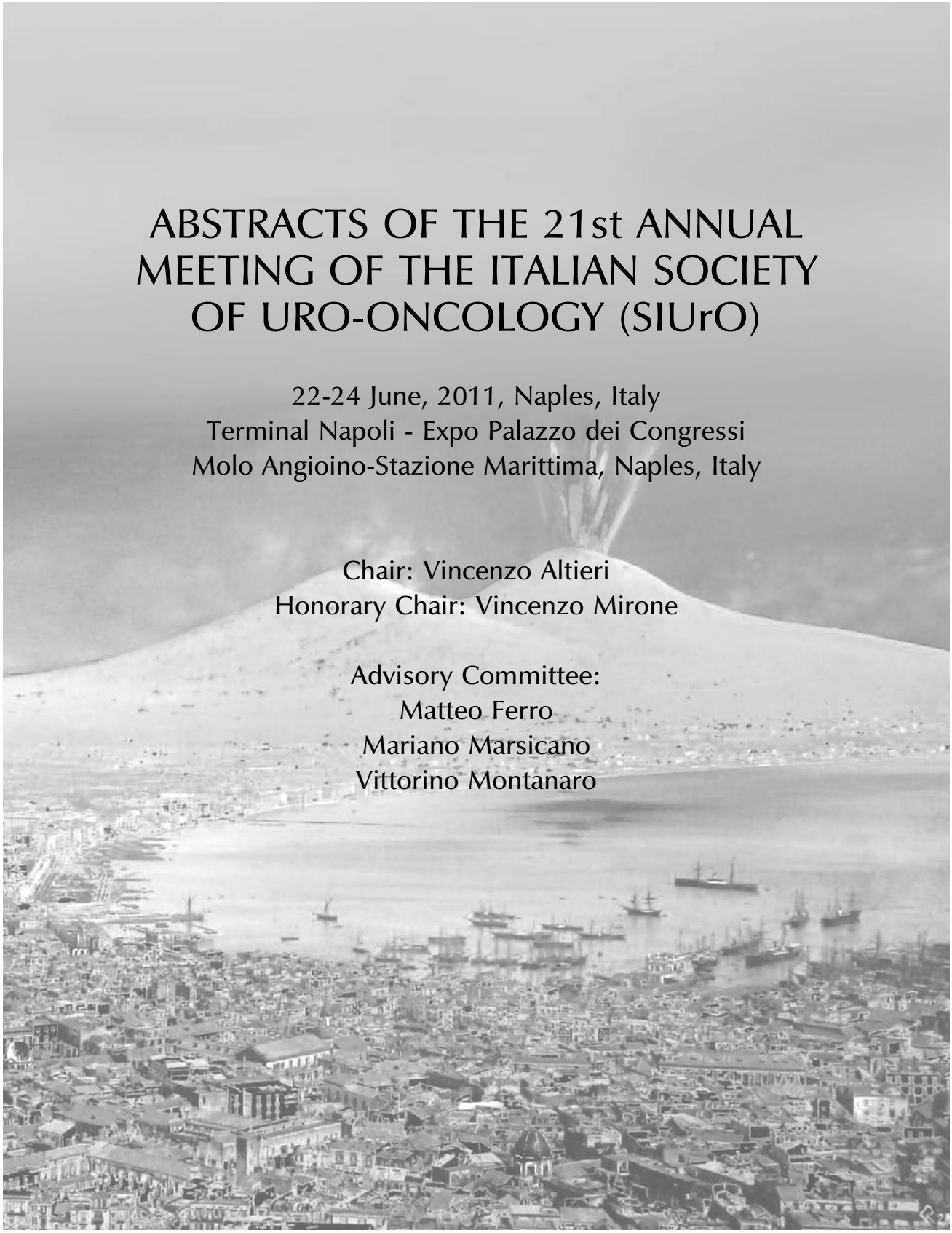

ABSTRACTS OF THE 21st ANNUAL MEETING OF THE ITALIAN SOCIETY OF URO-ONCOLOGY (SIUrO)

22-24 June, 2011, Naples, Italy
Terminal Napoli - Expo Palazzo dei Congressi
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1

OPTIMIZATION OF THE DETECTION RATE IN THE DIAGNOSIS OF LOCAL RECURRENCE OF DISEASE AFTER RADICAL PROSTATECTOMY: PERIANASTOMOTIC SATURATION BIOPSY SCHEME

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Background: Serial measurements of PSA level and digital rectal examinations are the standard tools used to monitor tumor recurrence after radical prostatectomy (RP) (1). Anastomotic biopsy is indicated in patients with clinically suspected local recurrence, which of course cannot be diagnosed only by serum PSA, digital rectal examination or imaging techniques (2). This study evaluated the optimization of the detection rate using a perianastomotic biopsy transrectal ultrasound scheme with eight biopsies in the diagnosis of local recurrence in patients with prostate cancer who underwent RP compared to four or six conventional standardized biopsies. These results were also related to the levels of PSA and Gleason score. *Patients and Methods:* Between July 2007 and February 2010, we evaluated 42 patients (range 56-74 years) who underwent consecutive RP (34 with the open technique and 7 with the laparoscopic technique) with recovery of biochemical disease (PSA>0.2 ng/ml). The pathologic stages of patients were: 18 with pT2, 23 with pT3 and 1 with pT4, respectively. All patients had negative lymph nodes and only one patient with pT4 disease had positive surgical margins. The staging examinations carried out at biochemical recurrence (chest radiography, abdominal CT and scintigraphy) were negative. All patients with a suspected local recurrence underwent rectal examination and transrectal ultrasound-guided biopsy perianastomotic transrectal ultrasound (BTP) using a G.E. ultrasound (LOGIQ 7) with an 'end-fire' multi-frequency convex probe under local anesthesia with lidocaine spray (10 g/100 ml). *Results:* Patients were divided into two groups. Group A: Twenty-five patients with mean PSA 2.6 ng/ml, who were subjected to BTP: 11/25 (44%) and 14/25 (56%) respectively with four and six biopsies. Group B: Seventeen patients with mean PSA 1.9 ng/ml who underwent the standard eight biopsies. Among patients in the latter group, three had already undergone four biopsies. One patient belonging to Group B did not complete the entire biopsy procedure because of discomfort. In the first group, there were no signs of local recurrence in 9/25 (36%), while in 16/25 (64%) local recurrence was found in three biopsies. In Group B: 10/17 (59%) patients were found to have relapsed prostate cancer, whereas under biopsy, 7/17 (41%) patients were found to have prostate tissue. Fibrous tissue and scarring was found in six biopsies. *Discussion and Conclusion:* The clinical significance of residual prostatic tissue in follow-up is most important since it can be responsible for biochemical failure and can increase in size, thus simulating a local recurrence (3). Although there was no evidence of a significant correlation between PSA levels and local recurrence, Gleason score and positive biopsy, the BTP conducted in a standardized manner with eight biopsies in patients with relapsed disease allowed the identification of the site of recurrence in 59% of cases, thereby significantly increasing the detection rate of the procedure. Further studies are needed, including a systematic execution of the BTP in patients with disease relapse after RP. This can be a valuable and statistically significant aid in identifying the presence of local recurrence in patients with prostate cancer.

1 Carroll P, Coley C, Mc Leood D *et al*: Prostate-specific antigen best practice policy. Part II. Prostate cancer staging and post-treatment follow-up. Urology *57*: 225-229, 2001.
2 Minardi D, Galosi AB, Dell'Atti L *et al*: Detectable serum PSA after radical prostatectomy. Clinical and pathological relevance of perianastomotic biopsies. Anticancer Res *24*: 1179-1185, 2004.
3 Sella T, Schwartz LH, Swindle PW *et al*: Suspected local recurrence after radical prostatectomy: endorectal coil MR imaging. Radiology *231(2)*: 379-385, 2004.

2

THE RELATION BETWEEN OBESITY AND PROSTATE CANCER: THE ROLE OF ABDOMINAL OBESITY AND BODY FRAME

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Background: A possible relationship between obesity evaluated by body max index (BMI) and prostate cancer aggressiveness has been demonstrated in several studies, mostly in patient series from the USA and confirmed by our group. However, the use of BMI presents several limitations in defining the type of obesity and alternative measures have been proposed. The aim of our study was to investigate the association between

abdominal obesity (AO), body frame (BF) and prostate cancer risk and grade in a group of patients scheduled for prostate biopsy. *Patients and Methods:* From 2008 onwards, 751 consecutive men undergoing 12-core prostate biopsy at three centers in Italy were enrolled to the study. Indications for a prostatic biopsy were PSA≥4 ng/ml and/or a positive digital rectal examination (DRE). BMI, as well as waist and hip circumference, were measured before biopsy. BF was defined as small up to a wrist circumference of 191 mm. AO was defined as a waist circumference >102 cm. *Results:* Out of 711 men, 273 (38%) were diagnosed with cancer on biopsy. The median age was 68 years, PSA 6.2 ng/ml, BMI 27.6 kg/m^2 and waist circumference 102 cm. According to BMI measurement, 153 men (21%) were obese. According to waist circumference, 319 (44%) men presented with AO. Large, medium and small BF were observed in 89 (13%), 479 (67%) and 143 (20%) men, respectively. No significant differences between age, prostate volume, PSA, BMI, waist and wrist circumferences, and prostate cancer incidence and Gleason score distribution were observed among the three centers. Out of 273 men with prostate cancer, 149 (55%) had Gleason score 6 (65 (43%) presented with AO) and 124 (45%) a Gleason score ≥7 (68 (55%) presented with AO). On univariate analysis, waist circumference (median value 101 cm in benign disease and 102 cm in cancer, respectively) was not significantly associated with prostate cancer diagnosis (p=0.12). Among men with cancer, higher waist circumference (median value for Gleason score 6 was 102 cm and for Gleason score ≥7 was 104 cm, respectively) on univariate (p=0.029) and multivariate analysis (p=0.04) was associated with high-grade disease (Gleason score ≥7). BF evaluation was not associated with prostate cancer diagnosis (p=0.79) or high-grade disease (p=0.24). *Discussion and Conclusion:* Among men undergoing prostate biopsy in different centers in Italy, our study confirmed that AO is associated with high-grade disease. However, further studies in a large patient population across multiple institutions and countries are needed to confirm our results and to allow us to better understand which precise factors related to obesity are responsible for the observed increase in high Gleason score tumors.

5
ANDROGEN LEVELS AND HIGH-GRADE PROSTATE CANCER: FREE TO TOTAL TESTOSTERONE RATIO ANALYSIS

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Background: Prostate cancer (PCa) and androgens have an unclear interrelationship. Some data suggest that low total testosterone levels may enhance tumor aggressiveness, while data on free testosterone remain controversial. We analyzed serum androgen concentrations in men who underwent initial prostate biopsy, focusing on the free (fT) to total testosterone (T) ratio (fT/T) as a predictor of the risk for low- and high-grade PCa. *Patients and Methods:* Between 2006 and 2010, we collected data on 812 Caucasian Italian men with no history of PCa who underwent 12-core biopsy. Digital rectal examination (DRE), body mass index (BMI), prostate volume, PSA, T and fT were measured on the day of biopsy. The fT/T ratio was computed by dividing free testosterone by total testosterone. T, fT and fT/T were examined as continuous variables. Crude and adjusted multinomial logistic regressions were performed to assess the association between T, fT, fT/T and the outcomes of low- (Gleason ≤6) and high-grade PCa (Gleason ≥7), both relative to the absence of cancer. Multivariate analyses were adjusted for age, PSA, BMI, prostate volume and DRE. The fT/T ratio was also examined using tertiles to evaluate the risk in different fT/T ranges. *Results:* Overall cancer detection was 40% (321/812): 136 men had low-grade and 185 men had high-grade PCa. Age, PSA, DRE, prostate volume and BMI all showed a significant difference in distribution across the three outcome clusters (all p≤0.001). The fT/T distribution also differed significantly across the outcome groups (p=0.017). On multivariate analysis, T (p>0.11) and fT (p>0.45) were not significantly associated with low- or high-grade PCa. Instead, a higher fT/T ratio was a significant predictor of high-grade PCa on both crude (p=0.01) and multivariate (p=0.02) analysis. No significant association was found with low-grade PCa (p≥0.38). The tertile analysis demonstrated a two-fold increased risk (OR=2.04, 95% CI=1.23-3.37, p=0.005) of high-grade PCa for patients in the highest fT/T tertile relative to the lowest tertile. *Discussion and Conclusion:* In Caucasian Italian men, a higher fT/T ratio significantly predicts against increased risk of high-grade PCa on initial prostate biopsy. Men in the highest fT/T tertile have a greater than two-fold increased risk of high-grade disease compared to men in the lowest tertile. This study provides evidence that a high fT/T ratio (*i.e.* high percentage of free testosterone) rather than absolute androgen levels may be associated with high-grade PCa. Nevertheless, the relationships between PCa and androgens remain complex and further studies are needed to confirm our findings.

6
PROSTATE BIOPSY ACCURACY: ANALYSIS OF 20- *VERSUS* 12-CORE TEMPLATES

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Background: Transrectal prostatic biopsy is considered the standard procedure for the diagnosis of prostate cancer. In recent years, sextant biopsy schedule has been replaced by new strategies consisting of sampling at least ten sites in the prostate; however, a standard number of cores is still to be agreed upon. The aim of our study was to evaluate and compare the impact of two different biopsy templates for the diagnosis of prostate cancer. *Patients and Methods:* From December 2008 to September 2010 all patients referred to our prostate clinics with a PSA value of more than 4 ng/ml or an abnormal digital rectal examination (DRE) were consecutively scheduled for their first TRUS prostatic biopsy with a 12- or a 20-core template, respectively. Patients with a PSA >30 ng/ml were excluded from the series. Prostate biopsy was carried out as an outpatient procedure. Antibiotic prophylaxis by means of levofloxacin 250 mg *b.i.d.* was started 48 h before the procedure and continued for 72 h after. All patients underwent a TRUS-guided biopsy using a Falcon ultrasound instrument (B-K Medical, Milan, Italy) equipped with a 5-10 MHz bi-convex probe (8808 probe; B-K Medical). A 16-gauge biopsy needle (Magnum 1000; BARD, Rome, Italy) and a dedicated spring-loaded biopsy gun (MG1522; BARD) were used. Periprostatic anesthetic block was performed for each patient 10 min before the biopsy. Differences in cancer detection rate were evaluated. One-way ANOVA and Chi-square were used as appropriate for statistical analysis. *Results:* A total of 550 patients were consecutively enrolled. The mean age was 69.6±7.4 years, mean body mass index (BMI) was 27.4±3.8 kg/m^2, the mean PSA value was 8.3±6 ng/ml and the mean prostatic volume was 45±26 ml. 275 patients underwent a 12-core biopsy (group A) and 275 a 20-core biopsy (group B). A total of 69 (25%) patients presented with a positive DRE in group A and 73 (26%) patients in group B (p=0.77). No significant differences for age, BMI, PSA, prostate volume and prostate cancer detection rate were observed between the two groups (see Table I). No significant complications requiring hospitalization were observed in both groups.

Table I.

	12-Core template	20-Core template	p-Value
Age (years)	67.7±7.9	66.3±8.3	0.51
BMI (kg/m^2)	26.9±3.5	27.6±5.9	0.11
PSA (ng/ml)	7.2±4.6	8±5.3	0.07
Prostate volume (cc)	52.4±24	48±29	0.06
Prostate cancer rate	119/275 (43%)	96/275 (35%)	0.06

Discussion and Conclusion: This study shows that increasing the number of biopsy cores is not associated with an increase in prostate biopsy performance in the detection of prostate cancer. These data suggest that the standard number of cores to be used in the first set of biopsies is still to be determined.

7
BONE SCAN IN NEWLY DIAGNOSED PROSTATE CANCER: EXTERNAL VALIDATION OF A NOVEL RISK STRATIFICATION TOOL

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Aim: To externally validate and test the performance characteristics of a novel risk stratification tool recently proposed by Briganti *et al.* (1) regarding the need for baseline staging bone scans in patients with newly diagnosed prostate cancer. *Patients and Methods:* From 2009 onwards, a consecutive series of patients with a diagnosis of prostate cancer were enrolled to the study. Indications for prostatic biopsy were a PSA ≥4 ng/ml and/or a positive digital rectal examination (DRE). All patients were staged with conventional total-body ^{99m}Tc MDP scintigraphy, performed regardless of baseline prostate cancer characteristics. The presence of skeletal metastasis (BM) on bone scan was defined when either solitary or multiple asymmetric areas of increased tracer uptake occurred. Patients with positive or equivocal bone scan findings also underwent computed tomography and/or magnetic resonance imaging to confirm the scintigraphy findings. No patient was on hormonal therapy at the time of the staging imaging. The AUC estimates were used to test the accuracy of the novel risk stratification tool (the regression tree (CART)) proposed by Briganti which recommended staging baseline bone scan for patients with a biopsy Gleason score >7 or with a PSA >10 ng/ml and palpable disease (cT2/T3) prior to treatment. The new tool was compared to the EAU guideline. The specificity, sensitivity, positive and negative predictive values of each model were also calculated *Results:* A total of 313 patients were consecutively enrolled. The median age was 68 (range 49-95 years), median PSA was 7 ng/ml (range 0.81-2670 ng/ml); median prostatic volume was 40 cc (range 10-189 cc). A total of 20 (6.4%) patients presented with BM at the bone scan. Of these patients, all presented at least a PSA≥30 ng/ml; 8 patients (40%) had a Gleason score 7, and 12 (60%) had a Gleason score >7; 10 patients (50%) presented with palpable

Table I.

	Bone scans performed using the EAU and CART, n (%)	Rate of BM within the recommended patient group, % (n)	Overall accuracy (%)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
EAU	151/313 (48%)	9.9% (15/151)	64%	75%	54%	97%	11%
CART	90/313 (29%)	16.6% (15/90)	75%	75%	74%	98%	16%

disease. The AUC for the EAU guidelines was 0.64 (CI: 0.52-0.761). However, the novel CART model was significantly more accurate (AUC: 0.75; CI: 0.632-0.859, p=0.001) than the EAU guideline (p<0.001). Table I reports the performance characteristics of CART and the EAU guideline. *Discussion and Conclusion:* In a group of patients with a diagnosis of prostate cancer, our study validated the novel risk stratification tool recently proposed by Briganti *et al*. and we confirmed that it does indeed offer a higher accuracy for baseline staging bone scan when compared to the EAU guideline. Furthermore, with this highly accurate approach, it is possible to further reduce (by about 60%) the use of staging baseline bone scans without compromising the ability to detect BM

1 Briganti A, Passoni N, Ferrari M *et al*: When to perform bone scan in patients with newly diagnosed prostate cancer: external validation of the currently available guidelines and proposal of a novel risk stratification tool. Eur Urol *57(4)*: 551-558, 2010.

8
ROLE OF THE TUMOR FOCALIZATION IN PROSTATE CANCER IN THE SELECTION OF PATIENTS FOR FOCAL THERAPY

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Background: Focal therapy has recently been proposed as a new strategy to treat low-intermediate risk prostate cancer (PCa). However, the traditional opinion that most cases of PCa are multifocal remains a possible obstacle to the application of focal therapy in most cases. It has been suggested that in multifocal disease, focal therapy is able to target only the largest (index) lesion, since secondary tumors are small and therefore unlikely to contribute to disease outcome. The aim of this study was to evaluate the role of PCa focalization in selecting patients for focal therapy. *Patients and Methods:* A total of 456 consecutive cases of whole-mount radical prostatectomy samples were evaluated (from January 2008 to December 2010). Pathology review evaluated the number of tumor foci, overall Gleason score (GsS), Gleason score (GsF), tumor volume (TTV), extracapsular extension (ECE) and seminal vesicle invasion (SVI). The index lesion was defined as the largest by volume. Patients suitable for focal ablation were defined as either having: (i) unifocal, organ-confined PCA, GsS <7, or (ii) multifocal PCa (pT2, GsS <7) with one large index lesion and the remaining foci demonstrating features of clinically insignificant disease (TTV of all secondary foci <0.5 cc with GsF <6). *Results:* The pathologist identified 627 tumor foci. PCa was more often multifocal: 489/627 (78%). There was no significant difference between unifocal and multifocal tumors with respect to total tumor volume (median 3.45 cc *vs*. 2.24 cc; p=0.39), proportion of GsS >7 (30.7% *vs*. 31.8%; p=0.9) and proportion of locally advanced disease (31.8% *vs*. 21.7%; p=0.33). In multifocal disease, TTV, GsG, ECE and SVI of the tumor were almost invariably defined by the index lesion. Of the 402 secondary foci, 347 (86.1%) had a volume <0.5 cc and 398 (99.0%) had Gleason score <6. Using the defined criteria, 232 (50.9%) patients were considered suitable for focal ablation of the index lesion. *Conclusion:* Although multiple cancer foci within the prostate gland is a common feature in RP specimens, histological features of poor prognosis are arguably associated with the index lesion. Secondary foci typically have a small volume and are well differentiated. Focal therapy may be suitable in a significant proportion of patients currently undergoing radical surgery. Further prospective IRB approved trials are needed to evaluate the role of focal therapy which tries to ablate only the index lesion.

9
INTRAOPERATIVE STENTING OF THE UPPER URINARY TRACT IS NOT NECESSARY AFTER RESECTION OF THE URETERIC ORIFICE DURING TRANSURETHRAL RESECTION OF THE BLADDER

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*Background:*The use of a ureteric JJ-stent is common practice when transurethral resection of the bladder tumor (TURBt) involves the ureteric orifice. We retrospectively analyzed our TURBt database and identified all patients that underwent resection of the ureteric orifice. We compared cases with and without the placement of ureteric stent concerning postoperative complications, stricture formations and tumor development in the upper urinary tract. *Patients and Methods:* From May 2005 to May 2010, 97 patients (65 males, 32 females) underwent resection of the ureteric orifice during TURBt of non-muscle-invasive bladder cancer. Intraoperative insertion of a ureteric stent ('stent'group) was compared to cases without stenting ('no-stent'group). Mean follow-up was 33 months (6-60 months). *Results:* A total of 63/97 (64.95%) patients had a urothelial bladder tumor directly in the ureteric orifice and 34/97 (35.05%) had a tumor growing out of the ureteric orifice. In 36/97 (37.5%) cases, a JJ-stent was inserted intraoperatively. Eight (13.1%) patients without a JJ-stent had no hydronephrosis at postoperative renal ultrasound and seven (11.4%) required drainage. Orifice strictures developed in 18 (18.6%) patients with JJ-stent and in 2 (3.3%) patients without. Upper urinary tract tumors developed subsequently in 7 (7.2%) patients with JJ-stent and in 3 (4.9%) patients without. *Conclusion:* Resection of the ureteric orifice during TURBt in non muscle-invasive bladder neoplasm does not necessarily require intraoperative insertion of a JJ-stent. We found a strong association between insertion of a JJ-stent and an increasing rate of ureteric orifice strictures, although stent insertion might be indicated by the surgeon in the most severe cases. JJ-stent does not seem to be associated with an increased risk of *de novo* tumor development in the upper urinary tract.

10
DIAGNOSTIC ACCURACY OF PROSTATE-SPECIFIC ANTIGEN–IgM IMMUNE COMPLEX IN MEN WITH PROSTATE CANCER

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Background: IgM immune complex of prostate-specific antigen (PSA–IgM) has been demonstrated to be a valuable biomarker of prostate cancer in multiple studies, showing higher accuracy for diagnosing patients with prostate cancer compared to PSA. A growing volume of evidence indicates that the PSA test has increased sensitivity for cancer detection in younger men using age-specific PSA reference ranges. To evaluate the diagnostic accuracy of the PSA–IgM assay compared to the PSA test in younger men, we assessed the circulating levels of PSA–IgM and PSA in 54 patients aged less than 65 years with different disease severity, including prostate cancer and benign hyperplasia (BPH). *Patients and Methods:* Serum samples from 54 male patients aged less than 65 years were collected by the Department of Urology, Villa Tiberia, Rome, Italy. Nineteen patients had histologically proven organ-confined prostate cancer and 35 patients suffered from BPH confirmed by histopathological examination. Serum levels of PSA–IgM were assessed using Prostate-IC kit (Xeptagen, Italy), while PSA levels were determined using Immulite 2000 (Medical Systems, Italy). *Results:* The diagnostic performance of PSA–IgM and PSA tests for discriminating prostate cancer from BPH was evaluated using the area under the ROC curve (AUC). The diagnostic accuracy measured with the PSA–IgM assay was significantly higher than that achieved with the PSA test (0.723 *vs*. 0.684, $p<0.001$). The point on ROC curves with maximum Youden index identified the optimal cut-off as 85 AU/ml for PSA–IgM and as 3.8 ng/ml for PSA. A sensitivity of 74% was obtained using the calculated cut-offs for both tests but the specificity of PSA–IgM (66%, 23/35) was higher than that of PSA (60%, 21/35). *Conclusion:* The analysis of serum levels of PSA–IgM leads to a better discrimination of prostate cancer from BPH compared to PSA levels, improving the diagnosis of prostate cancer in younger men with a consequent reduction of negative biopsies.

11
BRACHYTHERAPY WITH PERMANENT IMPLANT FOR RADICAL TREATMENT OF LOCALIZED PROSTATE CANCER: MEDIUM TERM RESULTS

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Background: Brachytherapy (BT), an option for radical treatment of localized prostate cancer (LPC), has been used in selected patients in our hospital from 2000. BT management has been performed by a dedicated brachytherapy specialist pool involving the Departments of Radiotherapy, Urology, Medical Oncology, and Health Physics. Preliminary results concerning clinical outcomes and quality of life (QL) have been presented in a previous SIUrO meeting (SIUrO XVII, abs 85, Modena 2007) and have been published in IJROBP (*66*: 31-37, 2006), respectively. Here, we present the medium term outcomes of the Trento experience. *Patients and Methods:* From May 2000 to December 2008, we treated a consecutive series of 409 patients with LPC by permanent ^{125}I implant as monotherapy

(145 Gy) in 380 patients and as a boost (100 Gy) in association with external beam radiotherapy (45-50.4 Gy) in 29 patients. A short course of hormonal therapy was performed pre-BT in 153 patients. The median age was 66 years (49-78); the NCCN risk class was low, medium and high in 68%, 30% and 2% of the patients, respectively. CT-based dosimetry at four weeks was used for post-planning evaluation. D90 and V100 were recorded for each patient, along with other dosimetric and clinical parameters. Biochemical relapse was defined according to Phoenix ASTRO Consensus Conference (nadir +2 ng/ml). From March 2005, QL was prospectively assessed by a self-filled QL validated questionnaire in a consecutive series of 228 patients. *Results:* A D90≥100% of prescribed dose and a V100 ≥90% of prostate volume were achieved in 83% of patients. After a median follow-up of 55 months, 36 patients developed biochemical relapse, with a clinical component in 8 patients. The 5- and 10-year relapse-free survival (RFS) was 92% and 79%, respectively. At this time, 30 patients had died (27 relapse-free), with a 5- and 10-year overall survival of 93% and 85%, respectively. The 5- and 10-year RFS in low-risk cancer was 95% and 80% *vs*. 88% and 73% in intermediate-high risk (*p*: NS). Patients with better dosimetric parameters (V100≥90% and D90≥100%) had a better RFS (5- and 10-year: 95% and 82% *vs*. 80% and 62%; $p<0.05$).

Table I. *Quality of life in relation to physical well-being (PHY), psychological well-being (PSY), social life (SL), physical autonomy (POW), and rectal (REC), urinary (URI) and sexual functioning (SEX).*

	BASAL POST	6 Months	12 Months	24 Months
PHY†	72.8	70.6	71.7	69.3	71.5
PSY†	80.2	84.9	81.0	82.0	81.7
SL†	78.9	71.4	82.8	78.9	75.9
POW†	91.1	92.5	93.4	90.6	89.3
URI§	10.7	25.4	23.6	20.4	17.6
IIEF†	16.4	12.2	12.4	13.0	11.3
SEX (UCLA PCI)†	54.5	38.8	38.1	41.9	33.4
RECT§	5.4	13.2	12.5	9.5	8.15

†Higher values: better function; §higher values: greater impairment.

Discussion and Conclusion: Our data reproduce the outcomes of larger published series. BT may be considered as an effective treatment also for intermediate-risk cases. Dosimetric quality parameters (D90 and V100) significantly influence biochemical outcome. BT negatively impacts on physical functions (rectal, urinary and sexual) within the first two years. The multidisciplinary management of BT represents an added value in enhancing patient selection and implant quality.

12
MIR-501 OVEREXPRESSION IN RENAL CARCINOMAS

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Background: MicroRNAs (miR) are small, non-coding RNAs (20-23 nucleotides) that regulate gene expression. In particular, miRs are involved in many biological processes, including cellular differentiation, proliferation and death. In addition to their physiological functions, miRs are found to be expressed aberrantly in certain carcinomas and to play oncogenic or tumor-suppressive roles in neoplastic cells (1). One in 75 people will develop renal cell carcinoma (RCC) during their lifetime, it being the seventh leading cause of cancer in men and eighth in women in the world. RCC is grouped into different types, where clear cell carcinoma (ccRCC) is the most frequent (2). Since little is known of the role of miRs in renal tumorigenesis, we screened the most common renal carcinomas, namely clear cell (ccRCC), papillary (pRCC) and chromophobe (chRCC), for miR expression, We investigated miR-501, 196b and 202 that we had found to be overexpressed in polycystic kidney disease, a hyperproliferative renal disease. In addition, miR-501 was found to be expressed predominantly in colon, lung and kidney. *Materials and Methods:* We selected and analyzed 41 tumor samples: 24 post-nephrectomy fresh frozen tissues (including 13 ccRCC, 7 pRCC, 1 chRCC, 1 liposarcoma and 2 oncocytomas) and 17 paraffin-embedded samples (12 ccRCC, 4 pRCC, 1 chRCC). Total RNA was extracted with RNeasy Plus Kit (fresh frozen tissues) or the RecoverAll® Total Nucleic Acid Isolation kit (paraffin-embedded tissues). Quantitative real-time PCR for mature miRs was performed using the TaqMan method. The level of miR expression was calculated by the ΔΔCt method by using U6 snRNA as reference, and vas related to that of normal tissue as fold change ($2^{-\Delta\Delta Ct}$). *Results:* No variations were observed in the expression of miR 196b and 202 in RCC compared to healthy tissues. Levels of miR-501 were instead expressed in a different manner in post-nephrectomy fresh-frozen tumors, as well as in paraffin-embedded tissues, compared to non-neoplastic tissues. In four patients, miR-501 expression was evaluated in both frozen and paraffin-embedded tissues to investigate any possible variability due to the different storage method. Expression levels found in paraffin-embedded tissues

were comparable to those obtained in frozen tissues. Based on miR-501 expression, renal carcinomas were divided into four groups: (i) low expression, <0.5-fold expression; (ii) normal expression, from 0.5- to 2-fold; (iii) weak overexpression, from 2- to 5-fold; and (iv) strong overexpression, >5-fold. Overall, miR-501 expression was down-regulated (group 1) in 12 patients (3 ccRCC, 7 pRCC, 1 chRCC and 1 oncocytoma); was normal in 10 patients (7 ccRCC, 2 pRCC and 1 lyposarcoma); weakly over-expressed in 7 patients (4 ccRCC, 1 pRCC, 1 oncocytoma and 1 chRCC); strongly over-expressed in 9 ccRCC patients. No correlation between miR-501 expression and tumor grading was observed. *Conclusion:* Our results demonstrate that miR-501 was mainly overexpressed in ccRCC, while it was mainly unchanged or down-regulated in chRCC and pRCC. The overexpression of miR-501 in ccRCC, therefore, may contribute to features of this type of cancer and may play a role in therapeutic response, metastasis development and survival.

1 Di Leva G and Croce CM: Roles of small RNAs in tumor formation. Trends Mol Med *16(6)*: 257-267, 2010.
2 Brannon AR and Rathmell WK: Renal cell carcinoma: Where will the state-of-the-art lead us? Curr Oncol Rep *12(3)*: 193-201, 2010.

13

RADICAL PROSTATECTOMY AND EXTENSIVE PELVIC LYMPH NODE DISSECTION FOR CLINICAL T3 PROSTATE CANCER: SINGLE-CENTER LONG-TERM RESULTS

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The objectives of this study were to evaluate the long-term oncological results of all cT3 Prostate cancer (PCa) patients who presented at our center from 2000 to 2005. Over- and under-staging, together with overall survival (OS), disease-specific survival (DSS) and the morbidity of surgery were evaluated. *Patients and Methods:* From the total of 1,195 radical prostatectomies (RPs) performed, 105 (8.8%) were staged as cT3, 31 of which were excluded from the study due to short follow-up, leaving 74 cT3 patients in the study. The mean age was 68.1 (range 51-76) years and the mean pre-operative PSA level was 24.5 (range 4-130) ng/ml. All the patients were M0 (negative bone scan and computed tomography). Bilateral extensive pelvic lymph node dissection (EPLND) was performed in all patients. The number of nodes removed varied from 20 to 45 (mean 32.5). The retrograde extraponeurotic approach with removal of Denonviller fascia was used. Nerve-sparing surgery was never attempted. Additional surgical margins (bladder neck, lateral, base and urethra) were taken for complete staging. *Results:* Pathological staging was: pT2=15/74 patients (20.3%): PT2a=6/15 (40%), pT2b=8/15(53.3%), pT2c=1/15(6.7%). pT3=50/74 (67.5%): pT3a= 19/50 (38%), pT3b= 31/50 (62%). PT4=9/74 (12.2%). A total of 29/74 patients had positive nodes (39.2%) and were all pT3 and pT4: pT3a=15.7%, pT3b=74.3%, pT4=66.6%.They all received immediate hormone therapy (HT). Overall, 45/74 cT3 pts. were N0 (60.8%). Grading: Gleason score <7=12/74 (16.2%), 7=20/74 (27%), 8-10=37/74 (50%), Gx=5/74 (6.8%). The mean follow-up was 99.6 (range 76-128) months. The positive surgical margin rate was 57% (42/74). The OS was 73% (54/74 patients), while DSS was 86.5% (64/74 patients). A total of 20/74 patients died: one in the postoperative period due to pulmonary embolus, nine from progression and metastasis in a mean time of 60.1 months, eight from other causes (mean time: 46.4 months), and finally two patients from unknown causes. A total of 46/73 pts received adjuvant HT (63%), while 25 did not (37%). Three patients received HT+ RT. At 99 months, 17/73 patients (23.3%) treated by RP alone had an undetectable level of PSA (0.001-01 ng/ml). A total of 25/73 patients on HT had an undetectable level of PSA (34.2%), while 11/73 (15%) had biochemical failure (PSA 0.57 to 100 ng/ml). Complications: mortality, 1/74 (1.3%); lymphocele, 33.5% (25% requiring puncture); ureteral re-implant, 1/74 (1.3%); rectal injury, 3/74 (4%) with intraoperative repair. *Conclusion:* RP with ELND was a valid option for cT3 PCa patients. The 99-month OS and DSS were 73% and 86.5%, respectively. Approximately 20% of patients were overstaged as being pT2. A total of 23.3% of patients had undetectable PSA after RP alone at 99 months. Morbidity was acceptable.

14

SMOKING STATUS, RECURRENCE RISK AND INTRAVESICAL CHEMOTHERAPY IN NON-MUSCLE-INVASIVE BLADDER CANCER

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Background and Aim: The influence of smoking status on the diagnosis of carcinoma of the bladder, on recurrence risk

and response to intravesical treatment has been scarcely studied. Available studies suggest a reduction in recurrence risk with cessation of smoking, however, most studies lack sufficient statistical power. The aim of the present analysis was to study the recurrence risk and the response to intravesical chemotherapy in terms of recurrence-free rate (RFR) and recurrence-free survival (RFS) in relation to smoking status at diagnosis in patients affected by intermediate-risk non-muscle invasive carcinoma of the bladder (NMI-BC). *Patients and Methods:* Tumor characteristics and smoking status were recorded for patients affected by NMI-BC treated by transurethral resection (TUR) and adjuvant intravesical therapy. All patients received intravesical epirubicin within six hours of TUR at a dose of 80 mg diluted in 50 ml of saline solution. Further adjuvant treatment in low- and high-risk patients was given according to physicians' choice. Two different schemes of intravesical chemotherapy with epirubicin were adopted at a dose of 80 mg in 50 ml for patients at intermediate risk. All patients were submitted to cytology and cystoscopy at three-monthly intervals for two years and then at six-monthly intervals for three more years. Multivariate statistical analysis was conducted to study the recurrence risk and the response to intravesical chemotherapy in terms of RFR and RFS in relation to smoking status at diagnosis. *Results:* Out of 577 consecutive patients, 241 (42%), 188 (33%) and 148 (25%) were current, former and never smokers, respectively. The mean number of cigarettes smoked per day was 20 for a median period of 30 years. Recurrent tumors were statistically more frequent in smokers that in never smokers. The percentage of recurrence increased from 20% to 42% ($p<0.0001$) for these who smoked less than 30 years compared to those who had smoked for longer. No significant difference between current and former smokers emerged in terms of RFR and RFS at a median follow-up of four years. On the other hand, a significant difference in terms of RFS between never and former smokers was evident ($p=0.019$). The 3-year RFS in never and former smokers was 71.3% and 57.6%, respectively. The above mentioned difference was completely removed 20 years after smoking cessation. An advantage in terms of RFR at 12 months emerged in favor of prolonged intravesical chemotherapy only in current smokers. *Conclusion:* Recurrent tumors are more frequent in smokers than in never smokers. Duration of smoking has a relevant impact on RFR. A significant difference in terms of RFS between never and former smokers was evident but the difference was completely removed 20 years after cessation of smoking. No statistically significant difference between current and former smokers emerged in our analysis. A statistically significant benefit from prolonged intravesical chemotherapy in terms of RFR emerged in current smokers only.

15

CHOICE OF ADJUVANT INTRAVESICAL THERAPY IN RECURRING INTERMEDIATE-RISK NMI-BC

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Objective: The therapeutic strategy for patients affected by intermediate risk non-muscle invasive bladder cancer (NMI-BC) recurring after intravesical therapy is not definitively established. Only few studies have been published on second-line intravesical therapy. BCG is advocated when intravesical chemotherapy fails and is often repeated. On the other hand, some patients that suffer recurrence repeat intravesical chemotherapy. A retrospective analysis of 179 intermediate-risk patients submitted to second-line intravesical therapy is reported. *Patients and Methods:* The clinical files of patients affected by intermediate risk NMI-BC and submitted to second-line adjuvant intravesical therapy were reviewed. Patients not receiving at least six instillations of BCG or intravesical chemotherapy after the first diagnosis and again after the transurethral resection (TUR) of the first recurrence were excluded. Only mitomycin c and epirubicin were accepted as chemotherapy. Only patients with intermediate-risk tumors with a recurrence-risk score between 5 and 9 according to the EORTC risk tables and in absence of Tis were selected. A multivariate analysis was performed for recurrence-free survival (RFS) and progression, considering first line intravesical therapy (BCG *versus* ICH), previous recurrence-free interval, tumor T category, G grade, multiplicity, second-line intravesical therapy (BCG *versus* ICH) and maintenance regimen. *Results:* The study included 179 patients. Chemotherapy was administered as first-line therapy in 131 (73.2%) and BCG in 48 (26.8%) patients. Second-line therapy was represented by BCG in 83 (46.4%) and chemotherapy in 96 (53.6%) patients, with maintenance of at least 12 months in 31% and 38% of patients, respectively. Of the 48 patients previously treated by BCG, 40 (83.3%) received BCG again, while of the 131 previously treated by chemotherapy, 88 (67.2%) repeated it and 43 (32.8%) received BCG. At a median follow-up of 29 months after the second TUR, 65 (36.3%) patients experienced recurrence, 25 (30.1%) and 40 (41.7%) after BCG and chemotherapy, respectively. Thirteen patients showed progression at a median interval of 19 months. At multivariate analysis, no statistically significant correlation was detected. Surprisingly, no statistical difference emerged in terms of recurrence-free interval between first- and second-line therapy and between BCG and chemotherapy as second-line therapy at recurrence after chemotherapy ($p=0.28$)

Conclusion: Almost 65% of patients experiencing recurrence after intravesical chemotherapy received intravesical therapy again. No difference in efficacy was detected between first- and second-line therapies or between BCG and chemotherapy given at recurrence after chemotherapy.

We wish to thank the GSTU Foundation for the statistical evaluations.

16

MINIMALLY INVASIVE OPEN TUMOR ENUCLEATION *VS*. PERCUTANEOUS RADIOFREQUENCY ABLATION *VS*. ACTIVE SURVEILLANCE OF SMALL RENAL MASSES <3 CM IN ELDERLY PATIENTS: LONG-TERM RESULTS OF A PROSPECTIVE FOLLOW-UP STUDY

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Background and Aim: The standard treatment of renal tumors is the resection or enucleation of the tumor (TE) through open or laparoscopic surgery. However elderly patients are at risk and a more conservative approach may be indicated. Percutaneous radiofrequency ablation (PRA) under a local anesthetic is an effective treatment for small renal tumors in the one-day surgery setting. Active surveillance (AS) has also been indicated for these patients. The objectives of this study were to evaluate and compare the oncological outcomes of elderly patients with renal tumors who received open surgery, PRA or AS and to record side-effects. *Patients and Methods:* From 2002 to 2006, 78 patients with small renal masses (<3 cm), as diagnosed on ultrasound and computed tomography, were included in this prospective study. All the patients included were ASA 3/4. A total of 27/78 patients, mean age 72.3 years (Group A), received open surgery: TE through a minimally invasive procedure. A small flank incision (6-7 cm) with *in situ* enucleation of the tumor without clamping the pedicle was adopted. Flow seal was used in nine patients for hemostasis, while 3/0 vicryl interrupted suturing was used in 16 patients. The technology and technique of PRA have been previously described and reported by us. A total of 26/78 patients, mean age 73.3 years, (Group B) received PRA. Finally, 22/78 patients, mean age 74.5 years, were only followed up (AS) (Group C). In Group A: males/females 23/4 *vs*. 20/6 in Group B *vs*. 16/6 in Group C. The mean tumor diameter was 2.1 cm, 2.5 cm and 2.2 cm in Groups A, B and C, respectively. General anesthesia was always used in Group A, while local anesthesia along the needle tract was used in patients receiving RFA. In this group, two patients were not treated because of the difficult tumor location. In the AS arm (Group C), patients were followed-up at six-month intervals with computed tomography. *Results:* Mean follow-up time was 60.1, 62.1 and 56.3 months in Group A, B and C, respectively. Histology: Group A: 23/27=renal cell carcinoma, one angiomyolipoma and three oncocytomas (11.1%). Grade: G1=6, G2=12, chromophobe=2, papillary=3. Mean blood loss was 127.6 (range 50-400) cc. Intraoperative margins were always negative (3-6 fragments). The mean hospital stay was 5.4 days. Complications: no major. A total of 3/27 patients (11.1%) had 2 units of blood transfused postoperatively. Group B: no biopsy was performed. Follow-up: Group A (5 years): 2/27 patients (7.4%) had died of pulmonary embolism and cardiac failure after 2 and 3 years from surgery; 25/27 (92.6%) had no evidence of disease. Renal function was normal in all the patients. Group B (62.1 months): mean hospital stay was 1 day. Complications: 1 patient had nausea. Total of 10/24 patients (42%) died of other causes. 2/24 patients (8.3%) had a complete response at CT, 3/24 (12.5%) had an increase in tumor diameter of 5 mm after 56, 59 and 72 months, and 17/24 patients (70.1%) had stable disease. Group C (56.3 months): 2/22 patients (10%) died of other causes, 3/22 (17%) progressed at 0.5, 0.6 and 2 cm in diameter. Two of these patients received surgery: pathology was adenocarcinoma; 1/3 still in AS. *Conclusion:* Open surgery (minimally invasive TE) was the best therapeutic option for elderly patients with small renal tumors. The oncological outcome was excellent and the complication rate low. RFA or AS can be offered to patients at a very high risk or refusing surgery.

17

INCIDENCE OF DELIRIUM IN ELDERLY PATIENTS UNDERGOING UROLOGIC SURGERY: THE ROLE OF COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IN DEFINING A HIGH-RISK POPULATION FOR DELIRIUM

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Background: Delirium is a common condition that occurs in hospitalized older patients, resulting in negative consequences, including higher rates of death, disability, permanent cognitive decline and institutionalization. Its incidence ranges from 15 to 35% in the postoperative phase and from 70 to 87% in intensive care. Several studies have attempted to set criteria that delineate a high-risk profile for developing delirium. *Aim:* To identify the domains of a comprehensive geriatric assessment (CGA) linked to the

incidence and characteristics of delirium in patients >70 years old hospitalized for elective surgical urology care. *Patients and Methods:* For this study, which is ongoing, elderly patients for which a surgical urology procedure has been planned are enrolled. A complete evaluation by geriatrician with CGA, urologist, and anesthesiologist is applied before hospital admission. During hospitalization nurses apply a confusion assessment method daily to define the incidence and clinical characteristics of delirium. Follow-up is planned at one and three months and one year after discharge to evaluate global health and, specifically, functional and cognitive status. *Results:* The study includes 37 patients, (81% male, 19% female, mean age 78.1±4.5 years). Among them, 33% were affected by benign prostatic hyperplasia; 22%, 26%, 15% by prostate, blood and kidney cancer, respectively, and 4% with a non-cancerous urinary tract obstruction. Mean anesthesiologist ASA score was 2.14±0.77, 41% of patients underwent general anesthesia and 59% spinal anesthesia. Overall, cognitive performance was mildly impaired (MMSE: mean 24.6±4.3); 17% of patients developed post-surgical delirium; in this sub-sample, the basal mean MMSE score was significantly lower, whereas no significant differences were found with respect to basal scores of depression and disability domains. *Conclusion:* In our sample, the incidence of delirium was lower than expected. This may be due the selected population having low co-morbidity, mild cognitive decline and a low rate of complications after the surgical procedure. It was not possible to fulfill the purpose of the study completely, but we feel confident that future sample enlargement will allow the definition of a risk-profile population that might benefit from specific programs devoted firstly to preventing the development of delirium and secondly to early treatment.

1 Inouye SK: Delirium in older persons. N Engl J Med *354(11)*: 1157-1165, 2006.

2 Inouye SK, Bogardus ST, Charpentier PA *et al*: A multi-component intervention to prevent delirium in hospitalized older patients. N Engl J Med *340(9)*: 669-676, 1999.

18
MANAGEMENT OF SMALL RENAL CANCER IN A CONTEMPORARY SERIES OF PATIENTS WITH VON HIPPEL-LINDAU DISEASE

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Background: Von Hippel-Lindau (VHL) disease is an autosomal dominant, inherited syndrome that occurs in 1 in 35,000 births. VHL is characterized by the development of retinal and CNS hemangioblastomas, pheochromocytomas, pancreatic neuroendocrine tumors, clear-cell renal carcinomas (RCC) and renal cysts. In particular, RCC occurs in approximately 40% of patients affected by VHL disease and is often bilateral and multifocal. The treatment of these patients, which usually relies on nephron-sparing surgery, is often very complex. The introduction of minimally invasive techniques can simplify and improve the management of renal lesions in these patients. We report our results in a recent series of patients in a multidisciplinary clinical care center, established at our hospital. *Patients and Methods:* From January 2000 to October 2010 a total of 22 patients affected by VHL disease were followed at our center. Twelve patients (57%) experienced at least one RCC before or during the follow-up period. Patients were preferentially offered percutaneous radiofrequency ablation (RFA). A lesion size greater than 4 cm at a site unreachable percutaneously was considered to be a contraindication to treatment. Cystic carcinomas were not considered a contraindication. The following data were retrospectively reviewed: medical history before coming to our center, features of the lesions (size, location and number), co-morbidities, oncological follow-up and renal function before and after the treatment. *Results:* From January 2000 to October 2010 a total of thirteen lesions were treated in eight patients. Another patient recently experienced two small lesions (12 and 10 mm) that are still on 'wait and see'. The mean age was 44 (range 19-65) years. Six patients had a history of previous contralateral radical nephrectomy and five patients had already undergone one or more partial nephrectomies. Eight lesions were easily treated with percutaneous RFA. The mean size of the lesion was 2.57 (range 1.5-3.5) cm. No complications were recorded. In one patient, a lesion of the upper pole of the left kidney, not percutaneously reachable, was treated through a laparoscopic RFA procedure. The other four patients underwent open partial nephrectomy (1 patient) or radical nephrectomy (3 patients). All patients that underwent RFA achieved a complete response and no worsening of renal function was recorded. No recurrence was recorded, with a mean follow-up for RFA-treated lesions of 32.7 (range 5-76) months. *Discussion and Conclusion:* Patients affected by VHL disease require a multidisciplinary approach for the various and severe manifestations of this syndrome. RCC in VHL occurs in younger patients, and is very frequently multifocal, bilateral and recurrent. For these reasons, oncological safety should not

compromise renal function in order to avoid precocious end-stage renal failure. The use of RFA, with extended indications, may improve the management of these patients, reducing the risk of renal failure and achieving a satisfying oncological result.

19
THE INHIBITION OF CHEMOKINE RECEPTOR CXCR7 MEDIATES TUMOR CELL GROWTH AND INVASIVENESS IN PRECLINICAL MODELS OF PROSTATE CANCER

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Background: The chemokine CXCL12/stromal cell-derived factor-1 (SDF-1) and its receptors CXCR4 and CXCR7 play a major role in tumor invasion, proliferation, and bone metastasis. *Aim:* To verify if CXCR7 receptor is differentially expressed during prostate cancer (PCa) progression and to identify the therapeutic potential of a CXCR7 receptor antagonist (CCX-733). *Materials and Methods:* The CXCR7 expression was evaluated by immunohistochemistry in tissues derived from radical prostatectomy (50 patients) and bone metastases (6 patients), as well as on 22rv1 xenografts obtained by injecting these cells with human osteoblasts and tissues, such as prostate, lymph nodes and lung metastases, obtained after orthotopical injection of DU145 and PC3 cell lines. Western blot analyses were performed on cell extracts derived from eight different prostate cancer cell lines having increased metastatic potential. The therapeutic potential CCX-733 was investigated. *Results:* In human PCa tissue, CXCR7 expression was higher in undifferentiated PCa (Gleason 8-10) when compared to that in differentiated tumors, with a further increase in bone lesions derived from patients with metastatic disease. In addition, CXCR7 expression was increased in cell lines harvested from metastatic lesions. Accordingly, high levels of CXCR7 were documented in locoregional lymph nodes and in lung metastases derived from PC3 and DU145 orthotopic *in vivo* models. Finally, tumors derived from 22rv1, subcutaneously injected together with human osteoblasts, expressed elevated amounts of CXCR7, with an evident positivity in tumor cells, endothelial cells and osteoblasts when compared to tumor derived from 22rv1 alone. *In vitro*, we observed that CXCR7 antagonism, by using the small molecule CCX-733, reduced basal and SDF1/OBCM-induced cell migration and matrigel invasion, through the reduction of MMP-9 and uPA secretion and activity. Moreover, CCX-733 reduced cell growth, with IC_{50} ranging between 50 and 250 nM. CXCR7 antagonism increased apoptosis induced by the absence of adhesion (anoikis), which is known to be a good model to study the initial phase of the metastatic process when tumor cell cross the endothelial barrier and follow the blood and lymphatic streams. *Conclusion:* Taken together, these results indicate a role for CXCR7 in PCa progression and suggest a potential role of CXCR7 antagonism for the management of advanced PCa.

20
HISTONE DEACETYLASE INHIBITOR, ROMIDEPSIN (FK228) IMPROVES ANTITUMOR EFFECTS OF DOCETAXEL AND CISPLATIN IN MODELS OF AGGRESSIVE PROSTATE CANCER

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Background: Once castration resistance is documented and secondary hormone therapy is ineffective, standard treatment of metastatic prostate cancer is with docetaxel (first-line) and platinum derivatives (second-line). *Aim:* We investigated the cytotoxicity and biology of the histone deacetylase inhibitor Romidepsin (FK228), as well as its capacity to restore sensitivity to docetaxel or cisplatin in hormone-refractory prostate cancer cells. *Results:* Romidepsin inhibited HDAC activity, produced acetylation of the histone proteins and induced dose-dependent apoptosis that was associated with prominent G_2/M arrest, decrease in S-phase population, increase in p21 protein expression, and down-modulation of cyclins B1 and D1. FK228 led to up-regulation of cleaved caspase-3 and PARP. BCL2 antagonists, such as HA-14-1, enhanced the effects of FK228 in these prostate cancer models. *In vivo*, FK228 (0.8 mg/kg *i.p.*) reduced tumor proliferation and induced apoptosis in both xenografts, up-modulating the expression of $p16^{INKA}$, BAX, BAK, $p21^{WAF1}$, and $p27^{KIP1}$, and inhibiting the activation of AKT and the expression of cyclin D1, BCL-2 and BCL-XL. Combined FK228 and chemotherapeutic agent (docetaxel and cisplatin) exposure resulted in strong synergistic apoptosis in all cell lines (combination indices ranged between 0.19 and 0.6).

Furthermore, compared to either agent alone, FK228/docetaxel and FK228/cisplatin combinations resulted in increased caspase cleavage and histone hyperacetylation. *In vivo*, this agent caused tumor growth delay without complete regression in xenograft systems. FK228 sensitized PC3 and 22rv1 xenografts to docetaxel and cisplatin treatments. These combinations were also tolerable in mice and superior to the use of either agent alone. *Conclusion:* As docetaxel and platinum derivatives are the standard first- and second-line chemotherapy for hormone-refractory prostate cancer, the development of chemotherapy-based combination therapies is of great interest for this disease stage. Our results provide a rationale for clinical trials on combination treatments with FK228 in patients with hormone-refractory and chemoresistant prostate tumors.

21

THE TORC1/TORC2 INHIBITOR, PALOMID 529 (P529), REDUCES TUMOR GROWTH AND SENSITIZES AGGRESSIVE HORMONE-REFRACTORY PROSTATE CANCER CELLS TO CHEMOTHERAPY AND RADIOTHERAPY BOTH *IN VITRO* AND *IN VIVO*

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Background: The AKT-mediated survival-signaling pathway is an attractive target for cancer therapy. This pathway is relatively inactive in resting cells and amplification of the *AKT* gene occurs in some tumors. The loss of the tumor suppressor gene *PTEN* (phosphatase and tensin homolog deleted on chromosome 10), present in about 30% of prostate primary tumors and in more than 50% of aggressive castrate-resistant prostate tumors, constitutively activates AKT, stimulating local invasion and neo-angiogenesis and reducing sensitivity to chemotherapeutics and radiotherapy. A novel PI3K/AKT /mTOR inhibitor, Palomid 529 (P529), shows inhibition of both AKT and mTOR signaling, as well as inhibiting tumor cell proliferation. *Materials and Methods:* We analyzed the *in vitro* effects of P529 on a panel of prostatic cancer cell lines with or without basal activation of AKT, as well as its *in vivo* effects on aggressive castrate-resistant PC3 and 22rv1 cell lines xenografted in nude mice. *Results:* P529 inhibited cell proliferation, with IC_{50} values ranging between 5 and 30 μM for 48 hours of treatment. These values seem to be scarcely related to basal AKT activity, since cells expressing low levels of AKT are also sensitive to P529. However, the re-expression of PTEN in the PTEN-negative PC3 cell line significantly reduced the effects of P529, and siRNA for PTEN sensitized DU145 and 22rv1 PTEN-positive cells to P529. However, we observed that the effects of P529 treatment were more marked when this drug was added to culture in clonogenic assays, suggesting that over longer periods of time, prostate cancer cells are able to increase AKT activity in an autocrine manner. For example, secretion of EGFR/Her2 ligands and exogenous addition of EGF (50 ng/ml) was indeed able to increase P529 efficacy. In this study, we showed that the inhibition of AKT pathway by P529 (Palomid) enhanced the sensitivity of both PTEN-positive and -negative prostate cancer cells to docetaxel and cisplatin *in vitro* and *in vivo*. We also demonstrated that P529 was able to reduce cell proliferation and to induce cell death, increasing the activity of death receptors TRAILR-5 and FAS and down-modulating the expression of cellular-FLICE-inhibitory protein (c-FLIP), BCL 2 and survivin. *Conclusion:* These combinatorial treatments may open a promising therapeutic approach for the elimination of hormone-refractory prostate cancer, which is largely resistant to conventional therapies.

22

HISTONE DEACETYLASE INHIBITOR, MS275, INCREASES RADIATION RESPONSES OF PROSTATE CANCER CELLS *IN VITRO* AND *IN VIVO*

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Background: Histone deacetylase (HDAC) inhibitors, which modulate chromatin structure and gene expression, represent a class of anticancer agents that hold particular potential as radiation sensitizers. This study examined the capacity of the HDAC inhibitor MS275 to modulate radiation response in human prostate tumor cell lines and explored potential mechanisms underlying these interactions. *Materials and Methods:* We analyzed cell proliferation and apoptosis in the presence of different doses of MS275 and for different culture times. In addition, we analyzed the effects of MS275 (0.2 M), radiation (2-6 Gy), or their combination, in order to define radiation survival by counting the number of colonies stained with crystal violet at different incubation intervals of 14±21 days. *Results:* MS275 induced a dose-dependent inhibition of proliferation in human prostate cancer cell lines. Exposure to

MS275 enhanced radiation-induced apoptosis as measured by caspase activity and PARP cleavage. The impact of MS275 on radiation response was further characterized using clonogenic survival analysis, which demonstrated that treatment with this agent reduced tumor survival after radiation exposure. We identified several oncoproteins and DNA damage repair proteins (epidermal growth factor receptor, AKT, DNA-PK, and RAD 51) that show differential expression after exposure to MS275. These proteins may contribute to mechanistic synergy between HDAC inhibition and radiation response. In addition, we demonstrated that MS275 ameliorates the response to radiation therapy in aggressive models of prostate cancer such as PC3 and 22rv1 *in vivo* xenografts. *Conclusion:* These preclinical results suggest that treatment with the HDAC inhibitor MS275 can enhance radiation-induced cytotoxicity in human prostate cells. This represents a rationale for future exploration in clinical trials.

25
ASSESSMENT OF SURGICAL MARGINS BY QUICK-STAINING CYTOLOGY IN NEPHRON-SPARING SURGERY

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Background: Nephron-sparing surgery is an established curative approach for the treatment of patients with T1 renal cell carcinoma (RCC) (1). The thickness of the surgical margin remains the subject of constant discussion (2-3). The standard procedure includes the performance of histological frozen section, which at our institution requires approximately 20 to 30 minutes. *Patients and Methods:* In this prospective study, we evaluated an alternative procedure to the frozen section. We compared quick-staining cytology, obtained by touch preparation of the tumor base, with frozen section result and the final histology. RCC was enucleated with a macroscopically normal parenchymal rim of 3-5 mm and sent to the pathology laboratory, where an imprint of the enucleated specimen and a frozen section were analyzed. *Results:* From August 2006 to August 2010, 48 patients with a mean age of 62.6 (25-83) years underwent 54 nephron-sparing surgeries for kidney tumors. The mean diameter of the tumors was 2.6 cm. The mean follow-up was 20.8 (3-120) months. The histological surgical margins were positive in 7/54 (12.9%) and the cytology was positive in 8/54 (14%) patients. Of the eight tumors with a positive cytology, six (75%) had a positive margin in histology. Of the 46 tumors with a negative cytology, 45 had a negative margin in histology. The sensitivity of cytology was 85%, with a positive predictive value of 75%; the specificity was 95.7%, with a negative predictive value of 97.8%. In 2/54 (3.7%) patients, a local recurrence was observed. One of the two patients had positive intraoperative cytology but negative histology; both tests were positive for the other patient. A total of 5/48 patients (10.4%) died but these deaths were not cancer-related. *Conclusion:* Intraoperative cytology is a rapid, sensitive and highly specific method to determine surgical margins. It reduces diagnostic time and might be a good alternative to intraoperative frozen sections.

1 Touijer K *et al*: The expanding role of partial nephrectomy: A critical analysis of indications, results and complications. Eur Urology *57*: 214-222, 2010.
2 Raz O *et al*: Positive surgical margins with renal cell carcinoma have a limited influence on long-term oncological outcomes of nephron-sparing surgery. Urology *75*: 277-281, 2010.
3 Dennis J *et al*: Utility of frozen section analysis of resection margins during partial nephrectomy. Urology *64*: 31-34, 2004.

26
LOCALLY ADVANCED SQUAMOUS CARCINOMA OF THE PENIS: DESCRIPTION OF A CLINICAL CASE AND REVIEW OF THE LITERATURE

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Penile carcinoma is a relatively rare neoplasm that usually originates from the prepuce or glans. In Europe and Western countries, the incidence is approximately 1 per 100,000 males. Primary risk factors are phimosis, human papillomaviruses (HPV 16-18), smoking, poor hygiene, therapy with sporalene, ultraviolet A phototherapy, chronic inflammatory conditions such as balanoposthitis, lichen and a history of multiple sexual partners. At present, with the improvement of living and hygiene standards, the incidence of penile carcinoma is in decline, especially for penile carcinoma of a large size. T3 and T4 stage are rare, accounting for only 5% of penile carcinoma in Europe. We describe a rare case of a huge squamous cell penile carcinoma in a 63-year-old patient with a history of tumor growth associated with the appearance of multiple surface ulcerations, in which total penectomy and perineal urethrostomy were carried out in our department. The presence of phimosis had been observed in previous years. A detailed clinical history showed that he was affected only by diabetes

mellitus and hypertension. The patient reported intermittent pain, fever, several episodes of gross hematuria and both irritative and obstructive urinary symptoms refractory to medical therapy. Physical examination revealed that the penis was worse, showing an increase in volume and consistent in its entirety, with a diffuse redness of the cutis. Four odorous purulent ulcerations involving the skin were present on the lateral surface. Inguinal lymph nodes could not be palpated on either side. The results of laboratory examinations were normal except for leucocytosis. A urinary catheter was therefore inserted and antibiotics were administered. We performed a wedge biopsy of the skin lesions previously described. The pathological examination revealed moderately differentiated squamous cell carcinoma with vascular invasion. Magnetic resonance of the lower abdomen and total body CT scan revealed the absence of distant metastases. After a negative sentinel node biopsy, a total penectomy with perineal urethrostomy was carried out. We decided to preserve both testicles. The affected area was corrected with a well-vascularized perineal skin flap. *Results:* The final histological examination confirmed the diagnosis of moderately differentiated squamous cell carcinoma. Extensive infiltration of the *corpora cavernosa* and urethra (pathological stage T3) were present with absence of lymphatic and vascular invasion with negative surgical margins. Furthermore, the patient underwent adjuvant chemotherapy with cisplatin. After 22 months, the patient is disease free. *Discussion and Conclusion:* Penile carcinoma is a rare malignancy in Western countries, with an incidence of 1,290 new cases and 290 deaths annually in the United States. In Europe, penile carcinoma represents fewer than 1% of all carcinomas. The five-year survival rate is approximately 80%. Pathological risk factors are perineural invasion, lymphovascular invasion, positive resection margins and urethral involvement. Despite severe implications for the quality of life, total penectomy (with wide surgical margins) with perineal urethrostomy is the standard surgical treatment for advanced disease (T3-T4). In T4 disease and in the presence of positive or relapsed nodes, adjuvant chemotherapy is strongly suggested. The presence of lymph node metastasis is probably the most important prognostic factor in squamous cell carcinoma of the penis; in fact, the disease-free survival at five years is less than 40% in node-positive patients but more than 80% in node-negative patients.

1 Barnholtz-Sloan JS, Maldonado JL, Pow-Sang J and Giuliano AR: Incidence trends in primary malignant penile cancer. Urol Oncol *25(5)*: 361-367, 2007.

2 Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, Carter JJ, Porter PL, Galloway DA, McDougall JK and Krieger JN: Penile cancer: importance of circumcision, human papillomavirus and smoking in *in situ* and invasive disease. Int J Cancer *116(4)*: 606-616, 2005.

3 Barocas DA and Chang SS: Penile cancer: clinical presentation, diagnosis, and staging. Urol Clin North Am *37(3)*: 343-352, 2010.

4 Pizzocaro G, Algaba F, Horenblas S, Solsona E, Tana S, Van Der Poel H and Watkin NA: EAU penile cancer guidelines 2009. Eur Urol *57(6)*: 1002-1012, 2010 [Epub 2010 Feb 4].

5 Pow-Sang MR, Ferreira U, Pow-Sang JM, Nardi AC and Destefano V: Epidemiology and natural history of penile cancer. Urology *76(2 Suppl 1)*: S2-6, 2010

27

PROLONGED RESPONSE TO CYTOREDUCTIVE SURGERY AND SUNITINIB IN AN ELDERLY PATIENT WITH SYNCHRONOUS MULTIPLE METASTASES FROM RENAL CELL CARCINOMA

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Renal cell carcinoma (RCC) is a cancer with a relatively low incidence, accounting for about 2-3% of all cancer cases. Multitargeted therapy of advanced RCC appears to be a better option than immunotherapy. Sunitinib is a multitarget tyrosine kinase inhibitor whose activity has been demonstrated in phase III and expanded-access studies. In the present paper, we report the case of an elderly patient with multiple metastases who attained a prolonged response to sunitinib. A 72-year-old woman with a Karnofsky performance status of 90, no significant medical history, and no comorbidities except hypertension treated with transdermal clonidine (TTS-1) was referred to our hospital in October 2006 complaining of flank pain and gross hematuria. At clinical examination, a mass in the right flank and a 2 cm subcutaneous nodule in the right breast were detected. Total-body computed tomography (CT) scan showed a right kidney neoplasm of 15 cm, a mass in the left adrenal gland, peripancreatic abnormal tissue, small lung nodules (three bilateral nodules of 1 cm) and extensive hilar-mediastinal lymphadenopathies (maximum diameter 3.8 cm). At cranial CT evaluation, a sub-centimetric (0.4 cm) thalamic lesion of uncertain etiology was identified. Bone scintigraphy was normal. At blood chemistry assay, mild anemia (Hb 11.7 g/dl) was present; LDH and calcium were in the normal range. Surgical excision of the subcutaneous breast nodule revealed an adenocarcinoma of metastatic origin. The patient underwent a right radical nephrectomy and abdominal cytoreductive surgery, including left adrenalectomy and distal pancreatectomy. No residual intra-abdominal gross tumor remained after surgery. Final pathology documented a 15×10×8

cm clear cell RCC, Fuhrman grade 2, pT3cN0M1, with pancreatic and contralateral adrenal involvement. After surgery, the patient recovered quickly and was placed on long-term corticosteroid treatment. Four weeks later (December 2006), she began subcutaneous interferon-alpha (IFN) 6 MU three times/weekly; higher doses were not tolerated. In February 2007, treatment was discontinued because of malaise and bone pain in the left hip. A CT scan of the pelvis revealed bone involvement of the left ischium. On CT and MRI, the thalamic lesion was found to have increased to 1 cm, with peripheral edema. The patient underwent stereotactic radiosurgery (Cyberknife) of the brain lesion. After cardiological assessment with ECG and echocardiography, in April 2007, she was placed on 50 mg sunitinib daily in a six-week cycle according to a 4/6 schedule (four weeks on treatment, two weeks off treatment. Up to June 2010, the patient was continuing sunitinib treatment and there was good control of arterial blood pressure with the three-drug combination, no electrocardiographic or echocardiographic alterations, normal thyroid function, grade 1 leukopenia and thrombocytopenia, and macrocytosis. The patient was in good performance status (Karnofsky 80) and was asymptomatic, but complaining of asthenia, especially during the four weeks of sunitinib administration, causing mild impairment of quality of life. The role of surgery in metastatic RCC is still debatable especially in this new era of targeted therapy. In conclusion, in the treatment of older people with targeted therapies, the following recommendations are made: assessment of the type and severity of co-morbidities; careful monitoring of cardiac, thyroid and metabolic dysfunctions, and assessment of the impact of every kind and grade of the developed toxicities on quality of life.

1 Flanigan RC, Mickisch GH, Sylvester R, Tangel C, Van Poppel H and Crawford ED: Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol *171*: 1071-1076, 2004.
2 Hofmann HS, Neef H, Krohe K, Andreev P and Silber RE: Prognostic factors and survival after pulmonary resection of metastatic renal cell carcinoma. Eur Urol *48*: 77-81, 2005.
3 Karellas ME, Jang TL, Kagiwada MA, Kinnaman MD, Jarnagin WR and Russo P: Advanced-stage renal cell carcinoma treated by radical nephrectomy and adjacent organ or structure resection. BJU Int *103*: 160-164, 2008.

29
QUALITY OF LIFE ISSUES IN URINARY DIVERSIONS: ORTHOTOPIC NEOBLADDER *VERSUS* ILEAL CONDUIT

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Background: During the last 20 years, the use of orthotopic neobladder has become the preferred choice for bladder replacement after radical cystectomy for muscle-invasive bladder cancer. The proportion of cystectomy patients receiving a neobladder has increased at medical centers to 30%-66%, while ileal conduit, once considered the gold standard, is now employed in 10%-64% of patients. It is generally believed that the use of an orthotopic neobladder might provide a better quality of life (QoL) because it should represent a true '*restitutio ad integrum*' but many studies have failed to demonstrate a better QoL score. We report our experience with EORTC QoL questionnaires. *Patients and Methods:* A total of 53 patients were given the EORTC QLQ-C30 (version 3.0) and the QLQ-BLM30 questionnaires. All patients underwent radical cystectomy for muscle-invasive bladder cancer. Twenty-six patients received an ileal conduit (group A), while 27 a Y orthotopic neobladder (group B). The mean follow-up was 53.65±29.02 months. The QLQ-C30 incorporates five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status/QoL scale, and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnea, loss of appetite, insomnia, constipation and diarrhea) and perceived financial impact of the disease. The QLQ-BLM30 is a phase-III module that specifically evaluates the impact of radical cystectomy and reconstructive surgery. The scores were linearly transformed (scale 0-100). A high score for a functional scale represents a high/healthy level of functioning, a high score for the global health status/QoL represents a high QoL, but a high score for a symptom scale/item represents a high level of symptomatology/problems. *Results:* All patients agreed to fill-in the questionnaires. As far as QLQ-C30 is concerned, all patients reported a good global health status/QoL (Group A: 60.58±21.42, group B: 68.21±23.69, p=0.22). No differences were recorded in physical, cognitive, emotional, and social functional scales. One of the questions of the role functioning scale recorded a statistically significant difference (group A: 50±27.08, group B: 66.67±29.24, p<0.05). Pain scaling also recorded statistically significant differences (Group A: 17.31±27.68, group B: 4.94±12.07, p<0.05). As far as QLQ-BLM30 is concerned, the patients of group B recorded few urinary symptoms (29.81±13.64), and the patients of group A recorded few urostomy problems (28.42±16.13). The 'future perspective' scale recorded significant differences in favor of orthotopic neobladder patients (group A 32.91±25.82 *vs*. group B 18.52±15.1 p<0.05). No differences were observed for abdominal symptoms and body image. Regarding sexual function, statistically significant differences (p<0.05) were recorded in

2/8 questions in favor of orthotopic neobladder. *Conclusion:* The use of EORTC QoL questionnaires was easy and effective. Both patients with orthotopic neobladder and those with ileal conduit reported a good global health status and QoL. The main differences were recorded in the role functional scale, pain, future perspective and sexual function: patients with orthotopic neobladder were less impaired in pursuing their hobbies or other leisure time activities, had fewer worries and were more interested in sex. Interestingly, no differences were observed for the perception of body image alterations.

1 Hautmann RE, Abol-Enein H, Hafez K *et al*: Urinary Diversion. Urology *69(Suppl 1A)*: 17-49, 2007.
2 Aaronson NK, Ahmedzai S, Bergman B *et al*: The European Organisation for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Nat Cancer Inst *85*: 365-376, 1993.

30

CONTRALATERAL DYNAMIC SENTINEL NODE BIOPSY IN PATIENTS WITH MONOLATERAL INGUINAL NODE METASTASES OF PENILE CANCER

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Background and Aim: Early detection of inguinal nodal metastasis from penile cancer is mandatory. Inguinal lymphadenectomy is advised in patients with invasive or high-grade cancer as stated by EAU guide lines; nevertheless) it has major morbidity (1). In high-volume centers, dynamic sentinel node biopsy (DSNB) is performed to reduce negative lymph node dissection in order to reduce morbidity (2). This study analyzed data from patients who underwent lymphadenectomy on the clinically positive inguinal side, while DSNB was performed on the opposite clinically negative side as revealed by physical and echographic examination. *Patients and Methods:* From January 2000 to December 2010, 55 patients underwent DSNB: in eight patients (median age 58 years, range 44-75), a controlateral lymphadenectomy on the metastatic side was performed at the time of surgery. The sentinel node was detected by a gamma camera study after lymphoscintigraphy performed three hours before and by blue dye which had been injected intradermally around the penile tumor or in the penile shaft just before surgery. Six partial penectomy (PP) procedures were performed in the same surgery section, one PP and one laser excision before lymph node dissection. After surgery, major complications were recorded and all patients started a follow-up schedule. *Results:* We recorded invasive squamous cell carcinoma (SCC: 3 pT1 and 5 pT2) with one G1, six G2 and one G3 carcinomas. The pathological nodal status on the metastatic side was: one pN0. three pN1, three pN2 and one pN3; while on the DSNB there were six N0. one N1 and one not conclusive. The positive DSNB patient underwent inguinal lymphoadenectomy (pN2) and he was the only patient with unusual complication of cutaneous spread, probably from inguinal scar. This patient died after 16 months due to metastatic disease despite chemotherapy. In the not conclusive DSNB patient, a close follow-up was initiated, with no actual evidence of relapse at six months. Seven patients were alive at the time of writing with no evidence of disease at a median follow-up of 20 months (range 1-81 months). *Conclusion:* Early detection of nodal metastases in SCC of the penis is mandatory and lymphadenectomy is the golden treatment as stated by EAU guidelines. Nevertheless, DNSB is safe, with limited major complications and good reliability also for patients with advanced cancer and clinical monolateral nodal metastases, as shown in this preliminary retrospective study. This procedure must be performed in high volume centers in order to ensure a reliable DNSB procedure. A close follow up is mandatory, even if a negative DSNB seems to be a good prognostic factor.

1 Pizzocaro G *et al*: EAU penile cancer guidelines 2009. Eur Urol *57*: 1002-1012, 2010.
2 Leijte JAP *et al*: Reliability and safety of current dynamic sentinel node biopsy for penile carcinoma. Eur Urol *52*: 170-177, 2007.

31

IMPACT OF MENTAL HEALTH ON QUALITY OF LIFE OF PROSTATE CANCER PATIENTS DURING ACTIVE SURVEILLANCE

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Background: Although active surveillance (AS) is not generally associated with poor quality of life (QoL), our preliminary

results revealed that at entrance into Prostate Cancer Research International Active Surveillance (PRIAS) patients with an impaired mental health (MH) showed lower levels of adjustment to disease and health-related quality of life (HRQoL). *Aim:* The aim of this study was to evaluate the association between MH status and QoL between the entrance into PRIAS and the first re-biopsy. *Patients and Methods:* From November 2007 to December 2010, 53 patients (median age 68 years, range 45-79) fully completed the follow-up assessment about 10 months (T1) after the first biopsy (time range between 9 and 11 months) and before the first re-biopsy. MH was measured by using the Symptom Checklist 90 (SCL-90) at entrance into PRIAS (T0). For each subscale (depression, anxiety, interpersonal sensitivity and hostility), we chose a cut-off point to identify patients with higher scores (85th percentile of the raw scores). QoL, which is a multidimensional construct, was evaluated at T1 by considering the following aspects: (i) HRQoL, measured by the Functional Assessment of Cancer Therapy - Prostate Version (FACT-P), subscales: physical wellbeing, emotional wellbeing, social well-being and functional wellbeing; and (ii) adjustment to cancer, measured by the Mini-Mental Adjustment to Cancer Scale (Mini-MAC), subscales: fighting spirit, anxious preoccupation, helplessness/hopelessness, fatalism and avoidance. *Results:* Most patients showed good levels of HRQoL and adjustment to disease at T1, in particular in terms of physical (98%) and emotional wellbeing (81%) (normalized scores ≥3) and fighting spirit (86%) (normalized scores ≥2). We performed the Kruskall-Wallis test to investigate the association between MH and QoL aspects and found that the MH status at the entrance into PRIAS was correlated with a dysfunctional style of coping with cancer and with poor HRQoL at T1. In particular: (i) patients with high scores in the anxiety domain showed greater fatalism (I=0.04, average rank (ar) 23.1 *vs*. 36.5), greater helplessness/hopelessness (I=0.017, ar 22.9 *vs*. 38.2), lower physical wellbeing (p=0.0013, ar 27.9 *vs*. 8.4) and emotional wellbeing (p=0.05, ar 27.3 *vs*. 13.8); (ii) patients with high scores in depression domain showed greater anxious preoccupation (p=0.02, ar 22.8 *vs*. 36.7), greater helplessness/hopelessness (p=0.0027, ar 22.3 *vs*. 40), greater avoidance (p=0.04, ar 23 *vs*. 35.3) and lower scores in emotional wellbeing (p=0.012, ar 27.9 *vs*. 11.8); and (iii) patients with high scores in interpersonal sensitivity domain showed greater helplessness/hopelessness (p=0.005, ar 21.9 *vs*. 35.9). *Discussion and Conclusion:* Consistent with our preliminary results and relevant literature regarding QoL in AS (van den Bergh, BJU, 2010), patients usually report a high subjective perception of QoL. Nonetheless, patients with impaired MH showed lower levels of adjustment to disease and HRQoL approximately ten months (T1) after the first biopsyand before the re-biopsy. In particular, we found that anxious patients showed a worse adjustment style to the disease, revealing hopelessness and loss of self-confidence, and depressed patients show high levels of anxious preoccupation about the disease, which is one of the potential drawbacks of AS. We emphasize that the helplessness/hopelessness style of coping with cancer was most frequently associated with impaired MH, particularly in terms of anxiety, depression and interpersonal sensitivity. It is likely that psychologically vulnerable patients would benefit from effective physician–patient communication and psychological support aimed to alleviate anxiety and uncertainty.

32
RELIABILITY AND SAFETY OF DYNAMIC SENTINEL NODE BIOPSY IN CLINICALLY INGUINAL NODE-NEGATIVE PENILE SQUAMOUS CELL CARCINOMA

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Background and Aim: Early detection of inguinal nodal metastasis from penile squamous cell carcinoma (SCC) is mandatory. Lymph-node dissection (LND) represents the standard management of nodal disease, but with severe morbidity. According to EAU guidelines LND is advised in patients with invasive and/or high grade cancer (pT1G2). In high volume centers, dynamic sentinel node biopsy (DSNB) is performed on selected patients for LND in order to limit morbidity. This study analyzed data from patients with clinically negative inguinal nodes (cN0), as determined by physical and ultrasound examination. The aims of this study were to assess the false-negative rate (FN), negative predictive value (NPV) and sensitivity, as well as complications of the DSNB procedure. *Patients and Methods:* The sentinel node was detected by gamma camera study after lymphoscintigraphy performed three hours before and detection of blue dye injected in the penile shaft immediately before surgery. From January 2000 to December 2010, 55 patients underwent DSNB: eight had clinical groin metastases in one side and were not considered for this study; the study population consisted of 47 patients (mean age 66 years, range 44-83) with bilateral cN0 nodes. In 39 patients, DSNB was detected successfully in both groins; in seven patients only in one groin and in one patient, there was no bilateral signal from the gamma camera. There was no signal (cNx) from the groins of 9/94 (9.5%) patients, while in 85/94 (91.5%) patients there was successful identification of DSN. In the groins of 6/85 (7.1%) patients, there was a positive DSNB followed by LND: Two patients had pN1 (DSN was the sole pathologic node), two had pN2 (more than one pathological node), and two had pN3 disease. After a median follow-up of five months (range 2-17), groins from 9

(10.6%) out of 85 patients with a negative DSNB developed inguinal metastases which were submitted to LND: eight had pN2 and one pN3 disease. In one out of nine undetected DSN (cNx), inguinal nodal metastases developed at two months as pN2 disease. Most probably, lack of visualization is due to tumor blockage of lymphatic vessels drainage and rerouting to a neo sentinel node. We had only 5 (7.4%) metastases among the groins of 68 patients which had had negative DSNB. Overall, we recorded 16/94 affected groins (17%), so that LND was spared in 83% (78/94) of patients. On the other hand, the FN rate was 10.6% (9/85), leading to a relatively good NPV of 82% (70/85), but to only fair sensitivity of 40% (6/15). The efficiency rate of the whole procedure (groins of 94 patients) is even lower, as we detected only 6 (37.5%) out of 16 metastases. We did not find major complications. Nonetheless, one patient developed an unusual intradermal metastatic spread, possibly due to a lymphatic drainage alteration after DNSB. *Conclusion:* DNSB is a safe procedure, with limited major complications which was able to spare LND in 83% of our patients. As false-positives are not actually possible, only NPV (82.3%) and sensitivity (40%) can be calculated. Moreover, the efficiency rate of the intention to diagnose is even lower, as it was only possible to detect 37.5% of metastatic nodes early. Small numbers, intrinsic to the rarity of the disease, do not allow one to draw definitive conclusions. A close follow-up is mandatory in cases of a lack of groin signal (cNx), as well as in cases of negative bilateral DSNB. Patients with penile SCC should be evaluated in high volume centers, in order to achieve greater accuracy in this procedure and the best chance of cure.

