Cavity shaving reduces involved margins and re-interventions without increasing costs in breast-conserving surgery: a propensity score-matched study

Fabio Corsi, M.D. Ph.D[a, b*], Luca Sorrentino, M.D.[a], Matteo Bonzini, M.D. Ph.D.[c], Daniela Bossi, M.D.[b], Marta Truffi, Ph.D.[d], Rosella Amadori, M.D.[e], Manuela Nebuloni, M.D. Ph.D.[f], Barbara Brillat, M.D.[a], Serena Mazzucchelli, Ph.D.[d]

[a]Surgery Division, Department of Clinical Sciences University of Milan, "Luigi Sacco" Hospital, via G. B. Grassi 74, 20157 Milano, Italy.

[b]Surgery Department, Breast Unit, IRCCS Maugeri Foundation Hospital, via Maugeri 4, 27100 Pavia, Italy

[c]Department of ClinicalSciences and Community Health, University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, via F. Sforza 28, 20122 Milano, Italy

[d]Department of Biomedical and Clinical Sciences University of Milan, "Luigi Sacco" Hospital, via G. B. Grassi 74, 20157 Milano, Italy.

[e]Division of Radiology, "Luigi Sacco" Hospital, via G. B. Grassi 74, 20157 Milano, Italy.

[f]Department of Pathology, Department of Clinical Sciences University of Milan, "Luigi Sacco" Hospital, via G. B. Grassi 74, 20157 Milano, Italy.

*Corresponding Author:

Prof. Fabio Corsi, MD

Department of Clinical Sciences, University of Milan, "Luigi Sacco" University Hospital, Via G. B. Grassi, 74, 20157 Milano, Italy

Surgery Department, Breast Unit, ICS Maugeri Foundation Hospital, via Maugeri 4, 27100 Pavia, Italy

E-mail: fabio.corsi@unimi.it

Phone: +39.02.3904.3449

Fax: +39.02.5031.9846

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Synopsis

Re-excision rates for involved margins remain high in breast-conserving surgery. Routine use of the cavity shave margins technique reduces positive margins and re-operations, without increasing costs. Cavity shaving is particularly effective in luminal cancers.

Abstract

Background: Currently re-interventions for involved margins after breast-conserving surgery remain common. The aim of this study was to assess the capability of the cavity shave margins (CSM) technique to reduce positive margin rates and re-operations compared to simple lumpectomy (SL). The impact of CSM on the various biological portraits of breast cancer and the costs were also investigated.

Methods: A retrospective review of 976 consecutive patients from a single center was performed: 164 patients underwent SL and 812 received CSM. All patients were treated with oncoplastic approach. Involved margins and re-operations were compared for each group. To avoid selection bias, propensity score-matched analysis was performed before applying a logistic regression model. Main outcomes were re-analyzed for each biological portrait. Surgery and hospitalization costs for SL and CSM were compared.

Results: Clear margins were found in 98.3% with CSM vs. 74.4% with SL, $p<0.001$. Re-operation rate was 18.9% with SL and 1.9% with CSM, $p<0.001$. After propensity score-matched logistic regression, OR for positive final margin status was 6.2 (95%CI 2.85-13.46, $p<0.001$) without CSM, while OR for re-intervention was 5.46 (95%CI 2.21-13.46, $p<0.001$). CSM significantly reduced positive margins and re-excisions for Luminal A, Luminal B and triple-negative breast cancers ($p<0.001$, $p<0.001$ and $p=0.0137$ respectively). SL had higher global costs compared to CSM: 193,630.6€ vs. 177,830€ for 100 treated patients, $p=0.009$.

Conclusions: CSM reduces re-excisions, mainly in luminal breast cancers, without increasing costs.

