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Intratissular expansion—mediated, serial fat grafting: A step-by-step working algorithm to achieve 3D biological harmony in autologous breast reconstruction[☆]

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KEYWORDS

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Summary *Background:* Breast reconstruction involves the use of autologous tissues or implants. Occasionally, microsurgical reconstruction is not an option because of insufficient donor tissues. Fat grafting has become increasingly popular in breast surgery. The challenge with this technique is how to reconstruct a stable and living "scaffold" that resembles a breast. *Methods:* Breast reconstruction ($n = 7$) was performed using intratissular expansion with serial deflation—lipofilling sessions. Mean age of the patients was 41 years (22–53). The expander generated a vascularized capsule at 8 weeks, which demarcated a recipient site between the skin and the capsule itself, and functioned as a vascular source for angiogenesis. Serial sessions of deflation and lipofilling were initiated at 8 weeks with removal of the expander at the completion of the treatment. An average of 644 ml (range, 415 ml–950 ml) of lipoaspirate material was injected to reconstruct the breast mound. An average of 4 (range, 3 to 5) fat-grafting sessions with a 3-month interval was needed to achieve symmetry with the contralateral breast. The average follow-up was 14 months (range, 9–29 months). MRI examination was performed at 8 months to analyze tissue survival and the residual volume.

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Results: MRI examination retained tissue survival and the mean reconstructed breast volume was 386 ml (range, 231 ml–557 ml). An aesthetically pleasant breast mound was created, with a high satisfaction rate.

Conclusion: We could reconstruct an aesthetically pleasant and stable breast mound in a selected group of patients by using intratissular expansion and fat grafting.

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Introduction

The objective in breast reconstruction is an oncologically safe and aesthetically pleasing, long-lasting result. Autologous- or implant-based techniques are available and associated with known advantages and disadvantages.^{1–4} A reconstructed breast should appear natural and symmetrical, with all the apparent features of a normal-looking breast.⁵ In this respect, an autologous-based reconstruction is superior to an implant-based reconstruction.^{1,6} Unfortunately, this implies the sacrifice of unaffected anatomical regions, and tissue transfer is often not an option because of insufficient or compromised donor tissue. Eventually, the choice of the technique will depend on many patient- and surgeon-related variables such as patient's wishes, associated risk factors, clinical presentation, the surgeon's skills and training, and the available infrastructure. A third "tissue engineering" approach has been added to the breast reconstructive armamentarium: the external volume expansion (EVE) Brava-assisted fat grafting.^{7–11} This technique requires a strict, daily compliance to the Brava treatment protocol, which can be inconvenient for some patients.^{7–11} Second, there is also some morbidity associated with the use of this device.^{7–11} Previously, we described our findings in adipose tissue—engineering research.^{12,13} This research recognized the ideal adipogenic environment and brought some insight in the survival process of fat grafts.¹² Fat grafting seems to "have it all" as it simply involves a relocation of grafts without major discomfort or visible scars—it is "nature's choice of filler".¹⁴ With this technique, the challenge is to reconstruct a three-dimensional (3D), high-density, and long-term—stable tissue construct with multilayered fat injections as "building blocks." The renowned unpredictable resorption rate is a major concern when predictable and reliable results are expected.^{15–17} The "breast reconstructive" working algorithm using fat grafting should include biological and physical end-points. Biologically, harmony should be established between the graft and the recipient site, whilst the physical goal is to mold the tissue construct into a breast-like framework with specific contours, projection, and shape.⁵ This paper describes an alternative working algorithm in autologous breast reconstruction based on fat grafting and tissue expansion.

Patients and methods

Between 2011 and 2014, we performed breast reconstruction using tissue expansion and fat grafting in 7 patients (Table 1). The study methodology was approved by the local ethics committee. Three patients had a primary reconstruction, of which 2 were diagnosed with localized

ductal carcinoma in situ (DCIS). They required no further adjuvant therapy. The third primary case was a tuberous breast anomaly (Meara Type III). Four patients had a delayed reconstruction. Two of them had a previously failed prophylactic free-flap reconstruction, and 2 patients presented 4 and 8 years, respectively, after a previous mastectomy with completed adjuvant therapy.

