

Breast Lipofilling: A Review of Current Practice

Abdul Kasem, Umar Wazir, Hannah Headon, Kefah Mokbel

The London Breast Institute, Princess Grace Hospital, London, UK

Lipofilling is a reconstructive and aesthetic technique that has recently grown in popularity and is increasingly being used in breast surgery. Previous concerns had been raised regarding its safety when used for remodelling and reconstruction of the breast; however, these concerns have since been dismissed. Over the subsequent two decades, little evidence has been found to support these early theoretical concerns, and growing numbers of proponents of the procedure are confident in its safety. Many developments and refinements in the technique have taken place in recent years, and several studies have been published regarding the safety of lipofilling in the breast. We reviewed the current literature regarding the use of different lipofilling techniques as well as the current evidence regarding the oncological safety of the procedure in patients seeking aesthetic breast enhancement and in patients requiring reconstruction after treatment for breast cancer.

Keywords Mammoplasty / Breast neoplasms / Lipectomy / Transplantation

Received: 10 Aug 2014 • Revised: 11 Oct 2014 • Accepted: 3 Nov 2014
 pISSN: 2234-6163 • eISSN: 2234-6171 • <http://dx.doi.org/10.5999/aps.2015.42.2.126> • Arch Plast Surg 2015;42:126-130

INTRODUCTION

The use of autologous fat for filling defects and remodelling body contours was reported over a century ago. The earliest description of the use of autologous fat as a filler is widely acknowledged to be by Czerny [1] in 1895, who augmented a breast with a lipoma removed from the patient's back [2]. Grafting of adipose tissue was a well-described procedure in the earlier part of the twentieth century [3]. However, it fell into disuse after concerns were raised in 1950 regarding the eventual loss of volume in such grafts [4].

The current usage of lipofilling dates back to 1987, when Bircoll [5] described a method that coupled liposuction with autologous transplantation of the harvested fat in the breast. The major advantage cited for this new technique was the presence of virtually limitless donor tissue that was soft and malleable [5].

However, there were early concerns that the procedure would cause scarring in the breast, which could interfere with breast

screening. This prompted the American Society of Plastic and Reconstructive Surgeons to release a statement in 1987 condemning the use of the procedure [6].

However, at approximately the same time, a growing body of literature emerged suggesting that other procedures performed on the breast, such as reduction mammoplasties, also lead to scarring in the breast that is visible during breast screening. Such scarring can be far in excess of what would be expected after lipofilling [7,8]. Furthermore, subsequent studies shown that these artefacts do not appreciably affect screening [9].

In addition, several case reports and case series have emerged over the years, which have not provided any definitive evidence to support these and other concerns. There have been significant refinements to the procedure since the initial description, resulting in increased confidence in its use, including for breast reconstruction and remodelling [10]. The recommendation against the procedure by the American Society of Plastic and Reconstructive Surgeons, now known as the American Society

Correspondence: Kefah Mokbel
 The London Breast Institute, Princess
 Grace Hospital, 45 Nottingham Place,
 London W1U 5NY, UK
 Tel: +44-75-8350-0187
 Fax: +44-75-8350-0187
 E-mail: kefahmokbel@hotmail.com

This study was funded by grants from
 the Breast Cancer Hope Foundation
 (London, UK).

No potential conflict of interest relevant
 to this article was reported.

of Plastic Surgeons, was reversed in 2009 [11].

CURRENT LIPOFILLING TECHNIQUES

Several techniques for fat harvesting and lipofilling are currently being employed. In all of these techniques, autologous fat is harvested, processed, and grafted. There is a paucity of high-level evidence to strongly recommend one choice over another. However, some evidence relevant for clinical decision-making has emerged over recent years [10].

Fat harvesting

The majority of extant lipofilling techniques employ a similar approach to fat harvesting, with variations between individual practitioners.

In the course of fat harvesting, a blunt cannula is inserted through a stab incision into fat tissue engorged with tumescent fluid consisting of intravenous normal saline, epinephrine, and local anaesthetics. Suction can be applied using a syringe or a pump system [12]. The shear stress exerted on harvested fat has been determined to be a factor affecting adipocyte viability, with low shear stress leading to improved graft survival. In contrast, adipocytes have been shown to tolerate a wide range of pressures (−0.85 to 6 atm) [13]. In addition, the bore of the cannula has been identified as a factor in graft viability, with a 5–6 mm cannula yielding superior results compared to smaller bores [14,15]. It has also been noted that freezing samples leads to increased adipocyte death, whereas samples stored at 4°C have a viability similar to fresh samples and can be stored for up to two weeks [14].

