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Original article

Impact of contra-lateral breast reshaping on mammographic surveillance in women undergoing breast reconstruction following mastectomy for breast cancer

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ABSTRACT

Background: The ultimate goal of breast reconstruction is to achieve symmetry with the contra-lateral breast. Contra-lateral procedures with wide parenchymal rearrangements are suspected to impair mammographic surveillance. This study aims to evaluate the impact on mammographic detection of mastopexies and breast reductions for contralateral adjustment in breast reconstruction.
Patients and methods: We retrospectively evaluated 105 women affected by uni-lateral breast cancer who underwent mastectomy and immediate two-stage reconstruction between 2002 and 2007.
We considered three groups according to the contra-lateral reshaping technique: mastopexy or breast reduction with inferior dermoglandular flap (group 1); mastopexy or breast reduction without inferior dermoglandular flap (group 2); no contra-lateral reshaping (group 3).
We assessed qualitative mammographic variations and breast density in the three groups.
Results: Statistically significant differences have been found when comparing reshaped groups with non reshaped groups regarding parenchymal distortions, skin thickening and stromal edema, but these differences did not affect cancer surveillance.
The surveillance mammography diagnostic accuracy in contra-lateral cancer detection was not significantly different between the three groups ($p = 0.56$), such as the need for MRI for equivocal findings at mammographic contra-lateral breast ($p = 0.77$) and the need for core-biopsies to confirm mammographic suspect of contra-lateral breast cancer ($p = 0.90$).
Conclusions: This study confirms previous reports regarding the safety of mastopexies and breast reductions when performed in the setting of contra-lateral breast reshaping after breast reconstruction. Mammographic accuracy, sensitivity and specificity are not affected by the glandular re-arrangement. These results provide a further validation of the safety of current reconstructive paradigms.

Introduction

The ultimate goal of breast reconstruction is to achieve symmetry with the contra-lateral breast [1]. Depending on the size and volume of the contra-lateral breast, this could not always be possible without a balancing procedure, in order to achieve a bilateral medium-sized cosmetic breast mound [2]. Contra-lateral surgery may include augmentation with implants or breast reduction or mastopexy [3].

Women treated for breast cancer are at higher risk of developing a second cancer in the contra-lateral breast than the general population [4,5].

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For this reason patients should perform a bilateral mammography every year as part of their follow-up [6]. Contra-lateral procedures with wide parenchymal rearrangements or implants placement are suspected to impair mammographic surveillance [7]. For instance it has been demonstrated that implants used for cosmetic breast augmentation may interfere with mammography causing delays in the detection of breast cancer [8–12].

Despite past evidences regarding the reliability of mammographic detection in breast reductions or mastopexies, it is widely accepted that post-operative changes may yield difficult interpretations of mammograms increasing the need for recalls, further imaging with MRI or tissue sampling. This may cause anxiety and distress to patients and has obvious economic implications [13–18].

This study aims to evaluate the impact on mammographic detection of mastopexies and breast reductions for contra-lateral adjustment during breast reconstruction with implants (Figs. 1–3).

Patients and methods

Study participants and data collection

We retrospectively collected from our prospectively-maintained database 105 women affected by uni-lateral breast cancer who underwent mastectomy and immediate two-stage reconstruction at our Institution between 2002 and 2007.

We considered three different groups according to the contra-lateral reshaping technique.

The first group included 35 women who underwent two-stage reconstruction and contra-lateral mastopexy or reduction with

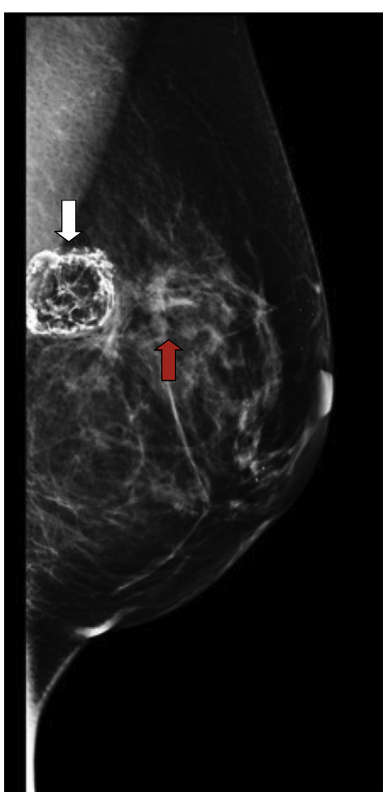

Fig. 1. Group 2. 1-year follow-up mammogram. MLO Projecton. Left breast. Fat-necrosis calcification (white arrow) and parenchymal distortion (red arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