Exclusion criteria included smokers, patients who had undergone planned adjuvant oncological treatment, insufficient donor fat tissue, unmotivated patients, and patients with unrealistic expectations regarding the volume to be reconstructed.

Expander insertion

Surgery was performed under general anesthesia. All patients were marked preoperatively in the upright position. Markings included limits of planned dissection, the existing inframammary folds, and the proposed new inframammary fold (IMF) in secondary reconstructions. Expanders (350 cc, CPX4 Contour Profile Tissue Expander, Mentor™) were inserted in a prepectoral plane with a closed suction drain (Figure 1). In secondary reconstructions, insertion was performed through an inframammary incision (4 cm length) (Figure 2). Previous scars on the skin envelope are not reopened to maintain the integrity of the skin envelope.

The expander was filled with 50 cc of NaCl 0.9% enriched with 5 cc methylene blue. Oral antibiotics were prescribed for 5 days (Amoxicillin 500 mg/Clavulanic acid 125 mg). Expansion started at week 2 postoperatively (Figure 3) and was continued for 8 weeks until the desired volume (symmetry with the contralateral side) was achieved.

Fat grafting

Coleman's structural fat grafting was performed at 8 weeks post-implant.^{18,19} In summary, donor sites (thigh, buttock area, and abdomen) were infiltrated with a liposuction solution (1 L NaCl 0.9%, 20 ml Xylocaine 1%, 1 ml Epinephrine 1.0 mg/1 ml). After a delay period of 20 min, fat was liposuctioned manually with a 50-cc syringe connected to a 3-hole Mercedes tip, 3-mm cannula. Lipoaspirate (LA) was transferred into 10-cc luer lock syringes and centrifuged at 12 g for 3 min (Sarstedt™, Centrifuge LC 24, 230 V). Before each lipofilling session, the expander was deflated and approximately one-third of its volume was extracted.

Concentrated LA was injected subcutaneously with a single-hole cannula (Coleman™ Concave Infiltration Cannula, Style I, 12g) in a layered, multidirectional fashion (Figure 1). The amount of injected fat was determined following clinical examination of the skin turgor, and care was taken not to

Table 1 Overview of patients who had an autologous breast reconstruction with fat grafting.

| Indications (n = 7) | Age | Lipofilling sessions | Follow-up (months) | Mean volume transferred per session (cc) | Total volume transferred (cc) | Total volume gained (cc) | Complications |
|---|-----------|----------------------|--------------------|--|-------------------------------|--------------------------|---|
| Failed DIEAP (prophylactic breast) | 49 | 5 | 12 | 168 | 840 | 549,64 | Scar revision |
| Failed DIEAP (BRCA patient) | 40 | 5 | 9 | 190 | 950 | 557,28 | Subcutaneous oil cyst drainage |
| Primary reconstruction (DCIS) | 37 | 4 | 11 | 177 | 710 | 231,55 | Infection of the expander (temporary removal) |
| Primary reconstruction (DCIS) | 53 | 3 | 9 | 138 | 415 | 332,86 | Oil cyst on MRI (2 × 2 cm) |
| Secondary reconstruction (5 y postop mastectomy and radiotherapy) | 35 | 4 | 16 | 155 | 620 | 262,92 | None |
| Tertiary reconstruction (8 y postop mastectomy and chemoR/) | 51 | 3 | 11 | 176 | 510 | — | None |
| Tuberous breast (Meara Type III) | 22 | 4 | 29 | 116 | 465 | — | None |
| Mean | 41 | 4 | 13.8 | 160 | 644 | N/A | N/A |