Introduction

The Society of Surgical Oncology (SSO) together with the American Society for Radiation Oncology (ASTRO) and the American Society of Clinical Oncology (ASCO) have stated that an adequate margin means “no ink on tumor”.[1,2] Currently, the re-operation rate for involved margins after lumpectomy ranges from 10% to 50%, whereas a recent consensus conference of the American Society of Breast Surgeons has set a reoperation rate <20% as a goal for 2020.[3,4]Re-interventions are undesirable because they lead to further sacrifice of breast tissue with inevitable aesthetic consequences, delay in adjuvant therapies, psychological discomfort for patients and increased re-hospitalization costs due to additionalsurgery.[5,6] Recently the cavity shave margins (CSM)technique has gained great interest, since it could reduce positive margins and re-interventions.[7,8] However, routine CSM is not a standard of care in breast-conserving surgery. Moreover, the correlation between biological subtypes of breast cancer and involved margins in CSM has been poorly investigated.[9] Our aim was to assess the capability of CSM to reduce positive margin rates and re-operations compared to simple lumpectomy (SL) in a large cohort of breast cancer patients treated in a single center. Secondary aims were to provide a cost analysis between CSM and SL, and to investigate if CSM impacted differently on different biological subtypes of breast cancer.

Methods

Case selection

A retrospective review of 976 consecutive stage I-II breast cancer patients referred to the Breast Unit at "Luigi Sacco" University Hospital (Milan, Italy) from January 2013 to April 2016, and who had received breast-conserving surgery, was performed. Patients with preoperative evidence of lesions >5 cm or with locally advanced or multifocal disease, and patients with an unfavorable tumor volume/breast volume ratio underwent mastectomy. Patients who received neoadjuvant chemotherapy were excluded from the study.

Surgery and perioperative procedures

All patients underwent preoperative localization by ultrasound as previously described.[10,11]The patient was set in supine position with the upper limb abducted, and the cutaneous projection of the lesion was marked on the breast skin. In cases of non-palpable lesions, an ultrasound visible clip (MammoMark, Artemis, Hayward, CA, USA) was located in the biopsy site and the skin was marked. On surgery day, a skin incision was made along the mark and lumpectomy was performed. One hundred and sixty-four patients (16.8%) were treated by SL, while 812 (83.2%) by CSM. In cases of SL, the lesion was identified by the surgeon after skin incision and excised together with a small portion of overlying skin and underlying pectoralis fascia. In cases of CSM, after lumpectomy the surgeon resected a portion of breast parenchyma immediately surrounding the surgical cavity on each margin (Figure 1). In all patients full-thickness lumpectomy specimens were obtained with a

basic oncoplastic approach, remodeling breast after resection by volume replacement with minimal local glandular flaps to improve cosmetic outcomes. In CSM patients, breast remodeling was performed after margin shaving. In all cases, the surgical specimen was oriented by marking the cranial and medial margins with stitches. Surgery was performed by the same surgical team.

In case of SL, the margin status was determined on all six planes of the resection and this represented the final margin status. In case of CSM, the margin status was assessed both on the lumpectomy specimen and on each cavity shaving. If one or more margins of lumpectomy were found to be involved but the margin status of the cavity shaving was negative, the final margins were considered adequate, and no further surgery was needed. Margins were considered adequate if no ink was found on the tumor.[1,2] If the final margin status was positive, a second surgical procedure was proposed. In case of single margin involvement surgery consisted in re-excision of the breast parenchyma surrounding the surgical cavity. In case of extensive involvement (>1 positive margins) or diagnosis of multifocality a total mastectomy was proposed. In selected patients with favorable features and with microscopically focal involvement of a single margin, adjuvant therapies and radiotherapy were proposed instead of surgery. When re-operation occurred in another Institute, data were retrieved from the re-operation center and included in the analysis.

Statistical analysis

Clinical data were collected in a prospectively-maintained database. The association between the use of CSM and final margin status and the re-intervention rate was assessed. Differences between the two study groups were assessed by chi-square or Fisher exact test for categorical variables and Student *t* test for continuous variables. Because of the non-random design of the study, we performed propensity score matching to reduce bias resulting from possible imbalance in observed

covariates between the SL and CSM groups. To generate the propensity score, a non-parsimonious logistic regression model was developed with CSM as the dependent variable. SL and CSM patients were matched in a 1:5 ratio and compared with a conditional logistic regression model adjusted according to post-operative variables significantly associated with outcomes, to avoid any bias.