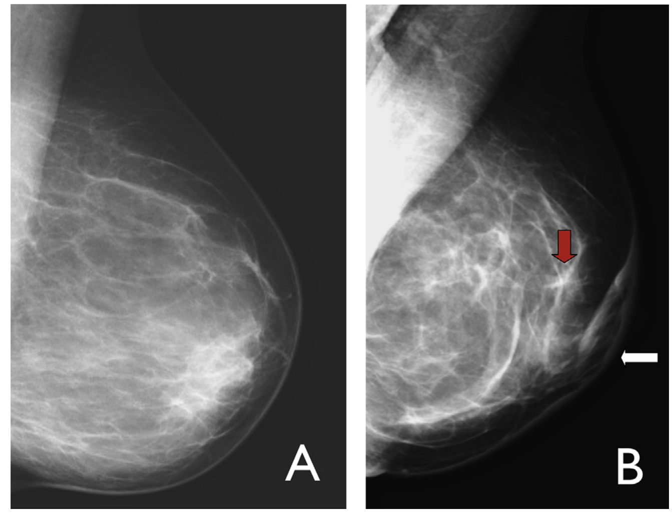

Fig. 2. Group 1. A. Pre-operative mammogram. BI-RADS Density 1. MLO Projection Left breast. B. 1 year follow-up mammogram. BI-RADS Density 1. MLO Projection. Left breast. Parenchymal distortion (red arrow) and skin thickening (white arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

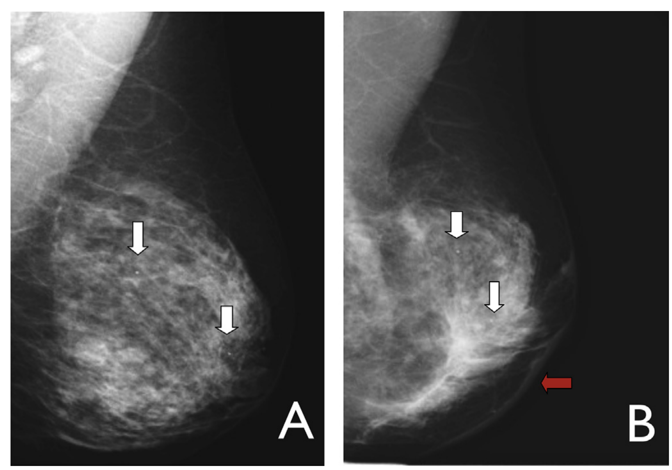

Fig. 3. Group 2. A. Pre-operative mammogram. MLO Projection. BI-RADS Density 4. Benign microcalcifications (white arrows); B. 1-year follow-up mammogram. MLO projection. BI-RADS Density 4. Skin thickening (red arrow), diffuse stromal edema, benign microcalcifications (white arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

preservation of an inferior dermal-glandular flap to enhance the breast projection (called “auto-prosthesis”).

The second group included 35 women treated by two-stage reconstruction and contra-lateral reduction or mastopexy with other techniques (without “auto-prosthesis”).

The third group included 35 women who underwent two-stage reconstruction and did not receive any kind of surgical treatment on the healthy breast.

We included 35 consecutive patients in each of the three groups according to the following inclusion criteria: absence of any previous form of surgery at the level of the healthy breast and availability of at least one pre-operative mammogram and two post-operative mammograms with at least 18 months of follow-up in the hospital database.

The baseline characteristics of this population (TNM, grading, histotype, Estrogen-receptor status, Progesterone-receptor status and Her-2 receptor status) are displayed in Table 1.