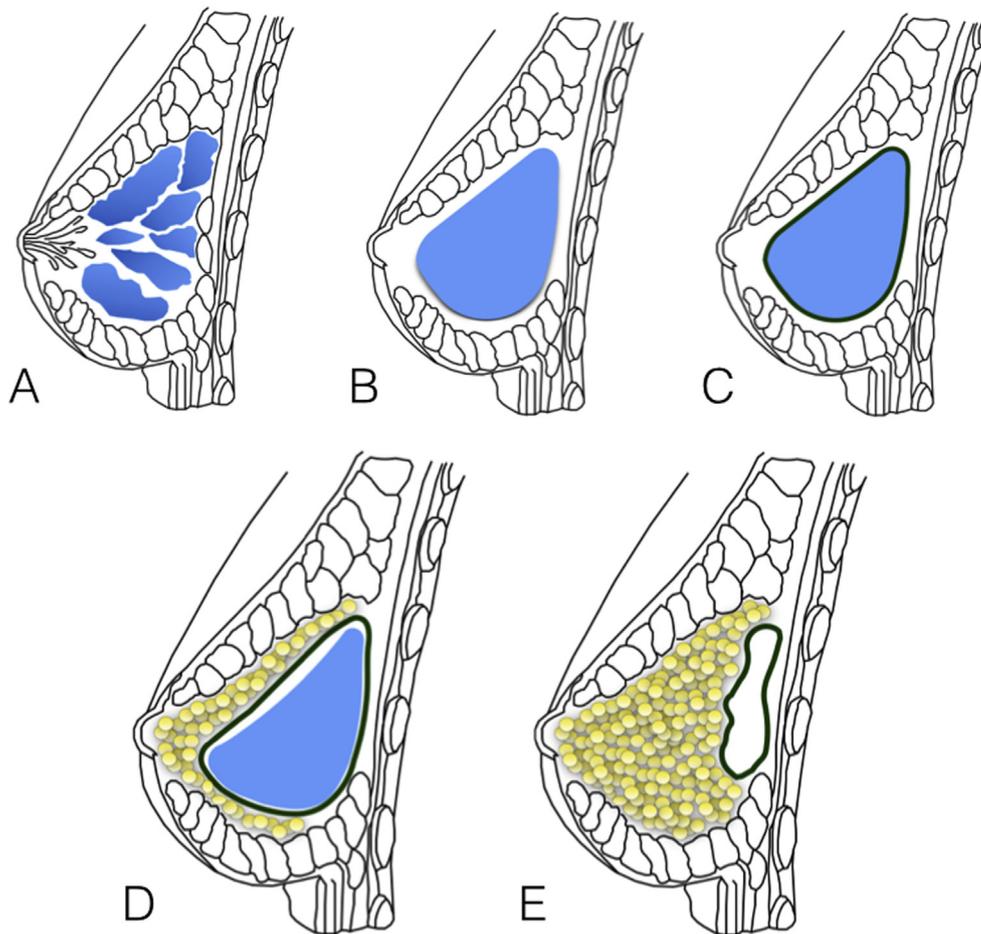


Figure 1 Normal breast anatomy (A). An expander is positioned in the prepectoral plane (B). Capsule formation as a normal physiological response (black line) (C). Serial deflation and fat grafting in the subcutaneous plane (D). Removal of the expander with capsule retained (E).

