SAFETY OF LIPOFILLING AS A SECONDARY PROCEDURE IN BREAST RECONSTRUCTION

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ABSTRACT

Introduction: Lipofilling is a useful surgical technique for breast reconstruction. However, there remains a concern regarding the long-term safety of fat grafting with its stem cell population in breast cancer patients. This study evaluated the safety of lipofilling procedure in breast reconstruction.

Materials and Methods: We conducted this observational study that included patients who underwent lipofilling with or without adipose-derived regenerative cells (ADRC) for breast reconstruction. We divided patients into 2 groups. Group I comprised of patients with lipofilling for lumpectomy defects. Group II included patients with post mastectomy reconstruction defects. These two groups were analysed using Chi-square test, P- Value of <0.05 was considered significant.

Results: A total of 53 patients had lipofilling for defects following breast cancer surgery. 25 patients had lumpectomy defects while 28 had post-mastectomy reconstruction defects. 29 out of 53 patients had lipofilling with ADRC. An average of 232 ml of fat (80-420 ml) was injected. The average follow-up was 50 months. Thirty-three percent (18/53) developed a palpable lump. Imaging confirmed benign changes including fat necrosis in 13, oil cyst in 3 and scarring in 2 patients. No loco-regional recurrence was identified in either group. Four patients developed metastasis at an average of 28 months following lipofilling and 56.6 months from primary breast cancer surgery. Out of four patients three had stage III disease and died of visceral metastasis.

Conclusion: Lipofilling is a safe technique for breast reconstruction. We found no increased risk of local recurrence or new cancer development. Patients with stage III disease were found to be at a higher risk of distant metastases.

KEYWORDS: Lipofilling, fat grafting, breast cancer, mammography

Introduction

One of the advances in breast reconstructive surgery is the restoration of breast volume or shape using lipofilling technique. The first use of free fat graft was reported by Neuber [1] in 1893. The first breast augmentation using autologous fat injection was reported by Bircoll in 1987 [2]. However, the same year The American Society of Plastic Surgeons did not recommend fat grafting to the breast [3]. It was due to the potential risk of interference with imaging and delay in cancer diagnosis. There was another concern that grafted fat may promote tumour formation or recurrence of cancer [4,5].

There are several studies that later reported the safety of this procedure in breast reconstruction without any delay in cancer diagnosis or increased cancer risk [6-11]. However, the use of...
We started lipofilling for breast reconstruction at our institution in 2008. It is an observational study with prospective data collection. Total of 64 patients had lipofilling for breast reconstruction or augmentation from September 2008 to May 2013. We included 53 patients, who had lipofilling for defects following breast cancer surgery. Eleven patients with benign indications for lipofilling were excluded. The historical information was collected including tumour pathology, type of reconstructive surgery following mastectomy and adjuvant therapy including radiation treatment. We divided patients into two groups. Group I comprised patients with lipofilling for defects following breast conservation surgery (BCS)/lumpectomy defects. Group II included patients with post-mastectomy reconstruction (PMR) defects. Breast imaging was performed as required before the lipofilling procedure. Patients were consented and informed of complications. These included risks of palpable lump, induration, fat necrosis, calcification, fat resorption and lack of long-term oncological safety following lipofilling. Patients also consented for pre and postoperative photographs to assess the cosmetic outcome.

**Materials and Methods**

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### Surgical Technique

**Fat Harvesting and Processing:**

Preoperative assessment and marking of the breast defects and donor sites were made with the patient in a standing position. Fat was harvested using wet tumescent technique under general anaesthesia with a 50-ml Toomey syringe attached to a Mercedes tip harvesting cannula (3mm x18 cm). The donor sites were abdomen and flank in all except two patients in which fat was harvested from the thighs. We used two techniques. Twenty-nine from fifty-three patients had centrifugation and purification techniques (Celution®800/CRS) to separate ADRC’s which was then mixed with the purified fat graft before injection. After NICE guidance in January 2012 which limited the use of ADRC in clinical trials setting only we used bilaminar filtration technique (Cytori Pure GraftTM) to purify the harvested fat.

**Fat Injection:**

Breast incisions were placed to allow the injection of fat graft into different directions following a Lattice pattern. Grafted fat was placed in small aliquots at many levels. We used both curved and straight cannulas attached to a 10 ml syringe for injection (16 G blunt tip). In patients requiring the release of scar tissue a V-dissecting tip cannula was used.