Patients mean age at surgery was 60.3 years (SD 8.6) in group 1, 59.2 years (SD 10.6) in group 2 and 58.9 years (SD 10.8) in group 3.

We evaluated the pre-surgical mammogram and then the first one in the follow-up (Time Point 1, TP1) and the latest one (Time Point 2, TP2) to assess qualitative mammographic variations (i.e. stromal edema, skin thickening, parenchymal distortions and calcifications).

Skin thickening was defined as a breast radiopaque profile larger than 1.5 mm [19].

The mean time from surgery to the first mammogram was respectively 15 months for group 1 (range 9–24 months), 13 months (range 6–24 months) for group 2 and 15 months (range 7–35 months) for group 3. The latest mammogram was performed after a mean time of 79 months for group 1 (range 25–119 months), 76 months (range 25–119 months) for group 2 and 59 months (range 22–97 months) for group 3.

Baseline mammographic characteristics for the three groups have been compared with the first follow-up mammogram and with the last follow-up mammogram for each group with an intra-group and inter-group analysis.

Data regarding group 1 and group 2 were evaluated separately and then matched together in order to create two comparisons:

Table 1
Baseline and clinico-pathological characteristics of the patients.

	Group 1 (n = 35)	Group 2 (n = 35)	Group 3 (n = 35)	p
Age (years) mean (SD)	60.3 (8.6)	59.2 (10.6)	58.9 (10.8)	0.83
Grading (%)				
G1	3 (8.6)	–	–	0.03
G2	19 (54.3)	23 (65.7)	15 (42.9)	
G3	13 (37.1)	12 (34.3)	20 (57.1)	
Histology (%)				
LCIS	1 (2.9)	–	–	0.13
DCIS	11 (31.4)	4 (11.4)	6 (17.1)	
LCIS/DCIS	1 (2.9)	–	–	
ILC	6 (17.1)	4 (11.4)	7 (20)	
IDC	14 (40)	23 (65.7)	22 (62.9)	
IDC/ILC	2 (5.7)	4 (11.4)	–	
pTNM (%)				
T				
Tis	13 (37.1)	4 (11.4)	6 (17.1)	0.13
T1	4 (11.4)	11 (28.6)	7 (20)	
T2	16 (45.7)	14 (40)	16 (48.6)	
T3	1 (2.9)	2 (5.7)	1 (2.9)	
T4	1 (2.9)	4 (11.4)	5 (14.3)	
N				
N0	26 (74.3)	15 (42.9)	15 (42.9)	0.04
N1	8 (22.9)	17 (48.6)	13 (37.1)	
N2	1 (2.9)	3 (8.6)	6 (17.1)	
N3	–	–	1 (2.9)	
Estrogen receptor status (%)				
Positive	32 (91.4)	22 (62.9)	24 (68.6)	0.01
Negative	3 (8.6)	13 (37.1)	11 (31.4)	
Progesterone receptor status (%)				
Positive	32 (91.4)	22 (62.9)	22 (62.9)	0.01
Negative	3 (8.6)	13 (37.1)	13 (37.1)	
Her-2 receptor status (%)				
Positive	7 (20.0)	13 (37.1)	12 (34.3)	0.25
Negative	28 (80.0)	22 (62.9)	23 (65.7)	

LCIS – Lobular carcinoma in situ; DCIS - Ductal carcinoma in situ; ILC - infiltrating lobular carcinoma; IDC - infiltrating ductal carcinoma.
Group 1: Autoprosthesis; Group 2: Other techniques; Group 3: No surgery.

- Autoprosthesis (group 1) vs. Other techniques (group 2)
- Surgical reshaping (group 1 + group 2) vs. No surgical reshaping (group 3)

We assessed mammographic modifications until mammographic stability (defined as two subsequent follow-up mammograms without any significant change) was reached.

In order to assess mammographic stability, all available yearly-performed mammograms from TP1 to TP2 have been evaluated for each patient.

We also evaluated changes in breast density according to the Breast Imaging-Reporting and Data System (BI-RADS) [20] density score as a consequence of post-surgical rearrangements. Secondary procedures such as further imaging with MRI or tissue sampling were also investigated in order to assess accuracy, sensitivity and specificity of the mammography.