Some practitioners advocate a “dry” method without the tumescent fluid. Cell viability in samples harvested in this manner has been found to be similar to that observed in samples harvested by the “wet” method [16]. However, the “dry” technique may lead to a greater requirement for analgesics [12].

Another technique with a distinct approach to fat harvesting is the Berlin autologous lipotransplantation, which involves the use of a proprietary water-jet system to harvest the tissue and collect it in a closed container [17]. This technique is said to have the advantages of minimal bruising and postoperative pain, faster harvesting time, and greater sterility. However, it should be noted that the apparatus is proprietary, and the studies cited in its support await external validation.

Fat processing

Ensuring graft viability is the focus of the various techniques for processing graft material. Fat grafting in the earlier part of the

last century did not involve any special processing. However, the results of such grafts were very unpredictable, as was noted in the seminal article by Peer [4] in 1950.

The strategies currently in use to improve graft survival vary significantly. This may be a function of the lack of clarity, let alone consensus, regarding the hierarchy of factors leading to better graft survival. Regardless, it is widely acknowledged that harvested fat tissue is far from inert, and that careful preparation may improve graft survival and reduce scarring [18].

The canonical method described by Bircoll [5] involves treating harvested tissue with insulin to improve cell survival. Similarly, vascular endothelial growth factor [19] and coenzyme Q10 [20] have been suggested as a treatment for improving graft survival. Little clinical evidence supports the efficacy of these or other similar strategies for improving graft viability.

The most widespread methodology is that described by Coleman, in which harvested tissue in syringes is refined by centrifugation in an essentially closed system. The supernatant fat and the lower, most aqueous layers are discarded, leaving concentrated viable fat cells [2]. Concentrating cells in this manner is expected to reduce postoperative volume loss [21]. Other authors advocate sedimentation [22], or washing the harvested tissue with saline and sterile gauze [23].

There is no clear evidence favouring one method over the other. Centrifugation unsurprisingly results in samples with better concentrations [24]. One study suggested that the viability of adipocytes suspended in fat was not impacted by centrifugation [25]. In contrast, Kim et al. [26] found that the ideal conditions for centrifugation are 3,000 rpm for three minutes, and that cell viability declines after five minutes of centrifugation. However, Rohrich et al. [27] suggested that centrifugation does not improve cell survival in fresh samples. Moreover, Conde-Green et al. [28] agreed that cell survival did not improve; however, they also noted that centrifugation resulted in good volume retention. Nevertheless, the majority of these studies were performed *in vitro* or involved a limited number of patients. Therefore, a definitive recommendation cannot be made without higher-level clinical evidence.

The role of stem cells in the viability of fat grafts has been increasingly recognised. Furthermore, adipose tissue has been identified as a readily available source of stem cells [29]. It has been observed that harvested adipose tissue contains relatively few stem cells. Therefore, studies have attempted to characterise the ability of various techniques to retain adipose-derived stem cells. A study including 51 patients indicated that serum lavage preserved more pre-adipocytes [30]. Pfaff et al. [31] reported that the preservation of adipose-derived stem cells was better after washing the grafts by Telfa-rolling compared to the preserva-

tion after centrifugation.

Matsumoto et al. [32] proposed a technique that they labelled cell-assisted lipotransfer, in which harvested fat tissue intended for grafting is enriched with adipose-derived stem cells. The adipose-derived stem cells can be extracted from the stromal vascular fraction and possibly cultured *ex vivo*. A recent randomised control trial suggested that this procedure does result in significant improvements in retaining graft volume [33]. In contrast, an internal trial comparing cell-assisted lipotransfer to Berlin autologous lipotransplantation demonstrated no significantly different results [34]. These results await external validation, and have yet to be replicated by other groups.

An alternative technique is mega-volume autologous lipotransfer after pre-grafting tissue expansion. Tissue expansion is achieved in the breast by using a BRAVA vacuum device (Brava LLC., Miami, FL, USA) over a period of months. It has been proposed that this leads to an increase in vasculature and causes the congenital bands to loosen, which makes it possible to transfer and support larger volumes of graft tissue. The proponents of this method have published studies with a cohort of approximately 500 patients, and have shown encouraging results in terms of volumes achieved and retained [35,36]. However, it is a cumbersome procedure requiring a high level of dedication on the part of the patient [37]. Furthermore, the results of the original cohort have yet to be replicated and the mechanism of action described by the authors does not take into account the current consensus regarding graft survival.

