International Journal of Surgery (2013) **11**(S1), S30–S35

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

ORIGINAL ARTICLE

# Efficacy, safety and effectiveness of image-guided percutaneous microwave ablation in cystic renal lesions Bosniak III or IV after 24 months follow up

Gianpaolo Carrafiello [a], Gianlorenzo Dionigi [b], Anna Maria Ierardi [a], Mario Petrillo [a], Federico Fontana [a], Chiara Floridi [a], Luigi Boni [b], Francesca Rovera [b], Stefano Rausei [b], Alberto Mangano [b], Sebastiano Spampatti [b], Alberto Marconi [c], Giulio Carcano [b], Renzo Dionigi [b]

[a] *Interventional Radiology – Department of Radiology, University of Insubria, Varese, Italy*
[b] *Department of Surgery – University of Insubria, Varese, Italy*
[c] *Division of Urology – Ospedale di Circolo, Fondazione Macchi, Varese, Italy*

ARTICLE INFO

*Keywords:*
Microwave ablation therapy
Kidney neoplasm
Bosniak category III or IV cystic lesion treatment
Heatsink effect

ABSTRACT

*Purpose of the study:* The aim of the study was to assess the efficacy, safety and effectiveness of percutaneous image-guided microwave ablation (MWA) in Bosniak category III or IV cystic renal lesions after 24 months follow-up duration.
*Methods*: Between May 2008 and December 2012, computed tomography (CT)- or ultrasound (US)-guided MWA was performed in 6 patients with 7 cystic renal lesions (range 13.8–27 mm, mean 17.02 mm, SD 8.5 mm) Bosniak catgegory III or IV. The number of treatment sessions, treatment results, lesion size changes and complications were evaluated. Technical success (TS), technical effectiveness (TE), local tumor progression rate (LTPR), cancer-specific survival rate (CSSR) and overall survival rate (OSR) were computed.
*Main findings:* TS was 100% (7/7) and TE was 100%; LTPR was 0%; CSSR and OSR were 100%. No major complications were observed.
*Conclusion:* Our preliminary experience with MWA shows a potential role for US/CT-guided percutaneous MWA in treating Bosniak category III or IV cystic renal lesions, as a safe approach to treat selected patients not suitable for surgery.



## 1. Introduction

Bosniak III or IV cystic lesions may carry a particular risk for malignancy even if some of these lesions (particularly Bosniak III lesions) are proven to be benign after biopsy or surgery. [1–3] Warren et al. summarized data obtained from several studies correlating pathology with Bosniak category, reporting the risks of malignancy for Bosniak III and IV lesions to be 16–100% and 90–100%, respectively. [4] Due to the high risk of malignancy in Bosniak IV lesions, an alternative role in sparing nephrectomy has been hypothesized for the image-guided percutaneous ablation technique. Image-guided percutaneous radiofrequency ablation (RFA) has been widely accepted as a minimally invasive treatment for surgically unresectable renal cell carcinomas (RCC) with good results in small solid renal tumors where complete ablation rates ranged from 90% to 100%. [5–8] Following the same approach, Park et al. proposed image-guided percutaneous RFA as a valuable alternative for cystic lesions unsuitable for surgery, with excellent results. [9] Since this approach is applicable to Bosniak IV lesions, it could be reasonably extended to Bosniak III lesions with a high risk for malignancy, where surgical excision is often advocated [10] in spite of the possibility that the lesions are found to be benign at biopsy or surgery. [1–3]

Its technical features render MWA an interesting technology, due to the minimized thermal dispersion obtained by reducing the "heatsink effect" as previously reported by Laeseke et al. [11] On this basis, we hypothesized that MWA would offer better performances for the treatment of malignant cystic renal lesions, particularly in patients who should not have undergone nephrectomy for co-morbidities, as well as for solid RCCs.

In this study we report our preliminary experience with the efficacy, safety and effectiveness of image-guided percutaneous MWA in Bosniak category III or IV cystic renal lesions after a 24-month follow-up period.