1 Leijte JAP *et al*: Reliability and safety of current dynamic sentinel node biopsy for penile carcinoma. Eur Urol *52*: 170-177, 2007.
2 Pizzocaro G *et al*: EAU penile cancer guidelines 2009. Eur Urol *57*: 1002-1012, 2010.

34

DIFFERENTIAL EXPRESSION OF MATRIX ATTACHMENT REGION-BINDING PROTEINS IN HUMAN PROSTATIC CANCER CELL LINES

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Background: Abnormal nuclear organization and alterations in the amount and distribution of heterochromatin have always been recognized as hallmarks of human cancer. However, neither the exact cause of these modifications nor how the activity/silencing of thousands genes can be orchestrated are currently known. In eukaryotes, the genome is compartmentalized into chromatin domains by attachment to a supporting structure termed the nuclear matrix (NM). The interactions of chromatin with the NM occur *via* AT-rich DNA sequences called matrix attachment regions (MARs). MARs exhibit several functions, including the organization of chromatin loops, the augmentation of transcription and the facilitation of replication; moreover, the attachment of the genome to the NM is a dynamic event that is cell type- or cell cycle-dependent (1). Several MAR-binding proteins have been identified, some are dramatically dysregulated in tumor cells and their expression is often significantly correlated with the more aggressive phenotype (2). Likewise, modifications of the interactions between NM proteins and MARs might be related to the large-scale chromatin organization observed in carcinogenesis. Research carried out in our and other laboratories seeking prostate cancer (PCa) markers with improved diagnostic and prognostic features has identified some NM proteins that are differentially expressed in PCa with respect to non-tumor tissue; a few of these proteins were significantly correlated with tumor aggressiveness and/or risk of biochemical progression (3). These findings prompted us to characterize the changes in the NM protein–MAR bond in PCa. *Materials and Methods:* In this study, using a proteomic approach along with two-dimensional Southwestern analysis, we characterized the NM protein–MAR bond in two prostatic cancer cell lines: the androgen-responsive LNCaP and the androgen-resistant PC3. For binding experiments, a highly repetitive bent DNA sequence of 370-bp (*Xmn*I) containing a base unpairing region was used as a probe. The variation of the expression of some MAR proteins was determined by quantitative Western blot. Both the nucleoplasm distribution and the co-localization with DNA were evaluated by confocal laser scanning microscopy. Using transmission electron microscopy (TEM) the high-order structure of chromatin was examined in the two cell lines. *Results:* Several NM proteins extracted from both cell lines strongly bind to the *Xnm*I sequence. It is possible to separate these proteins into two groups: I. MAR-binding proteins present in a large quantity also in other cellular types (MARPa, MARPb, hnRNPs, Lamin A, Lamin B, Matrin3) that may correspond to the proteins in contact with the constitutive MARs (*i.e.* the sequences demarcating permanent domain boundaries in all cell types). II. MAR-binding proteins corresponding to cell-type specific factors (PARPs, SATB1) that interact with facultative MARs (*i.e.* the sequences cell type- and activity-related and dependent on cell differentiation). In PC3 with respect to LNCaP cells, several changes in the ability of proteins to bind XnmI sequence were observed: the signal intensity of Matrin3, SATB1 and all basic hnRNPs decreased, showing that these proteins bind the DNA more weakly or are down-regulated in more aggressive cells. In contrast, MARPa, MARPb, PARP and its fragments increased. Confocal

microscopy demonstrated that also the co-localization of PARP with DNA was significantly lower. These changes were concomitant with a different compartmentalization of chromatin in the two cell lines, as shown by TEM. *Conclusion:* Our study provides evidence that several MAR-binding proteins undergo extensive changes in PC3 with respect to LNCaP cells, showing that the interactions between NM and the base of the chromatin loop are involved in cell differentiation. These proteins may turn out to be an important tool in the understanding of PCa carcinogenesis and may be novel targets of anticancer drugs.

1 Chattopadhyay S and Pavithra L: MARs and MARBPs: Key modulators of gene regulation and disease manifestation. *In*: Chromatin and Disease. Kundu TK and Dasgupta D (eds.). Springer, pp. 213-230. 2007.
2 Han HJ, Russo J, Kohwi Y and Kohwi-Shigematsu T: SATB1 reprogrammes gene expression to promote breast tumour growth and metastasis. Nature *452*: 187-193, 2008.
3 Barboro P, Rubagotti A, Boccardo F, Carnemolla B, Darrigo C, Patrone E and Balbi C: Nuclear matrix protein expression in prostate cancer: possible prognostic and diagnostic applications. Anticancer Res *25*: 3999-4004, 2005.

35
ROBOT-ASSISTED LAPAROSCOPIC RADICAL CYSTECTOMY AND INTRACORPOREAL URINARY DIVERSION

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Aim: To describe our technique of robotic cystectomy and intracorporeal formation of Studer neobladder for treatment of carcinoma of the bladder. *Materials and Methods:* We describe our surgical technique, stepwise describing the surgical procedure and pathologic outcomes. After cystectomy, the reconstruction phase starts from the ileo-urethral anastomosis about 40 cm from the ileocecal valve. We then proceeded to section the ileum through endoGIA. Detubularization of ileum neobladder is carried out using cold robotic scissors. Studer reconfiguration is performed by pds running suture. To reduce urinary reflux, we prefer the Wallace type of anastomosis, with a pro-peristaltic segment of nondetubularized ileum. *Results:* We performed 15 robotic-assisted intracorporeal neobladder procedures. Mean operating-room time of all patients was 6.3 h and mean surgical blood loss was 430 ml. We prefer to stent the ureteral anastomosis for two weeks. We have recorded only one major postoperative complication: an acute compartment syndrome of the lower leg. *Conclusion:* The clinical and oncologic follow-up of patients undergoing robot-assisted intracorporeal urinary diversion appears to be favorable in the short term. As our follow-up increases, we should expect to continue to truly define the long-term clinical appropriateness and oncologic success of this procedure.

36
PROSTATE CANCER BEFORE AND AFTER RENAL TRANSPLANTATION: OUR EXPERIENCE

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Background: Prostate cancer is the most common genitourinary malignancy in male renal transplant recipients. Renal transplantation is the preferred therapy in patients with end-stage kidney disease. Improvements in immunosuppressive therapy and in surgical techniques offer good renal allograft and patient survival times. Furthermore, the increased age of recipients leads to a high number of diagnoses of prostate cancer at the time of placement on the transplantation waiting list. *Patients and Methods:* From 1981 to 2010, 2,499 renal transplantations were performed at our center, 1610 of which were for males (64.4%). We found thirteen cases (Group 1) of prostate cancer at the time of placement on the waiting list and eight cases (Group 2) after kidney transplantation (from 1 month to 12 years after grafting). Patients in Group 1 underwent radical treatment: retropubic prostatectomy in three cases, perineal prostatectomy in six cases, HIFU in four cases (and one more HIFU after perineal prostatectomy for a pT3aNx with involved margins). After treatment, the follow-up for these patients consisted of a physical examination (including a DRE) and serial serum PSA measurements every three months. Patients in Group 2 underwent: perineal prostatectomy in three cases and radiation therapy in one case (for localized tumor), TUR-P in three cases (incidental tumors) followed by watchful-waiting, hormonal therapy with LH-RH analogs in one case (a patient with a Gleason Score of 5 who refused radical therapies). After treatment, the follow-up consisted of a physical examination (including a DRE) and serial serum PSA measurements every three months, abdominal US and chest X-rays every six months. *Results:* Patients in Group 1 submitted only to radical surgery (eight cases) were placed on the waiting list six months after the procedure: the mean serum PSA level was 0.03 ng/ml and they were considered free from disease. At the time of writing, four of them have received grafts, one is dead from infective complications, and three are still on the

waiting list. Patients in Group 1 submitted to HIFU (five cases, one of them after perineal prostatectomy) underwent a five-year period of follow-up. At the time of writing, three of them are dead from cardiovascular or infective complications during the follow-up period and two are still on the waiting list. All the patients in Group 2 (eight cases) are still alive and aid without metastasis or local recurrence of disease. *Conclusion:* Prostate cancer diagnosed at the time of placemat on the waiting list for renal transplantation can represent a management difficulty. These patients should be submitted to radical prostatectomy where possible. In our experience, we prefer a perineal instead of a retropubic approach because this allows us to avoid creating pelvic adherences that will make future grafting more difficult. When not possible, because of a PSA serum level >10 ng/ml and/or dubious lymph nodes at CT scan, regional lymphadenectomy is mandatory, by a retropubic approach. Regardless of the approach, radical prostatectomy allows these patients to be placed on the waiting list six months after the procedure, when the PSA serum is restored to a normal level. Patients diagnosed with prostate cancer after grafting should also be submitted to radical surgery. Even in these cases, the perineal approach reduces the risk of grafted organ lesions during the procedure. If radical surgery is not possible, a watchful waiting approach can be adopted for patients with incidental prostate cancer diagnosed after TUR-P.

1 Wicht A, Hamza A, Loertzer H, Dietl M, Heynemann H and Fornara P: Diagnostics and treatment of prostate cancer after kidney transplantation. Urologe A *45(1)*: 32-37, 2006 (in German).

37

PROGNOSTIC FACTORS IN A PROSPECTIVE SERIES OF NMIBC TREATED WITH BCG

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Aim: Several molecular markers were retrospectively analyzed in order to evaluate their predictive role in patients treated with BCG. The aim of this study was to prospectively evaluate the predictive role of p53, Ki67 and mitotic index (MI), along with the traditional prognostic variables in a homogeneous series of patients with NMIBC treated with BCG. *Patients and Methods:* From 1994 to 2004, 178 patients with intermediate- and high-risk NMIBC were enrolled. Specimens from initial pre-BCG TURB were obtained from all patients for p53, Ki67 immunoassay and MI. Traditional prognostic values included focalization, size of the lesion, associated CIS, recurrence status. The endpoints of the study were overall survival (OS), cancer-specific survival (CSS), recurrence-free survival and progression-free survival. Univariate survival analysis was conducted using the Kaplan-Meier method with 1og-rank test. In addition, multivariate analysis was performed with Cox's proportional hazard regression analysis. *Results:* The median age was 66 (range 40-90) years. Mean follow-up was 101.5 (range 2-229) months. Thirty-two patients underwent BCG induction alone because of side-effects or early disease progression. In univariate analysis, Ki67 (cut-off 20) was significantly associated with OS (95% CI=1.31-5.16, p=0.006) and CSS (95% CI=1.27-12.5, p=0.018). Neither p53 (cut-off 2.5) nor MI (cut-off 3) were statistically significant predictors of survival in our patient cohort (p>0.05). Interestingly, patients with values of p53 and MI lower than the median seemed to develop recurrences earlier (95% CI=0.35-0.78, p=0.002 and 95% CI=0.43-0.95, respectively, p=0.029). None of the three markers were significantly associated with progression. Multivariate analysis did not modify the predictive role of these markers. *Conclusion:* To our knowledge, this is the first study to evaluate prospectively the prognostic role of molecular markers in a cohort of patients treated with BCG. As previously assessed in literature, Ki67 may be a useful marker of response to BCG therapy. There is no consensus in the literature about the predictive value of p53 after BCG therapy. A recent study suggested that pretreatment p53 overexpression is associated with a high risk of recurrence, progression and cancer death; however, according to our data, p53 does not seem to be significantly associated with survival. MI was not a significant predictor of survival either. A tool to predict the response to BCG therapy is essential in order to identify more accurately the BCG non-responders and those at higher risk of recurrence and progression. Further analyses are required in order to confirm these preliminary findings.

38

MULTIFOCAL RETROPERITONEAL GANGLIONEUROMA: A CHALLENGING DIAGNOSIS

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Ganglioneuroma (GN) is the rarest and most benign of neuroblastic tumors and originates from neural crest cells wherever sympathetic nervous tissue exists, such as in the

retroperitoneum and in the adrenal gland. The diagnosis can be very challenging, given the rarity and the asymptomatic presentation of this neoplasia, and can be achieved only by means of histological evaluation. Although benign, only a few cases of metastatic ganglioneuroma have been reported in the literature. The prognosis, however, seems to be excellent after surgical resectionWe describe a rare case of multifocal retroperitoneal GN, diagnosed incidentally in a 46-year-old woman, with para-aortic and adrenal localizations. After the intraoperative pathological diagnosis was made, complete excision of all the visible masses was performed. The patient recovered well and was recurrence-free three months after surgery, without needing any adjuvant therapy. According to our knowledge, this is the first case reported of a multifocal retroperitoneal GN. Among the broad differential diagnosis of adrenal incidentalomas, an adrenal location of neuroblastic tumors should not be discounted.

39
OVERALL SURVIVAL DATA WITH SEQUENTIAL TARGETED THERAPIES IN METASTATIC RENAL CELL CANCER

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Background: Targeted therapies, including multi-kinase inhibitors, monoclonal antibodies and m-TOR inhibitors are the standard therapies for metastatic renal cell carcinoma (mRCC). The optimal sequence of all drugs is still unclear. *Patients and Methods:* Baseline characteristics and outcomes of 310 patients affected by mRCC receiving targeted therapies (TT) were collected from the database of the Istituto Nazionale Tumori of Milan, Italy. The main characteristics of patients were: ECOG PS 0/1/2: 168/123/19; gender M/F: 229/81; clear-cell histology 268 (86%); non clear-cell 42 (14%); previous nephrectomy 273 (88%); Fuhrman grade 1/2/3/4: 15/93/118/43 and unspecified in 41 (13%). According to the Motzer criteria, 100 cases (32%) had low risk, 146 (47%) had intermediate risk and 64 (21%) had poor prognosis. A total of 163 (53%) patients received only one TT, while 113 (36%), 30 (10%) and 4 (1%) received 2, 3 and 4 TT, respectively. Overall, 233 (75%) patients received sorafenib, 172 (55%) sunitinib, 32 (10%) bevacizumab and 20 (7%) other TT. The uni- and multivariate analyses were carried out using Cox proportional hazard regression analysis. Safety data, disease control rate (DCR) and progression-free survival (PFS) for targeted therapies were recorded. *Results:* After a median follow-up of 37 months, 179 patients (57%) had died. The median overall survival (OS) was 22 months and the 5-year OS was 23.4% (95% CI=16.7-30.0). The median and 5-year OS was 43 months and 42.8% in low-risk patients, 21 months and 15.9% in the intermediate-risk and 8 months in poor-risk patients. Table I shows the univariate OS analysis; Table II (next page) shows the multivariate OS analysis. *Conclusion:* The efficacy data suggest the absence of cross-resistance between antiangiogenic therapies and support the emerging use of sequential targeted treatments in mRCC.

Table I. *Univariate overall survival analysis.*

	HR (95% CI)	*p*-Value
Age		
10-year increment	0.98 (0.86-1.11)	0.735
Gender		
M *vs*. F	1.09 (0.77-1.55)	0.635
ECOG		
1 *vs*. 0	1.69 (1.25-2.29)	<0.001
2 *vs*. 0	2.62 (1.39-4.95)	
Cytokines		
Yes *vs*. No	1.28 (0.95-1.72)	0.101
Histology		
Papillary *vs*. Clear cell	1.39 (0.85-2.27)	0.247
Other *vs*. Clear cell	1.47 (0.75-2.89)	
Nephrectomy		
Yes *vs*. No	0.41 (0.26-0.65)	<0.001
Motzer		
Intermediate *vs*. Low risk	2.30 (1.57-3.35)	<0.001
High *vs*. Low risk	7.90 (5.07-12.31)	
Therapeutic choice		
Other option *vs*. Sorafenib + Sunitinib	0.77 (0.51-1.17)	0.212
Sunitinib + Sorafenib *vs*. Sorafenib + Sunitinib	0.69 (0.41-1.16)	

40
IS THERE A ROLE FOR TARGETED THERAPIES IN CARCINOMA OF THE COLLECTING DUCTS OF BELLINI?

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Background: Carcinoma of the collecting ducts (CDC) of Bellini in the kidney, although very uncommon, is one of the most aggressive urological entities. For this tumor, originating

Table II. *Multivariate overall survival analysis (Abstract No 39).*

	Adjusting for Motzer		Unadjusted	
	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value
Age				
10-year increment	0.98 (0.85-1.12)	0.767	0.91 (0.80-1.04)	0.180
Gender				
M *vs*. F	0.91 (0.62-1.32)	0.611	1.09 (0.76-1.59)	0.631
ECOG				
1 *vs*. 0	1.09 (0.78-1.54)	0.838	1.53 (1.11-2.12)	0.003
2 *vs*. 0	0.95 (0.48-1.89)		2.42 (1.27-4.59)	
Cytokines				
Yes *vs*. No	1.26 (0.91-1.75)	0.169	1.41 (1.03-1.94)	0.033
Histology				
Papillary *vs*. Clear cell	1.35 (0.81-2.24)	0.478	1.42 (0.86-2.35)	0.285
Other *vs*. Clear cell	1.19 (0.60-2.39)		1.38 (0.69-2.74)	
Nephrectomy				
Yes *vs*. No	0.59 (0.35-0.98)	0.041	0.40 (0.24-0.67)	0.001
Motzer				
Intermediate *vs*. Low risk	2.15 (1.44-3.21)	<0.001	-	-
High *vs*. Low risk	7.23 (4.42 ;11.83)		-	
Therapeutic choice				
Other option *vs*. Sorafenib + Sunitinib	0.84 (0.55-1.29)	0.388	0.85 (0.56-1.30)	0.675
Sunitinib + Sorafenib *vs*. Sorafenib + Sunitinib	0.70 (0.40-1.23)		0.85 (0.49-1.47)	

from the epithelium of Bellini ducts in the distal tubule and preferentially occurring in young populations, no standard effective therapy has been established to date. Indeed, results of previous clinical experiences with chemo- or immunotherapy have been disappointing. Documented efficacy in seven cases of CDC treated with targeted therapies is reported here. *Patients and Methods:* From December 2004 to May 2010, 333 patients with advanced RCC were treated with targeted therapies at the Istituto Nazionale Tumori of Milan. From the global database analysis, seven cases with histological subtype of CDC were identified. All patients had advanced disease and received a targeted therapy as first-line treatment. Six of them had undergone previous nephrectomy, all had nodal involvement and three had two or more sites of disease including lung, liver and adrenal glands. Four patients received sorafenib as first-line treatment: two sunitinib, and one temsirolimus. After failure with sorafenib, two patients received a second-line treatment consisting of both sunitinib and temsirolimus. *Results:* Five patients developed early progression of disease, with a very short four-month survival. One patient had a long-term partial response of 33 months with sorafenib additionally controlled, at progression, with sunitinib for another six months. The last patient reached a progression-free survival of six months with temsirolimus; when progression occurred, tumor shrinkage and a disease control for further six months was achieved during sunitinib therapy. These last two patients were alive after 50 and 12 months of the treatment, respectively. The most common adverse events, low or moderate in severity, consisted of fatigue, hand-foot skin reaction, diarrhea, hypertension and anemia. *Conclusion:* This retrospective analysis has limited value and does not support any conclusion. However, it discloses the likelihood of a role of targeted therapies for advanced CDC. Prospective trials are warranted.

41

AESTHETIC NEO-GLANS RECONSTRUCTION FOLLOWING PENIS-SPARING SURGERY FOR BENIGN, PREMALIGNANT OR MALIGNANT PENILE LESIONS

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Aim: To describe the technique and results of penis-sparing surgery combined with a cosmetic neo-glans reconstruction for benign, premalignant or malignant penile lesions. *Patients and Methods:* Twenty-one patients (mean age 61 years) with penile lesions of broad-spectrum histopathology underwent organ-sparing surgery with neo-glans reconstruction using a

free split-thickness skin graft (STSG) harvested from the thigh. Three patients were treated by glans-skinning and glans-resurfacing, ten patients by glansectomy and neo-glans reconstruction, four patients by partial penectomy and a neo-glans reconstruction, and four patients by neo-glans reconstruction after a traditional partial penectomy. *Results:* The mean follow-up was 45 months. All patients were free of primary local disease. All patients were satisfied with the postoperative phallic appearance and recovered their sexual ability, although sensitivity was reduced as a consequence of glans/penile amputation. *Conclusion:* In benign, pre-malignant or malignant penile lesions, penis-sparing surgery combined with a cosmetic neo-glans reconstruction may ensure a normally appearing and functional penis, without jeopardizing cancer control.

42

RESEARCH AND EVALUATION OF NEW MARKERS IN RENAL CELL CARCINOMA

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Background: Renal cell carcinoma (RCC), the most common malignancy of the adult kidney, accounts for approximately 3% of all malignancies. The incidence of RCC is increasing worldwide and more than 40% of patients with RCC die from their cancer. The discovery of disease markers by gene and protein expression profiling through DNA microarray and proteomics promises to deliver novel solutions for diagnosis, monitoring and therapeutics. *Aim:* The aim of this study was to identify new potential RCC protein markers by comparative proteomic approach for clinical applications. *Patients and Methods:* RCC samples (5-10 mg) obtained during radical nephrectomy and similarly sized samples from normal tissues were used. Pre-operatively, the patients also provided both urine and blood samples. Following extraction, proteins were solubilized and separated by 2-DE electrophoresis, as previously described (1). Afterwards, 2-DE maps of tumoral tissues were compared with normal tissue reference images and differential proteins were identified. Identifications were carried after in-gel proteolysis of the electrophoretic spots by MALDI-TOF analysis and peptide mass fingerprint. The study was approved by our Institution Ethical Committee. *Results:* All patients studied had renal cell cancer at histological examination. The comparison of protein patterns from healthy and carcinoma tissues showed a significantly modified level in carcinoma tissues of 15 proteins. The differentially expressed proteins identified were classified into different groups depending on their cellular compartment localization and their molecular function. Most of them (59%) were cytoplasmic proteins and mitochondrial proteins (18%), and 24% of them were cytoskeleton proteins, proteins of nucleus, secreted and endoplasmic reticulum proteins. The proteins that were most expressed in cancer tissue were reticulocalbin-1 and alpha-enolase. *Conclusion:* Using a minimal amount of tissue from RCC patients and proteome analysis, we identified differentially expressed proteins. Future studies will include the analysis of sera from cancer patients and healthy individuals to verify if the two studied proteins most expressed in cancer tissues elicit the production of auto-antibodies with diagnostic value.

1 Barbero G, Carta F, Giribaldi G, Mandili G, Crobu S, Ceruti C, Fontana D, Destefanis P and Turrini F: Protein/RNA coextraction and small two-dimensional polyacrylamide gel electrophoresis for proteomic/gene expression analysis of renal cancer biopsies. Anal Biochem *349*: 62-71, 2006.

43

LEFT KIDNEY REVASCULARIZATION BY SURGICAL INTRAHEPATIC VENA CAVA AND LEFT RENAL VEIN PATCH SHUNT IN RIGHT RADICAL NEPHRECTOMY PLUS EXTENDED CAVAL AND CONTROLATERAL RENAL VEIN THROMBECTOMY

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Background and Aim: Renal cancer with a thrombosis in the vena cava and fully extending into the controlateral renal vein is very rare. We describe the surgical technique in a 78-year-old male patient with a right kidney mass and a tumor thrombus extending from the bilateral iliac vein into the inferior vena cava (IVC) with complete thrombosis of the left renal vein. *Methods:* An asymptomatic 78-year-old male had a diagnosis of objective abdominal mass. A computed tomography scan showed right renal mass with extended thrombosis in IVC, iliac veins and controlateral renal vein. The patient underwent a urovascular approach with a double team. The tumor was approached through a median abdominal incision; laparotomy ruled out local metastasis. An incision in the root of the mesentery and Kocker maneuver allowed for

dissection of the aorta, hilum of the kidneys and the intra-hepatic VC with hepatic rotation. This maneuver exposed the right kidney, gonodal veins, ureter, IVC, left renal vein and the aorta. The right renal artery was ligated and cut in the cava-aortic space. The left renal vein was completely prepared from the IVC through the kidney. The hepatic vascular support was also clamped. We then proceeded with incision of the IVC until the iliac bifurcation and radical nephrectomy was then performed, and the extended cavo-iliac thrombus was removed. At this time, the blood flow from the iliac venal system appeared to be low and the IVC was tied at 5 cm above the iliac bifurcation. The operation was completed by incision of the left renal vein, removing the thrombus with high power flow from kidney. The vascularization of the kidney was performed by shunt through the intra-hepatic cavo-renail vein patch. *Results:* The total operation time was 3.5 hours, blood loss was 700 cc, requiring two transfusion units. There were no postoperative complications and the patient was discharged ten days after this major surgery. Pathology reported renal clear cell carcinoma, stage pt3c N0M0. Fuhram nuclear grade IV. One-year follow-up showed the patient to be of excellent health and metastasis free. *Conclusion:* The multidisciplinary approach in this case was the best treatment for the patient considering the clinical benefit and good prognosis for the clinical outcome.

44

SURGICAL TREATMENT OF RENAL CELL CARCINOMA WITH VENOUS TUMOR THROMBUS: COMPLICATIONS AND LONG-TERM SURVIVAL

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Background: Renal cell carcinoma is characterized by a marked tropism of the venous system. Involvement oftherenal vein and inferior vena cava occurs in 23% and 7% of cases, respectively. We present our experience with patients affected by clear cell renal carcinoma with tumor thrombosis treated at our department. *Patients and Methods:* From January 2004 to December 2010, 253 patients underwent radical nephrectomy. Twenty patients (8.5%) had a diagnosis of venous tumor thrombosis. The mean patient age was 68 (range 53-97) years. Nine patients had a renal vein thrombosis, nine had an inferior vena cava tumor thrombus below the diaphragm and two patients had an intrathoracic vena cava tumor thrombosis. We evaluated the pre-, intra- and postoperative complications and cancer-specific survival. *Results:* The man tumor size was 8.7 (range 4.5 to 26) cm and the length of the tumor thrombus was 7.6 (range 2.4 to 40) cm. Six patients (30%) had metastases at diagnosis: four patients had lung metastases, one patient had pleural metastases and one patient had skin metastases. In nine patients (45%), co-morbidities were present (diabetes, hypertension, chronic renal failure) at diagnosis. Eight patients had previously undergone abdominal surgery. Cancer-related symptoms were diagnosed in seven patients (hematuria in four patients, pain in one, palpable mass in one, severe fatigue and weight loss in one patient). The mean operative time was 174 (range 90 to 255) minutes, with a mean vena cava clamping time of 9 (range 7-18) minutes.The mean hospital stay was 11 (range 5-33) days. Estimated intraoperative blood loss was 1280 (range 200 to 4000) ml, with an average number of 2.6 (range 0-10) blood units infused intraoperatively. The preoperative creatinine level was 1.39 (range 0.56 to 9.3) mg/dl. Serum creatinine at admission was 1.69 (range 1 to 8.5) mg/dl. Six patients (30%) had early complications: acute respiratory failure (three patients), bronchopneumonia (one patient), pleural effusion (one patient), hemoperitoneum (one patient) that required surgery. The pathologic stage was as follows: pT3b, 18 patients; pT3c, two patients; G2, three patients; G3, seventeen patients; N1, two patients, N2, one patient. The mean follow-up was 37 (range 2-72) months. The overall cancer-specific survival was 89% at six months after surgery, 77% at 12 months after surgery, and 33% at 48 months after surgery. *Discussion and Conclusion:* Our experience shows that a significant percentage of patients affected by renal cell carcinoma have locally advanced disease. Surgery still remains the therapy of choice. Surgical treatment of both renal and vena caval tumor thrombus remains a major procedure, with a high risk of complications. However, surgery can improve the quality of life and prolong survival by making adjuvant therapies more effective.

1 Pouliot F, Shuch B, Larochelle JC, Pantuck A and Belldegrun AS: Contemporary management of renal tumors with venous tumor thrombus. J Urol *184(3)*: 833-841, 2010.
2 Boorjian SA and Blute ML: Surgery for vena caval tumor extension in renal cancer. Curr Opin Urol *19(5)*: 473-477, 2009.
3 Karnes RJ and Blute ML: Surgery insight: management of renal cell carcinoma with associated inferior vena cava thrombus. Nat Clin Pract Urol *5(6)*: 329-339, 2008.

45

IRREVERSIBLE ELECTROPORATION, A NOVEL TECHNIQUE FOR FOCAL ABLATION OF PROSTATE CANCER: RESULTS OF AN INTERIM PILOT SAFETY STUDY IN LOW-RISK PATIENTS

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Background and Aim: Irreversible electroporation (IRE) is a new non-thermal ablation modality that uses short pulses of direct electric current to create irreversible pores in the cell membrane, thus, causing cell death. The primary objective of the study was to test the procedural and short-term safety of the device to ablate localized microfocal, low-grade prostate cancer (PCa). A secondary objective was to evaluate the effectiveness of the treatment and its impact on quality of life of our patients. *Patients and Methods:* Eleven patients with PCa were enrolled after Ministry of Health, Ethical Committee approval and each patient gave informed consent. The mean age was 70.2 (range 60-78) years. Eligibility criteria: unilateral PCa on template perineal guided biopsies (1.37 cores per cc), PSA <10 ng/ml, Gleason score <7, stage cT1c/T2a. Mean pre-operative PSA was 6.43 (range 2.7-9.75) ng/ml, mean prostate volume on TRUS was 62.3 (range 33-120) cc. The mean number of cores biopsies was 85.4.The pre-operative continence rate was 100%. The mean pre-operative I-PSS was 9.54 (range 0-23). The mean pre-operative IIEF was 16.18 (range 14-24). Stage: cT1c=10 and cT2a=1. The procedure was performed under general anesthesia using the brachytherapy grid to reach the same area where PCa was detected at biopsy. The mean number of needles used to treat the tumor area was 6.3 (range 4-10). Mean treatment time was 7.8 (range 2-18) min. *Results:* All the patients were evaluated for toxicity and response. No major complications occurred during the procedure. Hospital stay was one day for all the patients. Patients were examined after 14, 30. 90 and 180 and 525 days (19.2 months) from IRE with PE, PSA, I-PSS and IIEF. Prostate biopsy of the treated area was performed after one month using local anesthesia. The mean number of biopsies taken was 24.72 (range 15-41). No major complications were observed after 14, 30. 90. 180 days and 19 months. A total of 1/11 patients (9%) had acute urinary retention and 3/11 patients (27%) had transient urge incontinence. The mean PSA after 30-90. 180 days and 19.2 months went down to 3.5, 2.9, 3.3 and 3.12 ng/ml respectively. The continence rate was 100%. I-PSS was reduced to 7.72, 7, 6.12, 4.28 and 4, respectively, while IIEF was 13.18, 10.45, 10.5, 11 and 17.3 months. The pathological report after 30 days was negative in 8/11 patients (73%). Coagulative necrosis, granulomatosis, fibrosis and hemosiderosis were commonly reported. Persistent adenocarcinoma was present in 3/11 patients (27%) (1, 1 and 2 foci), respectively. One patient received radical prostatectomy, one was re-treated and one is awaiting re-treatment. *Conclusion:* IRE is a safe procedure for focal therapy in localized low-risk PCa. It is relatively simple, minimally invasive and effective. Further larger studies with longer follow-up are needed to confirm these preliminary results.

46

THE SIGNIFICANCE OF PROSTATE VOLUME TO BIOPSY CORE SAMPLE RATIO ON CANCER DETECTION RATE

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Background: There has been extensive debate in the literature regarding the impact of prostate volume on the subsequent cancer detection rate. Similarly, much debate concerns the optimum number of biopsy cores necessary to maximize the cancer detection rate. This study investigates the ratio of prostate volume to the number of biopsy cores as a means of determining the optimal sampling volume to optimize the cancer detection rate. *Patients and Methods:* A retrospective review of a prospectively registered prostate biopsy database identified 1,678 consecutive patients undergoing prostate biopsy from January 2005 to January 2011. Of these patients, 480 (28.6%) were affected by cancer. We eliminated all patients showing high-grade PIN (HGPIN) and atypical small acinar proliferation (ASAP). Prostate volume to biopsy core ratios (volume/number of cores) was calculated and a comparative analysis was performed to determine its impact on the cancer detection rate. *Results:* The mean prostate volume was significantly smaller for those patients diagnosed with prostate cancer compared to those with negative biopsies (38.3 g *vs*. 50.7 g, $p<0.001$). The median number of core biopsies was the same for both groups of patients (median 12, $p=0.66$). The ratio of TRUS volume to number of cores differed significantly between the two cohorts of patients. The median TRUS/core volume ratio was 3.5 (IQR 2.5) for patients with identified cancer as compared to 4.7 (IQR 3.9) for those with negative biopsies ($p<0.001$). On multivariate logistic regression analysis, the TRUS/core ratio significantly impacted the cancer detection rate with a relative risk ratio of 1.29% (95% CI=1.1-1.5, $p=0.001$) even if adjusted for age, prostate volume, DRE and PSA. *Conclusion:* Prostate cancer detection can be enhanced by individualizing the number of cores to real-time prostate volume sampling. Our study demonstrates that optimal cancer detection rates were observed when a ratio of 3.5 g per tissue core was achieved. Proper prospectively designed studies must be performed to further validate our findings.

47

PREDICTIVE VALUE OF THE 2007 CHUN NOMOGRAM IN DIAGNOSING PROSTATIC CANCER AT REBIOPSY: THE VILLA TIBERIA CLINICAL EXPERIENCE FROM 2007 TO 2010

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Background: The aim of this study was to evaluate the use of Chun's nomogram in clinical practice as a predictive tool for prostatic cancer diagnosis at the time of re-biopsy. The feasibility of this nomogram might reduce the number of patients that are overtreated and might assist physicians in the decision-making process. *Patients and Methods:* From January 2007 to December 2010, 870 patients underwent ultrasound-guided prostatic biopsy. The method involves the use of at least 24 cores (range: 24-31) according to a pattern of at least 12 cores on both the peripherical zone and the transitional zone. Predictors of prostate cancer on repeat biopsy were patient age, digital rectal examination, prostate-specific antigen, percentage free prostate-specific antigen, number of previous negative biopsy sessions and sampling density (prostate volume/ numbers of cores). Mean age was 62.5 (range 47-78) years, mean PSA was 5 (range: 0.9-9.1) ng/ml and mean free PSA was 2.3 (range: 0.2-4.4) ng/ml. Previous negative biopsy sessions were three to five in 16% of patients, more than five sessions in 5% of patients and two sessions in 41% of patients; the remaining 38% of patients underwent only one biopsy. The mean sampling density was 2.05 (range: 1.1-2.99). Among all patients, 261 (30%) underwent positive digital rectal examination. *Results:* On histological analysis, 278 (32%) patients had prostate cancer. On multivariate analyses, all predictors were statistically significant ($p \leq 0.026$). After internal validation, the nomogram was fond to be 76.8% accurate. *Conclusion:* Chun's nomogram seems to be an accurate model in predicting the outcome of repeat prostate biopsy.

48

URACYST ENHANCES THE ANTITUMOR ACTIVITY OF DRUGS IN BLADDER CANCER CELLS

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Background: Non-muscle-invasive bladder cancer is the most common type of bladder cancer in Western nations. There are multiple risk factors for non muscle-invasive bladder cancer, which include exposure to tobacco and industrial chemicals, ingestion of arsenic-laced water, radiation therapy to organs adjacent to the bladder, therapeutic use of alkylating agents in chemotherapy regimens and infection with the trematode *Schistosoma haematobium*. The glycosaminoglycan layer at the bladder surface non-specifically blocks the adherence of bacteria, ions and molecules to the epithelium. It may be an important element in the first-line defence against infection, calculi and even carcinogens for the transitional cells of the bladder. Qualitative or quantitative defects in the glycosaminoglycan(s) (1) present may influence an individual's susceptibility to the development of bladder tumors. Approximately 80% of patients with transitional bladder cell carcinomas can be successfully treated with local endoscopic resection, although a significant number of these patients suffer recurrence with or without progression to invasive disease. Currently, there are few options other than cystectomy for the management of non muscle-invasive bladder cancer with intravesical chemotherapy using several drugs such as gemcitabine (GEM), mitomycin-C (MMC) and doxorubicin (DOX) (2). *Aim:* In this study, we investigated the effects of Uracyst (chondroitin sulphate) (3) on growth inhibition of the human bladder cancer cell lines J82, HT-1376 and MCR, and effects of the combination of GEM, MMC and DOX with Uracyst on the antitumor activity of drugs *in vitro*. *Materials and Methods:*Analysis of cell proliferation, as measured by MTT assay, and the drug combination studies were carried out by CalcuSyn software (4). *Results:* It was found that 72 h exposure of Uracyst , MMC, DOX and GEM induced approximately 50% of growth inhibition in human bladder J82, HT-1376 and MCR cancer cells. The data suggest that the three cell lines are sensitive to different extents to the treatments with drugs and that MCR cells were less sensitive as compared to the other two cell lines. On the basis of the obtained results, we hypothesize that Uracyst might potentiate the antitumor activity of MMC, DOX, and GEM. In detail, we evaluated the growth inhibition induced in bladder cancer cell line HT-1376 by 72 h exposure to different concentrations of Uracyst in combination with MMC, DOX, and GEM, respectively. We observed synergism when cells were treated with Uracyst in combination with MMC and GEM, respectively. In contrast, antagonism was observed when cells were treated with Uracyst and DOX. *Discussion and Conclusion:* In the human bladder cancer cell line HT-1376, pharmacologic combination of Uracyst with GEM and MMC, respectively, resulted in a strong synergism of growth inhibition. Such c ombinations may be able to overcome the multidrug resistance of bladder cancer. Therefore, these data encourage the investigation of the combined use of Uracyst with GEM and MMC in the treatment of human bladder cancer.

1 Bodenstab W, Kaufman J and Parsons CL: Inactivation of antiadherence effect of bladder surface glycosaminoglycan by a complete urinary carcinogen (*N*-methyl-*N*-nitrosourea). J Urol *129(1)*: 200-201, 1983.
2 Di Stasi SM, Dutto L and Verri C: Electromotive Drug Administration® (EMDA) intravescicale con Mitomicina-C nel trattamento dei tumori della vescica non-infiltranti la muscolare. Urologia *75(4)*: 214-220, 2008.
3 Hurst RE: Exogenous glycosaminoglycans coat damaged bladder surfaces in experimentally damaged mouse bladder. BMC Urology *5*: 4, 2005.
4 Chou J and Chou TC: Manual and Software. Biosoft, Cambridge, UK, 1987.

49

PREDICTIVE VALUE OF PARTIN'S NOMOGRAM IN DIAGNOSING PROSTATIC CANCER AT BIOPSY: THE VILLA TIBERIA CLINICAL EXPERIENCE FROM 2007 TO 2010

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Aim: To evaluate the use of Partin's nomogram in clinical practice as a predictive tool for prostatic cancer diagnosis at the time of biopsy in order to select the most appropriate therapy. *Patients and Methods:* Between January 2007 and December 2010, 485 patients with a histological diagnosis of prostate cancer were subjected to a surgical procedure after having undergone extended prostate biopsy. Patients were then subjected to a retrograde retropubic radical prostatectomy and also bilateral iliac-obturator lymphadenectomy when presenting with Gleason score >8 and PSA >10 ng/ml. In order to evaluate the prediction, the Partin table was applied to this group of patients, taking into account their pre-operative PSA, Gleason biopsy and clinical staging. The percentages of organ-confined disease (MOC), extra-capsular extension (EEC), seminal vesicle invasion (IVS) and lymph node invasion (IL) as given by the Partin table were compared with that observed postoperatively. *Results:* The observed postoperative MOC was 66%, EEC was 23%, IVS 0.9% and IL 2%. Partin tables gave 71% correct predictions for MOC, 59% for EEC and 78% and 75% for IVS and LN, respectively. *Conclusion:* In our experience, the Partin tables showed a low predictive value that does not allow their use in clinical practice for selecting the best treatment option.

50

ONE-STOP HEMATURIA CLINIC: FIRST EXPERIENCE IN ITALY WITH 100 CASES

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Background: Starting from a UK one-stop clinic experience, we decided to verify the feasibility and the advantages of this diagnostic pathway now established in an Italian hospital. We analyzed the outcomes in detecting transitional cell carcinoma (TCC) and other malignant and non-malignant conditions. *Patients and Methods:* Between April 2010 and December 2010, 100 patients presenting with hematuria were referred to our Institution's One-Stop Hematuria Clinic. Each patient underwent a urinary tract ultrasound and a cystoscopy, with a CT IVP in selected patients. If a TCC of the bladder was diagnosed, the patient underwent TUR-BT. In other cases (stones, BPH *etc*.) the appropriate therapeutic pathway was followed. *Results:* Bladder cancer was diagnosed in 25% of patients; 17% had a urinary stone (2% in the bladder); 2% had prostate cancer; 1% had a renal cell carcinoma. The mean age was 69.8 years. G3 disease was diagnosed in 6% of the patients (24% of patients with TCC of the bladder). The mean time from the day of the entry into the one-stop clinic to day of operation in cases of TCC of the bladder was 10.48 days. *Discussion and Conclusion:* The Italian experience of the one-stop clinic confirms a high rate of bladder cancer detection. Furthermore, a high rate of non-malignant conditions were detected, thus underling the importance of the one-stop clinic not only as a cancer clinic but as a complete general urological clinic. We report a shorter waiting time for operation, especially for TCC G3 patients.

51

PROSTATE CANCER ANGIOGENESIS: A PRELIMINARY EXPERIENCE WITH 64-ROW MULTIDETECTOR CT PERFUSION – DO QUANTITATIVE MEASUREMENTS DISTINGUISH TUMOR?

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Aim: To prospectively test the relationships in prostate cancer between quantitative computed tomography (CT) perfusion parameters and immunohistochemical microvascular density (MVD), considered a gold standard marker of angiogenesis. *Patients and Methods:* The study protocol conformed to the guidelines of the Declaration of Helsinki and each patient provided written consent in accordance with the requirements of our Institutional Review Board. Between July 2009 and April 2010, 21 consecutive men (mean age 59.7 years; age range 48-71 years) were enrolled. All patients were examined with 64 MDCT scanner for dynamic CT perfusion imaging, before prostatectomy surgery. Perfusion data-sets were analyzed by the scanner software (Prostate protocol, Perfusion 4.0). Values for each of the four perfusion CT parameters [blood volume (BV), blood flow (BF), meantransit time (MTT), permeability surface-area product (PS) measurements] were recorded and correlated with MVD and mean vascular area (MVA) calculated from macro-sections of corresponding areas. *Results:* ANOVA analysis revealed noticeable significant differences in BV, MTT and PS perfusion parameters ($p<0.01$). Two-tailed Spearman rank correlation analysis gave the highest correlation level between BV and PS measurements of prostate cancer squares (0.618 and 0.614, respectively), while MTT was inversely correlated (−0.475). BV and PS had the highest area under the curve (AUC) value in ROC analysis (0.769 and 0.708). *Discussion and Conclusion:* This complex study design was fitted to investigate if CT is a feasible technique in prostate cancer, and how CT perfusion parameters change on the basis of vascularization of malignant or benign prostate lesions. Results were encouraging and, above all, statistically significant. In particular, we found there were significant differences in mean values of BV, MTT and PS between benign lesions and malignant lesions as confirmed by other authors (1-3). Our results suggest that BV and PS measurements reflect angiogenesis and that perfusion CT with 64-row scanner is a feasible technique for assessing prostate cancer vascularization.

1 Ungersma SE, Pacheco G, Ho C, Yee SF, Ross J, van Bruggen N, Peale FV Jr., Ross S and Carano RA: Vessel imaging with viable tumor analysis for quantification of tumor angiogenesis. Magn Reson Med *63(6)*: 1637-1647, 2010.

2 Petralia G, Preda L, D'Andrea G, Viotti S, Bonello L, De Filippi R and Bellomi M: CT perfusion in solid-body tumors. Part II: technical issues. Radiol Med *2(1)*: 26-37, 2010.

3 Korporaal JG, van den Berg CA, Jeukens CR, Groenendaal G, Moman MR, Luijten P, van Vulpen M and van der Heide UA: Dynamic contrast-enhanced CT for prostate cancer: relationship between image noise, voxel size, and repeatability. Radiology *256(3)*: 976-984, 2010.

52

RADICAL CYSTECTOMY IN OCTOGENARIANS: WHEN AND WHY OUR EXPERIENCE

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Background: Radical cystectomy is considered the gold standard treatment for muscle-invasive bladder cancer (MIBC), although associated with significant morbidity. Therefore, considering the continuous ageing of the population, the treatment of the MIBC in octogenarians is becoming an important and discussed issue in urological practice. We evaluated the oncological and functional results of cystectomy performed in octogenarians. *Patients and Methods:* We retrospectively evaluated all the cystectomies performed in our Urological Center between June 2007 and June 2010. We enrolled 27 patients (9 female and 18 male), all over 80 years old. All the patients underwent staging transurethral bladder resection (TURB) (histological specimen: muscle-invasive urothelial carcinoma). The patients were divided into two groups: patients in group A (16 patients) had multiple urothelial bladder relapses, pT1/Ta high-grade, non-responsive to endovesical therapy; and patients in group B (11 patients) had their first bladder cancer diagnosis. Work-up before the cystectomy: urography CT for evaluation of the upper urinary tract. The patients underwent radical transperitoneal cystectomy, with 24 ureterocuteneostomy (UCS) and 3 Bricker ileal conduits. The pre-anesthetic risk was quantified using the American Society of Anesthesiologists score (ASA). Mean follow-up was 23.7±9.4 months. At follow-up, we performed an oncological and functional evaluation, with particular attention to postoperative surgical complications and the quality of life before and after TURB and cystectomy (using the EORTC QLQ C-30 questionnaire). *Results:* The mean age was 83.1±4.7 years (group A 83.5±5.75 years, group B 83.3±3.44). There were no significant differences in ASA score (score IV in three patients in group A and five patients I group B). In group A, there were 14 UCS and 2 ileal conduits: median surgical time was 175.5±25.7 min. In group B, 10 UCS and1 ileal conduit procedures were performed, and the median surgical time was 159.5±11.6 min. In group A, the time from the first bladder relapse (pT1/Ta high grade) to the cystectomy was 22.75±5.1 months, with over five TURB before the radical cystectomy. The final histological examination showed: group A: 12 patients with pT2b stage and 4 with ≥pT3 stage bladder cancer; group B: 5 patients with pT2b and 6 with ≥pT3 stage. Evaluation of the complications: there were no significant differences between the two groups in regard to non perioperative mortality. In group A, two patients had pulmonary embolism and four had symptomatic urinary

infections, while in group B, two patients had pneumonia and two had urinary infections. All patients had anemia: blood transfusion (hemoglobin <10 μg%) for 14 group A patients and for 7 group B patients. Before the cystectomy, blood transfusions of 8.1±14.7 units (1 unit=250 ml were given for group A, and of 3. 0±2.1 units for group B. After the cystectomy, 11.6±16.5 and 4.2±1.9 units of blood were transfused for patients in groups A and B, respectively. At mean follow-up: five patients had died in group A (31.25%) and three in group B (27.2%). After three months from cystectomy, there was a significant improvement of the quality of life. *Discussion and Conclusion:* Our results, although limited by the small patient population, show that radical cystectomy in octogenarians is associated with acceptable complications. Comparing the results from the two patient groups, we believe that delaying cystectomy can lead to a high risk of progression of bladder cancer (from pT1/Ta to muscle-invasive bladder cancer) and more surgical complications (we suppose that these patients have a catabolic situation leading to continuous relapse and chronic anemia with need for more blood transfusions). Finally, it should be considered that after cystectomy, the quality of life of the patients improves.

1 De Nunzio C, Cicione A *et al*: Extraperitoneal radical cystectomy and ureterocutaneostomy in octogenarians. Int Urol Neprol, Nov 26, 2010 Nov 26. [Epub ahead of print].
2 Tilki D, Zaak D, Trottmann M *et al*: Radical cytsetcomy in the elderly patient: a contemporary comparison of perioperative complication in a single institution series. World J Urol *28*: 445-450. 2010.
3 Farnham SB, Cookson MS, Alberts G, Smith JA Jr. and Chang SS: Benefit of radical cystectomy in the elderly patient with significant co-morbidities. Urol Oncol *22(3)*: 178-181, 2004.

53
A WELL-KNOWN LESION IN AN UNUSUAL LOCATION: GUM METASTASIS FROM PROSTATE CANCER

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We describe a rare case of prostatic cancer gum metastasis in a 69-year-old patient observed in a gum biopsy for a suspected alveolar abscess. The patient, who had undergone a right colectomy for adenocarcinoma three years previously, had an excisional biopsy of the gum for a solid ulcerated lesion, approximately 3 cm in diameter, in the left upper jaw, suspected to be alveolar abscess. Biopsy gave a diagnosis of metastatic adenocarcinoma. Pathologists treated the sample with hematoxylin-eosin and with immunohistochemical staining for cytokeratin pool, cytokeratin 7, cytokeratin 20 and PSA, suspecting prostate cancer metastasis, ruling out origin from the previous colon cancer. The patient was then referred to the Urological Department for a check-up, at which time a rectal examination showed the prostate to be increased in size and texture, with suspicious nodules along the right margin. The PSA value was 624 ng/ml. A prostate biopsy and a bone scintiscan were proposed, but the patient refused biopsy. The bone scintiscan showed the involvement of both the axial (left jaw, D3, D11, D12, L3, L5 and gill right pelvic bone) and of the appendicular skeleton (proximal epiphysis of left femur, proximal epiphysis of left humerus, proximal epiphysis of left femoral). Whole-body CT showed loss of 3 cm of the left maxillary sinus and lymph node swelling at the root of the right mesenteric artery. Once the presence of prostate cancer metastasis to bone and gum was confirmed, BAT hormone therapy was started. At the three month follow-up, the PSA level had dropped to 152 ng/ml. The patient is currently waiting to start treatment with zolendronic acid. Generally, metastases of prostate cancer are localized to the short and flat bones and rarely involve the soft tissues. At present in the literature, to our knowledge, only two cases of metastasis of prostate cancer to gum are described.

1 Shepherd SM and Lyon WK: Gingival bleeding: initial presentation of prostatic cancer. J Fam Pract *30(1)*: 98-100. 1990.
2 Piattelli A, Fioroni M and Rubini C: Gingival metastasis from a prostate adenocarcinoma: report of a case. J Periodontol *70(4)*: 441-444, 1999.
3 Chossegros C, Blanc JL, Cheynet F, Bataille JF and Tessier H: Metastatic localization in the buccal cavity. Case report and literature review. Rev Stomatol Chir Maxillofac *92(3)*: 160-164, 1991.

54
IDENTIFICATION OF PHOSPORYLATED PROTEINS IN URINE FROM BLADDER CANCER PATIENTS

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Background: As recently shown, urine and tissue specimens from patients affected by transitional cell bladder carcinoma (TCC) have high levels of proteins with phosphorylated tyrosine. Quantitative measurement of the level of tyrosine-phosphorylated proteins in urine have been shown to be very effective in discriminating between healthy individuals and these with cancer and is therefore under evaluation as a marker for urinary bladder cancer (1). Nevertheless, the identification of these proteins in urine is extremely complex due to their very minimal amount. We present the preliminary results of urinary phosphoprotein characterization. *Patients and Methods:* The study was approved by the Institution Ethical Committee. Urine samples (100 ml) were obtained from TCC patients and healthy volunteers. Phosphoproteins were enriched by the Cu-IMAC procedure, solubilized, separated by 1-D electrophoresis, and analyzed by anti-phosphotyrosine Western blot as recently described (1). Afterwards, 1-DE Western blot of urine samples from TCC patients were compared with those from urine samples from healthy individual. Differentially tyrosine-phosphorylated proteins were identified by MALDI-TOF analysis and peptide mass fingerprint after in-gel proteolysis of the electrophoretic bands. *Results:* Fifty urine samples from TCC cancer patients at histological examination and 50 urine samples from healthy individuals were analyzed by MALDI-TOF. It was shown that 26 proteins were more tyrosine-phosphorylated in TCC patients in comparison with healthy individuals. The identified differentially phosphorylated proteins were classified into different groups depending on their cellular compartment localization and their molecular function. Most of them (52%) were secreted proteins and cytoskeleton proteins (26%). The remaining 22% were cytoplasmic proteins, proteins of perinuclear region, cell membrane and endoplasmic reticulum proteins. It was seen that seven proteins were more differentially phosphorylated: glyceraldehyde-3-phosphate dehydrogenase, uromodulin precursor, apolipoprotein A-I, fibrinogen beta chain, alpha-1-antitrypsin, ceruloplasmin precursor and serotransferrin. *Discussion and Conclusion:* Using a Cu-IMAC enrichment procedure and MALDI-TOF analysis, we identified some new potential phosphotyrosine protein markers in the urine of TCC patients. The diagnostic and prognostic meaning of these identified proteins will be evaluated using a phosphoprotein-specific antibody chip, one of the ultimate goals for routine application of proteomics in the clinical setting.

1 Khadjavi A, Barbero G, Destefanis P, Mandili G, Giribaldi G, Mannu F, Pantaleo A, Ceruti C, Bosio A, Rolle L, Turrini F and Fontana D: Evidence of abnormal tyrosine-phosphorylated proteins in the urine of patients with bladder cancer: the road toward a new diagnostic tool? J Urol *185(5)*: 1922-1929, 2011.

55

CAN WE PREDICT BENIGN HISTOLOGY IN RENAL MASSES OF 4 CM OR LESS?

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Aim: To investigate whether clinical features are able to predict a benign histology in patients with small renal masses ≤4 cm. *Patients and Methods:* The study included 548 consecutive patients with unilateral, sporadic, non-metastatic renal mass with a diameter ≤4 cm, treated with radical or partial nephrectomy between 1990 and 2010. The relationship between clinicopathological features and the probability of detecting a benign histology was tested in univariate and multivariate logistic regression models. Clinical variables included age, gender, tumor size, symptomatology and BMI (≤25 *vs.* >25). *Results:* The study included 379 men and 169 women, with a median age of 62 years. Median tumor dimension was 3.1 cm. There were 130 renal masses up to 2 cm in size, 194 were between 2.1 and 3 cm, and 224 between 3.1 and 4 cm. Benign lesions, chromophobe, papillary or clear cell renal cell carcinoma accounted for 11.9%, 5.1%, 12.3% and 71.5% of cases, respectively. Women were more likely to have a benign histology (16.3% *vs.* 7%; $p<0.001$). The incidence of benign histology in cases of renal mass up to 2 cm, between 2.1 and 3 cm, and between 3.1 and 4 cm was 6%, 10% and 19%, respectively. At multivariate logistic regression analysis, female gender ($p=0.001$; HR 2.6) and tumor size ($p=0.007$) achieved the independent predictor status of benign histology, after adjusting for age, symptomatology and BMI. Specifically, renal masses between 2.1 and 3 cm, and up to 2 cm had 3-fold and 1.9-fold increased probability of having benign histology, with respect to renal masses between 3.1 and 4 cm, respectively. *Conclusion:* Female gender and tumor size are independent predictors of benign histology in patients with small renal masses ≤4 cm. No other clinical features are useful in predicting the benign or malignant pathology of these small masses. These findings seem to further support the need for needle biopsy in their evaluation.

56

CHARLSON CO-MORBIDITY INDEX PREDICTS OVERALL MORTALITY IN PATIENTS TREATED WITH SURGERY FOR RENAL CELL CARCINOMA

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Aim: To evaluate the Charlson co-morbidity index (CI) as a predictor of overall mortality (OM) in patients treated with partial or radical nephrectomy for renal cell carcinoma (RCC). *Patients and Methods:* We retrospectively analyzed data from 1,437 consecutive patients who underwent radical nephrectomy or nephron-sparing surgery for RCC between 1987 and June 2009. Univariate and multivariate Cox regression analyses were used to determine the effect of available predictors on OM. Covariates consisted of age, 2009 T stage, nodal status, presence of distant metastases, Fuhrman grade and CI. *Results:* Mean follow-up was 63 months (2-276). Mean age was 64 years (18- 90). CI was grouped into three categories: 0 (n=692) *vs*. 1-2 (n=575) *vs*. ≥3 (n=170). Five-year survival was 78%, 71% and 58%, respectively (log-rank $p>0.001$). At multivariate Cox regression analysis, CI achieved the independent predictor status for OM, after adjusting for age, pT stage, nodal status, presence of distant metastases and Fuhrman grade ($p<0.001$). CI ≥3 was associated with a two-fold higher risk of OM compared to mortality in those with no co-morbidity, and CI of 1-2 was associated with a 1.4-fold higher risk. We further tested CI in patients with venous tumor thrombosis (n=194). Patients with CI of 0. 1-2 and ≥3 had a median survival of 29, 24 and 6 months, respectively ($p=0.035$). At multivariate analysis, after adjusting for nodal status and presence of distant metastases, CI confirmed its independent predictor status for OM. Patients with CI ≥3 had a three-fold higher risk of OM. *Conclusion:* CI allows better risk stratification in patients undergoing surgery for RCC. Specifically, in patients with venous tumor thrombus, who should be submitted to challenging procedures, CI may help therapeutic decision making. Patients with CI ≥3 had a very limited survival and the need for surgical treatment should be accurately evaluated and individualized.

57
DIAGNOSIS OF ISOLATED HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA: PROPOSAL OF A NOMOGRAM FOR THE PREDICTION OF CANCER DETECTION AT SATURATION RE-BIOPSY

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Aim: To evaluate factors that may predict prostate cancer (PCa) detection after initial diagnosis of high-grade prostatic intraepithelial neoplasia (HGPIN) on 6-to 24-core prostatic biopsy. *Patients and Methods:* We retrospectively evaluated 262 patients submitted to prostate re-biopsy (rPBX) after initial HGPIN diagnosis in tertiary academic centres from 1998 to 2007. HGPIN diagnosis was obtained on initial systematic prostate biopsy with 6 to 24 random cores. All patients were re-biopsied with a 'saturation' rPBx with 20-26 cores, with a median time to rPBx of 12 months. All slides were reviewed by expert uropathologists. *Results:* Plurifocal HGPIN (pHGPIN) was found in 115 patients and monofocal HGPIN (mHGPIN) in 147 patients. One hundred and eight and 154 patients were submitted to >12-core initial PBx and ≤12-core, respectively. Overall PCa detection at rPBx was 31.7%. PSA (7.7 *vs*. 6.6 ng/ml; $p=0.031$) and age (68 *vs*. 64 years; $p=0.001$) were significantly higher in patients with PCa at rPBx. PCa detection was significantly higher in patients with a ≤12-core initial biopsy than in those with >12-core (37.6% *vs*. 23.1%; $p=0.01$), and in patients with pHGPIN than in those with mHGPIN (40% *vs*. 25.1%; $p=0.013$). At multivariate analysis, PSA value ($p=0.041$; HR:1.08), age ($p<0.001$; HR:1.09), pHGPIN ($p=0.031$; HR:1.97) and ≤12-core initial biopsy ($p=0.012$; HR:1.95) were independent predictors of PCa detection. A nomogram including these four variables achieved 72% accuracy in predicting PCa detection after an initial HGPIN diagnosis. *Conclusion:* PCa detection on saturation rPBx after initial diagnosis of HGPIN is significantly higher in patients with ≤12-core than those with >12-core initial PBx and in patients with pHGPIN than in those with mHGPIN. We developed a simple prognostic tool for the prediction of PCa detection in patients with initial HGPIN diagnosis, undergoing saturation prostate re-biopsy

58
PADUA SCORE ACCURATELY PREDICTS THE RISK OF COMPLICATION AND ISCHEMIC TIME IN PATIENTS WHO ARE CANDIDATES FOR NEPHRON-SPARING SURGERY

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Aim: To prospectively test the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification in a cohort of patients submitted to open nephron-sparing surgery (NSS) and to correlate the PADUA score to ischemia time. *Patients and Methods:* Between December 2009 and September 2010, 112 consecutive patients were treated with open NSS with the technique of hilar arterial clamping. Tumors were reclassified according to the PADUA classification. Complications were graded according to the modified Clavien system. Univariate and multivariate logistic regression analyses tested the predictive value of PADUA score for overall complication rate and for the ischemic time. *Results:* Sixty-one patients underwent extraperitoneal NSS through a flank incision, while 51 patients underwent a transperitoneal approach. the mean patient age was 61.8±13.3 years. The median tumor diameter was 3.4±1.5 cm. The median PADUA score was 8 (range 6-13). The mean ischemia time was 20±10 min. The overall complication rate was 18.7% (n=21). On Univariate analysis, the PADUA score correlated with complication rate (p=0.027) and with increased ischemia time, considered as a continuous variable as well as categorical one (≤25 min *vs*. <25 min) (p<0.001 and p=0.03, respectively). Complications were classified as modified Clavien grade I, II, IIIa and IVa in 3, 14, 3 and 1 patients, respectively. On multivariate analysis, PADUA score achieved independent predictor status for complication rate, after adjusting for body mass index and surgical approach. Patients with PADUA score 8-9 had a 4-fold increased risk of complication, while patients with PADUA score ≥10 had a 15-fold increased risk compared to those with scores of 6-7 (p=0.013). Moreover, patients with PADUA score ≥10 had a 6-fold increased risk of ischemic time >25 min (p=0.002). *Conclusion:* Our study confirms that PADUA score can be used to reliably predict risk complication and ischemic time in patients treated with NSS, independently from the extra- or transperitoneal approach. PADUA classification can help the selection of patients who may benefit from additional techniques such as hypothermic procedure.

59

IDENTIFYING FACTORS AFFECTING RENAL FUNCTION IN PATIENTS WITH PT1B RENAL CELL CARCINOMA WHO UNDERWENT RADICAL OR PARTIAL NEPHRECTOMY

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Aim: To examine our institutional experience for identifying factors affecting renal function in patients with pT1b renal cell carcinoma (RCC) treated with radical nephrectomy (RN) or partial nephrectomy (PN). *Patients and Methods:* From 1987 to 2007, 257 patients underwent surgery at our institution for pT1b sporadic, localized RCC, with a normal contralateral kidney (RN, n=194; PN=63). Renal function was evaluated by the estimated glomerular filtration rate (eGFR), comparing the variables to investigate the probability of renal function worsening (eGFR <60 ml/min/1.73m^2). The outcome was evaluated and compared with Cox proportional hazards regression models. *Results:* 35.6% of patients who underwent RN had renal function worsening compared to 16% of patients who underwent PN (p=0.006). A multivariate analysis including type of surgery, age, Fuhrman grade, Charlson Index, sex, hypertension, smoking, preoperative eGFR showed significance only for type of surgery (p=0.017) and age (p=0.001). We then stratified the cohort by year of surgery (cut-off: 1997), considering the increasing use of PN in the last decade: after 1997, only type of surgery (p=0.015) and age (p=0.011) were statistically significant, instead of hypertension (p=0.052), smoking (p=0.941) Charlson Index (p=0.495), Fuhrman grade 8 (p=0.384) and preoperative eGFR (p=0.490). The strong significance of age was evident even when stratifying for age quartiles (p<0.001), with a progressive worsening of renal function through the age quartiles. Furthermore, when considering age quartiles and type of surgery, we found a significant impact on renal function only for RN (p=0.001) compared to PN (p=0.462). *Conclusion:* When comparing the variables of a cohort of patients submitted to surgery for pT1b RCC, in identifying risk factors for renal function worsening after surgery, the only significant factor appears to be the age. However, on further analyses, RN is the strongest risk factor: it seems that PN is a protective factor against renal function worsening when performing surgery for pT1b RCC. PN, when technically feasible and oncologically correct, represents an imperative choice for the treatment of pT1b RCC.

60

RENAL CELL CARCINOMA WITH A DIAMETER OF 3 CM OR LESS: FACTORS PREDICTING SYNCHRONOUS OR METACHRONOUS DISTANT METASTASIS

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Aim: To investigate which clinicopathological factors are associated with a higher risk of developing distant metastases in patients with renal cell carcinoma (RCC) of 3 cm of diameter or less. *Patients and Methods:* The study included 266 consecutive patients with unilateral, sporadic RCC with a diameter of 3 cm or less, treated at two Departments, between 1986 and 2007. The relationship between clinicopathological features and the risk of developing distant metastases was tested in univariate and multivariate logistic regression models. *Results:* Histologically, the 266 cases of RCC included 211 clear cell, 33 papillary type I, 7 papillary type II and 14 chromophobe. Pathological T1a stage was found in 253 patients, and pT3a in 13 patients. Fuhrman grade 1-2 was found in 236 patients, and was grade 3-4 in 30. Tumor necrosis was found in 24 patients (9%). Two patients presented nodal invasion. Out of 266 patients, 24 (9%) developed distant metastases, of which 12 were synchronous. Univariate analysis showed that higher Fuhrman grade, presence of tumor necrosis and pathologic stage (pT1a *vs.* pT3a) were significant risk factors for distant metastasis. At multivariate logistic regression analysis, only the presence of tumor necrosis (p=0.027; HR 3.8) and Fuhrman grade (p=0.001; HR 5.5) achieved independent predictor status, after adjusting for pT stage, nodal status, histological subtype and age. *Conclusion:* Metastases develop in a limited percentage of RCC cases with a diameter of 3 cm or less. Higher Fuhrman grade and presence of tumor necrosis are associated with a higher risk of synchronous or metachronous distant metastasis. Patients with such features should be followed up more carefully.

61
ENDOVESICAL THERAPY IN HIGH-RISK NON-MUSCLE-INVASIVE BLADDER CANCER: A NEW CHEMOSENSITIVITY TEST

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Introduction: The treatment choice for high risk non muscle-invasive bladder cancer (NMIBC) is still controversial and no markers are yet available to guide the urologist in the individualization of therapy. Although intravesical chemo- and immunotherapy represent the gold standard in an adjuvant setting after transurethral resection of the bladder (TURB), the percentage of recurrence and progression under treatment is still high. We describe the design of a chemosensitivity assay based on the expression of genes involved in the resistance to standard intravesical regimens. *Patients and Methods:* A total of 64 patients with high-risk NMIBC were enrolled; all were candidates for TURB followed by intravesical treatment. All patients were evaluated by cystoscopy three and six months after TURB. A 1-mg sample of tumoral tissue from each patient was kept for molecular assay and was subjected to RNA extraction and RT-PCR amplification with primers specific for *MRP1, MRP2, hENT1, dCK* and α5β1 integrin in order to delineate the specific (for each patient) chemosensitivity profile to drugs commonly used in intravesical regimens, namely anthracyclines, mitomycin-C, gemcitabine and BCG. On the basis of the densitometric analysis of the amplification bands obtained by normalization with the *GAPDH* internal controls, we obtained a chemosensitivity molecular profile for each patient. The sensitivity to mitomycin-C, epirubicin, and doxorubicin was determined from the ratio *MRP/GAPDH*, with values <1, =1 and >1 corresponding to high, intermediate and low sensitivity, respectively. For gemcitabine resistance, the ratio *hENT-dCK/GAPDH* was considered, with values >1, =1 and <1 corresponding to sensitivity, intermediate sensitivity and resistance, respectively. Sensitivity to BCG was evaluated from the ratio of α5β1/*GAPDH* with values >1, =1 and <1 corresponding to high, intermediate and low sensitivity, respectively. We finally compared the molecular profiles of chemosensitivity to the clinical response to the intravesical regimen adopted in the first six months of follow-up. *Results:* This chemosensitivity test was able to predict response to treatment in 93% of patients. The assay was easy to perform, with low cost and rapid execution time. *Conclusion:* Our results are promising in view of an individualized therapeutic approach, allowing higher treatment success rates, while sparing patients unnecessary toxicity from drugs that are not suited to their tumor.

62
COMBINATION THERAPY OF ETHINYLESTRADIOL AND ESTRAMUSTINE PHOSPHATE REINTRODUCES OBJECTIVE CLINICAL RESPONSE IN PATIENTS WITH ANDROGEN ABLATION-REFRACTORY PROSTATE CANCER (EARLY EXPERIENCE)

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Background: Therapy for advanced prostate cancer focuses on suppressing systemic androgens and blocking activation of the

androgen receptor (AR). Despite anorchid serum androgen levels, nearly all patients develop castration-resistant disease. We hypothesized, on the basis of previous experience (1), that ongoing steroidogenesis within prostate tumors and the maintenance of intratumoral androgens may contribute to castration-resistant growth. Recently, Montgomery *et al*. (2) demonstrated that median testosterone levels within metastatic tumors from castrated men are approximately three-fold higher than the levels within primary prostate tumors from untreated eugonadal men. The study further showed statistically significant ($p<0.001$) up-regulation of expression of steroidogenic enzymes including FASN, CYP17A1, HSD3B1, HSD17B3, CYP19A1 and UGT2B17. Indeed, several clinical studies have proposed minimizing the levels of these extragonadal sources of testosterone and its precursors by using combinations of inhibitors targeting different points of steroidogenesis, such as ketoconazole and 5-α reductase inhibitors (3, 4). Here, we evaluated whether a combination therapy of ethinylestradiol and estramustine phosphate can reintroduce objective clinical responses in patients with metastatic androgen ablation-refractory prostate cancer (HRPC). *Patients and Methods:* A total of twelve patients (five patients with Gleason score 8 (4+4), five patients with Gleason score 9 (5+4) and two patients with Gleason score 10 (5+5)) with stage D3 disease and bone metastases, who had progression despite initial responses to combined androgen blockade and in whom anti-androgen withdrawal subsequently failed, discontinued combined androgen blockade and received 2 mg ethinylestradiol and 420 mg estramustine orally daily. Serum prostate-specific antigen (PSA), Eastern Cooperative Oncology Group performance status and bone pain scores were assessed at regular intervals. Median follow-up was 17 months (range, 8-26 months). *Results:* Eleven (out of 12) cases had an objective clinical response, defined as having PSA decrease >50% (median 87.1%, range 50.2% to 94.4%). PSA normalization (<4 ng/ml) was achieved in three cases. All patients reported significant and durable improvement in bone pain (median duration, 17.5 months) and performance status (median duration, 18 months). The most important side-effects were vein thrombosis (three patients) and gastric pain (two patients). *Conclusion:* This study showed that castrate-resistant prostate cancer is sensitive to androgens and, moreover, prostate cancer may become hypersensitive to low levels of androgens. Finally, the study established that prostate cancer produces androgens by itself. In the future, a therapeutic approach may be increasing estrogen dose (Estradurin® 80 mg) and/or using new androgen antagonists (*e.g.* abiraterone acetate, MDV300). Intracrine androgen synthesis produces a relatively hormone-refractory state and is a new research frontier.

1 Di Silverio F, Gagliardi V, Sorcini G and Sciarra F: Biosynthesis and methabolism of androgenic hormones in cancer of the prostate. Invest Urol *13(4)*: 286-288, 1976.

2 Montgomery RB, Mostaghel EA, Vessella R *et al*: Maintenance of intratumoral androgens in metastatic prostate cancer: a mechanism for castration-resistant tumor growth. Cancer Res *68*: 4447-4454, 2008.

3 Yap TA, Carden CP, Attard G and de Bono JS: Targeting CYP17: established and novel approaches in prostate cancer. Curr Opin Pharmacol *8*: 449-457, 2008.

4 Tindall DJ and Rittmaster RS: The rationale for inhibiting 5α-reductase isoenzymes in the prevention and treatment of prostate cancer. J Urol *179*: 1235-1242, 2008.

63

CIRCULATING TUMOR CELLS: A NEW PROGNOSTIC FACTOR FOR NON-MUSCLE - INVASIVE BLADDER CANCER

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Introduction: The prognosis of T1G3 bladder cancer is highly variable and not predictable, depending upon clinical and pathological prognostic factors. There is a need for improvement in risk stratification in this patient population. Understanding the molecular profile of individual patients may provide a more personalized and tailored treatment. The main objective of this study was to evaluate the prognostic significance of survivin in tumor tissues and that of survivin-expressing circulating tumor cells (CTCs) in T1G3 tumors. *Patients and Methods:* A total of 108 patients with T1G3 non muscle-invasive bladder cancer (NMIBC) were enrolled. Additional inclusion criteria were: tumor size <3 cm, absence of CIS and multifocalization. Planned follow-up was 24 months. Survivin was evaluated by RT-PCR in tumoral tissues. CTCs were isolated from blood by CELLection™ Dynabeads coated with the monoclonal antibody towards the human epithelial cell adhesion molecule. Cells were lysed and Dynabeads Oligo(dT) was used to capture poly A+ mRNA. cDNA was synthesized and analyzed for the expression of CD45, CK8 and survivin. The primary endpoint was disease-free survival (DFS). The favorable group at 24 months was defined as that without any clinical evidence of disease. The unfavorable group was that with evidence of recurrent disease or progressive disease. Tumoral survivin expression and the presence of CTC were correlated to DFS. Multivariate analysis was used to investigate whether CTC presence was an independent indicator of DFS. *Results:* Survivin was found in 50% of tumors. Survivin-positive patients had a longer DFS than survivin-positive patients ($\chi^2=4.572$, $p=0.029$). CTCs were found in 48/108 patients (44%) and 92% of CTCs expressed

survivin. The difference in DFS between CTC-negative and CTC-positive patients was statistically significant (χ^2=28.098, p<0.001). CTC presence was found to be an independent prognostic factor of DFS (p<0.001). *Conclusion:* CTC presence is an independent prognostic factor in high-risk NMIBC patients.

64
A NEW PROTOCOL OF CT CYSTOGRAPHY WITH DUAL-SOURCE TECHNIQUE IN THE DETECTION OF BLADDER LESIONS

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Aim: To assess a new computed tomography (CT) protocol of cystography (CTC) and virtual cystoscopy (VC) with dual-source technique in the detection of bladder lesions using cystoscopy with photodynamic diagnosis (PDD) as a reference standard. *Patients and Methods:* Thirty hematuric patients suspicious for bladder cancer and fourteen patients who had undergone transurethral resection of the bladder underwent CTC and VC with multi-detector CT and dual-energy technique after *i.v.* administration of contrast agent. The patient population was divided into three groups based on lesion size determined from PDD cystoscopy. Results of the CT study were compared with those of conventional and PDD cystoscopy. *Results:* PDD cystoscopy depicted 92 bladder lesions in the 44 patients examined. Sensitivity and specificity values of CTC and VC alone were constantly lower than those of the combined approach (group 1: 93.25% and 92.54%; group 2: 100% and 100%; group 3: 100% and 100%, respectively). Regarding lesion size, it was demonstrated that multi-detector row CT performed with thin-slice reconstructions (1 mm) has good sensitivity for the detection of lesions larger than 1 mm. Receiver-operator characteristics (ROC) analysis showed that the combined approach reduces the lower threshold of lesion size that can be detected (1.4 mm). The study of the bladder wall after the administration of contrast agent and using the dual-energy technique allowed superficial or infiltrative lesions to be distinguished in 89% of cases. *Conclusion:* CTC and VC are promising diagnostic approaches for bladder cancer, being able to measure lesions in the range of 1-5 mm and to distinguish superficial from infiltrative lesions. The main disadvantage of CTC and VC is their low sensitivity at depicting flat lesions, as demonstrated by PDD cystoscopy. CTC can be used for the evaluation of hematuric patients, confining standard cystoscopy to a therapeutical role.

65
PCA3 URINARY TEST *VERSUS* 3T 1H-MRS AND DCE-MRI IN THE DETECTION OF PROSTATE CANCER FOCI IN PATIENTS WITH BIOCHEMICAL ALTERATIONS

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Aim: To compare PCA3 test with magnetic resonance spectroscopic imaging (MRSI) and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) combined examination in the detection of prostate tumor foci in patients with persistently elevated prostate-specific antigen (PSA) levels and prior negative random transrectal ultrasound (TRUS)-guided biopsy. *Patients and Methods:* We recruited 43 patients with a first random biopsy negative for prostate adenocarcinoma, persistent elevated PSA and negative digital rectal examination. All patients underwent MRI examination (MRSI and DCE-MRI). The patients underwent attentive prostate massaging, in order to perform PCA3 assay. Afterwards, we performed 10-core laterally-directed random TRUS-guided prostate biopsies. *Results:* The overall sensitivity and specificity of a PCA3 score ≥35 for positive biopsy were 76.9% and 66.6%, respectively, with positive and negative predictive values of 80% and 62.5%, respectively. Regarding the MRI examination, sensitivity and specificity were 92.8% and 86.6%, respectively with positive and negative predictive values of 92.8% and 86.6%, respectively. Receiver-operator characteristics (ROC) analysis rates were 0.755 for PCA3 and 0.864 for MRI. *Conclusion:* Compared with PCA, the MRI examination, combining MRSI and DCE-MRI, improves cancer detection rates in patients with prior negative TRUS-guided biopsy and altered PSA serum levels. Instead of PCA3, this advanced MRI protocol allows more precise diagnosis of local invasion and is useful for optimizing subsequent biological procedures.

66
RADICAL CYSTECTOMY AND PELVIC LYMPHADENECTOMY FOR UROTHELIAL CANCER: FACTORS INFLUENCING PROGNOSIS

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Aim: The purpose of this study was to evaluate the role of prognostic factors in disease progression and cancer-specific mortality in patients undergoing radical cystectomy (RC) and bilateral pelvic lymphadenectomy (PLAD) for urothelial cancer. *Patients and Methods:* We retrospectively reviewed 116 RC + PLAD cases performed for urothelial bladder cancer at the San Paolo Hospital, University of Milan from February 2004 to April 2010. Of the 116 procedures, 80 were evaluable. All surgical procedures were performed by the same operator. Of the 80 patients, 60 were males (75%) and 20 females (20%). The mean age of patients was 70.3 (range 52-88) years and the mean follow-up was 31 (range 2-102) months. The criteria used to allocate patients to CR + PLAD were: muscle-invasive cancer, non muscle-invasive high-grade tumors (HG), recurrence or no response to immunoprophylaxis/therapy with Calmette-Guerin bacillus (BCG). The performed urinary diversions were 48 Wallace-type ureteroileocutaneostomy, 23 Studer-type orthotopic ileal neobladder, 2 vescica ileale Padovana, 8 ureterocutaneostomy and 1 nephrostomy. The prognostic factors evaluated were: age (cut-off <or ≥70 years), tumor stage (cut-off ≤pT2 or ≥pT3), number of tumor foci (cut-off <or ≥3), tumor size (cut-off <or ≥3 cm), lymph-node involvement according to TNM (cut-off =N0 or N1-2), lymph-node density (LND) (cut-off <or ≥20% and <or ≥25%), hydronephrosis (cut-off absent or mono-/bi-lateral). The role of prognostic factors was evaluated in disease progression and cancer-specific mortality, with progression being defined as the appearance of systemic disease (lung, liver, bone and lymph-node metastasis) after surgery. *Results:* Progression rate was 38.7%. General and cancer-specific mortality were 38.7% and 33.7%, respectively. Table I shows the results of the analysis of all prognostic factors considered. *Conclusion:* Age, size of tumor lesions, lymph-node involvement and LND with cut-off 20% and 25% were all found to be statistically significant as prognostic factors for tumor progression. Only pathological stage and lymph-node stage were found to be statistically significant for survival in patients undergoing CR. Considering all the variables examined, only lymph-node involvement assessed by the TNM staging system is significant both for disease progression and cancer-specific mortality. In agreement with literature reports, this study confirmed the prognostic importance of PLAD.

Table I.