CLINICAL CONSIDERATIONS

Breast cancer imaging

There were initial concerns regarding the potential effect of lipofilling on cancer screening. Specifically, it was suggested that the micro-calcifications introduced by the procedure might be indistinguishable from potentially malignant findings. As alluded to above, this led to the 1987 recommendation against the procedure by the American Society of Plastic and Reconstructive Surgeons [6]. These concerns have long been dismissed. Studies shortly after the Society's recommendation indicated that other elective procedures, such as breast reduction mammoplasty, lead to similar artefacts [9]. It has been amply proven that screening procedures can easily differentiate between benign and malignant micro-calcifications [38].

Oncological safety

Theoretical concerns were raised regarding the effect of fat grafts enriched with stem cells on the microenvironment of the breast, especially concerning the oncological safety [39]. There

is currently no strong high-level evidence to support these concerns. In the cases of lipofilling reported to date, only two patients developed cancer after the procedure [2,10]. Furthermore, Zocchi and Zuliani [40] followed 181 patients for a decade after they underwent the procedure and reported no cases of *de novo* carcinogenesis.

The evidence regarding the safety of the procedure in patients who have already been treated for breast cancer is similarly sparse, but increasing. In a recent randomised controlled trial investigating the use of cell-assisted lipotransfer in the treatment of post-mastectomy defects, no evidence of recurrence was found [41]. Among the 744 patients included in the currently available studies on breast cancer patients who underwent lipofilling, only 14 (1.88%) recurrences were identified [41-47].

Petit et al. [43] reported on a cohort of 321 patients with primary breast cancer who underwent lipofilling after treatment for the cancer. Each member of the cohort was compared to two matched controls. There was no significant difference in the overall risk of loco-regional recurrence [43]. Sub-group analysis suggested that a higher risk might exist in lipofilling patients who had been treated *in situ* for a neoplasia [43].

This issue was further explored in a matched cohort analysis of 118 patients with primary intra-epithelial neoplasias (mainly ductal carcinoma *in situ*) who had undergone lipofilling and were matched with two suitable controls. A statistically significant increase in local events was seen in the lipofilling group (6 cases vs. 3 cases, $P = 0.02$) [44]. Overall, the evidence suggests that the risk of neoplastic recurrence is low, with a caveat regarding the subset of the population with primary intra-epithelial neoplasia. However, the small sample size, retrospective nature of the study, and lack of data regarding the extent of the primary ductal carcinoma *in situ* and radiation treatment preclude any meaningful conclusions. Furthermore, these findings have yet to be replicated.

CONCLUSIONS

The experience of the last two decades has supported the use of lipofilling as a safe reconstructive technique. Whilst high-level evidence is still awaited, the use of this technique has not been associated with an increase in the risk of oncogenesis, or indeed in the overall risk of recurrence in patients with a primary invasive breast cancer. However, patients with intra-epithelial lesions such as ductal carcinoma *in situ*, especially those younger than 50 undergoing breast-conserving surgery for high grade ductal carcinoma *in situ* with a high proliferation index, should be informed of the questions that have been raised regarding a possibly higher risk of local recurrence and the need for further re-

search on this topic.

Of the refinements of the Coleman technique, the most extensive base of evidence supports cell-assisted lipotransfer. However, further studies are required to build a credible consensus regarding the optimal technique.