## 2. Methods and materials

Approval for this study was obtained from the local institutional review board (IRB). Informed consent was waived by the IRB given the retrospective nature of the study on an anonymized database. Between May 2008 and Dec 2012, 6 patients (5 males, 1 female, mean

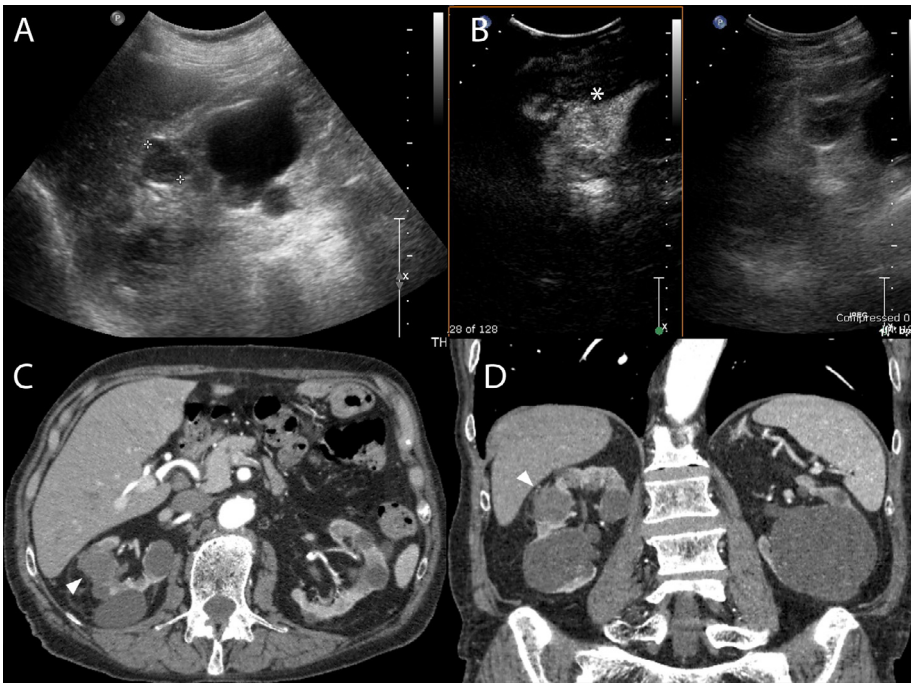


**Fig. 1.** (A) An exophytic rounded cystic lesion characterized by (B) an avid contrast enhancement along septa at CEUS examination. (C,D) The same lesion showed no enhancement at CECT (arrowhead); (D) a ring of fat-stranding due to persisting edema persists at CECT performed 1 month after treatment (arrowhead).

age 74 y, range 60–81) with 7 cystic renal lesions (one Bosniak III and six Bosniak IV lesions, range 13.8–27 mm, mean 17.02 mm, SD 8.5 mm) were treated with percutaneous MWA. [12,13] All patients were judged not suitable for surgery on the basis of their co-morbidities. Co-morbidities were distributed as follows: chronic renal failure (n = 2); respiratory and cardiac insufficiency (n = 2); cancer and abdominal aortic aneurysm (n = 1); amyotrophic lateral sclerosis and solitary kidney (n = 1). To be eligible for the procedure, patients have to meet the following criteria: Bosniak III or IV lesions no greater than 8 cm in size, the absence of renal vein thrombosis or extra-renal metastases, prothrombin time of less than 25 seconds, prothrombin activity higher than 40%, and a platelet count higher than $40\times10^9$ cells/L. Patients not eligible for surgery or refusing surgery, with an adequate route for percutaneous access, were eligible for percutaneous thermal ablation. Before the procedure, the number of cystic lesions, their size on multiplanar reformatted images (MPR) along the longest axis and the absence of renal vein thrombosis were evaluated by performing contrast enhanced ultrasonography (CEUS), as well as contrast enhanced computed tomography (CECT) or magnetic resonance imaging (MRI). All patients underwent a detailed pre-procedural assessment performed by CECT for staging, to evaluate lesion size, kidney location and proximity of adjacent organs and to evaluate the possibility of percutaneous access. Lesion locations were classified in upper (upper one-third), middle (middle one-third), and lower (lower one-third) poles based on Gervais et al. [14]