Characteristic	Cut-off value	Progression (*p*-value)	Progression (%)	Mortality (*p*-value)	Mortality (%)
Age (years)	<70	0.02	34.3	0.135	28.57
	≥70		42.2		37.77
Tumor stage	≤pT2	0.42	6.1	<0.001	13.95
	≥pT3		64.9		56.75
Number of tumor foci	<3	>0.05	40	0.510	35.5
	≥3		41		36.36
Tumor size (cm)	<3	0.04	35.3	0.292	29.41
	≥3		44.82		37.93
pN	N0	0.03	25	0.001	18.75
	N1-2		66.6		62.96
LND	<20%	0.00007	34.37	0.601	29.68
	≥20%		72.72		63.63
	<25%	0.000003	33.33	0.166	28.78
	≥25%		88.88		77.77
Hydro-nephrosis	None	>0.05	36.84	0.86	34.21
	Mono/Bilat.		51.85		40.74

1 Bassi P, Drago P, Piazza N, Spinadin R, Carando R, Pappagallo G and Pagano F: Prognostic factors of outcome after radical cystectomy for bladder cancer: a retrospective study of a homogeneous patient court. J Urol *161*: 1494-1497, 1999.

2 Kassouf W, Agarwal PK, Herr HW *et al*: Lymph node density is superior to TNM nodal status in predicting disease-specific survival after radical cystectomy foe bladder cancer: analysis of pooled data from MDACC and MSKCC. J Clin Oncol *26*: 121-126, 2008.

3 Osawa T, Abe T, Shinohara N *et al*: Role of lymph node density is predicting survival of patients with lymph node metastases after radical cystectomy: a milti-institutional study. Int J Urol *16*: 274-278, 2009.

67
SOMATOSTATIN RECEPTOR BINDING DOMAIN EXPRESSION IS UP-REGULATED BY ESTRADIOL IN PROSTATE CELLS

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Aim: The expression of somatostatin (SS) receptors (SSR) may be modulated by estrogens in breast cancer cells. The aim of this study was to evaluate the effects of estradiol (E_2) on SSR levels in prostate epithelial cells (PEC). *Materials and Methods:* We investigated the effects of E_2 on the expression of SSRs and the co-treatment with SS analog SOM230 on a PEC model (EPN). SSR proteins were evaluated by Western blotting, using specific monoclonal antibodies recognizing their binding domain epitopes

(Ypsilon Biotechnology, Napoli, Italy). Cells starved in red phenol-free DMEM and 1% charcoal treated FBS for five days were treated with 20 mM E_2 or 10^{-6} or 10^{-8} SOM230 or 20 mM E_2+ SOM230 (10^{-8} or $+10^{-6}$) for 48 h. Cells were differently harvested for semi-quantitative RT-PCR, Western blot or flow cytometry (FACS) analyses. *Results:* E_2 induced an up-regulation of SSR 1, 2 and 5 mRNA and proteins. E_2 and SOM 10^{-6} alone induced apoptosis and slightly reduced proliferation. The combined treatment of 20 mM E_2 + SOM230 (10^{-8} or 10^{-6}) induced a stronger rate of apoptosis and a greater decrease of proliferation compared to either alone. The synergistic action of SOM230 and E_2 induced a reduction in S-phase proliferation with an arrest in G_0/G_1 phase. Caspase-dependent apoptosis was induced by SOM230. while a reduction of BCL-2 levels was induced after the addition of E_2, which amplified SOM230 effects at lower doses. *Conclusion:* E_2 increases the inhibitory effects of SOM230 in a prostate cell model expressing ER alpha and beta, acting directly on cell growth and cell death control and up-regulating SSRs.

1 Tang X, Takekoshi S, Itoh J, Umemura S, Shoji S, Terachi T and Osamura RY: Somatostatin analogue inhibits the mobility of prostate carcinoma cells: A new therapeutic method for advanced prostate carcinoma. Int J Oncol *37(5)*: 1077-1083, 2010.
2 He Y, Yuan XM, Lei P, Wu S, Xing W, Lan XL, Zhu HF, Huang T, Wang GB, An R, Zhang YX and Shen GX: The antiproliferative effects of somatostatin receptor subtype 2 in breast cancer cells. Acta Pharmacol Sin *30(7)*: 1053-1059, 2009.
3 Kimura N, Takamatsu N, Yaoita Y, Osamura RY and Kimura N: Identification of transcriptional regulatory elements in the human somatostatin receptor sst2 promoter and regions including estrogen response element half-site for estrogen activation. J Mol Endocrinol *40(2)*: 75-91, 2008.

68
PROKINETICIN 1 STIMULATES THE MIGRATION AND PROLIFERATION OF PROSTATE EPITHELIAL CELLS *IN VITRO*

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Background and Aim: Increased PROK1 expression has been found in prostate hyperplasia and cancer, suggesting a role in prostate proliferative diseases. The aim of this study was to elucidate the role of PROK1 on prostate cell (PC) function and growth. We evaluated the effects of PROK1 on epithelial PC migration and proliferation using the androgen-dependent epithelial PC line EPN, and a stabilized PC line derived from prostate cancer (CPEC). *Materials and Methods:* Semi-confluent starved cultures were treated with recombinant PROK1 (5 nM), alone or associated with antiPROK1 monoclonal antibody or solvent. Cells were harvested 48 h after the treatment and stained with propidium iodide for flow cytometry of the cell cycle distribution by FACSCalibur or recovered for protein extraction for Western blot analysis, or for mRNA extraction for semi-quantitative RT-PCR. Cells grown on slides were also treated and harvested after 46 h for TUNEL assay. A wound assay was performed for the evaluation of cell motility after overnight incubation. For ERK phosphorylation assay, cell cultures were recovered after 5, 10. 20 and 60 min following treatment. *Results:* An increase of the cell number in S phase, with a decrease of cell counts in pre-G_1 and G_0/G_1 and a significant reduction of the percentage of fragmented nuclei was found after PROK1 treatment ($p<0.05$ *vs*. control). Treatment induced an increase of migration in CEPC only. These effects were abolished when antiPROK1 monoclonal anitbody was added. PROK1 induced a rapid and transient phosphorylation of ERK in EPN and had more sustained effects on CEPC. These effects were abolished by pretreatment with PD98059 (50 nM). Semi-quantitative PCR showed an increase of PROK-R2 transcript in treated cells. *Conclusion:* Our study demonstrates that PROK1 has stimulating effects on prostate epithelial tumor cells growth and migration *in vitro*, suggesting a role for PROK1 in neoplastic progression.

1 Pasquali D, Rossi V, Staibano S, De Rosa G, Chieffi P, Prezioso D, Mirone V, Mascolo M, Tramontano D, Bellastella A and Sinisi AA: The endocrine-gland-derived vascular endothelial growth factor (EG-VEGF)/Prokineticin 1 and 2 and receptor expression in human prostate: up-regulation of EG-VEGF/Prokineticin 1 with malignancy. Endocrinology *147(9)*: 4245-4251, 2006.
2 Zhou Q-Y and Meidan R: Biological function of prokineticins. Results Probl Cell Differ *46*: 181-199, 2008.
3 Monnier J and Samson M: Prokineticins in angiogenesis and cancer. Cancer Lett *296(2)*: 144-149, 2010.

69
ANTIPROLIFERATIVE EFFECTS OF LXR ALPHA AND LXR BETA ACTIVATION BY SYNTHETIC OXYSTEROL ON PROSTATE CELLS *IN VITRO*

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Aim: Oxysterols may exert antiproliferative effects on several cancer cells, including prostate cells (PC), acting on liver X receptors alpha and beta (LXRalpha and LXRbeta). Here, we evaluated the presence of LXRs and the effects of a synthetic oxysterol (T09) using the androgen-dependent cell lines EPN and a stabilized line, derived from prostate cancer (CPEC). *Materials and Methods:* Starved cultures were treated with T09 (3 or 10 μM) or DMSO and harvested 72 h after treatment, stained with propidium iodide for flow cytometry of cell cycle distribution by FACSCalibur or recovered for protein extraction for Western blot analysis or for mRNA extraction for quantitative real-time PCR. Cells grown on slides were also treated and harvested after 72 h for TUNEL assay. *Results:* LXRalpha and beta transcripts were found in both EPN and CPEC with higher LXRalpha levels in CEPC ($p<0.01$). In EPN, a reduction of S phase cells and an increase of cells with G_0/G_1 arrest were observed after T09 (3 and 10 μM). CDK4, p27 and p21 protein levels increased, while PIM-1 levels decreased, after treatment in a dose-dependent manner. In CEPC, no change of cell proliferation was found. No effects on pre-G_1 apoptotic peak and DNA fragmentation were found in both cell types. *Conclusion:* This study confirms an antiproliferative effect of T09 in PC cells. Our findings suggest that the variable effects of this oxysterol on PC growth *in vitro* may be explained by the relative LXRalpha/beta content in prostate cells.

1 Chuu C-P and Lin H-P: Antiproliferative effect of LXR agonists T0901317 and 22(R)-hydroxycholesterol on multiple human cancer cell lines. Anticancer Res *30(9)*: 3643-3648, 2010.

2 Chuu CP, Kokontis JM, Hiipakka RA and Liao SJ: Modulation of liver X receptor signaling as novel therapy for prostate cancer. Biomed Sci *14(5)*: 543-553, 2007.

3 Chuu CP, Hiipakka RA, Kokontis JM, Fukuchi J, Chen R and Liao S: Inhibition of tumor growth and progression of LNCaP prostate cancer cells in athymic mice by androgen and liver X receptor agonist. Cancer Res *66(13)*: 6482-6486, 2006.

72

SUTURELESS ELECTIVE LAPAROSCOPIC ENUCLEATION OF EXOPHYTIC CT1A RENAL MASSES: PERSONAL TECHNIQUE AND PRELIMINARY DATA

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Aim: To assess the technical feasibility, effectiveness and complications of elective laparoscopic enucleation without parenchymal hemostatic sutures in a consecutive series of patients in whom the only inclusion criterion was the clinical diagnosis of renal neoplasm T1a, protruding from the renal profile by ≥ 50% of its maximum diameter. *Patients and Methods:* From January 2005 to December 2010, we selected 10 consecutive patients who met the inclusion criterion (mean maximum diameter of tumors: 3.1 cm): eight were male and two female, with an average age of 67 years. All patients underwent laparoscopic enucleation through transperitoneal (4/10) or extraperitoneal access (6/10). The clamping of the renal artery was achieved with a double-loop elastic tape, after infusion of 120 ml 18% mannitol. Enucleation was performed with an ultrasonic scalpel. Parenchymal hemostatic sutures were not used. Hemostasis of the resection bed was achieved with bipolar forceps and with further placement of the active surface of fibrinogen/thrombin sponge (Tachosil) in contact with the enucleation field. Two oxidized cellulose absorbable hemostatic sponges were placed on the inactive surface of the Tachosil. We then proceeded to develop compression on the cellulose sponges by two Johann forceps, lasting for three minutes. The elastic tape was removed after achieving satisfactory hemostasis. Warm ischemia time, intraoperative blood loss, histology and surgical margins on pathological specimen, postoperative drainage loss, preoperative and discharge hemoglobin and creatinine, the number of whole-blood autologous and/or homologous packed cells transfusions, and the rate of peri- and postoperative reintervention were recorded. The mean follow-up period was 34 months (range, 12-60 months). Follow-up consisted of an abdominal ultrasound examination performed at six months from discharge and an abdominal computed tomography examination performed annually for five years. *Results:* The mean warm ischemia time was 15 min and average intraoperative blood loss was 400 ml. Histology showed that there was a clear-cell carcinoma in eight patients (six with Fhurman 2, the remaining with Fuhrman 3) and an oncocytoma in two patients. The minimum margin of healthy tissue on surgical specimens was 1 mm, while average postoperative blood loss was 120 ml. Average preoperative and discharge values were 13.7 and 10.8 g/dl, respectively, for hemoglobin, and 0.87 and 0.95 mg/dl, respectively, for creatinine. There was no postoperative bleeding which required blood transfusion or reintervention. No recurrence of disease was reported. *Discussion and Conclusion:* The elective enucleation enabled the removal of kidney solid masses, achieving both radical cure and sparing of healthy functioning

renal parenchyma. With respect to open enucleation, warm ischemia time affected laparoscopic rather than open access. The reported personal technique, saving time usually used for parenchymal hemostatic sutures, shortened the operative ischemia time, which in our series was found to be within the safe limits for the preservation of renal function, achieving good peri- and postoperative haemostasis. Our sutureless technique during elective laparoscopic enucleation for cT1a exophytic renal tumors was feasible and effective in reducing the complexity of laparoscopic maneuvers and warm ischemia time, without major bleeding complications.

73

MALIGNANCY IN HORSESHOE KIDNEYS: REVIEW AND OUR EXPERIENCE

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Background: Horseshoe kidney is one of the most common congenital anomalies of renal structure. The incidence of renal carcinoma in these abnormal kidneys is similar to that with normal anatomy and 85% of them are adenocarcinomas. Surgical treatment is difficult with regard to the anatomy of the isthmus and vascular malformations. We report a case of renal cell carcinoma in a horseshoe kidney and our experience in its management. *Case Report:* In October 2010, a 75-year-old man was referred to our institution and underwent abdomino-pelvic ultrasound, computed tomography and magnetic resonance imaging examinations. These examinations showed a 15-mm solid mass in the parenchymatous isthmus of a horseshoe kidney. The patient was without symptoms; the abdominal exploration was normal and there was no evidence of metastases. A partial nephrectomy was performed with an anterior bilateral intercostal Chevron-type incision. The pathological evaluation of the lesion gave evidence of chromophobe renal cell carcinoma of Fuhrman grade III. The immunohistochemical tests showed that the tumor tissue was positive for CK7. The follow-up was negative. *Discussion:* A horseshoe kidney is a rare, developmental anomaly that occurs in about 0.25% of the population, arising during the fourth week of embryonic development. There are two theories about the embryological development of a horseshoe kidney. The first is the classical mechanical theory according to which fusion of the inferior poles occurs, while the second theory is that of abnormal migration of the posterior nephrogenic area, which is now considered to be a more common causative factor. Recently reported data suggest that the theory of mechanical fusion is valid only for horseshoe kidneys with a fibrous isthmus, while the abnormal migration of the posterior nephrogenic area causes the majority of horseshoe kidneys, where the isthmus consists of parenchyma. Development of the isthmus through abnormal migration could predispose this location to renal cell carcinoma. *Conclusion:* The anatomical particularities of horseshoe kidneys should be taken into account during surgery because they render the treatment difficult and, thus, the presence of a horseshoe kidney should be determined before surgery. The key to successful surgery lies in careful and good preoperative planning. A computed tomographic scan with contrast agent is essential in the diagnosis and management of these cases.

74

CRANBERRY EXTRACTS REDUCE URINARY TRACT INFECTIONS DURING RADIOTHERAPY FOR PROSTATE ADENOCARCINOMA

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Introduction: Cranberry (*Vaccinium macrocarpon*) has been suggested to reduce the attachment of bacteria to uroepithelial cells, thus preventing urinary tract infections (UTI). Although the mechanism of action is not completely clear, flavonoids and proanthocyanidin oligomers are known to prevent bacterial attachment to host bladder mucosa. Because UTI is one of the most frequent adverse events during external beam radiotherapy (EBRT) of prostate carcinoma (PCa), with an incidence rate of about 20%, we have tested a cranberry extract (*V. macrocarpon* fruit titrated and highly standardized at 30% in proanthocyanidins), 200 mg/day/*p.o.*, to prevent cystitis in extreme conditions, such as partial bladder irradiation. *Patients and Methods:* From June 2007 to June 2009, 244 consecutive patients were enrolled in this study. All patients received hypofractionated intensity-modulated radiotherapy with simultaneous integrated boost to the prostate bed (with/without pelvis considering lymph nodal risk). A total of 120 patients were treated with cranberry extract and 124 were enrolled in the control group. Risk factors (diabetes, previous surgery, age, performance status, median dose to the bladder, V50 and V60) had a similar distribution between the two groups. Cranberry extract therapy started on the simulation day, when a bladder catheterization was performed. During EBRT (over 6-7 weeks), all patients underwent a weekly examination, recording urinary tract symptoms. Urine cultures were performed at 20 and 40 Gy and, eventually, when intense dysuria occurred. *Results:* All treated patients regularly took cranberry extract. No adverse effects due to the extract were observed, while two patients with chronic

gastritis had gastric pain, rapidly controlled by omeprazol. No allergies due to cranberry extract were observed. In the extract-treated group, 10 UTIs in 120 patients (8.3%) were diagnosed without relapses. In the control group, 25 UTIs in 124 patients (20.1%) were diagnosed, with recurrence in 4 of them. The difference between the two groups was statistically significant (χ^2=5.88, p=0.015, with a decrease of UTI incidence in the cranberry extract group of about 50%), especially considering *Escherichia coli* infections alone (3 *vs.* 15 in the cranberry extract and control groups, respectively). Compared to the control group, the extract-treated group had lower incidences of: dysuria (and, overall, lower seriousness of the symptoms G0: 62% *vs.* 34%, G1: 26% *vs.* 34%, G2: 11% *vs.* 21% and G3: 1% *vs.* 11%), nicturia (35% *vs.* 56%; χ^2=10.45, p=0.01), mictional urgency (34% *vs.* 64%; χ^2=20.76, p<0.01) and mictional frequency peak (7.59 *vs.* 8.94 times/day, Student's *t*-test, p=0.001). *Conclusion:* In the literature, cranberry extracts significantly reduce the incidence of UTIs (RR=0.65, 95% CI=0.46-0.90) when compared with placebo/control. The data of our study confirm these results, with a statistically significant decrease of cystitis incidence, even in critical situations such as mucositis due to partial bladder irradiation. Phenolic phytochemicals, including phenolic acids and flavonoids, contribute to the decrease in the the attachment of bacteria to uroepithelial cells, reducing clinical infective episodes. Furthermore, our data showed that cranberry extracts may have a protective role on bladder mucosa during EBRT. In fact, a significant decrease of urinary tract symptoms (dysuria, nicturia, frequency, mictional urgency) was recorded in the cranberry extract-treated group, probably due to local inhibition of cyclo-oxygenases and the effect of antioxidant properties on the bladder surface.

1 Jepson RG and Craig JC: Cranberries for preventing urinary tract infections. Update of Cochrane Database Syst Rev Cochrane Database Syst Rev, 2008.
2 Masson P, Matheson S, Webster A and Craig JC: Meta-analyses in prevention and treatment of urinary tract infections. Infect Dis Clin N Am *23*: 355-385, 2009.
3 Gupta K, Chou MY, Howell A, Wobbe C, Grady R and Stapleton AE: Cranberry products inhibit adherence of p-fimbriated *Escherichia coli* to primary cultured bladder and vaginal epithelial cells. J Urol *177(6)*: 2357-2360. 2007.

77

RETROSPECTIVE EVALUATION OF THE EFFECT OF PANAX GINSENG ON FATIGUE DURING PROSTATE IRRADIATION

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Aim: Panax ginseng CA Mayer G115 (PG) is a phytocomplex that contains 38 ginsenosides (saponins), phenol compounds and acid polysaccharides. The beneficial effects of this herbal extract on fatigue and the quality of life are well reported in the literature. Ergogenic activity, antidepressive effects, stimulation of memory performance and antioxidant, immunomodulatory, proapoptotic and antiproliferative actions of PG have been described. Furthermore, a light estrogenic activity is reported. Recently, it was also used for cancer-related fatigue. *Patients and Methods:* During 2009, PG was prescribed for 23 patients with fatigue during prostate irradiation without concomitant hormonotherapy. During radiotherapy, the patients were usually visited every 20 Gy or at request. All patients of this study had fatigue of more than grade 4 according to the VAS score and their symptoms started after 30-40 Gy of therapy. At that point, PG was prescribed, with treatment lasting for at least one month. The responses to therapy for fatigue were collected at the end of radiotherapy. The phytocomplex Monoselect Panax® - Phytosomial (distearoyl-phosphatidylcholine complex) Panax ginseng CA Mayer G115 was used, titrated and standardized in ginsenosides at 7% (HPLC), 150 mg *p.o.*/day. Treatment outcome was classified into three groups: complete response (no fatigue after one month), partial response (decrease of at least 3 points of the VAS score, but not complete resolution) and no response (if decrease of less than 3 points of the VAS score). *Results:* In our retrospective analysis, only 20 out of 23 patients were evaluated (3 patients were lost to follow-up). Among them, 3 patients (15%) were non-responders, 11 (55%) were partial and 6 (30%) were complete responders. No toxicities due to treatment or negative influence on radiation therapy were recorded. *Conclusion:* Panax ginseng is defined as an 'adaptogen' drug, a term that connotes an increased resistance to physical, chemical and biological stress. It is used to improve psychological functions, physical performance, immune response and antioxidants effects. Some studies have shown some activity of Panax ginseng in cancer- and cancer therapy-related fatigue with a perceived benefit for the patients (2). In our retrospective analysis, we observed a good response to therapy (85% of patients achieving partial or complete response) without toxicity and, for this reason we suggest that it may be widely used during radiotherapy. It is possible that G115 Panax ginseng is active in cancer fatigue due to its multifactorial (physical, neurological and immune) actions. Moreover, anticancer activity has been shown *in vitro* for several ginsenosides. For these reason, phase III studies are required in specific oncologic areas.

1 Wang J, Li S, Fan Y, Chen Y, Liu D, Cheng H, Gao X and Zhou YJ: Anti-fatigue activity of the water-soluble polysaccharides isolated from Panax ginseng C.A. Meyer. Ethnopharmacol *30(2)*: 421-423, 2010.

2 Barton DL, Soori GS, Bauer BA, Sloan JA, Johnson PA, Figueras C, Duane S, Mattar B, Liu H, Atherton PJ, Christensen B and Loprinzi CL: Pilot study of *Panax quinquefolius* (American ginseng) to improve cancer-related fatigue: a randomized, double-blind, dose-finding evaluation: NCCTG trial N03CA. Support Care Cancer *18(2)*: 179-187, 2010.
3 Qi F, Li A, Inagaki Y, Gao J, Li J, Kokudo N, Li XK and Tang W: Chinese herbal medicines as adjuvant treatment during chemo- or radiotherapy for cancer. Biosci Trends *4(6)*: 297-307, 2010.

78

PREPARATION OF THE URETHRA, BLADDER–URETHRAL ANASTOMOSIS AND FUNCTIONAL AND CANCER OUTCOMES IN RETROPUBIC RADICAL PROSTATECTOMY

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Background: We retrospectively analyzed the functional and oncologic results in a series of 530 patients who underwent retropubic radical prostatectomy (RRP) at our Department. *Patients and Methods:* From April 2002 to December 2010, 530 patients underwent RRP for clinically localized prostate cancer. The average age of the patients was 64 (range, 47-74) years and PSA ranged from 1.9 to 46.7 ng/ml. Our surgical technique involves saving pubo-prostatic ligaments, careful preparation of the urethra with its muscle–aponeurotic structures, section of the urethra at the prostatic apex, careful preparation of the bundle for the nerve-sparing technique, saving the bladder neck when sectioning the vesico-prostatic junction and eversion of the mucosa, calibrating the diameter of the bladder neck to the urethra. Anastomosis was performed with 5/6 interrupted sutures of Caprosyn 3/0 at Foley-type urinary catheter 22 ch, encompassing all the muscle–aponeurotic structures. The bladder catheter was usually removed in 12 postoperative days. *Results:* The mean follow-up was 52.6 months, while the pathological stage was pT2 in 83%, pT3a in 13% and pT3b in 7%. Gleason score was ≤7 in 78.5% and >7 in the remaining patients. Of the surgical margins, 8.4% were positive, while 91.6% were negative. A total of 493 out of 530 patients (93%) were completely continent (no pads), 27 patients (5%) had mild incontinence (1-2 pads daily), and 5 patients (1.8%) were incontinent (>2 pads daily). Continence was assessed at the removal of bladder catheter and at 1, 3, 6 and 12 months after the procedure; at these times, the percentage of continent patients was 59, 76, 88.5, 91 and 93%, respectively. Only 9 patients (1.7%) developed a vesico-urethral junction sclerosis in about 6 months after surgery, which was treated with cold incision of the stricture. *Discussion and Conclusion:* Our technique allowed us to prepare the prostate apex and urethra sphincter accurately, preserving the striated urethral support structures and preserving the maximum length of the urethra. Together with the preparation of the neurovascular bundle and the preparation of the bladder neck, this allowed us to obtain optimal functional results.

1 Delgado Oliva FJ, Caballero Romeo JP, García Serrado D, Prieto Chaparro L, Carro Rubias C, Chillón Sempere S, De Paz Cruz L and De Nova Sánchez E: Urinary incontinence after radical prostatectomy: Surgical technique historic evolution and present functional outcomes. Arch Esp Urol *62(10)*: 809-818, 2009.
2 Tewari A, Jhaveri J, Rao S, Yadav R, Bartsch G, Te A, Ioffe E, Pineda M, Mudaliar S, Nguyen L, Libertino J and Vaughan D: Total reconstruction of the vesico-urethral junction. BJU Int *101(7)*: 871-877, 2008.
3 Rocco F, Carmignani L, Acquati P, Gadda F, Dell'Orto P, Rocco B, Casellato S, Gazzano G and Consonni D: Early continence recovery after open radical prostatectomy with restoration of the posterior aspect of the rhabdosphincter. Eur Urol *52(2)*: 376-383, 2007.

79

MODIFIED CAMEY II ORTHOTOPIC ILEAL NEOBLADDER: DESCRIPTION OF THE TECHNIQUE AND INITIAL EXPERIENCE

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Background: The gold standard in the treatment of invasive or superficial bladder cancer at high risk of recurrence/progression is radical cystectomy with neobladder continent urinary diversion. In our Department, we commonly perform Camey II ileal neobladder procedure, comparable, from a functional point of view, to other neobladders, which, however, require longer times due to the greater complexity of their implementation. For about three years, we have introduced changes to the Camey II technique allowing us an easier descent of the reservoir into the pelvis and an easier uretero-ileal anastomosis, especially on the left side. *Materials and Methods:* Since January 2007, we have performed 12 neobladder procedures with this technique. The average time of the procedure was about 90 minutes, without long delays

compared to the traditional Camey II technique. *Results:* The results in the short postoperative follow-up did not seem to differ from those of the original technique in terms of morphology and urodynamics. However, our technique had a lower incidence of uretero-ileal anastomotic stenosis, especially of the left side. *Discussion and Conclusion:* Although the Camey II technique is well documented, we suggest that our modification of this surgical technique facilitates the descent of the reservoir into the pelvis and reduces the incidence of uretero-neovesical stenosis.

1 Hautmann RE, de Petriconi RC and Volkmer BG: Lessons learned from 1,000 neobladders: the 90-day complication rate. J Urol *184(3)*: 990-994, 2010.
2 Manoharan M, Ayyathurai R and Soloway MS: Radical cystectomy for urothelial carcinoma of the bladder: an analysis of perioperative and survival outcome. BJU Int *104(9)*: 1227-1232, 2009.
3 Hautmann RE, Abol-Enein H, Hafez K, Haro I, Mansson W, Mills RD, Montie JD, Sagalowsky AI, Stein JP, Stenzl A, Studer UE and Volkmer BG: Urinary diversion. World Health Organization (WHO) Consensus Conference on Bladder Cancer. Urology *69(1 Suppl)*: 17-49, 2007.

80
ROLE OF SELECTIVE UPPER URINARY TRACT CYTOLOGY IN PATIENTS WITH SUSPICIOUS TRANSITIONAL LESIONS

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Aim: To evaluate both sensitivity and specificity of urinary cytology obtained by selective upper-tract (UT) washing in predicting transitional cell carcinoma (TCC) when compared to bladder-voided cytology and radiological imaging in a selected series of patients with suspicious transitional tumor. *Patients and Methods:* Between 1991 and 2009, 127 consecutive patients with a clinical suspicion of UT-TCC underwent selective UT washing, bladder urinary cytology and radiological imaging. After completion of clinical assessment, all patients underwent a surgical approach for or biopsy of any suspicious lesion. Based on histology, both sensitivity and specificity of selective UT washing cytology were assessed and also compared with bladder-voided cytology and radiological imaging results. *Results:* The mean patient age was 65.9 (range: 34-84) years; 25 patients were female (19.7%). Eighty-eight patients (69.3%) had a previous history of bladder TCC. The suspicion of UT-TCC was based on radiological imaging in 69 patients (54.3%), positive voided cytology without evidence of bladder disease in 37 patients (29.2%) and hematuria in the remaining 21 patients (16.5%). All patients had at least one negative cystoscopy before surgery. Overall, 50 patients (39.4%) underwent surgery with histological diagnosis of UT-TCC (26 patients with transitional kidney cancer, 21 patients with ureteral transitional cancer and 3 patients with concomitant kidney and ureteral tumor), with high prevalence of high-grade cancer. The number of cases of pTa, pT1, pT2, pT3 and pT4 at surgery were: 13 (7.4%), 12 (6.9%), 6 (3.4%), 14 (8%) and 1 (0.6%), respectively. The remaining patients were only followed up. The mean follow-up was 36.5 (median: 12; range: 1-180) months. The sensitivity of voided urinary cytology was 48.65% and specificity was 69.35%, with positive and negative predictive values (PPV and NPV, respectively) of 48.65% and 69.35%, respectively. Sensitivity and specificity of selective UT washing were 76.60% and 91.25%, respectively, with PPV of 83.72% and NPV of 86.90%. In this series of patients, radiological imaging had a low accuracy (sensitivity, specificity, PPV and NPV were 85.29%, 29.82%, 42.03% and 77.27%, respectively). *Discussion and Conclusion:* Radiological imaging had high sensitivity for primary screening in patients with suspected UT-TCC. Selective UT washing cytology had higher specificity than either bladder cytology or radiology. These findings support the use of selective UT washing as a reliable second-level tool for patients with positive voiding cytology and negative or suspicious UT imaging.

81
PROSTATIC CAPSULE-SPARING CYSTECTOMY FOR ORGAN-CONFINED BLADDER CANCER: A SINGLE-INSTITUTION EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Background: Prostatic capsule and seminal-sparing cystectomy (CSSC) has been proposed for young (age <60 years) potent patients affected by organ-confined bladder cancer. Based on many published studies, very satisfactory functional outcome, in terms of urinary continence and preservation of erectile function, can be expected following this procedure. However, concerns about an increased risk for local and distant failure after CSSC compared to patients undergoing standard radical cystectomy have limited the use of this surgical procedure in

many clinical contexts. We report the long-term follow-up of patients undergoing CSSC in a single institution. *Patients and Methods:* Between 1997 and 2005, 28 patients with clinical stage ≤T2 were treated with CSSC at our institution. Preoperative assessment included definitive histology of biopsies and transurethral resection of the prostate (performed 7-10 days before surgery), as well as abdominal CT or MRI examination and completion of an erectile function questionnaire (IIEF-5) in all cases. Cystectomy included extended pelvic lymphadenectomy and complete bladder removal while preserving the prostate capsule, seminal vesicles and vas deferens. An ileal orthotopic bladder substitution was subsequently accomplished in all cases. Clinical, pathological and follow-up data were available for all patients. Kaplan-Meier analyses were used to calculate cancer-specific survival. Functional results at long-term follow-up were available for 16 patients (84.2%). *Results:* The mean age at the time of cystectomy was 52.4 (median: 52.3, range: 36-68) years. Definitive pathology documented pT0 in 10 patients (35.7%), pTa/Tis in 6 (21.4%), pT1 in 3 (10.7%), pT2 in 8 (28.5%) and pT3 in 1 patient (3.6%). Concomitant pTis was found in 3 patients (10.7%). Lymph-node invasion was present in 3 patients (10.7%). The median follow-up in patients who did not die from bladder cancer was 92 (mean: 90. range: 48-152) months. During follow-up, 8 patients (28.5%) died from bladder cancer. One patient died from other causes. The 5- and 10-year bladder cancer-specific survival rates were 88% and 65%, respectively. The 5- and 10-year recurrence-free survival rates were 66% and 28%, respectively. The IIEF-5 score preoperatively and at 12 months of follow-up was 28.9 and 27.9, respectively. At the last follow-up, 16 patients (84.2%) were continent and reported normal erectile function. Cox regression analysis was not able to identify the prognostic factors associated with optimal oncologic outcome in a definitive multivariate analysis, probably due to the small number of patients included in our study. *Discussion and Conclusion:* In our series, CSSC provided oncologic outcome comparable to that referred to in the literature for similar stage patients and length of follow-up after standard radical cystectomy. Satisfactory erectile function was definitively confirmed. Rigorous preoperative clinical assessment remains the most critical issue.

82

CLINICAL IMPACT OF WHO 2004 COMPARED TO WHO 1973 HISTOLOGIC CLASSIFICATION ON Ta PRIMARY BLADDER CANCER TUMORS: A SINGLE INSTITUTION EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Aim: To define both recurrence-free survival (RFS) and progression-free survival (PFS) in a series of patients with primary Ta bladder cancer (NMIBC) assessed by both WHO 2004 and WHO 1973 pathological classification system for grading. *Patients and Methods:* We retrospectively evaluated clinical data concerning 270 consecutive patients suffering from first-episode bladder cancer and diagnosed with Ta stage tumor at transurethral resection (TUR) between 2004-2008. In all cases, tumors were classified as low-grade according to the WHO 2004 classification system and as G1 or G2 according to the WHO 1973 classification system, by a single uro-pathologist. All patients received only a single early prophylaxis instillation with 50 mg epirubicin as adjuvant treatment. Follow-up examination included urine cytology and cystoscopy at three months after resection and then every six months for five years. Univariate analysis for RFS and PFS was performed using the Kaplan-Meier method with the log-rank test. *Results:* The mean age was 67.3 (median: 67, range: 27-91) years. Fifty patients were female (18.1%). Grade distribution was low according to WHO 2004 in all cases; grade was G1 in 87 patients (32.2%) and G2 in 183 patients (67.8%) according to WHO 1973. The median follow-up period was 25 (mean: 27.4, range: 1-72) months. The 5-year RFS rate was 62% for the G1 and 40% for the G2 groups. RFS rate was 49.4% for all patients (low-grade). The 5-year PFS rate was 97.6% and 93.3% for the G1 and G2 groups, respectively, and 93.5% for all patients (low grade). Only one case of progression to T1 was documented in the G1 group and 13 cases of progression (8 to T1, 2 to T2 and 3 CIS) in the G2 group. The differences in the 5-year RFS rate were statistically significant when comparing G1 and G2 patients (p=0.004). No statistically significant difference was found for the 5-year PFS rate when comparing G1 and G2 patients. *Discussion and Conclusion:* The WHO 1973 classification more accurately predicted Ta patients at higher risk of recurrence. However, the WHO 2004 classification was as accurate as the WHO 1973 classification in predicting the long-term PFS. These findings seem to confirm the clinical reliability of the new histological classification for the definition of both treatment and follow-up schedules of Ta tumors.

83

INTENSIVE INTRAVESICAL MITOMYCIN C REGIMEN *VERSUS* STANDARD SCHEDULE AS NEOADJUVANT THERAPY FOR NON MUSCLE-INVASIVE BLADDER CANCER: A RANDOMIZED PHASE II STUDY

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Background: It has been suggested that improved oncologic outcome can be expected when using a more intensive schedule for the administration of intravesical chemotherapy. *Patients and Methods:* This prospective randomized phase II study investigated both safety and subjective tolerability of a novel schedule of chemotherapy administration (3 times per week for 2 weeks) compared to the standard approach (1 time per week for 6 weeks) as neoadjuvant treatment of recurrent low-grade non muscle-invasive bladder cancer (NMIBC). The secondary endpoint of the study was the definition of complete tumor response (CR). Between January 2009 and September 2010, 52 consecutive patients diagnosed with recurrent NMIBC, single tumor smaller than 1 cm in size, with negative urinary cytology were recruited. All patients underwent pretreatment video cystoscopy with bladder map including the location and size of any tumor. Patients were then randomized to receive within 1 week: a neoadjuvant regimen according to the standard timing with mitomycin C 40 mg/40 ml saline at 1 instillation per week for 6 weeks (Group 1), or the experimental adjuvant regimen with mitomycin C 40 mg/40 ml saline at 3 instillations per week for 2 weeks (Group 2). Seven to ten days after treatment completion, video cystoscopy with bladder map and biopsy of every residual or suspicious lesion was performed for all patients. Local and systemic toxicity were investigated in both groups by means of a semi-structured questionnaire concerning lower urinary tract symptoms through three items (nocturia, frequency, dysuria and urgency) and the SF36 questionnaire being completed at the time of pre- and post-treatment cystoscopy. *Results:* The mean age was 63.4 (range: 34-82) years. All patients experienced recurrence after transurethral resection and biopsy for low-grade NMIBC. A total of 24 and 28 patients were assigned to groups 1 and 2, respectively. Overall, two patients in Group 2 were unable to complete the scheduled treatment due to severe lower urinary tract symptoms. Logistic regression analysis did not document statistical differences between the two groups in terms of lower urinary tract symptoms. One-way ANOVA evidenced only one significant difference between the two groups in terms of SF36 physical functioning (PF) after treatment (p=0.046). The mean PF score was 79.8 (standard deviation, 22.3) and 62.5 (standard deviation, 34.2) in groups 1 and 2, respectively. Overall 15/24 (65.5%) patients in Group 1 and 23/28 (82.1%) in Group 2 showed CR, including the two patients who were unable to complete the treatment. Due to the limited number of patients included in this study, we were not able to identify prognostic factors associated with optimal oncologic outcome in a definitive multivariate analysis. *Discussion and Conclusion:* The intensive schedule for intravesical mitomycin C administration was documented to be well tolerated. When compared to the standard approach, no difference in terms of local and systemic toxicity was registered.

84

A NEW MULTIMODAL ANESTHESIOLOGICAL AND NUTRITIONAL APPROACH IN RADICAL CYSTECTOMY WITH URINARY DIVERSION BASED ON ILEAL SEGMENT: A SINGLE-CENTER, PROSPECTIVE, RANDOMIZED STUDY

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Aim: To evaluate a new multimodal anesthesiological and nutritional approach for patients undergoing radical cystectomy (RC) and urinary diversion with ileal segment (orthotopic bladder substitution or Bricker ileo-cutaneous anastomosis). The main endpoints were: (i) to evaluate the reliability, tolerability and efficacy of intraoperative analgesia without opium derivatives; (ii) to describe the perioperative impact of non-administration of standard bowel mechanical preparation (BMP); and (iii) to report the effects of an early administration of oral nutrition (ON). *Patients and Methods:* Patients were randomized into two groups, three days before RC. In group I, the patients received standard treatment, namely administration of BMP with osmotic laxatives during the day before the operation, antibiotic prophylaxis with erythromycin and paromomycin, use of opium derivatives for the intraoperative analgesia, and administration of parenteral nutrition during the week before the operation. In group II, the patients received experimental treatment, namely administration of a standard enema the day before the operation, intraoperative analgesia without opium derivatives, and administration of ON with yoghurts and puddings starting on the third day after the operation. *Results:* A total of 46 patients were included in the study: 27 patients in group I and 19 patients in group II. The mean age at the time of operation was 68 years (range, 50-68). Flatus (used as an indicator of restarting of peristalsis) was reported after a mean time of 3.1 (range, 1-7) days in group I and after 2.3 (range, 2-4) days in group II. Canalization was observed after 4.5 (range, 1-15) days in group I and after 6.3 (range 2-11) days in group II. Surgical wounds were considered to be repaired after 9 (range, 9-19) days in both groups. ON was well tolerated by 98% (26/27) of patients of group II. Patients in group I were

discharged after 22.2 days, while patients in group II after 12.2 days. The complications in group I were: urinary leakage in 15% of cases (4/27), exitus in 3% (1/27), fever with temperature >38.3˚C in 26% (7/27). The complications in group II were: nausea and/or vomiting in 21% of cases (4/19), re-operation in 3% (1/19), sub-occlusion in 10% (2/19) and fever in 21% (4/19). *Discussion and Conclusion:* This new anesthesiological and nutritional approach in radical cystectomy with urinary ileal diversion allowed a more rapid restarting of peristalsis, ON was well tolerated, allowing a better recovery of the psycho-physical balance of the patients, and the time for discharge was reduced, leading to significant cost reduction. Further investigations are needed in order to confirm these preliminary results.

85
PERCEIVED SOCIAL SUPPORT AND ADJUSTMENT TO DISEASE IN PATIENTS UNDERGOING ACTIVE SURVEILLANCE

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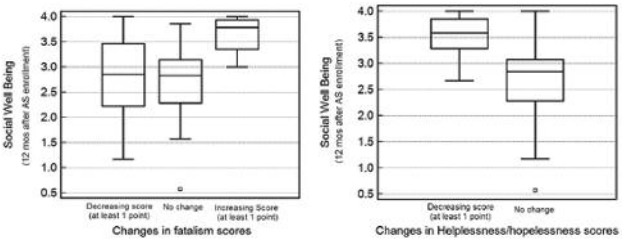
Background: Adaptation to cancer diagnosis and treatment is influenced by several psychosocial resources and social support plays an important role in coping with the disease. Several authors have found that social support is associated with well-being and the adjustment to the stress of cancer (Friedman *et al*., PsychoOncology 2006; Arora *et al*., PsychoOncology 2007). The aim of this study was to investigate whether social well-being in prostate cancer patients undergoing active surveillance (AS) in the framework of the PRIAS protocol is associated with the adjustment to the disease during the observational period. *Patients and Methods:* From November 2007 to January 2011, 146 patients entered the PRIAS Quality of Life protocol and 42 patients (median age, 66 years; range, 43-77 years) fully completed the basal assessment (T0, at AS enrollment) and the 12-month follow-up assessment (T2, about 12 months after the first biopsy and after the first re-biopsy). Social well-being (SWB) was measured by the functional assessment of cancer therapy, prostate version (FACT-P). Adjustment to cancer in terms of fighting spirit, anxious preoccupation, helplessness/hopelessness, fatalism and avoidance was measured by the mini-mental adjustment to cancer scale (Mini-MAC). SWB was considered as a continuous variable, while for each patient, differences in Mini-MAC scoring between T0 and T2 were calculated. A cut-off point=1 was chosen in order to identify patients who experienced a clinically significant change in their adjustment to disease during the first year of active surveillance. Non-parametric analysis (Kruskal-Wallis test) was performed in order to investigate the association between changes in adjustment to disease and SWB at T0 and T2. *Results:* SWB at T2 was correlated with effective styles of coping with cancer at T2. In particular, patients with higher scores of SWB showed at T2: (i) an increase of fatalism (p=0.035), with an average rank of 36.3 in patients with increased scores in the fatalism domain *vs*. 19.9 in patients who did not change or lowered their scores in the fatalism subscale, and (ii) a decrease of helplessness/hopelessness (p=0.007), with an average rank of 33.8 3 in patients with lowered scores in the helplessness/hopelessness domain *vs*. 19.4 in patients who did not change their scores in the helplessness/hopelessness subscale. Changes in anxious preoccupation, fighting spirit and avoidance scores were not significantly correlated to SWB. The following Figure gives a graphical representation of the Kruskal-Wallis test results.



Figure

Discussion and Conclusion: Consistent with the literature about the importance of social support and the association with well-being and adjustment to the stress of cancer, we found that for patients in AS, high levels of social well-being are correlated with a positive adjustment to the disease, in terms of increase of fatalism and decrease of helplessness/hopelessness during the first year of observational treatment. Although definitions of fatalism are rife and they differ across studies, and in contexts and methods of measurement, fatalism has been included together with fighting spirit within the positive attitude factor (Grassi *et al*., PsychoOncology 2005) of Mini-MAC (*e.g*., I've had a good life, what's left is a

bonus). A decrease of helplessness/ hopelessness has been identified as a very important variable related to quality of life (Andritsch *et al*., Support Care Cancer 2007) in cancer patients. To conclude, we highlight that social well-being represents an important variable related to a positive adjustment in patients undergoing AS.

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86

ROBOTIC RADICAL PROSTATECTOMY ANASTOMOSIS (RRP) ASSISTED BY V-Loc™ 180 ABSORBABLE CLOSURE SUTURE DEVICE: PRELIMINARY DATA AND PERSONAL SURGICAL EXPERIENCE

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Background: Robotic radical prostatectomy (RRP) anastomosis, suture of the lateral prostatic vascular pedicles, anterior retropubic Santorini's plexus and, when indicated, bladder neck reconstruction are stressed parts of robotic radical prostatectomy surgery. A new suture, namely the V-Lov 180 absorbable closure device, was tested with regard to various features of the RRP procedure. *Materials and Methods:* The V-Loc 180 consists of a barbed absorbable thread, armed with a surgical needle at one end and a loop end-effector at the other. The barb and loop end-effector design allows for tissue access without the need to tie surgical knots. The V-Loc 180 is completely absorbed in 180 days. This wound closure device is prepared from a copolymer of glycolic acid and trimethylene carbonate and is available in clear or green colors. The device is sterile, inert, non-collagenous and non-antigenic. United States Pharmacopoeia (U.S.P.) designations for diameter are applicable to the V-Loc 180 prior to barbing. After the creation of barbs, the V-Loc 180 is one size smaller than a non-barbed suture. This modification reduces the tensile strength of the suture similar to the effect of knot tying in a non-barbed suture. Therefore, the straight-pull tensile strength of the V-Loc 180 is comparable to the U.S.P. knot pull strength for a non-barbed suture of the equivalent size. The V-Loc 180 meets the requirements established by the U.S.P. and the European Pharmacopoeia for synthetic absorbable sutures for needle attachment only. The V-Loc 180 was tested in 15 Robotic Da Vinci RRP procedures. During the surgical steps, the suture of the lateral prostatic vascular pedicles and anterior retropubic Santorini's plexus were carried out using 15-cm V-Loc 180 material. The anastomoses were performed with two 15-cm or one 30-cm in length V-Loc 180. Comparisons between the Emo-loc clips and the V-Loc suture of the lateral prostatic vascular pedicles and between the traditional suture and the V-Loc suture in retropubic Santorini's plexus and anastomosis were performed. The following features of the RPP procedures were analyzed: safety of surgical steps, time required for anastomosis, surgical skill needed, check for intraoperative dry anastomosis, damage to the tissues by the suturing device, cost of suturing material, stay of the catheter and X-ray images of the anastomosis. *Results:* From July 2010 to January 2011, 20 V-Loc 180 RRP's were carried out. Multifactorial analysis was performed for the various features of the RPP procedure. Regarding the timing of the vesico-urethral anastomosis, the traditional method required 35 min on average, while the V-Loc averaged 20 min; there was no difference between the single 30-cm and the double 15-cm semicircular suture stitches. Overlocked bleeding control of the lateral prostatic vascular pedicles by the 15-cm V-Loc suture was an easy procedure, requiring a short time compared to the multiple Emo-loc clips. Using the V-Loc, elegant sutures were made in the Santorini's plexus and, when necessary, in the bladder neck reconstruction before the vesico-urethral anastomosis. Use of the V-Loc reduced hospitalization time because of the dry vesical-urethral anastomosis, as shown on early X-ray images. *Conclusion:* The V-Loc 180 absorbable wound closure device armed with a surgical needle at one end and a loop end-effector at the other is currently used in RRP procedures. The improved surgical skill, reduced surgical working time, the elegant approach to the different RRP steps and the reduced hospitalization due to the dry anastomosis make the V-Loc a promising device for complex pelvic urological surgical sutures.

89

LEIOMYOMA OF THE FEMALE URETHRA

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Background: Paraurethral leiomyoma is a rare benign hormone-dependent neoplasm of mesenchymal origin affecting women. Clinical evidence is variable but it tends to be asymptomatic or associated with the sensation of a foreign

body, while urinary symptoms are rarely described. Excision of the mass is the recommended treatment and diagnosis is confirmed by pathological analysis to rule out the presence of a sarcoma. A case of paraurethral leiomyoma associated with dysuria, dyspareunia and obstructive voiding symptoms is reported here. *Case Report:* A 28-year-old woman, presented with dysuria, dyspareunia and occasional urinary retention, associated with the presence in the vaginal introitus of a palpable, smooth, solid mass located above the urethral orifice just beneath the clitoris. Transvaginal ultrasonography showed a 25×25 mm hypoechoic mass, highly vascularized on colored Doppler imaging. The voiding cystogram did not show communication of the mass with the lower urinary tract but a constriction of the urethra was revealed. Axial T_1- and T_2-weighted MRI scans were performed and a neoplasm with signal similar to that of a uterine fibroid, compressing the urethra, was diagnosed. The patient underwent surgical excision of the mass, which was easily performed by blunt dissection, after 4-cm longitudinal incision of the anterior vaginal wall. The pathological analysis showed the presence of a paraurethral leiomyoma with less than 1 mitotic figure per 10 high-power fields. The patient had no immediate postoperative complications, the urethral catheter was removed two days after surgery and micturition was immediately restored. Urinary flow evaluation performed one month later revealed a normal Qmax nomogram and dyspareunia had disappeared. *Discussion:* Distinction between urethral, paraurethral, and anterior vaginal wall leiomyoma may be difficult due to their close anatomical proximity. Differential diagnosis of these lesions includes urethral diverticulum, Skene duct abscess, Bartolini gland cyst, Gartner duct cyst, vaginal wall cyst and urethral carcinoma. The literature supports the excision of these lesions to determine the mitotic count, which differentiates leiomyoma from locally recurrent or metastatic leiomyosarcoma, and this can help to predict the possibility of recurrence, which is extremely rare if there are fewer than 5 mitotic figures per 10 high-power fields. The case described here was unusual because of the symptoms (usually, there is paraurethral mass and increased urinary frequency, while voiding dysfunction and urinary retention, as presented here, are very rare) and the young age of the patient (28 years of age while the average age of patients at presentation is 47 years, with a range from 39 to 62 years).

1 Fry M, Wheeler JS Jr., Mata JA *et al*: Leiomyoma of the female urethra. J Urol *140*: 613-614, 1988.
2 Cattolica EV, Klein R and Knigge W: Paraurethral leiomyoma – an imitator. Urology *8*: 605-607, 1976.
3 Cornella JL, Larson TR, Lee RA *et al*: Leiomyoma of the female urethra and bladder: report of twenty-three patients and review of the literature. Am J Obstet Gynecol *176*: 1278-1285, 1997.

90

PROSTATE LOW-DOSE RATE BRACHYTHERAPY IN ELDERLY PATIENTS: OUTCOMES AND TOXICITY PROFILE

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Aim: To determine the toxicity and the biochemical disease-free survival (b-DFS) rate after low-dose rate ^{125}I permanent prostate brachytherapy implant (LDR-BRT) in elderly patients with prostate cancer. *Patients and Methods:* A total of 80 patients were treated between June 2003 and December 2008 and were retrospectively evaluated. Among them, 51 had low-risk (64%) and the remaining 29 had intermediate-risk (36%) prostate cancer. The median age was 75 (range 65- 86) years. All patients received LDR-BRT as monotherapy. The prescribed dose was 145 Gy to the prostate. Patients were divided into recurrence-risk groups according to the criteria of the National Comprehensive Cancer Network. Biochemical failure was defined according to the guidelines of the American Society of Therapeutic Radiology and Oncology. Toxicity was scored according to the RTOG scale. b-DFS was calculated from the implantation date to the date of biochemical recurrence. *Results:* With a median follow-up of 53 (range, 9-87) months, the global actuarial 5-year b-DFS rate was 91.3%. The 5-year overall survival rate was 95%. Acute genitourinary (GU) toxicity was mild; there was no acute grade G3 GU toxicity. Only four patients (5%) experienced late grade G3 GU toxicity. No patients experienced acute and late grade G3 gastrointestinal toxicity. *Discussion and Conclusion:* Older men receive potentially curative therapy for prostate cancer less often than younger men because of side effects, leaving the question of survival benefit open for these patients (1, 2). Our data suggest that LDR-BRT is effective and safe as monotherapy in elderly patients with prostate cancer.

1 Geinitz H, Zimmermann FB and Thamn R: 3D conformal radiation therapy for prostate cancer in elderly patients. Radiother Oncol *76*: 27-34, 2005.
2 Stangelberger A, Waldert M and Djavan B: Prostate cancer in elderly men. Rev Urol *10(2)*: 111-119, 2008.

91

PROSTATE LOW-DOSE RATE BRACHYTHERAPY WITH PERMANENT ^{125}I SEED IMPLANT: A SINGLE-INSTITUTION EXPERIENCE

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Aim: To evaluate biochemical disease-free survival (b-DFS) after low-dose rate ^{125}I permanent prostate brachytherapy implant (LDR-BRT) in patients with prostate cancer. *Patients and Methods:* Patients older than 18 years of age with diagnosis of prostate adenocarcinoma and adequate PSA follow-up time were analyzed in this retrospective study. LDR-BRT was performed as monotherapy, with a prostate total dose of 145 Gy. Patients were divided into recurrence-risk groups according to the criteria of the National Comprehensive Cancer Network. The guidelines of the American Society of Therapeutic Radiology and Oncology were used to define biochemical failure, which was calculated from the implantation date to the date of biochemical recurrence. Post-implant D90, defined as the minimum dose covering 90% of the prostate, was calculated for each patient. Univariate and multivariate statistical analyses were performed using SPSS software. For univariate analysis, cut-off points of 5.89 ng/ml for PSA and 5 for Gleason score (GS) were used. Clinical stage, pre-treatment PSA, GS, androgen deprivation therapy, D90 and risk groups were analyzed in the multivariate analysis. *Results:* From June 2003 to April 2007, 70 patients were treated and analyzed. Among them, 39 (56%) were at low risk, 23 (33%) at intermediate risk and the remaining 8 (11%) at high risk of recurrence. With a median follow-up time of 58 (range, 46-92) months, the global 5-year b-DFS rate was 86%. In the low-, intermediate- and high-risk groups, the 5-year b-DFS rate was 97.2%, 82.6% and 62.5%, respectively (p=0.006). In univariate analysis, initial PSA level, GS and risk group were significant predictors of biochemical failure (p=0.01, 0.01 and 0.006, respectively, by log-rank test). In multivariate analysis, only risk group and GS (p=0.005 and 0.03, respectively) were statistically significant predictors of b-DFS. *Discussion and Conclusion:* Our data compared favorably with the literature (1, 2) and confirmed the advantage of LDR-BRT, especially for low- and intermediate-risk patients with early prostate cancer.

1 Merrick GS, Butler WM and Galbreath RW: Five-year biochemical outcome following permanent interstitial brachytherapy for clinical T1-T3 prostate cancer. Int J Radiat Oncol Biol Phys *51*: 41-48, 2001.

2 Potters L, Cha C and Oshinsky G: Risk profiles to predict PSA relapse-free survival for patients undergoing permanent prostate brachytherapy. Cancer J Sci Am *5*: 301-306, 1999.

92

ADDED VALUE OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH NEGATIVE ULTRASOUND-GUIDED PROSTATE BIOPSY

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Aim: To prospectively investigate the incremental value of multiparametric magnetic resonance (MR) imaging compared with standard T_2-weighted imaging for biopsy planning. *Patients and Methods:* A total of 43 consecutive patients underwent T_2-weighted MR imaging supplemented with multiparametric 1.5-T MR imaging, consisting of proton (^{1}H) MR spectroscopy, diffusion-weighted (DW) imaging and dynamic contrast-enhanced (DCE) MR imaging. From the multiparametric MR imaging, quantitative maps of the following parameters were calculated: choline plus creatine to citrate ratio, apparent diffusion coefficient, and volume-transfer and exchange-rate constants. The prostate was divided into 20 standardized areas. Each area was classified as benign, inconclusive, or suspicious at T_2-weighted imaging, followed by quantitative evaluation of all inconclusive and suspicious areas with MR parameter maps. Transrectal ultrasound (TRUS) biopsy, guided by the MR findings, was performed for lesions classified as suspicious for cancer using at least one of the MR parameter maps after being overlain on the T_2-weighted images, and displayed in three dimensions. Diagnostic parameters were calculated on a per-lesion and per-patient basis for all combinations of T2-weighted images with MR parameter maps. *Results:* A total of 43 patients had a median of two prior TRUS biopsies with negative findings. Each patient had a median count of three suspicious lesions. Prostate cancer was demonstrated in 21 of 43 patients. Biopsy was performed for 128 lesions; 53 of them were positive for prostate cancer. Digital rectal examination was not suspicious for malignancy in 40 patients, while it indicated malignancy in only 3 cases. The biopsy Gleason score (GS) within this group was distributed as follows: 52% GS≤6, 33% GS=7, 14% GS≥8. *Conclusion:* Only the combination of T_2-weighted imaging with all three MR multiparametric techniques depicted all identifiable prostate carcinomas. The combination of T2-weighted imaging with only two MR multiparametric techniques (DW imaging and 1H MR spectroscopy or DW imaging and DCE MR imaging) missed 6%, reasonably reducing the number of areas needing biopsy.

94

ePTFE INFERIOR VENA CAVA PATCH RECONSTRUCTION SURGERY IN DELAYED CAVAL THROMBECTOMY IN A MALE PATIENT WITH PREVIOUS RADICAL NEPHRECTOMY DUE TO RIGHT KIDNEY TUMOR

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Background: Abdominal full vena cava thrombosis, abandoned after right radical nephrectomy, is very rare. We describe the complex surgical technique in a 38-year-old male patient with a full thrombus of the vena cava remaining after right radical nephrectomy. *Case Report:* A 38-year-old male with symptomatic abdominal pain was referred to our hospital one month after right radical nephrectomy due to kidney tumor. A CT scan prior to nephrectomy showed an 8-cm right renal mass with extended thrombosis in the inferior vena cava (IVC) until the iliac cross. No other abdominal mass had been previously described. The patient underwent right radical nephrectomy with abdominal Mercedes incision without caval surgery for thrombectomy. After the operation, the patient was referred to the oncologist for adjuvant therapy. The oncologist referred the patient back to the Urology Department for reconsideration of caval surgery. Xipho-pubic surgical abdominal incision was carried out with severe sub-hepatic abdominal viscerolysis of the ileum, right and transverse colon that occupied the previous right retroperitineal kidney space. An urovascular approach was adopted with a double team. It was impossible to perform the usual incision in the root of the mesentery and Kocker maneuver, allowing the dissection of the aorta and the sub-hepatic IVC, because of the previous surgery. After the approach to the aorta and vena cava, the intra-hepatic vena cava was completely exposed with hepatic rotation. The left renal vein was completely prepared from the IVC through the kidney. A clamp up to the sub-diaphragmatic vena cava was placed; the hepatic vascular support was also prepared and clamped. Subsequently, we proceeded with incision of the IVC until the iliac bifurcation and the extended cavo-iliac thrombus was removed. In the ligated hilum cross of the right kidney vascular support, the thrombus was fixed to the wall of the vena cava and extended for several centimeters. Consequently, a large part of the IVC was removed together with the thrombus. Regular suturing of caval tissue was impossible. Subsequently, polytetraethylene expanded (ePTFE) material was tailored for a reconstruction patch in the vena cava. The ePTFE was much more useful than Dacron material. *Results:* Total operation time was 3.5 h, with a blood loss of 700 ml and use of two transfusion units. No postoperative complication appeared and the patient was discharged in ten days. The 10-month outcome is excellent and the patient is metastasis-free. *Conclusion:* The multidisciplinary urovascular approach taken in this case is the gold standard, considering the possible outcome indicated by the kidney tumor pathology when the surgery is well done. A one-stage surgery, namely radical nephrectomy and the simultaneous removal of the thrombotic material, should always be considered in order to reduce early embolism phenomenon and early metastasis. Because of high perioperative mortality, it is strongly suggested these cases are referred to the surgical urovascular teams, which are familiar with such surgical procedures.

95

PRELIMINARY STUDY OF THE EFFECTS OF GEFITINIB, AN EGF-RECEPTOR INHIBITOR, ON PROSTATE CANCER STEM CELLS

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Background: Existing therapies for prostate cancer eradicate the bulk of cells within a tumor, but most patients go on to develop androgen-independent disease that remains incurable by current treatments. The progression of the disease seems to be caused by a small population of cells, named cancer stem cells, which show stem cell features: they are self-renewing, can differentiate and are highly tumorigenic *in vivo*. Using neurosphere culture strategies, unattached clusters of cells (prostaspheres) with cancer stem cell properties can be obtained from both malignant and non-malignant prostate tissues. The culture of prostaspheres is useful to obtain a consistent number of cancer stem cells and allows their propagation in an undifferentiated state. The epidermal growth factor receptor (EGFR) and its ligands (EGF, TGF-α) are overexpressed during the progression of benign, localized and metastatic forms of prostatic cancer. The up-regulated activation of EGFR signaling appears to sustain cell proliferation, vascularization, invasion and decrease of cell apoptosis. It has also been reported that the interruption of EGF–EGFR signaling by using a selective EGFR inhibitor, such as gefitinib, leads to growth inhibition and apoptotic death of many cancer cell types, including prostate tumor epithelial cells, both *in vitro* and *in vivo*. Moreover, gefitinib, combined

with cyclopamine, a selective inhibitor of the sonic hedgehog pathway, and docetaxel induced significant antiproliferative and apoptotic effects on side and non-side population cell fractions isolated from the WPE1-NB26 cell line (1, 2). This study investigated the antiproliferative effects of gefitinib on androgen-independent (DU145, PC3) and -dependent (LNCaP-C33) prostate cancer cell lines and on U285 non-malignant prostatic hyperplastic cells used as control. *Materials and Methods:* DU145, PC3 and LNCaP cell lines were cultured according to the supplier's instructions. U285 were cultured in RPMI medium with 10% FBS and 10% HS. Adherent cells of bulk cell lines were treated with gefitinib at different concentrations. After 24, 48 and 72 h of incubation, neutral-red and kenacid-blue stains on DU145, PC3 and U285 cells, and MTS assay on LNCaP cells were performed. *Results:* Data obtained from proliferation assays showed that gefitinib inhibited the cell growth in a concentration-dependent manner. IC_{50} values were obtained from the dose–response curves. The IC_{50} value after 48 h of incubation with gefitinib was higher than those after 24 h and 72 h of treatment in the LNCaP cell line. The IC_{50} value obtained using neutral-red staining revealed no significant differences in DU145 cells, whereas higher values were revealed after 24 h of treatment with gefitinib in the PC3 and U285 cell lines. Kenacid-blue assays showed the highest IC_{50} values after 24 h of treatment in all considered cell lines. *Discussion and Conclusion:* Gefitinib showed inhibitory effects on cell proliferation of differentiated prostate cancer and non-malignant prostatic hyperplastic cells. Further investigations are in progress to evaluate the cytotoxic and differentiative effects of gefitinib on prostate cancer stem cells obtained with the prostasphere culture method from the considered cell lines (DU145, PC3, LNCaP and U285).

1 Mimenault *et al*: Int J Cancer *118*: 1022-1031, 2006.
2 Mimenault *et al*: Mol Cancer Ther *9(3)*: 617-630, 2010.

96

CLINICAL IMPACT OF GENETICS ON RENAL CANCER: WHEN FOLLOW-UP NEEDS A MULTIDISCIPLINARY APPROACH

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Renal cancer occurs in hereditary and sporadic forms. The hereditary forms of the disease differ from the sporadic forms because they tend to be multifocal in the same kidney, bilateral and develop at young age. The true prevalence of hereditary kidney cancer is not known as many cases are unrecognized. It is estimated that 3-5% of kidney cancer patients have inherited forms of the disease. Known hereditary kidney cancer syndromes include von Hippel-Lindau (VHL) disease, familiar non-VHL clear-cell renal carcinoma (non-VHL CCRCC) with or without chromosome 3 translocation, hereditary papillary renal cancer, Birt-Hogg-Dube syndrome, hereditary leiomyomatosis and renal cell carcinoma syndrome, and tuberous sclerosis. Besides establishing the heredity of the tumors by family history, it is equally important to establish the associated clinical features, including the exact histology of the renal tumors in the family. Our experience considers a careful analysis of the patient's medical history and of the patient's family medical history as part of routine cancer follow-up. This approach may lead to support the cancer follow-up with the genetic counseling with a urinary assay of vanilmandelic acid, metanephrines, catecholamines and the constitutional karyotype analysis. The case study showed a CCRCC with a balanced translocation between chromosomes 3 and 4 (q12; p12), with a 50% risk of transmitting the same translocation to the offspring and a significantly increased risk of developing kidney cancer compared to the general population. The correct identification of familial adult renal neoplasia allows better management of the patient and their relatives, with early screening and careful follow-up, with the goals of minimizing disease-related morbidity and improving survival.

97

NOMOGRAM WITH PSA ACCELERATION PREDICTING HIGH-GRADE PROSTATE CANCER

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Background: Many patients diagnosed with low-grade prostate cancer have indolent disease and may not benefit from immediate therapy. Little is known about the relative utility of pre-diagnostic PSA kinetics to predict tumor aggressiveness. The aim of this study was to develop a model with PSA kinetics for high-grade prostate cancer risk and to determine its best range of values in terms of specificity and sensitivity. *Materials and Methods:* A prospective Institutional Review Board-approved database of 12-core prostate biopsies performed at the same Institution from January 2001 to June 2010 was searched for men with at least three consecutive PSA measurements for more than 730 days. The natural logarithm of PSA (log PSA) was used to create the best-fit line by least-squares' regression; the acceleration of PSA was the slope of this line (log PSA slope). A logistic

regression model to predict the presence of high-grade prostate cancer (Gleason score ≥7) at biopsy was fitted using age, digital rectal examination (DRE) findings, PSA, % free PSA, prostate volume and PSA acceleration. *Results:* A total of 630 men satisfied the inclusion criteria and, among them, 189 (30%) cancer cases were found at the ultrasound-guided prostate biopsies. Seventy-five (11.9%) had a Gleason score ≥7 and 73 (97%) of them showed a positive PSA acceleration. All men in the study were randomly divided into two groups with 315 cases each; the first group was used to develop the model, while the second group was used for validation. The step-wise multivariate logistic regression analysis showed that all factors except age and PSA, showed a significant ability to predict the presence of prostate cancer with Gleason score ≥7. A nomogram for a positive biopsy was developed from the final logistic-regression model findings. Using the validation data set, the receiver operating characteristics curve compared the performance of the model with the single variables alone. The area under the curve of the predicted results from the model of this validation cohort gave a value of 0.817 (95% confidence interval (95% CI)=0.770-0.858), better than PSA, free-to-total PSA ratio, PSA density and PSA acceleration ($p<0.05$). For a well-balanced sensitivity and specificity, a cut-off value of 17 was derived from the nomogram. This value corresponded to 69.3% specificity (95% CI=63.5-74.6), 85.7% sensitivity (95% CI=69.7-95.1), and a positive and negative predictive value of 2.79 and 0.21, respectively. *Conclusion:* We successfully developed an accurate model to predict prostate cancer with Gleason score ≥7. The addition of free-to-total PSA ratio, DRE, prostate volume and PSA acceleration sharply improved the accuracy of our model.

98

RADICAL PROSTATECTOMY AFTER PREVIOUS PROSTATE SURGERY: CLINICAL AND FUNCTIONAL OUTCOMES

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Aim: We evaluated the impact of previous prostate surgery performed for lower urinary tract symptoms (SxLUTS) in terms of overall perioperative and postoperative morbidity and early functional outcome in patients who underwent radical prostatectomy. *Patients and Methods:* From January 2001 to January 2010, 3,741 consecutive patients underwent open RP, of whom 283 (7.6%) had previously undergone SxLUTS. Perioperative and postoperative data were compared between group 1 (with previous SxLUTS) and group 2 (without previous SxLUTS). The functional results were assessed by validated questionnaires (IIEF and ICIQ). *Results:* Patients in group 1 were younger than those in group 2 (65.6 *vs*. 69.0 years, $p<0.001$). Preoperative risk groups according to D'Amico classification were: 35.7% *vs*. 44.0% (low risk), 42.3% *vs*. 39.4% (intermediate risk) and 22.1% *vs*. 16.7% (high risk) in groups 1 and 2, respectively ($p=0.01$). The preoperative rate of fully potent patients was significantly higher in patients not treated with SxLUTS (38.4% *vs*. 26.4%, $p=0.01$). Operative time (147 *vs*. 151 min), hospital stay (9.4 *vs*. 9.5 days), bladder catheterization (9.5 *vs*. 10.4 days) and blood loss (1108 *vs*. 1169 ml) were similar in groups 1 and 2, respectively (all $p>0.1$). Surgical complications, assessed according to the Clavien classification, were: grade 2 and 3 in 15.5% and 1.0% *vs*. 16.6% and 0.4% in group 1 and 2, respectively ($p=0.4$). The 1- and 2-year urinary continence recovery rates were not significantly different between the patients in groups 1 and 2 (72% *vs*. 69% and 79% *vs*. 74%, respectively). The 1- and 2-year erectile function recovery rates were not significantly different between the patients in groups 1 and 2 (38% *vs*. 48% and 39% *vs*. 46%, respectively). These data were confirmed with multivariate Cox regression analyses, where the variable depicting previous SxLUTS was not associated with urinary continence and erectile function recovery after accounting for patient age at surgery, surgical volume, nerve-sparing technique and preoperative functional and oncologic characteristics ($p>0.2$). *Conclusion:* Radical retropubic prostatectomy can be performed safely after previous prostate surgery for bladder outlet obstruction. Candidates for second-line prostate surgery should be informed that functional results may be achieved as satisfactory as those achieved after the same surgical approach in naïve patients.

99

CAN WE RELY ON CLINICAL CHARACTERISTICS TO PREDICT UNFAVORABLE DISEASE IN MEN WITH PROSTATE CANCER PREVIOUSLY TREATED WITH SURGERY FOR BENIGN PROSTATIC HYPERPLASIA? CLINICAL IMPLICATIONS

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Aim: We evaluated the effect of previous prostate surgery performed for lower urinary tract symptoms (SxLUTS) on the

ability to predict unfavorable tumors, using available clinical characteristics at prostate cancer (PCa) diagnosis. *Patients and Methods:* From January 2001 to January 2010, we collected 2,295 consecutive patients with clinical T1c-T3 PCa who underwent open radical prostatectomy (RP), of whom 165 (7.2%) had previously undergone SxLUTS. Univariate and multivariate logistic regression analyses addressed the ability of clinical characteristics, namely PSA, clinical stage and biopsy Gleason score, to predict unfavorable disease at RP, defined as extracapsular extension (ECE) and/or seminal vesicle invasion (SVI) and/or lymph node invasion (LNI) and/or RP Gleason score 8-10 (HGPCa). *Results:* The rate of unfavorable disease at RP was 31.6% *vs.* 28.5% in naïve patients and patients treated with previous SxLUTS, respectively (p=0.4). Patients treated with previous SxLUTS did not show any statistically significant differences compared to naïve patients with regard to age (64.3 *vs.* 69.0 years, p=0.1), PSA (8.7 *vs.* 6.2 ng/ml, p=0.7) and biopsy Gleason score (6, 7 and 8-10: 66.7%, 26.3% and 6.9% *vs.* 65.5%, 27.3% and 7.3%, p=0.9). Clinical stage was slightly lower in naïve patients compared to SxLUTS cases (cT1c, cT2 and cT3: 58.9%, 32.4% and 8.7% *vs.* 65.5%, 31.5% and 3.0%, p=0.03). Preoperative risk groups according to D'Amico classification were 37.7% *vs.* 44.2% (low risk), 45.7% *vs.* 44.2% (intermediate risk) and 16.6% *vs.* 11.5% (high risk) in naïve and SxLUTS patients, respectively (p=0.1). At univariate analysis, only biopsy Gleason score was associated with unfavorable disease at RP in patients treated with SxLUTS (p=0.01). At multivariate analysis, PSA, clinical stage and biopsy Gleason score achieved independent predictor status in naïve patients (all p<0.001). In patients previously treated with SxLUTS, only Gleason score at biopsy was an independent predictor of unfavorable disease at RP. *Conclusion:* When PCa is diagnosed in patients who had previously undergone prostate surgery, clinicians should exclusively base their ontological evaluation on biopsy Gleason score. PSA levels and clinical stage do not predict unfavorable disease at RP in patients known to have had prior prostate surgery.

100

IS 10-YEAR FOLLOW-UP LONG ENOUGH TO EVALUATE ONCOLOGICAL OUTCOMES OF PATIENTS AFTER RADICAL PROSTATECTOMY? IMPORTANCE OF LONG-TERM ASSESSMENT

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Background: Recurrence of prostate cancer is a common event. Although it has been reported that the majority of recurrences are observed in the first few years after surgery, only few series have reported the long-term results of patients treated with radical prostatectomy (RP). Here we report the long-term follow-up of patients treated with RP with a minimum follow-up of 10 years. *Patients and Methods:* Between 1985 and 2010, 5,957 patients were treated with RP for prostate cancer at a single tertiary referral center. For the purpose of this study, we focused on patients with a time interval between surgery and last evaluation of longer than 10 years. Kaplan-Meier and life-table analyses addressed the rates of overall mortality, cancer-specific mortality (CSM) and biochemical recurrence (BCR) according to the clinical and pathological characteristics of the patients. BCR was defined as two consecutive measurements of PSA >0.2 ng/ml. Moreover, life-table analyses were used to address the 10- and 15-year recurrence-free survival rates according to the pre-operative risk groups, namely low (PSA <10 ng/ml) and intermediate risk (all the remaining patients). Differences in patient outcome were addressed by using the log-rank test. *Results:* Of the 5,957 patients treated with RP, 728 (12.2%) had follow-up of more than 10 years. These patients were treated between 1986 and 2000. Mean and median follow-up were 152 and 144 months, respectively. At RP, mean and median PSA were 17.4 and 11.4 ng/ml, respectively. Pathological Gleason score was 2-6, 7 and 8-10 in 56.3, 22.8 and 14.9% of patients, respectively. Pathological stage showed organ-confined disease, extracapsular extension, seminal vesicle invasion and lymph node involvement in 57.2, 13.3, 20.8 and 20.4% of patients, respectively. Positive surgical margin(s) were found in 11.5% of patients. The 10- and 15-year BCR-free survival rates were 61 and 52%, respectively. The 10- and 15-year overall survival rates were 77 and 65% respectively. The 10- and 15-year CSM-free rates were 89 and 85%, respectively. Of 337 patients who recurred, 149 (44.2%) and 46 (13.6%) developed BCR beyond 5 and 10 years of follow-up. Of 85 patients who died of prostate cancer, 53 (62.3%) and 12 (14.1%) died beyond 5 and 10 years of follow-up, respectively. Interestingly, 11, 14 and 11% of low-, intermediate- and high-risk patients, respectively, experienced BCR beyond the 10-year landmark. *Conclusion:* CSM in patients selected for RP is low. Conversely, BCR represents a common event. If follow-up is adequately extended, a non-negligible proportion of patients develop BCR and CSM beyond the 5- and 10-year follow-up landmarks. About 10% of patients evaluated beyond the 10-year landmark experienced BCR, regardless of the preoperative risk of recurrence. Therefore, the results of RP series need to be evaluated only at long-term follow-up in low-, intermediate- and high-risk disease.

101
EXCLUSIVE RADIOTHERAPY OF PROSTATE CANCER WITH HELICAL TOMOTHERAPY: INITIAL EXPERIENCE

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Background: Prostate cancer (PCa) is the most common type of cancer in adult males. Many treatment strategies are feasible and the choice may depend on several factors. Exclusive radiation therapy for the local control of PCa is becoming more widespread due to the availability of new irradiation techniques allowing high-dose conformation and reduced toxicity. In January 2009, a helical tomotherapy (HT) system was installed at our Institution and, until June 2010, we treated 31 PCa cases exclusively with HT. Here, we report our results in terms of treatment effectiveness and short-/medium- term toxicity. *Patients and Methods:* HT, one of the most advanced external beam technologies, has many technical features improving treatment quality in comparison to conventional radiotherapy. It delivers the radiation dose in helical geometry, combining couch translation and source rotation, exactly like spiral computed tomography. The beam is shaped and modulated passing through a 64-leaf binary collimator. Treatment planning takes place in an 'inverse' modality, being wholly managed by specific mathematical functions to minimize undue dose and maximize target coverage. HT allows highly accurate (error <1 mm) positioning, based on imaging of the patient's internal organs (image-guided radiation therapy technology), reducing the required target margin and, therefore, the irradiated body volume. Our PCa irradiation protocol provides the delivery of two different dose levels at the same time (simultaneous integrated boost technology): 2 Gy/day to seminal vesicles and 2.18 Gy/day to the gland. The total dose is delivered in 33 sessions resulting in 66 Gy and 71.9 Gy for the two structures, respectively. Our 31-patient sample is characterized by the following parameters: mean age, 72.9 (range, 58-83) years; mean pretreatment PSA, 23.5 (range, 4.4 - 93.3) ng/ml and prevalent Gleason score, 6 (3+3) (range, 5-10). *Results:* Acute intestinal (rectal) and urinary toxicity (according to the international RTOG toxicity scale) did not exceed G2 for any of the patients included in the study. For instance, acute urinary toxicity G1 and G2 were found in 46.6% and 23.3% of patients, respectively, while acute intestinal toxicity was G1 and G2 in 60% and 10% of patients, respectively. Late urinary toxicity (medium-term, with a median follow-up of about 1 year) did not exceed G1 (50.4% of patients) and late intestinal toxicity was G1 and G2 in 35.5% and 9.7% of patients, respectively. Only in one patient was significant late rectal toxicity found, namely persistent bleeding and tenesmus, eight months after treatment; however, this patient was 81 years old and had already shown hemorrhoidal syndrome before treatment. A high number of patients surveyed showed erectile dysfunction, but this observation may not be meaningful due to the high mean age of the patients and the wide use of hormonal therapies. The average post-treatment PSA was 0.5 n (range, 0.02-5) g/ml, even though the majority of patients received hormonal therapy. In only two patients was biochemical disease recurrence found and no patient has yet experienced metastatic disease. *Discussion and Conclusion:* Since only mild urinary and intestinal toxicity was found in most cases, considering the absence of distant metastasis and the relatively low relapse rates, treatment exclusively with HT may represent an important therapeutic option in conventional radiotherapy for PCa, as well as being a valid alternative to surgical treatment. Given these encouraging results, we are also setting up a new dose hypofractionation protocol to increase the therapeutic index, while simultaneously reducing the number of sessions. Further studies are warranted in order to establish the clinical relevance of this technique.

102
SINGLE TESTICULAR METASTASIS OF PROSTATIC CANCER

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Background: Prognosis of prostate cancer is mainly determined by metastatic spread. The most common site of these metastatic lesions is bone. The testes are a very rare location for metastasis, especially when this recurrence is isolated. *Case Report:* A 58-year-old patient was diagnosed with prostatic hypertrophy and middle lobe adenoma, with a PSA value of 3.5 ng/ml. In September 2007, the patient underwent adenomyomectomy, revealing an incidental prostate adenocarcinoma with a Gleason pattern score (GPS) of 4+5. For this reason, two months later, a radical prostatectomy and lymphadenectomy (iliac and obturator lymph nodes) were performed. Definitive stage was pT3b (left seminal vessel), R1 (positive margin in prostatic apex), pN0 (0/7) cM0 GPS 5+4, Ki67-MIBI 20%. Before adjuvant radiation therapy, the patient underwent transurethral resection of the bladder neck for urethral stenosis with histological diagnosis of isolated nodular localization (2 mm, radical excision) of prostatic adenocarcinoma GPS 5+4. In March

2008, PSA fell to 0.0 ng/ml. From March 18 to May 6, 2008, the patient was treated with IMRT (rapid Arc, SIB technique), receiving 54.25 Gy to pelvic lymph node areas (1.75 Gy per fraction) and 71.3 Gy to the prostatic lodge (2.3 Gy per fraction). Regular follow-up was performed, with no signs of biochemical or clinical relapse, until November 2010, when PSA rose to 0.61 ng/ml, with a PSA doubling time (DT) of 2 months. All examinations (pelvic MRI, and C-11 choline PET) were negative, but a mass of 1.5 cm was clinically seen in the left testis. Because of suspicion of seminal tumor, a radical orchiectomy was performed on December 15, 2010. Microscopic and immunohistochemical findings showed a prostatic adenocarcinoma, PSA-negative. Postoperative PSA decreased to 0.0 ng/ml one month later. The patient refused adjuvant hormone therapy and a new course of follow-up started. On February15, 2011, the patient was in complete remission and PSA was 0.0 ng/ml. *Conclusion:* The testes are one of the rarest metastatic sites of prostatic adenocarcinoma, with fewer than 100 cases reported in the literature, affecting mainly patients treated with radical prostatectomy. When the lesion is single, its clinical presentation is similar to that of a primary testicular neoplasm. The neoplastic cells may arrive in the testis by retrograde venous extension or arterial embolism, or following the lymphatics of the vas deferens. Vascular change due to surgery may increase these ways of spreading.