### Follow-up

All patients were followed at intervals of 1 week, four weeks, six months and one year following the procedure. Patient satisfaction with the procedure in improving cosmetic outcome was recorded. The cosmetic outcome was graded as very good to excellent when the total score was >5, satisfactory to good when 3-5 score and unsatisfactory if <3 score. The endpoint of the study was the restoration of breast contour/symmetry or patient satisfaction.

Mammography was performed within a year after the procedure to assess any procedure related changes. Breast cancer patients were followed up to 5 years following cancer surgery according to local guidelines. Those patients discharged from follow up were contacted by phone or electronic hospital records were reviewed. Finally, the findings on post procedure breast imaging and biopsy results were recorded. The two patient groups and surgical techniques were compared using Fisher’s exact test. The level of significance was set at P <0.05.

### Results

A total of 57 lipofilling procedures were performed in 53 women from September 2008 to May 2013. Four patients’ had bilateral procedures. Patient ages ranged from 38 to 72 years, with a mean of 50 years. There was no family history of breast cancer or BRCA mutation. Group I included 25 patients (47 percent) who had lipofilling for BCS defects and group II included 28 patients (53 percent) with lipofilling for PMR defects. Post-mastectomy reconstruction included TRAM flap in 12, LD flap in 9 and implant-based reconstruction in 7 patients.

The primary breast cancer surgery in these patients was performed between 1996 and 2012. The study included 49 cases of invasive carcinoma (92 percent), 4 cases of in situ carcinoma (8 percent). Out of 49 invasive cancers, there were 28 cases of T1 (52 percent) and 21 cases of T2 to T4 (40 percent) size cancers. Twenty-seven patients (51 percent) had a history of adjuvant breast irradiation.

### Table 1 Clinicopathologic Characteristics of Patients before Lipofilling with Breast Cancer n=53.

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Mean age (years)</th>
<th>T(n)</th>
<th>N(n)</th>
<th>M(n)</th>
<th>Stage(n)</th>
<th>Mx(n)</th>
<th>BCS(n)</th>
<th>RT(n)</th>
<th>CT(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>53</td>
<td>50</td>
<td>T1 (28)</td>
<td>N1 (7)</td>
<td>0</td>
<td>1 (34)</td>
<td>(25)</td>
<td></td>
<td>(27)</td>
<td>(13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2 (17)</td>
<td>N2 (5)</td>
<td>0</td>
<td>2 (9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3 (1)</td>
<td>N3 (0)</td>
<td>0</td>
<td>3 (6)</td>
<td></td>
<td></td>
<td></td>
<td>Skin Sparing (8)</td>
</tr>
</tbody>
</table>

*ND- Axillary surgery not done in 2 patients (Breast conservation surgery for DCIS), Mx- Mastectomy, BCS – Breast Conservation Surgery, RT-Radiotherapy, CT – Chemotherapy.
Table 2 Comparison of clinical and oncological outcome in 2 groups following lipofilling BCS or PMR.

<table>
<thead>
<tr>
<th></th>
<th>Group I Lipofilling for BCS defects</th>
<th>Group II Lipofilling for PMR defects</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of procedures</td>
<td>25/53 (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat necrosis, oil cyst, calcifications</td>
<td>12 (48%)</td>
<td>6 (21%)</td>
<td>0.049*</td>
</tr>
<tr>
<td>Redo procedure</td>
<td>4 (7%)</td>
<td>2 (3.5%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Metastasis</td>
<td>1 (1.8%)</td>
<td>3 (5.6%)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

*P-value significant

Table 3 Comparison of clinical outcome in 2 groups following lipofilling with or without ADRC.

<table>
<thead>
<tr>
<th></th>
<th>Lipofilling with ADRC</th>
<th>Lipofilling with Pure GraftTM only</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>2008 - 2011</td>
<td>2012 - 2013</td>
<td>-</td>
</tr>
<tr>
<td>No. of patients</td>
<td>29 (55%)</td>
<td>24 (45%)</td>
<td>-</td>
</tr>
<tr>
<td>Mean volume of fat injected</td>
<td>270 ml (140 - 350)</td>
<td>160 ml (80 - 250)</td>
<td>-</td>
</tr>
<tr>
<td>Good to excellent cosmetic outcome</td>
<td>94%</td>
<td>86%</td>
<td>-</td>
</tr>
<tr>
<td>Patient satisfaction score*</td>
<td>5</td>
<td>4.3</td>
<td>-</td>
</tr>
<tr>
<td>Immediate complications</td>
<td>3</td>
<td>1</td>
<td>0.61</td>
</tr>
<tr>
<td>Redo procedure</td>
<td>2 (3.7%)</td>
<td>4 (7.5%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Metastasis</td>
<td>3 (10.3%)</td>
<td>1 (3.5%)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Patient satisfaction score* - 1 to 6 depending on patient rating, score 1 unsatisfactory outcome of scoring 6 excellent outcome.
Table 4 Clinical & pathological characteristics of patients with metastasis n=4/53.