During the percutaneous MWA procedure, patients lay in the prone or semi-prone position. Local anesthesia was performed on the antenna entrance site with subcutaneous injection of a 10-ml solution of 2% Mepivacaine. The procedure was performed with anesthesiologic assistance, under moderate sedation, through I.V. administration of Propofol (0.5–2.0 mg/kg/h, Fresenius SE & Co. KGaA, Bad Homburg, Germany), Fentanyl (1–2 μg/kg, Pfizer Pharmaceuticals Group, New York, USA) and Mydazolam (0.07–0.08 mg/kg, Pfizer Pharmaceuticals Group, New York, USA). Adequate antibiotic prophylaxis was achieved with intravenous administration of 1 g of cefazolin sodium (Ancef, SmithKline Beecham Pharmaceuticals, Philadelphia, USA) given every eight hours for three days prior to the procedure, ending two days post-procedure. During the entire ablation session, patients were monitored by an anesthesiologist. MWA was performed through a 915 MHz microwave generator (Evident™ microwave ablation system, Covidien Ltd., USA), connected via coaxial cable to one antenna that was positioned within the lesion to be ablated. According to manufacturer's indications, one antenna was used per each lesion < 3 cm, with a power of 45 W set up for ten minutes of total ablation time in order to obtain an optimal volume of necrosis. The antenna was continuously perfused with saline solution at room temperature with a flow rate of 60 ml/min to avoid possible thermal damage along the proximal semi-axis. Each single antenna was removed hot for the cauterization of the path (target–skin surface). Three procedures were performed under CT guidance and four under ultrasound (US) guidance, according to operator expertise. In all cases a CT scan or an US examination, depending on guidance, was performed to establish the correct antenna positions before starting treatment.

Immediately after the procedure, a CECT or CEUS was performed to assess technical success. Every image was reviewed by two experienced radiologists (G.P.C. and F.F., 20 and 15 years experience in radiology, respectively). Follow-up imaging with a CECT was scheduled to take place 1 month after completion of treatment and at 3, 6 and 12 months for the first year; subsequent follow up was scheduled to take place every 4 months through a CEUS and at 24 months through CECT (Fig. 1).

Grayscale Ultrasound and CEUS were performed using a Philips iU22 device (Philips, Best, Netherlands). All patients received an intravenously administered half-dose (2.5 ml) of the second-generation contrast agent SonoVue© (Bracco, Milan, Italy) followed by the injection of 10 ml of saline solution to homogenize the bolus.

CECTs were carried out by a 64-row scanner (Aquilion 64, Toshiba, Japan). Each examination was performed in pre-contrast, arterial, venous and excretory phases, obtained respectively with delays of 18 s, 70 s and 7 minutes using Sure Start© by the region of