Subsequently main outcomes were re-analyzed for each biological portrait of breast cancer, which was determined on histopathological features. This allowed the different effects of CSM with different molecular profiles of breast cancer to be verified. Finally a cost analysis (expressed in euro, €) was performed for SL and CSM using data from the Hospital Cost Management Office. Mean surgery times for the two groups were multiplied by 6.8€ per minute of surgery, including staff, medications, devices and sterilization costs. Hospitalization costs were calculated by multiplying 634€ for each day of patient stay in the Surgery Department. Pathology costs were calculated from tissue processing to staining of histological sections, considering margin assessment on lumpectomy specimen (3 paraffin blocks per patient, 17.5€) and on each cavity shaving (5-6 paraffin blocks per patient, 32.5€). Staff costs were calculated considering technical timing of 5 minutes for each lumpectomy (3.8€) and 15 minutes for cavity shavings (11.5€). In case of re-intervention the costs of operations, hospitalizations and pathological analyses were added. Mean total costs per patient were calculated. Considering the re-intervention rate in each treatment, the total summed cost for 100 treated patients was calculated and compared between the two groups. Data analysis was carried out using STATA software (v. 13, StataCorp, Austin, USA).

Results

Variables distribution between groups

Baseline features of SL and CSM patients are reported in Table 1. Microcalcifications and parenchymal distortions were more frequent in SL than CSM group (23.8% vs. 11.5% and 16.5% vs. 5.9% respectively, $p<0.001$). Ductal carcinoma in situ (DCIS) was more frequent among SL patients (20.1% vs. 7.4%, $p<0.001$), while more invasive lobular cancers were found in the CSM group (10.1% vs. 2.4%, $p<0.001$). CSM patients showed increased frequency of grade I (20.4% vs. 14.6%, $p=0.002$), pT1 (77% vs. 58%, $p<0.001$) and pN0/pNmic (76% vs. 70.1%, $p=0.029$) lesions than the SL group.

Margin status and re-intervention rates

Rates of involved margins on lumpectomy specimen were 25.6% for SL and 20.1% for CSM, $p=0.116$. Positive final margins decreased from 20.1% to 1.7% in CSM patients. Clear margins in the CSM group were found in 98.3% vs. 74.4% with SL, $p<0.001$. Residual cancer on cavity shave was detected in 20% of CSM patients, but performing CSM was sufficient to achieve adequate margins in 18.3% of cases. In the SL group 18.9% of patients (31/164) underwent a second surgical procedure to achieve adequate margins, while re-intervention was necessary in only 1.9% of CSM

patients (16/812), $p<0.001$ (Table 1). In SL group, 6.7% of patients (11/164) had involved margins but were not re-operated: 7 patients (4.3%) with favorable features had only a microscopically focal involvement of a single margin, therefore re-excision was avoided (supplementary Table S1); in 4 cases (2.4%) a re-excision was proposed but patients refused re-intervention. In CSM group, 0.2% of patients (2/812) had a negative final margins status but were re-operated because multifocality was incidentally detected on cavity shave.

Propensity score-matched analysis and multivariate logistic regression

Lesion types and stages were differentially distributed among groups (Table 1). Since these parameters were preoperatively defined with a potential bias in the chosen treatment, they were included together with age at diagnosis in the propensity score analysis. Matching was performed by a 1:5 ratio between SL and CSM patients, due to the high quantitative difference in the two populations. The total number of subjects included in such analysis was therefore 615.After propensity score matching, the risk of positive final margin status was significantly higher in patients treated by SL, with an OR equal to 14.51 (95%CI 4.95-42.57), $p<0.001$. The risk of re-intervention was also higher with SL than with CSM, with an OR of 7.73 (95%CI 2.88-20.77), $p<0.001$ (Table 2). Subsequently, the logistic regression models were implemented adding variables associated with poor outcome: histological type of lesion, grade and biological portrait. The adjusted OR for having a positive final margin status was 6.2 (95%CI 2.85-13.46, $p<0.001$) for SL, while the risk of re-intervention was 5.46 (95%CI 2.21-13.46, $p<0.001$) (Table 2).