<table>
<thead>
<tr>
<th>Age in years at cancer diagnosis</th>
<th>Surgery</th>
<th>TNM</th>
<th>Stage</th>
<th>Tumour grade / VI present</th>
<th>Adjuvant Chemo-/ Radiotherapy</th>
<th>Site of mets</th>
<th>Interval from lipofilling to mets</th>
<th>Interval from cancer surgery to mets</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>WLE+C</td>
<td>pT2pN2</td>
<td>IIIA</td>
<td>3/+</td>
<td>Yes</td>
<td>Lung + Liver</td>
<td>4 M</td>
<td>57 M</td>
<td>Died</td>
</tr>
<tr>
<td>47</td>
<td>Mx+C</td>
<td>pT4pN1</td>
<td>IIIB</td>
<td>3/+</td>
<td>Yes</td>
<td>Lung + Liver</td>
<td>11 M</td>
<td>51 M</td>
<td>Died</td>
</tr>
<tr>
<td>42</td>
<td>Mx+C</td>
<td>pT2pN2</td>
<td>IIIA</td>
<td>3/+</td>
<td>Yes</td>
<td>Lung + Brain</td>
<td>35 M</td>
<td>72 M</td>
<td>Died</td>
</tr>
<tr>
<td>71</td>
<td>Mx+S</td>
<td>pT3pN0</td>
<td>IIIB</td>
<td>3/-</td>
<td>No</td>
<td>Spine</td>
<td>63 M</td>
<td>114 M</td>
<td>Alive</td>
</tr>
</tbody>
</table>

WLE-Wide local excision, Mx- Mastectomy, S- Axillary node sampling, C- Axillary node clearance, Group I- Lipofilling with ADRC, TNM – Tumour, node and metastasis, VI- Vascular invasion, Mets-Metastasis, M- Months

The mean time from oncological surgery to the fat grafting procedure was 58 months (range 20 months to 17 years). Table 1 indicates baseline tumour characteristics before lipofilling in patients with a history of breast cancer.

The mean volume of fat injected was 240ml (range 80-350 ml) per breast. No immediate postoperative complications were seen. The mean hospital stay was one day. All our patients had a planned overnight stay for pain relief. Two patients needed prolonged stay, one due to painful swelling at donor site (thighs) while the other had a hematoma. Both were managed conservatively and discharged within three days. Recipient site infection and superficial skin necrosis (< 1 cm related to extensive scar release the following radiotherapy) was seen in one patient each and both were managed in an outpatient setting with no impact on the outcome.

Patient satisfaction survey showed > 90 percent of women with significantly improved breast contour and good to excellent cosmetic outcome Fig 1-2. A total of six patients needed a second / redo procedure (11 percent) due to resorption of grafted fat.

During follow-up, 18 patients (33 percent) had palpable nodules or lumps. Further investigations with mammography/ultrasound confirmed benign changes in all cases. The predominant finding was fat necrosis in 13 cases (24 percent), oil cyst in 3 cases and calcifications in 2cases. A percutaneous biopsy was required in 6 patients (11.3%) and one case needed surgical excision of lump. All had benign histological findings. We observed a higher risk of imaging changes in group I compared to group II (p = 0.049). The clinical and oncological outcome of lipofilling in 2 patient groups is compared in Table 2. The outcome of lipofilling with or without ADRC’s is presented in Table 3.

At 50 months’ follow-up following lipofilling procedure (range 20-80 months) and of 171 months after primary breast cancer surgery (range 36-240 months), no local recurrences were observed. Four patients developed distant metastasis at an average of 28 months following lipofilling and 56.6 months from primary cancer surgery. All four patients had advanced disease, three had mastectomies and received adjuvant chemo/radiotherapy. Only one patient out of 4 is alive with stable bone metastasis at 63 months while the other three patients died of visceral metastasis. The overall oncologic event rate was 7.5 percent (1.50 % per annum) Table 4.