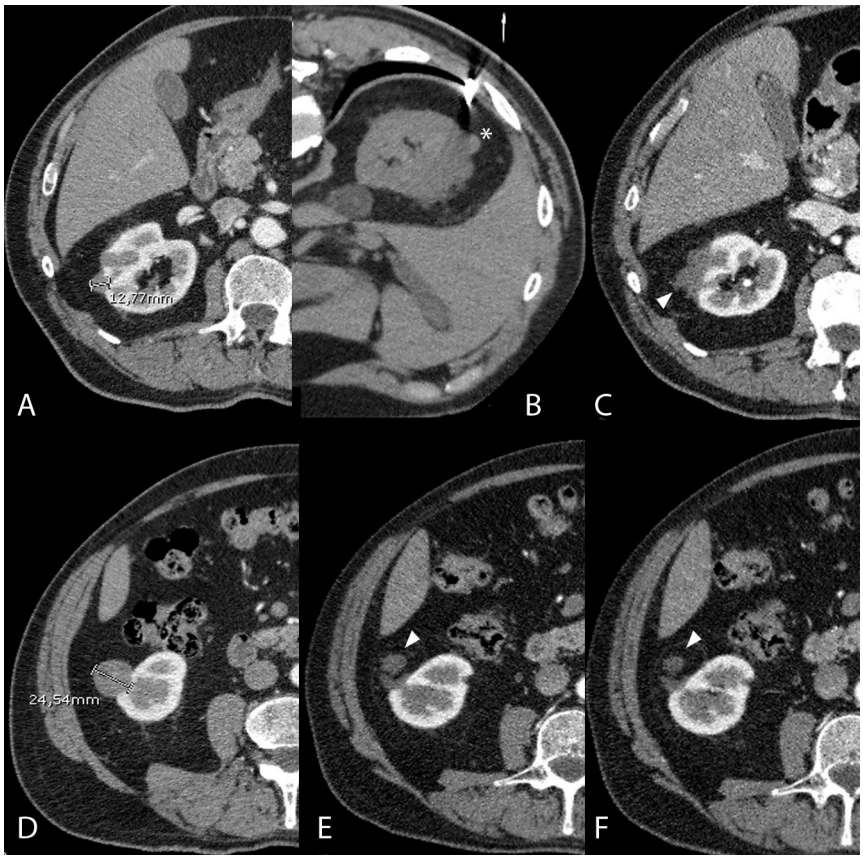


**Fig. 2.** Two different lesions observed and treated in the same patient (top and bottom panels). Top panel: (A) antenna entrance site; (B) lesion (asterisk); (C) this lesion appeared as completely necrotized without contrast enhancement at CECT performed 1 month after MWA treatment. Bottom panel: (D,E) the larger lesion appeared necrotized with a "halo" of fat-stranding 1 month after MWA treatment (arrowhead, E); (F) the "halo" progressively disappeared at CECT 24 months after treatment: a volume reduction of the ablated lesion was identified (arrowhead).

Table 1
Definitions used for study end-points

| End-point | Definition |
|---|---|
| Technical success (TS) | Correct positioning of the antenna inside the lesion to be ablated and the subsequent complete ablation checked on CECT/CEUS performed immediately after the MWA session |
| Technical effectiveness (TE) | Absence of thermo-ablative residues on CECT performed at one month ($1^{st}$ mo) after MWA treatment |
| Local tumor progression rate (LTPR) | Rate of patients in whom thermo-ablative residues are identified during follow up (beyond $1^{st}$ mo) in completely ablated lesions |
| Cancer-specific survival rate (CSSR) | The percentage of patients showing no local tumor progression at the chosen moment of follow up |
| Overall survival rate (OSR) | Global non-specific survival rate |

interest (ROI) positioning technique in abdominal aorta with a threshold of 100 Hounsfield units (HU). Scans were carried out after I.V. injection of non-ionic iodinated contrast media (350 mg I/mL), according to patient weight (respectively 85, 115 and 130 ml for $\leqslant$60 kg, $<$80 kg and $\geqslant$80 kg), at a rate of 4.5 ml/s followed by 40 ml of saline solution at the same flow rate. Complete ablation of a cystic renal tumor on CECT was defined as the absence of tumor enhancement with an attenuation value of a difference less than 10 HU when comparing follow-up unenhanced and contrast-enhanced CT images [9] (Fig. 2). On CEUS, residual non-ablated tissue was depicted as an irregular peripheral scattered, nodular or eccentric enhanced area. Non-ablated tumors could be re-treated if MWA treatment criteria persisted.

Definitions for the study end-points are reported in Table 1. Tumor features such as size, location, and HU values for each lesion on each CECT scan obtained during the arterial phase, and during all follow-up durations, are reported in Table 2. Ablation time, number of sessions, total applied energy for all lesions, and respective treatment results (i.e., the presence or absence of technical success, residual lesion, and tumor recurrence) were recorded. Complications, major or minor, when depicted by using US, CEUS, CECT, blood samples or clinical medical records, were defined according to S.I.R. criteria. [15]

## 3. Results

Seven cystic renal lesions were treated with a total of 7 ablations in 7 sessions (Fig. 3). The ablation time, the number of sessions and total applied energy for all lesions are as follows: 10 min, 1 (single) session, 45 Watt. TS was 100% (7/7); TE was 100% (7/7); LTPR was 0%; CSSR and OSR were 100%. There were no major complications; minor complications, resolved before discharging patients, included pain at needle insertion site, nausea, vomiting and fever.