Cost analysis

Regarding first surgery, the mean operative time was higher with CSM than with SL (72 min vs. 67.5 min, p=0.007). Based on operative times, first surgery costs were 459€ (±125.1€) for SL and 489.6€ (±132.6€) for CSM (p=0.007). Total costs per single patient were 1,748.3€ (±461.1€) for SL and 1,759.5€ (±463.2€) for CSM (p=0.778). In case of second surgery with local re-excision, the total summed costs per patient were 2,738.6€ (±601.8€) for SL and 2,747.8€ (±603.8€) for CSM, p=0.963. If mastectomy was performed as re-intervention, the total summed costs were 2,761.3€ (±601.8€) and 2,770.5€ (±603.8€) respectively, p=0.986. Global costs for 100 treated patients were 193,630.6€ (±38,562.1€) with SL vs. 177,830€ (±45,452.9€) with CSM, p=0.009 (Table 3).

Effects of cavity shave on margin status and re-interventions according to biological portraits

Biological portraits were equally distributed between the two groups (Table 1). A significant reduction in positive final margins was found upon CSM in Luminal A (from 27.3% to 1.8%, p<0.001), Luminal B (from 32.7% to 1.4%, p<0.001), and TNBC (from 16.7% to 0%, p=0.0137). Conversely, in cases of HER2-positive cancers no benefit was gained with CSM (0% vs. 4.3%, p=1.000). The re-intervention rates significantly decreased with CSM in Luminal A (from 16.9% to 2.3%, p<0.001), Luminal B (from 27.3% to 1.4%, p<0.001) and TNBC (from 16.7% to 0%, p=0.0137), while no difference was reported for HER2-positive lesions. All these data are reported in Table 4.

Discussion

Nowadays the rates of involved margins and re-excisions after breast-conserving surgery are still high.[12,13] Moreover, some breast surgeons are not confident with the novel definition of clear margin, and often propose unnecessary re-excision in order to gain wider margins.[12,14,15] CSM could be an interesting solution, since it resolves doubts whenever a margin is found positive on lumpectomy specimen. Indeed CSM avoids false positive margins arising from misleading interpretation of the pathologist, or from technical pitfalls related to specimen handling(e.g. ink infiltration into the specimen or dislocation of cancer cells near the resection margin).[16,17]

We observed a rate of involved margins on lumpectomy specimens as high as 21%. This rate is considered relevant, since it means that about 1 every 5 patients potentially needs a re-excision. [12,13]CSM significantly reduced involved margins and reinterventions. The clinical benefit from CSM was confirmed by the propensity score model adjusted with logistic regression: avoiding CSM exposed patients to 6.2-fold higher risk of positive margins, and 5.46-fold higher risk of re-intervention. We observed lower rates of positive margins and re-interventions compared to

previously published data. This probably relies on several features of the suggested toolbox to reduce re-operations that are standards of care in our institution, such as accurate lesion localization by ultrasound aided by clip markers, routine cavity shave of all margins, oncoplastic approach to obtain full-thickness specimens, and adoption of the updated definition of a proper margin.[4]

Marudanayagam has demonstrated a higher re-operation rate for SL than CSM (12.5% vs. 5.6%). [7]Zavagnohasfound an even higher frequency of reoperations without CSM (21.1% vs. 5.5%).[8]A case-matched study was published by Kobbermann who demonstrated a 9-fold reduction in the risk of reoperation by routinely adopting CSM, but they also re-excised close margins.[18]Currently no predictor for useful CSM has been identified.[19] Recently the first randomized clinical trial comparing CSM with SL was published, and reported a positive margin rate equal to 19% with CSM vs. 34% without CSM, with reduced re-operations from 21% to 10%.[20]Most of these studies were retrospective without a proper unbiased analysis, and the majority of them were prior to the publication of the latest guidelines on margins in breast-conserving surgery. Our study included all patients in which an oncoplastic approach was used, showing the benefit of CSM even in patients in which full-thickness specimens were obtained. Interestingly, thisfacthasnotbeenpreviouslyinvestigated.[21]

In Luminal B cancers, CSM reduced the involved margins rate from 32.7% (the highest among subtypes) to 1.4%, and re-operations from 27.3% to 1.4%. Conversely, CSM did not impact on margins or re-operations in HER2-positive breast cancers. Our data disagree with other literature, since HER2-positive disease is notoriously related to positive cavity shaves.[9] A possible explanation could be that since our study population included relatively small lesions associated to grade I-II and N0, the HER2-lesions here-analyzed did not exhibit the same local aggressiveness of HER2 cancers analyzed in other studies.[9,22]TNBC was associated with residual disease on cavity shaves in 25.9%, and in this subgroup of patients CSM reduced positive margins and re-excisions from 16.7%

to 0%. In a previous study, TNBC was associated with residual invasive disease on re-excision in 51% of cases.[23,24]The high rate in residual cancer and involved margins in Luminal B tumors has been previously observed, but its reasons are still unknown.[9,25-28] Of note, the majority of our patients had luminal cancers, therefore no significant conclusions could be inferred for TNBC and HER2-positive lesions.