Surgical technique

Breast reductions and mastopexies have been performed according to different techniques, in relation to the patient's breast shape and size [21–23].

The so-called "auto-prosthesis" technique represents a revised version of the technique described by Ribeiro [24].

The nipple areola-complex is based on a superior pedicle, with a Wise or vertical-scar skin reduction pattern. An inferior dermo-glandular flap is prepared at the central part of the lower pole of the breast and tunneled under the superior pedicle and the upper quadrants breast tissue and then fixed to the pectoralis major fascia, ensuring enough superior fullness.

Statistical analysis

The observed data are normally distributed (Shapiro–Wilk W-Test) and presented as means ± Standard Deviation (SD).

In order to investigate the differences between the three groups, sample size calculation was estimated by GPOWER software. The resulting total sample size, estimated according to a global effect size of 15% with type I error of 0.05 and a power of 95% was 105 patients.

The repeated measure ANOVA, Student's t test, and the Mann–Whitney U test and Kruskall-Wallis's test were used to compare continuous variables. The χ^2 test was used to compare discrete variables.

All p values presented are 2-tailed and a $p \leq 0.05$ was chosen for levels of significance. Statistical analyses were performed using SPSS 20 software package (SPSS, Inc., Chicago, IL).

Results

Time to achieve mammographic stability was 31 months in group 1 (range 12–60 months) and 29 months (range 12–48 months) in group 2. No significant mammographic modifications were observed in group 3.

The analysis of the qualitative mammographic changes demonstrated that there were no significant difference in the incidence of distortions in the comparison between the "autho-prosthesis" technique (group 1) and other surgical procedures for reduction or mastopexy (group 2) either at TP1 (group 1 = 68.6% vs group 2 = 62.9%; p = 0.13) and at TP2 (group 1 = 62.9% vs. group 2 = 60%; p = 0.24). We did not observe architectural distortions in group 3 (Tables 2 and 3).

Stromal edema was significantly lower in group 1 when compared with group 2 at TP1 (group 1 = 5.7% vs. group 2 = 51.4%; $p < 0.001$) but this resolved at TP2 (no mammographic signs of edema both in group 1 and group 2). Obviously no signs of post-surgical edema are reported for group 3 at each time point (Tables 2 and 3).

Skin thickening was also investigated and once again this was significantly lower for group 1 at TP1 (group 1 = 8.6% vs. group 2 = 14.3%; $p < 0.001$). Once again this post-surgical mammographic sign resolved at TP2. No changes in skin thickness across the follow-up were reported in group 3 (Tables 2 and 3).

A slightly higher incidence of calcifications was reported in the comparison between the "autoprosthesis" and other techniques at TP1 (group 1 = 62.9% vs group 2 = 51.4%; p = 0.03), these were still present, although not statistically significant, at TP2 (group 1 = 74.3% vs. group 2 = 62.9%; p = 0.13). When comparing the entire surgical cohort (group 1 + group 2) with the no-surgery group (group 3) we observed a higher but not significant incidence of calcifications at TP1 and TP2 in the surgical cohort (Tables 2 and 3).

We also assessed changes of BI-RADS density across the follow-up. No significant modifications were reported at each time point either comparing the two surgical groups (group 1 vs group 2) and both of them against no surgery (group 1 + group 2 vs. group 3) (Tables 2 and 3).

The need for further imaging with MRI and tissue sampling with core biopsies was also estimated without showing any significant variation between the three groups (MRI: group 1 = 2.85%, group 2 = 5.71%, group 3 = 2.85%; p = 0.77; Core biopsy: group 1 = 11.42%, group 2 = 11.42%, group 3 = 8.57%; p = 0.90) (Table 4).

To investigate accuracy, sensitivity and specificity we also evaluated the rates of contralateral metachronous cancers that even in this case did not show any statistically significant difference (group 1 = 8.6%, group 2 = 8.6%, group 3 = 5.7%; p = 0.87) (Table 4).