Table 2
Lesion sizes before (0) and at 1, 3 and 24 mo after MWA session, maximum contrast enhancement (Max CE) reached in each single lesion among all examinations performed, and location and type of the lesion

| Lesion | Size (mm) | | | | Max CE (HU) | Type [a] | |
|---|---|---|---|---|---|---|---|
| | 0 | 1 mo | 3 mo | 24 mo | | | |
| 1 | 24.7 | 26 | 24 | 22 | 5 | Anterior, Lower one-third, right kidney | Ex |
| 2 | 12.7 | 10 | 9 | 8.7 | 7 | Anterior, Upper one-third, right kidney | Ex |
| 3 | 18 | 19 | 18.2 | 16.6 | 3 | Posterior, Upper one-third, left kidney | Ex |
| 4 | 27 | 28 | 27.2 | 25 | 9 | Anterior, Lower one-third, right kidney | Ex |
| 5 | 14 | 18.6 | 18.1 | 17.3 | 7 | Posterior, Upper one-third, right kidney | Ex |
| 6 | 13.8 | 17.2 | 15 | 14.3 | 4 | Posterior, Upper one-third, left kidney | Ex |
| 7 | 21 | 22.3 | 22 | 21 | 8 | Posterior, Upper one-third, right kidney | Ex |

[a] Ex, exophytic.