A poorly explored issue is the cost-effectiveness of cavity shaving. CSM added 5 minutes to surgery times. Moreover, histopathology costs for each patient were higher with CSM than SL (65.3€ vs. 21.3€). However, reduced re-excisions in CSM patients mitigated the impact of CSM on total costs. Similar results have been reported in another cost-analysis, where comparable costs were demonstrated in SL and CSM groups, despite the shorter operative times in SL than CSM (66 vs. 76 minutes) and the higher pathological costs for CSM patients.[29]

Limitations of our study could be the lack of randomization due to retrospective design and the approximation of biological portraits of breast cancer on pathological features instead of genetic profiling. However propensity score analysis is widely accepted for surgical outcome in non-randomized studies to reduce the selection bias. Moreover, the mentioned approximation is extensively used in literature.[9]

Conclusions

Positive margins and re-excision rates are unacceptably high after breast-conserving surgery. Routine CSM associated to lumpectomy significantly reduced the need for re-excisions, especially in luminal cancers, even in patients treated with oncoplastic approach. A particularly low rate of re-excision was reached by accurate localization of breast lesions as indicated in the suggested toolbox for successful breast-conserving surgery. A clear advantage is expected in terms of psychological burden for patients and promptly starting adjuvant therapies, and the total costs of the treatment do not appear to increase.

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Tables

Table 1. Distribution of baseline features among patients treated by lumpectomy only and lumpectomy with cavity shave margins. Margin status and re-intervention rates with and without performing cavity shave margins.

	Lumpectomy (n = 164)	Lumpectomy + CSM (n= 812)	Total (n = 976)	p value*
Age at diagnosis	63.4 (±10.4)	63.6 (±10.8)	63.6 (±10.7)	0.828
Lesion size (mm)	15 (±9.5)	14.6 (±7.2)	14.7 (±7.7)	0.541
Lesion type				
Lump	98 (59.7%)	671 (82.6%)	769 (78.8%)	<0.001
Microcalcifications	39 (23.8%)	93 (11.5%)	132 (13.5%)	
Parenchymal distortion	27 (16.5%)	48 (5.9%)	75 (7.7%)	
Histological type				
DCIS	33 (20.1%)	60 (7.4%)	93 (9.5%)	<0.001
Invasive ductal	114 (69.5%)	663 (81.6%)	777 (79.6%)	
Invasive lobular	4 (2.4%)	82 (10.1%)	86 (8.8%)	
Others	13 (7.9%)	7 (0.9%)	20 (2.1%)	
Biological portrait**				
Luminal A	77 (47.0%)	436 (53.7%)	513 (52.6%)	0.123
Luminal B	55 (33.5%)	288 (35.5%)	343 (35.1%)	0.655
HER2-positive	10 (6.1%)	23 (2.8%)	33 (3.4%)	0.054
Triple-negative	18 (11.0%)	54 (6.7%)	72 (7.4%)	0.069
N.A.	4 (2.4%)	11 (1.3%)	15 (1.5%)	
Grade				
I	24 (14.6%)	166 (20.4%)	190 (19.5%)	0.002
II	65 (39.6%)	370 (45.6%)	435 (44.6%)	
III	49 (29.9%)	142 (17.5%)	191 (19.5%)	
N.A.	26 (15.9%)	134 (16.5%)	160 (16.4%)	
T stage				
Tis	33 (20.1%)	60 (7.4%)	93 (9.5%)	<0.001
T1	95 (58.0%)	625 (77.0%)	720 (73.8%)	
T2	22 (13.4%)	110 (13.5%)	132 (13.5%)	