All contralateral cancers have been diagnosed at mammography and confirmed at core-biopsy: core-biopsy has been performed in 4 (11.42%) patients to confirm mammographic suspect of contralateral breast cancer both in the first and the second group, assessing 3 contra-lateral breast cancers in each group. The remaining 2 patients had a diagnosis of benign epithelial hyperplasia (considered as false positives at mammography). Three (8.57%) patients in the third group performed core-biopsy, diagnosing 2 contra-lateral breast cancers and one benign epithelial hyperplasia (considered as false positive).

The annual risk of contra-lateral tumors was 1.43% in the first and second group and 0.95% in the third group.

All contralateral cancers have been diagnosed at stage I (pT1N0).

Mammographic sensitivity rate was 100% in the three groups; specificity was 94.1% either in group 1 and group 2 and 97% in group 3; accuracy was 94.6% in group 1 and group 2 and 97.2% in group 3 (Table 5).

Discussion

Extensive use of contra-lateral reshaping as part of breast reconstruction with implants allowed us to reduce the use of more complex autologous tissue flaps. Modern anatomical implants resemble the shape of a juvenile medium-sized extra-projected gland and for this reason patients with large or ptotic breast need a contralateral adjustment (mastopexy or breast reduction) to reach a good symmetry [2].

Several authors described the impact of cosmetic procedures on mammographic detection [13–18]. A historical study by Brown et al. [18] investigated forty-two patients who had at least one mammographic examination following reduction mammoplasty providing evidence regarding alterations of the peri-areolar and inferior pole soft-tissues in almost all cases 6 months after operation with a decrease in the following years of follow-up. The authors concluded that changes after breast reduction are predictable and can be easily differentiated from those associated with cancer.

The effects of remodeling the breast upon mammographic cancer detection as part of the screening program was evaluated in a recent study by Muir [17]. Data of women with a previous history of breast reduction were extracted from a population based screening: the authors concluded that post-operative breast changes following reduction mammoplasty do not significantly hinder analysis of the screening mammogram.

A recent study from Losken et al. [25] investigated the impact of partial breast reconstruction using reduction techniques on post-operative cancer surveillance. Two groups of patients were retrospectively reviewed (standard breast conserving surgery vs. therapeutic reduction mammaplasties). Interestingly they did not find differences in the two groups regarding the typical post-operative mammographic. There were also no significant differences in the breast density scores. The rate of tissue sampling in the study group was significantly higher (53%) when compared with the control group (18%). However this study presented several limitations related to the small size of the sample (34 patients in total) and the lack of a control group of healthy patients who underwent cosmetic procedures.

Although reasonable evidence regarding the safety of breast rearrangements (mastopexy or reduction) was provided by the studies already mentioned, the presence of post-surgical changes is still considered a challenge for the effective detection of metachronous cancers [13–15]. In our study we investigated the radiological impact of these surgical operations when performed in patients who had a mastectomy and are at a higher risk of developing a second contra-lateral cancer. As a secondary end-point we investigated the impact of an alternative technique for mastopexies (so called "auto-prosthesis") in which an inferior dermoglandular flap is de-epithelialized and placed underneath the superior pedicle. This technique generates a very pleasant cosmetic result but creates two overlapping tissues and could hinder the mammographic detection.

The results of this study are largely in line with other previous works. As expected the surgical changes are evident in the two subgroups of patients who underwent either standard mastopexy/breast reduction or the auto-prosthesis technique. In detail, architectural distortions are present in both groups and do not change

Table 2
Mammographic findings and BI-RADS density at TP1. Inter-group comparisons.

	Group 1	Group 2	Group 3	p (comparison 1)	p (comparison 2)
Parenchymal distortions	68.6%	62.9%	–	0.13	<0.0001
Stromal edema	5.7%	51.4%	–	<0.001	<0.0001
Skin thickening	8.6%	14.3%	–	<0.001	<0.0001
Calcifications	62.9%	51.4%	40%	0.03	0.24
Birads-density	2.71	2.81	2.74	0.75	0.42

Group 1: Autoprosthesis; Group 2: Other techniques; Group 3: No surgery.
Comparison 1: Group 1 vs. Group 2; Comparison 2: (Group 1 + Group 2) vs. Group 3.

Table 3
Mammographic findings and BI-RADS density at TP2. Inter-group comparisons.