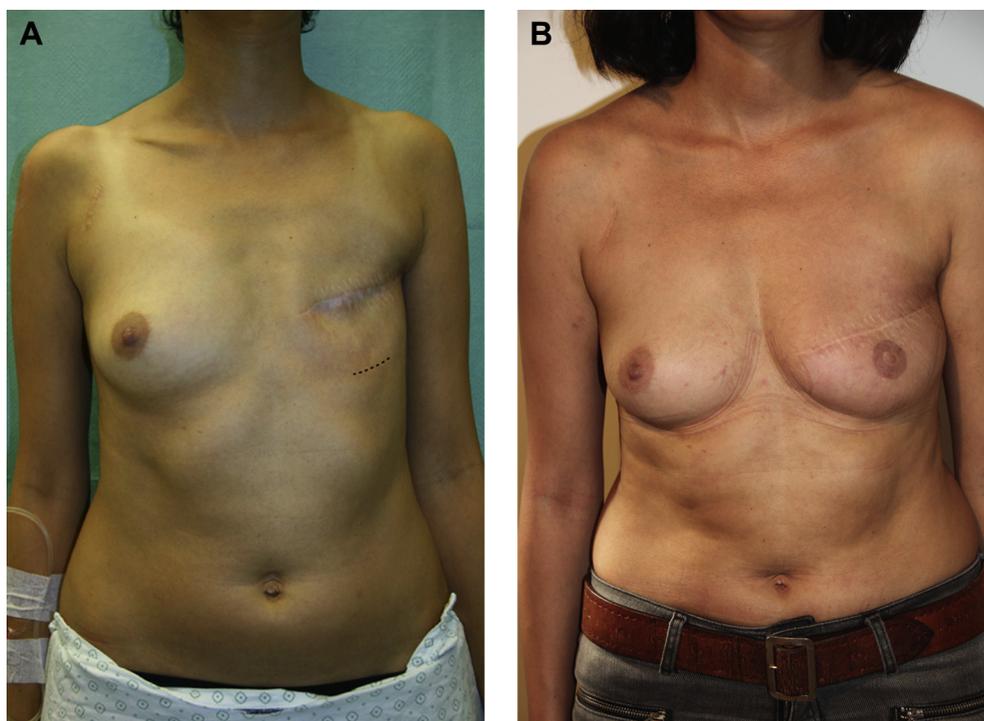


Figure 2 Secondary breast reconstruction in a 29-year-old patient (A). An expander was inserted in a prepectoral position to expand the skin envelope through an imaginary inframammary fold (IMF) incision (dotted line). She had 4 fat-grafting sessions with a total volume of fat graft injection of 620 ml. Magnetic resonance imaging was used to calculate a final volume of 262 ml at 2-year follow-up (B).

compromise the skin's turgor to avoid obstruction of the capillary perfusion. Overall, the volume of injected fat was twice the volume of the fluid extracted. Fat grafting sessions were performed with a 3-month interval until good symmetry was obtained with the contralateral side. The expander was eventually removed during the last lipofilling session through the existing inframammary incision.

Videoendoscopy

A standard carpal tunnel videoendoscope (4 mm*30°, 25 mm focal length, Smith&Nephew™) was used to visualize the morphological features of the breast recipient site in



Figure 3 The expansion not only recreates the skin envelope but also induces the formation of a capsule. This capsule is well vascularized at 8 weeks and resists the effect of the fat-grafting procedure. It prevents lipoaspirate to diffuse into the expander's pocket.

three patients. The endoscope was inserted subcutaneously through a stab incision of 4 mm in the breast envelope and data of fibrous capsule formation, vascularity, and graft positioning were recorded.

MRI analysis

All patients underwent preoperative Computerized Tomography (CT) scan or Magnetic Resonance Imaging (MRI) imaging of the chest wall region. CT scan imaging was performed in the 2 patients with previous failed free-flap reconstruction, which is the standard preoperative investigation in deep inferior epigastric artery perforator (DIEAP) flap reconstruction. All the other patients received MRI imaging preoperatively. Five patients underwent a post-operative MRI imaging of the reconstructed breast at least 9 months following surgery (Table 1). The 2 other patients were not included because of organizational problems. The volume of the reconstructed breast was calculated on T1 images. Prepectoral adipose tissue within the breast pocket was marked in the transverse sections. The designated area of fatty tissue included roughly an area located 1 cm subcutaneously and 1 cm prepectoral to avoid misinterpretation with the native tissue (Figure 4). Every section (1.5-mm thick, FS: 1.5) throughout the reconstructed volume was counted. The sum of all sections approximated the final reconstructed volume.