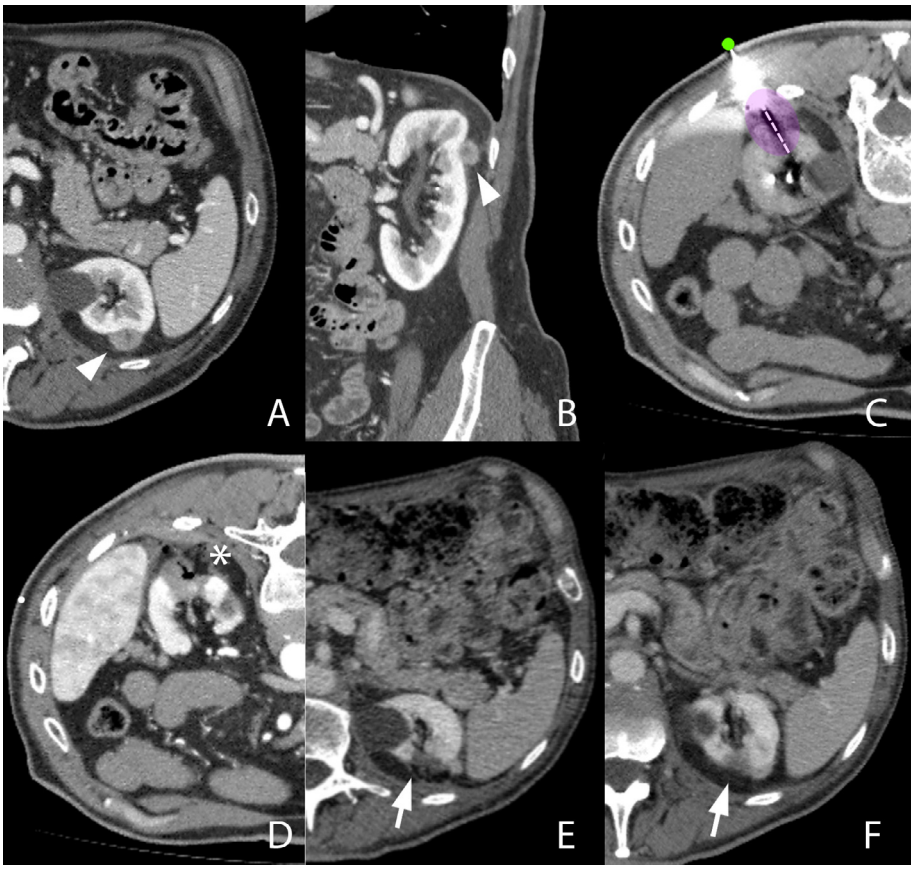


**Fig. 3.** (A,B) A small rounded exophytic lesion on axial (arrowhead, A) and coronal (arrowhead, B) reformatted CECT images before MWA treatment. (C) The same lesion during the MWA session: the dotted line shows the planned antenna track, the green circle the antenna entrance site and the violet oval the planned ablation area (diameter 3.7 cm). (D) The asterisk shows the ablated area on CECT performed immediately after MWA treatment; in particular some air bubbles of vaporization near the ablated site may be observed. (E,F) CECT performed 1 month (arrow, E) and 24 months (arrow, F) after MWA treatment showing absence of residue/recurrence.

## 4. Discussion

Surgery, when feasible, is widely accepted [10] as the treatment of choice for solid tumors; nucleo-resection or spare nephrectomy is preferred when possible [solitary, small lesions (<4 cm), located in a peripheral seat]. Ablative techniques have been introduced with the aim to control the spreading of a local tumor and to preserve the surrounding parenchyma's function, with curative or local control as the primary objectives, when surgery is not feasible. Different ablation techniques such as radiofrequency ablation (RFA), cryoablation (CA) or microwave ablation (MWA) have been available for some time, resulting in few complications, most of which are self-limited or readily treated, with great advantages if compared with surgical management. [5–8,16–19]

When suspected malignant cystic lesions of the kidney are considered, such as Bosniak III or IV lesions (malignancy rates 16–100% and 90–100%), [4] despite the interesting results in solid RCC, the use of RFA or CA still remains questionable, given that the overall performances and procedural tips for these treatments are not well established. Boss et al. [20] reported low effectiveness of RFA for cystic renal tumors, whilst Park et al. [9] reported optimal results with a shorter duration of energy application when compared with solid renal tumors similar in size. The most important limitation of RFA is the "heatsink effect" with a low efficacy related to a small necrosis

area caused by undesired RF energy dispersion. This effect is more evident in highly vascularized tissues or in fluid-filled, prominent lesions if large volumes are considered.

To offer an alternative by minimizing this phenomenon, Laeseke et al. [11] showed the interesting properties of MWA in a porcine model: this technique appeared less susceptible to perfusion-mediated cooling, especially in highly perfused tissue, such as kidney tissue, which is more subject to thermal dispersion. Inspired by this study, Yu et al. showed that US-guided percutaneous MWA could be a feasible alternative to obtain a safe and effective approach in managing RCC [16] due to the minimized thermal dispersion gained by MWA.

On this basis we hypothesized that MWA could open new perspectives in approaching suspected malignant cystic renal lesions, acting as a viable alternative when surgery was not feasible. In our CECT evaluation, based on residual lesion enhancement after MWA treatment, values ranged from 3 HU to 9 HU, showing that it could be acceptable to assume the absence of residual disease and no recurrences during follow up. These findings led to optimal results (shown in Table 3) with the absence of major intra- or peri-procedural

Table 3
Results for study end-points

| End-point | Result |
|---|---|
| Technical success (TS) | 100% |
| Technical effectiveness (TE) | 100% |
| Local tumor progression rate (LTPR) | 0% |
| Cancer-specific survival rate (CSSR) | 100% |
| Overall survival rate (OSR) | 100% |

complications or recurrences at 24 months. In our opinion, the small lesion size (<3 cm) may assume a relevance in our results: it was one of the most important criteria to reach a complete ablation with high technical success rate and improved clinical efficacy. It acted by enforcing synergistic effects obtained by linking the minimized "heatsink effect", formerly reported as extremely minimized in MWA, and the small volume of fluid-filled content, both factors that could determine thermal dispersion in RFA-treated cystic lesions. [9]