1 Janssen S, Bernhards J, Anastasiadis AG and Bruns F: Solitary testicular metastasis from prostate cancer: a rare case of isolated recurrence after radical prostatectomy. Anticancer Res *30(5)*: 1747-1749, 2010.
2 Smaali C, Gobet F, Dugardin F and Pfister C: Testicular metastasis of prostatic cancer. Urology *75(2)*: 249-250. 2010.
3 Deb P, Chander Y and Rai RS: Testicular metastasis from carcinoma of prostate: report of two cases. Prostate Cancer Prostatic Dis *10(2)*: 202-204, 2007.

103
CONTRIBUTION OF TRAP AND FISH APPROACHES TO INCREASING THE DIAGNOSTIC ACCURACY OF BLADDER CANCER IN SYMPTOMATIC PATIENTS

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Background: The importance of urine telomerase activity in detection of bladder cancer has been consistently reported in recent studies (1, 2). However, so far its diagnostic accuracy has mainly been investigated in case–control studies (3). The aim of the present study was to validate its use in symptomatic patients and to analyze the sensitivity and specificity attained by telomerase activity and *in situ* hybridization analysis in comparison to, or in combination with, conventional cytology. *Patients and Methods:* Between 2007 and 2008, 270 consecutive patients [223 males, 47 females; median age 70 (range 28-92) years] who presented with urinary symptoms but with no prior history of bladder malignancy at the Urology Department of Morgagni-Pierantoni Hospital in Forlì were recruited. All patients underwent cytology, cystoscopy and telomerase activity determination by telomerase repeated amplification protocol (TRAP) assay or fluorescence *in situ* hybridization (FISH) analysis. *Results:* Sensitivity was 0.39 for cytology and 0.66 for TRAP, increasing to 0.78 for the combination of cytology and TRAP. Specificity was 0.72 for TRAP, increasing to 0.93 with the combination of TRAP and FISH. All differences in specificity and sensitivity observed for telomerase alone or combined with FISH were statistically significant compared to those of conventional cytology ($p \leq 0.011$). *Conclusion:* The present study provides evidence that TRAP assay and FISH analysis play a potential role in the diagnostic work-up of urinary symptoms. Compared to cytology alone, the combination of cytology, TRAP and FISH provides the best trade-off between the increase in sensitivity and the loss of specificity, especially in non-bleeding patients and in those with low-grade, early-stage cancer. Further research is needed to develop an effective multimodal approach.

1 Bravaccini S, Sanchini MA, Granato AM, Gunelli R, Nanni O, Fabbri C, Amadori D, Calistri D and Silvestrini R: Urine telomerase activity for the detection of bladder cancer in females. J Urology *178(1)*: 57-61, 2007.
2 Casadio V, Bravaccini S, Gunelli R, Nanni O, Amadori D, Calistri D and Silvestrini R: Accuracy of urine telomerase activity to detect bladder cancers in symptomatic patients. Int J Biol Markers *24(4)*: 253-257, 2009.
3 Sanchini MA, Gunelli R, Nanni O, Bravaccini S, Fabbri C, Sermasi A, Bercovich E, Ravaioli A, Amadori D and Calistri D: Relevance of urine telomerase in the diagnosis of bladder cancer. JAMA *294(16)*: 2052-2056, 2005.

104
URETERAL METASTASIS SECONDARY TO ADENOCARCINOMA OF THE PROSTATE: A CASE REPORT

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Background: Ureteral metastasis is rare, arising usually from melanoma, breast cancer and colon cancer (1-4). Only a few cases are described secondary to carcinoma of the prostate (5). *Case Report:* An 80-year-old man, who had a diagnosis of adenocarcinoma of the prostate (cT2N0M0) two years before and undergoing treatment with a luteinizing hormone-releasing hormone analog, was admitted to hospital because of gross hematuria and right renal pain. His PSA value was 5.5 ng/ml. Abdominal ultrasound showed right hydronephrosis, while a computerized tomography scan showed a stone in the lumbar ureter, with only partial obstruction and a stricture about 1-cm long in the ureter below the stone, with no lymphadenopathy. The patient's bone scan was normal. We treated the patient with ureteropyeloscopy and a biopsy was performed of the ureteral stenosis, where an irregular and elevated mass was present. The histological examination revealed clear-cell adenocarcinoma stained positively for PSA. *Discussion:* The case presented had no direct extension of the tumor to the bladder and ureterovesical junction. A metastatic involvement of the ureter with no direct extension of prostatic carcinoma is rare and was probably caused by lymphatic invasion. In the case presented, ureteral metastasis was the only recurrence of the disease.

1 Ferrozzi F, Campani R and Garlaschi G: La tomografia computerizzata nello studio delle metastasi: aspetti e sedi unusuali. Radiol Med *94*: 233-246, 1997.
2 Canossi B, Renzi E and Santini D: Metastasi ureterale da carcinoma mammario lobulare. Radiol Med *90*: 158-160, 1995.
3 Stenner J, Arista-Nasr J, Lenero-Llaca E *et al*: Adenocarcinoma of the ampulla of Vater and head of pancreas metastatic to ureter: report of 2 cases. J Urol *156*: 1765-1766, 1996.
4 Straub B, Muller M, Schrader M *et al*: Recurrent intraluminal ureteral metastasis of a testicular seminoma. J Urol *164*: 443-444, 2000.
5 Jung YJ, Kim HK and Roh YT: Long-standing ureteral metastasis secondary to adenocarcinoma of the prostate after bilateral orchiectomy. J Urol *164*: 1298-1299, 2000.

107
PSEUDOLYMPHOMA OF THE KIDNEY ASSOCIATED WITH HIGH-GRADE BLADDER UROTHELIAL CARCINOMA

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Background: Pseudolymphoma is an inflammatory response that results in a lymphomatous-appearing but benign accumulation of lymphoid cells or histiocytes. It may exhibit histological and, sometimes, clinical features suggestive of malignant lymphoma. Unlike lymphomas, pseudolymphomas usually undergo spontaneous remission. Causes for pseudolymphoma include idiopathy, drugs, contact allergens, photosensitivity, insect bites, scabies and infections. Cases of pseudolymphoma have been reported for the stomach, lung, skin, orbit, salivary gland, tongue, tonsils, larynx and intestines. Immunohistochemical and molecular pathological investigations for B-and T-cell clonality are conventionally used to differentiate between lymphomas and their mimics (1). However, interpretation of clonality studies also poses some difficulties. Clonal B- or T-cell populations have been encountered, in fact, in clearly benign conditions and cannot be considered to be synonymous with malignancy. Here, we report a case of pseudolymphoma of the kidney, associated with a high-grade bladder urothelial carcinoma. To the best of our knowledge, this is the second reported case of pseudolymphoma of the kidney (2) and the first case of such an association. Patient and *Methods:* A 70-year-old man presented at our hospital for the onset of hematuria, back pain and malaise. Personal and family history, physical examination, laboratory data and urinalysis were unremarkable. Ultrasonography revealed a hypoechoic mass in the left kidney associated with an ulcerative lesion of the bladder. Post-contrast computed tomography showed an area of low density in the left kidney. The clinical and radiological diagnosis was bladder and renal cell carcinoma. Accordingly, left radical nephrectomy, ureterectomy, cystectomy, prostatectomy and retroperitoneal lymph node dissection were performed. *Results:* Grossly, the kidney was a firm-to-hard, whitish mass (5-cm in maximum diameter) occupying the renal sinus, the pelvis and the proximal ureter. In the bladder, an ulcerate, firm, grayish lesion of the right wall was observed, infiltrating the bladder wall and the perivesical fat. On microscopy, the kidney lesion consisted of a proliferation of small-to-medium size lymphocytes, mostly $CD20^+$, sometimes arranged in follicular structures with germinal centers associated with plasma cells. Mitotic figures, pleomorphism and nuclear atypia were absent. The bladder lesion was a high-grade flat urothelial carcinoma infiltrating the perivesical fat tissue. An acinar adenocarcinoma with Gleason score 6 was also present in the prostate. GeneScan analyses of multiplex polymerase chain reaction (PCR)-based evaluation of clonal IgH rearrangements showed oligopolyclonal IgH

rearrangement. *Discussion:* This is the second case of pseudolymphoma of the kidney and the first with a complete pathological and molecular characterization. The pathological diagnosis required a differential diagnosis between pseudolymphoma and malignant lymphoma. We stress that a definite diagnosis cannot be made based only on the clinical and radiological data because there are no characteristic findings. Instead, pathological analysis of the tissue lesion is necessary, reaching a strict correlation between morphology, immunohistochemistry and molecular biology. In particular, GeneScan analyses of multiplex polymerase chain reaction-based rearrangement of IgH seem to be necessary to avoid potential pitfalls in the diagnosis of lymphoid proliferations.

1 Holm N, Flaig MJ, Yazdi AS and Sander CS: The value of molecular analysis by PCR in the diagnosis of cutaneous lymphocytic infiltrates. J Cutan Pathol 29: 447-452, 2002.
2 Hozumi F, Yoshihiro I, Youji N and Riichiro T: Pseudo-lymphoma of the kidney: a case report. J Urol *153*: 387-388, 1995.
3 Boer AR, Bresch M and Falk TM: Pseudoclonality in cutaneous pseudolymphomas: a pitfall in interpretation of rearrangement studies. Br J Dermatol *159*: 394-402, 2008.

111
PELVIC UROTHELIAL CARCINOMA WITH NESTED GROWTH PATTERN AND AN UNCOMMON CLINICAL PRESENTATION

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Background: Nested variant of urothelial carcinoma (NVUC) is a rare and often unrecognized urothelial neoplasia with a reported prevalence of 0.3% (1) and male predominance. Hematuria is the most common clinical presentation, while other symptoms are increased urinary frequency and dysuria (2). The diagnosis is based only on morphology and there are no reported immunohistochemical or cytogenetic differences distinguishing this entity from usual high-grade urothelial carcinoma. *Patients and Methods:* A 49-year-old woman affected by HCV hepatitis presented with fever, vague cystitic symptoms and hypertension. Computed tomography showed a sclerosing inflammatory process involving the connective and adipose tissue of the renal sinus. In the absence of renal or pelvic masses, an underlying malignancy was excluded and renal abscess or tuberculosis were suspected. Renal scintigraphy indicated the loss of left kidney function. Accordingly, nephrectomy and proximal ureterectomy were performed. After the nephroureterectomy, the patient recovered from hypertension and dysuria. Two months later, distal ureterectomy was performed. *Results:* Grossly, calices, renal pelvis and pyelo-ureteral junction appeared modestly dilated, with whitish, thickened and uneven mucosa. Microscopically, the urothelial lining of the renal pelvis and the pyelo-ureteral junction were spared. The subepithelial connective tissue, the fibromuscular layer and the renal sinus fat were diffusely infiltrated by small nests composed of medium-to-large urothelial cells with abundant eosinophylic cytoplasm and slightly atypical nuclei. Differential diagnosis included cystic ureteritis, von Brunn nest, collecting duct renal carcinoma and paraganglioma. Immunohistochemically, the cells showed diffuse and intense expression of p63, while they were negative for chromogranin and synaptophysin. On the basis of the morphological and immunohistochemical features, the diagnosis of NVUC was made. The distal tract of the ureter was unremarkable. *Conclusion:* We reported a case of upper urothelial tract NVUC, underlining the clinical and pathological diagnostic difficulties that can delay the diagnosis of such aggressive and potential deadly neoplasia. In fact, neither the symptomatology, nor imaging or scintigraphy were helpful in the diagnosis that was incidental during the management of a suspicious pyelonephritis and nephrovascular hypertension.

1 Holmang S and Johansson SL: The nested variant of transitional cell carcinoma – a rare neoplasm with poor prognosis. Scand J Urol Nephrol *35*: 102-105, 2001.
2 Dundar E, Acikalin MF and Can C: The nested variant of urothelial carcinoma: an aggressive tumor closely simulating benign lesions. Pathol Oncol Res *12*: 105-107, 2006.
3 Ooi SM, Vivian J, Sinniah R and Troon S: Nested variant of urothelial carcinoma: A rare presentation. Urology *67(4)*: 845.e3-5, 2006.

113
THE ROLE OF IMAGE-GUIDED RADIOTHERAPY IN PREVENTING URINARY AND RECTAL TOXICITIES IN PATIENTS WITH PROSTATE CANCER TREATED WITH RADIOTHERAPY

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Aim: To evaluate acute urinary and rectal toxicities in patients with prostate cancer submitted to image-guided radiotherapy (IGRT). *Patients and Methods:* From June 2009 to March 2010, 29 patients (median age: 70 years, range: 48-82 years; median Gleason score: 7, range: 5-10) underwent radical radiotherapy and 12 patients (median age: 67 years, range: 54-78 years; median Gleason score: 7, range: 5-9) underwent adjuvant radiotherapy. All patients underwent simulation computed tomography (CT) without contrast injection in supine position. The CT scans were used to delineate the organs at risk, namely bladder, rectum, coxo-femoral joints and penis bulb. For patients receiving radical radiotherapy, the seminal vesicles were excluded at an absorbed dose of 66 Gy. For this group of patients, the total delivered dose was 74 Gy, while for patients who underwent adjuvant radiotherapy, the total delivered dose was 66 Gy. The planning target volume (PTV) was obtained from the expansion of the clinical target volume (CTV) by 8 mm anteriorly, laterally and caudally, 10 mm cranially and 5 mm posteriorly. The isocenter position-check protocol was performed with the use of MV cone-beam CT on the first, second and third day, successively, once a week. Correct positioning was evaluated using the bone structures of the pelvis as reference. Corrections of isocenter position were made with a semi-automatic modality. Acute urinary and rectal toxicities were evaluated administering IPSS before radiotherapy, during the weekly clinical examinations and at the end of the radiotherapy. At the same time, we used the RTOG scale for acute and late adverse events to evaluate toxicities. We also calculated the median error of isocenter position indicated by virtual simulation and cone-beam existing in the left-right (L-R), cranial-caudal (C-C) and anterior-posterior (A-P) directions. *Results:* At the end of IGRT, we found a median IPSS score of 8 (range: 0-14) for the 12 patients treated with adjuvant radiotherapy; 50% of patients had IPSS scores between 0-7. The worst scores corresponded to the first, fourth and seventh questions. In addition, we recorded prevalent G1 rectal toxicity and G2 urinary toxicity at end of treatment. In the group of patients who underwent radical radiotherapy, the median IPSS score at the end of treatment was 9 (range: 1-28) and 58.6% of patients had IPSS scores between 0-7. The worst scores corresponded to the second and seventh questions. There was prevalent G1 rectal toxicity and G2 urinary toxicity in 93.1% and 44.8% of patients, respectively, at the end of treatment. At the last follow-up (March 2010), in both groups, rectal and urinary toxicities were G0, while IPSS scores between 0-7 were observed in 82.6 and 100% of patients in the radical and adjuvant radiotherapy groups, respectively. Median values of L-R, C-C and A-P directions were 3, 2 and 3 mm, respectively. In order to match precision and workload criteria, thresholds for the standard deviation of the corrections were set as: 2.96, 3.78 and 2.78 mm in the L-R, C-C and A-P directions, respectively. *Conclusion:* Treatment was well tolerated. We observed low toxicity rates and a high compliance to treatment. IGRT, performed for first fractions, may be helpful for eliminating gross systematic errors, especially after virtual simulation.

114
TOTAL INTRAVENOUS ANESTHESIA (TIVA), TARGET-CONTROLLED INFUSION AND DA VINCI ROBOT-ASSISTED PROSTATECTOMY

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Background: Robotic prostatectomy provides a prolonged Trendelenburg position of about 40° and CO_2 pneumoperitoneum for surgical exposure with potential significant changes in hemodynamic and respiratory parameters for the patient, such as the rising of central venous pressure (CVP) and pulmonary capillary wedge pressures. CVP measures the filling pressure of the right ventricular volume and gives an estimate of the intravascular volume status and the interplay of the circulating blood volume venous tone. Measuring CVP is widely considered a useful aid in the management of a patient's fluid status during surgery. Target-controlled infusion (TCI) is a total intravenous anesthesia (TIVA) technique that maintains constant plasma and effect-site concentrations of anesthetic agents due to the pharmacokinetic models incorporated in the TCI pump. The precise dosing of the anesthetic drugs leads to superior hemodynamic stability and fast recovery after surgery for patients. The use of propofol/remifentanil TIVA-TCI in combination tends to have a synergistic action and the rate of equilibration between blood and effect-site depends on cardiac output, central blood volume, cerebral blood flow, lipid solubility and degree of ionization of drug. We evaluated TIVA-TCI of propofol and remifentanil and hemodynamic and respiratory parameters during Da Vinci robot-assisted prostatectomy. *Patients and Methods:* In our retrospective study, we evaluated 15 consecutive patients scheduled for robot-assisted endoscopic radical prostatectomy in TIVA-TCI with non-invasive monitoring of arterial blood pressure, heart rate, pulse oximetry, end-tidal (ET) CO_2, peak and plateau airway pressure and state entropy (SE), assessing anesthetic depth and continuous invasive CVP on a S/5 Datex-Ohmeda monitor. Accurate measurement of CVP was obtained with cannulation of the internal jugular vein. The depth of anesthesia was obtained with TIVA-TCI in propofol/

remifentanil combination and cisatracurium as muscle relaxant and was maintained at 40-60 SE. We maintained ET CO_2 at 30-40 mm Hg by ventilation. Observations were continued until the end of surgery and early postoperative period. *Results:* The respiratory plateau pressure gradually increased from 15 (±4) to 28 (±5) cm H_2O and CVP was up to 24 (±4) mmHg. Target effect-site concentrations for propofol (1.9-2.3 μg/ml) and remifentanil (4.3-6.2 ng/ml) were less than those predicted to maintain adequate SE during surgery. No conscious awareness was detected. The parameters evaluated by Aldrete's score in the early postoperative recovery period returned to the normal clinical range for all patients. Two cases of periorbital and facial edema required intravenous central line infusion of 18% mannitol (100 ml bolus) without significant changes of clinical signs. There was only one case of cognitive and behavioral disorder seven days after surgery. *Discussion and Conclusion:* Pneumoperitoneum and head-down position increase filling pressures, without any clinical effect on cardiac performance but have significant effects on the pharmacokinetics of propofol and remifentanil, thus reducing target concentrations in comparison with other surgical procedures. TCI is effective in inducing a good anesthetic effect, maintaining hemodynamic and respiratory stability and ensuring rapid recovery.

1 Kalmar AF *et al*: Influence of steep Trendelenburg position and CO_2 pneumoperitoneum on cardiovascular, cerebrovascular and respiratory homeostasis during robotic prostatectomy. Br J Anaesth *104(4)*: 433-439, 2010.

2 Wang LP *et al*: Low and moderate remifentanil infusion rates do not alter target-controlled infusion propofol concentrations necessary to maintain anesthesia as assessed by bispectral index monitoring. Anesth Analg *104(2)*: 325-331, 2007.

115
SIMULTANEOUS INTEGRATED BOOST RADIOTHERAPY IN HIGH-GRADE PROSTATE CANCER: RESULTS OF TOXICITY WITH IGRT

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Background: In the past decades, three-dimensional conformal radiotherapy (3D-CRT) has become the standard treatment technique for prostate irradiation. There is now growing evidence supporting the benefit of hypofractionated and intensity-modulated radiation therapy (IMRT) with simultaneously integrated boost (SIB). *Patients and Methods:* At our institution between November 2009 and January 2011, we treated 27 patients with high-risk prostate carcinoma (T3 or Gleason score >8 or PSA >20 ng/ml). The median age was 73 (range, 67–82) years. Median PSA at diagnosis was 10.5 (range 3.89-45.4) ng/ml. Stage was cT1c in 1/27 (3.7%) patients, cT2a in 1/27 (3.7%), cT2b in 5/27 (18.5%), cT2c in 1/27 (3.7%), cT3a 8/27 (29.6%) and cT3b in 11/27 (40.7%) patients. Gleason score was 6 in 7/27 (25.9%) patients, 7 (3+4) in 8/27 (29.6%) and 8 in 12/27 (44.4%) patients. All patients underwent a simulation computed tomography (CT) scan with 2.5 mm slice thickness to execute 3D conformal planning. They were immobilized with a footlocker in supine position. Half an hour before the CT scan, all patients urinated and drank 0.5 l of water. Magnetic resonance imaging scans were fused with the planning CT scan for all patients to help delineation of the clinical target volume (CTV). Subsequently, the patients were submitted to image-guided radiation therapy (IGRT) for implementation of linear accelerator with on-board imaging system. CTV1 included the pelvis, CTV2 included the seminal vesicles and CTV3 included only the prostate. The margins for the planning target volume (PTV) were 5 mm in all directions. All patients were submitted to IMRT developed with the Eclipse System. All patients underwent additional neoadjuvant hormonal therapy, concomitant with adjuvant radiotherapy for a total of nine months, starting three months before radiotherapy with anti-androgen (bicalutamide 150 mg) in 13/27 (48.14%) patients and LHRG analog in the remaining 14/27 (51.85%) patients. Radiation was delivered in 25 fractions in total, with 4 fractions per week. The total radiation dose was 45 Gy to the pelvis (1.8 Gy per fraction), 55 Gy to PTV2 (2.2 Gy per fraction) and 68.75 Gy to PTV3 (2.75 Gy per fraction). All patients were monitored during treatment daily with a portable imaging system equipped with a cone-beam kilovoltage CT. All patients were visited once a week during treatment, one month after the completion of radiotherapy and every three months during follow-up. *Results:* Median follow-up for all patients was 6 (range 2-12) months. We considered acute toxicity, in particular, because of the shortness of follow-up, although we did not observe any late effects in patients with a follow-up longer than three months. We observed only acute grade 1 genitourinary toxicity in 3/27 (11.1%) patients during treatment and after one month from radiation therapy. Regarding gastrointestinal toxicity, two patients (7.4%) presented grade 1 and 2 diarrhea, cured with medical therapy. During the follow-up period, no patients experienced worsening of their symptoms. *Discussion and Conclusion:* Technological progress enables the implementation of new technologies such as IMRT and IGRT. IMRT is capable of minimizing the volume of normal tissue irradiated, notably reducing acute radiation-induced toxicity in patients.

116
IS BIOPTIC DIAGNOSIS OF LOW-RISK PROSTATE CANCER REAL? SINGLE-CENTER EXPERIENCE

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Background: Clinically insignificant prostate cancer defined as cT1c stage, Gleason score ≤6, PSA ≤10 ng/ml, and tumor volume ≤0.5 mm is characterized by limited biologic malignancy and is, possibly, suitable for non-radical treatment. The purpose of this study was to perform a retrospective analysis of the outcome of patients with clinically insignificant prostate cancer, who underwent radical prostatectomy, in order to assess the predictors of cancer-related outcome. *Patients and Methods:* From January 2004 to December 2010, we performed 958 retropubic radical prostatectomies. Among these patients, 111 (12%) had clinically insignificant prostate cancer according to the biopsy criteria. Biopsy and specimen Gleason score, prostate biopsy sampling (standard *vs.* saturation), pathological stage, extraprostatic involvement and surgical margin status were evaluated. During follow-up, the patients had semiannual PSA test and clinical evaluation. *Results:* A total of 89 patients (80%) had clinically significant prostate cancer in the prostatectomy specimen, with 81% of the patients having organ-confined disease. Gleason score was 6 in 66% of the cases. Surgical margins were positive in 21 cases (19%) and extraprostatic involvement occurred in 21 cases (19%). Concordance between biopsy and specimen Gleason score was limited, with clinical undergrading occurring in 49 cases (44%), regardless of the biopsy scheme. The median follow-up duration was 38 months. At follow-up, extraprostatic extension and surgical margin status were independent predictors of biochemical recurrence-free survival (p=0.008). *Discussion and Conclusion:* The risk of overtreatment in patients with prostate cancer ranges from 0 to 48% according to literature data. As yet, major variables predictive of clinically insignificant prostate cancer are not available. In our experience, only 20% of patients undergoing radical prostatectomy for clinically insignificant prostate cancer had clinically insignificant cancer in the prostatectomy specimen, whereas in 19% of the cases, a high-risk disease was found. Although low-risk prostate cancer does exist, predictive variables allowing such patients to be identified are still lacking. The risk of overtreatment is present but currently counterbalanced by the risk of undertreatment.

117
HYPOFRACTIONATED RAPIDARC™ INTENSITY-MODULATED RADIOTHERAPY FOR POSTOPERATIVE OR SALVAGE TREATMENT OF PROSTATE CARCINOMA

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Aim: To assess the feasibility and acute toxicity of a mildly hypofractionated intensity-modulated radiotherapy (IMRT) treatment for prostate cancer in a postoperative or salvage setting, delivered to the prostatic bed and, in selected cases, pelvic lymph nodes, using a Linac with recently implemented RapidArc™ technology, Trilogy™ – Varian (RA-IMRT). *Patients and Methods:* Between January 2010 and December 2010, 70 prostate cancer patients (median age: 68 years, range: 54-79 years; median GS score: 7; median iPSA: 8.5 ng/ml) were treated in a postoperative (45 patients) or salvage setting (25 patients) after an open (42 patients), laparoscopic (3 patients), or robotic prostatectomy (24 patients). Pelvic radiotherapy (RT) was added in cases of pN1 or cN0/pNx, if the estimated risk of lymph node involvement was >30%, calculated on pre- and/or postoperative data using the available online Memorial Sloan–Kettering Cancer Center nomogram, RA-IMRT was delivered using a mildly hypofractionated schedule. The prescription dose to the prostate bed was 2.2 Gy per fraction ×30 fractions totaling 66 Gy (equivalent to 69 Gy, according to the linear quadratic model with alpha/beta ratio of 1.5 Gy) in cases of undetectable postoperative PSA, or 2.2 Gy per fraction ×31 fractions totaling 68.2 Gy (equivalent to 72 Gy), or 2.3 Gy per fraction ×30 fraction totaling 69 Gy (equivalent to 75 Gy) in cases of detectable postoperative PSA or salvage therapy. In cases of pelvic lymph-node therapy, the simultaneous integrated boost (SIB) approach was employed and a dose of 1.7 or 1.8 Gy per fraction ×30 fractions totaling 51-54 Gy was delivered to the N0 or N+ sites, respectively. Patients were invited to have a full bladder (drinking 0.5 l of water 1 h before each RA-IMRT session) and empty rectum and were treated in the supine position, with legs immobilized with a Combi-Fix™ device. The clinical target volume (CTV) for the tumor (CTV-T) included the prostatic bed only. The

margins of CTV-T to the planning target volume (PTV) for the tumor, PTV-T, were 10 mm in all directions, except for the posterior direction, where they were 5 mm, and the prostatic bed plus pelvic lymph nodes volume; this CTV-N volume was encompassed within an 8-mm margin (avoiding bone, bladder, muscle and mesorectum). An additional 5-mm margin expansion was added to create the respective PTV-N volume. Dose–volume histograms (DVHs) were elaborated for the organs at risks (urinary bladder, rectum, anal canal, peritoneal cavity, penis, penile bulb, testicles and femoral heads) and considered for each RA-IMRT plan according to the institutional DVH constraints. Target localization was performed with cone-beam CT for the first three RA-IMRT sessions and weekly thereafter. An institutional action level protocol was applied to correct daily errors in the set-up due to organ motion. *Results:* All but one patient completed the RA-IMRT course with a median total treatment time of 43 (range: 36-66) days. For one patient, the treatment was stopped due to deterioration of his general condition after 27 out of 30 fractions. Median RA-IMRT session duration was 10 min, with a median beam-on time of 2.5 min. Acute toxicity was low and included G1 genitourinary events in 19 patients (27.1%), G2 events in 5 patients (7.1%) and G3 events in 1 patient (1.4%); and G1rectal events in 27 patients (38.6%), G2 events in 2 patients (2.9%) and G3 events in 1 patient (1.4%). No acute G4 events were observed. Treatment interruptions due to toxicity were registered in two cases, one due to cystitis and the other due to fecal urgency and mucous discharge. In seven cases, treatment interruption occurred due to technical problems. *Conclusion:* The mildly hypofractionated RA-IMRT in a postoperative or salvage setting for prostate cancer patients seems a feasible approach, with an excellent acute toxicity profile and high patient compliance. Longer follow-up periods and higher patient numbers are warranted in order to verify the long-term outcomes of the RA-IMRT technique.

118
ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY IN A CENTER WITH LOW VOLUME OF CASES: OUR EXPERIENCE

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Background: We assessed the outcomes of robot-assisted laparoscopic prostatectomy (RALP), including the learning curve, in the setting of a single center with a low caseload. *Patients and Methods:* A total of 42 consecutive patients underwent RALP between September 2007 and 2011, carried out by a single experienced surgeon, an expert in open surgery but with no experience of pure laparoscopic prostatectomy. All patients had histologically confirmed prostate adenocarcinoma. A three-arm Da Vinci robot was employed. We prospectively evaluated the baseline patient and tumor characteristics, the perioperative parameters and the early surgical, functional and oncologic outcomes, with up to four years of follow-up. *Results:* The first three cases were mentored by a surgeon trained in robotic surgery. The mean age of patients was 64 years. Mean preoperative PSA was 7.35 ng/ml and median Gleason sum was 6 (range, 5-8). Clinical stages were: T1c (79%), T2a (14%), T2b (2%) and T2c (2%). The mean operative time did not decrease below four hours until the first 30 cases. The mean hemoglobin decrease was 2.93 g/dl. Three patients required blood transfusions. There were no major complications and no conversions to open surgery. The mean hospital stay was 6.6 days. On average, the patients were required to maintain the bladder catheter for ten days. Pathological stages were: T2a (7%), T2b (2%), T2c (51%) and T3a (39%). Mean postoperative Gleason sum was 7 (range, 6-9). Overall, the rate of positive surgical margins (PSM) was 18.6%, while stage-specific PSM rates were 14% and 37% for T2c and T3a, respectively. Mean postoperative PSA after one month was 0.06 ng/ml. Biochemical recurrence was recorded in four patients, with a mean time to biochemical recurrence of four months. Fourteen patients regained early continence within three months, while ten patients needed only one pad/day. At 12 months of follow-up, 63.8% of patients were fully continent. Fifteen patients underwent either bilateral or monolateral nerve-sparing RALP. Of them, 66% regained partial or full potency at one year of follow-up, after sexual rehabilitation. Pelvic lymphadenectomy was performed in eight cases, with a mean of ten lymph nodes removed. *Conclusion:* Notwithstanding the low caseload and the inclusion of the learning curve cases, RALP allowed acceptably good oncologic and functional outcomes. The main drawback of the low number of procedures is reflected in the operative time, which did not decrease below four hours until after the first 30 cases.

119
HYPERLIPIDEMIA DURING SUNITINIB ADMINISTRATION IN PATIENTS WITH MRCC

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Background: Sunitinib malate is a tyrosine kinase inhibitor currently approved for the treatment of metastatic renal cell carcinoma (mRCC). Hyperlipidemia is not reported among patients on sunitinib; however, it may induce a hypothyroid

state, possibly causing an increase of serum lipids. Here, we describe the incidence and severity of hypertriglyceridemia and hypercholesterolemia in a cohort of patients receiving sunitinib for mRCC. *Patients and Methods:* Between July 2008 and November 2010, we prospectively evaluated serum triglycerides and cholesterol (expressed as total serum cholesterol, LDL and HDL cholesterol) in 25 patients receiving sunitinib for mRCC (50 mg daily, according to the classic 6-week schedule). The median patient age was 62.9 years. On average, the patients received sunitinib for 7.2 cycles (range, 2-22). Serum lipids were measured before the beginning of treatment and at the end of each sunitinib 'ON' period. Thyroid function was also measured at each cycle. *Results:* At baseline, the median serum level of triglycerides was 141.78 mg/dl (±22, 95% confidence interval (CI)) and the median serum total cholesterol was 196.8 mg/dl (±21.8, 95% CI). Three patients presented mild hypercholesterolemia before the beginning of treatment; in one of them, this was associated with hypertriglyceridemia. During sunitinib administration, 16 patients (64%) presented an elevation of serum lipids. These abnormalities usually developed within 2 cycles (range, 1-3). In these patients, a maximum increase of median triglycerides and cholesterol of 160% and 36.1%, respectively, was observed. Patients who developed hypercholesterolemia presented an increase of both HDL and LDL cholesterol. We did not observe a relationship between hyperlipidemia and a hypothyroid state. Considering all patients on sunitinib, median serum triglyceride levels were 237.57, 208.27 and 277.22 mg/dl at the second, fourth and sixth cycle, respectively, showing a relative increase from baseline of 67.7, 46.9 and 95.6%, respectively. The median serum cholesterol levels were 214.1, 205.8 and 216.1 mg/dl at the second, fourth and sixth cycle, respectively, showing a relative increase from baseline of 8.7, 4.5 and 9.8%, respectively. *Conclusion:* An elevation of serum triglycerides and cholesterol developed in a high percentage of patients on sunitinib. This is a side-effect commonly described with the use of mTOR inhibitors, which are prescribed sequentially to sunitinib in mRCC patients. Therefore, an elevation of triglycerides and cholesterol may persist for a long time in these patients. However, whether this phenomenon may have consequences, especially on the cardiovascular system, is not yet known. We recommend careful monitoring of serum triglycerides and cholesterol of patients on sunitinib, and more extensively so during the treatment of mRCC, especially considering possible consequences on the cardiovascular system.

120

TKI-INDUCED CARDIOTOXICITY IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA: A MANAGEABLE ADVERSE EVENT

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Background: Cardiovascular events (CVE), namely congestive heart failure (CHF) and coronary artery disease (CAD), may occur in up to 10% of patients treated with tyrosine kinase inhibitors (TKI). CVE recognition, TKI interruption and appropriate therapy based on ACE inhibitors and/or β blockers, are the only effective treatment for this severe complication. Cardiovascular monitoring during TKI treatment may underline early signs of myocardial damage. *Patients and Methods:* We prospectively analyzed patients receiving sunitinib or sorafenib as first-line treatment for metastatic renal cell carcinoma (mRCC). Between April 2009 and January 2011, a total of 21 patients (median age: 69 years, range: 50-82 years) were treated with either sunitinib (19 patients, 90%) or sorafenib (2 patients, 10%) as first-line treatment. The median duration of treatment was 6.4 (range, 22.5-0.3) months. All patients were analyzed for CAD risk factors, hypertension, rhythm disturbances and heart failure. ECG, echocardiography and cardiology consultation were performed at baseline and after three and six months of TKI treatment. We prospectively recorded the following patient features: cardiovascular history, blood pressure, NYHA class, renal function and antihypertensive therapy. *Results:* At baseline, we found 16 patients (76%) with hypertensive disease (HD). On TKI therapy, the pre-existing HD in 13 of these patients worsened and was controlled with adequate medical treatment which did not cause a discontinuation of TKI therapy. Furthermore, 4 patients (19%) developed HD. In 9 out of 21 patients (42.8%), there was reduction of left ventricular ejection fraction (LVEF) (median ≥10%) compared to the baseline value (p=0.003). Eight patients (out of 21) were asymptomatic and only one presented symptoms of CHF and discontinued the treatment. This patient had global myocardial hypokinesia at echocardiography. Paradoxically, in five patients (23%) we observed an increase of LVEF after treatment. The median baseline LVEF was 66% (range: 55-85%), while the median LVEF on treatment was 60% (range: 45-77%); this difference was not statistically significant. Six patients (28%) showed ECG changes (in the ST segment and T-wave), while 15 patients (72%) had a stable ECG. *Conclusion:* Cardiac damage in TKI-treated patients with mRCC is often underestimated; however, it is manageable with careful cardiovascular monitoring and cardiac treatment at first signs of myocardial damage. Only the early identification and treatment of patients at risk of developing

CHF may reduce this adverse event and TKI treatment discontinuation.

121
RE-CHALLENGE WITH DOCETAXEL IN PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER: ASSESSMENT OF PREDICTIVE FACTORS OF RESPONSE

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Background: Responders to first-line docetaxel (DOC) therapy, who have stopped the treatment in the absence of progression, usually experience disease progression within a few months. In recent years, re-challenge (ReC) with DOC has emerged as a therapeutic option for these patients, who are able to achieve a response again. In clinical practice, the possibility of obtaining a new response by DOC ReC may be considered on the basis of the response to the previous treatment. The available data usually report on the clinical outcome of patients who have received one or two ReCs, but it is unclear whether more ReCs may be offered to these patients and whether there are additional factors that allow patients who may respond to ReC to be identified. *Materials and Methods:* From March 2002 to December 2010, a consecutive series of 45 patients with castration-resistant prostate cancer received at least one ReC after first-line DOC, for a total of 91 ReC courses (median 2, range 1-7). ReCs consisted of 4-6 DOC cycles and were proposed until the appearance of a true resistance to DOC: we considered DOC-resistant patients to be those showing a clinical and/or biochemical progression during DOC treatment. For each ReC course, the following parameters were recorded: treatment schedule (three-week *vs*. one-week interval), estramustine use (yes *vs*. no), PSA response (>50% reduction) at the previous DOC course, baseline parameters (hemoglobin, alkaline phosphatase, pain presence, ECOG PS), number of previous DOC courses, PSA parameters (slope log, doubling time, velocity) during both previous DOC course and treatment 'holiday', duration of treatment 'holiday' before ReC. A binary logistic regression analysis was applied. Continuous variables were categorized by quartiles and chosen for the initial model after a univariate chi-square analysis. *Results:* A PSA reduction >50% was observed in 67% of 91 ReCs. After a median follow-up of 25 months, the median survival was 32 months and the estimated two-year overall survival was 77.5%. In our experience, multiple ReCs were well tolerated, with no more than grade 1-2 hematological and non-hematological toxicities. Having an interval log-PSA ≥0.62 (exp(beta) 8.965; p=0.020), an interval from the previous cycle ≥23 weeks (exp(beta) 8.212; p=0.002), and a response to the previous cycle (exp(beta) 7.658; p=0.014) were independently predictive of a response to ReC. *Conclusion:* In our experience, multiple DOC ReCs may be administered to DOC-sensitive patients with castration-resistant prostate cancer. This may provide long-term disease control, with a remarkable survival rate, and allow second-line treatment to be delayed until the appearance of true DOC resistance. Response to the previous cycle, interval log-PSA ≥0.62 and an interval from the previous cycle of at least 23 weeks are factors able to identify those patients having more probability of responding to ReC.

122
COMPARISON OF INTENSITY-MODULATED RADIOTHERAPY AND TWO DYNAMIC ARC TECHNIQUE FOR PROSTATE CANCER: ACUTE AND LATE TOXICITY

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Background: To evaluate acute and late gastrointestinal (GI) and genitourinary (GU) toxicity during intensity-modulated radiotherapy (IMRT) and two-dynamic arc (2DA) therapy for treatment of adenocarcinoma of the prostate. *Patients and Methods:* Sixty patients with non-metastatic cancer were included in the study: 30 patients were treated with IMRT and 30 patients were treated with 2DA. The total dose was 80 Gy in 40 fractions over eight weeks. Dose–volume histograms (DVHs) were computed and DVHs of planning target volume (PTV), rectum, urinary bladder and femoral heads were evaluated. Doses given to 50% bladder (V50), to 30% of rectum (V30), to 60% of rectum (V60) and to 50% of femoral head (V50) were reported as a percentage of the total dose. Toxicity was scored according to the Radiation Therapy Oncology/European Organization for Research and Treatment of Cancer criteria. *Results:* With a median follow-up of 14 months, acute grade 1 (GI) toxicity occurred in 12 patients (40%) and in 11 patients (36.6%) under treatment with IMRT and 2DA, respectively, while acute grade 2 toxicity occurred in 10 patients (33.3%) and in 9 patients (30%), respectively.

Acute grade 1 (GU) toxicity occurred in 8 patients (26.6%) and in 7 patients (23.3%), respectively. Acute grade 2 (GU) toxicity occurred in 5 patients (16.6%) using both techniques. Acute grade 3 GI and GU toxicity was absent. Grade 1 late toxicity occurred in 13.3% (4 patients) and 10% (3 patients) for GI and GU with IMRT and 2DA, respectively. Late grade 2 GI and GU toxicity was absent. *Conclusion:* We concluded that there is no difference in acute and late GI and GU toxicity comparing IMRT and 2DA. The evaluation of response by PSA decrement was the same for both techniques.

123

ACUTE AND LATE TOXICITY IN 762 PROSTATE CANCER PATIENTS TREATED WITH CONFORMAL DYNAMIC ARC RADIOTHERAPY

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Background: To evaluate acute and late gastrointestinal (GI) and genitourinary (GU) toxicity in 762 prostate cancer patients treated with conformal dynamic arc radiotherapy. *Patients and Methods:* We reviewed 762 patients that were diagnosed with prostate cancer between 2004 and 2010. Of these patients, 502 and 260 received definitive or postoperative radiotherapy, respectively. All patients underwent radiotherapy with two conformal dynamic arc technique. Toxicity was scored according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer Criteria (RTOG-EORTC). *Results:* A total of 762 were analyzed. The median age was 65 (range 59-82) years. A total of 502 patients underwent definitive radiotherapy (mean dose 78 Gy), while 260 patients underwent postoperative radiotherapy (mean dose 72 Gy). Median follow-up time was 52 (range 24-75) months. Acute GU toxicity was G0 in 450 patients (59%), G1 in 200 patients (26.25%), G2 in 112 patients (14.7%), and was greater in patients who underwent surgery. Acute GI toxicity was G0 in 270 patients (35.4%), G1 in 250 patients (32.8%), G2 in 152 patients (19.9%) and G3 (90 patients: 11.8%). Late GU toxicity was G0 in 508 patients (66.7%), G1 in 202 patients (26.5%) and G2 in 52 patients (6.8%). Late gastrointestinal toxicity was G0 in 455 patients (59.7%), G1 in 182 patients (23.9%) and G2 in 125 patients (16.4%). The severity of acute toxicity (grade 2 or greater) was predictive of the severity of late toxicity for both rectal and urinary events. *Conclusion:* Conformal dynamic arc radiotherapy is associated with low rates of severe GU and GI toxicity after treatment for prostate cancer.

124

LATE BLADDER METASTASES FROM COLON ADENOCARCINOMA PRESENTING WITH SEVERE HEMATURIA

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Background: Metastasis to the bladder from distant organs is rare (1), but any adenocarcinoma of the bladder should raise suspicion of a distant primary cancer. We report a case of bladder metastasis from a sigmoid adenocarcinoma four years later. *Patients and Methods:* In February 2010, a 65-year-old woman came to our observation for uncontrolled massive hematuria. In September 2006, she had undergone laparoscopic assisted sigmoidectomy for sigmoid cancer. Pathological examination revealed the presence of a colonic adenocarcinoma, stage pT1 N1 G2. One cycle of chemotherapy was started, but was stopped immediately due to adverse reaction. Because of severe hemorrhagic anemia, the patient underwent an emergency cystoscopy. At cystoscopy, blood clots were evacuated, and a large base 4×2 cm, non papillary, white-gray mass with focal hemorrhagic area was seen on the urothelium of the anterior wall and the fundus of the bladder. The histology showed tubular and pseudoglandular structures, intermixed with solid foci of mucin-producing signet-ring cell type adenocarcinoma, partially covered by an intact urothelium. The malignant cells were very similar to the original colon cancer, showing positive staining for cytokine CK20 but no staining for CK7. The patient was stable, voided spontaneously without hematuria, and was followed-up closely for four weeks. There were small-volume intermittent bleeding episodes during this time period. The patient returned for CT evaluation for the purpose of staging. This revealed a large mass with a heterogeneous and multilobulated appearance, 4×5×5 cm in diameter, invading the bladder and probably originating from the ileum. Based on the patient's clinical history and evaluation, it appeared safest to proceed with open surgical resection. The tumor was identified only on the exterior of the bladder dome without any intestinal involvement. The lesion was circumscribed and resected while maintaining a safe margin. Postoperative course was uneventful and the patient underwent oncologist evaluation. Postoperative chemotherapy was given, but three months afterwards abdominal and thoracic CT showed recurrent disease in the bladder and multiple lung metastases. *Discussion and Conclusion:* There are no consistent epidemiological data in the literature regarding secondary bladder tumor. Bates *et al*. studied 5533 surgical specimens and 756 autopsy specimens of bladder cancer and reported 2.3% cases of metastatic involvement in

the surgical specimens and 20.2% in the postmortem cases. Tumors can metastasize to the bladder by direct spreading or by means of hematogenous or lymphatic spread (2). In one study, approximately 54% of metastases from bladder cancer were located near the bladder neck and trigone areas, however, metastatic colon cancer commonly involves the fundus (3). The treatment of secondary bladder cancer can be performed by an open or transurethral resection, and/or by a combination of chemo- and radiotherapy. However, due to the rarity of these conditions and to the lack of any large series comparing the various surgical options, the optimal treatment is unclear. The possibility of metastasis should be considered in patients with a history of colonic adenocarcinoma who present with adenocarcinoma of the bladder. The use of an immunohistochemical panel is recommended to differentiate between primary and metastatic tumors (3).

1 Kobayashi T, Kamoto T, Sugino Y, Takeuchi H, Habuchi T and Ogawa O: High incidence of urinary bladder involvement in carcinomas of the sigmoid and rectum: a retrospective review of 580 patients with colorectal carcinoma. J Surg Oncol *84(4)*: 209-214, 2003.
2 Bates AW and Baithun SI: Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumors: clinicopathological and histological features of 282 cases. Histopathology *36(1)*: 32-40. 2000.
3 Velcheti V and Govindan R: Metastatic cancer involving bladder: a review. Can J Urol *14(1)*: 3443-3448, 2007.

125

SETUP ACCURACY WITH THE USE OF CBCT IMAGE-GUIDED RADIOTHERAPY IN THE TREATMENT OF PROSTATE CANCER

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Background: Modern radiotherapy in prostate cancer can be delivered with sophisticated techniques, such as 3D conformal radiotherapy, and intensity modulated radiation treatment (IMRT), which allow for a shaped distribution of dose around the target with an acceptable toxicity for the nearby healthy organs (bladder, rectum). There has also been a parallel advancement in the methods available to verify accuracy of the patient setup. The aims of the present study were: (i) to evaluate the effectiveness of cone beam-computed tomography (CBCT) to determine set-up accuracy in radiotherapy treatment for prostate cancer; and (ii) to validate an internal online correction protocol with the goal of reducing systematic errors, thus establishing the proper clinical target volume (CTV) to planning target volume (PTV) margin. *Patients and Methods:* The study population consisted of 20 low-/intermediate-risk prostate cancer patients undergoing definitive radiotherapy to a total dose of 76 Gy with the use of an Elekta linear accelerator mounting a CBCT scanner (Elekta Synergy S, Elekta Oncology Systems Ltd, Crawley, U.K.). Patients were treated in the supine position with a full bladder and empty rectum; proper immobilization devices (Orfit industries, Wijnegem, Belgium) were adopted. The CTV was identified as the prostate gland and the entire seminal vesicles plus a 7 mm margin everywhere, except for 5 mm in the posterior direction and for 1 cm in the superoinferior (SI) direction. Pre-treatment image registration was performed using a soft-tissue algorithm applied to a region of interest including the whole PTV. CBCT was executed for the first three fractions to detect systematic errors with an action level of 3 mm; subsequent registrations were performed every seven fractions. Only translational (no rotational) errors were considered by the present analysis. The overall mean shift (M), the SD of the group systematic error (Σ), the root mean square of the SD of all patients (σ) and the 3D vector of displacement were calculated. The Van Herk formula (1) ($2.5\ \Sigma + 0.7\ \sigma$) was used to determine CTV to PTV margins. The impact of the correction protocol was determined by quantifying the set-up accuracy without the application of systematic adjustments. *Results:* A total of 168 CBCT scans (average 8 per patient, range 6-11), resulting in 504 positional errors along the mediolateral (ML), SI and anteroposterior (AP) axes, were analyzed. A systematic correction was requested in 60% of patients, mostly (66%) in AP direction. The values of M were –0.2, 1.5 and 0.8 mm in the 3 axes, respectively. The SD of the group systematic error (Σ) was 1.8, 2.1 and 1.9 mm along ML, SI and AP directions, respectively; these values rose to 2.5, 2.5 and 4.1 mm in the 3 axes if systematic corrections were not considered. The values of σ were 2.4, 3.3 and 3.6 mm in the three directions. The mean 3D vector of displacement was 3.48±1.4 mm. CTV-PTV margins were 6.18, 7.56 and 7.27 mm along the three axes. In the absence of systematic corrections, a CTV-PTV margin of 7.93, 8.59 and 12.77 mm in ML, SI and AP directions was required, respectively. *Discussion and Conclusion:* CBCT image registration ensures accurate targeting in prostate radiotherapy. The internal correction protocol allowed for a significant reduction of CTV-PTV margins, especially in the AP direction. A PTV margin of 8 mm in all directions seems appropriate: a margin of 5 mm in the posterior direction to reduce rectal toxicity could be achievable (i) by the introduction of a dietary protocol (2) to decrease both systematic and random errors, and (ii) by increasing the number of image-guided fractions. The acquisition of post-treatment CBCT might be helpful in quantifying intrafraction prostate motion.

1 van Herk M *et al*: Errors and margins in radiotherapy. Semin Radiat Oncol *14*: 52-64, 2004.
2 Smitmans HP M *et al*: The influence of a dietary protocol on cone beam CT-guided radiotherapy for prostate cancer patients. Int J Radiat Oncol Biol Phys *71*: 1279-1286, 2008.

126
A CASE OF EPITHELIOID ANGIOMYOLIPOMA AND REVIEW OF LITERATURE

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Background: Renal angiomyolipoma (AML) is a rare benign renal tumor. Epithelioid AML has malignant potential, as described in the WHO Classification of renal tumor: EAML is a potentially malignant mesenchymal neoplasm, composed of histologically and immunohistochemically distinctive perivascular epithelial cells (1). *Case Report:* The case of a 48-year-old female with diagnosis of tuberous sclerosis and repeated episodes of pain in the right abdominal wall is described. In December 2010, the patient underwent a thoraco-abdominal CT that demonstrated a bulky (15×9×2.5 cm) solid tumor with multiple solid lesions in the right kidney, with perirenal fascia and fat thickening. The radiologist defined these aspects as possible angiomyolipoma. In January 2011, the patient underwent a right radical nephrectomy. The histological examination gave evidence of multicenter epithelioid angiomyolipoma with multiple cortico-medullary extensions but with the absence of infiltrative capsular transmurality and without involvement of the hilum vascular-excretory district. The cells were immunoreactive for CD117. *Discussion:* Epithelioid AML is a rare renal neoplasm that has adverse outcomes in approximately one-third of patients, with neoplastic progression, recurrence, systemic and lymph node metastasis (2). Negative prognostic factors are older age, tumor size, necrosis, multicentricity, lymph node and renal vein involvement, and a higher percentage of epithelioid component (1). Generally, surgical therapy alone is curative in patients with AML. In contrast, in epithelioid AML, surgical therapy may be associated with chemotherapy. At present, some cases are treated with doxorubicin or with mTOR inhibitors (2). *Conclusion:* Epithelioid AML is a rare renal neoplasm with malignant potential. The diagnosis is based on histological and immunohistochemical examination and the expression of melanocytic markers (HMB45 and Melan-A). In the case reported here, the patient received a radical surgical treatment alone without adjuvant therapy.

1 Pure epithelioid PEComas (so-called epithelioid angiomyolipoma) of the kidney: a clinicopathologic study of 41 cases: detailed assessment of morphology and risk stratification. Am J Surg Pathol *35(2)*: 161, 2011.
2 Renal epithelioid angiomyolipoma: a malignant disease. J Nephrol *24(1)*: 18, 2011.

128
A NEW PATIENT-REPORTED OUTCOME (PRO) QUESTIONNAIRE SPECIFIC FOR ILEAL ORTHOTOPIC NEOBLADDER (IOB) RECIPIENTS: THE IOB-PRO

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Background: The expression 'patient reported outcome' (PRO) refers to questionnaires used in clinical practice that ask patients about their perceptions of symptoms, activities of daily living and other aspects relating to quality of life. There is a lack of specific PROs for ileal orthotopic neobladder (IOB) for patients who undergo radical cystectomy, although outcome questionnaires are available for other types of urinary diversion. The goal of this study was to show how such a need has been met in questionnaire design and construction. *Materials and Methods:* Questionnaire development was planned in seven steps. Phase (a) can be summarized as follows: 35 in-depth interviews of IOB recipients (mean age 63.3 years; males=28) were performed in seven Italian centres. Phase (b) can be summarized as follows: materials collected through narrative interviewing were analyzed. Over 80 sentences were produced. Coding procedures clustered sentences into eight macro concepts. The scale of symptoms was shortened to 43 items, distributed into 6 dimensions using a clinical overview. *Results:* The questionnaire is divided into two parts. Part 1 includes all sections and items specified above and is summarized in Table I. The questionnaire is edited according to the findings of cognitive research on the visual design of questionnaires: a specimen is given in Table II. Part 2 of the questionnaire design belongs instead to the so-called individualized approach in which the patient is free to express their point of view. *Conclusion:* The IOB-QOL Part 1 will undergo first item reduction while patients acceptability

of Part 2 is tested. An international harmonization meeting will take place in order to select the definitive questionnaire that will undergo further psychometric validation on extended groups of patients.

Table I.

Symptoms
Incontinence, day time; Incontinence, night time; Urinating regularly; Feverish sensations; Difficulty urinating.
Neobladder self management
Neobladder compression/decompression exercises; Emptying neobladder; Waking-up at night.
Activities of daily living
Difficulties in carrying out light daily activities; Fear of not being close to a toilet when out of the home; Limits in drinking liquids; Organizing daily time table; Problems in using public transport; Level of performance at work; Limited in staying far from home; Limited in doing work.
Sleep and tiredness
Sleeping well; Being tired during the day; Waking-up refreshed; Need to rest during the day; Run out of energy easily in doing things; Problems of thinking clearly in doing things; Having to interrupt activity because of tiredness; Interrupting activity because of tiredness
Emotional
Feeling dependent; Adaptation to living with neobladder; Feeling angry because of the condition; Panicking; Feeling irritable; Hopelessness; Fear that cancer enhanced; Worry for the future; Feeling handicapped; Loss of self-esteem.
Social
Support from family members; Difficulty in getting on with people; Giving up leisure activities; Avoiding going out; Fear others smell urine; Being embarrassed in small places (elevators, *etc*.); Feeling different; Fear in meeting new people; Fear of being refused; Avoiding physical contact with family members; Avoiding sexual relations.

Table II. *Your emotional life*.

During the last week…	Always	Sometimes	Rarely	Never
Did you feel independent?	☐	☐	☐	☐
Did you feel angry because of your condition?	☐	☐	☐	☐
Did you feel panic?	☐	☐	☐	☐
Did you feel irritable?	☐	☐	☐	☐

1 Yossepowitch O, Dalbagni G, Golijanin D, Donat SM, Bochner BH, Herr HW, Fair WR and Russo P: Orthotopic urinary diversion after cystectomy for bladder cancer: implications for cancer control and patterns of disease recurrence. J Urol *169*: 177, 2003.

2 Hobisch A, Tosun K, Kinzl J, Kemmler G, Bartsch G, Höltl L and Stenzl A: Life after cystectomy and orthotopic neobladder *versus* ileal conduit urinary diversion. Semin Urol Oncol *19*: 18, 2001.

3 Mansson A, Davidsson T, Hunt S and Mansson W: The quality of life in men after radical cystectomy with a continent cutaneous diversion or orthotopic bladder substitution: is there a difference? BJU Int *90*: 386, 2002.

129
PELVIC IMRT AND HYPOFRACTIONATED SIMULTANEOUS INTEGRATED BOOST TO HIGH-RISK PROSTATE CANCER

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Aim: During the past decade, significant advancements have been made in external beam radiotherapy. With recent evidence demonstrating the positive effects of dose escalation on tumor control, the trend has been toward irradiating smaller areas with greater doses. This has led to the development of conformal radiotherapy and, more recently, intensity-modulated radiotherapy (IMRT). We describe our technique and preliminary toxicity profile for ultrasound-guided outpatient placement of intraprostatic fiducial markers before simultaneous integrated boost (SIB)-IMRT for high-risk prostate cancer. *Patients and Methods:* A total of 15 men with prostate cancer who underwent hypofractionated IMRT between January 2009 and May 2010 were included in the study. All patients underwent ultrasound-guided transrectal placement of three gold intraprostatic fiducial markers under local anesthesia using our standard technique. Daily on-line image guidance adjustments were made according to the location of the fiducial markers. Before the beginning of the radiation therapy, flexible rectoscopy with rectal biopsies was performed for evaluation of all the patients. In the event of toxicity, further rectoscopy with mucosal biopsy was carried out. The SIB-IMRT treatments were designed to deliver 67.5 Gy in 25 fractions (2.7 Gy/fraction) to the prostate, while simultaneously delivering at least 56.25 Gy (2.25 Gy/fraction) to the seminal vesicles and 50 Gy (2.0 Gy/fraction) to the

pelvic lymph nodes. All treatment planning was performed using the Oncentra MasterPlan system (Nucletron, NL) and delivered with five equispaced 6 MV IMRT beams (every 72˚) from a VARIAN Clinac 600C/D Linac, equipped with a 120-leaf MLC. This number of fields had been determined to give acceptable dose distributions whilst being practical for quality analysis verification and treatment. In optimization, dosimetric target coverage was considered to be achieved when 95% of the volume received at least 95% of the prescribed dose, while for organs at risk, dose–volume limits were derived using best estimates from the relevant literature. The dose distributions were also studied to ensure that there were no significant hot-spots in uncontoured normal tissue. The charts were reviewed to evaluate the acute toxicity profile of IMRT hypofractionation with fiducial markers during the treatment course using the Common Toxicity Criteria, version 3.0. The goal was to score late toxicity according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) scale. The International Prostate Symptom Score, International Index of Erectile Function-5 (IIEF-5), clinical stage, and Gleason score were tabulated. *Results:* Fiducial marker placement proceeded without complications. All patients were classified as being at high risk (NCCN score). Grade 1 perineal dermatitis occurred in three patients. Acute genitourinary (GU) toxicity manifested in five patients (28%) as grade 1 or 2 urethritis. No patients developed urinary retention requiring catheterization and no patients had any episode of gross hematuria. No cases of acute gastrointestinal (GI) toxicity grade 2 were observed. No late GI or GU toxicity according to the RTOG/EORTC scale or significant change in the International Prostate Symptom Score were found at nine months in patients with available follow-up. *Conclusion:* The placement of intraprostatic fiducial markers before SIB-IMT radiation therapy is a safe and efficacious method for prostate localization and produces an excellent toxicity profile; however, additional investigation is required into the long-term clinical benefits.

1 Zelefsky MJ, Leibel SA, Gaudin PB *et al*: Dose escalation with three-dimensional conformal radiation therapy affects the outcome in prostate cancer. Int J Radiat Oncol Biol Phys *41(3)*: 491-500. 1998.

2 Zietman AL, DeSilvio ML, Slater JD *et al*: Comparison of conventional-dose *vs*. high-dose conformal radiation therapy in clinically localized prostate cancer. JAMA *294*: 1233-1239, 2005.

3 Langen KM and Jones DTL: Organ motion and its management. Int J Radiat Oncol Biol Phys *50*: 265-278, 2001.

130
EARLY CLINICAL EXPERIENCE OF HELICAL TOMOTHERAPY FOR HYPOFRACTIONATED RE-IRRADIATION OF RECURRENT LOCALIZED PROSTATE CANCER

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Background: The local recurrence rate for localized prostate cancer after curative external beam radiotherapy (EBRT) is between 25% and 32%. The standard curative salvage treatment for disease that is still organ confined is radical surgery. Cryotherapy and brachytherapy have recently been proposed. The use of re-irradiation by three-dimensional conformal radiation therapy is traditionally limited by low cure and high complication rates. Highly conformal radiotherapy techniques, *e.g*. helical tomotherapy, with their adaptive capabilities offer new treatment options, providing the opportunity to evaluate new indications such as hypofractionated re-irradiation in locally recurrent prostate cancer. *Patients and Methods:* Between July 2009 and November 2010, we used tomotherapy to re-irradiate the prostate gland in five patients. All but one patient experienced biochemical and local recurrence (documented by ^{18}F-choline PET/CT) of prostate cancer previously treated by curative EBRT. One patient with newly diagnosed prostate cancer had received prior irradiation to the pelvis because of rectal cancer. All patients were treated with a hypofractionated accelerated course of radiotherapy (25 Gy in five daily fractions of 5 Gy each). *Results:* Dose–volume histograms for targets and organs at risk were satisfactory. Treatments were well tolerated. No toxicities ≥grade 2 were observed. Side-effects were limited to an increase in urinary frequency. A lowering of PSA value was seen in 4/5 patients three months after treatment completion. One patient had biochemical and nodal progression. *Discussion and Conclusion:* Our experience suggests that hypofractionated re-irradiation of the prostate gland performed by helical tomotherapy is feasible and safe. A larger number of cases and longer follow-up are now needed to evaluate the effectiveness of these treatments.

131
3D CONFORMAL *VERSUS* INTENSITY-MODULATED RADIOTHERAPY IN POST PROSTATECTOMY PATIENTS: A DOSIMETRIC COMPARISON

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Aim: Adjuvant radiotherapy for locally advanced prostate cancer improves biochemical and clinical disease-free survival. While comparisons for intact prostate cancer show a benefit for intensity-modulated therapy (IMRT) over 3D conformal planning (3DCRT), this has not been studied for post-prostatectomy radiotherapy to date. The aim of this study was to compare the dosimetric parameters of IMRT and 3DCRT to predict the relative possible clinical benefit of the treatments. *Patients and Methods:* This study analyzed ten patients who were candidates for post-prostatectomy radiotherapy. All volumes were delineated by the same radiation therapist in accordance with EORTC consensus guideline. A CTV (prostate-bed) expansion of 1 cm (5 mm posterior) was used to determine the PTV. The urinary bladder, rectum and penile bulb were also delineated. For all patients, two treatment plans were performed: one used a five-beam conformal therapy and the other a five-beam step-and-shoot IMRT with inverse planning optimization. For each plan, 66Gy in 33 fractions were prescribed to the PTV. Differences in dose volume histograms (DVHs) between the plans were evaluated using two-tailed paired Student's *t*-test. In addition, to study the coverage and conformity of PTV with respect to 95% isodose, for both techniques, the target coverage (TC) and conformity index (CI) were evaluated. *Results:* DVHs showed comparable PTV coverage (mean TC=89.4% for IMRT *versus* 84.7% for 3DCRT) with a better conformity for IMRT plans (mean CI=1.03 for IMRT *versus* 1.23 for 3DCRT). We also decided to compare the two treatment plans with respect to the volume of the organ at risk that received three high dose levels: 60 Gy (V60), 50 Gy (V50) and 40 Gy (V40). In particular, for the bladder, V60 was found to be 30% and 50% for IMRT and 3DCRT, respectively; V50 was found to be 45% and 75%, respectively; finally, V40 was found to be 65% and 95%, respectively. For the rectum, V60 was found to be 20% and 30% for IMRT and 3DCRT, respectively; V50 was found to be 30% and 40%, respectively; and V40 was found to be 40% and 55%, respectively. For the penile bulb, V60 was found to be 10% and 30% for IMRT and 3DCRT, respectively; V50 was found to be 50% and 75%, respectively; and V40 was found to be 75% and 75%, respectively. We also evaluated the mean dose to these organs: for the bladder it was found to be 48 Gy and 58 Gy for IMRT and 3DCRT, respectively; for the rectum, it was found to be 40 Gy and 46 Gy, respectively; for the penile bulb, it was found to be 49 Gy and 54 Gy, respectively. All these differences had a significance of $p<0.1$. *Discussion and Conclusion:* According to these data, the IMRT plans give a greater sparing of normal tissues at low doses, with slightly better coverage of the PTV. This should result in a resolute decrease of acute genitourinary and rectal toxicity. Another relevant finding is that IMRT reduces the dose to penile bulb so that patients that undergo nerve-sparing prostatectomy with preservation of erectile function should have a positive possibility for continued sexual activity. Further research in clinical trials is necessary to determinate the significance of the better planned dose of IMRT compared to 3DCRT on patient outcome.

1 Zelefsky MJ, Fuks Z *et al*: High dose radiation delivered by intensity modulated conformal radiotherapy improves the outcome of localized prostate cancer. J Urol *166*: 876-881, 2001.
2 Kao J, Turian J *et al*: Sparing of the penile bulb and proximal penile structures with intensity-modulated radiation therapy for prostate cancer. Br J Radiol *77*: 129-136, 2004.
3 Meier R, Mark R *et al*: Postoperative radiation therapy after radical prostatectomy for prostate carcinoma. Cancer *70*: 1960-1966, 1992.

132

IGRT WITH ON-LINE KV-CBCT AND HEXAPOD ROBOTIC COUCH IN PROSTATE CANCER: ASSESSMENT OF INTER-FRACTION ERRORS

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Aim: Recent studies have shown that different filling conditions of the bladder and rectum can significantly influence the inter- and intra-fraction position of the prostate during radiotherapy, with consequent modifications of dose distribution to the target and adjacent organs. This may result in an impairment of local control and/or increased risk of late sequelae. The aim of this study was primarily to determine the inter-fraction set-up error and organ motion assessed with a kilovoltage cone beam CT (kVCBCT) in patients treated for prostate cancer with radical radiotherapy. *Patients and Methods:* The study involved 18 patients treated with radical radiotherapy between January 2009

and January 2010. All patients were instructed to empty their rectum and fill their bladder, drinking 500 ml of water 30 min before the planning CT/therapy. For all patients, the prostate position had been assessed before each fraction through kVCBCT image guidance (XVI, Elekta). Patients were positioned first by using lasers and skin tattoos and then kVCBCT acquisition was performed. For each fraction, the daily CBCT scan was registered with planning kilovoltage CT images and positioning adjustments were assessed using a robotic table with six degrees of freedom (Hexapod Evo, Elekta-Medical Intelligence). Registration was based on a rigid-body approach and was performed according to the following procedure: (i) a fully automatic registration based on bony anatomy assessed the set-up error; (ii) a physician and a radiotherapy technologist manually adjusted the matching on the target through a gray-value algorithm, assessing the total inter-fraction error (set-up plus organ motion), and (iii) after the matching procedures, the final corrections were automatically applied to the robotic treatment couch for three translational and three rotational deviation vectors and the patient was treated. For each fraction, values of inter-fraction set-up and total error (set-up plus organ motion) assessed at steps (i) and (ii) were registered for three principal axes (L-R, A-P, C-C) and for three angle rotations (pitch, roll and jaw). For each patient, the average deviation μi and the standard deviations σi for both set-up and organ motion were calculated in each direction. Moreover, for the entire population of patients, we calculated the global systematic error (M), the distribution of the systematic errors (Σ) and the distribution of the random errors (σ). *Results:* To assess inter-fraction set-up and organ motion errors, data from 680 kVCBCT were analyzed. Concerning set-up errors, in L-R, C-C and A-P directions, deviations for M were found to be 0.9, –0.1 and 0.5 mm, with Σ of 2.9, 1.9 and 4.3 mm and σ of 2.4, 2.2 and 3.3 mm, respectively. Rotation deviations were <1° for M, Σ and σ. Concerning inter-fraction organ motion relative to bony anatomy, deviations for M were found to be –0.9, –1.2 and 1.5 mm, with Σ of 0.2, 0.3 and 2.4 mm and σ of 0.4, 0.3 and 0.3 mm for L-R, C-C and A-P, respectively. Rotation deviations were <1° for M, Σ and σ. *Conclusion:* Daily kVCBCT is a simple and highly efficient procedure that permits an accurate positioning of the patient and a reliable localization of the target. A current task in our center is to evaluate the opportunity to assess individual margins for patients who undergo prostate treatments with IGRT, also setting the stage for hypofractionation studies and adaptive radiotherapy.

133
MONOLATERAL NERVE-SPARING PROSTATECTOMY: REVIEW OF INDICATIONS, FUNCTIONAL AND ONCOLOGIC OUTCOME

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Background and Aim: The literature describes well-documented indications for nerve-sparing radical prostatectomy. However, to date, there is no clear reference to the monolateral preservation of the bundles. The purpose of this study was to identify patients who are candidates for monolateral nerve-sparing prostatectomy (MRP) and to evaluate the oncologic and functional results. *Patients and Methods:* The study included 936 patients who underwent consecutive radical retropubic prostatectomy (RRP) for clinically localized prostate cancer. In 463 patients (49.5%), neurovascular bundles were not preserved; in 359 (38.3%) patients, it was possible to preserve both bundles (BRP); while in 114 (12.2%) patients, an MRP was performed. The 114 MRP patients included in the study filled out an IIEF questionnaire pre-operatively and 3, 6, 12, 18 and 24 months after surgery. We performed MRP in patients not suitable for BRP, with Gleason score ≤7, preoperative PSA<20 ng/ml, one lobe involvement at biopsy and IIEF-5>19.The Kaplan–Meier method was used to assess the biochemical recurrence-free survival and the χ^2 test was used to investigate the correlation between MRP and RRP. *Results:* The mean age at surgery was 62.8 years, mean PSA was 8.52 (range: 3-19.6) ng/ml, 70% of patients had a Gleason score <7 at biopsy and 26.7% of patients had a Gleason score of 7 at biopsy (mean of ten samples, range 6-24) and was positive for cancer bilaterally in 30% of patients (mean of 4 samples, range: 2-7) while in 70% of them only one lobe of the prostate was involved (mean of 3 samples, range: 1-5). The mean preoperative IIEF-5 was 22.1 (range: 14-25). The final histopathological staging showed 56 cases of pT2 (49.2%) and 45 cases of pT3a (39.2%). Thirteen patients with pT3b and pT4 disease and three patients with positive lymph nodes were excluded from the study. In seven patients (7.4%) there were positive surgical margins on the side of the preserved bundle. There was a low incidence of positive surgical margins in the MRP group but it was not statistically significant when we stratified the overall population for RRP, MRP and BRP (12.9,7.4 and 11.5% respectively, *p*-value was non-significant; MRP *vs*. RRP, *p*-value was non-significant). The mean follow-up was 48.4 (range: 16-119) months. The biochemical recurrence-free survival for RRP, MRP and BRP at 60 months was 71.7, 80.9 and 86.3%, respectively (p=0.0001; (MRP *vs*. RRP, p=0.01). Overall, spontaneous sexual potency (or using PDE5-I) was obtained in 62 patients (54.2%) in the MRP group in comparison to 73.1% in the BRP group (p=0.0015). The patients who underwent MRP presented a mean IIEF-5 of 18.3

(range: 5-22) and had a mean age of 62.1 (range: 45-72) years. *Conclusion:* The retrospective review of this patient series suggests the potential role of preservation of one of the neurovascular bundles. In this patient series, MRP allowed recovery of sexual function in >50% of patients, with good oncologic outcome. However it is necessary to conduct prospective studies for further evaluation.

134

THE EFFECT OF THE PRESENCE OF A MEDIAN LOBE ON THE OUTCOMES OF ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY

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Aim: To report the effect of the presence of a median lobe on perioperative outcomes, positive surgical margin (PSM) rates and short-term urinary continence outcomes after robot-assisted laparoscopic radical prostatectomy (RARP). *Patients and Methods:* We analyzed data from 1,693 consecutive patients who underwent RARP by a single surgeon for treatment of clinically localized prostate cancer. Patients were categorized into two groups based on the presence or absence of a median lobe identified during RARP. Outcomes analyzed included operative time, estimated blood loss (EBL), nerve-sparing procedure, overall complication rates, length of hospital stay, days with catheter, presence of anastomotic leakage on cystogram, number of bladder neck reconstruction procedures, tumor volume, pathological stage, PSM rates, pathological Gleason score and continence rates. Continence was defined as the use of 'no pads' based on the patient responses to the Expanded Prostate Cancer Index Composite questions at 1, 4, 6, 12 and 24 weeks after catheter removal. *Results:* Median lobe was intraoperatively identified in 323 (19%) patients. Patients with a median lobe were slightly older (median 63 *vs*. 60 years, $p<0.001$), had higher PSA levels (median 5.7 *vs*. 4.7 ng/ml, $p<0.001$) and higher AUA-SS before RARP (10 *vs*. 6, $p<0.001$). The number of bladder neck reconstruction procedures (93.5% *vs*. 65.7%, $p<0.001$) and the median prostate weight (64 *vs*. 46 g, $p<0.001$) were also higher. Both groups had equivalent EBL, length of hospital stay, days with catheter, pathological stage, pathological Gleason score, nerve-sparing procedures, complication rates, anastomotic leakage rates, mean tumor volume, PSM rates and PSM rate at the bladder neck. The median OR time was slightly greater in patients with median lobe (80 *vs*. 75 minutes, $p<0.001$). There was no difference in the operative time between the two groups when stratifying this result by prostate weight. Continence rates were also equivalent between patients with and without a median lobe at 1 week (27.8% *vs*. 27%, $p=0.870$), 4 weeks (42.3% *vs*. 48%, $p=0.136$), 6 weeks (64.1% *vs*. 69.5%, $p=0.126$), 12 weeks (82.5% *vs*. 86.8%, $p=0.107$) and 24 weeks (91.5% *vs*. 94.1%, $p=0.183$). Finally, the median time to recovery of continence was similar between the groups based on the Kaplan–Meier curves (median: 5 weeks, 95% CI=4.41-5.59 *vs*. median: 5 weeks, 95% CI=4.66-5.34; log rank test, $p=0.113$). *Conclusion:* The presence of a median lobe does not affect perioperative outcomes, PSM rates and early continence outcomes in patients undergoing RARP performed by an experienced surgeon. There was a slight increase in the operative time in patients with a median lobe which was, however, related to the larger prostate size in this group.

135

ANALYSIS OF THE CLINICAL PARAMETERS COMMONLY USED TO CHOOSE NERVE-SPARING PROSTATECTOMY FOR PATIENTS WITH POSITIVE BIOPSY AT THE TRANSITION ZONE ALONE

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Aim: The aim of this study was to analyze the indication for nerve-sparing surgery for patients with positive prostate biopsies at the level of the transition zone (even in patients with PSA above10 ng/ml), the impact of this factor on biochemical recurrence-free survival (BCR) and extracapsular extension (ECE). *Patients and Methods:* The study included 273 patients undergoing open radical prostatectomy and pelvic lymphadenectomy for clinically organ-confined prostate cancer (OC), not submitted to neoadjuvant therapy, with preoperative biopsy of peripheral (PZ) and transitional zone (TZ). Clinical and pathological data were available from our prospectively maintained institutional registry of 936 consecutive patients. The correlation between clinicopathological parameters and the site of the biopsy were investigated with the chi-square and Mann–Whitney *U*-tests. The impact of these variables on biochemical progression-free survival was evaluated by Kaplan–Meier survival curves. *Results:* The mean follow-up was 26.9 (range, 7 62, median 24) months. The mean age was 65.7 (range 49-78, median 66) years. At the final pathological examination, 152/273 (55.6%) patients presented OC disease,

while 121 patients presented ECE, with a prevalence of 44.4%. We identified 54/273 patients (19.8%) with positive biopsies at the level of TZ only. Among these, 36 (66.7%) had PSA <10 ng/ml, 15 (27.7%) had a PSA in the range 10-20 ng/ml, and 3 (5.6%) >20 ng/ml. Of the 18 patients with PSA >10 ng/ml, only 3 presented ECE. The OC disease incidence in patients with positive biopsy only in the TZ and with PSA >10 ng/ml was significantly higher than in those patients with same PSA level and positive biopsy in the PZ alone ($p<0.05$). Patients with positive biopsy of the TZ showed a significantly higher incidence of OC tumor (83.3%) compared to those patients with positivity in the PZ alone (50.5%) ($p=0.014$). In univariate analysis, the localization (TZ or PZ) of the tumor did not prove to be predictor of relapse-free survival (p-value was non-significant): the BCR at five years amounted to 94.4% and 90.2%, respectively. Of the 54 patients with positive samples in the TZ, 51 (94.4%) had bioptic GS ≤6, three (5.6%) had bioptic GS=7, while 33 (61.1%) had a pathological GS ≤6, and 21 (38.9%) had a GS=7. *Conclusion:* Our records show that tumors diagnosed in the TZ alone are associated with a lower risk of ECE after radical prostatectomy. In particular, even with PSA >10 ng/ml, the probability of OC disease remains significantly higher than in patients with positivity of the PZ alone. These data should be assessed in order to extend the possibility of a nerve-sparing surgery to patients with positive bioptic cores only in the transitional zone and PSA>10 ng/ml.

136
PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL: OUTCOME IN POST WHO/ISUP GRADING SYSTEM OF A SINGLE-CENTER COHORT

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Background: Few long-term single-center studies have shown the outcome in patients affected by papillary urothelial neoplasm of low malignant potential (PUNLMP). The present study evaluated the behavior of *de novo* primary bladder PUNLMP lesions (Primary-PUNLMP) as well as Surveillance-PUNLMP (diagnosed during follow-up of a higher grade urothelial neoplasm). *Patients and Methods:* From January 2006 to January 2010, 478 patients (male=340. female=138; mean age 71.8±9.2 years) underwent transurethral resection (TURBT) of all visible tumors. We retrospectively analyzed our TURBT database and identified all patients with a histological examination which revealed a PUNLMP lesion type. *Results:* We identified a total of 43 PUNLMP of the bladder; 25 (58%) patients were categorized as Primary-PUNLMP and the remaining 18 (42%) patients were categorized as Surveillance-PUNLMP. During follow-up (range: 12-48 months), in the Primary-PUNLMP group, 14/25 (56%) patients did not develop any recurrences *vs*. 6/18 (33%) in the Surveillance-PUNLMP group. In the first group, 4/25 (16%) patients developed PUNLMP recurrence (1-2 episodes in 1-4 years) and 8/25 (32%) progressed to a higher grade lesion within 1-4 years. Grade progression was non-invasive low-grade urothelial carcinoma (LG-TCC) in 7 patients (28%) and non-invasive high-grade urothelial carcinoma (HG-TCC) in 1patient (4%). None of the Primary-PUNLMP patients developed muscle-invasive carcinoma or died because of disease progression. Tumor size did not correlate with the likelihood of recurrence. In the second group, 12/18 patients (67%) had PUNLMP during surveillance for higher grade urinary bladder lesions. These included 7 (58.3%) prior LG-TCC, 4 (33.3%) prior HG-TCC and 1 (8.3%) found in cystectomy for invasive neoplasm in bladder diverticula. Grade progression to LG-TCC occurred in 5 patients (27.7%), while progression to HG-TCC occurred in 6 (33.3%). Two patients (11.1%) died in the HG-TCC group and one patient (5.5%) died in the LG-TCC group died after developing a high-grade upper urinary tract tumor. *Conclusion:* Bladder PUNLMP can occur either as a *de novo* lesion or during surveillance for prior higher grade urinary bladder urothelial neoplasm. None of the Primary-PUNLMP patients in this study developed invasive carcinoma or died because of the disease despite 48% recurrence and 32% grade progression rates. Surveillance-PUNLMP was associated with a worse outcome (61.1% grade/stage progression, 16.6% deaths because of disease progression), most likely due to their initial higher grade/stage urothelial neoplasm.

137
DOES PROSTATE WEIGHT AFFECT PERIOPERATIVE OUTCOMES, POSITIVE SURGICAL MARGIN RATES AND FUNCTIONAL OUTCOMES AFTER ROBOT-ASSISTED RADICAL PROSTATECTOMY PERFORMED BY AN EXPERIENCED SURGEON?