Discussion

Despite various reconstructive options to restore breast symmetry, lipofilling has a unique place as used successfully not only to reconstruct BCS defects but also to improve cosmetic results following PMR. There is evidence that up to 30 percent of women following BCS will have a residual deformity that might require surgical intervention [14-18]. In this series almost 50 percent of patients had lipofilling to correct BCS defects.

We found it a safe technique without any significant post-operative complications. We found 1.7 percent of our patients developed breast infection that is slightly higher compared to the acceptable rate of 0.6-1.1% [13]. It could be explained by the fact that none of our patients received prophylactic antibiotics that are given routinely in most centres.

To date, there is no consensus that lipofilling technique confers the best results. Nor there is any specific method to assess fat resorption. Calculated fat reabsorption rate and need for re-injection reported in the literature ranges from 8% to 40% [13, 17]. In this study, no objective method was used to assess fat resorption. However, we observed that the need for re-do procedure in our patients (11 percent) is comparatively lower than that reported in the literature. It could be due to our surgical technique involving minimal handling of harvested fat, use of ADRC’s and larger volume of fat graft compared to other centres. The other possible explanation could be the lower cosmetic expectations of our patients compared to other major centres.

Published literature has already excluded any increase in the risk of imaging changes or interference in cancer detection following fat grafting to the breast [18, 19]. In our experience, imaging changes after lipofilling were almost all benign. The risk of imaging changes and biopsy following lipofilling was not significantly higher compared to other breast procedures [20]. Fat necrosis was the predominant imaging finding, most were a
few millimetres in size and managed conservatively.

To date, there is no randomised controlled trial to evaluate the oncological risk of lipofilling to breast tissue. As cancer histology, staging and treatment can directly influence the oncological outcomes, the direct effect of lipofilling on the cancer recurrence cannot be measured accurately without a control group. RESTORE-2 was the first prospective clinical trial using ADRC enriched fat grafting for breast and reported no adverse outcome at 12 months oncological follow-up in 71 patients [21].

In another review by Largo et al. [22] that included 1453 patients with fat grafting to healthy breast tissue, only two cases (0.1 percent) of breast cancer were reported with one in an area not grafted with fat. Petit et al. [23] and Rigotti et al. [24] reported local recurrence rates of 1.35 - 2.19 percent and 0.72 percent per year respectively. The other series reported the risk of local recurrence following lipofilling similar to those without fat grafting. Emmanuel Delay [7] published the largest series of 880 fat grafting procedures to the breast over ten years and showed the procedure is safe and effective with no increased rate of recurrence or new cancer development. Recently published studies and meta-analysis have also established the oncological safety of lipofilling in breast cancer patients [9-11, 25, 26]. Only a few studies have reported metastasis following lipofilling in the range of 5.9 to 7.6 percent [24, 27]. There are a few recent case reports of local recurrence of invasive cancer within 4 to 10 months after fat grafting raising the controversy and possibility of promoting latent cancer or metastasis [28, 29].

In this series with almost five years’ follow-up following the lipofilling procedure, we observed no local recurrences or new cancers in either patient group. Four of our patients developed metastasis. We found no statistically significant difference in the risk of metastasis in patients underwent lipofilling with or without ADRC’s. Three out of four patients with metastasis had stage III disease and relapsed more than five years following cancer surgery. The reported five-year survival in stage III disease is reported to be 72 percent and as expected these patients were at a higher risk of distant metastases. Our results support the safety of lipofilling procedure in breast cancer patients. There is no evidence to suggest increased breast cancer occurrence or recurrence after lipofilling but we do understand the limitations of this observational study with small sample size and lack of long-term oncological follow-up.

Conclusion
Based on our experience we suggest that lipofilling is a safe procedure for breast reconstruction with no increased risk of cancer recurrence. In our practice, it has become an indispensable adjunct to breast reconstruction conferring a good cosmetic outcome. Further, multicentre studies with longer follow-up are needed to support our results and develop guidelines for the implementation of fat grafting in breast reconstruction.

Abbreviations
BCS (Breast Conservation Surgery); BCT (Breast Conservation Therapy); PMR (Post-Mastectomy Reconstruction); ADRC’s (Adipose Derived Regenerative Cells); NSSM (Nipple and Skin Sparing Mastectomy)

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None

Authors’ Statements
Competing Interests
The authors declare no conflict of interest.

Statement of Ethical Standards
Ethical approval was not required for the study as this was the routine follow-up of a surgical procedure under NICE guidance. Informed consent was obtained from patients prior to use of images in publication.

References