T3	2 (1.2%)	3 (0.4%)	5 (0.5%)	
N.A.	12 (7.3%)	14 (1.7%)	26 (2.7%)	
N stage				
N0/Nmic	115 (70.1%)	617 (76.0%)	732 (75%)	0.029
N1	32 (19.5%)	158 (19.4%)	190 (19.5%)	
N2	12 (7.3%)	26 (3.2%)	38 (3.9%)	
N3	5 (3.1%)	11 (1.4%)	16 (1.6%)	
Involved margins on lumpectomy	42 (25.6%)	163 (20.1%)	205 (21.0%)	0.116
Clear margins on lumpectomy with no residual disease on CSM	//	647 (79.8%)	647 (79.8%)	
Clear margins on lumpectomy and residual disease on CSM (multifocality)	//	2 (0.2%)	2 (0.2%)	
Involved margins on lumpectomy with residual cancer on CSM (cleared margins)	//	149 (18.3%)	149 (18.3%)	
Involved margins on lumpectomy with residual cancer on CSM (still involved margins)	//	14 (1.7%)	14 (1.7%)	
Final margins status				
Involved	42 (25.6%)	14 (1.7%)	56 (5.7%)	<0.001
Clear	122 (74.4%)	798 (98.3%)	920 (94.3%)	
Re-intervention				
Yes	31 (18.9%)	16 (1.9%)	47 (4.8%)	<0.001
Local re-excision	25 (15.2%)	15 (1.8%)	40 (4.1%)	
Total mastectomy	6 (3.7%)	1 (0.1%)	7 (0.7%)	
No	133 (81.1%)	796 (98.1%)	929 (95.2%)	

* Comparison between the two study groups: Student t test for continuous variable, Fisher exact test for categorical variables

** Biological portraits were approximated as following: luminal A (positive hormone receptors and negative HER2, Ki67 <14%), luminal B (positive hormone receptors and negative or positive HER2, Ki67 ≥14%), HER2-positive (negative hormone receptors and positive HER2), and triple-negative (negative hormone receptors and negative HER2).

Table 2. Results from the logistic regression analysis after propensity score matching (1:5 ratio, 615 patients). OR and 95%CI estimating the risk of positive final margins status (A and B) and the risk of undergoing re-intervention (C and D).

A) Risk of positive margins after propensity score matched analysis by relevant preoperative variables, unadjusted model				B) Risk of positive margins, adjusted model for relevant post-operative variables			
	Coeff.	**95%CI**	**p value**		**OR**	**95%CI**	**p value**
Age at diagnosis	-0.002	-0.019-0.013	0.75	Histological type	1.78	1.25-2.54	0.001
Lesion type	0.78	0.54-1.02	<0.001	Grade	0.84	0.58-1.22	0.36
Stage	0.2	-0.02-0.43	0.08	Biological portrait	0.91	0.65-1.27	0.57
Positive margins status	**OR**	**95%CI**	**p value**	**Positive margins status**	**OR**	**95%CI**	**p value**
Lumpectomy without CSM	14.51	4.95-42.57	<0.001	Lumpectomy without CSM	6.2	2.85-13.46	<0.001
C) Risk of re-intervention after propensity score matched analysis by relevant preoperative variables, unadjusted model				D) Risk of re-intervention, adjusted model for relevant post-operative variables			

	Coeff.	95%CI	p value		OR	95%CI	p value
Age at diagnosis	-0.002	-0.019-0.013	0.75	Histological type	1.85	1.26-2.72	0.002
Lesion type	0.78	0.54-1.02	<0.001	Grade	0.88	0.58-1.35	0.56
Stage	0.2	-0.02-0.43	0.08	Biological portrait	0.98	0.67-1.43	0.92
Re-intervention	**OR**	**95%CI**	**p value**	**Re-intervention**	**OR**	**95%CI**	**p value**
Lumpectomy without CSM	7.73	2.88-20.77	<0.001	Lumpectomy without CSM	5.46	2.21-13.46	<0.001

Table 3. Cost-analysis.