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Aim: To determine whether prostate weight has an impact on pathological, perioperative and early functional outcomes after

robot-assisted laparoscopic radical prostatectomy (RARP). *Patients and Methods:* We analyzed 1,831 consecutive patients who underwent RARP by a single surgeon. Patients were stratified into three groups on the basis of pathological prostate weight: group 1: <30 g, group 2: 30 to 49.9 g, group 3: 50 to 69.9 g and group 4: >70 g. Continence was defined as the use of 'no pads'. Potency was defined as the ability to achieve and maintain adequate erections for penetration more than 50% of the time with or without the use of PDE-5 inhibitors. Only patients with preoperative SHIM score >21 and who underwent bilateral nerve-sparing procedure were included in the study. Groups were compared using one-way ANOVA on ranks test and the Dunn's method for multiple comparisons when statistically significant differences were found. *Results:* Patients with a larger prostate (group 4) were older (median age 65 years), had higher pre-treatment PSA (median 5.8 ng/ml), higher AUA-SS (median 9), longer operative time (median 80 min) and higher estimated blood loss (median 100 cc) ($p<0.001$ for all variables). There was no association between prostate size and body mass index, biopsy Gleason score, clinical stage, catheterization time, pathological stage, hospital stay, anastomotic leak rates, specimen Gleason score and continence rates (at one, three and six months). Overall positive surgical margin rates were lower in patients with prostate size larger than 70 g when compared to the other groups (14.4% *vs.* 12.5% *vs.* 10.2% *vs.* 7.2%, respectively, $p<0.001$). There was a trend towards lower potency rates in patients with prostates larger than 70 g at four weeks (45.4% *vs.* 35% *vs.* 32% *vs.* 25%, $p=0.065$) and three months (72% *vs.* 75% *vs.* 75.2% *vs.* 65%, $p=0.07$) after RARP, although the potency rates were similar among the groups at six months after surgery. *Conclusion:* RARP performed by an experienced surgeon in patients with an enlarged prostate is feasible, with slightly higher operative time and estimated blood loss and without any impact on early continence rates. There was a trend towards lower early potency rates in patients with larger prostates, which can probably be explained by the greater age of these patients. Pathologically larger prostates were associated with lower overall PSM rates even though the pathological stage and specimen Gleason score were similar in the groups.

138
LOW DOSE RATE I-125 BRACHYTHERAPY OF EARLY-STAGE, GOOD-PROGNOSIS PROSTATE CANCER: SAN FILIPPO NERI HOSPITAL EXPERIENCE

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Background: Early-stage prostate cancer is usually treated with radical prostatectomy (RP) or external beam radiotherapy (EBRT). Long-term results [biochemical progression-free survival (bPFS): 98.6% and overall survival (OS): 77% at 12 years] (1) show that low dose rate (LDR) ^{125}I brachytherapy might represent an effective and patient-friendly modality, with equivalent results in both bPFS and OS, being more respectful of erectile function and urinary continence for low-risk prostate cancer (2). Post-implant CT-based dosimetry has become the gold standard for assessing the quality of permanent prostate brachytherapy and the actual dose delivered to prostate and normal surrounding structures. The purpose of this study was to assess dosimetric results and clinical outcome in patients with early-stage, good-prognosis prostate cancer treated at our institution with LDR ^{125}I brachytherapy. *Patients and Methods:* At our institution, all prostate cancer patients are managed by a multidisciplinary team to apply tailored therapy in order to treat the cancer, to respect sexual potency, urinary continence and also to reach acceptable genitourinary (GU) and gastrointestinal (GI) tolerability. LDR 125I brachytherapy was proposed to patients with PSA ≤10, Gleason score ≤6, T1-T2 (3), good urinary functionality and prostate volume ≤50 g. The transperineal seed implant was performed under regional anesthesia. After ultrasound imaging of the prostate, rectum and urethral volumes and intraoperative dosimetric planning, the brachytherapy needles, loaded with customized strand ^{125}I seeds, were inserted through a guidance template. The prescription dose was 145 Gy. One month after the implant, a CT scan was performed for post-implant dosimetric planning: a prostate D90 value ≥140 Gy was considered the measure of good implant quality (4). All patients received a three month multidisciplinary follow-up, including digital rectal examination and PSA determination. For the purpose of this analysis, we recorded the following data: post-implant dosimetric parameters, time needed to perform the procedure, the acute and late GU and GI toxicity according to EORTC/RTOG criteria, erectile function and urinary continence preservation and post-implant PSA levels. *Results:* Between February 2009 and February 2011, 22 low-risk prostate cancer patients were evaluated, with the LDR ^{125}I brachytherapy as primary treatment. The mean age was 62.7 (range: 50-74) years, mean pre-treatment PSA value was 6.77 (range: 3.87-10.77) ng/ml, with a mean prostate volume of

35.89 (range: 17.25-58.16) cm^3. Two patients received a transurethral resection of the prostate, six and seven years before implant. At one-month post-planning, mean prostate D90 was 143.61 (range: 123.95-166.64) Gy. As a result of experience gained over two years of applying this treatment regime, the time needed to perform the procedure decreased from 270 to 90 minutes. With a median follow-up of nine months, the observed toxicity was low with no acute or late urinary obstruction: 45% and 9% of patients presented grade 1 (G1) and grade 2 (G2) acute GU toxicity, respectively, and only 9% of patients developed G1 acute GI toxicity. A total of 27% of patients presented G1 late GU toxicity not requiring medication. At the time of writing, urinary continence and erectile function are preserved in the whole group. All patients are free from biochemical and local recurrence, with mean PSA values reduced by 70%, 85% and 86.1% at three, six and nine months, respectively. *Conclusion:* Our data confirm that LDR ^{125}I brachytherapy is a safe and effective curative modality for selected low-risk prostate cancer patients who wish to maintain erectile function and urinary continence. The outcome seems strongly dependent on a multidisciplinary approach, as well as on the high technical ability of dedicated professionals and the careful selection of the patients to be treated.

1 Taira Al V, Merrick G, Wayne Y *et al*: Long-term outcome for clinically localized prostate cancer treated with permanent interstitial brachytherapy. Int J Radiation Oncology Biol, in press, 2010.
2 Inciūra A, Jarusevicus L, Vaiciūnas K and Juozaityte E: Review on the effectiveness of prostate cancer brachytherapy. Medicina (kaunas) *45(8)*: 660-671, 2009.
3 Nag S, Beyer D, Friedland J, Grimm P and Nath R: American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. Int J Radiation Oncology Biol Phys *4*: 789-799, 1999.
4 Nath R, Bice WS, Butler WM, Chen Z, Meigooni AS, Narayana V, Rivard MJ and Yu Y: Recommendations on dose prescription and reporting methods for permanent interstitial brachytherapy for prostate cancer: report of Task Group 137. Am Ass Phys Medicine Med Phys *36(11)*: 5310-5322, 2009.

139
SALVAGE ROBOT-ASSISTED RADICAL PROSTATECTOMY: SINGLE SURGEON EXPERIENCE

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Aim: The objective of this study is to report the perioperative, functional and oncologic outcomes of salvage robot-assisted radical prostatectomy (sRARP). *Patients and Methods:* We identified 19 patients who underwent sRARP with bilateral limited pelvic lymph node dissection by a single surgeon between July 2002 and October 2010. RT consisted of XRT in nine cases, brachytherapy in seven cases, brachytherapy plus XRT in two cases and proton beam therapy in one case. Biochemical failure was defined as a PSA of >2.0 ng/ml over the absolute nadir. Continence was defined as the use of 'no pads' after surgery and potency was defined as the ability to achieve and maintain adequate erection for penetration, with or without PDE-5 inhibitors. Biochemical recurrence (BCR) was defined as a PSA of >0.2 ng/ml after sRARP. *Results:* The median (IQR) age, BMI, SHIM score and AUA score were 66 (range: 60-70.5) years, 30 (range: 37-32.5) kg/m^2, 5 (range: 4-15), and 12 (range: 7.5-13), respectively. The median PSA nadir after RT and the median PSA before surgery were 4.3 (range: 3.4-4.9) and 1.2 (range: 0.75-1.2) ng/ml, respectively. Six patients were placed on ADT. The median OR time and blood loss were 92.5 (range: 90-107.5) min and 100 (range: 100-100) ml, respectively. A partial nerve-sparing surgery was performed in five (26.3%) patients, while all other patients underwent non nerve-sparing surgery. On histopathological evaluation, five patients (26.3%) had pT2 disease, eight (42.1%) had pT3a, while five (26.3%) had pT3b. Due to intense scarring, it was not feasible to accurately stage one prostate. Three patients (15.8%) had a positive surgical margin. The median Gleason score, prostate weight and tumor volume were 8 (range: 7-8), 34 (range: 25-43) g and 25% (range: 16-32%), respectively. The median length of hospital stay and days on catheter were 1 (range: 1-2) day and 8 (range: 7-11) days, respectively. Two (10.5%) patients had three complications (15.8%). Two patients had anastomosis leak (1d), both treated by extended Foley's catheterization. One of these developed an anastomotic stricture (Clavien 3a) at six months and was treated by direct internal urethrotomy. There were no rectal injuries or bladder neck contractures. Fifteen patients had at least six months of follow-up, of whom twelve (80%) were continent. The median time to achieve continence was 5.5 (range: 2.6-9) months. Only two patients who had partial nerve-sparing surgery had six months of follow-up, and none of them were potent. On a median follow-up of 24 (range: 6-45) months, 4 patients (21%) had BCR. *Conclusion:* sRALP is a technically challenging but feasible procedure. The challenge lies in extensive fibrosis and loss of dissection planes, secondary to radiation therapy. This is the

largest published single surgeon series and it shows encouraging perioperative, continence and oncologic outcomes.

140

ROBOT-ASSISTED RADICAL PROSTATECTOMY IN PATIENTS WITH A HISTORY OF ENDOSCOPIC TREATMENT FOR BENIGN HYPERPLASIA OF THE PROSTATE

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Aim: The purpose of this study was to determine whether previous prostate surgery has an adverse effect on the perioperative, histopathological and functional outcomes of robot-assisted radical prostatectomy (RARP). *Patients and Methods:* We retrospectively identified 42 patients (Group 1) who had a history of endoscopic prostate surgery for the treatment of benign prostate hyperplasia (BPH). We performed one-to-one matching based upon ten variables (age, BMI, PSA, SHIM, AUA-SS, c stage, biopsy Gleason score, median lobe presence, pathological stage and the extent of nerve-sparing) using a propensity score matching algorithm to generate a control group (Group 2). The perioperative, histopathological and functional outcomes were compared between these groups. All the patients were evaluated for continence outcomes, while only those patients who had a preoperative SHIM score of 17 and had a nerve-sparing surgery (unilateral, bilateral or partial) were examined for potency outcomes. *Results:* The patient demographics after matching are listed in Table I. The perioperative histopathological and functional outcomes were evaluated. There was no statistically significant difference at any point in time for either continence or potency outcomes *Conclusion:* RARP is a safe and effective procedure in patients who have a history of endoscopic prostate surgery. Although the OR time is higher in these patients, the PSM rates, complications, histopathological and functional outcomes are comparable to those of patients who have no prior prostate surgery.

141

RENAL LEIOMYOMA: A RARE BENIGN TUMOR OF KIDNEY. A CASE REPORT

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Aim: We present a case of renal leiomyoma in a 31-year-old man who presented with hematuria and abdominal pain on the left flank at the first aid unit of our institution. *Case Report:* Ultrasonography and computed tomography (CT) were performed. A conventional pathological analysis, including immunohistochemistry, was performed after radical nephrectomy. Ultrasonography detected enlargement of the left kidney with a mass occupying the caudal half of the organ, hypoechoic with irregular central fluid collection and de-structuration of the normal renal echo-structure. The power-Doppler appearance was hypovascular without visualization of the renal vein. At CT scan, the lesion was described as a voluminous heterogeneous mass of 8.6×11 cm in the lower pole of the left kidney. Before contrast medium injection, the lesion appeared hyperdense compared with the surrounding renal parenchyma, with signs of bleeding. It also revealed a renal pelvis and ureter dilatation with non-flow of contrast medium into the bladder. Radical nephrectomy was performed. On gross examination, the mass was well circumscribed and encapsulated, with a well-defined limit between the thin rim of renal tissue and the lesion. The outer surface was lobular and the cut surface showed a solid whorled white appearance. The tumor was very hard in consistency. No cystic change, hemorrhage, or necrosis was evident. On microscopic examination, the lesion showed fascicles of long spindle cells, showing a whirling pattern with intervening areas of collagen deposition. Nuclei were regular oval with bland chromatin. Mitoses were not evident. No tumor cell pleomorphism, epithelial components or immature elements were evident on multiple sections that were studied. On immunohistochemical evaluation, tumor cells were strongly positive for smooth muscle actin and negative for cytokeratin and HMB 45. *Discussion and Conclusion:* Renal leiomyomas are rare benign tumors of the kidney originating from muscle cells. A few cases of leiomyoma are described in the literature. They can be found directly at autopsy as they are asymptomatic, or diagnosed by the appearance of symptoms (abdominal/flank pain, hematuria, palpable mass). Today the widespread use of ultrasonography and CT has increased the detection of clinically asymptomatic renal leiomyomas. Ultrasonographic evaluation detects leiomyoma as a hypoechoic lesion that may appear solid or cystic. At CT scan leiomyomas appear hyperdense compared to the surrounding tissue, with density similar to that of muscles. The differential diagnosis between leiomyoma and other malignant lesions (above all renal cell carcinoma and leiomyosarcoma) is still possible only by histological examination. Macroscopically, leiomyoma is described as a white or red peripheral lesion, well defined, with a solid aspect and elastic consistence. Color is related to mass vascularization. Histologically, renal

leiomyomas appear to be composed of fusocellular elements, showing absence of mitotic figures, pleomorphism, hyperchromatism and, above all, with an absence of perilesional invasion. Finally, despite the diagnostic difficulties, the gold standard of therapy is still surgery.

142
LOCALIZED PROSTATE CANCER TREATED WITH THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY (3D-CRT): A SINGLE INSTITUTION EXPERIENCE

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Background and Aim: Three-dimensional conformal radiation therapy (3D-CRT) is often used as a curative treatment for clinically localized prostate cancer. Development of sophisticated imaging modalities, coupled with irradiation treatment planning technologies, allows for precise localization of the prostate gland and other target tissues with respect to the treatment beam (1). The aim of this study was to assess the benefit and the toxicity of 3D-CRT for the treatment of localized prostate cancer. *Patients and Methods:* We retrospectively reviewed the cases of 222 men treated with 3D-CRT at the Radiotherapy Department of Foggia from 2006 to 2009. Forty patients were lost to follow-up and our analysis thus included 182 patients treated for localized prostate cancer. The median age was 75 (range: 55-89) years. All patients underwent biopsy and analysis of histological specimens showed adenocarcinoma, with a median Gleason score of 7. Median pre-radiotherapy PSA was 11 ng/ml. Clinical tumor stage was T1 for 18 patients, T2 for 159 patients and T3 for 5 patients. Hormonal therapy was prescribed for 148 (81.3%) patients and they all received hormonal therapy before starting radiotherapy. Fifty-five (30%) patients also received pelvic radiotherapy according to the Roach formula, with a median dose of 44 Gy to pelvic nodes, while the total median dose to the prostate gland was 73.8 Gy. Toxicity was assessed with RTOG scale. Biochemical failure rate, disease-free survival (DFS) and overall survival (OS) were calculated. *Results:* The median follow-up was 28 months. Radiotherapy was well-tolerated and all patients received the prescribed dose. Acute toxicity included rectal (G0, 89%; G1, 11%; G2, 0%) and urinary events (G0, 80.8%; G1, 13.7%; G2, 5.5%). Late toxicity included rectal (G0, 93.9%; G1, 5.5%; G2, 0.6%) and urinary events (G0, 93.4%; G1, 6.6%; G2, 0%). Three patients (1.6%) experienced biochemical failure after radiotherapy and one patient had bone metastasis. Three-year OS and DFS were 94.5% and 89%, respectively. Five-year OS and DFS were 91% and 85%, respectively. *Discussion and Conclusion:* Our retrospective analysis showed good results in terms of OS and DFS, with very low acute and late toxicities. 3D-CRT should be considered as a valid option for treatment of prostate cancer patients, since it is a safe and well-tolerated treatment.

1 Zelefsky MJ, Yamada Y, Fuks Z, Zhang Z, Hunt M, Cahlon O, Park J and Shippy A: Long-term results of conformal radiotherapy for prostate cancer: impact of dose escalation on biochemical tumor control and distant metastases-free survival outcomes. Int J Radiat Oncol Biol Phys *71(4)*: 1028-1033, 2008.

143
TOXICITY AND HEALTH-RELATED QUALITY OF LIFE IN ELDERLY PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Background and Aim: Adjuvant radiotherapy has been associated with improved freedom from biochemical failure as compared with radical prostatectomy alone and it is often delivered after surgery for high-risk patients (1, 2). The aim of this study was to assess the benefit and the toxicity of postoperative radiotherapy after surgery for prostate cancer. *Patients and Methods:* We retrospectively analyzed the cases of 80 men treated with adjuvant radiotherapy at the radiotherapy department of Foggia Hospital from 2006 to 2009. All patients underwent radical prostatectomy and pelvic lymphadenectomy. The median age was 65 (range: 43-77) years. Analysis of histological specimens showed positive margins in 68 patients (85%), extracapsular spread in 50 patients (62.5%) and nodal involvement in 2 patients (2.5%). Median pre-surgery PSA was 9.5 ng/ml and median Gleason score was 7. Hormonal therapy was prescribed for 51 patients (63.7%), of whom 28 (55%) received total androgen deprivation and 23 (45%) received bicalutamide alone (150 mg/day). Radiotherapy was delivered with a median dose of 68 Gy (2 Gy/day). Disease-free survival (DFS) and overall survival (OS) were calculated and toxicity was assessed with RTOG scale. *Results:* The median follow-up was 25 months. The median PSA value after adjuvant radiotherapy was 0.07 ng/ml. Radiotherapy was well-tolerated; only one patient

interrupted treatment due to rectal bleeding. Acute toxicity included rectal (G0, 66.2%; G1, 30%; G2, 3.8%) and urinary events (G0, 50%; G1, 22.5%; G2, 27.5%). Late toxicity included rectal (G0, 96.3%; G1, 2.5%; G2, 1.2%) and urinary events (G0, 73.8%; G1, 22.5%; G2, 3.7%). Three-year OS and DFS were 93.5% and 85%, respectively. Five-year OS and DFS were 89.5% and 80.5%, respectively. *Discussion and Conclusion:* This study showed good results in terms of OS and DFS and also acute and late toxicities were acceptable. Radiotherapy should be considered as an adjuvant treatment for high-risk prostate cancer, especially with positive margins or extracapsular spread, since it is a safe and well-tolerated treatment.

1 Rossi CJ Jr., Joe Hsu IC, Abdel-Wahab M, Arterbery VE, Ciezki JP, Frank SJ, Hahn NM, Moran BJ, Rosenthal SA and Merrick G: ACR appropriateness criteria postradical prostatectomy irradiation in prostate cancer. Am J Clin Oncol *34(1)*: 92-98, 2011.
2 Vargas C, Kestin LL, Weed DW, Krauss D, Vicini FA and Martinez AA: Improved biochemical outcome with adjuvant radiotherapy after radical prostatectomy for prostate cancer with poor pathologic features. Int J Radiat Oncol Biol Phys *61(3):* 714-724, 2005.

144

ADJUVANT RADIOTHERAPY FOR HIGH-RISK PATIENTS AFTER RADICAL PROSTATECTOMY: BENEFITS AND TOXICITY IN OUR EXPERIENCE

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Introduction and Aim: Adjuvant radiotherapy has been associated with improved freedom from biochemical failure as compared with radical prostatectomy alone and it is often delivered after surgery for high-risk patients (1, 2). The aim of this study was to assess the benefit and the toxicity of post-operative radiotherapy after surgery for prostate cancer. *Patients and Methods:* We retrospectively analyzed 80 men treated with adjuvant radiotherapy at the Radiotherapy Department of Foggia from 2006 to 2009. All patients underwent radical prostatectomy and pelvic lymphadenectomy. Median age was 65 years (range: 43-77). Analysis of histologic specimens showed positive margins in 68 patients (85%), extracapsular spread in 50 patients (62.5%) and nodal involvement in 2 patients (2.5%). Median pre-surgery PSA was 9.5 ng/mL and median Gleason score was 7. Hormonal therapy was prescribed for 51 patients (63.7%) of whom 28 (55%) received total androgen deprivation and 23 (45%) received bicalutamide alone (150 mg/die). Radiotherapy was delivered at a median dose of 68 Gy (2 Gy/die). Disease Free Survival and Overall Survival were calculated and toxicity was assessed with RTOG scale. *Results:* Median follow-up was 25 months. Median PSA value after adjuvant radiotherapy was 0.07 ng/mL. Radiotherapy treatment was well-tolerated, only one patient interrupted his treatment due to rectal bleeding. Acute toxicity included rectal (G0, 66.2%; G1, 30%; G2, 3.8%) and urinary events (G0, 50%; G1, 22.5%; G2, 27.5%). Late toxicity included rectal (G0, 96.3%; G1, 2.5%; G2, 1.2%) and urinary events (G0, 73.8%; G1, 22.5%; G2, 3.7%). Three-year Overall Survival and Disease Free Survival were 93.5% and 85%. Five-year Overall Survival and Disease Free Survival were 89.5% and 80.5%, respectively. *Discussion and Conclusion:* This study showed good results in terms of OS and DFS and also acute and late toxicities were acceptable. Radiotherapy should be considered as adjuvant treatment for high-risk prostate cancer, especially with positive margins or extracapsular spread, since it is a safe and well-tolerated treatment.

1 Rossi CJ Jr, Joe Hsu IC, Abdel-Wahab M, Arterbery VE, Ciezki JP, Frank SJ, Hahn NM, Moran BJ, Rosenthal SA, Merrick G: ACR appropriateness criteria postradical prostatectomy irradiation in prostate cancer. Am J Clin Oncol *34(1)*: 92-98, 2011.
2 Vargas C, Kestin LL, Weed DW, Krauss D, Vicini FA, Martinez AA. Improved biochemical outcome with adjuvant radiotherapy after radical prostatectomy for prostate cancer with poor pathologic features. Int J Radiat Oncol Biol Phys *61(3)*: 714-24, 2005.

145

RADICAL THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY (3D-CRT) FOR OLD PATIENTS WITH LOCALIZED PROSTATE CANCER

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Background: Radiation therapy and radical prostatectomy are curative treatment options for patients with localized prostate cancer but surgery is seldom offered to prostate cancer patients beyond the age of 75 years. For these patients, radiation therapy is often the only curative option. *Aim:* The aim of the present study was to analyze outcome and acute and late side effects of three-dimensional conformal radiation therapy (3D-CRT) for localized prostate cancer in patients aged 75 years and older. *Patients and Methods:* Ninety-two localized prostate cancer patients aged >75 years were treated at the Radiation Oncology Department in Foggia between January 2007 and December 2009. All patients were affected by intermediate-

risk disease, with PSA 20 ng/ml or less and tumor category T2c or less. Each patient was scored by using the Cumulative Illness Rating Scale (CIRS) Severity Index comorbidity scale. All men were treated with radical 3D-CRT with or without hormonal therapy. None of the patients received treatment of the pelvic lymphatics. Acute and late side-effects were analyzed according to the toxicity criteria of the Radiation Therapy Oncology Group (RTOG). Overall survival, biochemical recurrence, local recurrence rate and metastasis rate were calculated. *Results:* The median follow-up was 25 months and the mean age was 78 years (range: 75-89 years). CIRS Severity Index was none (0) for eight patients, mild (1) for 42 patients, moderate (1.01-2) for 29 patients and severe (2.10-3) for 13 patients. Clinical stage was T1 for 65.2% and T2 for 34.8% of patients. The Gleason score sum was 4 for 16.3%, 6 for 30.4%, 7 for 50% and 8 for 3.3% of patients. Thirty-seven percent of men also received hormonal therapy. The mean total prescribed radiotherapy dose was 76.5 Gy, with a range of 72 Gy to 80 Gy, and all patients reached the total prescribed radiotherapy. Acute side-effects observed were urinary toxicity of G1 for 47.8% of patients, G2 for 19.6% and G3 for 6.5%, while rectal toxicity of G1 was observed for 43.5% of patients, G2 for 13% and G3 for 2.2%. Late side-effects observed were urinary toxicity of G1 for 23.9% and G2 for 3.3%. Late rectal toxicity was G1 for 19.6% of patients and G2 for 6.5% of patients. All patients were still alive at last examination performed in 2010, without metastasis and without local recurrence, and only twelve patients (13%) experienced a biochemical recurrence during follow-up. *Conclusion:* This analysis showed that 3D-CRT of localized prostate cancer is well tolerated by patients over 75 years old. Despite the short follow-up time, our results demonstrate excellent local control and overall survival, and the benefits of this treatment should be offered to all men with prostate cancer >75 years old. Radiotherapy should be considered as a valid treatment for elderly patients with the same modalities of younger patients, where circumstances and medical conditions permit.

146

SALVAGE RADIOTHERAPY FOR CANCER PATIENTS WITH PSA RELAPSE AFTER RADICAL PROSTATECTOMY: OUR EXPERIENCE

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Background and Aim: A detectable serum PSA level after radical prostatectomy is referred to as biochemical relapse and it typically occurs months to years before there is clinical evidence of tumor recurrence. Most studies define biochemical relapse as equal to two or three PSA values that are at least 0.2 ng/ml after prostatectomy. Salvage radiotherapy is often considered as a valid option for these patients (1, 2). In this study, we analyzed the benefit and toxicity of salvage radiotherapy after biochemical relapse. *Patients and Methods:* We retrospectively analyzed the cases of 18 patients who underwent radiotherapy for PSA recurrence after surgery between January 2007 and December 2009 at the Radiation Oncology Department in Foggia. Biochemical relapse was defined as equal to three PSA values that were at least 0.2 ng/ml after radical prostatectomy. At the time of diagnosis of recurrence, the median PSA value was 5 (range 0.5-30.1) ng/ml. Biopsy findings showed local recurrence in ten patients (55.5%). Patients received a median of 72 Gy to the prostate bed without treatment of the regional lymphatics. Recurrence-free survival and overall survival were calculated and toxicity was assessed with RTOG scale. *Results:* The median follow-up was 24 months. Radiotherapy treatment was well tolerated and all patients received the prescribed dose. Acute toxicity included rectal (G0, 72.3%; G1, 16.6%; G2, 11.1%) and urinary events (G0, 66.8%; G1, 22.1%; G2, 11.1%). Late toxicity included rectal (G0, 88.9%; G1, 11.1%; G2, 0%) and urinary events (G0, 77.8%; G1, 11.1%; G2, 11.1%). Three-year overall survival and recurrence-free survival were 94.5% and 89.5%, respectively. Five-year overall survival and recurrence free survival were 90% and 84.5%, respectively. *Conclusion:* Salvage radiotherapy is an effective treatment after radical prostatectomy, and in cases of persistent PSA following surgery for prostate cancer, it can be used with a significant chance of overall survival and recurrence-free survival. Complications are similar to those reported for adjuvant irradiation.

1 Neuhof D, Hentschel T, Bischof M, Sroka-Perez G, Hohenfellner M and Debus J: Long-term results and predictive factors of three-dimensional conformal salvage radiotherapy for biochemical relapse after prostatectomy. Int J Radiat Oncol Biol Phys *67(5)*: 1411-1417, 2007.

2 Peyromaure M, Allouch M, Eschwege F, Verpillat P, Debré B and Zerbib M: Salvage radiotherapy for biochemical recurrence after radical prostatectomy: a study of 62 patients. Urology *62(3)*: 503-507, 2003.

147

HYPOFRACTIONATION *VERSUS* CONVENTIONALLY FRACTIONATED RADIATION THERAPY FOR PROSTATE CANCER: LATE TOXICITY

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Background: Recent analyses suggest that the fractionation sensitivity of prostate tumors is high and many hypofractionated protocols are being tested (1). Since the alpha/beta ratio estimates for prostate cancer are much lower than the typical values for many other types of tumor (2), we performed a small randomized trial to compare a hypofractionated *versus* a conventional schedule for radiotherapy in localized prostate carcinoma. We have already reported the acute toxicity (3). Now our aim is to evaluate late gastrointestinal (GI) and genitourinary (GU) toxicities in the two patient groups and to assess the mathematical model theoretically predicting equivalent fractionations. *Patients and Methods:* From September 2008 to July 2009, 40 patients with cT1-T2N0M0 prostate cancer were randomized to receive either a conventional or a hypofractionated radiation therapy with curative intent. Patients were stratified according to stage, Gleason score and presenting prostate-specific antigen level; 9 patients were at low risk and 31 patients were at intermediate risk according to Partin classification. The latter patient group received neoadjuvant hormonal therapy that started two months before the radiotherapy onset and continued during radiotherapy. Treatments were delivered using four to six coplanar 10-18 MV photon beams at a dose of 72- 78 Gy in 36-39 fractions within 7-8 weeks, or 64.8-70.2 Gy in 24-26 fractions within 5 weeks. Based on standard linear-quadratic modeling, the hypofractionated protocol was designed to keep late complications constant in rectal tissues. GI and GU toxicities were scored according to the RTOG/EORTC system. Efficacy of radiotherapy, based on clinical, radiologic and prostate-specific antigen data, was also evaluated every three months for two years and every six months subsequently. *Results:* All patients completed the whole course of radiotherapy without interruptions. Minimum follow-up was one and a half years; median follow-up was 25 months. None of the patients experienced grade 3-4 toxicity. Grade 1 and grade 2 GI and GU toxicities occurred during and soon after treatment in both groups without significant differences. In the long term, 35% of patients in the hypofractionated group and 40% of patients in the control group reported increased frequency of urination or nocturia ($p>0.5$). Their symptoms cannot be scored as G1 because they did not reach twice the level of the pretreatment habit. Only one patient in the hypofractionated group presented an actinic proctitis ($p>0.5$); moreover, this patient suffered from a pre-existing hemorrhoidal disease. *Discussion and Conclusion:* No difference was noted in the chronic complications between hypofractionated and conventionally fractionated radiotherapy groups. As regards late rectal side-effects, according to the linear-quadratic formula in our study design, late toxicity was already expected to be equivalent in the two treatment groups. Our study confirms that hypofractionation is a promising regimen for prostate cancer radiotherapy and that a linear-quadratic formula is a reliable radiobiological model. The follow-up period was long enough to conclude that the hypofractionated schedule was well tolerated in both the short and long term and the incidence of clinically significant GI and GU toxicity after conventional and hypofractionated radiotherapy appeared to be similar. Longer follow-up is mandatory to evaluate the effectiveness of the two regimens. Regarding tumor control, assuming a low alpha/beta ratio for prostate carcinoma, we expect an interesting therapeutic gain.

1 Brenner DJ *et al*: Direct evidence that prostate tumors show high sensitivity to fractionation (low α/β ratio), similar to late-responding normal tissue. Int J Radiat Oncol Biol Phys *52*: 6-13, 2002.
2 Dasu A: Is the α/β value for prostate tumors low enough to be safely used in clinical trials? Clinical Oncol *19*: 289-301, 2007.
3 Spagnoletti G *et al*: Hypofractionated *versus* conventionally fractionated radiation therapy for prostate cancer: our first results. Anticancer Res *30*: 1472-1473, 2010.

148

VIRTUAL HDR CYBERKNIFE® TREATMENT FOR LOCALIZED PROSTATE CANCER. PRELIMINARY EXPERIENCE

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Aim: The Cyberknife is an imaging-guided device for delivering high radiation doses to a precisely defined three-dimensional target volume. The Virtual HDR Cyberknife is indicated for patients with localized cancer prostate (T1-T2b) with favorable prognosis (Gleason score ≤6, PSA ≤10 ng/ml) and selected patients with intermediate prognosis (Gleason score of 7, PSA 10.2-20 ng/ml). The low α/ß ratio for prostate cancer requires high radiation with an hypofractionated schedule of dose for tumor control and it has been shown to be biologically lethal for prostate cancer cells. In this report, we summarize preliminary experience with planning emulating HDR brachytherapy dose distribution. *Patients and Methods:* At our institution, over a period of 36 months, 11 patients with a median age of 78 (range 73-86) years and a median Gleason score of 6 (range 5-7) were submitted to treatment with the Virtual HDR Cyberknife. The planning target volume (PTV), defined with MRI and CT imaging, included the prostate and seminal vesicles, plus 2 mm of expansion for favorable prognosis or 5 mm for intermediate prognosis in all directions,

except posteriorly. The prescription dose was 38 Gy in four fractions with an extraurethral PTV Dmax at least 150% of the prescription of dose. The Fiducial Tracking System follows the fiducials that are placed one week before. *Results:* A dose of 38 Gy in four fractions with a median dose of 60% (range 57-75%) was prescribed for all patients. No biochemical failures were observed in a median follow-up of 12 (range 3-36) months. The median value of pre-treatment PSA was 8.8 (range 4.5-14.3) ng/ml and this decreased in patients with a follow-up of more than three months, with a median value of 0.16 (range 0.032-1.21) ng.ml. Acute and late grade 2-3 rectal or urinary toxicities were observed in some patients. Only one patient had acute G3 rectal toxicity. One patient died of other causes. *Conclusion:* The Virtual HDR Cyberknife is a non-invasive and safe method for low-intermediate risk prostate cancer, improving PSA response. Further work is needed to investigate late complications and effective tumor control.

150
RECTAL AND URYNARY TRACT TOXICITY IN IPOFRACTIONATED 3DCRT PROSTATE CANCER

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Background: Recent analysis of patient outcome after radiotherapy has led to the assumption that the α/β ratio of prostate cancer is low. To deliver an equivalent biological dose to the prostate using fewer and larger fractions than the conventional 2 Gy (hypofractionation), the total dose must be reduced proportionally. If the α/β ratio is lower in the tumor than in the surrounding late-responding healthy tissue, the equivalent total dose delivered to the tumor tissue will translate into a significant reduction of the total equivalent 2 Gy dose absorbed by the healthy tissue, with a potential decrease in the late side-effects. *Aim:* The aim of the study was to estimate rectal and urinary tract toxicity when prostate and seminal vesicles receive hypofractionated (310 cGy/day) 3DCRT for all patients (lower, intermediate and high risk recurrence). *Patients and Methods:* Fifty consecutive patients were treated with hypofractionated 3DCRT 310 cGy/day to 62 Gy to the prostate and vesicles between September 2009 and August 2010. The mean age was 72 years (median 73, range 59-83 years). Based on prognostic classification according to guidelines by the National Comprehensive Cancer Network, all patients were divided into the following groups: favorable prognosis, 9 patients (18%); intermediate prognosis, 16 patients (32.8%); and unfavorable prognosis, 25 patients (50%). The mean PSA at diagnosis was 36 ng/ml (median 11.6 ng/ml, range 1.84-465). The mean Gleason score was 7 (median 7, range 4-10). Hormonotherapy was administered in 45 patients (90%). Total androgenic deprivation was used in 60% of patients, peripheral antagonist in 30%, and LH-RH in 10%. The mean treatment time was 38 days. The mean dose to planning treatment volume (PTV) was 62.45 Gy (median 62.26 Gy). The mean percentage of rectal volume receiving 38 Gy (rV38) was 43%. The mean percentage of rectal volume receiving 54 Gy (rV54) was 22%. The mean percentage of bladder volume receiving 38 Gy (rV38) was 34%. The mean PTV volume was 151 cc. The mean follow-up was of 12 months. The patients were treated according to Memorial Sloan–Kettering Cancer Center set-up (Zelefsky IJROBP1994): 6 fields, MLC conformation, photons of 6 or 15 MV. DVH was calculated for PTV, rectum, bladder and femoral heads. For OAR delineation on TPS, bladder wall and rectum wall was drawn. All patients were clinically evaluated for urinary and rectal complications according to RTOG acute effects score. Results and *Conclusion:* According to the American Society for Therapeutic Radiology and Oncology, a rise by 2 ng/ml or more above the nadir PSA is considered the standard definition for biochemical failure after radiotherapy, with or without hormonotherapy. Only one patient had biochemical recurrence and one patient systemic disease (bone metastasis). Regarding acute toxicity, we registered 13/50 G1(26%) and 9/50 G2(18%) urinary complications, and 9/50 G1(18%) and 1/50 G2(2%) gastrointestinal complications. No G3 and G4 acute complications were registered. Hypofractionation allowed reduction of treatment time.

151
ADAPTIVE RADIOTHERAPY WITH GOLD MARKERS TO REDUCE RADIOTHERAPY-RELATED TOXICITY IN LOW-RISK PROSTATE CANCER PATIENTS

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Aim: The main aim of this study was to highlight the good bladder and rectum tolerance recorded in a group of patients with low-risk prostate cancer when treated with an adaptive on-line radiotherapy protocol. *Patients and Methods:* Twenty-eight low-risk patients with cT1-2 prostate-confined adenocarcinoma were submitted to an image-guided radiation therapy protocol at the Radiotherapy Department of Ancona, between January 2007 and November 2010. Three gold markers (1.2 mm×3 mm) were placed in the prostate (left base, apex and right mid-gland) under ultrasound guidance by the referring urologist (AG); before implantation, patients had an enema and were placed on antibiotics; local rectal anesthesia was performed.

The correct gold marker positions were verified by fluoroscopy. The planning computed tomography (CTsim) was acquired (1 mm axial slices) five days after implantation, when stability of the markers had been achieved. Polyurethane foam was individually tailored to immobilize the legs and to ensure a stable positioning of the patient's pelvis; the patients were asked to keep a full bladder and an empty rectum in order to reduce inter-fraction organ-filling variability. The prostate without the seminal vesicles as clinical target volume (CTV) was delineated by the same expert physician (GM). An initial 3D conformal RT plan (pre-planning) was performed, prescribing 78 Gy (2 Gy per fraction) to the planning target volume (PTV) and using a standard CTV-to-PTV margin of 1 cm except for 0.5 cm on the posterior edge. A daily match of marker positions between CBCT and CTsim was performed in order to correct inter-fraction prostate motion. After the first week of treatment, a new treatment plan was performed for each patient where the first five CBCTs were used to create a patient personalized PTV , as a merged volume, including the 5-day prostate position variability (plus 2 mm due to operator and Linac mechanical inaccuracy). Patient symptoms were monitored regularly (at least each 3-4 months up to the time of writing). The observed toxicity was recorded and classified according to the RTOG score. *Results:* The applied adaptive on-line protocol with scheduled re-planning to compensate for the anterior prostate tilt (incorrigible with a linear shift) allowed us to reduce CTV-PTV margin in the majority of patients: the median CTV-PTV margin in the pre-planning phase was 98.82±25.70 cc (range 29.73-134.14 cc), while the median CTV-PTV margin in the re-planning phase was 20.38±12.56 cc (range 4.79-56.09 cc), with a median advantage of 78.44±21.67 cc (range 24.94-117.57 cc). The reduction of re-planning margin allowed a reduction of the dose to the rectum and bladder, and resulted in low acute and late toxicity. Late rectal toxicity was recorded only in three patients (one G1, one G2 and one G3 patient) and late bladder toxicity in 13 patients (eight G1, four G2 and one G3 patients); all the patients, except one, presented sexual impotence, mainly as worsening of pre-radiotherapy impotence due to hormonal therapy; only one patient showed true radiotherapy-related impotence. *Conclusion:* Image-guided radiation therapy is helpful to personalize and reduce the CTV-PTV margin. Consequently, toxicities were very low, with few cases of G1-G2 acute and late bladder and rectal effects, and only two cases of G3 toxicity.

153
INTRAOPERATIVE RADIOTHERAPY DURING RADICAL RETROPUBIC PROSTATECTOMY

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Aim: To evaluate the efficacy, complications and outcome of intraoperative radiotherapy (IORT) during retropubic prostatectomy (RRP). *Patients and Methods:* From January 2009 to February 2010, twelve patients were submitted to RRP, obturatory lymphadenectomy and IORT. At clinical staging, six tumors were T2c, three presented with perineural infiltration, two showed seminal vesicle infiltration and one extracapsular disease. Mean preoperative PSA value was 14 (range 11-23) ng/ml and the Gleason score at biopsy was 7-9. None of the patients presented preoperative incontinence. Vesico-urethral anastomosis was performed with 6-8 stitches. IORT was administered with linear electron accelerator and administration of energy of 12 MeV. *Results:* The time surplus for IORT administration was 45 minutes (±30-60 minutes according to the difficulty in finding the correct position of the probe underneath the pubic bone),with the entire procedural time being 200 (±30) minutes. Bleeding was less than 500 cc, without need for transfusions. Three tumors were pT2c, three were pT3a, one was pT3b, one was pT2cN1 and four patients presented R+. Perioperative complications were not observed. Bladder catheter was removed after ten days. At three months follow-up, five patients presented stress-incontinence (three pads/day); at six months, one patient still presented the same problem. Erectile dysfunction was reported by all patients. PSA failure was not present at mean follow-up of 16 (range 13-23) months. *Discussion:* IORT during RRP can be used safely in the treatment of prostate cancer with locally advanced disease or with high Gleason score. Oncologic follow-up was too short and the number of patients was too low in our series to lead to conclusions on the outcome, but the absence of PSA failure is encouraging. The use of a linear electron accelerator with maximum energy administration of 12 MeV does not seem to expose the patients to significant adverse effects. *Conclusion:* Selected patients affected by prostate cancer can benefit from radical surgery associated with a supplementary treatment as IORT, without evidence of significant adverse side-effects.

154
RARE NON-GERM CELL TESTICULAR TUMOURS: LEIOMYOSARCOMA AND ADULT TYPE GRANULOSA CELL TUMOUR

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Background: Non-germ cell tumors of the testicle include the sex cord/gonadal stromal tumors (Leydig cell, Sertoli cell and granulosa cell) and non-specific stromal tumors (leiomyosarcoma). These tumors are very rare and account for only 2-4% of adult testicular tumors. Primary testicular leiomyosarcomas are soft-tissue tumors, arising from the undifferentiated smooth muscle cells of mesenchymal origin. Risk factors are reported to be high-doses of anabolic steroids, chronic inflammation, radiotherapy, or an association with testicular germ cell tumors. Testicular granulosa cell tumors are divided into two histological types: adult and juvenile. Adult type tumors arise from epithelial tissue of the gonads. The average age at presentation is 44 years and the tumors are usually >7 cm diameter. *Case Report A:* A 65-year-old man presented at our clinic with a six-month history of left testicular pain and swelling. His past medical history was significant for a left testicular trauma that had occurred several years before. Scrotal ultrasound showed an intratesticular mass (4×4 cm), while whole-body computed tomography (CT) scans and tumor markers were normal. The patient underwent left radical orchiectomy and histopathological examination of the excised mass was consistent with high-grade leiomyosarcoma. There was no evidence of recurrence or metastasis 16 months postoperatively. *Case Report B:* A 26-year-old man presented at our clinic with a two-month history of left testicular pain. Ultrasound showed left sex cord and testicular inflammation and a small nodule (7 mm) of the left testis. The pain resolved after medical therapy and two months afterwards an ultrasound examination confirmed the presence of the nodule. The patient underwent surgical resection of the nodule. The histological picture was consistent with adult type granulosa cell tumor. There was no evidence of recurrence or metastasis ten months postoperatively. *Discussion:* Granulosa cell tumors and leiomyosarcoma of the testis are uncommon neoplasms and, to date and our knowledge, only 17 cases of leiomyosarcoma and only 25 cases of adult type granulosa cell tumors have been reported in the literature. All leiomyosarcomas and 20% of the adult type granulosa cell tumors are malignant. In both cases, distant metastases are relatively rare. The standard treatment is orchiectomy. Adjuvant treatments, such as chemotherapy, radiotherapy or retroperitoneal lymph-node dissection, do not seem able to improve prognosis, which remains good in cases of localized tumors. *Conclusion:* In our opinion, scrotal trauma, associated with chronic inflammation, should be considered as a risk factor for testicular cancer. In cases of small testicular nodules (<1 cm), an initial conservative approach may be considered. A reasonable follow-up for these rare adult testicular carcinomas requires, in our opinion, a six-month clinical examination with CT.

155

RARE HISTOLOGIC VARIANTS OF UROTHELIAL BLADDER CANCER AT ANALYSIS OF RADICAL CYSTECTOMY SPECIMENS: OUR EXPERIENCE

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Background and Aim: Urothelial bladder cell carcinoma has a propensity for divergent differentiation that has increasingly been recognized in recent years due to heightened awareness and improved immunohistochemical techniques. Moreover, some authors suggested that urothelial cancer with divergent differentiation, even if it occurs only rarely, has a worse prognosis when compared with pure urothelial cancer. However, the management options for this disease are still under discussion. The aim of this study was to evaluate the prognosis of patients affected by uncommon pathological variants of bladder cancer who had undergone radical cystectomy. *Materials and Methods:* Radical cystectomy specimens, collected from January 2000 and December 2009, were reviewed pathologically in order to identify the pathological variants of urothelial bladder cell carcinoma. All pathological analyses were carried out by a single uropathologist. Clinical, pathological and instrumental data at radical cystectomy were collected. Moreover, all clinical data regarding patient outcome were analyzed. *Results:* A total of 66 pathological variants of bladder cancer were collected over the entire study period. Pathological analysis showed: 41 cases of squamous cell carcinoma, 8 cases of micropapillary carcinoma, 4 cases of clear cell carcinoma, 3 cases of adenocarcinoma, 2 cases of small cell carcinoma, 2 cases of sarcomatoid differentiation, 3 cases of lymphoepithelioma-like tumor, 1 case of giant cell tumor and two undifferentiated cases. Moreover, we found one pT1, 14 pT2, 2 pT2 with carcinoma *in situ*, 29 pT3a, 5 pT3b, 15 pT4, and 5 N1, 7 N2 and 2 N3. At a mean follow-up period of 97.6 (range 10 to 114) months, 19 patients were alive without disease, 5 were alive with disease progression and 42 had died from their disease (mean survival time=9.7 months). We found that squamous differentiation was the most common variant and was correlated with higher grade and stage. Moreover, bladder carcinoma with sarcomatoid differentiation had a poorer prognosis and patients affected by clear cell carcinoma or micropapillary carcinoma had a better prognosis. *Conclusion:* The present study, by means of a long-term follow-up, showed

that the uncommon pathological variants of urothelial bladder cell carcinoma are specific clinical and pathological entities to be taken into account. Moreover, we should have a high index of clinical suspicion for aggressive disease in patients who present with either urothelial cancer with divergent differentiation or non-urothelial histology at pathological analysis after TURBT.

156

DURATION OF HORMONE SENSITIVITY AND PRE-CHEMOTHERAPY PSA ARE PREDICTORS OF RESPONSE TO DOCETAXEL IN CASTRATION-RESISTANT PROSTATE CANCER

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Background: Castration-resistant prostate cancer (CRPC) after second-line hormonal manipulation is usually treated by a chemotherapeutic regimen based on docetaxel (75 mg/kg/3 weeks)–prednisone (10 mg/day) combination. Nowadays, this therapy represents the gold standard for the treatment of metastatic CRPC, allowing an improvement in the overall survival (OS) and quality of life (QoL) as shown by the landmark trial TAX 327. The best moment at which to start chemotherapy and the pathological features which can affect therapy response are both matters of debate amongst uro-oncologists. The aim of this study was to assess the differences in terms of biochemical/clinical progression-free survival (PFS) and OS in patients with various pathological features of CRPC treated with docetaxel/prednisone (D/P). *Patients and Methods:* We retrospectively reviewed the medical charts of 30 patients with CRPC treated with 3-week docetaxel at 75 mg/kg plus prednisone 10 mg/day in the period 1999-2010. We recorded pathological features of each patient, including PSA at the time of chemotherapy, presence of metastasis, duration of hormone sensitivity, reduction in PSA ≥50% for at least three weeks after chemotherapy induction and adverse events. The end-points were the assessment of biochemical progression intended as three consecutive increments in PSA from PSA nadir, clinical progression intended as development or increase in number and dimension of visceral/bone metastasis and OS. We estimated the interval to biochemical/clinical progression and death according to the pathological features using the Kaplan–Meier method and compared this distribution in a multivariate analysis using the Mantel–Cox test. *Results:* Biochemical progression occurred in 19 cases (63%) after an average of 8.1 (range: 1-22) months, PFS and cancer-related death occurred in 15 (50%) and 16 patients (53%) after an average of 9.1 (range: 3-21) and 11.8 (range: 2-27) months, respectively. In the univariate analysis, we observed a statistically significant increase of clinical PFS in those patients with a reduction in PSA ≥50% after chemotherapy induction or with hormonal sensitivity longer than 50 months (14.9 months, p=0.04 and 16.3 months, p=0.08, respectively). Prolonged OS was observed in those patients in which chemotherapy was started with a PSA<50 ng/ml compared to those in which PSA at therapy induction was ≥50 ng/ml (17.5 vs.12.7 months, p=0.02). Patients who developed CRPC after 50 months of hormonal treatment showed a prolonged OS compared to patients with a hormone sensitivity of less than 50 months (20 vs.11.7 months, p=0.01). Evidence of bone/visceral metastasis did not significantly affect either the biochemical/clinical PFS or OS. The multivariate analysis showed a prolonged biochemical/clinical PFS (p=0.01; HR=7.02, 95% CI=1.3-36.2) and OS (p=0.01; HR=6.9, 95% CI=1.5-31.3) in patients with hormone sensitivity ≥50 months; a prolonged clinical PFS in case of PSA reduction ≥50% (p=0.02; HR=11.01, 95% CI=1.3-89.82) and hormone sensitivity ≥50 months (p=0.01; HR=10.6, 95% CI=1.6-67.9). Docetaxel/prednisone treatment was generally well tolerated, with grade 1-2 adverse events, the most common of them being anemia and neutropenia in four (13%) and six patients (20%), respectively. *Conclusion:* According to our data, the duration of hormonal sensitivity represents a significant predictor of chemotherapy response, while PSA reduction ≥50% after chemotherapy induction is correlated with a prolonged clinical PFS. Initiation of chemotherapy with a PSA <50 ng/ml conferred an increase in OS in the univariate model. Studies based on larger series are needed to support these findings.

157

ASSOCIATION OF *N*-ACETYLTRANSFERASE 2 POLYMORPHISM WITH RISK FACTORS IN UROTHELIAL CANCER

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Aim: Biological and epidemiological data suggest that genetic polymorphisms of enzymes involved in activation and detoxification processes may play a role in determining susceptibility to bladder cancer, especially in cases of

environmental carcinogenic exposure. Two isoforms of *N*-acetyltransferase, NAT1 and NAT2, are involved in the detoxification of arylamine contained in cigarette smoke and certain foods. The inactivation of arylamine by NAT2 must be rapid to prevent the formation of an electrophylic compound that on binding to DNA may cause mutations which can lead to tumorigenesis. Gene polymorphism produces a 'slow acetylator' phenotype with a reduced capacity to inactivate carcinogens. The purpose of this study was to verify the presence of *NAT2* gene polymorphism in patients with bladder carcinoma and in healthy individuals exposed to risk factors. *Materials and Methods:* Analysis of *NAT2* gene polymorphism was studied on DNA extracted from peripheral blood. The *NAT2* gene was amplified by PCR. DNA bands were visualized by restriction fragment-length polymorphism (RFLP) analysis. Finally, an allele-specific amplification of *NAT2*5* was carried out. A volume of 50 μg of protein from each lysate was run on 10% SDS-PAGE and subsequently transferred to PVDF membrane. The membranes were blocked with 5% non-fat dry milk in TPBS and then incubated with the NAT2 antibody. Samples from 160 individuals were analyzed (48 female and 112 male), of whom 80 were bladder cancer patients (71 smokers and 20 exposed to environmental carcinogens) and 80 were healthy individuals (27 smokers and 24 exposed to environmental carcinogens). *Results:* In the 80 patients, *NAT2*5* polymorphism consisted of T341C specific nucleotide substitution for this allele. Independently of histological grade (G3 n=57, G2 n=15, G1 n=8) and stage (Ta n=21, T1 n=37, T2 n=10. T3 n=7, T4 n=5), all bladder cancer patients had *NAT2* polymorphism. Moreover, nearly all healthy individuals at risk of bladder cancer had *NAT2* gene polymorphism. In patients with carcinoma, the *NAT2*5* allele was associated with a significant reduction or absence of protein expression compared with healthy individuals (p=0.001). *Conclusion:* NAT polymorphism characterization may help to identify people who are not at risk of developing bladder cancer even if exposed to environmental carcinogens. The mechanism responsible for reduction of protein expression in bladder cancer is under investigation.

158

RENAL CELL CARCINOMA: DOES TRANSCRIPTIONAL DEREGULATION OF ADULT RENAL STEM/PROGENITOR CELLS LEAD TO ONCOGENESIS?

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Background: Cancer stem cells (CSCs) are a subset of undifferentiated cells responsible for tumor initiation, maintenance and progression. They possess an unlimited potential for proliferation, self-renewal ability and generation of differentiated progeny cells that become the most important cell population of the tumor. Recently, in an experimental model of severe combined immunodeficient mice, a population of $CD133^+$ stem cells isolated from human renal cell carcinoma (RCC) and which was able to initiate tumor growth was detected. *Aim:* The aim of this study was the isolation and characterization of $CD133^+$ cells derived from human clear cell RCC in order to study the features of the progenitor/stem cells, including the ability for self-renewal. *Patients and Methods:* Fresh human renal cortical tissue was harvested from 15 patients diagnosed with RCC. Tissue fractions of both healthy and tumorous renal tissue were used for the isolation of progenitor/stem cells. Two healthy cell populations were isolated: one resident in the renal tubules and the other in the glomeruli. The same procedure was also used for the pathological tissue, but in this case it was impossible to distinguish tubules and glomeruli since this portion appeared deprived of a compartmentalized structure. The isolated cells were purified for stem cell marker CD133. The $CD133^+$-derived clones were purified for CD24. This marker allowed us to distinguish resident renal stem cells from hematopoietic ones. The expression of classic markers of stemness (CD133, PAX-2, CD24, BMI-I, OCT-4) and tumorigenicity (NCAM, CD10 and VEGFR/KDR) was assessed by cytofluorimetric analysis. Therefore, lysate protein from $CD133^+/CD24^+$ cells was used to perform a protein array including 16 stem cell markers (OCT3/4, NANOG, SOX2, E-cadherin, α-fetoprotein, GATA4, HNF-3β/FOX A2, PDX-1/IPF1, SOX17, OTX2, TP63/TP73L, Gosecoid, SNAIL, VEGF R2/KDR/FLK1, and HCG). *Results:* We isolated viable renal stem cells (CD133+/24+) from healthy and neoplastic renal tissue. By cytofluorimetric analysis, we confirmed the expression of the following markers in CSCs: CD133, CD24, PAX-2, BMI-I, and OCT-4. Only a small percentage of this population was $NCAM^+$. The quantitative analysis of cellular proteins obtained from the array confirmed the stemness of $CD133^+/24^+$ CSCs and the increased expression of particular proteins NANOG, OCT3/4, SOX2, SOX 17, OTX2 and SNAIL *versus* the normal stem cells isolated from the same patient. *Discussion and Conclusion:* Taken together, these results showed that stem cells are present in clear cell RCC and that they are more undifferentiated than normal stem cells due to their expression of embryogenesis-derived markers. It is conceivable, therefore, that only the eradication of CSCs or, alternatively, the induction of differentiation in cells without self-renewal potential, is able to lead to effective treatment of

cancer. Stem cell identification in RCC and the uncovering of more specific markers could be useful for optimizing therapeutic strategies and for gaining prognostic and predictive information in RCC patients.

1 Blana A, Murat FJ, Walter B *et al*: First analysis of the long-term results with transrectal HIFU in patients with localized prostate cancer. Eur Urol *53*: 1194-1203, 2008.
2 Pasticier G, Chapet O, Badet L *et al*: Salvage radiotherapy after high-intensity focused ultrasound for localized prostate cancer: early clinical results. Urology *72*: 1305-1309, 2008.
3 Riviere J, Bernhard JC, Robert G *et al*: Salvage radiotherapy after high-intensity focused ultrasound for recurrent localized prostate cancer. Eur Urol *58(4)*: 567-573, 2010.

159

CASE REPORT: SALVAGE RADIOTHERAPY IN PROSTATE CANCER RECURRENCE AFTER HIGH-INTENSITY FOCUSED ULTRASOUND

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Background: Although not validated and still controversial, high-intensity focused ultrasound (HIFU) has been used in recent years for the treatment of localized prostate cancer. Salvage radiotherapy after radical prostatectomy has been widely used for many years. We report a patient treated with salvage radiotherapy for a histologically proven local recurrence after HIFU treatment. *Case Report:* In November 2005, a 72-year-old man affected by Parkinson's disease was bioptically diagnosed with a prostatic adenocarcinoma, Gleason pattern score 2+3 (1/6 cores positive; clinical stage 1c). Basal PSA was 3.74 ng/ml. No staging procedures were implemented. In May 2006, he was treated with HIFU, with control of the disease but with an associated complete incontinence. In March 2010, because of progressively increasing PSA (1.6 ng/ml), the patient underwent magnetic resonance imaging of the pelvis, showing abnormal solid tissue with contrast enhancement measuring 20×9 mm in the left posterior region with interruption of the prostatic capsule and extraprostatic fat infiltration. A bioptic sample histologically confirmed the cancer recurrence. The patient was initially treated with hormone therapy (bicalutamide 150 mg daily *per os*). We treated the patient with conformal radiotherapy (CRT) at a dose of 74 Gy in 37 fractions. The treatment was performed with periodic control of the treatment set-up by cone beam CT (image-guided radiotherapy). The treatment was well tolerated. Toxicity was measured using the RTOG scale (gastrointestinal toxicity of grade 1 and a genitourinary toxicity of grade 2). At the end of treatment, PSA was 0.57 ng/ml. Hormone therapy was continued during the treatment and interrupted six months after. After one year, the patient is free of recurrence and without evidence of late toxicity. *Conclusion:* Salvage radiotherapy after HIFU is feasible and safe, with a tolerable acute toxicity, while a longer follow-up is needed to define the impact on late sequelae and outcome.

160

COMPARISON BETWEEN INCIDENCE OF COMPLICATIONS, STRATIFIED ACCORDING TO CLAVIEN SYSTEM IN OPEN *VERSUS* ROBOTIC PROSTATECTOMY

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Background: The introduction of PSA monitoring has assisted in the downstaging of prostate cancer and diagnosis in younger men, consequently meeting oncological goals and achieving a good quality of life in terms of continence, potency, hospitalization and morbidity. According to EAU 2010 guidelines, radical prostatectomy is considered the gold standard of treatment for prostate cancer. Robotic approaches have been developed to achieve these outcomes. In 1992 and 2004, Clavien (1) proposed a simple grading system for surgical complications, which was then used by Coehlo *et al*. (2) to classify robot-assisted radical prostatectomy. The aim of this study was to compare incidence of complications, stratified according to the Clavien system, in retropubic radical prostatectomy (RRP) *vs*. robot-assisted radical prostatectomy (RARP). *Materials and Methods:* From February 1999 to May 2008, we performed 953 RRP procedures and from November 1st 2006 to December 31st 2010, we performed 697 RARP procedures. To avoid population bias related to the learning curve, we selected the last 197 RRP procedures that were performed two years before the first RARP procedure, and 358 consecutive RARP procedures that were performed from February 2008 to February 2010. All RARP were performed according to Patels description, with rhabdosphincter reconstruction according to the Rocco-Patel technique; pelvic lymphadenectomy was performed for intermediate-risk patients according to the Kattan nomogram. At the preliminary analysis, RRP and RARP populations were comparable. We collected data regarding perioperative complications, defined according to Clavien and Dildo as any

deviation from the normal postoperative course. *Results:* A total of 115 overall complications were recorded in the RRP group *vs*. 87 in the robotic group (p-value=0.001). A total of 45.2% of patients who underwent RRP had one complication *vs*. 19.0% of patients in the robotic group. The following observations were made: inguinal hernia, 9 *vs*. 7 in the RRP *vs*. the RARP group, respectively; drained hematoma, one 1 *vs*. 4; acute urine retention, 5 *vs*. 9; perianastomotic leakage, 30 *vs*. 31; drained lymphocele, 6 *vs*. 2; balanitis, 10 *vs*. 0; pneumonia 0vs.2; needed blood transfusion 44 vs.19; and ureteral fistula, 1 *vs*. 0, respectively. A single patient in each group experienced an early anastomotic stenosis. A total of 7.9% vs.11.8% of the patients in the RRP *vs*. the RARP group, respectively, had Clavien I complication, 83.1% *vs*. 73.2% had Clavien II complication, 9% *vs*. 2.9% had Clavien IIIa complication and 0 *vs*. 11.8% had Clavien IIIb complication, respectively. Univariate and multivariate analyses of potential predictors for postsurgical complications showed that surgical technique, presurgical hemoglobin value and blood loss >500 ml were independent variables correlated with an increased risk. *Discussion:* Patel *et al*. reported complication rates of 5% in a series of 2500 patients. Higher complication rates were reported by Murphy *et al*., who showed a complication rate of 15.7%, with 5.2% being Clavien III complication, and by Novara *et al*., who showed an overall complication rate of 21%, with 3% being Clavien III and 0.2% being Clavien IV complications. As far as comparison between RRP and RARP is concerned, recently published studies reported comparable perioperative overall complication rates; Ficarra *et al*. showed only a non-statistically significant trend in favor of RARP (2). Carlsson *et al*. (3), when comparing RRP and RALP, showed a lower incidence of overall and major complications with the robotic approach. *Conclusion:* RARP is a safe option for treatment of localized prostate cancer, presenting lower overall complication rates than open surgery. It seems that even if less frequent, adverse events can be more serious than when an open approach is used.

1 Dindo D, Demartines N and Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg *240(2)*: 205-213, 2004.

2 Coelho RF, Palmer KJ, Rocco B, Moniz RR, Chauhan S, Orvieto MA, Coughlin G and Patel VR: Early complication rates in a single-surgeon series of 2500 robotic-assisted radical prostatectomies: report applying a standardized grading system. Eur Urol *57(6)*: 945-952, 2010.

3 Carlsson S, Nilsson AE, Schumacher MC, Jonsson MN, Volz DS, Steineck G and Wiklund PN: Surgery-related complications in 1253 Robot-assisted and 485 open retropubic radical prostatectomies at the Karolinska University Hospital, Sweden. Urology *75*: 1092-1099, 2010.

161

ADJUVANT *VS*. SALVAGE RADIOTHERAPY AFTER RADICAL SURGERY FOR PROSTATE CANCER: EXPERIENCE AT THE NIGUARDA CA' GRANDA HOSPITAL

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Aim: The optimal role of radiotherapy (RT) in prostate cancer after radical prostatectomy is controversial. This retrospective review compares postoperative modalities of RT to investigate the optimal timing of RT. The aim of the study was to determine any advantage between the different modalities of treatment. *Patients and Methods:* Between 1994 and 2008 at the Niguarda Ca' Granda Hospital in Milan, 338 patients were treated with external beam RT to the prostate bed after radical prostatectomy (pT2R+, pT3). These patients were divided into three groups: 137 patients (40.5%) who underwent RT within six months from surgery and whose post-prostatectomy PSA level was undetectable (group A); 98 patients (29%) treated with RT within six months, but with persistent PSA values (PSA >0.02 ng/ml) (group P); and 103 patients (30.5%) who underwent RT in the salvage setting, following a delayed rise in PSA or based on clinical evidence of relapse (group S). Adjuvant androgen ablation was given in 17/137 patients in group A, 27/98 patients in group P and 16/103 patients in group S. In group P, the mean value of PSA was 0.36 (range 0.02-7.7) ng/ml, while the mean PSA for group S was 0.78 (range 0.1-5.5) ng/ml. For the three groups, the median RT dose was 64.8 (range 59.4-72) Gy. The Kaplan–Meier method was used to estimate the probabilities of biochemical relapse-free survival (b-RFS) and overall survival (OS). The log-rank test was used to test the significance between the three groups with respect to selected endpoints. *Results:* For all groups, gastrointestinal and genitourinary toxicities were never higher than grade 2 according to RTOG classification. In group A, there were six deaths, four unrelated to prostate cancer and two due to metastatic disease; in group P, there were five deaths (three due to cancer and two due to other disease) and in group S there were six deaths (four related and two not related to prostate cancer). We evaluated biochemical relapse of disease according to ASTRO criteria. A total of 27/137 patients (19.7%) in group A, 35/98 patients (35.7%) in group P, and 64/103 patients (62.1%) in group S showed a biochemical relapse. The three groups showed a statistically significant difference in b-RFS (p<0.01), while there was no significant difference in OS. Univariate analysis was performed for two subgroups (GS <or ≥8 and RT dose ≥or <70 Gy). For all three groups, patients with GS<8 showed a significantly better b-RFS than those withGS≥8, while the

dose of radiotherapy did not significantly affect b-RFS, possibly because of the small number of patients receiving a dose ≥70 Gy (5/137 in group A, 21/98 in group P and 39/103 in group S). *Conclusion:* Our data confirm that clinical outcome after salvage RT is poorer if compared to outcome after adjuvant treatment. In the adjuvant setting, the detectability of PSA impacts negatively on clinical outcome. Further data will be presented on the impact of GS and of RT dose on outcome.

162
FROZEN SECTION EXAMINATION IN INTRAOPERATIVE DIAGNOSIS OF TESTICULAR CANCER: OUR EXPERIENCE

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Background: Testicular cancer represents between 1% and 1.5% of all male neoplasms and 5% of urological tumors, with there being an increase in the incidence in the last 30 years in the majority of industrialized countries in North America, Europe and Oceania. Testicular cancer normally appears as a casually found, painless, unilateral mass in the scrotum; ultrasound confirms the presence of a testicular mass and exploration of the contralateral testis can lead to diagnosis in cases where the testicular mass is not palpable and in cases of retroperitoneal or visceral lesions or elevated serum markers. All patients with a suspected testicular mass must undergo inguinal exploration; immediate orchiectomy with division of the spermatic cord at the internal inguinal ring must be performed if a tumor is found. If the diagnosis is not clear, a testicular biopsy is taken for frozen section histological examination. Frozen section histological examination is also required in cases of solitary testis or bilateral testicular lesions. We retrospectively reviewed our experience concerning the reliability of frozen section examination in primary testicular tumors by comparing each frozen section examination result to the final diagnosis. *Patients and Methods:* From 2001 to 2009, at IEO, 323 patients underwent orchiectomy. In 80 of these patients (24.7%), the surgeon clamped the spermatic cord and performed a biopsy for frozen section histological examination; this was required for patients with a small tumor without elevated serum markers and for patients with bilateral lesions or single testis, both of which were considered to be cases of doubt. Specimens were well oriented and resection margins properly inked and the pathologist performed a perpendicular section of the tumor with margin including the entire tumor and uninvolved testicular parenchyma. All procedures had to be completed within 20 minutes since the spermatic cord was clamped. In cases of malignancy, radical orchiectomy was performed and in cases of benign findings, the lesion was simply enucleated. Slides of frozen section and the permanent sections were reviewed and compared with regard to the histological diagnosis and presence/absence of malignancy. *Results:* Of the 80 specimens analyzed, 18 (22.5%) were negative for malignancy and 15 (18.7%) were benign lesions such as tumors of non-specific stroma, Leydig cell tumor, cystadenomas, or simple cysts. A total of 50.1% of cases of malignant lesion were diagnosed, in particular, 10 were seminoma, 16 were non seminoma germ cell tumor, 4 were intratubular germ cell neoplasia, 10 were lymphoma, leiomyosarcoma and others. In 8.7% of cases, the diagnosis was delayed. The definitive pathology confirmed the diagnosis in 90% of cases of seminoma, in 95.5% of cases of non seminoma germ cell tumors and in 94.5% of cases of benign lesions. *Discussion:* A total of 80-90% of all testicular masses are malignant germ cell tumors and patients should undergo orchiectomy. On the other hand, benign testicular lesions are recognized in approximately 10-20% of cases, enabling testis-sparing surgery based on the findings of frozen section examination results. Frozen section is accurate for distinguishing benign from malignant lesions and testicular function is preserved, whenever possible, requiring close collaboration between the surgeon and the pathologist. In a study of 317 patients, comparing frozen section examinations results with definitive pathology, Elert *et al*. obtained a correct frozen section diagnosis for all benign lesions, 90% of seminoma and 92% of non seminoma. *Conclusion:* Intraoperative frozen section examination correctly identified more than 90% of malignant and benign testicular masses. Surgical management of testicular tumors based on frozen section examination results is safe and helpful in clinical practice.

1 Elert A, Olbert P, Hegele A, Barth P, Hofmann R and Heidenreich A: Accuracy of frozen section examination of testicular tumors of uncertain origin. EAU guidelines 2010. Eur Urol *41(3)*: 290-293, 2002.

163
LOSS OF LKB1 EXPRESSION IS AN EARLY MOLECULAR EVENT IN PROSTATE CARCINOGENESIS

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Background: In recent years, prostate cancer research has focused on the screening for mutations in genes whose function is critical for cell growth control. However, the molecular mechanisms leading to the development and progression of prostate cancer still are not yet fully understood. Recently, in a murine model, a conditional *Lkb1* knockout was able to induce atypical hyperplasia and prostate intraepithelial neoplasia. Furthermore, the lack of LKB1 positively correlated with beta-catenin nuclear accumulation and Wnt signaling deregulation. In humans, *LKB1* germline mutations cause Peutz-Jeghers syndrome, an inherited condition predisposing to mucocutaneous pigmentations and several types of both benign and malignant neoplasm. *Materials and Methods:* We performed a retrospective analysis of 22 human prostate carcinomas to investigate the possibility of a causative role of *LKB1* deregulation in prostate cancer. Exhaustive analysis of the *LKB1* gene at DNA and protein level was performed by means of direct sequencing, MLPA analysis, methylation PCR, and Western blotting. The LKB1 staining pattern was evaluated by means of immunohistochemistry in different cell subtypes and in different pre-neoplastic and fully malignant cancer specimens. Finally, to test whether the restoration of LKB1 expression and function would affect prostate cancer cell growth, we used DU145 LKB1-deficient cells. *Results:* A significant decrease of LKB1 expression was observed in tumoral tissue compared to healthy tissue. Moreover, a significant inverse correlation of LKB1 protein expression with tumor grade was found. However, none of the samples analyzed, independently of the stage and grade, showed evidence of *LKB1* inactivation by canonical mutational events (point mutation, CpG island methylation). Our immunohistochemical analysis showed that LKB1 had an increased expression in proliferative inflammatory atrophy (PIA), while it was reduced in prostate intraepithelial neoplasia, and totally absent from prostate carcinoma. We also found no evidence of Wnt pathway activation. Finally, we found that reconstitution of a functional LKB1 protein in cancer-deficient cells interfered with cell cycle progression and inhibited tumor cell growth. *Conclusion:* In this study, we report the first molecular analysis of the *LKB1* gene at DNA and protein levels in human prostate cancer. *LKB1* inactivation appears to be a crucial step for prostate cancer initiation and progression, suggesting that *LKB1* can act as a tumor suppressor. The loss of LKB1 expression in high-grade prostate intraepithelial neoplasia occurring in areas of PIA indicates that if PIA represents a precursor lesion of prostate cancer, *LKB1* needs to be silenced in order for such a lesion to progress toward a fully malignant stage.

164
RENAL CELL CARCINOMA AND THYROID METASTASIS WITH THROMBOSIS OF THE INTERNAL JUGULAR VEIN: CASE REPORT

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Background: Approximately 25-33% of patients with renal clear cell carcinoma (RCC) present metastasis at the time of diagnosis, and 40-50% develop metastases later. Metastasis to the thyroid gland is rather uncommon (2-3%). In clinical series, such metastasis is related to a favorable clinical history, with an average time from diagnosis of the RCC to metastasis of more than 100 months (1). The tendency of RCC to extend by means of neoplastic thrombi to larger veins is well known. We present a case of a patient with a palpable thyroid mass which was diagnosed as RCC metastasis. *Patients and Methods:* An 83-year-old woman (with a history of hypertension, hypercholesterolemia, and stroke with left hemiparesis and aphasia, completely restored) presented with a palpable thyroid mass that was clinically suspected to be a multinodular thyroid goiter. Thyroid function serum values were just slightly abnormal: TSH 0.16 Q UI/ml, fT3: 2.22 pg/ml, fT4: 1.33 ng/dl and she had no kidney symptoms. Ultrasound examination of the neck showed an enlarged thyroid with multiple hypoechoic nodules. Biopsy revealed RCC localization. A computed tomography scan revealed a large, nonhomogeneous and partially necrotic mass involving the mid-lower part of the right kidney, without evident renal vein or inferior vena cava thrombosis. No lung or bone lesions were evident. Thus, the patient underwent a robot-assisted nephrectomy (RAN) with a Da Vinci Œ Standard Surgical System, followed by a total, parathyroid-sparing, thyroidectomy. During the procedure, thrombosis of internal jugular vein and right superior thyroid vein was suspected and confirmed by intraoperative echo Doppler, so thrombectomy and ligature of the internal jugular vein were performed. *Results:* The primary tumor was diagnosed as a Fuhrman grade 2 RCC, with initial invasion of the renal vein and with focal invasion to the perinephric fat. The thyroid was involved, with multiple RCC metastases and macro-/microfollicular nodular hyperplasia. There were no postoperative complications and the patient was discharged on

day three after surgery, with thyroid substitutive therapy. *Discussion:* The thyroid gland is a rare site of solid tumor metastasis, despite its rich blood supply: the prevalence of intrathyroid metastasis ranges from 1.9% to 25% in autopsy series of patients who have died of malignant tumors of other primary sites. The most common carcinomas metastasizing to the thyroid gland are lung, breast, kidney, stomach and melanoma (2). Leva was the first to describe, in 1891, thyroid metastasis from RCC. Thompson *et al*., in one of the largest series of RCC metastasis to thyroid, described the microscopic pattern as neoplastic cells infiltrating the capsule with invasion of vessels; nevertheless, macroscopic involvement of the internal jugular vein was reported in only four other cases. Complete excision of a single intrathyroid metastasis is associated with a better prognosis (2). Patients with metastases from RCC have a longer survival (80% at two years after thyroidectomy) than those with any other type of metastasis (20% at two years after thyroidectomy) (3). *Conclusion:* Invasion of the internal jugular vein by the neoplastic thrombus of a RCC thyroid metastasis is very rare. Radical surgery may improve survival, especially in case of synchronous metastasis. A robot-assisted (minimally invasive) approach allowed a successfully radical nephrectomy, associated with total thyroidectomy.

1 Nakhjavani MK, Gharib H, Goellner JR and van Heerden JA: Metastases to the thyroid gland. A report of 43 cases. Cancer *79*: 574-578, 1997.
2 Dionigi G, Uccella S, Gandolfo M, Lai A, Bertocchi V, Rovera F and Tanda ML: Solitary intrathyroidal metastasis of renal clear cell carcinoma in a toxic substernal multinodular goiter. Thyroid Res *1(1)*: 6, 2008.
3 Heffess CS, Wenig BM and Thompson LD: Metastatic renal cell carcinoma to the thyroid: a clinicopathologic study of 36 cases. Cancer *95*: 1869-1878, 2002.

165
SALVAGE RADIOTHERAPY IN MUSCLE-INVASIVE BLADDER CANCER: EXPERIENCE OF THE S. GIOVANNI CALIBITA FATEBENEFRATELLI HOSPITAL IN ROME

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Aim: The object of this study was to report on the use and results of salvage radiotherapy, in terms of overall survival (OS) and disease free survival (DFS), in the treatment of muscle-invasive bladder cancer, at the Department of Radiotherapy, Ospedale San Giovanni Calibita Fatebenefratelli in Rome. *Patients and Methods:* From January 2006 to September 26 patients (18 men and 8 women) with muscle invasive bladder cancer, who had previously been treated surgically, underwent salvage radiation therapy; 21 of those patients underwent transurethral endoscopic resection and 5 of them underwent radical cystectomy. The median age was 75 (range 49-90) years. Up until 2007, patients were treated with 3D conformational technique and from 2008 until the time of writing, with intensity-modulated radiation therapy (IMRT). Treatment volumes included pelvis and bladder in 18 patients, with total doses of 45-50 Gy prescribed to the pelvic nodes and up to 60-70 Gy to the bladder or bladder bed, with single daily fractions of 1.8-2 Gy. In eight patients, the treatment was directed only to the bladder, with doses of 60 Gy in two patients, of 66 Gy in two patients and of 70 Gy in four patients. Five patients received concomitant chemotherapy, based on cisplatin with or without gemcitabine. *Results:* The median follow-up was 14 (range 6-39) months. Radiation therapy-related toxicity was acceptable with G3-G4 acute toxicity of the gastrointestinal tract (GIT) in 10% of patients and G3-G4 acute toxicity of the genitourinary tract (GUT) in 15% patients. Late toxicity of the GIT two years after completing radiotherapy was absent, and was G4 in 2% patients in the GUT. The median OS and DFS were 19 and 18 (range 1-39) months, respectively. At the time of writing, 54% of the patients were alive and 71% were without clinical evidence of disease. Over 80% of the patients who previously underwent bladder-sparing therapy retained bladder function. *Discussion and Conclusion:* Our data suggest a clear benefit from salvage radiotherapy in terms of OS and DFS, allowing more than 80% of patients, alive without disease progression, to retain bladder function.

166
DIABETES MELLITUS IN RENAL CELL CARCINOMA: ROLE OF OGG1 AND TUBERIN

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Background: There is strong evidence that the incidence of renal cell cancer (RCC) increases in patients with diabetes

mellitus (DM) but mechanisms underlying this association are still largely unknown. DM is associated with elevated production of reactive oxygen species, leading to DNA damage. The gene encoding for the DNA repair enzyme that recognizes 8-oxodG DNA damage is 8-oxoG-DNA glycosylase (*OGG1*). Loss of *OGG1* function in RCC may contribute to carcinogenesis. A recent study showed that polymorphism of *OGG1* is associated with type 2 diabetes in Mexican American families, supporting a role for alterations of *OGG1* in the pathogenesis of DM. In addition, DM induces phosphorylation of tuberin, a tumor suppressor gene that also predisposes to RCC. Therefore, in the present study, we investigated the effect of DM on tumor progression and the molecular mechanisms involved. *Patients and Methods:* Between 1979 and 2000, we enrolled 462 patients treated with radical nephrectomy or nephron-sparing surgery for unilateral sporadic RCC, with (Group I) and without diabetes (Group II), with a median follow-up of 43 months. The pathological features studied included histological subtype, tumor size, 2002 TNM primary tumor classification, nuclear grade, coagulative tumor necrosis and presence of sarcomatoid differentiation. To test for the association of DM with survival end-points, the Kaplan–Meier method and Cox multivariable logistic regression models were applied. We collected renal tissue samples from 13 patients from Group I and 13 patients from Group II to evaluate protein expression of phospho-tuberin, tuberin, and OGG1 (immunofluorescence/immunohistochemical and immunoblotting). *OGG1* gene expression was studied by real-time PCR. *Results:* After a median follow-up of 43 months, the overall survival was of 34.3 and 67.5 months in Group I and Group II ($p<0.05$), respectively. Progression-free survival was 26.4 and 64.6 months in Group I and Group II, respectively. In multivariate analysis, diabetes (HR=4.90; $p<0.001$) along with stage (HR=2.01; $p=0.01$), tumor size (HR=1.09; $p=0.02$) and UISS stage system (HR=1.82; $p=0.01$) were independent predictors of cancer related-mortality. Interestingly, we observed a significant increase ($p<0.05$) in tuberin phosphorylation and a down-regulation of *OGG1* protein and gene expression ($p=0.002$, $p=0.03$, respectively) in Group I compared to Group II. A reduction of OGG1 expression in Group I were confirmed by immunostaining ($p=0.0006$). Moreover, on kidney tissue from patients with DM, up-regulation of tuberin phosphorylation that co-localized with tuberin protein compared to patients without DM was observed ($p=0.00002$). *Conclusion:* Patients with RCC and DM have a shorter overall survival, increased risk of recurrence and higher risk for kidney cancer mortality compared to those without DM. Down-regulation of *OGG1* and an increase of tuberin phosphorylation may play a key role on progression of RCC.