Morphological analysis

One patient requested additional correction of the reconstructed breast. A mastopexy-reduction procedure

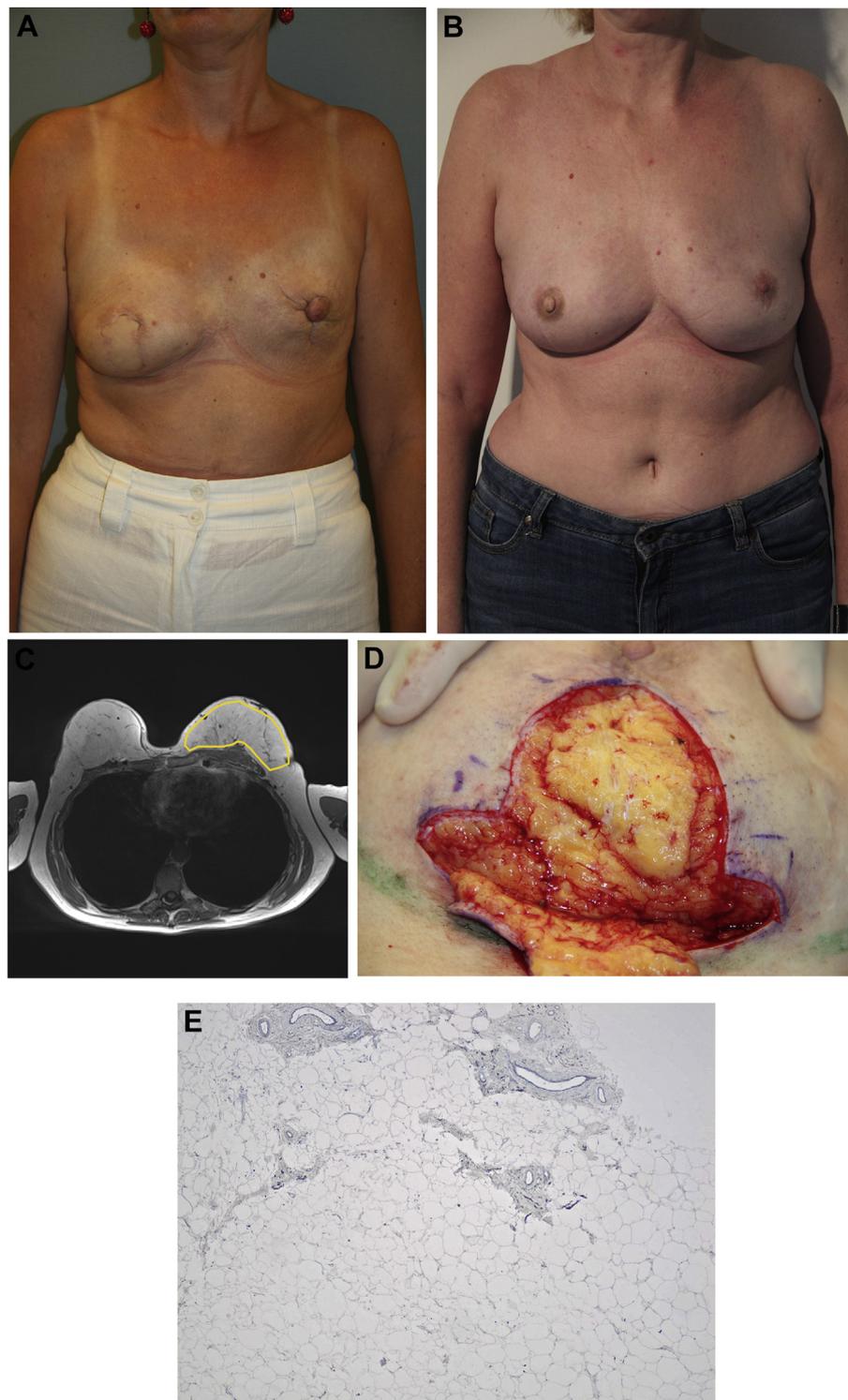


Figure 4 Breast reconstruction after previous failed flap reconstruction (BRCA patient) (A). Good symmetry with the contralateral breast at 1 year and viable adipose tissue were observed in MRI (B, C). The yellow marking shows the area of the grafted adipose tissue to measure the final volume (C). The patient requested additional mastopexy-reduction, and intraoperative views show nicely vascularized adipose tissue confirmed by histology (Orcein staining) (D, E).

was performed, and biopsies were taken from the deep layers of clearly visible grafted tissue (Figure 4). Samples were cut into 5- μ m sections, mounted onto slides, and stained with hematoxylin and eosin, elastin, and

orcein. Smooth muscle actin (SMA) and Ets-related gene (ERG) immunohistochemistry was performed to identify smooth muscle cells and endothelium in the capillaries, respectively.

Results

Patient age ranged from 22 to 53 years (mean, 41 years). The mean follow-up was 13.8 months (range, 9 to 2.5 years). One patient developed an infection of the expander, which was removed. Infection subsided with antibiotic treatment and a new expander was inserted. The ambulatory expansion protocol was uneventful and well tolerated by all patients.

Fat transfer