A questionable point in our series was the lack of a histological diagnosis before MWA treatment. Some studies reported that a biopsy of renal mass could be useful in evaluating the Bosniak II or III cystic renal mass [1,2] whilst other studies reported that the biopsy could be unreliable, particularly in pathologically diagnosing cystic masses. [13,21,22] Considering the lesions treated in our series, all classified as Bosniak category III/IV on the basis of imaging, surgery would have been considered in all cases (positive or negative histological presence of malignant cells). If the biopsy specimen was positive for malignancy, this result merely confirmed the need for surgery, whereas on the other hand, a negative test for malignancy did not impact the decision for surgery, not excluding the possibility of a sampling error or a potential future degeneration. Moreover, in some cystic RCCs where cystic architecture dominates the morphological appearance of the tumors, an adequate sample of malignant cells was not always available for a conclusive histological assessment, making biopsy not useful. [23] Previous studies reported that biopsy was not performed in two cystic renal masses despite RFA treatment and that there was a repeated negative biopsy for malignancy in a complex cystic–solid renal mass. [8,14] According to literature in our series, a careful CECT evaluation allowed the diagnosis of Bosniak III/IV lesions, avoiding invasive management. Moreover, the absence of contrast enhancement inside the ablated lesion after treatment was judged as a sufficient sign of absence of viable tissue persistence, especially considering the disease-free survival at 24 months in all cases.

A technical note regards percutaneous MWA guidance; in our experience the choice of image-guiding during renal ablation was strictly related to operator expertise and lesion features. Ultrasound has great advantages in the capability of real-time monitoring and its lack of ionizing radiation. However, being operator-dependent, it was compromised in certain settings, for example, in patients with a large body habitus, in the presence of abundant bowel gas, or when the tumor is near bowel. Moreover, US drawbacks are linked to the hyperechoic bubbles produced by vaporization during the procedure that could impact image quality. On the other hand, CT was typically associated with fewer changes in the imaging pattern of ablated renal masses, although intratumoral hyperdensity and gas generated during ablation sometimes could limit visualization. [24]

Only minor complications were observed in our patients, in particular pain at needle insertion site, vomiting or fever; this symptomatology was judged tolerable by patients. Therefore the procedure may be considered acceptable and safe, especially if compared with a surgical approach.

Limitations of the study are the retrospective evaluation; the selection bias based on type of lesion; and the small cohort of patients that included only small malignant cystic renal lesions (less than 4 cm in diameter). The last limitation was strictly linked to the strength of inclusion in patient selection, hypothesizing an MWA approach only when a clear benefit for the patient is expected after following a decision-making process well established with referent nephrologists.

In summary, our preliminary experience with MWA, notwithstanding the small number of cases and the need for further investigation, defines a potential role for US/CT-guided percutaneous MWA in treating Bosniak category III or IV cystic renal lesions, resulting in an efficient, effective and safe approach to treat selected patients not suitable for surgery.

*Funding*
None.

*Disclosure statement*
The authors have no conflicts of interest to declare.

## References

1. Harisinghani MG, Maher MM, Gervais DA, et al. Incidence of malignancy in complex cystic renal masses (Bosniak category III): should imaging-guided biopsy precede surgery? *AJR Am J Roentgenol* 2003;**180**:755–8.
2. Lang EK, Macchia RJ, Gayle B, et al. CT-guided biopsy of indeterminate renal cystic masses (Bosniak 3 and 2F): accuracy and impact on clinical management. *Eur Radiol* 2002;**12**:2518–24.
3. Hora M, Hes O, Michal M, et al. Extensively cystic renal neoplasms in adults (Bosniak classification II or III) – possible "common" histological diagnoses: multilocular cystic renal cell carcinoma, cystic nephroma, and mixed epithelial and stromal tumor of the kidney. *Int Urol Nephrol* 2005;**37**:743–50.
4. Warren KS, McFarlane J. The Bosniak classification of renal cystic masses. *BJU Int* 2005;**95**:939–42.
5. Pavlovich CP, Walther MM, Choyke PL, et al. Percutaneous radiofrequency ablation of small renal tumors: initial results. *J Urol* 2002;**167**:10–5.
6. Farrell MA, Charboneau WJ, DiMarco DS, et al. Imaging-guided radiofrequency ablation of solid renal tumors. *AJR Am J Roentgenol* 2003;**180**:1509–13.
7. Mayo-Smith WW, Dupuy DE, Parikh PM, Pezzullo JA, Cronan JJ. Imaging-guided percutaneous radiofrequency ablation of solid renal masses: techniques and outcomes of 38 treatment sessions in 32 consecutive patients. *AJR Am J Roentgenol* 2003;**180**:1503–8.
8. Gervais DA, McGovern FJ, Arellano RS, McDougal WS, Mueller PR. Radiofrequency ablation of renal cell carcinoma: part 1. Indications, results, and role in patient management over a 6-year period and ablation of 100 tumors. *AJR Am J Roentgenol* 2005;**185**:64–71.
9. Park BK, Kim CK, Lee HM. Image-guided radiofrequency ablation of Bosniak category III or IV cystic renal tumors: initial clinical experience. *Eur Radiol* 2008;**18**(7):1519–25.
10. Whelan TF. Guidelines on the management of renal cyst disease. *Can Urol Assoc J* 2010;**4**(2):98–9.