167

HELICAL TOMOTHERAPY IN HIGH RISK (WITH N+) AND NODAL RECURRENCES OF PROSTATE CANCER: PRELIMINARY RESULTS

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Background and Aim: The aim of our study was to assess the feasibility of image-guided radiotherapy by helical tomotherapy (HT) in patients affected by high risk prostate cancer (HRPC) with metastatic locoregional lymph nodes, or affected by nodal recurrence, with or without local relapse, after radical treatment. In both cases, difficulties exist in treating different volumes at different dose levels, which can be addressed through the use of intensity-modulated radiotherapy with the simultaneous integrated boost technique. In particular, additional difficulties occur in cases where prior radiation therapy has been given. HT allows a high conformation and dose escalation on tumor volumes with considerable sparing of organs at risk (OAR) if computed tomography (CT) is performed daily before treatment. *Patients and Methods:* Between October 2010 and February 2011, we treated five patients with nodal relapse after radical treatment (in one patient there was recurrence at the level of a single lymph node and in four patients there was recurrence in more than one lymph node) and two patients with HRPC with metastatic locoregional lymph nodes (in external and internal iliac chain). The average age was 63.9 years. In one patient with nodal recurrence and relapse in the prostate gland after radiotherapy, the treatment strategy was radiotherapy to nodal volume and HIFU to the prostate. All patients received hormonal therapy. All patients underwent fluorocholine positron-emission tomography (PET) for staging. Five patients underwent virtual simulation for treatment planning, using a CT simulator and two patients received PET-CT virtual simulation. The treatment volumes were the lombo-aortic and/or pelvic chains (irradiated with prophylactic doses), the PET-positive nodes (with curative doses) and the prostatic bed (with curative doses). Prescription doses were: 51-54-54.4 Gy in 30-32 fractions of 1.7-1.8 Gy to prophylactic pelvic and lombo-aortic chain; 60-66 Gy in 30-32 fractions of 1.9-2-2.2 Gy to PET-positive nodes and 75.2 Gy in 32 fractions of 2.35 Gy to the prostate bed. The OAR were: rectum, bladder, penis bulb, ureters, femoral heads, small bowel, kidneys, liver and pancreas. In previously irradiated patients, the prior treatment planning was reviewed in order to evaluate any overlapping of the irradiated volumes. *Results:* Patients were evaluated in terms of acute and late toxicity and prostate-specific antigen control. Toxicity was evaluated according to the RTOG-EORTC scale. Abdominal MRI was

performed 45 days after treatment. Liver, kidney and pancreatic function were assessed by blood tests. *Results:* All patients completed treatment, which was well tolerated. Gastrointestinal acute toxicity was evaluated in all patients and was the following: G1 in five patients (nausea and/or moderate diarrhea not requiring drugs); G2 in one patient with extensive irradiation volume (diarrhea requiring drugs); no G3-G4 toxicity was observed. Genitourinary acute toxicity was G4 in one patient, with acute urinary obstruction requiring catheter, but this occurrence appeared after only three sessions (at a dose of 7.05 Gy), and it resolved quickly with antibiotics, steroids and alpha 1 blockers; in addition, this patient had a history of previous episodes of acute urinary obstruction requiring catheter. Hematological toxicity was G1 in two patients (slight decrease of white and red blood count and hemoglobin) and G0 in the others. In one patient, there was a slight increase of pancreatic amylase. Late toxicity was not evaluated because of the limited follow-up (three months). MRI, performed in one patient, revealed remission of previously positive lymph nodes. Prostate-specific antigen level was evaluated and decreased in all patients. *Discussion and Conclusion:* Our initial experience shows that HT enables a good daily check of internal anatomy to ensure proper set-up for patients. Under this observation, treatment of extensive volumes, near dose-limiting for OAR, and dose escalation on target volume, can be performed with reduced acute toxicity. These results are however preliminary and further follow-up is necessary to evaluate outcome and late toxicity.

1 Malinverni G, Landoni C, Stasi M , Picchio M, Gatti M, Delmastro E, Bona C, Gabriele P and Fazio F: Clinical application of 11C-choline PET in patients with biochemical relapse of prostate cancer. ECCO Meeting, Parigi, 2005.

2 Jereczek-Fossa BA, Beltramo G, Fariselli L, Fodor C, Santoro L, Vavassori A, Zerini D, Gherardi F, Ascione C, Zanetti IB, Mauro R, Bregantin A, Bianchi LC, De Cobelli O and Orecchia R: Robotic image-guided stereotactic radiotherapy, for isolated recurrent primary, lymph node or metastatic prostate cancer. Int J Radiat Oncol Biol Phys, 2011.

3 Engels B, Soete G, Tournel K, Bral S, De Coninck P, Verellen D and Storme G: Helical tomotherapy with simultaneous integrated boost for high-risk and lymph node-positive prostate cancer: early report on acute and late toxicity. Technol Cancer Res Treat *8(5)*: 353-359, 2009.

168
INTRAOPERATIVE RADIOTHERAPY FOR LOCALLY ADVANCED PROSTATE CANCER: TREATMENT TECHNIQUE AND PRELIMINARY OUTCOMES

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Aim: To present a technique adopted for intraoperative radiotherapy (IORT) for locally advanced prostate cancer and preliminary outcomes. *Patients and Methods:* Between June 2005 and December 2010, 50 consecutive patients with non-metastatic, intermediate-risk or locally advanced, prostate cancer were treated with IORT before prostatectomy as part of their surgical procedure. The median age was 65 years. The median iPSA was 14 ng/ml and the median bioptic Gleason score was 7. According to NCCN 2010, the risk group distribution was as follows: four patients at intermediate risk (8%), 43 patients at high risk (86%) and three patients at very high risk (6%). A total of 21 patients (42 %) were treated with neoadjuvant hormonal therapy. Immediately before IORT, prostate dimensions and rectum depth were measured with intraoperative ultrasound in order to select the electron beam energy and the applicator size properly and to estimate the doses to target and organs at risk. IORT was delivered by a mobile linear accelerator in the operating room, using 8-10 MeV electron energies and 5-7 cm diameter applicators. The prescribed dose was 12 Gy at the 90% isodose. According to the pathological findings, it would be possible to administer further adjuvant radio- or hormonal therapy: three months later, postoperative external beam radiotherapy (EBRT) was prescribed to the prostatic bed alone and whole pelvis in cases of pT3-4 pN0 and pN1 disease, respectively. *Results:* According to the Memorial Sloan Kettering Cancer Center nomograms, the mean preoperative probability of organ-confined disease, extracapsular disease and lymph node involvement were 15%, 45% and 22%, respectively. Postoperative histological findings were as follows: median GS 8, pT2 disease in 8 patients, pT3 in 37 patients, pT4 in 5 patients, pN0 in 27 patients and pN1 in 23 patients. One patient died from postoperative pulmonary embolism. Organ-confined disease with negative surgical margins (R0) was diagnosed in four patients and no further radiation treatment was prescribed. Adjuvant pelvic and prostatic bed EBRT was administered to 21 and 19 patients, respectively. No patient had major acute rectal toxicity. Twenty-three patients had G1-G2 urinary acute toxicity and two patients had G3 acute urinary toxicity (iatrogenic monolateral urethral stricture and acute urinary retention, respectively). No increased risk of

urinary incontinence was recorded. After a median follow-up of 31 months, seven patients had evidence of biochemical failure, two of them with evidence of clinical failure (lymph node and bone metastasis). *Conclusion:* IORT delivered before prostatectomy appears to be a feasible and safe approach for locally advanced prostate cancer, but longer follow-up is needed to evaluate late toxicity and clinical control. Further investigation is warranted in order to identify the patients that benefit most from this treatment modality.

169

PERMANENT BRACHYTHERAPY AS SALVAGE THERAPY FOR LOCALLY RECURRENT PROSTATE CANCER AFTER EXTERNAL BEAM IRRADIATION

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Aim: To estimate the incidence of acute and late toxicity and to evaluate the biochemical outcome after transperineal ultrasound-guided permanent prostate brachytherapy (PPB) for local failure after initial external beam radiotherapy for prostate cancer. *Patients and Methods:* Between August 2000 and May 2010, 18 patients underwent salvage PPB using ^{125}I for intraprostatic recurrence after external beam radiotherapy (EBRT). The median patient age was 68 years. Risk group distribution at initial diagnosis was as follows: four patients at low risk (22.2%), five patients at intermediate risk (27.8%) and nine patients at high risk (50%). All patients were treated using perioperative treatment planning with dedicated hardware and software. The total re-irradiation dose was 145 Gy. Prior to PPB 12 patients were treated with androgen-deprivation therapy. Urinary symptoms (International Prostatic Symptom Score, IPSS) and uroflowmetry were evaluated before treatment: the median IPSS was 4 and the median maximum flow rate was 14 ml/s. Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer criteria and Houston-Phoenix definition (PSA nadir + 2 ng/ml) were used for evaluation of toxicity and biochemical failure, respectively. *Results:* The median follow-up was 28 months. One patient developed acute urinary retention. No patient developed urinary incontinence. No rectal toxicity was observed. One patient died from prostate cancer after biochemical failure; two patients died from other causes. Eight patients (47.1%) were alive without biochemical failure at the time of writing. At last follow-up, the biochemical control rate using risk category at first diagnosis was 50%, 60%, and 44% in patients with low-, intermediate- and high-risk prostate cancer, respectively. *Conclusion:* Salvage PPB after irradiation is feasible, with low urinary and rectal morbidity. The main limitations of this study include a small number of patients and a short follow-up; further experience and longer follow-up are needed to evaluate the role of PPB in the treatment of local recurrences and to identify patients most likely to benefit from it.

170

CURATIVE RADIOTHERAPY IN PROSTATIC CARCINOMA: IMPACT OF AGE ON INTESTINAL AND UROLOGICAL ACUTE TOXICITY

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Aim: Prostate carcinoma is an age-related cancer with high incidence in elderly men, which requires care to achieve a favorable balance of risk in its treatment. The aim of this study was to analyze the impact of age on acute intestinal and urological toxicity in patients with prostate cancer treated with external beam radiotherapy. *Patients and Methods:* Between June 2008 and May 2010, 101 patients with non metastatic localized and locally advanced prostate cancer were treated at our institution with curative conventionally fractionated three-dimensional conformal radiotherapy. Only two patients were treated with intensity-modulated radiation therapy. For intermediate- and high-risk patients, the total dose to the prostate ranged from 78 Gy to 80 Gy (2 Gy/fraction); the total dose to the seminal vesicles ranged from 64 Gy to 70 Gy. Low-risk patients received 80 Gy to the prostate and the base of seminal vesicles. The median age of patients was 73 (range 51-81) years. Patients were stratified into two groups according to age: Group 1 consisted of 72 patients ≤75 years of age (71.3%) and Group 2 consisted of 29 patients >75 years of age (28.7%). Acute toxicity was evaluated weekly on the basis of the RTOG scale. Bivariate analysis was performed using the Chi-square test and multivariate comparisons were realized using Cox's method. The following parameters were included in this analysis as covariates: age, dose to the seminal vesicles and adjuvant hormonal therapy. *Results:* No patient

in either group showed >G2 acute intestinal or urological toxicity. Among Group 1 patients, 32 (44.4%) had no urinary toxicity and 40 (55.6%) had G1-G2 urinary toxicity; 51 patients (51.8%) had no rectal toxicity and 21 (29.2%) had G1-G2 rectal toxicity. Among Group 2 patients, 9 (31%) had G0 urinary toxicity and 20 (69%) had G1-G2 urinary toxicity; 25 patients (86.2%) had G0 rectal toxicity and 4 patients (13.8%) had G1-G2 rectal toxicity. There was no significant correlation between acute urinary or rectal toxicity and the age of patients (p=0.43 and p=0.269, respectively) under bivariate analysis. There was no significant correlation for acute intestinal and urological toxicity under multivariate analysis. *Discussion and Conclusion:* Radical radiotherapy for localized prostate carcinoma is an effective treatment option in elderly patients. This analysis demonstrates that age has no significant impact on radiation-induced intestinal and urological acute toxicity and can be safely used as curative treatment for prostate cancer patients older than 75 years.

171
HYPOFRACTIONATED IG-IMRT AND ACUTE TOXICITY IN PROSTATE CANCER: THE EXPERIENCE OF THE DEPARTMENT OF RADIOTHERAPY SANT'ORSOLA-MALPIGHI HOSPITAL, BOLOGNA

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Background: In recent years, image-guided radiation therapy (IGRT) has taken a leading role in prostate cancer treatment, allowing optimization of the target irradiation technique through the use of the intensity-modulated radiation therapy (IMRT) supplied in a hypofractionated regime. The endpoint is to improve patient outcome, both in terms of local control of the disease and in terms of reduction of radiotherapy toxicity. *Aim:* The aim of this study was to provide preliminary data of our experience related to gastrointestinal (GI) and genitourinary (GU) toxicity profiles of those patients who have completed this treatment. *Patients and Methods:* Between October 2010 and February 2011, 18 patients affected by intermediate- to high-risk prostate cancer have been treated at the Radiotherapy Department of Policlinico S. Orsola-Malpighi of Bologna. The placement of three gold fiducial markers inside the prostatic gland was planned first by the use of ultrasound guidance, and then, after two to three weeks, computed tomography and magnetic resonance imaging. The total dose delivered to clinical target was 67.5 Gy (25 fractions of 2.7 Gy each). *Results:* Acute toxicity was evaluated during treatment through the use of the EORTC-RTOG toxicity grading scale with the following results. GI toxicity: 15 patients G0, 3 patients G1. GU toxicity: 13 patients G0, 5 patients G1. *Conclusion:* Although this study did not include a sufficiently meaningful number of patients, it is possible to conclude that the hypofractionated regime with IG-IMRT is a very well tolerated treatment.

172
HIGH-DOSE CURATIVE RADIOTHERAPY FOR PROSTATE CANCER: RECTAL DOSE-VOLUME CONSTRAINTS AND ACUTE INTESTINAL TOXICITY

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Aim: To assess the impact of rectal dose-volume constraint on acute gastrointestinal (GI) toxicity in patients with non-metastatic localized and locally advanced prostate cancer treated with high-dose curative radiotherapy. *Patients and Methods:* Between June 2008 and May 2010, 101 patients with prostate cancer received conventionally fractionated three-dimensional conformal radiotherapy in our institution. For intermediate- and high-risk patients, total dose to the prostate ranged from 78 Gy to 80 Gy (2 Gy/fraction) and total dose to the seminal vesicles ranged from 64 Gy to 70 Gy. No patient received pelvic lymph node irradiation. Low-risk patients (eight patients) received 80 Gy to the prostate and the base of seminal vesicles. The median age of the patients was 73 (range 51-81) years. The median PSA was 9.3 (range 0.89-89.3) ng/ml and 31% of patients had Gleason score (GS) ≤6, 32% of patients had GS=7 and 37% of patients had GS≥8. Almost all patients (91%) received hormonotherapy before and during radiotherapy. GI toxicity was assessed weekly according to the RTOG toxicity scale. The complete rectal wall, from the rectosigmoid flexure to the anal verge, was contoured as an organ at risk. An empty rectum (rectal volume <100cc) was required for both simulation and treatment; this condition was obtained by careful patient training. According to dose constraints used in our institution, no patient had rectal V50>55% nor V70>25%. We retrospectively re-assessed our data according to the recent constraints proposed by the

QUANTEC report (V30<80%; V40<65%; V50<50%; V60<35%; V70<20%; V75<15%). We investigated the differences in rectal acute toxicity evaluating these constraints at the dose-volume histograms (DVH). Bivariate analysis was performed using the Chi-square test. The statistical analysis was conducted using SPSS Software (release 12.0). *Results:* No patient had >G2 acute GI toxicity. The results of our correlation are reported in the following table:

		Number of patients	G0 (%)	G1-G2 (%)	*P*-value
V30	<80%	56	78.6	21.4	0.393
	>80%	45	70.5	29.5	
V40	<65%	33	72.7	27.3	0.777
	>65%	68	76.5	23.5	
V50	<50%	46	76.1	23.9	0.09
	>50%	55	74.5	25.5	
V60	<35%	67	76.1	23.9	0.514
	>35%	34	73.5	26.5	
V70	<20%	44	79.5	20.5	0.584
	>20%	57	71.9	28.1	
V75	<15%	81	76.5	23.5	0.826
	>15%	20	70	30	

Discussion and Conclusion: Our retrospective analysis did not show a statistically significant relationship between the rectal dose-volume constraints as proposed by recent reports and the development of acute GI toxicity in patients treated with high dose curative radiotherapy for prostate cancer. Nevertheless, the overall toxicity was mild (G1-G2). A larger number of patients may be needed to show a real impact of constraints on acute toxicity. Our short follow-up does not allow the evaluation of the impact of these constraints on late toxicity.

174
TOMOTHERAPY IN POSTOPERATIVE PATIENTS WITH PROSTATE CANCER: EVALUATION OF ACUTE TOXICITY

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Background: After radical prostatectomy, the risk of biological recurrence at five years varies from 10% to 40%, leading to the proposal of using radiation therapy to supplement surgery. When the recurrence risk is essentially local, supplementary radiotherapy is justified with the aim of improving biological recurrence-free survival, local control, metastasis-free survival and specific and global survival, while respecting patient quality of life. Aims: To estimate the acute toxicity in postoperative hi-art tomotherapy for prostate cancer. *Patients and Methods:* Between 2009 and 2010, we treated 28 patients for localized prostate cancer to 62 Gy or 66 Gy using hi-art tomotherapy. The median age at diagnosis was 65 (range 54-77) years. The median Gleason score was 7 (range 5-9). The median PSA was 18.6 (range 1.9-35.4) ng/ml. Ten patients were treated with bicalutamide, four were treated with bicalutamide + leuprorelina acetate and one was treated with leuprorelina acetate. Computed tomography was performed for all patients for centering and to prepare a restraint system. CT was used for centering and radiotherapy sessions were conducted under conditions of full bladder and upright vacuum. The gross tumor volume (GTV) was represented from the tumor bed in 17 patients and tumor bed and the corresponding nodal stations in 11 patients with simultaneous integrated boost (SIB). The planned tumor volume (PTV) was represented by the GTV + 7 mm of expansion in all directions except posteriorly by 5 mm. The daily dose was 2 Gy for fractions to the tumor bed and 1.6 Gy for fractions to the nodal PET-positive stations. For plan validation, particular attention was paid to the doses of tolerance to the organs at risk and to the cover of the PTV with an isodose of at least 95%. Toxicity was graded according to RTOG, IIEF and IPSS. The acute rectal and bladder toxicities were compared with those reported in the literature for patients treated with 3DCRT. *Results:* The incidence of late rectal toxicity RTOG grades 1, 2, and 3 was 25% (seven patients) and 7.1% (two patients) vs.15% (literature value) and 0% *vs*. 7% (literature value), respectively. The incidence of late urinary toxicity RTOG grade 1, 2, and 3 was 21.4% (six patients), 7.1% (two patients) vs.12% (literature value) and 0% *vs*. 6% (literature value), respectively. The urinary and rectal toxicities were higher in the group of patients whose targets also included the pelvic lymph nodes. *Conclusion:* Using hi-art tomotherapy for adjuvant treatment in patients with prostate cancer significantly reduces not only the acute toxicity but, from a preliminary analysis with a follow-up to 12 months, also chronic toxicity. Based on the excellent results obtained, the low toxicity and literature studies, we have begun new protocol escalation dose, largely for high-risk patients.

175
INTER-OBSERVER VARIABILITY IN THE ASSESSMENT OF HISTOLOGICAL SUBTYPE AND FUHRMAN GRADE OF RENAL TUMOR BIOPSIES: RESULTS OF A PROSPECTIVE STUDY

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Background and Aim: Indications for percutaneous biopsy of renal tumors are increasing. The accuracy in the assessment of histological subtype (HS) and Fuhrman grade (FG) of renal tumor biopsies (RTBs) is important when this information is used for clinical decision making. The aim of this study was to assess the inter-observer variability in determining HS and FG on RTBs performed on surgical specimens after radical or partial nephrectomy. *Patients and Methods:* RTBs were performed on surgical specimens from 43 patients who underwent radical or partial nephrectomy for a renal tumor between March 2009 and July 2010. The median tumor size was 50 (IQR 32-70) mm. In all cases, four cores were obtained with an 18G automatic needle (two cores in the central part and two cores in the peripheral part of the renal mass). All cores and surgical specimens were analyzed blindly by two expert pathologists. The concordance between the pathologists in the assessment of adequacy of the tissue to obtain a diagnosis, HS and FG was evaluated using the Cohen's kappa coefficient (CKC) either for central and peripheral RTBs. The results were also stratified based on tumor size (group A <4 cm; group B 4-7 cm and group C >7 cm). Statistical analysis was performed with SPSS v. 15.0 e R v. 2.11.0. *Results:* Central and peripheral RTBs were defined by the two pathologists as adequate to obtain a diagnosis in 70-79% and 79-84% of the patients, respectively. The adequacy of central biopsies increased with decreasing tumor size. CKC for the concordance on biopsy adequacy was 0.82 (very good) for central biopsies and 0.91 (very good) for peripheral biopsies. All adequate RTBs allowed the diagnosis of HS for both pathologists. CKC for the concordance on the diagnosis of HS was 0.94 (very good). The concordance between HS on RTBs and surgical specimen was perfect in all cases. The diagnosis of FG was possible on central biopsies and peripheral biopsies in 68-74% and 79-82% of patients, respectively. CKC for the concordance on FG was 0.52 (moderate) for central biopsies and 0.63 (good) for peripheral biopsies. FG on RTBs and surgical specimens was concordant in 82% of cases. *Discussion and Conclusion:* Central RTBs appear to be less frequently adequate for histological assessment than peripheral RTBs, especially for larger renal masses. The concordance between pathologists in the assessment of HS on RTBs is very good. Determination of FG is easier and inter-observer concordance on FG is higher for peripheral RTBs. Based on these results, peripheral RTBs should be favored over central RTBs for histological diagnosis of renal tumors.

176

FLUORESCENT CYSTOSCOPY WITH HEXAMINOLEVULINATE: DIAGNOSTIC ACCURACY FOR NON-MUSCLE-INVASIVE BLADDER CANCER

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Background: The sensitivity of white light cystoscopy (WLC) can be improved, especially for the detection of flat urothelial neoplasms. Fluorescent or blue light cystoscopy (BLC) has the potential to overcome the limitations of WLC. *Aim:* The aim of this study was to compare the diagnostic accuracy of WLC and BLC in the diagnosis of urothelial cancer and to identify the conditions where BLC can provide the highest diagnostic advantage over WLC. *Patients and Methods:* A total of 65 patients with a suspicious primary or recurrent bladder tumor were enrolled in the study. Patients who had intravesical instillations in the three months before the procedure were not eligible. After intravesical instillation of 85 mg hexaminolevulinate one hour before the procedure, the patients underwent WLC followed by BLC. All observed lesions were reported in a diagram, biopsied or resected. The correct and false-detection rates of the two techniques were compared. Data were stratified according to pathology of bladder lesions and bladder site where the lesions were observed. A subset analysis was also performed to assess the diagnostic accuracy of WLC and BLC in patients who had (n=34) or had not (n=31) undergone previous intravesical treatments to prevent recurrence and progression. *Results:* Overall, 256 bladder lesions were detected (97 with BLC only). At pathology, 219 lesions were found to be malignant, while 37 were benign. The detection rate was 67.1% for WLC (147/219) and 97.2% for BLC (213/219). The highest diagnostic advantage for BLC was observed for the diagnosis of carcinoma *in situ* (100% *vs*. 25%) and for lesions located at the bladder dome (100% *vs*. 53%). The false-detection rate was 8.6% for WLC (14/161) and 14.2% for BLC (36/252). Overall, in 24/65 patients (36.9%), BLC allowed the diagnosis of at least one carcinoma *in situ*, dysplastic or papillary lesion that would have otherwise been missed at WLC. The subset analysis showed that the detection rate of BLC did not decrease in patients who had undergone previous endovesical treatment (97.6% *vs*. 98.3%), and also that the false-detection rate did not increase (14.3% *vs*. 14.2%). *Discussion and Conclusion:* BLC is a promising technique that has a significantly higher detection rate than WLC. The high diagnostic advantage with BLC can be obtained for the diagnosis of carcinoma *in situ* and of lesions located at the bladder dome. The detection rate of BLC does not decrease in patients who have undergone previous endovesical treatment when the last instillation is not performed in the three months before the procedure.

177
RENAL CELL CARCINOMA WITH Xp11 TRANSLOCATION AND IMMUNOHISTOCHEMICAL CATHEPSIN K EXPRESSION: A CASE REPORT

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Background: Renal cell carcinoma with a translocation involving Xp11 (Xp11-RCC) has recently been included as a separate entity in the new version of the WHO classification of kidney tumors (2004). This rare variant is characterized by different chromosomal translocations involving Xp11 and results in a gene fusion (1). The correlation between translocation subtype and tumor behavior is still unclear. Xp11 RCC frequently affects children and young adults but rare cases of patients over 40 years old have been recently reported. The diagnosis was based on morphological findings, transcription factor E3 (TFE3) immunohistochemical staining and cytogenetic studies. Recent studies showed that TFE3 mediates the expression of cathepsin-K, a potent cysteine protease, in osteoclasts, and it probably has the same effect in Xp11 translocation carcinomas (2). *Case Report:* We here report the case of an Xp11 translocation carcinoma in a 28-year-old man who presented with macroscopic hematuria in August 2008, without significant medical history. A computed tomography scan showed a 9×7 cm solid renal mass, suspicious for malignancy, with massive right renal vein thrombosis reaching the vena cava confluence. The patient underwent a radical right nephrectomy with venous thrombectomy in September 2008. The pathological examination showed a renal carcinoma with mixed clear cell, papillary and solid patterns containing areas of hemorrhage and necrosis. Features of aggressiveness, such as perirenal fibroadipous tissue infiltration and massive vascular invasion, were observed. Immunohistochemistry showed that the neoplastic cells were strongly and diffusely positive for TFE3 and CD10 but had a weak staining for cytokeratin. Staining for CD13 was negative. Moreover, tissue samples showed strong immunohistochemical positivity for cathepsin-K and alpha-methylacyl-CoA-Racemasi. Molecular cytogenetic analysis showed a rearrangement of the *TFE3* gene located on the short arm of chromosome X. On the basis of the clinical, microscopic, immunohistochemical and genetic examinations, this case was classified as Xp11 translocation RCC. After nephrectomy, in December 2008, the patient received sunitinib as adjuvant treatment, and there was no measurable disease until October 2009, when he had a relapse involving bone, liver and renal cavity. In June 2010, the patient underwent a D7-D9 decompressive laminectomy for the appearance of neurological symptoms. In August 2010, the patient started RAD001/everolimus therapy, but after three months experienced disease progression. From December 2010 to date, the patient is under treatment with 400 mg of sorafenib *b.i.d*. *Discussion:* We observed a rare case of juvenile Xp11-RCC confirmed by morphological, immunohistochemical and cytogenetic analyses. The immunohistochemical analyses on tumor samples showed a strong cytoplasmic cathepsin-K staining. As recently reported, cathepsin-K is selectively expressed in over 75% of cases of Xp11 RCC, whereas common renal cell neoplasm subtypes are negative for this marker (2). In Xp11 RCC, cathepsin-K is a highly specific marker but not completely sensitive. Nevertheless, not all TFE3-positive carcinomas express cathepsin-K; this is likely due to the presence of different translocations involving chromosome Xp11 (2). The expression of cathepsin-K in Xp11 RCC may not only be a marker useful in differential diagnosis but also a possible therapeutic target. Unlike other published case reports (3, 4), we observed only a minimal response to tyrosine kinase inhibitors and mTOR inhibitors. The molecular pathways activated in Xp11 RCC are different from those involved in the common RCC subtypes. For this reason, standard therapeutic agents such as tyrosine kinase inhibitors and mTOR inhibitors may be less effective in Xp11 RCC. This molecular pattern may represent the rationale for a therapeutic approach using a selective inhibitor of cathepsin-K.

1 Komai K *et al*: Adult Xp11 translocation renal cell carcinoma diagnosed by cytogenetics and immunohistochemistry. Clin Cancer Res *15*: 1170-1176, 2009.
2 Martignoni G *et al*: Cathepsin-K immunoreactivity distinguishes MiTF/TFE family renal translocation carcinomas from other renal carcinomas. Modern Pathol *22*: 1016-1022, 2009.
3 Choueiri T *et al*: Vascular endothelial growth factor-targeted therapy for the treatment of adult metastatic Xp11.2 translocation renal cell carcinoma. Cancer *15*: 5219-5225, 2010.
4 Malouf G *et al*: Targeted agents in metastatic Xp11 translocation/TFE3 gene fusion renal cell carcinoma (RCC): a report from the Juvenile RCC Network. Ann Oncol *21(9)*: 1834-1838, 2010.

178
HYPOFRACTIONATED REGIMEN IN PROSTATE CANCER PATIENTS: A MULTICENTER STUDY

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Background: To evaluate feasibility and toxicity of a hypofractionated regimen in the treatment of prostate cancer using 3D conformal technique or IMRT. *Patients and Methods:* Patients with localized prostate cancer were treated with a hypofractionated regimen of 2.7 Gy/day in 24 fractions with a total dose of 64.8 Gy to the prostate. Seminal vesicles were excluded from the fields when a total dose of 45.9 Gy was delivered. Dose constraints were: rectum: V50 <33%; femoral heads: V36 <50%; bladder V59 <50%. Toxicities were evaluated weekly for all patients during treatment. *Results:* A total of 19 patients were entered into the study between the dates 22.04.10 and 01.02.2010. The median age was 77 (range 61-82) years. All had adenocarcinoma, with a median Gleason score of 6 (3+3) (range 5-9). The median value of PSA at diagnosis was 11.25 (range 4.4- 28.20) ng/ml. A total of 14 patients were submitted to total androgenic block. Acute genitourinary toxicity was: G0 in 14 patients (73.7%) and G1 in five patients (26.31%). Six patients (31.6%) had G1 rectal toxicity and G3 toxicity was reported in a single patient. *Conclusion:* The hypofractionated regimen used in this study seems to be feasible, with a very low toxicity profile. Longer follow-up is necessary to evaluate long-term results.

179

CONFORMAL RADIOTHERAPY (3DCRT) IN THE MANAGEMENT OF LOCALIZED PROSTATE CANCER: OUTCOME AND ANALYSIS OF ACUTE AND LATE TOXICITY

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Background: Use of a treatment decision tree in localized prostate cancer is related to prognostic factors such as PSA level, Gleason score and clinical T-stage at the time of diagnosis, as well as age and comorbidity. At the Radiotherapy Department of S.M. Goretti Hospital in Latina we have been using the risk grouping system adopted by the National Comprehensive Cancer Network (NCCN) v.1.2008, to retrospectively review the records of the patients. We report our results. *Patients and Methods:* From January 2002 to June 2008, 267 patients diagnosed with localized prostate cancer (cT1-3N0M0) were referred to the Radiotherapy Department of the S.M. Goretti Hospital. Out of 267 patients, 200 were considered evaluable for clinical outcome and toxicity report. According to NCCN v.1.2008, patients were stratified into groups of low risk (LR): PSA <10 ng/ml and GS<6 and clinical T-stage <2a; intermediate risk (IR): PSA 10-20 ng/ml or GS 7 or clinical T-stage 2b-2c; high risk (HR): PSA >20 ng/ml or GS 8-10 or clinical T-stage 3a. The treatment consisted of a course of 3DCRT to the prostate (low risk) or prostate and seminal vesicles (intermediate and high risk, respectively). A total dose of 76 Gy in 38 daily fractions was delivered. A course of neoadjuvant hormone therapy (monthly LHRH analog plus bicalutamide 50 mg/day) was administered to 98% of patients, with the intent of achieving a reduction in the prostate volume and allowing a more tolerable treatment regime. High-risk patients received concomitant and adjuvant hormone therapy, lasting a median of two years (range 2-76 months). From January 2002 to November 2005, a 5-field 3DCRT technique was employed for the first one hundred patients (group 1). From December 2005 on, a 7-field 3DCRT technique was used (group 2). Patient characteristics are reported in Table I.

Table I.

Variable	5-Field 3DCRT			7-Field 3DCRT		
Median age, years (range)	71	(56-79)		72	(55-82)	
Risk category	LR 43%	IR 18%	HR 39%	LR 22%	IR 15%	HR 63%

We report acute and late rectal and urinary toxicity according to the RTOG/EORTC scale (G0-1-2-3-4) and correlation with dose-volume parameters. To state rectal toxicity, we recorded the dose to a volume of rectal wall (V40, V50, V60, V70, V72) for each patient. Overall and cancer-specific survival were also analyzed. Biochemical relapse was defined according to the ASTRO-Phoenix criterion. *Results:* All patients received the prescribed radiation dose. No G3 acute rectal or urinary toxicity was observed. G3 late rectal toxicity rates were as follows: 19% in group 1 (5-field 3DCRT) and 4% in group 2 (7-field 3DCRT), p=0.001. Severe rectal bleeding was submitted to argon plasma coagulation or hyperbaric oxygen therapy and all patients except one were managed medically. No patient was considered to be in need of surgical removal of the rectal ulcer. No correlation was found between dose-volume parameters (V40, V50, V60, V70, V72) for rectal wall volume and the onset of late rectal toxicity.

Table II.

	Median value				
3DCRT	V40	V50	V60	V70	V72
5-Field	65	55	40	25	20
7-Field	60	38	30	23	20

No G3 acute urinary toxicity was observed. Mild to moderate incontinence was reported in 2.5% of cases for each group, and urethral stenosis in 1.5% of the whole patient series. Table III shows cancer-specific survival (CSS), overall survival (OS), metastasis-free survival (MFS) and biochemical relapse-free survival (b-NED) at five and at ten years, after a median follow-up of 86.5 (range 25-142) months.

Table III.

Parameter	Five years	Ten years
CSS	99%	92%
OS	94.1%	67%
MFS	93.8%	80%
b-NED	87%	77%

Conclusion: 3DCRT technique can be considered a safe and effective treatment for patients affected by localized prostate cancer. The 7-field technique has a significantly better late rectal toxicity than 5-field 3DCRT. Although no correlation was found between dose-volume parameters and G3 late rectal toxicity, we suggest that a low dose of radiation therapy given to an extended rectal wall volume causes perfusion damage and represents the basis for mucosal ulcer and severe rectal bleeding.

180
RADICAL PROSTATECTOMY AND INTRAOPERATIVE RADIATION THERAPY FOR CLINICALLY LOCALLY ADVANCED PROSTATE CANCER: CLINICAL ASPECTS AND RESULTS OF A PROSPECTIVE SERIES

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Aim: Intraoperative radiation therapy (IORT) is a new technique that can deliver high doses of radiation during surgical treatment. Four years ago, we started a prospective feasibility study of IORT during radical prostatectomy (RP) for locally advanced prostate cancer (PCa). Here we report data on morbidity, toxicity (RTOG scoring criteria), functional and oncologic outcomes of our prospective series. *Patients and Methods:* From September 2005, 72 patients with locally advanced PCa were treated with IORT during RP. A total of 67 patients had follow up ≥6 months. Inclusion criteria were: age <75 years, clinical stage T3-T4 N0-1 M0, probability of extracapsular disease >25% (Kattan's nomograms) and no inflammatory bowel disease. During surgery, the prostate was exposed with dissection of endopelvic fascia and pubo-prostatic ligaments. The distance between the prostate and rectum was measured with ultrasound. A collimator (Mobetron, Intraop, California, U.S.A.) with a median diameter of 5.5 (range 4.5-7) cm and an angle 'bevel' of 15-30° was introduced into the surgical field and a dose of 10-12 Gy with 9-12 MeV was delivered. The dose was prescribed to a 90% isodose. The volume treated included prostate, seminal vesicles and periprostatic area. RP was then completed and an extended lymphadenectomy was performed. Postoperative RT treatment three months after IORT, based on histological findings, was planned for 38/44 patients. A 3D conformal technique was used and a dose of 50 Gy (2 Gy/day) was delivered. Hormonal therapy (HT) was prescribed when indicated. *Results:* The median patient age was 67.2 (IQR 62.3-73.0, min-max 51-75) years and median PSA at diagnosis was 21.8 (IQR 6.6-31.1, min-max 2.0-67.5) ng/ml. Biopsy Gleason score ranged from 4 to 9. A total of 23 patients (35%) received neoadjuvant treatment. The majority of patients had clinically locally advanced PCa (78%). We observed no intra- or perioperative complications. The median dose absorbed by the rectum was 4.6 (range: 0.4-9.1) Gy. Pathological stage was: T2 in 21 patients, T3 in 40 patients and T4 in 5 patients. Positive lymph nodes were detected in 17 patients (25.7%) and positive surgical margins (PSM) in 41 patients (61%). A total of 56 patients (85%) underwent postoperative RT treatment, with a median follow-up of 24 months (6-46). Rectal and urinary RT toxicity are detailed in Table I, according to the RTOG scale.

Table I.

N=66	Grade, N (%)			
Toxicity	G0	G1	G2	G3
Gastrointestinal, acute	52 (78.8)	7 (10.6)	6 (9.1)	1 (1.5)
late	60 (90)	2 (3)	3 (4.5)	1 (1.5)
Genitourinary, acute	44 (66.6)	13 (19.6)	8 (12.3)	1 (1.5)
late	57 (86.5)	1 (1.5)	6 (9)	2 (3)

Table I.

%	UTI	Mild incontinence I-II	Severe incontinence III	Urethral stenosis	Bladder neck strictures	AUR	Recto-urinary fistula
All patients	14	21	3	7	10	8	1
Group A	11	18	3	7	8	6	1
Group B	3	3	0	0	2	2	0

UTI: Urinary tract infection; AUR: acute urinary retention.

Minor surgical complications were observed in 12 patients (18%), including seven lymphoceles (10%), two pelvic hematomas (3%) and three bladder neck strictures (6%). The mean hospital stay was 5 (range 4-8) days. At last follow-up, all patients were alive. *Discussion and Conclusion:* IORT during RP represents a safe procedure, with acceptable surgical time and minimal toxicity for patients with locally advanced PCa. A larger series and a longer follow-up are needed to confirm these findings and to assess long-term side-effects and biochemical control.

181
MALIGNANT HISTIOCYTOMA OF THE PENIS: A CASE REPORT

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Background: Penile malignant fibrous histiocytoma is an extremely rare tumor, with only 5% of penile tumors being mesenchymal tumors. We present here a four-year follow-up of a patient affected by primary malignant fibrous histiocytoma of the penis. To the best of our knowledge, this is the first published report of such a case. *Case Report:* An uncircumcised 64-year-old male presented in April 2007 with a 4-cm solid lesion on the penile right base (*Corporum cavernosum*). There was no history of sexually transmitted disease, constitutional symptoms or dysuria. Physical examination revealed the absence of palpable abnormalities in the inguinal region. Inguinal ultrasound did not show any abnormal nodes. Penile needle biopsy revealed a malignant mesenchymal tumor. This case was treated surgically with total penectomy. Histopathological examination concluded the tumor was a G2 malignant histiocytoma, with negative surgical margins. Immunohistochemical stains were positive for vimentin and negative for cytokeratin, desmin, S-100, AE1/AE3, CK34, Be12, actin, desmin, CD31, CD34 and p63. Results and *Conclusion:* At the 4-year follow-up, the patient was in very good condition, without local or distant metastasis, and with normal uroflowmetry is normal He has, however, developed a depressive syndrome mainly related to the absence of a penis. Malignant fibrous histiocytoma is rarely reported in the literature and primary involvement of the genitourinary tract is very rare. Because of the rarity of such tumors, there is no agreement concerning the best method for staging and management of these patients.

1 Parsons MA and Fox M: Malignant fibrous histiocytoma of the penis. Eur Urol *14*: 75-76, 1988.
2 Moran CA and Kaneko M: Malignant fibrous histiocytoma of the glans penis. Am J Dermatopathol *12*: 182-187, 1990.
3 Tripathi VNP and Dick VS: Primary sarcoma of the uro-genital system in adults. J Urol *101*: 898-904, 1969.
4 Zaffagnini V: Il sarcoma del pene. Contributo anatomo-clinico e sintesi bibliografica. Arch Ital Anat Istol Pat *37*: 322-339, 1963.

182
CAN SPLITTING TURP AND HIFU INTO TWO SESSIONS REDUCE COMPLICATION RATES?

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Aim: To evaluate whether splitting transurethral resection of the prostate (TURP) and high-intensity focused ultrasound (HIFU) into two sessions can reduce complication rates in patients with localized prostate cancer. *Patients and Methods:* From November 2004 to September 2010, 103 patients affected by localized prostate cancer underwent HIFU following TURP. In 39 patients, both procedures were performed in the same session (Group A); in 64 patients, HIFU was delayed (Group B). Follow-up included serial PSA measurements and prostate biopsies 6 months after treatment for all patients. Biochemical recurrence was defined as PSA nadir + 2 ng/ml (ASTRO 2005 criteria). We evaluated complication rates in Groups A and B. *Results:*

The mean (±SD) patient age, PSA and prostate volume were: 73.3 (±5.4) years, 8.2 (±19.3) ng/ml and 29 (±8.3) ml, respectively. The mean procedure duration was 128 min and the mean hospitalization time was 3.4 days. Complications occurred in 30 patients. Complication rates were not associated with clinical stage (T1 *vs*. T2) (p=0.67), Gleason score (p=0.62), age (p=0.2), prostate volume (p=0.06) or PSA (p=0.9). Complication rates were lower when HIFU was delayed after TURP (Group B) (Table I). Complications occurred in 61% (24/39) of Group A patients and in 9.3% (6/64) of Group B patients (p<0.001). No significant differences were seen between Group A and B patients in terms of clinical stage (p=0.9), Gleason score (p=0.2), prostate volume (p=0.3), age (p=0.4) and PSA (p=0.46). *Conclusion:* Splitting TURP and HIFU into two different sessions seems to reduce postoperative complications and improve patient tolerance of the procedure. Longer follow-up and larger patient populations are needed to obtain robust evidence for this finding.

183
POSTOPERATIVE RADIOTHERAPY IN PROSTATE CANCER PATIENTS: RETROSPECTIVE ANALYSIS OF A SINGLE-INSTITUTION SERIES OF 282 PATIENTS

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Background: Outcome after radical prostatectomy (RP) is suboptimal in patients whose cancer extends beyond the prostatic capsule (pT3) or reaches the resection margins (R1). The role of adjuvant radiotherapy (RT) still remains controversial. Therapeutic alternatives include active surveillance, adjuvant RT and hormonal therapy. The aim of our study was to review the results of postoperative RT in patients who had undergone radical prostatectomy. *Patients and Methods:* Clinical records of 283 consecutive patients who had undergone adjuvant RT after prostatectomy between January 1999 and December 2008 were reviewed. Patients treated with salvage RT for biochemical relapse were not included in this analysis. RT was planned on 5-mm-thick spiral CT slices with patients in supine position. A 3D conformal technique was used with four individually shaped fields including the prostatic bed and the space of the seminal vesicles in 232 patients and the pelvis plus prostatic bed in 50 patients. The median radiation dose was 66 (range, 45-70) Gy to the prostatic bed and 45 Gy to the pelvic lymph nodes. Biochemical failure was defined as any increase in the PSA level greater than the pre-RT PSA level in two consecutive PSA measurements. Acute and late toxicity were scored according to the RTOG scale. *Results:* The median age, preoperative PSA and Gleason score were: 66.7 (range, 44-76) years, 17.91 (range, 1.7-399.0) ng/ml and 6.6 (range, 4-9), respectively. The patients were divided into preoperative risk categories according to NCCN criteria, as follows: 102 patients had low risk, 92 patients had intermediate risk and 88 patients had high risk. Pre-surgery hormone therapy was administered in 55 patients (20.1%). Radical prostatectomy was performed in 168 patients, while radical prostatectomy plus regional lymph node dissection was performed in 114 patients. Four patients underwent a laparoscopic approach. Pathologic tumor stage was pT2 in 41 patients (14.5%), pT3a in 100 patients (35.4%), pT3b in 118 patients (42%) and pT4 in 23 patients (8.1%). Twenty-five patients (8.8%) were pN1 and 203 patients (71.9%) had positive surgical margins. Median postoperative Gleason score and PSA were: 7 (range, 4-10) and 0.066 (range, 0.0-20.0) ng/ml, respectively. Adjuvant hormone therapy was prescribed in 150 patients (53%). Follow-up ranged from 6 to 118 months. Acute genitourinary toxicity was: grade 1 in 58 patients (20.5%), grade 2 in 27 patients (9.5%) and grade 4 in 9 patients (3.2%); no patient reported grade 3 toxicity. Acute gastrointestinal toxicity was: grade 1 in 81 patients (28.7%), grade 2 in 30 patients (10.6%) and grade 3 in 2 patients (0.7%). Late genitourinary toxicity was: grade 1 in 35 patients (12.4%), grade 2 in 7 patients (2.4%) and grade 3 in 2 patients (0.7%). Late gastrointestinal toxicity was: grade 1 in 9 patients (3.2%), grade 2 in 7 patients (2.5%) and grade 3 in 2 patients (0.7%). Median PSA at the last follow-up was 0.02 ng/ml. Disease-free survival rates at 2, 5 and 8 years were: 90, 76 and 62%, respectively. Overall survival rates at 2, 5 and 8 years were: 97, 90 and 79%, respectively. Sixteen patients (5.6%) experienced both biochemical and clinical progression: 15 presented bone metastasis and 1 lumbo-aortic lymph node metastass. *Discussion and Conclusion:* In this retrospective single-institution study, patients at high risk of disease recurrence after radical prostatectomy benefited from adjuvant radiotherapy, with acceptable acute and late toxicity.

184
LAPAROSCOPIC RESOLUTION OF COMPLICATIONS DURING RADICAL PROSTATECTOMY

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Background: Since its introduction, laparoscopic pre-peritoneal radical prostatectomy (LPPRP) has been undergoing continuous refinements which have made it a feasible and reproducible operation. Nevertheless, intraoperative complications often necessitate conversion to open surgery. However, it is possible to repair rectal and vascular injuries without conversion during pre-peritoneal radical prostatectomy. *Materials and Methods:* Two examples of LPPRP are described. In the first case, because of strong adhesion between the prostate and the rectum, injury of the anterior rectal wall occurred. After cutting Santorini's plexus and urethra, the prostate was placed in an endobag. The rectal lesion was repaired with Vicryl™ sutures. A sponge of Tachosil™ was applied to the repaired rectal wall using a laparoscopic dedicated device. In the second case, a lesion of the right external iliac vein occurred during the removal of a needle from the abdominal cavity. The vein was isolated and clamped by a self-made tourniquet. The lesion was repaired with a Prolene suture. A Surgicel™ sheet was applied to the vein. Bladder-neck biopsy and water-tight urethrovesical anastomosis with double running suture, as described by van Velthoven, were performed. *Results:* In both cases, the laparoscopic surgical procedure was performed without any major consequences. *Conclusion:* LPPRP is a feasible and reproducible technique that may be subject to intraoperative complications requiring conversion to open surgery. Nevertheless, it is possible to resolve major complications, such as rectal and vascular injuries, without conversion to open surgery.

185

BILATERAL LAPAROENDOSCOPIC SINGLE-SITE SURGERY: FIRST TWO CASES

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Background: Since 2007, several cases of laparoendoscopic single-site surgery (LESS) have been performed in our institution, especially nephrectomy, partial nephrectomy and adrenalectomy. We demonstrated, in agreement with published literature, that LESS surgery is safe and offers minimal scarring, as well as reduced postoperative pain and quick recovery. Here, we present the first two cases of bilateral LESS performed in our institution. With this report, we propose LESS as the technique of choice for surgeons with laparoscopic skills, being able to reduce pain and the number of scars, especially in the case of bilateral surgery. *Patients and Methods:* The first case was a non-simultaneous bilateral LESS adrenalectomy performed in a 61-year-old man affected by lung cancer with a 6-cm non-functioning adrenal mass in each adrenal. The first surgical procedure was left adrenalectomy. The second procedure was performed one month after the first. The patient had a BMI of 27.8 kg/m^2, ASA score of 3 and preoperative Hb level of 13 g/dl. We performed a transperitoneal approach with subcostal insertion of a Triport™ . The patient was in the flank position and we used standard straight (non-articulating) 5/10-mm devices without additional port. Operating time was 150 min, estimated blood loss (EBL) was 50 ml, length of stay (LOS) was 4 days, visual analog scale (VAS) score was 2 in the first postoperative day (POD) for the first procedure. We recorded an operating time of 110 min, with an EBL of 10 ml, LOS of 3 days and VAS score of 2 in the first POD for the second procedure; no intra- or perioperative complications were observed. The skin incision was 3 cm for the first and 3.5 cm for the second procedure and the patient was satisfied with the scar. The second case we describe in this report was a non-simultaneous bilateral LESS partial nephrectomy in a 50-year-old man affected by RCC (T1a) in each kidney, without comorbidity. The second surgical procedure was performed 6 months after the first. The patient had a BMI of 27 kg/m^2, ASA score of 2 and preoperative Hb level of 16 g/dl. Firstly, the tumor in the left kidney was extirpated. We performed a transperitoneal approach with pararectal insertion of a Triport™ on the left and an X-cone (Karl Storz) on the right. The patient was in the flank position and we used standard straight (non-articulating) 5/10-mm devices without additional port on the right side. On the left side, we used two 5-mm additional ports for suturing the parenchymal defect. For the left procedure, operating time was 160 min, with an EBL of 550 ml, LOS of 3 days and VAS score of 3 in the first POD. On the right-side surgery, we recorded an operating time of 110 min, with an EBL of 80 ml, LOS of 2 days and VAS score of 1in the first POD. No intra- or perioperative complications occurred. Tumor size was 4.3 and 2.2 cm on the left and right sides, respectively, with negative surgical margins. The skin incision was 3.5 cm for each procedure and the patient was very satisfied with his scar. Results and *Conclusion:* Bilateral surgery is rarely required but we suggest that in these cases, more than a unilateral approach, a surgeon with laparoscopic experience should consider the use of a technique that seems to offer advantages in terms of cosmetics, decreased port-site complications and decreased postoperative pain and hospital stay. Although LESS has some disadvantages, such as difficulty in instrument angulation and movement, especially in bilateral surgery, it should be considered as a new surgical strategy.

1 Cindolo L, Berardinelli F, Gidaro S and Schips L: Laparoendoscopic single-site partial nephrectomy without ischemia. J Endourol *24(12)*: 1997-2002, 2010.

2 Cindolo L, Gidaro S, Neri F, Tamburro FR and Schips L: Assessing feasibility and safety of laparoendoscopic single-site surgery adrenalectomy: initial experience. J Endourol *24(6)*: 977-980, 2010.

3 Lee JY and Lee SW: Concomitant laparoendoscopic single-site surgery for ureterolithotomy and contralateral renal cyst marsupialization. Korean J Urol *52(1)*: 64-67, 2011.

187

LAPAROSCOPIC PARTIAL NEPHRECTOMY FOR FOREIGN BODY SIMULATING RENAL CANCER

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Background: We report the case of a 61-year-old male presenting with an upper pole right renal mass suggestive of renal cell carcinoma which was found to be a retained surgical gauze. *Case Report:* The patient, who had a history of previous nephrolithotomy 30 years previously with subsequent percutaneous nephrolitotomy and ESWL, presented with flank pain. Abdominal ultrasound and CT scan were suggestive of a malignant renal mass of the upper pole of the right kidney. A right transperitoneal laparoscopic radical nephrectomy was planned. After performing a renal biopsy, we noticed a gauze oozing out from the lesion. Consequently, we decided to perform a partial nephrectomy. The renal vessels were carefully dissected and isolated; mannitol was given intravenously before pedicle clamping. The renal artery and vein were clamped with a self-made tourniquet. The lesion was excised with Ligasure™ . Renal parenchyma was repaired with Vicryl™ sutures, secured with Hem-O-lock clips™ . The vein and the artery were unclamped. The lesion was extracted in Endobag. After checking the peritoneal cavity, a drain was placed into the abdomen. No perioperative complications occurred and the patient was discharged on day 4. *Conclusion:* A retained surgical gauze should always be suspected in all patients with an abdominal mass and with a history of previous renal surgery, regardless of the time lapsing between surgery and the discovery.

188

PHARMACOKINETICS, PHARMACOLOGICAL STABILITY, SAFETY AND ACTIVITY OF MMC ADMINISTERED WITH A NEW HYPERTHERMIA DEVICE (UNITHERMIA)

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Background: Patients with BCG-refractory non-muscle-invasive bladder cancer (NMIBC) represent a widely argued therapeutic challenge. Many conservative treatments have been proposed. Bladder wall thermochemotherapy seems to be an interesting treatment option. UniThermia is a new device that provides bladder wall thermochemotherapy with uniform hyperthermia (44.5˚C) all over the bladder with a high flow of a heated mitomycin C (MMC) solution. The aim of this study was to evaluate drug stability, pharmacokinetics, tolerability and activity of this technique. *Patients and Methods:* A total of 28 patients with BCG-refractory NMIBC (intermediate and high risk) were treated with a course of six instillations after transurethral resection of bladder tumor (TURBT): one early single and five weekly instillations. The drug solution was completely replaced at the halfway point of each instillation. After the treatment, patients underwent cystoscopy every three months for the first year and every six months afterwards. *Results:* There was a significant loss of MMC in the first half of instillation, while in the second half, most of the drug was retrieved. This observation suggests that there was a significant absorption of MMC during the first half of instillation which was minimal in the second half. Plasmatic *Cmax* was considerably lower than the reported threshold concentration for toxicity (400 ng/ml). Most side-effects were not beyond grade II, showing a good safety profile. Data about activity are partial, with 1-year follow-up available for only 16 patients. Among them, six were disease-free, six presented progression and four recurrence.

189

PSA ACCELERATION: THE NEW TOOL FOR PROSATE CANCER DIAGNOSIS

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Background: Prostate-specific antigen (PSA) acceleration can be calculated as the slope of log(PSA) *vs*. time, where log is the natural logarithm. We determined the best interval where PSA acceleration can be calculated with the best result in terms of specificity and sensitivity for diagnosis of prostate cancer. *Patients and Methods:* A total of 741 patients entered the study. They underwent transrectal ultrasound-guided prostate biopsy with 12 or more cores and at least 3 prior consecutive PSA measurements in at least 365 days. PSA acceleration was calculated as the slope of log(PSA) *vs*. time, using a minimum of three PSA measurements. PSA acceleration was evaluated at different intervals, including 1 year (365 days), 2 years (730 days), 3 years (1,095 days), 4

years (1,460 days), 5 years (1,825 days) and 6 years (2,190 days) before the last measurement. *Results:* A total of 255 cancer cases (34.4%) were found. On receiver operator characteristics (ROC) analysis, the area under the curve (AUC) of PSA acceleration (mean=0.728, 95% confidence interval (95% CI)=0.694-0.760) was better than that of PSA, PSA velocity and PSA doubling time. The highest AUC of PSA kinetics was for PSA acceleration, calculated within 3 to 4 years (731 to 1,460 days) before the last measurement. *Conclusion:* Three or more PSA measurements within 3 to 4 years (731 to 1,460 days) before the last measurement enabled more accurate calculation of PSA acceleration than measurement within 1 to 2 years (0 to 730 days).

190

ACUTE TOXICITY IN PROSTATE CANCER PATIENTS TREATED WITH HYPOFRACTIONATED INTENSITY-MODULATED RADIOTHERAPY

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Background: Intensity-modulated radiotherapy (IMRT) using inverse treatment planning and dose–volume constraints for normal tissues allows the delivery of highly conformal radiotherapy (RT) and has the potential to reduce toxicity by limiting the radiation dose given to the rectum and bladder. The aim of this study was to assess the toxicity resulting from hypofractionated IMRT in prostate cancer patients. *Patients and Methods:* Between May 2009 and January 2011, 37 consecutive patients with prostatic adenocarcinoma underwent IMRT. Patient characteristics were as follows: median age 74 (range: 66-83) years; stage: T1N0 in 7 patients (18.91%), T2bN0 in 4 patients (10.81%), T2cN0 in 22 patients (59.45%), T3N0 in 3 patients (8.10%) and T4N0 in 1 patient (2.7%); Gleason score: 2-6 in 23 patients (62.16%), 7 in 11 patients (29.72%) and 8-10 in 3 patients (8.1%). The median basal PSA was 7.6 (range: 5.34-19.21) ng/ml. Twenty patients (54.05%) received hormonal therapy because of high-risk features; the therapy consisted of LHRH analog and/or anti-androgen. IMRT was delivered with 15 MV photons using a five-field technique. The target volume included the prostate in 23 patients (62.16%), prostate and seminal vesicles (SV) in 14 patients (37.83%) on the basis of the risk of involvement or direct involvement of SV. Planning target volume (PTV) consisted of the clinical target volume (CTV) plus 1 cm in all directions except for the prostate fossa-rectal interface where a 0.5-cm margin was added. The prescribed dose to prostate ±SV was 74.25 Gy in 33 fractions at 2.25 Gy/fraction, equivalent to 78 Gy in 2-Gy fractions; SV received 62 Gy in 33 fractions at 1.879 Gy/fraction using a simultaneous integrated boost when the risk of involvement was >15%. The median prostate volume was 42.99 (range 22.573-105.65) cm^3. Acute toxicity was scored using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Biochemical failure was defined according to the Phoenix definition (PSA level at least 2 μg/l greater than the PSA nadir after RT). *Results:* The median follow-up time was 7.7 (range: 0.8-18.5) months. The median pre- RT and post-RT PSA levels were 8.17 (range: 0.11-15.65) ng/ml and 1.2 (range: 0.08-10.35) ng/ml, respectively. At the time of data analysis, 34/37 patients (91.89%) were alive without disease, while the remaining 3 patients (8.1%) were alive with biochemical relapse, locoregional recurrence, or distant metastasis. Acute gastrointestinal (GI) toxicities, mainly urgency, anal pain and increased frequency, were observed in 11 patients (29.7%): G1 in 9 (24.3%) and G2 in 2 patients (5.4%). There was no G3 or G4 acute toxicity. Acute genitourinary (GU) toxicities, mainly nicturia, dysuria, urgency and frequency of urination, were observed in 24 patients (64.8%): G1 in 15 (40.5%), G2 in 4 (10.8%) and G3 in 5 (13.5%). *Conclusion:* Hypofractionated IMRT delivered with simultaneous integrated boost is safe, with acceptable acute GI and GU toxicity rates. A longer follow-up is necessary to evaluate recurrence rate and late toxicity.

191

A NEURO-FUZZY SYSTEM FOR DIAGNOSIS OF HIGH-GRADE PROSTATE CANCER

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Background: Fuzzy systems and neural networks are complementary technologies in the design of adaptive intelligent system. An artificial neural network (ANN) learns from scratch by adjusting the interconnections between layers. A neuro-fuzzy system is simply a fuzzy inference system trained by a neural network-learning algorithm. The aim of this work was to develop a neuro-fuzzy system for the selected diagnosis of high-grade prostate cancer (Gleason score 7-10). *Patients and Methods:* We retrospectively reviewed 1,280 patients who underwent prostate biopsy. All men had a PSA level of less than 20 ng/ml. Of the 1,280 men, 469 (36.6%) had prostate cancer. A neuro-fuzzy system was developed using a coactive neuro-fuzzy inference system model. The

model was composed of an input layer with four neurons (PSA, percent free PSA, PSA density and age) and an output neuron representing the output value of the predictor. The cases were randomly divided into a training test group (800 cases) and a validation group (480 cases). *Results:* In the validation group, the mean area under the receiver operating characteristic curve for the neuro-fuzzy system output was 0.777. Furthermore, pairwise comparison of the area under the curve evidenced differences among PSA, percent free PSA and PSA density in the neuro-fuzzy system. *Conclusion:* This study presented a neuro-fuzzy system based on both serum data (total PSA, percent free PSA and PSA density) and clinical data (age) for the selected diagnosis of high-grade prostate cancer (Gleason score 7-10).

192
CONFORMAL POSTOPERATIVE RADIOTHERAPY IN PATIENTS WITH POSITIVE RESECTION MARGINS AND/OR pT3-4 PROSTATE ADENOCARCINOMA

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Background: There is increasing evidence that adjuvant radiotherapy (RT) reduces the risk of biochemical and/or local relapse in patients with pT3 disease and/or positive margins and undetectable PSA values. The aim of this study was to evaluate treatment outcome and toxicity of high dose (66-70 Gy) conformal RT after radical prostatectomy (RP). *Patients and Methods:* Between August 1998 and December 2007, 182 consecutive patients with positive resection margins and/or pT3-4 prostatic adenocarcinoma underwent conformal postoperative RT. Patient characteristics were as follows: median age 65 (range: 51-77) years; stage: pT3aN0 in 41 patients (22.5%), pT3bN0 in 76 patients (42%) and pT4N0 in 17 patients (9.5%) ; 136 patients (75%) had surgical margins involved by disease; Gleason score: 2-6 in 42 patients (23%), 7 in 79 patients (33.5%) and 8-10 in 61 patients (43.5%). The median pre- and postoperative PSA levels were 9.45 (range: 0.57-108) ng/ml and 0.04 (range: 0.00-4.67) ng/ml, respectively. The median time from surgery to radiotherapy was 5.3 (range: 1.2-8.8) months. A total of 110 patients (60.5%) received hormonal therapy because of high-risk features, consisting of LHRH analog or anti-androgen. RT was delivered with 15-18 MV photons to the tumor bed using a three- or four-field conformal technique, within 3 to 6 months from surgery. The prescribed median dose to the prostate bed was 66.6 (range: 50-70) Gy. *Results:* Median follow-up time was 60.9 (range: 17.26-140.66) months. Biochemical relapse occurred in 28 patients (15.4%) at a median of 23.55 (range: 2.8-100.96) months. The probability of biochemical relapse-free survival was 90% at 3 years, 80% at 5 years and 70% at 10 years. Locoregional relapse occurred in only 4 patients (2.2%) at a median time of 35.7 (range: 28.66-39.56) months. The probability of locoregional relapse-free survival was 100% at 3 years, 90% at 5 years and 90% at 10 years. Distant metastasis developed in 16 patients (8.8%) at a median of 38.38 months (range: 4.6-83.9). The probability of distant metastasis-free survival was 95% at 3 years, 90% at 5 years and 85% at 10 years. At the time of data analysis, 128/182 patients (70.3%) were alive without disease, 41 patients (22.6%) were alive with biochemical relapse or locoregional recurrence or distant metastasis, 4 patients (2.2%) had died of disease progression, 3 patients (1.6%) had died of a second cancer and 6 patients (3.3%) had died of other causes. The probability of overall survival was 95% at 3 years, 90% at 5 years and 80% at 10 years. In univariate analysis, T stage and preoperative and pre-RT PSA were significant factors of biochemical relapse and pre-RT PSA was a significant predictor of distant metastasis. In multivariate analysis, risk factors for biochemical relapse were T stage, preoperative and pre-RT PSA, and hormone therapy given for 402 days or more, while pre-RT PSA was the only independent predictor of distant metastasis. Due to the few observed events, no correlation was found between locoregional relapse and any of the risk factors indicated above. None of the above indicated risk factors was significant for overall survival in either univariate or multivariate analysis. Acute genitourinary and gastrointestinal toxicities were observed in 72 (39.6%) and 91 (50%) patients, respectively, while late toxicities occurred in 28 (15.4%) and 14 (7.7%) patients, respectively. *Conclusion:* High-dose (66-70 Gy) postoperative RT in patients with high-risk pathological features is associated with a low risk of biochemical and local recurrence, achieving minimal morbidity.

193
CRITICAL RETROSPECTIVE EVALUATION OF THE INCLUSION CRITERIA FOR BRACHYTHERAPY IN PATIENTS WITH LOW-RISK PROSTATE CANCER

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Background: The treatment of low-risk prostate cancer is still open to debate in the published literature and several options can be proposed to patients. In our institute, patients with low-risk prostate cancer are usually treated with retropubic prostatectomy (RRP), brachytherapy (BT) or robotic prostatectomy (RALP), depending on the patient's characteristics and preference. The aim of this study was to assess the predictive value of the main preoperative criteria for the diagnosis of low-risk prostate cancer, by comparison with the definitive pathological parameters assessed after RRP and RALP, in order to revise critically the role of BT in this group of patients. *Patients and Methods:* In the period between 1996 and 2010, 748 open or laparoscopic radical prostatectomies were carried in our institute. Among them, 215 procedures were due to low-risk prostate cancer according to AUA criteria, namely PSA ≤10 ng/ml, clinical stage T1c or T2a and Gleason score <7. All pathological specimens from these cases were revised by the same expert pathologist in order to avoid any statistical bias related to different classification criteria after such a long period of time. After this retrospective revision, 109 patients (mean age: 64.3 years) were confirmed to be affected by low-risk prostate cancer (mean PSA: 7 ng/ml, mean Gleason score: 5.7). The preoperative parameters related to these patients were compared with those shown at the definitive pathological reports, namely Gleason score, T stage, grading, perineural invasion and positive surgical margin rate. *Results:* At the definitive pathological reports, 3/109 (1.8%) patients had pT0 stage disease, while 75/109 (68.8%) and 31/109 (28.4%) patients had pT2 and pT3 tumors, respectively. With regard to grading, 3/109 (1.8%) patients had G0 tumor, while 3/109 (1.8%), 71/109 (65.1%) and 32/109 (29.3%) patients had G1, G2 and G3 tumors, respectively. Comparing the preoperative with the postoperative Gleason scores, we assessed an upgrading of 42.9% and a downgrading of 3.6%. Moreover, 60/109 (54.9%) patients had perineural invasion, while 10/109 (9.1%) pT2 patients had positive surgical margins. *Conclusion:* The assessment of extracapsular extension and higher Gleason scores in 28.4% and 42.9% of patients, respectively, at the definitive pathological report demonstrated preoperative understaging and undergrading. This data, which is already reported in literature, suggest the need for critical evaluation of the role of conservative treatments, such as BT, in the management of low-risk prostate cancer patients.

1 Bresee J, Spuma P, Lipsky M *et al*: What is the 'true' incidence of active surveillance and brachytherapy candidates in men undergoing robot-assisted prostatectomy? J Endourol *24*: 1671-1674, 2010.

2 Large MC and Eggener SE: Active surveillance for low-risk localized prostate cancer. Oncology *23*: 974-979, 2009.

3 Oliveira IS, Pontes-Junior J, Abe DK *et al*: Undergrading and understaging in patients with clinically insignificant prostate cancer who underwent radical prostatectomy. Int Braz J Urol *36*: 292-299, 2010.

194

FREE PSA KINETICS FOR PROSTATE CANCER DIAGNOSIS

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Background: There are limited data on the predictive value of longitudinal percentage free PSA measurements for subsequent prostate cancer detection. To evaluate the clinical importance of percentage free PSA kinetics prior to 12-core prostate biopsy, we compared longitudinal percentage free PSA in prostate cancer patients and in controls. *Patients and Methods:* A prospective, Institutional Review Board-approved database of 2,208 12-core prostate biopsies performed in our institution from February 2002 to January 2009 was searched for patients with four or more total and free PSA measurements performed in one or more years before biopsy. The slope of percentage of free PSA over time was calculated with linear regression analysis. *Results:* A total of 256 men entered the study. Seventy-nine (30.8%) cancer cases were found at ultrasound-guided prostate biopsy. The median PSA before the biopsy was 7.05 (range: 1.4-52.7) ng/ml, the median age was 62 (range: 36-84) years. The median percentage free PSA was 16.67% (range: 1.48-50.7%). The median PSA density was 0.14 (range: 0.03-0.99). The median PSA doubling time (PSADT) was 4.49 (range: 2.1-5.54) months. The median percentage free PSA slope was –0.45 for prostate cancer patients and 0.28 for controls ($p<0.001$). On univariate and multivariate analyses, percentage free PSA, the slope of the natural logarithm of PSA and percentage free PSA slope showed a significant ability to predict the outcome of a 12-core prostate biopsy. At ROC analysis, the area under the curve (AUC) of PSA was 0.555 (95% confidence interval (CI)=0.492-0.617) and the AUC for percentage free PSA slope was 0.659 (95% CI=0.597-0.717) with a statistically significant difference ($p=0.041$) between prostate cancer patients and controls. A value of percentage free PSA slope equal to zero corresponded to a sensitivity of 65% and a specificity of 60%. *Conclusion:* We found that percentage free PSA slope is an independent predictor of prostate cancer at 12-core prostate biopsy.

195
ROBOT-ASSISTED RENAL TUMORECTOMY FOR A SMALL RENAL CELL CANCER

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Aim: To demonstrate the method for performing a robot-assisted renal tumorectomy for a small left renal cell cancer. *Case Report:* A 66-year-old female patient, affected by a small (3 cm) exophytic tumor, localized in the medium part of the left kidney, underwent robot-assisted renal tumorectomy in our institute using the Da Vinci surgical robot. The patient was placed in the flank position. The access was controlled by a 12-mm camera port, 2 cm from the umbilicus on the left pararectal line and two 8-mm robotic trocars, introduced on the left midaxillary line in a C configuration. A fourth trocar was introduced during the procedure. After incision of the left paracolic gutter and exposure of the renal lodge, the left renal vein and artery were isolated. Gerota's fascia was then incised, with complete isolation of the tumor, and the renal capsule was scored in order to design the margin of tumor dissection. The renal artery was clamped with a bull-dog clamp and cold dissection of the tumor was performed during warm ischemia. After removing any blood clots, an absorbable fibrin sealant patch (Tachosil) was put into the inner defect and then renorrhaphy was performed using Vycril 2/0 sliding clips. The bull-dog clamp was removed after 13 min of warm ischemia and Gerota's fascia was sutured. The specimen was retrieved into the endobag through the camera port. The operative time was 120 min. Blood loss was minimal. *Results:* No peri- or postoperative complications occurred. The patient was discharged on the fourth day after surgery. Pathological examination reported pTaG1 renal cell cancer. Follow-up was regular. *Conclusion:* The Da Vinci surgical robot significantly helps the surgeon during the tumor dissection and the suture of renal parenchyma, shortening the warm ischemia time and providing easier reproducibility of this laparoscopic technique.

1 Benway BM, Bhayani S, Rogers C *et al*: Robot-assisted partial nephrectomy: an international experience. Eur Urol *57*: 815-820, 2010.
2 Petros FG, Patel MN, Kheterpal E *et al*: Robotic partial nephrectomy in the setting of prior abdominal surgery. BJU Int, 2010.
3 Rogers C, Sukumar S and Gill IS: Robotic partial nephrectomy: the real benefit. Curr Opin Urol *21*: 60-64, 2011.

197
COMPARISON OF DOSIMETRIC RESULTS AND TOXICITY PATTERNS BETWEEN SIB-IMRT AND HIGH-DOSE 3D-CRT IN PROSTATE CANCER

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Aim: To evaluate the risk of rectal and bladder toxicity in intensity-modulated radiation therapy (IMRT) of the prostate compared to 3D conformal radiation therapy (3D-CRT) in localized prostate cancer patients, based on the dose coverage of the planning and clinical target volumes and the frequency of the acute and late adverse events. *Patients and Methods:* Between November 2007 and December 2009, 29 patients with localized prostate cancer were selected for this comparative study at the Operative Unit of Radiotherapy of V. Fazzi Hospital of Lecce, during the implementation of dynamic-arc-IMRT with NomoStat System® for serial tomotherapy. Clinical target volume (CTV) 1, CTV-1, included the prostate and the seminal vesicles, while CTV-2 included the prostate and the base of the seminal vesicles. To obtain planning target volume (PTV) 1, PTV-1, the CTV-1 was expanded with a 10-mm margin in all directions except for the posterior direction, where the margin was limited to 6-7 mm. A 3D margin of 6 mm was added to the CTV-2 resulting in the PTV-2. Thirteen patients were treated with standard 3D-CRT to 60 Gy to PTV-1, plus a 16-Gy sequential boost to PTV-2 with conventional fractionation (2 Gy/fraction in 38 fractions). In sixteen patients, IMRT treatment plans were designed to deliver 66.5 Gy (1.9 Gy/fraction) to the seminal vesicles while simultaneously delivering 78.5 Gy (2.24 Gy/fraction) to the prostate in 35 fractions, using simultaneous integrated boost (SIB) technique. The bladder, rectum and femoral heads were delineated as organs at risk (OAR). OAR dosimetry evaluation was based on dose-volume histograms. Association of these dose parameters with acute and late toxicity was performed. Side-effects were classified according to the RTOG scale for acute and late gastrointestinal (GI) and genitourinary (GU) toxicity. Additional symptoms, such as rectal blood loss, urgency, incontinence and erectile dysfunction were investigated. *Results:* Average values of the volume that received at least 95% of the prescription dose (V95), target volume coverage by 100% of the prescription dose (V100%) and conformity index within the PTV were: 99.3%, 97.8% and 0.9 in SIB-IMRT and 95%, 68.8% and 0.65 in 3D-CRT, respectively. The mean dose to the bladder was 38.8 (range, 34-55) Gy and 26.8 (range, 22-35) Gy with 3D-CRT and IMRT, respectively, with an applied dose limit of

V50<30%. The volume of the rectum receiving 70 Gy or more (V70) was 18% in SIB-IMRT and 33% in 3D-CRT, with an applied dose limit of V45<30%. The mean dose to the femur with SIB-IMRT was approximately 30% lower than that obtained with 3D-CRT. The most common acute grade 2 events were cystitis (23 *vs*. 36.7%) and urinary urgency/frequency (15 *vs*. 26.7%) in the SIB-IMRT and 3D-CRT groups, respectively. Only one case of grade 3 rectal bleeding was observed in the 3D-CRT treatment. At a median follow-up of 12 months, late toxicity was uncommon in the SIB-IMRT group with only two patients with urinary urgency *vs*. five patients with erectile dysfunction and urinary urgency and two patients with chronic pelvic pain in the 3D-CRT group. *Discussion and Conclusion:* IMRT with serial tomotherapy achieved more conformal dose distribution to the PTV than 3D-CRT, in return for a larger, but acceptable, dose inhomogeneity and markedly reduced doses to critical structures. SIB-IMRT, moreover, was well-tolerated in this patient series, with low rates of grade 2 or greater acute and late toxicity. The improved dosimetric results achieved with SIB-IMRT allowed dose escalation to the prostate, while hypofractionation seemed to improve the toxicity pattern. This was probably due to different α/β ratio and different biological equivalent dose (BED) in the prostate and the rectum, namely in the prostate: α/β=1.5, BED=83 Gy; in the rectum: α/β=3, BED=81 Gy.

1 Purdy JA: Dose to normal tissues outside the radiation therapy patient's treated volume. Health Phys *95(5)*: 666-676, 2008.
2 Vieillot S, Fenoglietto P *et al*: Which intensity-modulated radiation therapy? From 'step and shoot' to volumetric modulated arc therapy. Cancer Radiother *14(6-7)*: 550-553, 2010.
3 Pirzkall A *et al*: Comparison of intensity-modulated radiotherapy with conventional conformal radiotherapy for complex-shaped tumors. Int J Radiat Oncol Biol Phys *48*: 1371-1380, 2000.

198

EFFECTS OF THE ERBB1/ERBB2 KINASE INHIBITOR GW2974 ON THE GROWTH AND NSE, CHROMOGRANIN A AND OSTEOPONTIN CONTENT OF THE ANDROGEN-INDEPENDENT PROSTATE CANCER CELL LINE PC-3

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Aim: To investigate the effects of GW2974, a dual inhibitor of ERBB-1 and ERBB-2 tyrosine kinase activity, on the growth, and on cytosol content of NSE, chromogranin A and osteopontin of the androgen-independent prostate cancer cell line PC-3. *Patients and Methods:* Androgen-independent PC-3 cells were obtained from the American Type Culture Collection. Cells were grown at 37˚C in DMEM supplemented with 10% fetal bovine serum (v/v) (Invitrogen), 1% glutamine (Sigma Aldrich) and antibiotics (100 units of penicillin and 100 μg of streptomycin). Cells were treated with several concentrations of GW2974 (Sigma Aldrich). As a control, cells were treated with DMSO, the solvent for GW2974. After 48 h, the medium was removed, the cells were washed with PBS and scraped in ice, then subjected to five rounds of homogenization in buffer (10 mM Tris HCl at pH 7.4, 50 mM NaCl, 1% aprotinin, 1% PMSF and 5 mM EDTA). The homogenate was centrifuged for 10 min at 1500 ×g, then the supernatant was divided into aliquots and stored at −20˚C until used to quantify NSE, chromogranin A and osteopontin, or solubilized in 1× Laemmli buffer for immunoblotting. Proteins were determined by the Bradford procedure. *Results:* The growth of PC-3 cells was significantly reduced ($p<0.05$) by each individual GW2974 dose, with an inhibitory effect of about 14% at 1 μM, 23% at 2 μM, 28% at 3 μM and 38% at4 μM. NSE cytosol content was significantly increased ($p<0.05$) by treatment with GW2974 dose. Chromogranin A levels were significantly increased ($p<0.05$) by adding each single dose of the dual ERBB1/ERBB2 inhibitor to the PC-3 cell culture medium. Osteopontin mean levels were not significantly different ($p>0.05$) in PC-3 cells treated with 0.1 μM (6.47±0.30 ng/well), 1 μM (6.48±0.32 ng/well) or 2 μM (6.58±0.28 ng/well) of GW2974 compared to vehicle-treated cells (6.44±0.38 ng/well). *Discussion and Conclusion:* We demonstrated that in PC-3 cells, ERBB1/ERBB2 blockade caused growth inhibition and NE-related marker expression increase, whereas it had no effect on osteopontin cell content. Since it has been shown that somatostatin analogs, such as lanreotide, in combination with other agents are able to reduce NE phenotype in patients with castration-resistant prostate cancer, it may be informative to test the response of androgen-independent prostate cancer cells to combined treatment with lanreotide and GW2974 or lapatinib.

199

PROSTATE HEALTH INDEX (PHI) IS ABLE TO DISCRIMINATE BENIGN AND PRECANCEROUS CONDITIONS FROM PROSTATE CANCER

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Background: PSA has been widely used for the detection of prostate cancer (PCa) for more than two decades. However, the major drawback of PSA is its relative lack of specificity, most of all in the critical diagnostic range of 4-10 ng/ml, with a large consequent number of unnecessary prostate biopsies. PSA is organ specific but not cancer specific. Thus, serum levels may be elevated in the presence of benign prostatic hyperplasia (BPH), prostatitis and other non-malignant conditions. A significant improvement in the discrimination of PCa from BPH was achieved by evaluating the serum free-to-total PSA ratio. Free PSA (fPSA) comprises different subforms of inactive PSA, such as the pro-enzyme called pro-PSA. Recently, with this aim, the prostate health index PHI has been proposed, calculated according to the formula PHI=(p2PSA/fPSA)×√tPSA, where tPSA is the total PSA and p2PSA is a PSA isoform. *Patients and Methods:* We tested the ability of the PHI to discriminate between benign and malignant disease in a population composed of 120 patients [49 with BPH, 38 with PCa and 33 with precancerous lesions, such as prostatic intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP)]. *Results:* We found that median PHI levels were significantly higher in PCa patients compared with either BPH or precancerous patients (p=0.005 and 0.034, respectively). ROC curve analysis confirmed this finding (AUC=0.67 for either comparison, BPH *vs*. PCa or PIN, and ASAP *vs*. PCa). *Conclusion:* The prostate health index PHI seems to be able to discriminate PCa from BPH, PIN and ASAP.

1 Le BV, Griffin CR, Loeb S *et al*: -2,Proenzyme prostate-specific antigen is more accurate than total and free prostate-specific antigen in differentiating prostate cancer from benign disease in a prospective prostate cancer screening study. J Urol *183*: 1355-1359, 2010.
2 Jansen FH, van Schaik RH, Kurstjens J *et al*: Prostate-specific antigen (PSA) isoform p2PSA in combination with total PSA and free PSA improves diagnostic accuracy in prostate cancer detection. Eur Urol *57*: 921-927, 2010.
3 Sokoll LJ, Sanda MG, Feng Z *et al*: A prospective, multicenter, National Cancer Institute Early Detection Research Network study of -2,proPSA: improving prostate cancer detection and correlating with cancer aggressiveness. Cancer Epidemiol Biomarkers Prev *19*: 1193-1200, 2010.