In total, 28 autologous fat transfers were performed to reconstruct 7 breasts (Table 1). An average of 4 lipofilling sessions (range, 3 to 5 sessions) was necessary to achieve volumetrical symmetry with the contralateral breast. The mean volume transferred per session per breast was 160 ml, and the total mean volume of grafted fat was 644 ml per breast (range, 415 ml–950 ml). During the fat graft sessions, perforation of the expander or its capsule with possible diffusion of fat grafts did not occur.

Endoscopic imaging (Figure 5)

Endoscopic imaging visualized the boundary conditions of the subcutaneous recipient site and confirmed the presence of a young vascular plexus on top of the capsule surrounding the expander. The fat grafts were structurally positioned without diffusion into the pocket occupied by the expander.

MRI volumetric analysis (Figure 4)

MRI measurements in 5 patients at least 9 months (range, 9–16 months) after the reconstruction showed a mean reconstructed volume of 386 ml (range, 231 ml–557 ml).

No areas of tissue necrosis were seen except for some diffusely located, small oil cysts measuring less than 0.5 cm. A complete collapse of the capsule was observed with no residual dead space.

Clinical assessment

In the immediate postoperative period, we retained one palpable, subcutaneous cyst of 2 cm in a primary reconstruction, which was drained with transcutaneous