REFERENCES

1. Czerny V. Plastischer ersatz der brustdruse durch ein lipom. *Verhandl Deutsche Ges Chir* 1895;24:216-7.
2. Coleman SR, Saboeiro AP. Fat grafting to the breast revisited: safety and efficacy. *Plast Reconstr Surg* 2007;119:775-85.
3. Lexer E. Freie fettransplantation. *Dtsch Med Wochenschr* 1910;36:340.
4. Peer LA. Loss of volume in human fat grafts. *Plast Reconstr Surg* 1950;5:217.
5. Bircoll M. Cosmetic breast augmentation utilizing autologous fat and liposuction techniques. *Plast Reconstr Surg* 1987;79:267-71.
6. Report on autologous fat transplantation. ASPRS Ad-Hoc Committee on New Procedures, September 30, 1987. *Plast Surg Nurs* 1987;7:140-1.
7. Brown FE, Sargent SK, Cohen SR, et al. Mammographic changes following reduction mammoplasty. *Plast Reconstr Surg* 1987;80:691-8.
8. Isaacs G, Rozner L, Tudball C. Breast lumps after reduction mammoplasty. *Ann Plast Surg* 1985;15:394-9.
9. Danikas D, Theodorou SJ, Kokkalis G, et al. Mammographic findings following reduction mammoplasty. *Aesthetic Plast Surg* 2001;25:283-5.
10. Largo RD, Tchang LA, Mele V, et al. Efficacy, safety and complications of autologous fat grafting to healthy breast tissue: a systematic review. *J Plast Reconstr Aesthet Surg* 2014;67:437-48.
11. American Society of Plastic Surgeons. Fat transfer/fat graft and fat injection: ASPS guiding principles [Internet]. Arlington Heights, IL: American Society of Plastic Surgeons; 2009 [cited 2014 Dec 24]. Available from: <http://www.plastic-surgery.org/Documents/medical-professionals/health-policy/guiding-principles/ASPS-Fat-Transfer-Graft-Guiding-Principles.pdf>.
12. Klein JA. Tumescence technique for local anesthesia improves safety in large-volume liposuction. *Plast Reconstr Surg* 1993;92:1085-98.
13. Lee JH, Kirkham JC, McCormack MC, et al. The effect of pressure and shear on autologous fat grafting. *Plast Reconstr Surg* 2013;131:1125-36.
14. Erdim M, Tezel E, Numanoglu A, et al. The effects of the size of liposuction cannula on adipocyte survival and the optimum temperature for fat graft storage: an experimental study. *J Plast Reconstr Aesthet Surg* 2009;62:1210-4.
15. Kirkham JC, Lee JH, Medina MA 3rd, et al. The impact of liposuction cannula size on adipocyte viability. *Ann Plast Surg* 2012;69:479-81.
16. Agostini T, Lazzeri D, Pini A, et al. Wet and dry techniques for structural fat graft harvesting: histomorphometric and cell viability assessments of lipoaspirated samples. *Plast Reconstr Surg* 2012;130:331e-339e.
17. Ueberreiter K, von Finckenstein JG, Cromme F, et al. BEAULI: a new and easy method for large-volume fat grafts. *Handchir Mikrochir Plast Chir* 2010;42:379-85.
18. Smith P, Adams WP Jr, Lipschitz AH, et al. Autologous human fat grafting: effect of harvesting and preparation techniques on adipocyte graft survival. *Plast Reconstr Surg* 2006;117:1836-44.
19. Chung CW, Marra KG, Li H, et al. VEGF microsphere technology to enhance vascularization in fat grafting. *Ann Plast Surg* 2012;69:213-9.
20. Witort EJ, Pattarino J, Papucci L, et al. Autologous lipofilling: coenzyme Q10 can rescue adipocytes from stress-induced apoptotic death. *Plast Reconstr Surg* 2007;119:1191-9.
21. Coleman SR. Hand rejuvenation with structural fat grafting. *Plast Reconstr Surg* 2002;110:1731-44.
22. Munch DP. Breast augmentation with autologous fat: experience of 96 procedures with the BEAULI-technique. *Handchir Mikrochir Plast Chir* 2013;45:80-92.
23. Li FC, Chen B, Cheng L. Breast augmentation with autologous fat injection: a report of 105 cases. *Ann Plast Surg* 2014;73 Suppl 1:S37-4.
24. Ferraro GA, De Francesco F, Tirino V, et al. Effects of a new centrifugation method on adipose cell viability for autologous fat grafting. *Aesthetic Plast Surg* 2011;35:341-8.
25. Pulsfort AK, Wolter TP, Pallua N. The effect of centrifugal forces on viability of adipocytes in centrifuged lipoaspirates. *Ann Plast Surg* 2011;66:292-5.
26. Kim IH, Yang JD, Lee DG, et al. Evaluation of centrifugation technique and effect of epinephrine on fat cell viability in autologous fat injection. *Aesthet Surg J* 2009;29:35-9.
27. Rohrich RJ, Sorokin ES, Brown SA. In search of improved fat transfer viability: a quantitative analysis of the role of centrifugation and harvest site. *Plast Reconstr Surg* 2004;113:391-5.
28. Conde-Green A, Wu I, Graham I, et al. Comparison of 3 techniques of fat grafting and cell-supplemented lipotransfer in athymic rats: a pilot study. *Aesthet Surg J* 2013;33:713-