200

PATHOLOGICAL OUTCOMES OF CANDIDATES FOR PRIAS AND JOHNS HOPKINS ACTIVE SURVEILLANCE PROTOCOLS TREATED WITH IMMEDIATE RADICAL PROSTATECTOMY

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Background: Active surveillance (AS) represents an emerging option for selected patients with low-risk prostate cancer. The aim of AS is to decrease the rate of definitive therapy and its side-effects in patients whose biological tumor characteristics pose a minimal threat to their life expectancy. We tested the two most commonly used European and American AS protocols (PRIAS (1) and John Hopkins (JHP) (2), respectively) in patients who met their selective entry criteria, but underwent radical prostatectomy (RP) as first-choice treatment, in particular their ability to correctly select patients with low-risk prostate cancer, excluding patients with unfavorable prostate cancer characteristics at final pathological examination. *Patients and Methods:* The records regarding a total of 616 patients were extracted from our institutional urological oncology database of all men who underwent radical prostatectomy between 2005-2010. For all patients, full records of biopsy and RP specimen pathological reports were available. Following central review of all slides, pathological tumor volumes were calculated using 3-D stereology (as the product of tumor area per section and thickness section) based on a whole-mount section 3-mm step analysis. We selected two groups of patients: firstly, those who met the PRIAS inclusion criteria, namely: T1-cT2, biopsy Gleason ≤3+3, PSA ≤10, PSA density <0.2 and positive cores ≤2 (1); secondly, those who met the JHP inclusion criteria, namely: T1c, biopsy Gleason ≤3+3, PSA density <0.15 and positive cores ≤2, ≤50% any core involvement (2). The primary outcome was pathological upstaging (defined as stage pT3a or T3b or pN1). Pathological upgrading (Gleason pattern 4 or 5) was identified as a secondary outcome. We excluded 26 patients who had used hormonal therapy, including 5-alpha-reductase inhibitors. Therefore, 147 and 126 patients were evaluated in PRIAS and JHP criteria, respectively. *Results:* A total of 147/616 cases (23.8%) met PRIAS criteria and were submitted to immediate RP: 32/147 patients (20%) were upstaged on final pathology up to N1 disease (26/30 pT3a, 3/30 pT3b, 1/30 pT4, 2/30 pN1). A Gleason score upgrading between biopsy and RP was recorded in 56/147 patients (38%) (3+4=7 in 47/57, 4+3=7 in 8/57, 4+5=9 in 1/57). Insignificant prostate cancer volume in RP specimens (<0.5 cm3, organ-confined disease and Gleason score ≤3+3) was found in 61/147 patients (41.7%). A total of 108/616 cases (17.5%) met JHP criteria and were submitted to immediate RP: 16/108 patients (13.5%) were upstaged on

final pathology (all pT3a), no cases with lymph node or seminal vesicle involvement were reported. A Gleason score upgrading between biopsy and RP was recorded in 35/108 (32%) (3+4=7 in 32/35, 4+3=7 in 3/35). Insignificant prostate cancer volume in RP specimens was found in 51/108 patients (47.2%). *Conclusion:* A total of 23.8% and 17.5% of patients treated with RP were considered potential candidates for PRIAS and JHP AS protocols, respectively. Upstaging rates were 20% and 13.5% for PRIAS and JHP criteria, respectively, while upgrading rates were 38% and 32%, respectively. Using more stringent AS criteria, according to JHP, the risk of seminal vesicle and lymph node invasion is reduced if compared to PRIAS. Insignificant cancer cases were correctly predicted in 41.7% and 47.2% of cases by PRIAS and JHP, respectively. All protocols can underestimate the true nature of prostate cancer by 30%, but JHP performed better than PRIAS in identifying candidates for AS in this patient series.

1 Van den Bergh RC, Vasarainen H, van der Poel HG *et al*: Short-term outcomes of the prospective multicenter Prostate Cancer Research International Active Surveillance study. BJU Int *105(7)*: 956-962, 2010.
2 Carter HB, Kettermann A, Warlick C, Metter EJ, Landis P, Walsh PC and Epstein JI: Expectant management of prostate cancer with curative intent: an update of the Johns Hopkins experience. J Urol *178(6)*: 2359-2364, 2007.

201
PCA3 COMPARISON WITH PROSTATE HEALTH INDEX (PHI) IN REPEAT BIOPSY PATIENTS

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Background: Prostate cancer (PCa) diagnosis is currently based on serum prostate-specific antigen (PSA) levels and digital rectal examination (DRE). The low specificity of PSA is responsible for a large number of unnecessary prostate biopsies to confirm diagnosis. PCA3 score has been shown to be a non-invasive tool for improving diagnosis. PCA3 measurement requires urine sample after DRE. Recently, the prostate health index (PHI) has been proposed as an easily available blood test with a specificity higher than that of percentage free PSA (fPCA) to discriminate between benign prostatic hypererplasia (BPH) and PCa. PHI is calculated according to the formula PHI=(p2PSA/fPSA)×$\sqrt{}$tPSA, where tPSA is the total pSA and p2PSA is a PSA isoform. *Patients and Methods:* We compared the ability of PHI and PCA3 to identify prostate malignancy in a population of 40 patients selected for re-biopsy [17 with BPH, 14 with PCa and 9 with precancerous lesions such as atypical small acinar proliferation (ASAP)]. *Results:* We found that the median PCA3 levels were significantly higher in PCa patients compared to BPH cases (p=0.023); the difference in PCA3 levels between PCa and ASAP cases was not statistically significant. On the contrary, we did not observe any significant difference in PHI values between PCa and BPH or ASAP cases. ROC curve analysis showed that PCA3 has a better ability to discriminate BPH and PCa than PHI (AUC= 0.69 and 0.58 for PCA3 and PHI, respectively). *Conclusion:* Compared to PHI, PCA3 seems to be a better indicator of malignancy before re-biopsy.

1 Groskopf J, Aubin SM, Deras IL *et al*: APTIMA PCA3 molecular urine test: development of a method to aid in the diagnosis of prostate cancer. Clin Chem *52*: 1089-1095, 2006.
2 Marks LS, Fradet Y, Deras IL *et al*: PCA3 molecular urine assay for prostate cancer in men undergoing repeat biopsy. Urology *69*: 532-535, 2007.
3 Haese A, Van Poppel H, Marberger M *et al*: The value of the PCA3 assay in guiding decision which men with a negative prostate biopsy need immediate repeat biopsy: preliminary European data. Eur Urol Suppl *6*: 48 (abs. 101), 2007.

202
URACYST ENHANCES THE ANTITUMOR ACTIVITY OF DRUGS IN BLADDER CANCER CELLS

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Background: Non-muscle-invasive bladder cancer (NMIBC) is the most common type of bladder cancer in the Western world. There are multiple risk factors for NMIBC, which include exposure to tobacco and industrial chemicals, ingestion of arsenic-laced water, radiation therapy to organs adjacent to the bladder, therapeutic use of alkylating agents in chemotherapy regimens and infection with the trematode *Schistosoma hematobium*. The glycosaminoglycan layer on the bladder surface non-specifically blocks the adherence of

bacteria, ions and molecules to the epithelium. It may be an important element in the first line of defense against infection, calculi and even carcinogens for the transitional cells of the bladder. Qualitative or quantitative defects in the glycosaminoglycan(s) present may influence an individual's susceptibility to the development of bladder tumors (1). Approximately 80% of patients with transitional bladder cell carcinomas can be successfully treated with local endoscopic resection, although a significant number of these cases exhibit recurrence, with or without progression to invasive disease. Currently, there are few options other than cystectomy for the management of NMIBC with intravesical chemotherapy using several drugs, such as gemcitabine (GEM), mitomycin-C (MMC) and doxorubicin (DOX) (2). In this study, we investigated the effects of Uracyst® (chondroitin sulphate) (3) on the growth inhibition of human bladder cancer cell lines J82, HT-1376 and MCR and the effects of the combination of GEM, MMC and DOX with Uracyst on the antitumor activity of these drugs *in vitro*. *Materials and Methods:* Cell proliferation was measured by MTT assay and the drug combination studies were analyzed using CalcuSyn software (4). Apoptosis was evaluated by FACS scan after double labeling with propidium iodide and FITC-annexin V. *Results:* We found that Uracyst, MMC, DOX and GEM induced a dose- and time-dependent growth inhibition in human bladder J82, HT-1376 and MCR cancer cells. The data suggest that the three cell lines had different sensitivities to the treatment with these drugs and that the MCR cells were the least sensitive among the three cell lines. On the basis of the obtained results, we hypothesized that Uracyst may potentiate the antitumor activity of MMC, DOX and GEM. Specifically, we evaluated the growth inhibition induced by different concentrations of Uracyst in combination with MMC, DOX or GEM at 72 h in the bladder cancer cell line HT-1376. We observed a synergistic effect when the cells were treated with Uracyst in combination with MMC or GEM at an equimolar ratio. On the other hand, an antagonistic effect was observed when the cells were treated with Uracyst in combination with DOX. The synergism observed was also independent of the sequence of administration of the drugs. Moreover, with Uracyst/GEM and Uracyst/MMC combinations at concentrations which were able to induce synergism on growth inhibition, a strong potentiation of apoptosis was recorded. *Discussion and Conclusion:* In human bladder cancer cell line HT-1376, the pharmacologic combination of Uracyst with GEM or MMC resulted in a strong synergism on cell growth inhibition and apoptosis. This strategy may resolve the multidrug resistance of bladder cancer, and may be used to overcome the tolerance of cancer cells to chemotherapeutic agents. These data encourage further investigations on the combined use of Uracyst with GEM or MMC in the treatment of human bladder cancer.

1 Bodenstab W, Kaufman J and Parsons CL: Inactivation of antiadherence effect of bladder surface glycosaminoglycan by a complete urinary carcinogen (*N*-methyl-*N*-nitrosourea). J Urol *129(1)*: 200-201, 1983.
2 Di Stasi SM, Dutto L and Verri C: Electromotive Drug Administration® (EMDA) intravescicale con Mitomicina-C nel trattamento dei tumori della vescica non-infiltranti la muscolare. Urologia *75(4)*: 214-220, 2008.
3 Hurst RE: Exogenous glycosaminoglycans coat damaged bladder surfaces in experimentally damaged mouse bladder. BMC Urology *5*: 4, 2005.
4 Chou J and Chou TC: Manual and Software. Biosoft, Cambridge, UK, 1987.

203

ARE 18 CORES BETTER THAN 12 CORES DURING TRANSRECTAL PROSTATE BIOPSY TO DETECT PROSTATE CANCER? OUR EXPERIENCE

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Background: We retrospectively investigated the detection rates of prostate cancer, high-grade prostatic intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP) by initial 18- and 12-core prostate biopsy. *Patients and Methods:* A total of 192 consecutive patients with prostate-specific antigen (PSA) between 1.5 and 100 ng/ml underwent 12- (114 patients) or 18- (78 patients) core prostate biopsy under local anesthesia in our department. The biopsies were evenly distributed throughout the prostate in six sectors. In the 12-core prostate biopsies, two samples were obtained from each sector, while in the 18-core prostate biopsies, one additional core was taken from each sector. *Results:* Cancer detection rate in the 18-core biopsy group was not statistically different from the rate in the 12-core biopsy group (41% and 45.6%, respectively; p=0.25). Similarly, the detection rates of ASAP and high-grade PIN did not differ significantly between the two groups (ASAP: 2.9% and 3.3%, respectively, p=0.49; high-grade PIN: 23% and 27%, respectively, p=0.7). The cancer detection rate was similar in 18- and 12-core prostate biopsies in patients with a prostate volume of 55 cm3 or greater (44 patients; rates of 4% and 18%, respectively; p=0.33) and also in those with a prostate volume smaller than 55 cm3 (75 patients; rates of 20% and 37%, respectively; p=0.41). *Discussion:* The 18-core prostate biopsy did not detect a greater number of cases with prostate cancer, ASAP or high-grade PIN than the 12-core prostate biopsy. Based on our data, we did not register a significant difference between the 18- and 12-core prostate biopsy.

205

CLINICAL OUTCOMES IN SIMULTANEOUS INTEGRATED BOOST-IMRT WITH SERIAL TOMOTHERAPY PLUS HORMONAL THERAPY FOR PROSTATE CANCER

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Background: The management of patients with prostate cancer is clearly multidisciplinary. The aim of this study was to quantitatively evaluate the clinical benefits of radiation therapy (RT), specifically simultaneous integrated boost intensity-modulated radiation therapy (SIB-IMRT), combined with hormonal therapy (HT) for localized prostate cancer, based on the frequency of acute and late adverse events. *Patients and Methods:* Between November 2007 and February 2009, at the Operative Unit of Radiotherapy of V. Fazzi Hospital of Lecce, during the implementation of dynamic-arc-IMRT with NomoStat System® for serial tomotherapy, 16 patients with localized prostate cancer were selected from the Prostate Cancer Unit and treated with SIB-IMRT. Radiation doses of 78.5 Gy (2.24 Gy/fraction) and 66.5 Gy (1.9 Gy/fraction) in 33 fractions were prescribed to the prostate and the seminal vesicles, respectively. Radiation doses to the bladder, rectum, small bowel and femoral heads were used as toxicity predictors. All patients received short-course neoadjuvant HT (bicalutamide, 50 mg/day; goserelin, 3.6 mg every 28 days) starting 2-4 months before RT, depending on risk factors, such as PSA, Gleason score and clinical stage, and continuing until the end of irradiation. A total of 16 patients received adjuvant HT (bicalutamide, 150 mg/day) for 6 months. The median pretreatment PSA was 9 ng/ml. Patients were seen on a weekly basis during treatment, and every one or three months thereafter. During follow-up, the periodical PSA score, acute (<120 days) and late (>120 days) gastrointestinal (GI) and genitourinary (GU) side-effects and erectile dysfunction were investigated. To evaluate acute toxicity, the Radiation Therapy Oncology Group (RTOG) scoring system was used and the maximum score was reported. Additional symptoms, such as rectal blood loss, urgency and incontinence, were scored. Late toxicity was scored according to the slightly adapted RTOG/European Organization for Research and Treatment of Cancer (EORTC) criteria. *Results:* The median follow-up time was 28 (range, 23-39) months. The most common acute grade 2 events were cystitis (23%) and urinary urgency/frequency (15%); no patient experienced acute grade 3 events. Five patients developed acute grade 2 or higher rectal toxicity, while 34% of the patients experienced no GU symptoms (grade 0) during treatment. Late toxicity was uncommon (two patients had urinary urgency and one patient had nocturia) and no patient experienced more severe symptoms or developed erectile dysfunction, urinary urgency and chronic pelvic pain. The PSA relapse-free survival provided a good indication of the efficacy of RT-HT. The median 12-month PSA was 0.45 ng/ml. The 12- and 24-month PSA relapse-free survival (PRFS) rates were 100% and 99.5%, respectively. We recorded biochemical relapse in two patients; both had poor prognostic factors at initial diagnosis of prostate cancer. *Conclusion:* SIB-IMRT offers optimal clinical results in terms of acute toxicity, allows dose escalation to the target volumes and, therefore, appears to be a promising method for the improvement of radiation local control and disease-free survival. Our data demonstrated the feasibility and safety of SIB-IMRT with serial tomotherapy for patients with localized prostate cancer and provided proof that this method allows safe dose escalation with low severe toxicities to the normal tissues.

1 Guckenberger M *et al*: Toxicity after intensity-modulated, image-guided radiotherapy for prostate cancer. Strahlenther Onkol *186(10)*: 535-543, 2010.

2 Latorzeff I, Mazurier J, Boutry C *et al*: Benefit of intensity-modulated and image-guided radiotherapy in prostate cancer. Cancer Radiother *14(6-7)*: 479-487, 2010.

3 Lawton CA, Desilvio M, Roach M 3rd *et al*: An update of the phase III trial comparing whole pelvic to prostate only radiotherapy and neoadjuvant to adjuvant total androgen suppression: RTOG 94-13. Int J Radiat Oncol Biol Phys *69*: 646-655, 2007.

4 Peeters ST, Heemsbergen WD, van Putten WL *et al*: Acute and late complications after radiotherapy for prostate cancer: results of a multicenter randomized trial. Int J Radiat Oncol Biol Phys *61(4)*: 1019-1034, 2005.

206

VERUMONTANUM AS ANATOMICAL LANDMARK FOR COMPLETE SAVING OF STRIATED SPHINCTER DURING RADICAL PROSTATECTOMY

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Aim: The aim of our study was to investigate functionally and oncologically the role of verumontanum as a landmark for the complete saving of striated sphincter in patients undergoing radical prostatectomy. *Patients and Methods:* Verumontanum can be considered an anatomical landmark in saving the longest portion of the urethra and, consequently, the largest

part of the striated sphincter. By the antegrade approach to the radical prostatectomy, it is possible to have an anatomical preparation of the urethral sphincter with an excellent visualization of the apex, due to cranial traction of the completely mobilized prostate. At this point, the urethra can be resected with maximum respect of the anatomical boundaries of the urethral sphincter and minimizing the risk of leaving prostatic tissue *in situ*. From January 2007 to April 2008, we prospectively collected data from 102 patients undergoing antegrade radical retropubic prostatectomy (ARRP) for clinically localized prostate cancer. We determined two cohorts: Group A (50 patients) underwent ARRP without the saving of verumontanum, and Group B (52 patients) underwent ARRP with the saving of verumontanum. Both groups were homogeneous in terms of preoperative PSA, pathological staging and pathological Gleason score. Continence was evaluated with ICIQ-SF questionnaire at months 1, 3, 6 and 12 after the operation. *Results:* The mean follow-up was 27.3 (range, 24-33) months for Group A and 28.3 (range, 24-34) months for Group B. In 2/50 (4%) cases of Group A and in 3/52 (5.8%) of Group B, a positive apical surgical margin was found (p=0.4383). Of these patients, one in Group A and one in Group B developed biochemical recurrence (p=0.4877). Overall, 94% of Group A and 96.1% of Group B patients completely fulfilled our continence criteria (no pads and ICIQ-SF=0) at a minimum follow-up of 12 months. Continence was obtained within the first month in 36 patients of Group A (72%) *vs*. 41 patients of Group B (78.8%). The number of patients in groups A and B achieving continence within three, six and twelve months were: 41 (82%) *vs*. 46 (88.5%), 45 (90%) *vs*. 49 (94.2%), and 47 (94%) *vs*. 50 (96.1%), respectively. The saving of verumontanum resulted in a significant overall continence; moreover, this technique strongly influenced the early recovery of continence (p<0.0001). *Conclusion:* Verumontanum can be considered an anatomical landmark in saving most of the striated sphincter. In our experience, ARRP with saving of verumontanum resulted in an early recovery of continence without increasing the risk of leaving prostatic tissue *in situ*. This study was limited by the small patient numbers of both groups and the exiguity of events.

207

A PROGRESSION SCORE FOR BLADDER PT1 HIGH-GRADE UROTHELIAL CARCINOMA: PRELIMINARY DATA

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Aim: The aim of the study was to evaluate the combination of immunohistochemical markers in elaborating a prognostic score of recurrence and progression of non muscle-invasive high-grade urothelial bladder carcinoma. *Patients and Methods:* We retrospectively reviewed clinical and pathological data of 23 patients who had undergone transurethral resection of bladder tumor (TURBT) with histological diagnosis of T1 high-grade (19 cases, 82.6%) or carcinoma *in situ* (4 cases, 17.4%). Additional inclusion criteria were: negative anamnesis for previous urothelial tumors, post-TURBT treatment with BCG, known follow-up, available microscopic slides and paraffin blocks of each case (first and follow-up biopsies). The slides and tissue blocks of all first diagnosis specimens were selected for immunohistochemical analysis, including galectin-3, CD44, E-CAD, CD138, p16, HYAL-1, survivin and TOP-2α. For a semiquantitative assessment of the immunohistochemical data, the mean percentage of positive tumor cells was determined at ×400 magnification for each section. Sections were graded on the basis of the percentage of stained tumor cells as: 0 (negative), 1 (<10%), 2 (10-49%) and 3(>50%). The intensity of staining was graded as: 0 (negative), 1 (weak), 2 (moderate) and 3 (strong). The grades for percentage tumor cells and staining intensity were multiplied to generate weighted points for each tumor specimen (range, 0-9) and evaluated using the following scoring system: 0 (weighted points between 0 and 3) =weak or no staining; 1 (weighted points between 4 and 9) =moderate/intense staining. The first group was defined as 'negative', the second as 'positive'. A grading score (0 or 1) was assigned to each immunohistochemical staining and, for each patient, it was added to the grading score of the eight studied immunohistochemical markers to obtain a score for assessing the progression score. *Results:* After treatment with BCG, 10 patients showed no recurrence/progression at a mean follow-up of 16.6 (range, 12-34) months, 9 patients developed recurrence at mean follow-up of 14.7 (range, 2-48) months and 4 patients underwent radical cystectomy for muscle-invasive bladder cancer at a mean follow-up of 14.5 (range, 2-23) months. TOP-2α, p16, CD44, survivin and galectin-3 demonstrated a strong statistical correspondence to recurrence and progression of urothelial carcinoma. Of the three remaining markers (E-CAD, CD138 and HYAL-1), only CD138 showed a trend for being significantly correlated with the recurrence or progression of urothelial carcinoma. The progression score was calculated by the addition of the grading score of each immunohistochemical marker, with a range from 0 (best prognosis) to 7 (worst prognosis). A score ≥5 corresponded to specificity, sensitivity, positive and negative predictive values of progression of 78.9%, 100%, 50% and 100%, respectively. The ROC curve at this cut-off gave an area under the curve of 0.974 and a 95% confidence interval of 0.807-1.000 (p<0.001). *Conclusion:* The progression score applied to urothelial bladder carcinoma

demonstrated high specificity and sensitivity in predicting local recurrence and progression, despite intravesical treatment with BCG after TURBT. The progression score may help clinicians to focus on patients who may need a close follow-up or early radical treatment. The present study should be considered a preliminary report and should be substantiated by a larger patient series.

208

CONTRAST-ENHANCED ULTRASOUND FOR CHARACTERIZATION AND FOLLOW-UP OF RENAL LESIONS

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Aim: The aim of the study was to evaluate the usefulness of contrast-enhanced ultrasonography (CEUS) in the characterization and follow-up of renal lesions. *Patients and Methods:* From March to September 2010, we performed CEUS in 29 patients to evaluate 42 renal lesions. Of them, 37 lesions (88%) were detected with previous contrast-enhanced CT (CECT) and CEUS was used to better characterize them. In 4 patients (5 US-questionable lesions) with initial renal failure, CEUS was directly performed after grayscale US to avoid contrast-induced nephropathy (CIN); in this set of patients, CEUS confirmed US-suspected solid renal masses and the patients underwent CECT evaluation. CEUS was performed by a single experienced radiologist (with more than 20 years of practice in urologic ultrasound and more than one year in CEUS) using a commercially available scanner (Esaote® MyLab 70 Gold) equipped with software dedicated to the CEUS study and with a convex multi-frequency broadband (3-8 MHz) probe. Lesions were first scanned with gray-scale and color Doppler US to obtain their location and size and the best imaging plane to observe the lesions and the normal adjacent renal parenchyma. Thereafter, a contrast agent (SonoVue; Bracco®, Milan, Italy) was injected intravenously as a bolus (average flow, 2.5 ml/s) of 4.8 ml dose followed by 10 ml of normal saline flush. Each examination lasted about 3 min following bolus injection. One post-contrast cine clip was acquired lasting approximately 150 s. If necessary, the injection was repeated 15 min later. Quantitative analysis of enhancement was performed using dedicated software for the quantification of perfusion (Qontrast, manufactured by Esaote for Bracco Group). This software elaborates color maps and process time/intensity (T/IS) curves on a region of interest (ROI). CECT studies (completed with Siemens SOMATOM Sensation 16) were performed by experienced radiologists (practicing urological CT imaging for 10 years on average) blinded to the CEUS diagnosis. For the interpretation of both CECT and CEUS findings, we used the Bosniak scheme for the classification of cystic lesions. *Results:* CEUS better defined the US features in all cases (p=0.001) and demonstrated a matching diagnosis with CECT in 38/42 lesions (90.4%). In the remaining four cases, CT failed to show tumor blood flow in small lesions, while the ability of CEUS to quantify perfusion demonstrated the presence of subcentrimetrical renal masses, discovered to be clear-cell renal carcinoma, histopathologically confirmed. The diagnostic value of CEUS was comparable to that of CECT. Moreover CEUS was found to have higher sensitivity in characterizing small renal lesions (<1.5 cm in the greatest dimensions) and suspected cysts (B IIF, B III) (p<0.0001). None of the patients suffered adverse reactions to the CEUS contrast agent, and no renal function worsening was suspected. *Conclusion:* CEUS appeared to be more sensitive in detecting slight tumor blood flow than CECT, with an improved characterization of small renal tumors. CEUS allowed better visualization of septa number, wall thickness, solid component and enhancement of some renal cystic masses than CECT. Moreover, the dedicated software (Qontrast) gave confirmation and detailed definition of the observed features by creating colorimetric maps and time–intensity curves. This safe, cost-effective procedure may be useful to better define renal lesions in patients undergoing surgery, or to tailor an active surveillance of small masses or postoperative follow-up.

209

SEQUENTIAL TARGET THERAPY FOR METASTATIC RENAL CELL CARCINOMA: COMPARISON OF SUNITINIB+SORAFENIB *VS.* SORAFENIB+SUNITINIB

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Background: Sunitinib (SUN) is a targeted therapy most commonly used as first-line treatment of metastatic renal cell carcinoma (mRCC), while sorafenib (SOR) is the treatment of choice in the second line. However, for different reasons (mainly the local availability of drugs or compassionate use), some patients have been treated with sequences of these drugs not considered by the guidelines. The present study reviewed our experience in regard to the results of the sequences SUN+SOR *vs*. SOR+SUN. *Patients and Methods:* Since 2005, 67 patients with mRCC have been treated with a target therapy in our institution. Among them, 34 cases treated with the

sequence SUN+SOR (24) or SOR+SUN (10) were reviewed. Statistical analysis was not performed due to the small sample size and the disparity of the cases. *Results:* The following Table summarizes the features of the patients and the results obtained.

Feature	SUN+SOR	SOR+SUN
Mean age, years (range)	64.1 (47.0-76.0)	58.5 (37.0-82.0)
Male gender	58.3%	50.0%
Previous therapy	37.5%	40.0%
Clear cell histology	100.0%	90.0%
Previous nephrectomy	95.8%	100.0%
Synchronous metastasis	35.3%	16.7%
Number of metastatic sites		
1	43.5%	11.1%
2	21.7%	33.3%
>2	34.8%	55.6%
Mean number of courses of therapy	11.6 (8.0+3.6)	14.3 (5.0+9.3)
Median progression-free survival (months)	10.0 (10.0+0.0)	15.5 (6.5+9.0)
Median overall survival (months)	17.0 (13.0+4.5)	26.8 (12.0+14.8)
Response		
Stable disease	31.1% (39.1%+26.1%)	21.0% (22.2%+20.0%)
Regressive disease	20.8% (34.8%+8.7%)	42.1% (33.3%+50.0%)
Progressive disease	48.1% (26.1%+65.2%)	36.8% (44.4%+30.0%)
Discontinuation of therapy due to adverse events	16.7%+4.2%	0.0%+0.0%
Patients alive at end of study	33.3%	60.0%

Discussion and Conclusion: Comparing the sequences SUN+SOR and SOR+SUN for the two groups of patients with similar or slightly unfavorable clinical features for the sequence SOR+SUN (*e.g.* number of metastatic sites), a longer survival time (both disease-free and overall) and better response rates were observed for the sequence SOR+SUN. This advantage is mainly due to the good activity of SUN shown both in the first- and second-line treatment. These results are not in agreement with guidelines, where SUN should be employed exclusively in the first-line treatment and SOR in the second-line treatment. Even though this conclusion should be carefully regarded due to the small number of patients and the retrospective design of the study, the possible use of SUN after failure of SOR can be considered. The need for a better and more individualized selection of patients for target therapy in mRCC is further emphasized by this retrospective study.

210

FIVE- AND TEN-YEAR OUTCOME IN PROSTATE CANCER TREATED WITH THREE DOSE LEVEL 3D-CRT

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Aim: The aim of this study was to evaluate the prognostic role of several clinical variables in a patient population with localized prostate cancer treated with a dose-escalated three-dimensional conformal radiation therapy (3D-CRT) and with hormonotherapy, and to determine the biochemical and clinical outcome after the end of radiotherapy. *Patients and Methods:* From January 1999 to December 2005, 1,004 patients with prostate cancer (mean age 72, range 47-83 years) underwent external beam radiation therapy (EBRT) at the Radiotherapy Department of the IRCC in Candiolo and at Mauriziano Umberto I Hospital in Turin. Patients were treated with 3D-CRT (6 beam, 18 MV, MSKCC of New York modified technique), with three levels of dose (72, 75.6 and 79.2 Gy) to prostate volume and seminal vesicles with/without pelvic nodes. The ICRU prescription median dose was 46 Gy to pelvic volume (9% of the patients) and 76 Gy to prostate volume using standard fractionation (1.8-2 Gy/fraction). Hormonotherapy was employed in 785 patients (78.2%): low-risk patients (13%) received neo-adjuvant hormonotherapy for two to three months before radiation therapy; intermediate-risk patients (59%) received neo-adjuvant and concomitant hormonotherapy for a total of about 5 months; and, finally, high-risk patients (28%) received neo-adjuvant, concomitant and adjuvant hormonal therapy for a total of about two years. The distribution according to clinical stage was T1: 21%, T2: 66% and T3: 13%. The distribution according to Gleason score (GS) was grade 2-6: 54%, grade 7: 31% and grade 8-10: 15%. The distribution according to pretreatment PSA levels (in ng/ml) was 0-10: 47%, 10-20: 27% and >20: 26%. The comorbidity of patients treated was: diabetes 6%, hemorrhoids 5%, diverticulitis 2% and obesity 1%; 86% of the patients had no comorbidity. Average follow-up was 61.4 (range: 13.2-127.9) months. *Results:* Overall survival at five and ten years after the end of radiotherapy was 93% and 88%, respectively. Disease-free survival at five and ten years was 92% and 72%, respectively (Kaplan–Meier method). Log-rank test was performed to evaluate the survival function across groups. The parameters significantly correlating with overall survival were

GS and clinical stage. With regard to GS, we saw a statistically significant difference between patients with GS <7 and GS=7 (p=0.034) and patients with GS <7 and >7 (p=0.0002). With regard to clinical stage, there was a statistically significant difference between stage II and III disease (p=0.028). The radiation dose to the tumor was not significantly correlated with overall survival. In univariate logistic analysis (UVA), the overall survival had a trend in favor of age >75 years (p=0.0585, OR=0.55) and unfavorable for GS >7 (p=0.0068, OR=2.37). In UVA, disease-free survival was related to GS >7 (p=0.0274, OR=1.87), age >75 years (p=0.035, OR=0.57) and stage III disease (p=0.0274, OR=1.87). In multivariate logistic analysis, the disease-free survival was strongly related to GS >7. *Conclusion:* 3D-CRT is a feasible modality allowing for dose escalation. GS also correlates very strongly with the outcome as reported in the literature. Our results confirmed a series of studies which suggested that age plays a protective role in overall survival; in effect, we observed that patients over 75 years of age survive longer than patients under 75 years of age. However, in our study the dose increase from 76 to 80 Gy was not associated with better tumor outcome, perhaps because treatment dose was selected according to the patient risk level (most patients at low risk were treated at 72 Gy, intermediate risk at 75.6 Gy and high risk patient at 79.2 Gy). Further investigations are warranted aiming to provide a better understanding of the dose effect for prostate cancer.

211
XANTHOGRANOLOMATOUS PYELONEPHRITIS: ATYPICAL DIFFERENTIAL DIAGNOSIS OF RENAL CARCINOMA WITH CAVAL THROMBOSIS

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Background: Xanthogranolomatous pyelonephritis (XGPN) is an inflammatory renal disease, usually associated with urinary lithiasis, with ultrasound (US) and computed tomography (CT) features similar to those of renal cancer. Exceptionally, it presents with venous thrombosis, emphasizing the difficulties of the differential diagnosis and posing specific technical demands at surgery. Here, we present a case of XGPN with caval thrombosis. *Case Report:* An 85-year-old female, otherwise healthy, presented with recurrent right-flank pain. At abdominal US and CT, a 5-cm necrotizing right renal mass with subdiaphragmatic caval thrombosis was detected. The patient was submitted to right radical nephrectomy, cavectomy and extraction of the caval thrombosis filling the caval lumen. The clinical course was uneventful and the patient was discharged after eight days. At histological examination, XGPN with venous thrombus was diagnosed, having uniform cellularity. *Discussion and Conclusion:* This was only the fourth case of XGPN with caval thrombosis reported in the literature (1-3) over the last 30 years. The case had a particular surgical complexity related to the extension of the thrombus along the vena cava proximal to the overlying veins, the complete filling of the caval lumen and, moreover, a specific anesthesiological difficulty due to the patient's advanced age. Therefore, such a rare differential diagnosis should be taken into account. In view of the recent proposals of a neoadjuvant role of targeted therapy in advanced renal cancer, the need for pre-therapy biopsy is further emphasized.

1 Gupta G, Singh R, Kotasthane DS *et al*: Xanthogranulomatous pyelonephritis in a male child with renal vein thrombus extending into the inferior vena cava: a case report. BMC Pediatr *10*: 47, 2010.
2 Tiguert R, Gheiler EL, Yousif R *et al*: Focal xanthogranulomatous pyelonephritis presenting as a renal tumor with vena caval thrombus. J Urol *160(1)*: 117-118, 1998.
3 Mitchell DG, Friedman AC, Druy EM *et al*: Xanthogranulomatous perinephritis: unusual cause of renal vein and vena caval thrombosis. Urol Radiol *7(1)*: 35-38, 1985.

212
RECURRENT CYSTIC NEPHROMA IN A WOMAN AFTER CYSTECTOMY AND CONTRALATERAL NEPHRECTOMY: A CASE REPORT

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Background: Cystic nephroma is an uncommon benign tumor of the kidney, with uncertain etiology. Radical nephrectomy is the gold standard to treat this pathology (1). We present an unusual case of a 50-year-old woman with cystic nephroma, who had undergone contralateral nephrectomy and cystectomy in the past and was treated with partial right nephrectomy. *Case Report:* Left radical nephrectomy was performed when the patient was two years old because of recurrent pyelonephritis in a silent and dilated kidney. Two years later, an orthotopic and ipsilateral ureterocele was removed with a transvesical technique. At the age of 18, the old right ureteral stenosis was treated in Switzerland with an unspecified endoscopic approach. In June 2009, cystoscopy revealed a small tumor around the right ureteral orifice and a pelvic minus mass was seen at retrograde pyelography. Therefore, a surgical approach was planned and an intraluminal polycystic lesion of the kidney was removed, together with distal ureterectomy with ureteral re-implantation. The histological

examination showed a benign polycystic lesion of the kidney and a poorly differentiated squamous carcinoma of the ureteral orifice with detrusor infiltration. Consequently, the patient underwent radical cystectomy with orthotopic ileal neobladder reconstruction and colposacropexy with no evidence of carcinoma in the removed specimen. One year later, because of the onset of persistent fever, lumbar pain and acute renal failure, two nephrostomies were temporarily applied and a recurrent polycystic obstructive mass was found in the right kidney. The patient underwent partial nephrectomy in the middle of the kidney with removal of the entry of the lesion in a medium calyx. The tumor was completely removed. The histological examination showed a recurrent cystic nephroma. *Results:* At 6-month follow-up, the patient was free from disease, with a creatinine level of 1.43 mg/dl, and abdominal US showing mild dilatation of renal cavities and no sign of recurrence. *Conclusion:* In selected patients, partial nephrectomy can be a safe therapeutic option for the removal of a cystic nephroma.

1 Kuzgunbay B, Turunc T, Bolat F and Kilinc F: Adult cystic nephroma: a case report and a review of the literature. Urol Oncol *27*: 407-409, 2009.

213
3D-TEMPLATE-GUIDED TRANSPERINEAL SATURATION BIOPSY (3D-TTPSB): INDICATIONS, TECHNIQUE AND OUR INITIAL EXPERIENCE

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Background: All imaging techniques, as well as prostate biopsy, are considered inadequate for detecting early prostate cancer (PCa) in small tumors (diameter <5 mm). Furthermore, the index tumor lesion may be missed even by extended transrectal ultrasound biopsy (TRUSB); false-negatives (10-18%), understaging (30%) and undergrading (20-40%) are notable risks for error. These risks need to be considered particularly when new strategies such as active surveillance (AS) and focal therapy (FT) are used. Recently, 3D transperineal template-guided saturation biopsy (3D-TTPSB) has been proposed for 3D histological mapping of the prostate. Based on the current literature, in this report, we have identified the indications for 3D-TTPSB in clinical practice; moreover, we describe our up-to-date technique and report on our initial experience. We describe our initial experience based on six cases. *Patients and Methods:* 3D-TTPSB was used to obtain a definitive diagnosis in: (i) three men with a persistent clinical suspicion of PCa despite previous negative TRUSBs and (ii) three men with minimal cancer on initial biopsy who could have been suitable for AS or FT. In addition, we carried out a critical analysis of articles on 3D-TTPSB (Medline search). *Results:* We identified two groups with the indications for 3D-TTPSB: (i) Diagnosis: a persistent clinical suspicion of PCa (PSA doubling time <4 years, doubtful DRE, familiar history, PIN and/or ASAP) despite previous negative biopsies; and (ii) Staging: patients with low- or very low-risk cancer on initial TRUSB who are considered for AS or FT. With regard to the 3D-TTPSB technique, the following are true: (i) Required equipment: bi-plane transrectal ultrasound machine with a probe stabilization tool; stepwise linear movement; grid-mounting and imaging capabilities. The setup is analogous or equivalent to the brachytherapy or cryoablation model. (ii) Light general anesthesia or, preferably, spinal anesthesia; the patient in the lithotomy position. A Foley catheter is passed to better visualize the urethra and to help avoid urethral injury during the biopsy. (iii) The prostate is divided into eight regions, with respect to the three reference planes commonly used, labeled as follows (1): left anterior distal, left anterior proximal, left posterior distal, left posterior proximal, right anterior distal, right anterior proximal, right posterior distal, and right posterior proximal. Each octant is divided into three zones and midline biopsies are segregated. (iv) 2-5 Cores are taken anywhere (1 core every 5 mm of distance) within each region plus 2-4 cores from the midline (a total of 50-124 biopsies, depending on prostate size), and the specimens transferred to prelabeled containers. (v) A catheter is left indwelling at least for one day. Patients are prescribed five days of oral antibiotics at home or two days *i.v.* in the hospital. A summary of our initial experience with 3D-TTPSB follows. In our diagnostic group, we detected 2/3 PCa, both with small focus and Gleason pattern of 4. One of the patients underwent radical prostatectomy (final pathology: pT2cN0R0, volume<0.5 cm^3, Gleason score: 4+3=7) and the other underwent radiotherapy. In the staging group, we confirmed 3/3 PCa; disease in one patient was upgraded to Gleason score 3+4 and he underwent surgery (final pathology: pT2cN0R0, volume: 0.08 cm^3, Gleason score: 3+4=7); the second patient is on AS and the last one is scheduled for cryoablation. Radical prostatectomies after 3D-TTPSB were not perceptibly more difficult than those without 3D-TTPSB and there were no major complications (such as sepsis or severe hematuria), only minor complications (2/6 moderate hematuria, 1/6 retention). *Conclusion:* 3D-TTPSB is a safe and effective technique to detect PCa in high-risk patients whose cancer has been missed or is undetectable by standard TRUSB. It has an important role in mapping the location and the extent of PCa and, therefore, in choosing the most appropriate treatment among several option, including radical treatments, FTs and AS. To date, this procedure is considered the best in

minimizing the risks of undersampling, understaging and undergrading. However, increased morbidity has also been reported and long-term effects on subsequent treatments are not yet known. In our early experience, the procedure is well tolerated with a low rate of complications.

1 Onik G and Barzell W: Transperineal 3D mapping biopsy of the prostate: an essential tool in selecting patients for focal prostate cancer therapy. Urol Oncol *26(5)*: 506-510, 2008.
2 Onik G, Miessau M and Bostwick DG: Three-dimensional prostate mapping biopsy has a potentially significant impact on prostate cancer management. J Clin Oncol *27(26)*: 4321-4326, 2009.
3 Barzell WE and Melamed MR: Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3D pathologic mapping of the prostate - a 4-year experience. Urol *70(Suppl 6A)*: 2007.

214

MATRIX METALLOPROTEINASE-2 AND -9 IN THE URINE OF PROSTATE CANCER PATIENTS

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Background: The matrix metalloproteinase (MMP) family of enzymes are critically important extracellular proteases whose activity has been implicated in a number of key normal and pathological processes. The latter processes include growth, progression and metastasis of cancer, as well as dysregulated angiogenesis associated with these events. The MMPs are secreted by all types of cells, and they also degrade the extracellular matrix, allowing cancer cells to take root and metastasize. Endogenous inhibitors typically hold MMPs in check but in cancer, the balance shifts against the inhibitors and in favor of MMPs, which ultimately spill over from blood into urine. *Patients and Methods:* Thirty-eight patients were chosen for the study and their first morning urine was collected before surgical or other therapeutic intervention. Of these patients, 30 had prostate cancer, with Gleason scores of 6 (13 patients), 7 (12 patients), 8 (2 patients) and 9 (3 patients), while 8 patients had benign prostate hyperplasia (BPH). MMP activity in concentrated urine of patients with prostate disease was verified by gelatin zymography. *Results:* Zymography showed four dominant gelatinolytic bands of 240, 130, 92 and 72 kDa in prostate disease. The most abundant lytic activity was at 92 kDa (MMP-9), whereas MMP-2 was present in lesser quantities. Moreover, MMP-9 activity was enhanced in the urine from patients with BPH compared with that from cancer patients. No correlation between gelatinolytic activity and Gleason score or pathological findings was found. *Discussion and Conclusion:* The results suggest that the inexpensive measurement of MMP-9 in concentrated urine may serve as a suitable supplementary tool to distinguish between patients with prostate cancer and patients with BPH. The addition of this enzyme to the currently available serum PSA and/or the free-to-total PSA ratio may provide clinicians with additional objective information on prostate neoplasias.

1 Yan L, Borregaard N, Kjeldsen L and Moses MA: The high molecular weight urinary matrix metalloproteinase (MMP) activity is a complex of gelatinase B/MMP and neutrophil gelatinase-associated lipocalin (NGAL). J Biol Chem *276*: 37258-37265, 2001.
2 Roy R, Louis GL, Loughlin KR, Wiederschain D, Kilroy SM, Lamb CC, Zurakowski D and Moses MA: Tumor-specific urinary matrix metalloproteinase fingerprinting: identification of high molecular weight urinary matrix metalloproteinase species. Clin Cancer Res *14*: 6610-6617, 2008.
3 Di Carlo A, Terracciano D, Mariano A and Macchia V: Matrixmetalloproteinase-2 and matrix metalloproteinase-9 type IV collagenases in serum of patients with pleural effusions. Int J Oncol *26*: 1363-1368, 2005.

215

MALIGNANT MESOTHELIOMA OF *TUNICA VAGINALIS*: MANAGEMENT, PROGNOSTIC FACTORS AND ADJUVANT THERAPIES

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Background: If malignant mesotheliomas (MMs) of pleura, pericardium and peritoneum are uncommon, testicular MMs are extremely rare, accounting for fewer than 5% of all MMs. They can be associated with a previous exposure to asbestos and usually occur in patients older than 45 years, with a median age of 60 years. Despite aggressive surgical procedures, prognosis remains poor. MMs have an expansive and infiltrative growth pattern and metastasis occurs *via* the lymphatic system to inguinal and para-aortic nodes. Two thirds of recurrences occur within the first two years after diagnosis. Clinicians do not agree about adjuvant therapy: many of them report results following surgery alone; others report survival with postoperative chemotherapy and/or radiotherapy even in advanced diseases. *Case Report:* In 2008, a 77-year-old man presented with a growing swelling of the left hemiscrotum. Ultrasonography revealed a left

hydrocele. The patient underwent cytoanalysis of the hydrocele fluid: many mesothelial cells with nuclear and cytoplasmic atypias were found. Preoperatively, the patient was studied with whole-body CT. He was treated with left hemiscrotectomy in January 2009. Grossly, the testicle was filled with a whitish plurinodular, in places pseudocystic and gelatinous neoformation, which involved the *Tunica vaginalis*, *Tunica albuginea* and scrotal tissues and reached the epididymis. Histopathology demonstrated an MM arising from the *Tunica vaginalis*, characterized by a epithelioid pattern and tubulopapillary architecture; focal necrosis and endovascular invasion were found. Immunochemistry showed high cytokeratin, epithelial membrane antigen (EMA) and calretinin positivity. No adjuvant treatment was administered. *Results:* The patient lived without evidence of disease until October 2010, when left-groin adenopathies developed. Ultrasonography confirmed the presence of four metastastic nodes, the largest one of 4 cm, and also revealed a suspicious node in the right groin. A nodal biopsy in the left groin resulted in the diagnosis of MM metastasis. A subsequent PET/CT scan demonstrated radioactive tracer fixation in both groins and in para-aortic nodes. The patient was enrolled in a chemoradiation therapeutic program. He has just completed three cycles of pemetrexed-based chemotherapy with passable results and will undergo radiotherapy to all sites of the disease. According to the literature, radiotherapy can be even more effective than chemotherapy in patients with metastatic disease. *Discussion and Conclusion:* Our case report underlines the importance of a correct preoperative diagnosis and an accurate staging because these tumors often present as a hydrocele or an epididymal cyst. The diagnosis of MM of the *Tunica vaginalis* should be considered in any patient presenting with a rapidly growing hydrocele. Because most cases of MM are found intra- or postoperatively, many patients undergo suboptimal resection and the diagnosis of malignancy is achieved late. Instead, the only useful treatment is radical orchiectomy through an inguinal approach or hemiscrotectomy, in the case of initial involvement of the scrotum. There is no role for inguinal or iliac lymph-node dissection when there is no suspicion of metastasis. Our patient was well-studied preoperatively and underwent adequate surgery. Unfortunately, in a considerable proportion of patients, risk of local recurrence is high: nearly 40% of patients present with negative prognostic factors, such as local invasion to subtunical connective tissues and testicular parenchyma, and 12% develop recurrence after surgery. In the light of literature findings, surveillance after orchiectomy can be considered a valid policy for many patients. However, there are some conditions which are predictors of relapse and should be taken into account when considering the opportunity for an immediate adjuvant treatment, as our case report highlights. Moreover chemotherapy and/or radiotherapy to the sites of relapse can be adopted as salvage treatment. Finally, this case report emphasizes the importance of oncologic follow-up after surgery.

1 Ashis G *et al*: Malignant mesothelioma of the *Tunica vaginalis* of the testis without exposure to asbestos. Cases Journal *1*: 310, 2008.
2 Chen JL and Hsu YH: Malignant mesothelioma of the *Tunica vaginalis* testis: a case report and literature review. Kaohsiung J Med Sci *25(2)*: 77-80, 2009.
3 Liguori G *et al*: Inguinal recurrence of malignant mesothelioma of the *Tunica vaginalis*: one case report with delayed recurrence and review of the literature. Asian J Androl *9(6)*: 859-860, 2007.

216
ACTIVE SURVEILLANCE FOR PROSTATE CANCER: NOMOGRAM PREDICTING THE RISK OF UPGRADIG/UPSIZING AT ONE-YEAR REPEAT BIOPSY

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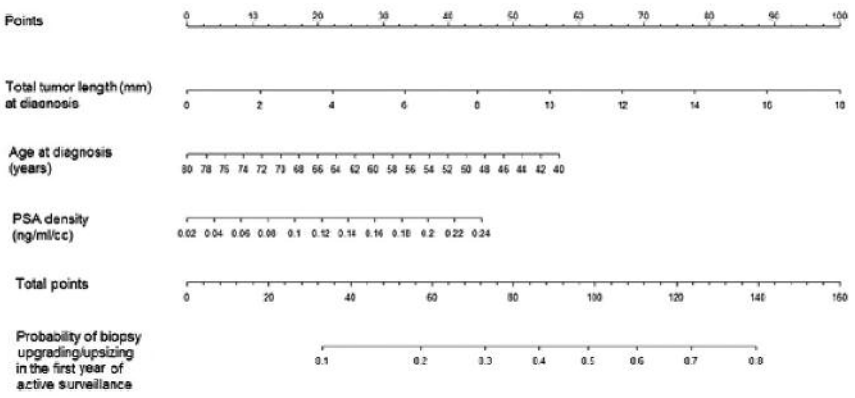
Background: Since 2005, we have been proposing the use of active surveillance (AS) for low-risk prostate cancer (PCa). Variables influencing upgrading/upsizing at the first repeat biopsy (one year after the beginning of AS) are analyzed here to identify patients with a higher probability of upgrading/upsizing after a short time in AS, and a preliminary nomogram is presented. *Patients and Methods:* The AS institutional protocol (SAINT) started in March 2005 and was accepted by 86 patients. Entry criteria were: iPSA≤10 ng/ml, Tstage≤T2a, GPS≤3+3, positive biopsy cores≤20%, maximum core length containing cancer ≤50%. Patient drop out was: PSADT≤3 years, PSA>10 ng/ml, upgrading/upsizing at re-biopsy or personal choice. In November 2007, the PRIAS protocol was embraced: 126 patients were enrolled until October 2010. PRIAS *vs*. SAINT differs on: maximum 2 positive cores and PSA density<0.2 ng/ml/cm^3. Multivariable logistic regression (MVLR) was used to analyze correlations between variables and upgrading/upsizing at first repeat biopsy and a nomogram was developed using R software (www.r-project.org). *Results:* Statistical analysis was performed on data for 109 patients (39 SAINT and 70 PRIAS patients) with complete records (one-



Figure

year min follow-up). A total of 20/109 patients had upgrading/upsizing after repeat biopsy, switching to radical treatment. Age, iPSA, PSA density, number of positive cores, percentage of positive cores, absolute biopsy tumor length (ABSmm) and T-stage were all considered factors potentially influencing upgrading/upsizing. GPS was not considered (all patients had GPS=3+3). Backward and forward MVLR resulted in a three-continuous variable best fit model (overall p=0.05): ABSmm (p=0.07, OR=1.20), age (p=0.37, OR=0.97), and PSA density (p=0.24, OR=6.9). A nomogram (see the figure) was built on this result. *Conclusion:* A nomogram including biopsy details coupled to age and PSA density can help identifying patients who have a higher probability of upgrading/upsizing after a short time in AS. More data are required to strengthen the statistical power of this preliminary analysis.

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217
STEREOTACTIC BODY RADIATION THERAPY FOR ISOLATED NODAL RECURRENCES OF PROSTATE CANCER

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Aim: To evaluate the feasibility, tolerability and preliminary outcomes of stereotactic body radiation therapy in patients with nodal recurrences of prostate cancer. *Patients and Methods:* Between May 2006 and July 2009, 12 patients (10 with isolated nodal recurrences and 2 with multiple adjacent adenopathy) underwent stereotactic body radiation therapy delivered by a linear accelerator (Linac 2100, Varian). The patient age ranged from 51 and 87 (median, 70) years. Primary treatment was radical prostatectomy in 7 patients, prostatectomy and postoperative radiotherapy in 2 patients and exclusive radiotherapy, androgen deprivation and radiotherapy with rescue prostatectomy in 3 patients. The initial disease category according to the National Comprehensive Cancer Network 2011 was defined as intermediate, high, very high and metastatic (pN1) in 1, 2, 5 and 3 patients, respectively (1 unknown). At the time of radiation therapy, 3 patients did not receive androgen deprivation, 7 patients received some forms of androgen deprivation and the remaining 2 patients were hormone-resistant. Ten patients underwent ^{11}C-choline positron-emission tomography/computed tomography (^{11}C-choline PET/CT) examination, while the remaining 2 patients underwent a magnetic resonance imaging (MRI) and a CT scan, respectively, for the diagnosis of the recurrence and in order to exclude the presence of other sites of disease. All patients had a CT scan with contrast centering; 10 mm were added to the macroscopic disease or gross tumor volume (GTV) to create the planning target volume (PTV). Ten patients received a total dose of 30 Gy/3 daily fractions for lesions of dimensions between 1.2 and 2 cm (pelvic disease). Two patients received 35 Gy/5 fractions and 27 Gy/3 fractions, respectively, because of the large size of the adenopathy (5 cm) and its critical location near the bone marrow (para-aortic lymph nodes). *Results:* There was no report of acute and late toxicity. The mean follow- up was 38 (range, 18-58) months. Eight patients had a complete response to radiotherapy with negative imaging exams (^{11}C-choline PET/CT, MRI and CT) with 3 of them never having received neoadjuvant or concomitant/adjuvant hormonal therapy; 3 patients had stable disease/partial response, and the remaining patient had progressive disease in the irradiated field. Clinical progression was observed in 9 patients after a mean time of 11 (range, 5-24) months from the completion of the stereotactic body radiation therapy. One patient had regional lymph node progression, while 3 patients had regional and distant nodal progression. Two patients experienced distant metastasis involving bones, while 3had biochemical disease progression.

At the time of analysis (February 2011), 10 patients were alive and 2 dead from disease progression. *Discussion and Conclusion:* In the single regional lymph nodal recurrence of prostate cancer after primary treatment, locoregional treatment may still play an important role and prevent distant metastasis, and may also delay the onset and duration of action of hormonal therapy. Instead of surgical dissection, which is not always feasible because of patient age and comorbidities, irradiation of isolated nodal recurrence by stereotactic techniques is feasible, with excellent results in terms of local disease control and the almost complete absence of side-effects (3). In our experience, stereotactic body radiation therapy seems to be a safe, non-invasive and effective treatment. It offers excellent tumor control in the field in the absence of toxicity and could probably be used as an alternative to surgery in selected patients with isolated, early detected, nodal disease.

1 Chang BK and Timmerman RD: Stereotactic body radiation therapy: A comprehensive review. Am J Clin Oncol *30*: 637-664, 2007.
2 Friedland JL, Freeman DE, Masterson-McGary ME *et al*: Stereotactic body radiotherapy: An emerging treatment approach for localized prostate cancer. Technol Cancer Res Treat *8*: 387-392, 2009.
3 Jereczek-Fossa BA, Fariselli L, Beltramo G *et al*: Linac-based or robotic image-guided stereotactic radiotherapy for isolated lymph node recurrent prostate cancer. Radiother Oncol *93*: 14-17, 2009.

218
IS PROSTATE BIOPSY STILL NECESSARY?

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Background: The deficiencies of serum prostate-specific antigen (PSA) as a prostate-cancer-specific diagnostic test are well recognized, thus creating a new diagnostic dilemma: only a fraction of men with increased serum PSA have detectable prostate cancer. Men with at least one negative biopsy often have persistently increased serum PSA, primarily attributable to an enlarged gland and benign prostatic hyperplasia (BPH). However, a significant proportion of men with slightly increased serum PSA (2.5±4.0 ng/ml) either have, or will develop, clinically significant prostate cancer (1). Although biopsy remains the gold standard for prostate cancer detection, more accurate tests with better specificity are needed to decide whether or not to biopsy the prostate. In recent clinical trials, the potential diagnostic value of the PCA3 urine test was established, as well as the role of combined proton ^{1}H magnetic resonance spectroscopic imaging (^{1}H-MRSI) and dynamic contrast-enhanced imaging magnetic resonance imaging (DCE-MRI) in the management of prostate cancer. The aim of our study was to evaluate the ability of ^{1}H-MRSI /DCE-MRI combined with PCA3 urinary test to improve prostate cancer detection in cases of PSA increase and precious negative prostate biopsy. *Patients and Methods:* This was a prospective single-center study on patients with prior negative random transrectal ultrasound (TRUS)-guided prostate biopsy and persistent elevated PSA levels. Including criteria were: a first random TRUS-guided prostate biopsy negative for prostate adenocarcinoma or high-grade prostate intraepithelial neoplasia, persistent elevated PSA levels (mean total PSA: 6.37, range: 4-10 ng/ml) and negative digital rectal examination (DRE). Exclusion criteria for the study were: previous hormonal, surgical or radiation therapies for prostatic diseases, lack of urine sample collected after DRE and prior to prostate biopsy, inadequate prostate biopsy with fewer than 10 cores and cases where an MRI examination with ^{1}H-MRSI and DCE-MRI was not possible. All patients were submitted to ^{1}H-MRSI and DCE-MRI. Prior to that the patient's urine was collected by an expert urologist, following an attentive prostate massage (three compressions for each prostatic lobe), in order to perform PCA3 assay. All biopsies were performed according to a standard biopsy protocol: 10-core laterally directed random TRUS-guided prostate biopsy (two cores from the basal portion lateral and paramedial, two from the mid-gland lateral and paramedical, and one from the apex, on each side of the gland for each patient, plus additional biopsies from other areas suspicious for prostate cancer at MRI. *Results:* 41/43 urinary samples (95.3%) were analyzed successfully. The performance of the PCA3 test was evaluated in terms of sensitivity and specificity by comparing the PCA3 score to the biopsy results. The overall sensitivity and specificity of a PCA3 score >35 alone for positive biopsy in this cohort were 76.9% and 66.6%, respectively, with positive and negative predictive values of 80% and 62.5%, respectively. With regard to MRI, sensitivity and specificity were 92.8% and 86.6%, respectively, with positive and negative predictive values of 92.8% and 86.6%, respectively. The sensitivity and specificity of PCA3, MRI (^{1}H-MRSI/DCE-MRI) and their combination were explored using receiver operating characteristic (ROC) analysis. The area under the ROC curve was 0.755 for PCA3, 0.864 for MRI and 0.92 for their combination. *Discussion and Conclusion:* Our results showed that the combination of both diagnostic methods, PCA3 and MRI, may lead to a very high diagnostic accuracy compared to either individual test. If this finding is confirmed in a large prospective study it may lead to the establishment of new

oncological markers in the near future, calling for re-evaluation of the role of prostate biopsy.

1 Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL *et al*: Prevalence of prostate cancer among men with a prostate-specific antigen level 4.0 ng per milliliter. N Engl J Med *350*: 2239-2246, 2004.
2 Fradet Y, Saad F, Aprikian A, Dessureault J, Elhilali M, Trudel C, Masse B, Piche L and Chypre C: uPM3, a new molecular urine test for the detection of prostate cancer. Urology *64*: 311-315, 2004.
3 Sciarra A, Panebianco V, Ciccariello M, Salciccia S, Cattarino S, Lisi D, Gentilucci A, Alfarone A, Bernardo S, Passariello R and Gentile V: Value of magnetic resonance spectroscopy imaging and dynamic contrast-enhanced imaging for detecting prostate cancer foci in men with prior negative biopsy. Clin Cancer Res *16(6)*: 1875-1883, 2010.

219
A SINGLE-CENTER EXPERIENCE OF 3D CONFORMAL RADIATION TREATMENT IN PROSTATE CANCER

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Background: High-energy external radiotherapy is one of the most popular methods of local treatment in non-metastatic prostate cancer. A clear dose–effect relationship has been shown in terms of biochemical control and side-effects. Since 2003, we have used a dose escalation program in localized prostate cancer with progressively increasing doses from 74 to 78 Gy. We have evaluated the effects of escalating dose according to acute and late side-effects and tumor control. *Patients and Methods:* Between October 2003 and December 2009, 92 patients with prostate cancer were treated. They were classified according to D'Amico risk groups. In the low-risk group, only the prostate and the basis of seminal vesicles were considered in the target volume; in the intermediate- and high-risk groups, the complete seminal vesicles were considered in the initial target volume. Patients in this second group received neoadjuvant hormone therapy for three months and adjuvant therapy between six months and two years. No patient underwent whole pelvic irradiation. Acute side-effects were evaluated weekly and graded according to the RTOG scoring system. Late side-effects and tumor had been monitored every three months for at least two years. *Results:* Acute side-effects were generally mild. Late effects were more pronounced regarding genitourinary toxicity, with four cases of urinary incontinence and two cases of ureteral dilatation. Only three patients experienced gastrointestinal toxicity grade ≥2. In the high-risk category, three patients developed metastatic disease and eight patients had biochemical failure. In the low- and intermediate-risk groups, four patients developed PSA failure. *Conclusion:* High-radiation dose levels allowed excellent biochemical control in low- and intermediate-risk groups, with acceptable radiation related side-effects. Since 2010, patients in the high-risk group have being undergoing whole pelvic irradiation.

220
A CASE OF RENAL CARCINOMA METASTASIS SIMULATING A THYROID GOITER

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Background: Although the thyroid is a highly vascularized gland, it is not a common target of metastasis from extrathyroidal cancer. Clear-cell renal carcinoma (cRCC) frequently metastasizes to the thyroid, representing 2-3% of all adult tumors, and more than 40% of patients present with metastases at diagnosis. The presence of cRCC thyroidal metastases makes the differential diagnosis from thyroid clear-cell carcinoma extremely difficult. *Patients and Methods:* A 70-year-old woman presented with a mild compressive symptomatology due to a recent multinodular thyroid goiter with a 'simple' multinodular ultrasound pattern, in the absence of signs of malignancy and with normal findings for hormonal and immunological assessment. Clinical history presented chronic renal failure under hemodialytic treatment subsequent to a right nephrectomy carried out 2 years before for an unspecified cause. A volumetric increase of the whole gland was evident, with absence of laterocervical adenopathy. A total thyroidectomy was performed. *Results:* Histological examination showed an enlargement of the thyroid with a distorted shape; the cross-section showed multiple nodules, some with firm appearance and others with colloidal appearance. The sections showed nodules with firm appearance surrounded by a complete fibrous capsule and

characterized by proliferation of large cells, with abundant optically clear cytoplasm and well-defined margins, arranged in an alveolar-tubular pattern (nests and cords). The nuclei exhibited mild to moderate atypia and single or multiple nucleoli. Few mitoses were observed. Within the nodules, several dilated vascular structures were visible, some of which showing angiolymphatic invasion. The neoplastic cells were strongly immunoreactive for CD10 (commonly expressed in cRCC) and vimentin. By contrast, thyroid transcription factor-1 (TTF-1), thyroglobulin and CK7 were not found in tumoral cells and this ruled out a primary tumor of the thyroid. On the grounds of the morphological and immunohistochemical findings, along with the patient's medical history, a diagnosis of intrathyroid metastasis of cRCC was made. Contacting the patient's relatives for more information about his renal disease, they revealed that the nephrectomy had been due to cRCC, which had been concealed from the patient. This clarification confirmed the histological diagnosis of thyroid metastasis of cRCC, on a background of micro- and macrofollicular colloidal goiter. The patient underwent a whole-body CT scan and bone scintigraphy that was negative for metastases. Therefore, being at low-risk and under hemodialytic treatment, the patient was sent for oncologic follow-up. *Discussion and Conclusion:* Many patients suffering from thyroid metastases present a local symptomatology which is not easy to distinguish from that caused by primary pathologies of the thyroid. In the case we described here, the difficulty of diagnosis was not only due to the rarity of this condition, but was also complicated by the lack of information about the cause of the previous nephrectomy. In secondary thyroid lesions, it is necessary to ensure the total eradication of the gland (even for suspected malignant pathology) in order to guarantee oncologic radicality and extend the patient's survival.

221
LIDOCAINE-PRILOCAINE CREAM COMBINED WITH LIDOCAINE-KETOROLAC GEL PROVIDES BETTER PAIN RELIEF THAN WHEN COMBINED WITH PERIPROSTATIC NERVE BLOCK DURING TRANSRECTAL PROSTATE BIOPSY

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Aim: To compare the efficacy and safety of perianal-intrarectal lidocaine-prilocaine (PILP) cream when combined with lidocaine-ketorolac (LK) gel and with periprostatic nerve block (PPNB) in relieving pain during transrectal prostate biopsy (TPB). *Patients and Methods:* A total of 200 patients were randomized to receive PI LP cream combined with LK gel (group 1), or combined with PPNB (group 2) before TPB. The 0-to-10 point visual analog scale (VAS) was used for assessing pain at probe insertion and movements (VAS-1), periprostatic infiltration (VAS-2) when applied and at prostate sampling (VAS-3), as well as maximal procedural pain (MPP). Complications occurring up to 20 days after the procedure were recorded. *Results:* The groups were comparable for patient age, serum PSA, prostate volume and cancer detection rate. All patients tolerated the procedure well. The two anesthetic regimens provided almost equal mean VAS-1 (0.33 *vs*. 0.37 for groups 1 and 2, respectively; p=0.701) and VAS-3 (0.52 *vs*. 0.51 for groups 1 and 2, respectively; p=0.954) scores, but patients in group 2 reported significantly greater MPP scores (0.68 *vs*. 1.53 for groups 1 and 2, respectively; p<0.0001), as periprostatic infiltration was the most painful part of the procedure (mean VAS-2=1.33). The complication rate was similar in the two groups (1% *vs*. 2% for groups 1 and 2, respectively; p=0.38). *Conclusion:* The novel combination of PILP cream and LK gel provided the same probe- and sampling-related pain relief as the combination of PILP cream and PPNB. Moreover, by preventing the non-negligible periprostatic infiltration pain, it provided significantly better overall patient compliance with the procedure. It also was safe and easy to administer.

222
A LONGITUDINAL DEFINITION OF LATE FECAL INCONTINENCE AFTER 3D-CRT FOR PROSTATE CANCER: ANALYSIS AND NOMOGRAM

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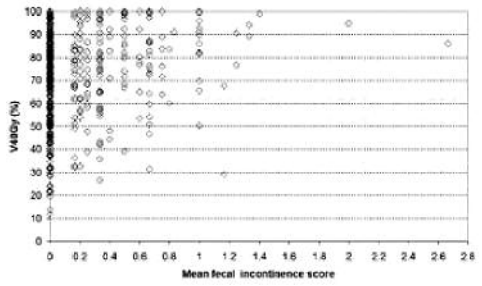

Figure 1

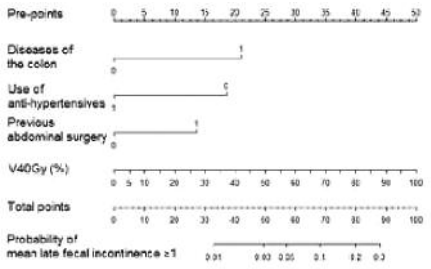

Figure 2

Aim: To evaluate the relationship between clinical/dosimetric factors and late fecal incontinence (linc) after high-dose radiotherapy (RT) in prostate cancer patients (patients) accrued in AIROPROS 0102 trial (RT doses: 70-80 Gy, 1.8-2 Gy/fraction). Toxicity was defined using a longitudinal parameter (mlinc) which took into account both the severity and duration of symptoms. *Patients and Methods:* Self-reported questionnaires of 586 patients enrolled in the AIROPROS 0102 trial with a minimum follow-up of 36 months were analyzed with respect to linc. Only patients with a G0 basal linc were included (550/586). mlinc was defined as the mean score for fecal incontinence calculated over the whole follow-up period. G1 linc was scored if unintentional stool discharge was sometimes experienced; G2 linc was scored if unintentional stool discharge was experienced often or if patients used sanitary pads sporadically; G3 linc was scored if patients reported daily unintentional stool discharge or use of sanitary pad more than twice/week. The correlation between pretreatment morbidities, hormonal therapy, drug prescription, presence of diabetes or hypertension, abdominal surgery prior to RT, presence of acute lower gastrointestinal toxicity, irradiation of pelvic nodes and seminal vesicles, mean rectal dose, constraints of dose–volume histograms (from V20Gy to V75Gy) and mlinc was investigated by uni- and multivariate logistic analyses. *Results:* mlinc was a continuous variable (range, 0-2.7 in this population). A total of 197/550 patients had mlinc >0, thus, 35.8% of patients experienced some linc symptoms during the follow-up period; 22/550 patients had mlinc ≥1; thus, 4% of patients had either a persistent G1 linc or a G2-G3 linc which never completely recovered. Figure 1 shows mlinc as a function of V40Gy. A clear relationship can be seen between the dose at V40Gy and mlinc. In multivariate analysis (overall p=0.0034), V40Gy (continuous variable, p=0.02, OR=1.035), use of antihypertensive protective factors (p=0.02, OR=0.28), presence of colon morbidity before RT (p=0.04, OR=4.3) and abdominal surgery before RT (p=0.17, OR=2.5) were correlated to mlinc ≥1. A nomogram was developed for the prediction of mlinc ≥1 (Figure 2). *Conclusion:* The use of a longitudinal definition of linc was useful for taking both the duration and the severity of symptoms into account. The use of mlinc provided additional information which was not seen by analyzing linc, as peak toxicity (corresponding to the maximum grade of linc) and a stronger relationship between dosimetric (V40Gy) and clinical risk factors (use of antihypertensives, presence of colon morbidity before RT and previous abdominal surgery) were revealed.

223

IMPACT OF TRANSRECTAL PROSTATE BIOPSY ON ERECTILE FUNCTION: A PROSPECTIVE STUDY USING THE INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF)

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Background: Erectile dysfunction (ED) is a rare, although possible, complication after prostate biopsy. Nevertheless, only few studies have prospectively analyzed this issue through validated questionnaires. The aim of this study was to evaluate the impact of transrectal prostate biopsy (TPB) on erectile function through the use of the International Index of Erectile Function-5 (IIEF-5) questionnaire. *Patients and Methods:* Between June 2008 and June 2010, all patients scheduled for TPB in our Department completed the IIEF-5 questionnaire before the procedure. A total of 200 among them who were diagnosed with prostate cancer and scheduled for retropubic radical prostatectomy (RRP) were asked to complete the IIEF-5 questionnaire again before RRP. *Results:* The mean patient age was 56 years, mean PSA was 6.3 ng/ml and mean prostate volume was 47 cm3. The mean IIEF-5 score was 21 before TPB and 20 before RRP, and this difference was not significant. However, while in patients ≥65 years of age, the mean IIEF-5 score was 19 before TPB and before RRP, in patients <65 years of age, the mean IIEF-5 score decreased from 22 before TPB to 19 before RRP (p<0.001). Overall, 107 patients (53.5%) underwent non-nerve-sparing RRP, whereas

39 and 54 patients (19.5 and 27%, respectively) underwent unilateral and bilateral nerve-sparing RRP, respectively. Of the 104 patients <65 years of age, 33 (31.7%) were not considered eligible for a nerve-sparing RRP because of tumor characteristics (27) or IIEF-5 score before TPB <17 (6). If we had used IIEF-5 before RRP, another 14 (19.7%) out of the 71 patients who underwent nerve-sparing RRP would have been excluded because of IIEF-5 <17. *Discussion and Conclusion:* The present study showed that in patients <65 years of age, a TPB yielding the diagnosis of prostate cancer may lead to a significant reduction in the IIEF-5 score. Since this index is currently used to decide a patient's eligibility for nerve-sparing radical prostatectomy, it should better be evaluated before TPB rather than before RRP.

Table I. *Histopathological results (453 patients).*

Gender	
Male: 386	327 Ta-T1 (84.2%); 61 T2a or more (15.8%)
Female: 67	57 Ta-T1 (85.1%); 10 T2a or more (14.9%)
Stage	
Ta	231 (51%)
T1	151 (33.3%)
T2a or more	71 (15.7%)
Grade	
G1	220 (48.6%)
G2	153 (33.7%)
G3	80 (17.7%)

Table II. *Correlations between cystoscopic findings and muscle invasion.*

		Muscle invasion		
	n	Yes	No	*p*-Value
Cystoscopic evaluation (performed by single operator)	453	84 (18.5%)	369 (81.4%)	
Neoplasm configuration				<0.0001
Papillary	372	12 (3.2%)	360 (96.8%)	
Non-papillary	81	59 (72.8%)	22 (27.2%)	
Finding of stalk of tumor				<0.0001
Pedunculated	314	13 (4.1%)	301 (95.9%)	
Sessile	139	58 (41.7%)	81 (58.3%)	
Number of neoplasms				0.1956
Single	192	15 (7.8%)	177 (92.2%)	
Multiple	261	56 (21.5%)	205 (78.5%)	
Maximum size of neoplasm				<0.0001
≤1 cm	201	4 (2%)	197 (98%)	
1-≤2 cm	175	24 (13.8%)	151 (86.2%)	
≥2 cm	77	43 (55.8%)	34 (44.2%)	

224

PREDICTIVE VALUE OF CYSTOSCOPIC FINDINGS IN MUSCLE-INVASIVE BLADDER CANCER

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Background: The definitive diagnosis of bladder cancer is possible only through cystoscopy. Urinary cytology, performed on the basis of clinical suspicion (micro- and/or macroscopic hematuria, dysuria in the absence of obstruction), or the presence of a bladder neoplasm on ultrasound, although it can help to assess the degree of tumor aggressiveness, does not provide information about the pathological stage. In this study, we tried to assess how and whether it is possible to predict the infiltration of muscle cancer on the basis of personal experience and data obtained with cystoscopy carried out before transurethral resection, using multivariate logistic regression analysis. *Patients and Methods:* From January 1998 to December 2007, 453 patients with histologically confirmed primary bladder cancer were evaluated in our department following endoscopic treatment. The patient age ranged from 32 to 83 (mean, 66.4) years; 386 were men, with a male-to-female ratio of 5.8:1. Pathological staging was reassessed according to the UICC classification (2002), and the pathological degree according to the WHO criteria (2004). Before endoscopic surgery, all patients underwent renal and bladder ultrasonography and urinary cytology. The cytology was positive in 291 patients (54.3%). Prior to transurethral resection, the operator expressed an opinion, based on personal experience, on the possibility that the cancer was invasive or not, paying particular attention to the following tumor characteristics: number of tumors, size (in case of multiple tumors, the largest lesion was assessed), appearance (papillary or non-papillary), finding on the stalk of the tumor (sessile or pedunculated). All patients were at the first manifestation of disease. Multivariate logistic regression analysis was used to determine which variables significantly predicted muscle invasion. *Results:* The pathological results after endoscopic resection are shown in Table I. Most bladder tumors were transitional cell carcinomas, with the presence of squamous-cell type in a small number of cases. Of the 71 patients with invasive cancer (15.7%), 56 underwent radical cystectomy. Histopathological examination showed that tumors in 27, 11, 4, 8 and 6 patients were pT2a, pT2b, pT3a,

pT4 and pT3b, respectively. Fifteen patients received palliative care for general comorbidities. Patients who presented with superficial bladder cancer (382; 84.2%) were treated following the EAU guidelines. Correlations between cystoscopic findings and muscle invasion are summarized in Table II. The results indicate that the non-papillary form, sessile stalk of tumor and tumor size >1 cm are the most representative characteristics significantly associated with a higher risk of muscle infiltration. *Discussion and Conclusion:* The treatment of bladder cancer was correlated with the pathological stage of the primary cancerous lesion. Our experience confirmed that the appearance, stalk and size of the tumor are independent risk variables associated with muscle infiltration. If these independent risk factors are associated with each other, there is a statistically significant increased risk of muscle invasion. The finding of a tumor with a diameter greater than 1 cm in combination with a sessile form and a non-papillary configuration is associated with an increased risk of detrusor infiltration and an estimated 54% chance of muscle invasion. Although the majority of data reported in the literature suggest that cystoscopy is the most accurate examination in the diagnosis of bladder cancer, it is not yet clear whether tumor muscular invasion may be diagnosed based on cystoscopic findings. Our results may confirm the experience of urologists in assessing the muscle invasion of bladder cancer through cystoscopic findings.

1 Herr HW, Donat SM and Dalbagni G: Correlation of cystoscopy with histology of recurrent papillary tumors of the bladder. J Urol *168(3)*: 978-980, 2002.
2 Satoh E, Miyao N, Tachiki H and Fujisawa Y: Prediction of muscle invasion of bladder cancer by cystoscopy. Eur Urol *41(2)*: 178-181, 2002.
3 Herr HW: Does cystoscopy correlate with the histology of recurrent papillary tumours of the bladder? BJU Int *88(7)*: 683-685, 2001

225

AN ELEVATED POST-VOID RESIDUAL URINARY VOLUME IS PREDICTIVE OF A NEGATIVE PROSTATE BIOPSY

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Background: To date, the indication for prostate biopsy (PBx) is mainly based on serum prostate-specific antigen (PSA); nevertheless, this tumor marker has no particularly high sensitivity and specificity for diagnosis of prostate cancer. Various PSA-based parameters, such as PSA density, PSA velocity and free-to-total PSA ratio, have been suggested to play a role in indicating PBx, but none has reached high levels of accuracy. The present study aimed to determine the role of urodynamical parameters, such as the maximum flow (Qmax) rate and the post-void residual (PVR) in predicting the outcome of PBx. *Patients and Methods:* From December 2005 to October 2009, all non-catheterized patients scheduled for first PBx because of elevated PSA (>4 ng/ml) and/or abnormal digital rectal examination underwent uroflowmetry before PBx. The value of PSA, prostate volume, PSA density (PSAd), Qmax, and PVR in predicting or excluding the diagnosis of prostate cancer was then analyzed. *Results:* Of 1004 patients, 10 were excluded because they were affected by prostatic intraepithelial neoplasia (PIN, 5 cases) or atypical small acinar proliferation (ASAP, 5 cases). Of the remaining 994 patients, 373 (37.5%) were affected by prostate cancer. In univariate analysis (ANOVA test), all clinical and urodynamical parameters were predictive of prostate cancer; In multivariate analysis, however, PVR was the most important prognostic factor ($p<0.0001$). *Discussion and Conclusion:* PVR correlated inversely with the diagnosis of prostate cancer, resulting in it being the best predictive factor in the multivariate analysis. Being simple and non-invasive, PVR should be used routinely in the decision-making process for PBx. The identification of reliable cut-off values and the possible inclusion of this parameter in ad hoc nomograms could help prevent a number of unnecessary PBx.

227

UPPER URINARY TRACT TCC RECURRENCE RATE FOLLOWING RADICAL CYSTECTOMY FOR BLADDER CANCER: A META-ANALYSIS OF 13,185 PATIENTS

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Background: Patients who have undergone radical cystectomy for urothelial cancer are at risk for recurrence of transitional cell carcinoma (TCC) on the upper urinary tract. Previous studies identified several risk factors for TCC recurrence, although the predictive value of each factor still remains controversial. Both European and American urological guidelines lack these topics, referring only to isolated works with large causative studies. *Materials and Methods:* A bibliographic search covering the period from January 1970 to July 2010 was conducted on PubMed, MEDLINE and EMBASE. The analysis was based on 27 studies that fulfilled

the predefined inclusion criteria. Data were analyzed in two ways: a fixed-effect logistic regression approach and a classical meta-analysis. *Results:* A total of 13,185 patients were included. Follow-up was described in 22 studies, ranging from 0.36 to 349.2 months. The overall prevalence of recurrence of the upper urinary tract after cystectomy ranged from 0.75 to 6.4%. TCC recurrence evidence appeared after 0.4 to 164 months. The presentation was in an advanced (64.6%) or metastatic way (35.6%). Both situations had poor survival rates. Patients affected by low-grade disease showed a strong significant difference in TCC recurrence compared to those having higher grade disease. The same difference in TCC recurrence was reported between patients with carcinoma *in situ* or superficial disease and those with muscle-invasive disease. Patients with a history of carcinoma *in situ* did not have statistically significant different recurrence rates from those presenting with solitary bladder TCC. Moreover, there was no statistically significant difference in TCC recurrence rates between the different types of diversion adopted. In 24 studies, follow-up was carried out through periodic radiological assessment of the upper urinary tract, while in 20 studies, urinary cytology was used in the follow-up. In 14 studies, 166 recurrences were reported. For 63 patients (63/166; 38%), the upper urinary tract recurrence was diagnosed due to the follow-up. The other recurrences (62%) were diagnosed after the appearance of symptoms. Among the 5537 patients who underwent the follow-up pathway with a urinary cytological examination, recurrences were diagnosed in 1.8‰. This rate rose to 7.6‰ with a follow-up performed with periodic upper urinary tract imaging. *Conclusion:* The recurrence values appear low considering the panurothelial field defect theory, but these values reflect the mortality related to the initial bladder cancer. A group of patients at high risk does exist, considering their anamnesis and their definitive pathological examination taken from cystectomy specimens. An extensive regular follow-up with cytology and upper urinary tract imaging gives insufficient benefit. Periodic CT scans with a pyelographic study combines upper urinary tract imaging with the identification of any secondary parenchymal, osseous or lymph-nodal metastatic lesion.