	Group 1	Group 2	Group 3	p (comparison 1)	p (comparison 2)
Parenchymal distortions	62.9%	60%	–	0.24	<0.0001
Stromal edema	–	–	–	–	–
Skin thickening	–	–	–	–	–
Calcifications	74.3%	62.9%	40%	0.13	0.40
Birads-density	2.40	2.61	2.74	0.72	0.43

Group 1: Autoprosthesis; Group 2: Other techniques; Group 3: No surgery.
Comparison 1: Group 1 vs. Group 2; Comparison 2: (Group 1 + Group 2) vs. Group 3.

Table 4
MRI and core biopsies for equivocal mammographic findings at the reshaping side; contralateral cancers at mean 6-year follow-up.

	Group 1	Group 2	Group 3	p
MRI	1 (2.85%)	2 (5.71%)	1 (2.85%)	0.77
Core biopsies	4 (11.42%)	4 (11.42%)	3 (8.57%)	0.90
Contralateral cancers	3 (8.6%)	3 (8.6%)	2 (5.7%)	0.87

Group 1: Autoprosthesis; Group 2: Other techniques; Group 3: No surgery.

Table 5
Mammographic accuracy.

	Group 1	Group 2	Group 3	p
Sensitivity	100%	100%	100%	1
Specificity	94.1%	94.1%	97%	0.56
Accuracy	94.6%	94.6%	97.2%	0.56

Group 1: Autoprosthesis; Group 2: Other techniques; Group 3: No surgery.

over time, acute post-surgical changes such as stromal edema and skin thickening tend to resolve in the long term. Interestingly we observed that the auto-prosthesis technique reduced significantly the post-operative edema at a stromal level and in the skin. This can be due to the morphological properties of patients candidate to auto-prosthesis that usually have smaller breast with medium to moderate ptosis in comparison to woman candidate to other techniques such as breast reductions or mastopexies for severe ptosis.

The presence of calcifications was also assessed and no significant differences were identified in the comparison between the first and the second group and between both surgical groups (when matched together) and the cohort of patients who did not receive any operation.

Imaging features of post-operative calcifications due to fat necrosis vary depending on its stage of evolution [26]. Imaging may suffice to differentiate fat necrosis in the early stage from pathologic calcifications and malignancy, while differentiation in the late stage may result more challenging.

We did not face this kind of problem leading to the possibility of a larger number of second level exams, because we could evaluate early post-operative mammograms for each of the patients in the study, having the possibility of defining the occurence of post-surgical calcifications, without suspects of malignancy, and following their evolution in the mammographic follow-up.

We considered the BI-RADS glandular density an interesting parameter to be investigated in the presence of severe glandular re-arrangements. Even in this case the surgical treatment (irrespective of the surgical technique employed) did not alter the mammographic results and the final mean BI-RADS density score is very similar to that reported by Losken [25]. Contrary to us, Losken observed a higher incidence of further testing while we did not find any difference with not treated patients. This can be explained because their study was performed on the affected side while we studied the contra-lateral healthy breasts. The annual incidence of metachronous contralateral cancers has been reported at 0.5%–1% per annum, with the annual hazard rate being constant up to 15 years after the diagnosis of the first primary [27], which is two to three times that of the general population [28]. These results are in line with our observation. Also sensitivity and specificity are in accordance with data reported in literature [13,17,18].

Conclusion

This study confirms previous reports regarding the safety of mastopexies and breast reductions when performed in the setting of contra-lateral breast reshaping after breast reconstruction. The mastopexy with auto-prosthesis has been demonstrated to be as safe as standard techniques and performs better in terms of post-operative short-term edema and skin thickening. Mammographic accuracy, sensitivity and specificity are not affected by the glandular re-arrangement.

This study has some limitations related to the relatively small and not entirely matched sample of patients and its retrospective nature. All the procedures were performed in a highly specialized cancer center by dedicated radiologists and this may have affected the final results.

A larger prospective cohort of patients assessed in general hospitals may provide further information regarding the safety of this surgical approach. These results provide a further validation of the safety of current reconstructive paradigms.

Conflict of interest statement

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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Ethical approval

Ethical approval not required.

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