- 21.
29. Zuk PA, Zhu M, Ashjian P, et al. Human adipose tissue is a source of multipotent stem cells. *Mol Biol Cell* 2002;13:4279-95.
30. Khater R, Atanassova P, Anastassov Y, et al. Clinical and experimental study of autologous fat grafting after processing by centrifugation and serum lavage. *Aesthetic Plast Surg* 2009;33:37-43.
31. Pfaff M, Wu W, Zellner E, et al. Processing technique for lipofilling influences adipose-derived stem cell concentration and cell viability in lipoaspirate. *Aesthetic Plast Surg* 2014;38:224-9.
32. Matsumoto D, Sato K, Gonda K, et al. Cell-assisted lipotransfer: supportive use of human adipose-derived cells for soft tissue augmentation with lipoinjection. *Tissue Eng* 2006;12:3375-82.
33. Kollé SF, Fischer-Nielsen A, Mathiasen AB, et al. Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: a randomised placebo-controlled trial. *Lancet* 2013;382:1113-20.
34. Peltoniemi HH, Salmi A, Miettinen S, et al. Stem cell enrichment does not warrant a higher graft survival in lipofilling of the breast: a prospective comparative study. *J Plast Reconstr Aesthet Surg* 2013;66:1494-503.
35. Khouri RK, Khouri RK Jr, Rigotti G, et al. Aesthetic applications of Brava-assisted megavolume fat grafting to the breasts: a 9-year, 476-patient, multicenter experience. *Plast Reconstr Surg* 2014;133:796-807.
36. Khouri RK, Eisenmann-Klein M, Cardoso E, et al. Brava and autologous fat transfer is a safe and effective breast augmentation alternative: results of a 6-year, 81-patient, prospective multicenter study. *Plast Reconstr Surg* 2012;129:1173-87.
37. Ho Quoc C, Delay E. Tolerance of pre-expansion BRAVA and fat grafting into the breast. *Ann Chir Plast Esthet* 2013;58:216-21.
38. Rubin JP, Coon D, Zuley M, et al. Mammographic changes after fat transfer to the breast compared with changes after breast reduction: a blinded study. *Plast Reconstr Surg* 2012;129:1029-38.
39. Lohsiriwat V, Curigliano G, Rietjens M, et al. Autologous fat transplantation in patients with breast cancer: "silencing" or "fueling" cancer recurrence? *Breast* 2011;20:351-7.
40. Zocchi ML, Zuliani F. Bicompartimental breast liposculpting. *Aesthetic Plast Surg* 2008;32:313-28.
41. Perez-Cano R, Vranckx JJ, Lasso JM, et al. Prospective trial of adipose-derived regenerative cell (ADRC)-enriched fat grafting for partial mastectomy defects: the RESTORE-2 trial. *Eur J Surg Oncol* 2012;38:382-9.
42. Semprini G, Cattin F, Zanin C, et al. About locoregional recurrence risk after lipofilling in breast cancer patients: our experience. *Minerva Chir* 2014;69:91-6.
43. Petit JY, Botteri E, Lohsiriwat V, et al. Locoregional recurrence risk after lipofilling in breast cancer patients. *Ann Oncol* 2012;23:582-8.
44. Petit JY, Rietjens M, Botteri E, et al. Evaluation of fat grafting safety in patients with intraepithelial neoplasia: a matched-cohort study. *Ann Oncol* 2013;24:1479-84.
45. Sarfati I, Ihrai T, Duvernay A, et al. Autologous fat grafting to the postmastectomy irradiated chest wall prior to breast implant reconstruction: a series of 68 patients. *Ann Chir Plast Esthet* 2013;58:35-40.
46. Iannace C, Di Libero L, Manetta F, et al. Coleman lipofilling: experience of an Italian group and review of the literature. *Chir Ital* 2009;61:67-75.
47. Panettiè P, Marchetti L, Accorsi D. The serial free fat transfer in irradiated prosthetic breast reconstructions. *Aesthetic Plast Surg* 2009;33:695-700.