228

EXTERNAL VALIDATION OF PREOPERATIVE AND POSTOPERATIVE PROGNOSTIC KARAKIEWICZ NOMOGRAMS FOR RENAL CELL CARCINOMA: A MULTICENTER EUROPEAN STUDY

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Background: Pre- and postoperative prognostic models for patients with renal cell carcinoma (RCC) were recently released, considering only clinical parameters such as symptoms, TNM and tumor size, as prognostic variables. These models have been internally validated and they still require external validation. Our aim was to externally validate the pre- and postoperative model developed by Karakiewicz predicting cancer-specific survival in patients affected by RCC. *Patients and Methods:* Our multicenter retrospective study consisted of a total of 2570 cases from 7 European sites. Patients who underwent either radical or partial nephrectomy were enrolled. For each patient, prognostic scores were calculated according to two models: the preoperative Karakiewicz (2009) model and the postoperative Karakiewicz (2007) model. According to the original studies, the primary endpoint was cancer-specific survival (CSS). Survival curves were estimated by Kaplan–Meier method. Discriminating ability was assessed by the Harrell C-index for censored data stratified by center and with 95% confidence intervals (CI). *Results:* A total of 2046 patients were eligible for the analyses (mean age at diagnosis: 61±11 years; male-to-female ratio: 1.6; mean tumor size: 5.7±3.1 cm). Local and systemic symptoms were present in 383 (18.7%) and 181 (8.8%) of the patients, respectively. The median follow-up was 46 months. At the last follow-up, 460 patients had died (305 cancer-related deaths), with a 1-, 3- and 5-year CSS equal to 95%, 88% and 85%, respectively. Both models discriminated well. The stratified C-index for CSS was: 0.776 (95% CI=0.741-0.811) for the preoperative model (on 2011 patients) and 0.840 (95% CI=0.811-0.868) for the postoperative one (on 1997 patients). *Conclusion:* Our study better defined the general applicability of these prognostic models for predicting survival in patients with RCC treated with nephrectomy. Our results suggest that the postoperative model discriminates substantially better than the preoperative model. These

nomogram-based predictions may be used as benchmark data for pretreatment and postoperative decision making in patients with various stages of RCC. Further studies are needed to confirm their calibration before their definitive introduction into clinical practice.

229

PARTIAL NEPHRECTOMY OF RENAL METASTASIS FROM THYROID FOLLICULAR CARCINOMA

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Background: We report a rare case of laparoscopic surgery for renal metastasis of thyroid carcinoma. *Case Report:* A 67-year-old woman with a history of total thyroidectomy for a follicular thyroid carcinoma was admitted to our Department for the treatment of a renal node discovered during radiometabolic treatment with ^{131}I for bone and lung metastatic disease. The strong radiohalogen accumulation in the left kidney and the high levels of blood thyroglobulin led us to suspect a metastasis of the thyroid carcinoma. The patient underwent laparoscopic enucleation of the metastasis at the level of the inferior pole of the left kidney. The histological exam showed follicular thyroid carcinoma metastasis with negative surgical margin. *Results:* The laparoscopic approach allowed the removal of the renal node without complications and bleeding, with early recovery and mobilization, intact bowel function and oral feeding ability, which are all necessary conditions for any therapeutic regime.

230

THE PCA-3 ERA: PRELIMINARY RESULTS OF A SINGLE-CENTER PRAGMATIC STUDY

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Background: With increasing evidence that screening based on prostate-specific antigen (PSA) reduces disease-specific mortality but coincides with unacceptable levels of unnecessary testing, more specific biomarkers are necessary. Within this context, the use of the prostate cancer gene 3 (PCA-3) test is growing progressively. The primary endpoint of this pragmatic study was to assess the current indication for performing the PCA-3 test in a consecutive patient population from South Italy. Secondary endpoints were to assess the adequacy of the results with subsequent clinical decisions and the performance of the assay. *Patients and Methods:* A total of 1100 patients who underwent PCA-3 test between September 2009 and December 2009 were interviewed. The following data were collected: physician who prescribed the PCA-3 test, pretest total serum PSA (tPSA), PCA-3 score, possible performance of prostate biopsy after test and histopathological findings. Sensitivity and specificity of the test at different PCA3 cut-off values were also evaluated. *Results:* To date, complete data on 207 patients have been collected. Patients treated with 5-alpha reductase inhibitors were excluded from the study (n=122). In 206/207 (99.5%) cases, the PCA-3 test was prescribed by the urologist. A total of 63/207 (30%) patients had never undergone a prostate biopsy and 144/207 (70%) had undergone one or more biopsy sets for tPSA>3.0 ng/ml and/or abnormal digital rectal examination before the PCA-3 test. The mean pretest tPSA was 8.9 (range: 0.6-44) ng/ml. After PCA-3 test, 92 (44.5%) patients underwent prostate biopsy, with a mean PCA-3 score of 70 (range: 6-253) and a mean tPSA of 9.2 (range: 1.45-34) ng/ml. In 115 patients with a mean PCA-3 score ≤29 and mean tPSA ≤9.3 ng/ml, a prostate biopsy was not performed. Prostate cancer was found in 29/92 (31.5%) of patients who underwent biopsy after the PCA-3 test. In this patient group, the mean PCA-3 score was significantly higher than in the patients with negative prostate biopsy (93.5 *vs*. 54.7, respectively; $p<0.01$). We found the best results at a PCA-3 score cut-off of 50; specifically, positive predictive value, sensitivity, specificity and clinically significant cancer missed were 48%, 86%, 58% and 13.7%, respectively. *Discussion and Conclusion:* The preliminary results of this study demonstrated the enthusiasm of the urologists for this new biomarker, but also their desire to use it as a screening test for prostate cancer. Moreover, we found a tendency not to perform prostate biopsies after the test: Blind faith in a new biomarker that is still under investigation?

231

LONG-TERM COMPLICATIONS IN NON-SURGICALLY TREATED PATIENTS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Prostate cancer is the most common malignant neoplasm in males and the incidence is increasing every year. Oncologic and morbidity studies are necessary to improve therapeutic treatment options. We observed a group of patients

not treated surgically as primary treatment, having uro-oncologic complications long after primary treatment. We report the histories of these patients in an attempt to gain a better understanding of an unclear field of prostate cancer treatment. *Patients and Methods:* This was a retrospective observational study of a cohort of 74 patients with a mean age of 78.2 (range: 55-95) years at diagnosis, not treated with radical prostatectomy for prostate cancer. Diagnosis of prostate cancer was by transrectal ultrasound (TRUS)-guided biopsy. Prostate-specific antigen (PSA) at diagnosis was, on average, 197.8 (range: 4.3-61.24) ng/ml. The mean Gleason score was 7, with most common pattern of 3+4. After clinical and instrumental staging, we found 17 patients (23%) with metastasis at diagnosis; specifically, 15 patients (20%) with bone metastasis and 2 patients (3%) with nodal and bone metastasis. Patients were not treated surgically because of advanced age, advanced disease, inoperability, or simply patient choice. With regard to first-line therapy, 23 patients (31%) were treated with external beam radiotherapy (EBRT), 21 (37%) with pharmacological therapy using luteinizing hormone-releasing hormone (LHRH) analogs, 20 (27%) with combined androgenic blockade (CAB) and 4 (5%) with anti-androgenic drugs. Patients were observed for a median follow-up of 42 (range: 32-56) months. *Results:* During the follow-up, we divided complications per first-line type of treatment. In patients treated primarily with EBRT, we found: 7% with hematuria, 4% with proctitis, 4% with urinary incontinence, 30% with outlet bladder obstruction, 18% with hydronephrosis and 40% without symptoms. In patients treated exclusively with pharmacological therapy there was: 2% hematuria, 40% with outlet bladder obstruction, 5% with hydronephrosis, 35% without symptoms and 14% with vertebral fractures and neurological symptoms. We calculated the mean number of blood units with respect to first-line therapy: EBRT 6, LHRH 12, CAB 4, anti-androgens 2. *Discussion and Conclusion:* Considering the low number of patients, we observed a high rate of complications and a high number of blood units for patients treated with non-surgical treatments. Long-term case–control studies or randomized controlled trials are required to confirm our observations.

232

OVERVIEW OF UPPER URINARY TRACT LAPAROENDOSCOPIC SINGLE-SITE SURGERY: A MULTI-INSTITUTIONAL EXPERIENCE

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Background: Laparoendoscopic single-site (LESS) surgery is evolving as a promising alternative for mini-invasive surgery. This registry was designed to prospectively document early results of LESS procedures in urology among a large group of clinical cases. The aim of this study was to present the perioperative outcomes in an observational cohort of patients who underwent LESS surgery at advanced laparoscopic centers for upper urinary tract diseases. Three centers from three countries were approved to participate in the study. LESS surgery was clinically applied in 162 patients. Intra- and postoperative parameters were prospectively documented. *Patients and Methods:* Demographic data including age, body mass index, operative variables, estimated blood loss, operative indications, complications and postoperative visual analog pain scale scores were accrued. Patients were followed postoperatively for evidence of adverse events. *Results:* Between September 2007 and December 2010, 162 patients underwent LESS surgery of the upper urinary tract. The mean patient age was 54 years and the mean body mass index was 27 kg/m^2. Specifically, the following LESS procedures were performed: cryoablation (n=6), adrenalectomy (n=6), renal cyst decortication (n=7), partial nephrectomy (n=24), simple nephrectomy (n=20), radical nephrectomy (n=44), nephroureterectomy (n=6), donor nephrectomy (n=27), dismembered pyeloplasty (n=20), resection of a perirenal nodule (n=1) and nephropexy (n=1), accounting overall for 32 ablative, 107 extirpative and 21 reconstructive procedures. Our intra- and perioperative data were consistent with published data. the overall mean operative time was 170 min (177 min for renal extirpative procedures and 211 min for pyeloplasty), with a mean blood loss of 157 ml. The mean scar size was 3.8±1.1 cm. In 57 cases, an additional 2- or 5-mm port was added. Eight patients required conversion to standard laparoscopy. No major intraoperative complications occurred, but three cases with intraoperative bleeding required conversion to open surgery; the overall conversion rate was 6.7%. A postoperative complication rate of 11.7% was recorded (19 events), with Clavien I-II complications representing 89% and III-IV 11%. The pain scale score at discharge was 1.4/10. The mean length of stay was 4.3±1.7 days. *Conclusion:* The LESS surgery for the upper urinary tract is technically feasible for a variety of ablative and reconstructive applications. With proper patient selection, conversion and complication rates are low. Further clinical research is warranted to determine selection criteria, to fully prove the benefits of LESS surgery over conventional laparoscopy and to define the role of LESS in the field of minimally invasive surgery. Improvement in instrumentation and technology is likely to expand the role of LESS in minimally invasive urological surgery.

233
SINGLE-PORT ADRENALECTOMY: TECHNIQUE AND OUTCOMES

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Background: The objective of this study was to describe the surgical technique, to analyze the outcomes and to provide an overview of the current status of laparoendoscopic single-site (LESS) adrenalectomy using evidence-based analysis. *Materials and Methods:* A PubMed search was performed for all relevant urological literature regarding LESS and adrenal surgery. In addition, experience gained at the Authors' own institutions was considered. Laparoscopic adrenalectomy is considered the standard surgical procedure for patients with benign adrenal adenomas. LESS adrenal surgery can be effectively performed for all patients eligible for laparoscopic surgery and has the same indications as standard laparoscopy (1). LESS adrenal surgery can use both transperitoneal and retroperitoneal approaches. The most common position for access is the umbilicus, for esthetic benefits. Nevertheless, umbilical access can be extremely challenging due to the angle of approach, the long distance from the entry port to the target organ and difficult organ retraction. Different approaches, such as a subcostal or retroperitoneal approach, are emerging in adrenal LESS surgery to obviate these problems. The surgeon faces the same surgical steps of standard transperitoneal or retroperitoneoscopic adrenalectomy, but with the recognized ergonomic constraints and limitations related to LESS, mainly arising from instrument crushing and the lack of true triangulation. The use of articulating instruments can resolve the problems of triangulation but they are encumbered by difficult use, poor ergonomics and the lack of sufficient strength to provide robust retraction and dissection. Surgeons have adopted intraoperative strategies, such as cross- or one-handed manipulation. This may contribute to an increase in tissue re-grasping and suboptimal angle for a precise and safe dissection and can ultimately translate into prolonged operative time. Specific access devices allow multiple instruments to be passed through them at the same time. Numerous types of ports have been described for LESS adrenalectomy, such as TriPort, SILS, and OCTOport. Over the last two years, several groups have reported their early outcomes of LESS adrenalectomy. These series are all limited by a small sample size and mostly address the feasibility of the procedure. Jeong *et al*. (2) compared the outcomes of 9 LESS adrenalectomies with 17 conventional laparoscopic adrenalectomies. Intra- and perioperative complications were similar between the two groups. No differences were found in terms of mean operative time, blood loss and postoperative hospital stay. Postoperative pain was significantly lower in the LESS group. In a study comparing the outcomes of 19 LESS adrenalectomies with 38 retroperitoneoscopic adrenalectomies, the authors found no difference in terms of the estimated blood loss, postoperative hospital stay and postoperative complications. The LESS group had a longer median operative time, whereas the in-hospital use of analgesics was significantly less. Ishida *et al*. found no significant differences in operative time, estimated blood loss or resumption of oral intake between 10 consecutive transumbilical LESS adrenalectomies and 10 conventional laparoscopic adrenalectomies for benign adrenal tumors. In the LESS group only, time was needed to adjust the roticulator. After subtracting the time needed for adjustment, the operative time between two groups was more comparable. In the largest comparative matched-control study (3) (50 single-access retroperitoneoscopic adrenalectomies *vs*. traditional retroperitoneoscopic three-port approach), the operative time was longer for the LESS group. In the LESS group, pain medication was less frequently administered and the mean hospital stay was also shorter. Results and *Conclusion:* Despite promising early outcomes, the benefits of LESS are not obvious at present, with the only claimed advantage being cosmetic. Further clinical research studies, including those with a long-term follow-up, are warranted to determine selection criteria, to elucidate the cost effectiveness and the benefits over conventional laparoscopy and to define the oncologic safety of LESS adrenal surgery.

1 McCauley LR and Nguyen MM: Laparoscopic radical adrenalectomy for cancer: long-term outcomes. Curr Opin Urol *18(2)*: 134-138, 2008.
2 Jeong BC, Park YH, Han DH and Kim HH: Laparoendoscopic single-site and conventional laparoscopic adrenalectomy: a matched case–control study. J Endourol *23*: 1957-1960, 2009.
3 Walz MK, Groeben H and Alesina PF: Single-access retroperitoneoscopic adrenalectomy (SARA) *versus* conventional retroperitoneoscopic adrenalectomy (CORA): a case–control study. World J Surg *34(6)*: 1386-1390, 2010.

234
BIOPSY FOLLOW-UP IN PATIENTS WITH ISOLATED ATYPICAL SMALL ACINAR PROLIFERATION ON PROSTATE NEEDLE BIOPSY

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Aim: The aim of this retrospective study was to evaluate the incidence of prostate cancer with a medium term follow-up in patients with isolated atypical small acinar proliferation (ASAP) results on initial prostate biopsy. *Patients and Methods:* A total of 124 out of 140 ASAP only cases were selected. Selection criteria were: ASAP only in biopsy, central review of all slides, clinical follow-up of at least six months with at least one re-biopsy. Sixteen cases were excluded: ten cases were lost to follow-up and six declined re-biopsy. From 1998 to 2010, 140 patients with ASAP were selected from our prostate biopsy database, composed of 3360 unscreened cases who underwent transrectal ultrasound-guided biopsy. Clinical parameters (age, digital rectal examination findings, total and free PSA and prostate volume) and biopsy parameters (site, side and number of cores per biopsy set) were available for all cases. Indications for re-biopsy and follow-up strategies were discussed on an individual patient basis, depending on patient age, serum PSA values, imaging (transrectal ultrasound or MRI), digital rectal examination findings and urologist preference. Follow-up was considered from the initial biopsy with ASAP to the last follow-up visit or diagnosis of cancer. Surgical specimens were analyzed by a step-section protocol according to TNM system. Central review of all slides (including initial and follow-up biopsies) and surgical specimens was carried out by a single uropathologist. ASAP diagnosis was obtained by performing 6 to 24 random biopsies (median: 12 biopsies). The mean patient age was 64.8±7.4 (confidence interval (CI)=52-76) years; the mean PSA was 7.0 ±4.8 (CI=2-15.9) ng/ml and mean prostate volume was 53±21 cm^3. *Results:* Isolated ASAP was identified in 140/3360 cases (4.1%): 124 selected cases with isolated ASAP underwent at least one follow-up biopsy; 35, 11, 5, 2 and 1 patient had a second, third, fourth, fifth and sixth follow-up biopsy, respectively. Cancer was detected overall in 56/124 follow-up biopsies (45.2%): 40/56 (71%), 12/56 (21%), 3/56 (5.3%), 1/56 (1.7%) cancer cases were detected in the first, second, third and fourth follow-up biopsies, respectively. The mean follow-up was 32 (range=6-131, CI=6-80, median=24) months. A total of 21/124 patients (16.9%) had biopsy before ASAP diagnosis. All clinical parameters were associated with cancer, with statistical relevance. Cancer was treated with radical prostatectomy in 21 patients; re-biopsy of these cases revealed 10 insignificant cancer cases and 11 relevant cancer cases. Extracapsular disease or seminal vesicle invasion (5 patients) and/or positive margins (3 patients) were observed in 5/21 patients with small volume cancer located in the subcapsular anterior or apical gland, or the medial suburethral gland. *Conclusion:* In patients with isolated ASAP, the overall cancer detection rate was 45.2%. Nearly all cancer cases (98%) were detected with the third biopsy after 24months of follow-up. Cancer detected after initial ASAP is still curable; however 5 out of 21 cases (23%) submitted to surgery had adverse pathological features. Such cases, with small volume tumor and unusual cancer locations (anterior, subcapsular or suburethral), may be undersampled by standard biopsy approaches, increasing the risk of extracapsular extension, early seminal vesicle invasion and positive margins. We suggest that the first repeat biopsy using a saturation strategy could reduce the need for further biopsies; however a different biopsy strategy should be considered in order to detect a potential aggressive cancer located in unusual sites.

235

HUMAN PAPILLOMAVIRUS AND NON-MUSCLE INVASIVE UROTHELIAL BLADDER CANCER: POTENTIAL RELATIONSHIP FROM A PILOT STUDY

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Background: The relationship between urothelial bladder cancer and high-risk human papillomaviruses (HR-HPV) is still poorly understood, even though some studies have supposed a possible correlation. The aim of the present study was to assess the potential relationship between the presence of HR-HPV and non-muscle invasive urothelial bladder cancer (NMIBC). *Patients and Methods:* A total of 137 individuals (78 patients affected by NMIBC and 59 controls) were recruited in this prospective study. HR-HPV DNA was evaluated both in urine and tumor tissues. Data from patients were compared with data from healthy controls. The relationship between patients and controls, in terms of HR-HPV presence, was analyzed. Moreover, the relationship between all pathological data and HR-HPV presence in the patient group was investigated. *Results:* HR-HPV DNA in tissue was found in 27 out of 78 (34.6%) tumor samples and in 6 out of 59 (10.1%) specimens from TURBK, with a statistically significant difference (p=0.0009; df=1; chi square=10.98). HR-HPV DNA in urine was found in 36 out of 78 (46.1%) samples obtained from patients compared to only 8 out of 59 (13.5%) samples from controls (p<0.0001: df=1; chi square=16.37). A statistically significant difference in terms of HR-HPV frequency between high- and low-grade urothelial bladder cancer was found (p=0.032; RR=0.52, 95% CI=0.27-0.93; OR=0.34, 95% CI=0.13-0.90). *Conclusion:* In conclusion, this study highlighted the correlation between

urothelial bladder cancer and high-risk-type HPV infection, suggesting the potential etiopathogenetic role of HR-HPV in the development of urothelial bladder cancer.

236

GERM-CELL TESTICULAR TUMORS: FROM CALAMITY TO CURABLE DISEASE

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Background: The aim of this paper was to provide urologists, medical oncologists and radiotherapists detailed information on the evaluation of management of germ-cell testicular tumors from 1900 to 2010. *Materials and Methods:* The Testut and Jacob "Traite de Anatomie" published in 1904, the up-to-date version published by UTED in 1950, the review of 11300 PubMed papers from 1951 to 2010, and our personal experience since 1968 were used for a critical and objective evaluation of germ cell testicular tumors in the last century. *Results:* The first step in understanding the natural histology of testicular germ-cell tumors was the finding of lymph node metastasis to para-aortic lymph nodes, upward to cisterna chyli. Initial progress in the management of retroperitoneal metastases was due to radiotherapy and retroperitoneal lymph node dissection (RPLND) in combination with an understanding of the different natural sensitivity to radiotherapy of pure seminoma and non-seminoma, even if some northern European countries were reluctant to use RPLND for a long time. The second significant step was chemotherapy improvement in the 1970s, which led from the complicated VAB 1-5 to the easy and active vinblastine-bleomycin combination and to cisdiammino-dichloro-platinum from initial PVB, to improved PEB, followed by TIP and high-dose chemotherapy for salvage. *Discussion:* Sensitivity to chemotherapy is not the same for cases with different histology. It is excellent for pure seminoma and embryonal carcinoma; yolk-sac tumor is responsive but with late relapses; immature teratoma is partially responsive, mature teratoma is refractory because of poor mitosis. Consequently, residual masses after primary chemotherapy do need postchemotherapy radical surgery. *Conclusion:* Radical primary RPLND has nearly been abandoned for non-seminomatous tumors and it should not be used for seminoma because of lymphangeous dissemination in these tumors. Only major surgical indications such as postchemotherapy residual disease, late relapses and brain metastases will remain for surgeons, who will need great experience to perform such difficult surgeries.

238

PROGNOSTIC IMPACT OF SECOND-LOOK TURB IN PRIMARY T1G3 BLADDER CANCER

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Aim: To evaluate the usefulness of second-look transrectal ultrasound biopsy (TURB) and determine whether pathological outcomes of restaging TURB (ReTUR) have a prognostic impact on recurrence and progression of primary T1G3 bladder cancer. *Patients and Methods:* Patients affected by primary T1G3 transitional cell carcinoma of the bladder underwent ReTUR 4-6 weeks following the initial TURB. Patients with muscle-invasive disease underwent radical cystectomy; those with non-muscle-invasive residual tumor (NMIRT) and those with no residual tumor (NRT) received an intravesical BCG therapy. In order to evaluate the prognostic significance of ReTUR outcomes, we compared recurrence and progression rates, and recurrence- and progression-free survival in NMIRT patients and NRT patients at ReTUR. A cumulative survival curve was drawn using the Kaplan–Meier method (log-rank test). *Results:* From January 2002 to October 2010, 147 patients (mean age: 68.8±10.0 years, mean follow-up: 25.2±22.8 months) were enrolled in the study. At first TUR, 103 patients had a solitary tumor and 44 had multiple lesions; 3 patients showed concomitant carcinoma *in situ* (CIS). At ReTUR, residual cancer was detected in 65 (44.2%) patients. There was no significant statistical association between primitive tumor focalization and evidence of residual cancer at ReTUR: 43.7% (45/103) of patients with solitary tumor had residual cancer compared with 45.4% (20/44) of patients with multiple lesions (p=0.85). Of the patients with residual cancer at ReTUR, 27 (18.3%) presented identical stage and grade, while 24 (16.3%) were upstaged to T2. Histological outcomes of the other patients with residual cancer were: 4 patients with TaG1, 1 patient with TaG3, 2 patients with T1G1, 1 patient with T1G2, 2 patients with T1G2 associated with newly diagnosed CIS and 4 patients with CIS. There were significant differences in the follow-up period (33.6 *vs*. 22.8 months; p=0.008) and recurrence rate (25.6% *vs*. 41.5%; p=0.05) between NRT and NMIRT patients, respectively. Progression of the disease occurred in 13.4% and 14.6% of NRT and NMIRT patients, respectively (p>0.05). *Conclusion:* ReTUR of T1G3 TCC is a safe procedure that allows a considerable number of residual and understaged tumors to be identified (44.2% and 16.3%, respectively). However, the foremost finding in our study is the statistically significant difference in recurrence rate between patients with and without residual cancer on ReTUR.

240

RADIOTHERAPY AND CONCOMITANT DOCETAXEL IN HIGH-RISK PROSTATIC CANCER

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Background: High-risk prostate cancer patients (cT3, N1, PSA ≥20 ng/ml and/or Gleason score ≥8) have a 5-year biochemical failure rate after surgery or radiation of 50% or greater. Neoadjuvant, concomitant and adjuvant hormonotherapy (HT) are currently the only systemic treatments with escalation dose of radiation therapy. Because of the heterogeneity of prostate cancer cells and the desire to improve the outcome with radiotherapy (RT), weekly chemotherapy during RT in localized, high-risk prostate cancer is being explored. Docetaxel has demonstrated significant antitumor effect and impact on survival in hormone-refractory prostate cancer and a strong sensitization of tumor cells to radiation injury. *Patients and Methods:* From 2005 to 2010, 16 very high-risk patients were treated with high dose of RT and concomitant docetaxel. All patients had clinically (10/16) or pathologically (6/10) advanced disease. The median age was 65 (range: 56-65) years. Gleason score was: 8 in six patients, 9 in nine patients and 10 in one patient. The median PSA level at diagnosis was 15.45 (range: 2.5-71.3) ng/ml, while pre-RT PSA was 0.15 (range: 1.8-0.02) ng/ml. The median RT dose for all patients was 76 (range: 70-80) Gy, while for radical RT it was 80 (range: 76-80) Gy. Docetaxel was administered at a standard weekly dose (30 mg for patients with surface area <2 m^2 and 40 mg for patients with ≥2 m^2). The median cycle of chemotherapy was 7 (range: 2-8) months. All patients began HT before and during RT and continued the treatment for 2 years after RT. *Results:* At median follow-up of 36 (range: 8-60) months, only one patient, after 11 months, had recurrent disease (in the bones). The median PSA three months after the end of RT was 0.08 (range: 0.01-0.31) ng/ml, while at follow-up it was 0.1 (range: 0.01-0.4) ng/ml. With regard to toxicity: gastrointestinal grade I was reported in 12/16 patients and urological grade I was reported in 3/16 patients. One patient stopped chemotherapy infusion after two chemotherapy cycles because of systemic toxicity. *Conclusion:* These preliminary data confirmed the feasibility and the tolerability of weekly docetaxel in combination with RT in men at high risk of disease progression. No patient suffered performance status worsening during the scheduled treatment. At a median follow-up of 36 months, only 6% of patients experienced disease relapse and this was a remarkable result, considering that the patients were at very high risk. For such very high-risk patients, multimodal treatments combining HT, chemotherapy and RT will, possibly, be the treatment of choice in the future; however, at the moment, such treatments are only available in clinical trials and patients should be encouraged to participate in them.

242

TELOMERE LENGTH, TELOMERASE ACTIVITY AND TELOMERE-BINDING PROTEINS IN BLADDER CANCER: RELATIONSHIP WITH GRADING AND RECURRENCE

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Aim: To evaluate the relationship between telomere length (TL), telomerase activity and telomere-binding proteins (TBP) and grading and recurrence rate in patients with superficial bladder cancer (SBC). *Patients and Methods:* In 35 patients (tumor group; age: 63.9±10.6 years) with SBC, samples from the bladder tumor and disease-free bladder mucosa were obtained. In the control group of 23 healthy individuals (age: 65.3±10.1 years), samples from the bladder mucosa were collected. In all samples, TL was detected by Southern blot, while the expression of hTERT and of several TBP (TRF1, TRF2, PARP1 and TANK) were detected by Western blot. Histological examination was carried out on all samples. The patients underwent immuno- or chemotherapy, and for all of them, cytoscopy was performed at 3, 6 and 12 months. Statistical analysis of the results was performed using the parametric ANOVA test and the post-hoc Bonferroni test. Statistically significant results were considered when $p<0.05$. *Results:* The histological examination in the tumor group revealed 15 (42.9%) high-grade (HG) SBC and 20 (57.1%) low-grade (LG) SBC. The stage varied between Ta and T1. A statistically significant difference was found between the control and the tumor group (LG and HG) for all parameters tested (TL, hTERT, TRF1, TRF2, PARP1 and TANK). No statistically significant difference was found within the tumor group between LG and HG for TRF2. In the biopsies performed on the apparently healthy mucosa of the patients with LG and HG SBC, a statistically significant difference was observed for TBP and hTERT but not for TL. Compared with the control samples, the samples of healthy mucosa of patients with SBC were found to be significantly different for all parameters analyzed. At the cystoscopic follow-up, a total of 11 tumor recurrences were observed: 8 of them in the previous

HG (2 at 3 months, 4 at 6 months and 2 at 12 months) and 3 in the LG (2 at 6 months and 1 at 12 months). Regarding the correlation of the parameters tested and tumor recurrence/grading, the Pearson Chi-square test showed a tendency for statistical significance ($p<0.06$). A significant correlation was observed between TL, hTERT and PARP-1 values and the risk of recurrence (RR). No significant correlation was found between RR and TRF1, TRF2 and TANK. Only TRF1 and TRF2 assessed on samples of healthy mucosa of the tumor group were significantly associated with RR. *Discussion:* Compared with the control group, the SBC group showed a statistically significant reduction of TL (more evident in HG than in LG tumors), a reduced expression of TRF1 and TRF2, and an overexpression of hTERT, TANK and PARP-1. Significant correlations with SBC grading were demonstrated; HG tumors showed shorter telomeres, lower TRF1 and TRF2 values and higher hTERT, TANK and PARP-1 values compared to LG tumors. A statistically significant correlation between the RR and grading was also shown. There was an earlier appearance of recurrence in patients with shorter telomeres and higher hTERT and PARP-1 values. No statistically significant correlation was found between the earliness of recurrence and TBP expression. *Conclusion:* The data of this study allowed us to confirm that TL, and especially its shortening, plays a crucial role in the multistep process of malignant transformation of urothelial cells. This instability appears to be largely influenced by the dysfunction of some TBP and by the permissive role of telomerase reactivation, which, in turn, represents a key moment in cancer cell immortalization.

1 Fernandez-Gomez J, Escaf Barmadah S, Gosalbez D, Rodriguez-Faba O, Jalon A, Gonzalez R, Garcia Miralles T and Calas A: Telomere length on bladder washing samples from patients with bladder cancer correlates with tumor characteristics flow cytometry method for quantitative fluorescence *in situ* hybridization (flow-FISH technique). Eur Urol *48(3)*: 432-437, 2005.

2 McGrath M, Wong JY, Michaud D, Hunter DJ and De Vivo I: Telomere length, cigarette smoking, and bladder cancer risk in men and women. Cancer Epidemiol Biomarkers Prev *16(4)*: 815-819, 2007.

3 Leuenroth S, Riethdorf S, Erbersdobler A, Riethdorf L, Löning T, Huland H and Friedrich MG: Detection of human telomerase RNA in the tumour-surrounding mucosa of bladder carcinomas as a marker for premalignant transformation. BJU Int *96(4)*: 553-557, 2005.

243

RETROSPECTIVE EVALUATION OF THERAPY WITH KETOCONAZOLE IN HORMONE-REFRACTORY PROSTATE CANCER (HRPC)

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Aim: Ketoconazole, an antifungal drug which affects the synthesis of androgens and other steroids, has shown direct cytotoxic effects in prostate cancer. It is used to palliate disease symptoms and prolong the time to prostate-specific antigen (PSA) progression after standard hormonal therapy. This study described our ongoing experience with a ketoconazole-based treatment for hormone-refractory prostate cancer (HRPC). *Patients and Methods:* Of 25 patients enrolled in this study, 7 were in treatment, while 18 completed the treatment (stopped due to progression). The latter were evaluated in this analysis. All patients had HRCP and were previously treated with LH/RH agonist (plus two concomitant lines of peripheral anti-androgens) and afterwards with estramustine. When biochemical progression occurred after estramustine, treatment commenced with a schedule based on ketoconazole (600 mg/day), dutasteride, hydrocortisone, gastric protection with rabeprazol and liver protection with Monoselect Sylibum® (*Silybum marianum* L. Fruits ES, fitosomial, slow release, 210 mg standardized in sylimarin). Three patients did not take sylimarin and dutasteride. Every month, clinical examination, CBC, PSA and hepatic function were recorded to verify possible toxicity. PSA was used as a surrogate endpoint for response to treatment. *Results:* All patients regularly took ketoconazole. With regard to PSA response (change from baseline), decline was recorded in 9 patients (50%), stabilization in 3 (17%) and increase in 6 (33%). With regard to the duration of response (time to progression), the average was 5.3 (median: 4, range: 3-16) months. The average time to reach PSA nadir was 2.1 months. Among the three patients who did not take sylimarin, one had drug acute hepatitis, whereby the treatment was ended and another had an increase of transaminases (×2.5). Only one patient treated with sylimarin had an asymptomatic increase of transaminases (×2) and bilirubin (×2). *Conclusion:* A schedule, blocking multiple steps in androgen synthesis and activity, was used in this study, namely ketoconazole to inhibit CYP17A1 and dutasteride to inhibit type I and II 5alpha-reductases. Moreover, liver protection was used to increase tolerance to treatment. Sylimarin (especially, its component sylibinin) appeared to be suitable for this purpose, also considering its antineoplastic activity (it inhibits cell growth and induces apoptosis in human prostate cancer cells). In the literature, the response rate to ketoconazole ranges from 40% to 56%, with a median duration of response ranging from 3 to 6.75 months, sometimes further prolonged and, occasionally, lasting for years. Our data were in agreement with these values. Because prostate cancer usually has a long asymptomatic course, ketoconazole can be used to prolong the

symptom-free period and the time to chemotherapy. Therefore, low-dose ketoconazole may cover the gap in the continuum of treatment for patients with HRPC and for whom cytotoxic chemotherapy may have a significant impact on their quality of life. Low-dose ketoconazole may thus be considered an appropriate third-line agent in HRPC, after standard androgenic blockage and estramustine, causing a PSA decline, symptomatic relief and minimal toxicity. In agreement with literature reports, we conclude that ketoconazole (in our series, used in combination with dutasteride and sylimarin) may prolong time to PSA progression in patients with HRPC, with a good toxicity profile, low cost and ease of administration.

244
RADICAL LAPAROSCOPIC PROSTATECTOMY SERIES AT THE DEPARTMENT OF UROLOGY, UNIVERSITY OF BOLOGNA: ONCOLOGICAL AND FUNCTIONAL RESULTS

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Background: Prostate neoplasia is a disease with a high social impact. Surgery is the most common among radical treatments but has certain adverse effects. The purpose of this study was to evaluate the oncologic and functional outcomes of laparoscopic radical prostatectomies performed at the Department of Urology, University of Bologna. *Patients and Methods:* This study retrospectively analyzed a cohort of 297 patients who had undergone laparoscopic radical prostatectomy between 2002 and 2008. All data were collected from questionnaires and medical records completed during hospitalization, outpatient procedures and telephone interviews. The surgical technique adopted was, initially, a transperitoneal Montsouris approach and, subsequently, a modified technique including an extraperitoneal approach. *Results:* Biochemical relapse-free survival (BRFS) at 42 months was 90%. Patients with PSA<4 ng/ml had a BRFS in 5.88% of cases, while those with preoperative PSA>10 ng/ml, had a BRFS rate of 23%. At 42 months, the following functional results were observed: urinary continence (use of ≤1 minipad/day): 89%; sexual potency (satisfactory sexual intercourse with or without oral therapy): 83%; average intraoperative blood loss: 200 ml (need for transfusion: 3%); average duration of surgery: 125 (range: 60-190) minutes; permanence of the urinary catheter: 11 days; average time of hospital stay: 5 days; postoperative lymphocele: 1%; average postoperative use of analgesics: 25 mg equivalent morphine. *Discussion and Conclusion:* Laparoscopic radical prostatectomy outcomes are similar to those of open surgery, particularly regarding the onset of biochemical relapse and disease progression. Moreover, regarding the functional results, the technique has also proven its effectiveness, both in terms of continence and potency (when a nerve-sparing approach is taken). Laparoscopic radical prostatectomy should be proposed as a first-choice surgical treatment in centers where laparoscopy is performed routinely.

1 Guillonneau B, el-Fettouh H, Baumert H, Cathelineau X, Doublet JD, Fromont G *et al*: Laparoscopic radical prostatectomy: oncological evaluation after 1000 cases at Montsouris Institute. J Urol *169(4)*: 1261-1266, 2003.
2 Lepor H: A review of surgical techniques for radical prostatectomy. Rev Urol *7(suppl 2)*: S11-S17, 2005.
3 Riskin DJ, Longaker MT, Gertner M and Krummel TM: Innovation in surgery: a historical perspective. Ann Surg *244(5)*: 2006.

245
REDUCING THE NUMBER OF PROSTATE BIOPSY CORES USING A REAL-TIME TOOL

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Background: Prostate cancer (PCa) is one of the most frequent neoplasias, with almost 30,000 new cases/year in Italy and 338000 new cases/year in Europe (EU-27). PCa can be accurately detected only by prostate biopsy (PBx), while is not clearly detectable using transrectal ultrasound (TRUS) and other diagnostic methods such as measurement of PSA level. For this reason, guidelines for PCa diagnosis suggest random tissue sampling (at least 8-12 cores, depending on gland volume) be performed when PCa suspicions arise from standard diagnostic methods. The PBx sampling procedure is TRUS-guided and roughly costs 20€/core, including the cost of the subsequent histological analysis. Even though accuracy grows with the number of PBx cores taken, the cost, patient discomfort and the adverse-event probability grow as well. It is thus desirable to reduce the number of PBx cores without having a negative impact on diagnostic accuracy. *Patients and Methods:* This work describes the follow-up of a retrospective study aiming to evaluate the feasibility of a reduction in the number of PBx cores through the application of a custom-built real-time computer-aided biopsy (rtCAB) tool. The technique

enhances TRUS video streams with a live false-color overlay image. Relative organ-to-transducer movements are tracked and compensated in order to provide a stable classification map, which is useful to guide the physician during tissue sampling. The recorded signal is split into regions of interest (ROIs) and statistical parameters are estimated with an optimized algorithm. Finally, a nonlinear supervised classification model discriminates between PCa risk levels and the results are superimposed on the TRUS image. The monocentric, single-operator prostate gland adenocarcinoma database built to train rtCAB was expanded to enlist 129 patients (50 of them with pathological disease) for a total of 1303 PBx cores and 26060 ROIs. For each core, several data were collected, in particular the ultrasound image intensity and the histological outcome, making it possible to estimate the correspondence between the pathological state of the tissue and its ultrasound signature. *Results:* The system was optimized for reducing the number of false positives while preserving an acceptable number of false negatives. Motion tracking improved the stability of the classification between frames. In addition, the extended database allowed us to better estimate the positive predictive value of the classical double-sextant PBx (23.6%) and the rtCAB method (38.9%). *Discussion and Conclusion:* Thanks to its real-time image processing capabilities, the proposed method may increase the detection rate and may be helpful in finding regions sufficiently representing the cancer. As a consequence, if used to guide biopsies, the method may provide a significant (>30%) reduction in the number of biopsy cores required to obtain the same detection rate achieved by the standard double sextant biopsy, with reduced healthcare costs. The reduction in the number of biopsy cores may also reduce the probability for post-mapping complications and, even more importantly, improve patient compliance.

1 Ferlaya J, Parkinb DM and Steliarova-Fouche E: Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer *46(4)*: 765-781, 2010.
2 Testoni N, Maggio S, Galluzzo F, De Marchi L and Speciale N: A diagnostic tool for reducing unnecessary prostate biopsy cores. Proc 2010 Int Ultrasonic Symp, San Diego, CA, USA, 2010.
3 Bertaccini A, Fandella A, Prayer-Galetti T, Scattoni V, Galosi AB, Ficarra V, Trombetta C, Gion M and Martorana G: Systematic development of clinical practice guidelines for prostate biopsies: a 3-year Italian project. Anticancer Res *27(1B)*: 659-666, 2007.

246

ACTIVE SURVEILLANCE IN PATIENTS WITH LOW-RISK PROSTATE CANCER: PRIAS EXPERIENCE AT THE NATIONAL CANCER INSTITUTE (MILAN)

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Background: Since 2005, we have been proposing active surveillance (AS) as an alternative to radical therapies in low-risk prostate cancer (PCa) patients. The Prostate Cancer Research International: Active Surveillance (PRIAS) protocol was embraced in November 2007. Here, we present results on the first 150 patients who were enrolled in PRIAS up to February 2011. *Patients and Methods:* PRIAS entry criteria were as follows: informed consent, initial prostate-specific antigen (iPSA) ≤10 ng/ml, clinical stage ≤T2, Gleason pattern score (GPS) ≤3+3, maximum 2 positive biopsy cores and PSA density <0.2 ng/ml/cc. Follow-up was scheduled with PSA measurement every 3 months, digital rectal examination (DRE) every 6 months, re-biopsy after 1 year of AS. When PSA doubling time (PSADT) was between 3 and 10 years, a yearly repeated biopsy was scheduled. Whenever during the follow-up the PSADT was less than 3 years, the clinical stage was >T2 or the repeat biopsies showed more than two positive cores or a GPS >3+3, the protocol advised a change to active treatment. The quality of life (QoL) of patients participating in the PRIAS protocol was also evaluated. QoL data were collected through two questionnaires: the mini mental adjustment to cancer (MINI-Mac) and the functional assessment of chronic illness therapy-prostate (FACT-P). QoL evaluation was planned for a 5-year period, through 8 screening phases. We present a preliminary evaluation of QoL evolution between AS enrolment and 15 months after PRIAS acceptance. *Results:* A total of 150 patients were enrolled in PRIAS (February 2011). At a median follow-up of 18 (range: 3.2-44.6) months, 119/150 patients remained under observation. Three patients dropped out due to comorbidities, one due to personal choice (anxiety), two due to lack of compliance with the PRIAS protocol and one due to non-PCa-related death. A total of 24/150 (16%) patients dropped out because of cancer progression: eight due to PSADT, three due to upgrading (first re-biopsy), five due to disease upsizing (four at first and one at second re-biopsy) and eight due to both upsizing and upgrading (six at first and two at second re-biopsy). The actuarial treatment-free survival was 86.3% and 72.9% at 13 and 25 months, respectively (all causes). When considering biopsy-related drop-out, the respective rates were 90.6% and 86.8% (25 months), while they were

99.1% and 88.4% when considering PSA-related drop-out. To date, no unfavorable outcome has been observed. The following parameters were not significantly associated with PCa progression: iPSA, age, stage, GPS, number of positive cores at biopsy, maximum core length containing cancer, PSADT and DRE. The QoL investigation showed an improvement with time in coping with the disease. Specifically, the percentage of patients experiencing avoidance was reduced from 30% (at AS enrollment) to 18.2% (at 15 months after PRIAS acceptance); anxious preoccupation and helplessness/hopelessness were reduced from 11.5% and 3.4% (at AS enrollment) to 2.3% and 0% (at 15 months), respectively. Physical, emotional, social and functional well-being was high and showed no relevant changes during the investigated screening period. *Conclusion:* AS is feasible in selected men with early prostate cancer. Ongoing studies are trying to optimize AS protocols in order to become efficient at detecting patients with disease progression. The one-year repeat biopsy is an important examination which can be used as a diagnostic clarification point. Further follow-up is necessary to detect the effect of deferred treatment on disease control. Despite the limited number of patients, the results of the QoL study showed that exhaustive information, good communication between patients and clinicians, and on-demand psychological support can help patients cope with anxiety and uncertainty related to AS acceptance.

247

PROSTATE CANCER UNITS IN EUROPE: FROM UTOPIA TO DREAM TO REALITY?

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The multidisciplinary approach is particularly important in prostate cancer (PC), where, according to the clinical state of disease, there are multiple treatment options, as well as observational strategies, to choose from. Multidisciplinary, multi-professional management facilitates administration of high-quality medical procedures, collaboration among dedicated specialists, and tailoring of treatment and observational strategies to the patients' needs. Access to specialist counseling, supportive care and rehabilitation are also fundamental. Prostate cancer units (PCU) are places where men with PC can be cared for by specialists working within a multidisciplinary team and these appear to be the most suitable structures for the care of patients at all stages, from newly diagnosed to advanced disease, including preventing and managing disease-induced or treatment-induced complications, whether physical, emotional or psychological. Following the German PC model, the British example with urological malignancies and the example of European breast cancer units, general recommendations and mandatory requirements for a PCU were identified. General recommendations include: European certification process based on the fulfillment of mandatory requirements, a focus on research and clinical trials, teaching for junior staff and students, and management of a PCU budget. Mandatory requirements include: a critical mass of a minimum size to serve a population of 300,000 people that is capable of attracting ≥100 newly diagnosed PC patients (at all ages and stages) who are willing to accept all treatment and observational strategy protocols conducted under the direction of the Unit's Multidisciplinary team; documentation/audit recording of data on diagnosis, pathology, radical, adjuvant and palliative treatments, observational strategies, clinical outcomes, follow-up, side-effects audit meeting once a year with written protocols for diagnosis and management of PC at all stages. There should be a core team whose members (PCU Clinical Director, ≥1 uropathologist, ≥2 urologists, ≥2 radiation oncologists, ≥1 medical oncologist, at least 1 nurse specialist in prostate care, ≥1 dedicated data manager, 1 professional responsible for monitoring the compilation of patient data and scheduling evaluations) all have specialist training in PC, spend an agreed amount of time working in PC, attend multidisciplinary meetings (MDM) for case management and audit purposes; associated services and non-core personnel are those the PCU should have access to: ≥1 radiologist, ≥1 nominated medical physicist, ≥2 radiation therapy technologists, ≥1 physiotherapist, ≥1 palliative care specialist, 1 clinical psychologist with experience in seeing

prostate patients, 1 sexologist or andrologist, 1 geriatrician and ≥1 clinical trial coordinator. All core team members should attend weekly MDM to discuss at least 90% of the cases referred to PCU. Decisions should be documented in patient charts. The PCU should offer all treatment options (radical prostatectomy, external radiotherapy, brachytherapy, observational strategies, hormonal therapy, chemotherapy, novel therapeutics, psychological support and palliative care) and ensure the patient's right to information and self-determination. Patients should be provided with a detailed written record of the treatment and follow-up plan. PC patients should have access to a weekly multidisciplinary clinic with a urologist, a radiation oncologist and a medical oncologist, synchronously or in rapid succession. If possible, a psychologist should participate. PC patients should be offered follow-up supervised by one core member responsible for the treatment. Patients with advanced, recurrent or metastatic PC should be offered clinic access every two weeks. The PCU should possess or have access to all the technological equipment for imaging, radiotherapy, pathology. Establishing a PCU will require the re-organization of current PC services, workflow and attitudes but it should have a favorable economic impact and avoid multiple consultations and inappropriate treatments. Certification of a PCU should be considered the necessary step forward to ensure optimal treatment and care of men with PC.

248
MULTIDISCIPLINARY CLINIC FOR PROSTATE CANCER AT ISTITUTO NAZIONALE TUMORI, MILAN: 6 YEARS' EXPERIENCE

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Background: The Istituto Nazionale Tumori started the multidisciplinary (MD) translational prostate program in 2004, re-arranging and activating experimental and clinical research on prostate cancer (PC) within a disease-focused frame. Priorities in clinical activity were sharing diagnostic, therapeutic, and observational guidelines as a working methodology to manage PC patients and setting up a MD clinic for PC patients. *Patients and Methods:* After determining institutional guidelines, the following MD clinics started in March 2005: (i) a clinic for newly diagnosed, untreated patients and for patients in all states of disease who seek a second opinion: a urologist, radiation oncologist, medical oncologist and psychologist simultaneously meet ten patients once a week; after recording the anamnesis, digital rectal examination and evaluating co-morbidities, possible therapeutic, observational, and follow-up strategies or research protocols are proposed if the case is univocally interpreted, if the case is complex and no shared decision is reached, it is referred to the multidisciplinary case discussion; patients may request psychological support for the decision-making and individual, couple, family or group counseling, with supportive, rehabilitation and palliative care given on demand; (ii) a follow-up clinic for patients on active surveillance (AS) and watchful waiting: a urologist and radiation oncologist meet eight and 6 patients once a week, respectively; (iii) a case discussion (once a week, CME activity): specialists working in the MD and the prostate program (urologists, radiation oncologists, medical oncologists, psychologists, uropathologists, radiologists, experimental researchers, and prostate program administrative personnel) discuss cases seen multidisciplinarily plus complex cases examined monodisciplinarily, share decisions taken in the clinic, tailor strategies to individual patients whenever possible, include patients in trials and check adherence to institutional guidelines and quality assurance. *Results:* From March 2005 to December 2010, 2150 MD clinics were run. The disease distribution was analyzed from 2006, when an electronic chart was introduced. While the number of patients with high-risk and metastatic PC decreased, the number of patients with low-risk PC increased constantly, with a peak in 2009 (61%). This is probably due to the anticipation of diagnosis and to the fact our Institute is one of the few Italian centers where AS is routinely proposed within a research protocol (PRIAS study). Considering the distribution of therapies in a low-risk group population, while in 2006, only 44% of low-risk patients accepted AS, this increased to 81% in 2009. This is probably due to the change in patients' attitudes towards observational strategy and the credit of our Institute as a reference center for AS. Considering the small number of patients with metastatic, advanced and recurrent disease (5.5%) and of no shows, a nurse coordinator was introduced in September 2010 to collect basic information on the cases to be seen and reorganize the clinic lists according to the state of disease, thus optimizing human resources and having the medical oncologist on call for selected patients. A total of 98.4%

patients seen multidisciplinarily were discussed in the case discussion meetings. It was possible to check adherence to guidelines, evaluate the quality of the multidisciplinary team's activity and modify the work-flow to adapt to changing situations. Treatment plans prescribed by physicians working outside our institute were changed for 236/2150 patients (11%). Indications formulated in the clinics were changed in the case discussion for 129/2150 patients (6%) after checking adherence to our institutional guidelines. *Conclusion:* Our MD clinic is proving efficient in the management of PC patients. The synchronous presence of different specialists enables all possible therapeutic and observational options to be proposed. Case discussion meetings allow agreement on the strategies offered to patients, multidisciplinary management of complex cases, performance of quality checks, stimulation of interdisciplinary working and facilitation of team building.

251

BRAIN METASTASES INCIDENCE IN PATIENTS RECEIVING TARGET THERAPIES FOR ADVANCED RENAL CELL CARCINOMA

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Background: Treatment of metastatic renal cell carcinoma has changed significantly in recent years thanks to targeted therapies. In the literature, brain metastases are reported to occur in 2-17% of patients with metastatic renal cell carcinoma. The aim of this study was to analyze the incidence and characteristics of patients with brain metastases from RCC treated with targeted therapy. *Patients and Methods:* From March 2007 to October 2010, 43 consecutive patients affected by metastatic renal cell carcinoma without brain metastasis were analyzed. Patient characteristics were: 35 males (81.3%) and 8 females (18.7%), with a median age of 54 (range 35-76) years, KPS 100 (range 60-100). A clear renal cell histology was observed in 41 patients (95.3%) and other histology in 2 patients (4.7%). Thirty-eight patients (88.3%) underwent surgery and 31 patients (72%) patients were treated as first-line, and 12 (28%) were pre-treated. *Results:* With a median follow-up of 32 (range 1-43) months, 6 patients (13.9%) progressed with brain metastases. Median time of treatment was 10 (range 5-27) months. The median age was 55 (range 46-70) years, KPS 100 (range 60-100), clear renal cell histology was observed in 5 patients (83.3%), other histology in 1 patient (16.7%). Of this group, two patients (33.3%) experienced relapse in an extra cerebral site. No difference was observed in the two groups as regard site of metastasis and no patients changed ongoing treatment because of onset of brain metastasis. In 3 patients (50%), brain metastases were symptomatic. Three patients (50%) underwent gamma-knife treatment, one patient (16.7%) external radiotherapy and two patients (33.3%) anti-edema therapy. *Conclusion:* The occurrence of brain metastases in the course of treatment with targeted therapy is a significant event. The assessment of these patients requires systematic evaluation of the brain with CT scans and specific local treatments. This aspect should be investigated with a broadening of the series through a multicenter study.

252

VARIANTS OF ADRENOCORTICAL CARCINOMA: MORPHOLOGICAL, PHENOTYPICAL AND MOLECULAR FINDINGS AND CLINICO-PATHOLOGICAL CORRELATIONS

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Adrenocortical carcinoma (ACC) diagnostic criteria (>3/9 Weiss parameters) do not apply well with special variants, including oncocytic (OACC) and myxoid tumors. A review of 194 ACCs showed that the oncocytic variant (20 patients: 14 pure OACCs with oncocytes >90% of the tumor; 6 mixed, with clear cell component ranging from 10 to 50%) can hardly be classified using the Weiss system since cytoplasmic eosinophilia, atypia and diffuse growth are intrinsically present (thus requiring a higher diagnostic threshold). The mitochondrial DNA profile of OACCs was analyzed by means of real-time PCR and FISH, detecting in 5/20 cases the so-called '4977 bp common deletion', which was previously identified in many oncocytic tumors of other organs (*e.g.* kidney, thyroid and salivary gland). Myxoid tumors (17 patients: 14 pure myxoid, of which 1 borderline and 13 malignant tumors; 3 with focal myxoid changes in otherwise conventional ACCs) are characterized by cords or nests of medium-size scanty atypical cells in a myxoid background, with a peculiar neurofilament expression. The Weiss system might be inadequate to reliably detect malignancy in myxoid ACCs because a few criteria are hard to assess or are poorly represented in myxoid areas (such as small vessel invasion, diffuse growth pattern and nuclear atypia). The prognosis of patients with these ACC variants seems more comparable to conventional ACCs regarding the myxoid, and more favorable as compared to pure oncocytic ACCs, whereas this does not hold true for ACCs having an oncocytic component.

253

AGE IS PREDICTIVE OF IMMEDIATE URINARY CONTINENCE AFTER RETROPUBIC RADICAL PROSTATECTOMY

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Background and Aim: Long-term continence after open radical retropubic prostatectomy (RRP) is linked to the surgical technique, surgical volume and patient age. The immediate postoperative continence (IPC), which is one of the main outcomes for patient satisfaction, is not well investigated. The aim of this study was to evaluate the correlating factors of IPC after catheter removal. *Patients and Methods:* Between July 2002 and November 2009, 373 patients were treated for localized prostate cancer. Among them, 130 patients underwent brachytherapy and 243 patients underwent RRP. The follow-up of the RRP group was limited to 202 patients, prospectively evaluated, who resided in the local geographic region. RRP was performed by a single surgeon (MM) following Walsh's procedure and preserving the urinary sphincter. On the fifth postoperative day, the catheter was removed after filling the bladder with 100 ml of saline to test the immediate continence. Continence was considered to be preserved if the patient was dry. A multivariate analysis was performed to evaluate the association between IPC and preoperative, operative, clinical, hormonal, and pathological variables. The long-term continence was also evaluated at one, three, six and twelve months according to Catalona's criteria. The sexual potency was evaluated at one year postoperatively. *Results:* The mean patient age was 63.8 (range 49-75) years, 52.5% of the patients had a Gleason score ≤6, 80.7% of patients had T1c stage disease and 82.7% of patients had PSA ≤10 ng/ml. The IPC rate at catheter removal was 69%. The logistic multivariate regression analysis showed statistical association between IPC and age less than 65 years (p=0.02) and sexual potency (p=0.02). No statistical association was shown for others factors, such as preoperative (biopsy Gleason score, clinical stage, PSA, D'Amico risk group, and prostate weight), operative (nerve sparing procedure), hormonal (testosterone, LH, FSH, and fT3 levels), pathological (surgical margins, extracapsular extension, pT, and Gleason score) variables. At 12-month follow-up, 85% of patients were completely dry, 12.5% with only occasional drops of urine and 2.5% were incontinent. *Conclusion:* Age is a factor correlating to IPC at catheter removal after RRP. Patients less than 65 years old have a 2.6-fold increased likelihood of being continent on the fifth postoperative day, and IPC patients are 3.6-fold more likely to be sexually potent within 12 months.

254

EFFICACY OF USE OF CRANBERRY (GISOMA) IN PATIENTS WITH SUPERFICIAL BLADDER CANCER

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Aim: This work aimed at investigating the efficacy of cranberry on prevention of urinary tract infection in patients with intravesical instillation of chemo-/immunotherapeutic agents. *Patients and Methods:* We evaluated 82 patients with papillary tumor from October 2009 to February 2011. *Results:* According to the treatment protocols, 38 patients (28 male and 10 female) with non-invasive papillary carcinoma (T_a/TIS) or minimally invasive tumor (T_1) were treated with intravesical chemotherapy induction, weekly schedule with mitomycin (eight weeks), or gemcitabine (six weeks) in tumor recurrence or BCG-refractory disease. A total of 44 patients (37 male and 7 female), with high-grade superficial lesion or multifocal lesion were treated with BCG (six weeks). After weekly therapy and negative cystoscopy, patients continued with monthly maintenance therapy (12 months with BCG, or schedule of one weekly dose for three weeks every six months for two or three years, and eight months with mitomycin and 11 months with gemcitabine). Repeat cystoscopy was performed after four-monthly therapy and urinary cytological examination. Urine culture after TUR and cystoscopy, and urine test were carried out before inserting a catheter. During antibiotic therapy (Floxacin, previous day and two days after intravesical instillation), patients received cranberry: two times a day for three days for weekly therapy; for monthly therapy two times a day for seven days, then one time a day for seven days. At the time of writing, 76 patients had completed the treatment without any evidence of urinary infection. Six patients stopped treatment; two patients died of other comorbidities: three patients due to systemic disease progression, one patient due to infection during instillation with BCG. We retrospectively evaluated 198 patients with papillary tumor, from January 2007 to September 2009. Out of 80 patients treated with intravesical immunotherapy with BCG, urinary infection with symptoms of frequency, urgency and dysuria (especially during weekly therapy) was observed in 37 cases and therefore the treatment was postponed. After the first few months' therapies, 17 patients (age ≥65 years) stopped the treatment due to infection. Of 112 patients with intravesical instillation with mitomycin, it was observed that treatment was postponed due to infection in 53 patients. *Conclusion:* Treatment with cranberry appears to be effective in the prevention of urinary tract infection. At the time of writing, 25 new patients continue to receive monthly or weekly cranberry with intravesical instillation.

255

ACCURACY OF ENDORECTAL MRI AND DYNAMIC CONTRAST-ENHANCED MRI IN THE PREOPERATIVE LOCAL STAGING OF PROSTATE CANCER: A PROSPECTIVE STUDY OF 46 PATIENTS

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Aim: To assess the accuracy of endorectal magnetic resonance imaging (MRI) at 1.5 Tesla in association with dynamic contrast-enhanced MRI (DCE-MRI) in the pre-operative local staging of prostate cancer (PCa). *Patients and Methods:* After at least six weeks from prostate biopsy, 46 consecutive patients with biopsy-proven intermediate- or high-risk PCa were prospectively evaluated with MRI in association with DCE-MRI within two weeks before radical prostatectomy (RP). Conventional clinical staging methods included digital rectal examination (DRE) and transrectal ultrasound (TRUS). Assessment of radiological images and RP specimens were performed dividing the prostate into 14 regions: 12 prostatic locations (base, intermediate and apex, on the left/right side and in the anterior/posterior position) and two seminal vesicle locations. T1- and T2-weighted MRI and DCE-MRI were interpreted contemporarily by two expert radiologists (in agreement) who scored the likelihood of extracapsular extension (ECE) and seminal vesicle invasion (SVI) on a 5-point scale in each of the 14 regions. We assessed sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy with ROC analysis of MRI, DCE-MRI and conventional staging methods using pathological findings as reference standard. *Results:* The mean age was 65.7 years, the mean PSA was 7.9 ng/ml, the mean prostate volume was 65.7 ml and the mean pathological Gleason score was 7.45. At histopathology, 11/46 (24%) patients had pathological extraprostatic involvement: 5 patients with unilateral ECE, 2 patients with bilateral ECE and 2 patients with unilateral SVI (with concomitant bilateral ECE) and 2 patients with bilateral SVI (with concomitant bilateral ECE). Overall, 552 prostatic regions and 92 seminal vesicle regions were evaluated. Table I shows results of diagnostic accuracy of the different staging methods. DCE-MRI did not improve the diagnostic accuracy of T1- and T2-weighted MRI in the evaluation of ECE or SVI. *Conclusion:* Endorectal T1- and T2-weighted MRI adds important information regarding the preoperative local staging of PCa. With regard to individual patient analysis, T1- and T2-weighted MRI provides higher values for diagnostic accuracy, in particular, for the evaluation of ECE. The region-by-region analysis shows a high negative predictive value, which can be helpful before choosing a nerve-sparing approach. DCE-MRI does not improve the diagnostic accuracy of MRI in the local staging of PCa.

256

PROGNOSTIC SIGNIFICANCE OF POSITIVE SURGICAL MARGINS AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER

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Aim: We evaluated the impact of positive surgical margins (PSMs) on biochemical relapse (BCR)-free survival after radical prostatectomy. *Patients and Methods:* We evaluated 837 consecutive patients submitted to RP between October 1995 and June 2009. Exclusion criteria were: (i) a follow-up period <12 months, (ii) neoadjuvant or adjuvant therapy,

Table I.

	Per patient analysis				Per region analysis			
	Prostate (n=46)		Seminal vesicles (n=46)		Prostate (n=552)		Seminal vesicles (n=92)	
	DRE/TRUS	MRI	DRE/TRUS	MRI	DRE/TRUS	MRI	DRE/TRUS	MRI
Sensitivity	27.3	81.8	0	25.0	5.0	36.4	2.0	20.0
Specificity	100	91.4	100	100	96.7	98.1	94.7	98.9
PPV	100	75.0	91.3	100	7.7	44.4	4.7	50.0
NPV	81.4	94.1	-	93.3	94.9	97.4	93.9	95.6
AUC	0.701	0.894	0.661	0.607	0.509	0.657	0.500	0.586

(iii) incomplete follow-up data, (iv) pT0 or pN1 disease, and (v) incomplete pathological details. BCR was defined as a PSA level higher than 0.2 ng/ml. *Results:* The median follow-up was 54.0 (range 12-159) months. A total of 614 patients (73.4%) had negative surgical margins (R0), while 146 (17.4%) had a single PSM and 77 (9.2%) had a multiple PSMs (R1). Among the 837 patients, only c-stage, p-stage and p-Gs had an independent significant relationship with the BCR at multivariate analysis; after stage stratification, the margin status was a significant predictor of BCR only in pT2 patients (Table I). In pT3b patients, there were no significant factors correlated with BCR. Figure 1 shows the Kaplan–Meier curve for BCR-free survival in the 837 patients stratified into five groups according to margin status and p-stage ($p<0.001$). At Cox analysis, pT3b patients (group 5) had a higher BCR rate than the other groups and pT2 patients with R0 (group 1) had a lower BCR rate than the other groups; there were no significant differences in the BCR rate among groups 2 to 4. *Conclusion:* In our series, the presence of PSMs influences the BCR rate only in patients with pT2 disease. Moreover, in men with no seminal vesicle invasion but a PSM and/or extracapsular extension, the presence of both pathological features did not portend a worse prognosis than the presence of either one alone.

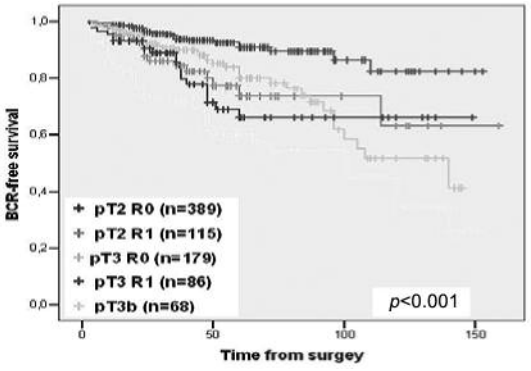

Figure 1.

Table I.

	Reference group			
	Group 1	Group 2	Group 3	Group 4
Group 2				
HR	2.877 (1.592-5.202)	/	/	/
P-Value	<0.001			
Group 3				
HR	2.615 (1.578-4.334)	0.909 (0.520-1.587)	/	/
P-Value	<0.001	0.737		
Group 4				
HR	3.220 (1.797-5.772)	1.119 (0.597-2.099)	1.231 (0.713-2.128)	/
P-Value	<0.001	0.726	0.456	
Group 5				
HR	5.745 (3.411-9.676)	1.996 (1.126-3.539)	2.197(1.362-3.543)	1.784 (1.019-3.124)
P-Value	<0.001	0.018	<0.001	0.043

257

THE EXTENT OF PELVIC LYMPH-NODE DISSECTION CORRELATES WITH THE BIOCHEMICAL RECURRENCE RATE IN PATIENTS WITH INTERMEDIATE- AND HIGH-RISK PROSTATE CANCER

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Aim: To assess the impact of pelvic lymph-node dissection (PLND) and the number of lymph nodes (LN) retrieved during radical prostatectomy (RP) on biochemical relapse (BCR) in pNX/0/1 patients according to the clinical risk of lymph-node invasion (LNI). *Patients and Methods:* We evaluated 872 consecutive patients (pT2-4 NX/0/1) who underwent RP between October 1995 and June 2009. Exclusion criteria were: (i) a follow-up period <12 months, (ii) neoadjuvant or adjuvant therapy, (iii) incomplete follow-up data, (iv) pT0, and (v) incomplete clinical and pathological data. BCR was defined as prostate-specific antigen (PSA) >0.2 ng/ml. The patients were divided into three groups according to the clinical risk of LNI: low-risk group (cT1a-T2a and cGs ≤6 and PSA <10 ng/ml), intermediate-risk group (cT2b-T2c or cGs =7 or PSA=10-19.9 ng/ml) and high-risk group (cT3 or cGs= 8-10 or PSA >20 ng/ml). The patients were also divided into two groups according to the number of LNs removed: group 1, with 0 to 9 LNs removed, and group 2 with ≥10 LNs removed. The primary endpoint was BCR-free survival. *Results:* The mean follow-up was 55.8 months. Overall, 305 patients (35%) had pNx tumor and 567 patients (65.0%) pN0/1. In the 567 patients who underwent PLND, the mean number of LNs dissected was 10.9; 49 of these patients (8.6%) had pN1. In the 402 patients at low-risk of LNI, the number of LNs removed was not a significant predictor of BCR at the univariate analysis. On the contrary, in the 470 patients at intermediate- and high-risk of LNI, patients in group 2 (≥10 LNs removed) had a significantly lower BCR-free survival at the univariate and multivariate analyses ($p=0.021$) (Figure 1). In the 33 pN1 patients with ≤2 LN metastasis, patients in group 2 had a significantly lower BCR-free survival at the univariate and multivariate analysis ($p=0.006$) (Figure 2). *Conclusion:* In our study population, a more extensive PLND positively affected BCR-free survival, regardless of the nodal status in patients with intermediate- and high-risk prostate cancer.

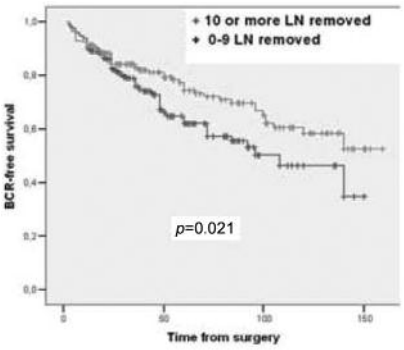

Figure 1 (Abstract 257).

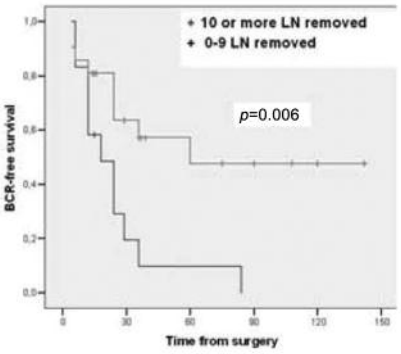

Figure 2 (Abstract 257).

258

THE IMPACT OF THE EXTENT OF LYMPH-NODE DISSECTION DURING RADICAL CYSTECTOMY FOR BLADDER CANCER ON CANCER-SPECIFIC SURVIVAL

Riccardo Schiavina, Alessandro Baccos, Hussam Dababhne, Ziv Zukerman, Cosimo Bizzarri, Daniele Romagnoli, Alessandro Bertaccini, Fabio Manferrari, Eugenio Brunocilla, Marco Garofalo and Giuseppe Martorana

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Background: We evaluated the associations between the number of lymph nodes retrieved during radical cystectomy (RC) for bladder cancer (BC) and the cancer-specific survival (CSS). *Patients and Methods:* We evaluated 229 consecutive patients who had undergone RC for BC between November 1995 and October 2009 with complete follow-up data. Exclusion criteria were: (i) neoadjuvant or adjuvant therapy, (ii) palliative RC, (iii) pNx, and (iv) incomplete clinical and pathological data. A total of 167 patients were evaluated, divided into two LN groups according to the number of LNs retrieved: group 1 (n=56, 33%) had 1 to 12 LNs removed, while group 2 (n=111, 67%) had ≥13 LNs removed. The primary endpoint was the evaluation of CSS. *Results:* The mean follow-up was 52.6 (range: 1-172) months. Overall, the CSS rate was 67.1% and 57.7% at five and ten years, respectively. Cancer-specific death was observed for 51 (30.5%) patients. The mean number of LNs removed was 16.5 (range: 1-43); in pN+ patients, the mean number of positive LNs was 5.6 (range: 1-19). Figure 1 shows the Kaplan–Meier curves for CSS for the two groups of patients, divided according to the number of LNs removed. Table I shows the univariate and multivariate Cox analysis for clinical and pathological characteristics correlated with CSS. Patients with lower pathological stage, negative LN status, conventional transitional cell carcinoma (TCC) and large number of LNs retrieved had better CSS. *Conclusion:* In our study, patients

Table I (Abstract 255).

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value
Age (years)	1.018 (0.982-1.056)	0.326	-	-
Gender (female *vs*. male)	1.940 (0.827-4.549)	0.128	-	-
Pathological stage	1.791 (1.410-2.276)	<0.001	1.416 (1.093-1.833)	0.008
Histological subtype (other subtype *vs*. TCC)	3.539 (1.268-9.877)	0.016	5.679 (1.753-18.400)	0.004
Tumor grade (high *vs*. low)	2.273 (1.138-4.540)	0.020	-	-
LN status (pN+ *vs*. pN0)	8.380 (4.087-17.184)	<0.001	7.931 (3.248-19.370)	<0.001
Number of positive LNs	1.183 (1.110-1.260)	<0.001	-	-
LVI (presence *vs*. absence)	2.090 (1.158-3.773)	0.014	-	-
Number of LNs retrieved (for each LN)	0.961 (0.925-0.997)	0.036	0.929 (0.889-0.971)	0.001

HR: Hazard ratio; 95% CI: 95% confidence interval.

who underwent a more extensive pelvic lymph-node dissection (PLND) had a better CSS than those who underwent a more limited one. Our data support a possible role of PLND in cancer outcome. Although the extent of PLND may indirectly influence BCR because of the Will-Rogers phenomenon, the inclusion of both node-positive and node-negative patients may partially exclude this bias.

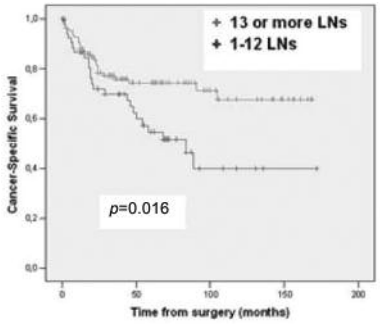

Figure 1.

259

SIURO-PRIAS-ITA: FIRST YEAR ITALIAN EXPERIENCE IN THE PRIAS INTERNATIONAL COLLABORATIVE STUDY ON ACTIVE SURVEILLANCE

Giario Conti[1], Tiziana Magnani[2], Roberto Salvioni[3], Sergio Villa[4], Michele Gallucci[5], Rocco Papalia[5], Giuseppe Martorana[6], Cosimo Bizzarri[6], Roberto Sanseverino[7], Giorgio Napodano[7], Pierpaolo Graziotti[8], Gianluigi Taverna[8], Roberto Peschechera[8], Andrea Turci[9], Giacomo Cicchetti[9], Enrico Bollito[10], Maurizio Colecchia[11], Rodolfo Montironi[12], Steno Sentinelli[13], Monique Roobol[14] and Riccardo Valdagni[2,4]

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PRIAS is the acronym for Prostate cancer Research International: Active Surveillance, a large collaborative international study on observational strategy in low-risk prostate cancer patients, coordinated by the Erasmus University Medical Center in Rotterdam. Over two thousand patients have been enrolled since 2006. The Italian Society of Urological Oncology (SIUrO) joined the protocol in December 2009. Eligibility criteria were: PSA ≤10 ng/ml, Gleason score ≤6 or Gleason 3+4 in men >69 years old with <10% positive cores, T1c or T2, PSA-D ≤0.20, ≤2 positive biopsy cores (<10% positive cores in cases of saturation biopsy), an adequate number of samples at the biopsy (related to the prostate volume), namely 8 samples for prostate volume ≤40 cm^3, 10 for volume 40-60 cm^3 and 12 for volume >60 cm^3. Follow-up was based on periodic PSA, clinical evaluation (Table I) and biopsy samples (in the first, fourth and seventh year). Different from PRIAS, in SIUrO-PRIAS-ITA, extensive information on the disease, comorbidities, education and habits were collected and three questionnaires administered: IPSS to evaluate LUTS, IIEF to evaluate sexual situation and FACT-P to evaluate the

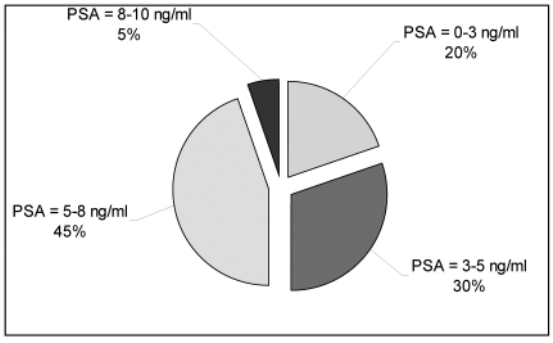

Figure 1. *PSA at diagnosis.*

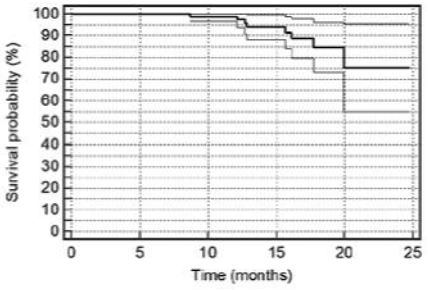

Figure 2. *Active treatment-free survival.*

Year	1					2				3		4		5		6		7	
Month	0	3	6	9	12	15	18	21	24	30	36	42	48	54	60	66	72	78	84
PSA-test	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
DRE	✓		✓		✓		✓		✓		✓		✓		✓		✓		✓
Biopsy	✓				✓								✓						✓
Evaluation	✓		✓		✓		✓		✓		✓		✓		✓		✓		✓

Table I. *Follow-up schedule*.

health-related quality of life. Exit criteria were: ≤3 years PSA-DT, progression in number of positive cores and/or Gleason score ≥7 at the follow-up biopsies (Gleason 3+4 is accepted in men >69 years old with <10% positive cores). From December 2009 to March 2011, 118 patients from seven Italian centers entered the study; the mean patient age was 66.5 years, 75% patients had an iPSA between 3 and 8 ng/ml, and 20% iPSA <3 ng/ml (Figure 1); 104 patients are still on protocol, while 14 discontinued active surveillance based on protocol or personal decision. The actuarial treatment-free survival is represented in Figure 2. Active surveillance is an important option in the spectrum of treatments for low-risk prostate cancer, is well-accepted and sometimes requested by the patients themselves; moreover, it provides the opportunity to avoid overtreatment and treatment-related toxicities in patients with a high probability of harboring an indolent tumor.

Authors Index*

(Figures indicate abstract number. *Missing abstracts were withdrawn.

Acquati P, 137
Albisinni S, 5
Albo G, 134
Alessandro M, 129
Ambrosio MR, 107
Antonelli A, 209, 211
Baldazzi V, 119
Ballaré A, 143
Barboro P, 34
Beldì D, 183
Bellardita L, 31
Bellastella G, 68
Bellavita R, 190, 192
Benecchi L, 97, 189, 191, 194
Bertelli E, 208
Bertini R, 56
Bollito E, 252
Bonetta A, 74, 77, 102, 243
Borrelli D, 174
Bortolato B, 159, 161
Bortolus R, 240
Brausi M, 13, 16, 17, 45
Bravaccini S, 103
Busetto GM, 64, 65
Cammarota F, 101
Caparrotti P, 165
Caraglia M, 48
Cardinali M, 151
Carmignani L, 50
Catanzaro MA, 32
Chiara F, 188
Chiumento C, 90
Cindolo L, 228, 232, 233
Cisternino A, 43, 86, 94
Cividini R, 244
Cochetti G, 229
Colombo R, 81
Conti G, 259
Cormio L, 221, 225
Cova G, 116
Cricca A, 251
De Berardinis E, 61, 63
De Cobelli O, 160
De Nunzio C, 2, 6, 7
Dell'Atti L, 1
Delle Cave A, 79
DeStefanis P, 18, 29, 42, 54
Di Lallo A, 104
Di Silverio F, 62, 218
Dionisi F, 125
Errico A, 170, 172
Fandella A, 92, 95
Fellin G, 11
Ferrera G, 219
Ferro M, 198, 199, 202, 214
Festuccia C, 19, 20, 21, 22
Fiorentino A, 91
Fiorino C, 222
Fontana A, 179
Frezza G, 132
Galleggiante V, 158
Galosi A, 234
Garibaldi E, 167
Giberti C, 193, 195
Giulianelli R, 8, 9, 10, 46, 47, 49, 136
Iori F, 224
Lacetera V, 200, 213
Lacquaniti S, 72
Lanciotti M, 135
Lanzi F, 206
Lasaponara F, 36
Liguori G, 124
Lo Monte AI, 220
Longo F, 66
Lorusso F, 223
Lotrecchiano G, 78
Lucarelli G, 163
Maccagnano C, 84
Macchione N, 53
Maffezzini M, 253
Maggioni M, 27
Magnani T, 248
Maines F, 177
Malizia M, 203
Mangolini A, 12
Marchioro G, 180
Marenghi C, 246
Marino L, 122, 123, 178
Marino R, 254
Martin G, 131
Martorana G, 256
Masieri L, 133
Mazza M, 171
Melegari S, 162, 164
Mombelli G, 212
Monaco F, 115
Montanari M, 96
Mucciardi G, 242
Neri F, 181
Neri F, 185

Nucciotti R, 35
Oderda M, 37, 38, 118
Palermo S, 25
Palloni T, 138
Palmieri F, 26, 44
Palminteri E, 41
Panaia R, 210
Papaleo A, 205
Pappagallo GL, 121
Parziani S, 153
Pastore AL, 51
Pellucchi F, 80, 82
Perdonà S, 201
Pernetti R, 73
Perugia G, 89
Petralia G, 59
Petrongari MG, 217
Picozzi S, 227
Pizzirusso G, 52
Pizzocaro G, 236
Pontoriero A, 148
Prati V, 120
Prezioso D, 67
Procopio G, 39
Pultrone CV, 141
Rancati T, 216
Raspollini MR, 207
Ravo V, 113
Rocca BJ, 111
Rocchini L, 83
Rocco B, 139, 140
Romeo A, 130
Roscigno M, 55, 57, 58, 60
Russo D, 197
Rutigliano M, 157
Sanseverino R, 182, 184, 187, 238
Scattoni V, 98, 99, 100
Schiavina R, 255, 257, 258
Serretta V, 14, 15
Siracusano S, 126, 128
Spagnoletti G, 142, 144, 145, 146, 147, 215
Spilotros M, 156
Testoni N, 245
Tiscione D, 154, 155, 235
Torelli T, 30
Tosco L, 231
Totaro A, 230
Tramacere F, 150
Valdagni R, 247
Vavallo A, 166
Vavassori A, 168, 169
Verzoni E, 40
Villani D, 85
Visconti C, 114
Visconti D, 69
Volpe A, 175, 176
Zerini D, 117