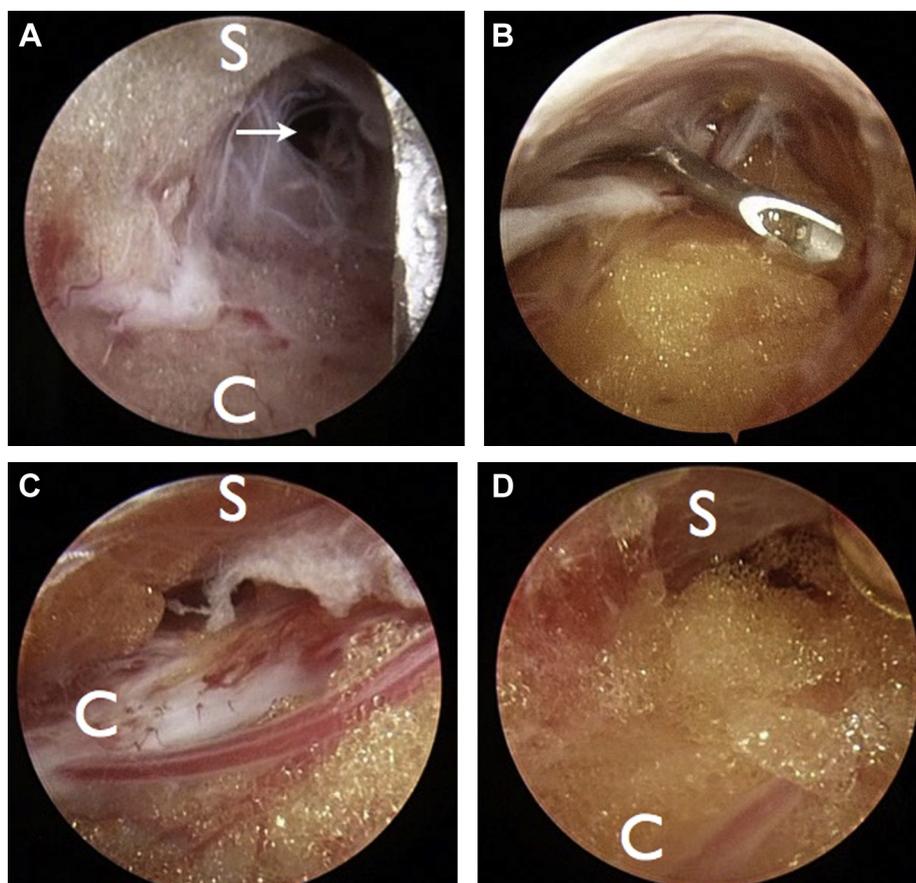


Figure 5 Intraoperative views show the boundary conditions of the compliant recipient site (arrow) (A). They define a suitable niche for fat grafts to survive. The injection cannula is introduced easily within this recipient site without the risk of perforating the capsule, which is firm enough by 8 weeks (B). The expanded capsular tissue develops into a large-scale vascular plexus and increases in vascularity by 8 weeks (C). Fat grafting is performed easily with the positioning of fat grafts in close proximity of the vascular plexus (D). Grafts appear as “islands of cells” that need to be revascularized. *S*: skin; *C*: capsule.

aspiration. In all patients, volume loss did not occur from 9 months since the last fat grafting session, and even an increase in volume of the reconstructed breast compared to the contralateral side was noticed in 2 patients (one primary reconstruction and the tuberous breast anomaly) (Figure 6). This increase was probably due to weight gain; one patient requested an additional revision mastopexy-reduction (Figure 4). Intraoperatively, vascularized fatty tissue was resected from the deep layers and sent for histological analysis, which showed healthy vascularized adipose tissue (Figure 4). In all patients, we achieved a good symmetry in relation to the contralateral breast.

Discussion

Small defects after breast conservative surgery have been treated with fat grafting. Lipofilling has been used recently for total, autologous breast reconstruction.^{7-11,14,20-23} In our department, a microsurgical breast reconstruction is our first choice, but unfortunately, it was excluded because of insufficient donor tissue. Moreover, some patients are not willing to undergo microsurgery or an implant-based reconstruction. This clinical impetus and the inconvenience of external expansion (BRAVA) led to the development of this autologous-based technique.^{12,13,18,19}



Figure 6 Tuberous breast pathology Meara Type III (A). Intratissular expansion and fat grafting with the result at 1 year (B). Breast enlargement/hypertrophy seen at 2.5 years postoperatively (C).

The challenge with lipofilling is to reconstruct 3D tissue. Strictly speaking, a liquiform material (LA) is used as a building block for a geometrical framework that should appear like a breast, has a pleasant shape and consistency, and stays stable in the long term.