	Simple Lumpectomy (n = 164)		Lumpectomy + CSM (n = 812)		p value
	Mean (± SD)	**Costs (± SD)**	**Mean (± SD)**	**Costs (± SD)**	
Operative time (first surgery) - 6.8€ per min	67.5 (±18.4)	459€ (±125.1€)	72 (±19.5)	489.6€ (±132.6€)	0.007
Hospitalization stay (first surgery) - 634€ per day	2 (±0.7)	1,268€ (±443.8€)	1.9 (±0.7)	1,204.6€ (±443.8€)	0.095
Pathology costs (first surgery)		21.3€		65.3€	
Total cost per patient (first surgery only)		1,748.3€ (±461.1€)		1,759.5€ (±463.2€)	0.778
Operative time (second surgery) - 6.8€ per min*	21.3 (±10.3)	144.8€ (±70€)	21 (±10.7)	142.8€ (±72.8€)	0.936
Hospitalization stay (second surgery) - 634€ per day*	1.3 (±0.6)	824.2€ (±380.4€)	1.3 (±0.6)	824.2€ (±380.4€)	1.000
Pathology costs (second surgery)		21.3€ if local re-excision 44€ if mastectomy		21.3€ if local re-excision 44€ if mastectomy	
Total cost per patient (first + second surgery, local re-excision)		2,738.6€ (±601.8€)		2,747.8€ (±603.8€)	0.963
Total cost per patient (first + second surgery, mastectomy)		2,761.3€ (±601.8€)		2,770.5€ (±603.8€)	0.986
Patients with first surgery only (%)	81.1%	141,787.1€ (±37,395.2€)	98.1%	172,606.9€ (±45,439.9€)	
Patients re-operated with local re-excision (%)	15.2%	41,626.7€ (±9,147.4€)	1.8%	4,946€ (±1,086.8€)	
Patients re-operated with mastectomy (%)	3.7%	10,216.8€ (±2,226.7€)	0.1%	277.1€ (±60.4€)	
Total cost on 100 patients		**193,630.6€ (±38,562.1€)**		**177,830€ (±45,452.9€)**	**0.009**

*In case of re-intervention performed in another Institute, costs of the second surgery were approximated as if they were performed in our Breast Unit

Table 4. Effects of cavity shave on margin status and re-interventions according to biological portrait

	Luminal A	Luminal B	HER2-positive	TNBC	p value
Margins on lumpectomy	**(n = 513)**	**(n = 343)**	**(n = 33)**	**(n = 72)**	
Involved	99 (19.3%)	83 (24.2%)	3 (9.1%)	17 (23.6%)	0.105
Clear	414 (80.7%)	260 (75.8%)	30 (90.9%)	55 (76.4%)	
Final margins status (patients treated by lumpectomy only)	**(n = 77)**	**(n = 55)**	**(n = 10)**	**(n = 18)**	
Involved	21 (27.3%)	18 (32.7%)	0 (0.0%)	3 (16.7%)	
Clear	56 (72.7%)	37 (67.3%)	10 (100.0%)	15 (83.3%)	
Final margins status (patients treated by lumpectomy + CSM)	**(n = 436)**	**(n = 288)**	**(n = 23)**	**(n = 54)**	Luminal A: <0.001 Luminal B: <0.001 HER2-positive: 1.000 TNBC: 0.0137
Involved	8 (1.8%)	4 (1.4%)	1 (4.3%)	0 (0.0%)	
Clear	428 (98.2%)	284 (98.6%)	22 (95.7%)	54 (100.0%)	
Residualcancer on CSM					
Yes	79 (18.1%)	65 (22.6%)	3 (13.0%)	14 (25.9%)	0.26
No	357 (81.9%)	223 (77.4%)	20 (87.0%)	40 (74.1%)	
Re-intervention after lumpectomy only	**(n = 77)**	**(n = 55)**	**(n = 10)**	**(n = 18)**	
Yes	13 (16.9%)	15 (27.3%)	0 (0.0%)	3 (16.7%)	
No	64 (83.1%)	40 (72.7%)	10 (100.0%)	15 (83.3%)	
Re-intervention after lumpectomy + CSM	**(n = 436)**	**(n = 288)**	**(n = 23)**	**(n = 54)**	Luminal A: <0.001 Luminal B: <0.001 HER2-positive: 1.000 TNBC: 0.0137
Yes	10 (2.3%)	4 (1.4%)	1 (4.3%)	0 (0.0%)	
No	426 (97.7%)	284 (98.6%)	22 (95.7%)	54 (100.0%)	

Figure Captions

Fig. 1 Cavity shave margins technique: all margins were separately shaved (the skin was resected with the lumpectomy specimen.