11. Laeseke PF, Lee FT Jr, Sampson LA, van der Weide DW, Brace CL. Microwave ablation versus radiofrequency ablation in the kidney: high-power triaxial antennas create larger ablation zones than similarly sized internally cooled electrodes. *J Vasc Interv Radiol* 2009;**20**(9):1224–9.
12. Bosniak MA. The current radiological approach to renal cysts. *Radiology* 1986;**158**: 1–10.
13. Israel GM, Bosniak MA. How I do it: evaluating renal masses. *Radiology* 2005;**236**: 441–50.
14. Gervais DA, McGovern FJ, Wood BJ, Goldberg SN, McDougal WS, Mueller PR. Radiofrequency ablation of renal cell carcinoma: early clinical experience. *Radiology* 2000;**217**:665–72.
15. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. *J Vasc Interv Radiol* 2009;**20**(7 Suppl): S377–90.
16. Yu J, Liang P, Yu XL, et al. US-guided percutaneous microwave ablation of renal cell carcinoma: intermediate-term result. *Radiology* 2012;**263**(3):900–8.
17. Zagoria RJ, Traver MA, Werle DM, Perini M, Hayasaka S, Clark PE. Oncologic efficacy of CT-guided percutaneous radiofrequency ablation of renal cell carcinomas. *AJR Am J Roentgenol* 2007;**189**(29):429–36.
18. Carrafiello G, Mangini M, Fontana F, et al. Single-antenna microwave ablation under contrast-enhanced ultrasound guidance for treatment of small renal cell carcinoma: preliminary experience. *Cardiovasc Intervent Radiol* 2010;**33**(2): 367–74.
19. Zagoria RJ, Childs DD. Update on thermal ablation of renal cell carcinoma: oncologic control, technique comparison, renal function preservation, and new modalities. *Curr Urol Rep* 2012;**13**(1):63–9.
20. Boss A, Clasen S, Kuczyk M, Schick F, Pereira PL. Image-guided radiofrequency ablation of renal cell carcinoma. *Eur Radiol* 2007;**17**:725–33.
21. Renshaw AA, Granter SR, Cibas ES. Fine-needle aspiration of the adult kidney. *Cancer* 1997;**81**:71–88.
22. Dechet CB, Zincke H, Sebo TJ, et al. Prospective analysis of computerized tomography and needle biopsy with permanent sectioning to determine the nature of solid renal masses in adults. *J Urol* 2003;**169**:71–4.
23. Rybicki FJ, Shu KM, Cibas ES, Fielding JR, vanSonnenberg E, Silverman SG. Percutaneous biopsy of renal masses: sensitivity and negative predictive value stratified by clinical setting and size of masses. *AJR Am J Roentgenol* 2003;**180**: 1281–7.
24. Venkatesan AM, Wood BJ, Gervais DA. Percutaneous ablation in the kidney. *Radiology* 2011;**261**(2):375–91.