Large-volume reconstructions with lipofilling alone are not feasible yet because it requires a layered, multidirectional injection technique to benefit most from plasmatic imbibition.^{15,16} Additionally, fat grafts need an anchoring framework that not only prevents dispersion but also facilitates the coordination of multicellular processes involved in survival and morphogenesis.^{24,25}

This expansion-mediated approach creates such a geometrical recipient site. The normal biological foreign-body response creates a peri-prosthetic capsule, which has a dual role. It not only acts as a barrier of the recipient site that prevents dispersion of the fat grafts within the pocket (Figure 5A), but also provides a vascular support for grafted fat (Figure 5C). Previous reports have shown that expanded capsular tissue contains a large-scale vascular plexus in its outer layer by 8 weeks.^{26–28} Our methodology creates a vascularized niche comparable to the tissue-engineering chamber, which has a highly adipogenic environment.¹²

The stretchy but resilient capsule allows a subcutaneous volume augmentation (fat grafting) and a retro-capsular volume reduction (deflation of the expander). Thus, the breast is progressively built up in a layered pattern.

Initial fat grafting seemed to be more susceptible to resorption than those in following sessions. Interestingly, on the basis of the MRI findings, injection of 100 cc of LA resulted in a 3D volume restoration of approximately 55 cc (range, 32.5 cc–80 cc).

Khouri reported his experience on megavolume fat grafting with a mean volume grafted of 225 ml per breast per operation, with an average reconstruction requiring 4.5 operations per patient.⁸ Although we are presenting a small series in a selected group of patients, the overall grafted volume was 160 ml per breast per session with an average of 4 fat-grafting sessions per patient.

From a practical point of view, we found that the fat-grafting sessions should focus initially on the lower pole, and one should avoid overinjection initially. Overinjection is assessed clinically by palpating the skin's turgor.

The interval between two consecutive fat-grafting sessions was set at 3 months. This arbitrary time period was chosen to allow the fat grafts to settle, angiogenesis to occur, and to limit the total duration of the treatment. Although resorption has been described as an ongoing phenomenon for at least 1 year, this time frame seemed to be ideal to achieve acceptable results.^{16,17}

Intraoperative videoendoscopic findings, MRI findings, histological data, and a clinical manifestation of post-operative breast hypertrophy in 2 patients confirmed homeostasis of the grafted tissue and its interaction with physiological processes (weight gain).

This reconstructive approach is an alternative for a selective group of patients: those who prefer not to have microsurgery, revision microsurgery, or implant-based reconstructions. The ideal clinical presentation is a motivated patient with small-to-moderate size breasts with sufficient donor adipose tissue. Patients who are not motivated to undergo several fat-grafting sessions or patients with larger

breasts could benefit from fat grafting with an additional implant insertion.

To call this a "tissue-engineering approach" would be overrated, but principles from our tissue-engineering research have been implemented in this working algorithm: creating space together with a supportive environment with a potent vascular source and combining it with cell sources (fat grafts) that can survive.^{12,13,29} The lipofilling technique is likely the missing, translational link to bridge the gap between tissue-engineering expectations and clinical applications in autologous breast reconstruction.

Moreover, fat grafting in breast reconstructive surgery could profit from tissue-engineering knowledge using the body's own biological processes as a vector to support the long-term homeostasis of the grafted adipose tissue. Further research in adipose tissue survival, fabrication of biocompatible matrices, and the development of cryopreservation protocols could be the beginning of ambulatory breast reconstruction based on this algorithm.

Conclusion

This reconstruction algorithm with intratissular expansion and serial fat grafting is a reconstructive strategy based on the divide between the practical, the doable, and the ideal. It can be offered to patients as an alternative for microsurgery in specific indications or as an alternative after previous failed attempts in breast reconstruction. The unpredictable resorption rate, a major concern in fat grafting, is addressed with the in vivo fabrication of a well-vascularized capsule with distinct boundaries. It is an autologous-based approach, and further technical refinements and biological research (matrix development) could possibly introduce this technique to reconstruct larger-volume breasts in the future with minimal morbidity for the patients.

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None.

Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary video related to this article can be found at <http://dx.doi.org/10.1016/j.bjps.2016.09.013>.

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