Evaluation of the role of autologous fat transfer in reduction of radiation complications in implant based breast reconstruction

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Background
Implant-based breast reconstruction (IBBR) is the most common method of reconstruction after mastectomy.(1) Postoperative radiotherapy is associated with a significant increase in complications. We report our experience with the use of autologous fat transfer (AFT) to reduce radiation complications in (IBBR) and assess survival of the transferred fat after breast radiation.

Patient and methods
This study was a prospective comparative study of 20 patients who were divided into two groups using the closed envelope technique: group (A) consisted of 10 patients treated with (AFT) during the first phase of (IBBR), group (B) consisted of 10 patients not treated with (AFT) during the first phase of (IBBR), both groups underwent postmastectomy radiotherapy (PMRT).
A survey was done to analyze radiation complications and assessment of fat survival using computed tomography.

Results
Both groups (A) and (b) consist of 10 patients (9 unilateral and one bilateral) with 11 treated breasts in both groups Mean follow-up was 6 months. Complication rates in group (A) versus group (B) were as follows: surgical-site infection, 0% versus 9.1%; Superficial mastectomy flap necrosis, 9.1% versus 18.2%; wound dehiscence, 0% versus 9.1%; minor capsular contracture grade 1 2, 36.4% versus 54.5%; major capsular contracture grade 3,4 0 percent versus 18.2%; Radiation dermatitis 9.1% versus 27.3%; no hematoma, Seroma, Full-thickness mastectomy flap necrosis nor extrusion in both groups
The average fat retention percentage after radiation was 74.82±4.21%.

Conclusions
Early data of the use of AFT as a protective measure in prepectoral IBBR in Patients with postmastectomy radiation therapy show promising results.

Keywords:
breast cancer, breast reconstruction, fat transfer, implant-based reconstruction, lipofilling, radiation

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Abbreviations: AFT, Autologous Fat Transfer; IBBR, Implant-Based Breast Reconstruction; PMRT, Postmastectomy Radiotherapy; XRT, radiation therapy.

Introduction

The most popular kind of postmastectomy reconstruction is implant-based breast reconstruction (IBBR), which has a low complication profile, quick recovery times, low cost, and attractive results [1]. In the United States, 107 238 individuals had postmastectomy breast reconstruction in 2019, and 72.306 of them underwent 2-stage IBR [1]. and [2] have demonstrated that immediate breast reconstruction can produce very patient-satisfying cosmetic results without postponing adjuvant chemotherapy or radiation treatment (XRT) or raising the risk of cancer recurrence [3–7].

Adjuvant breast XRT is performed in ~40% of patients requiring mastectomy and therefore has significant implications for postmastectomy breast reconstruction [7–10]. Implant-based breast reconstruction performed in the setting of postoperative XRT is associated with a significant increase in complications, including dehiscence, capsular contracture, infection, and even reconstruction failure, as well as the risk of unfavorable cosmesis [7,11,12]. In the long term, greater resistance to expansion, pain, capsular contracture, thinning of the skin, and visibility of the prosthesis were observed [13,14].

Postmastectomy radiotherapy (PMRT) also results in an increased incidence of undesirable aesthetic and functional outcomes, including a tighter tissue envelope, higher position of the implant or expander on the chest wall, overlying skin lesions, poor skin flap quality, and increased scarring, due to decreased quality and quantity of breast microvascular blood supply and skin flap fibrosis [9,15,16]. These complications are inevitable, and the plastic surgeon does his best to prevent them during the first and second phases of reconstruction.

The use of AFT has been used since 2002 [17] with a significant increase in the last 20 years [18]. It is beneficial in patients undergoing (IBBR) with irradiated tissue [19], as it reduces the previously mentioned complications [20].

AFT makes it possible to correct volume, contour defects, scars, and asymmetries after (IBBR) surgery for breast cancer, as well as to increase tissue thickness and enhance irradiated tissue to optimize the final result [20], Over time, the technique has been perfected [21] and numerous studies have been published demonstrating its safety [22]

As a surgical technique, the procedure offers minimal donor site morbidity, ease of reproducibility, and long-term patient satisfaction of up to 80% [23]. Potential complications of the technique include Fat necrosis, oil cyst formation, accumulation of liquefied necrotic fat, cellulitis, and abscess, which are very rare at 8% to 12% in the literature [13,24].

In 2007, Rigotti and colleagues demonstrated significant improvement in skin and soft tissue healing after transplantation of liposuction fluid in reconstructions tissues with fibrosis due to irradiation. These investigators postulated that fat-derived cells have proangiogenic capabilities that promote tissue regeneration [17].

Patient and methods

This is a prospective comparative study. 20 patients admitted to the surgical oncology and plastic and reconstructive surgery units between April 2021 and September 2022 were recruited for the study. These 20 patients were divided using the closed envelope technique into two groups. Group (A) consisted of 10 patients who underwent autologous fat transfer (AFT) during the first stage of implant-based breast reconstruction (IBBR) and then received postmastectomy radiation therapy (PMRT). Group (B) consisted of 10 patients who underwent the first phase of IBBR reconstruction without AFT and subsequently received PMRT.

Inclusion criteria

(1) Operable breast cancer eligible for mastectomy (skin-sparing, nipple-sparing, and skin-reducing mastectomy)
(2) All patients who required postmastectomy radiation therapy (PMRT).

Exclusion criteria

(1) Patients who did not receive postmastectomy radiation.

Patients were initially evaluated by a multidisciplinary team (breast surgeon, plastic surgeon, and medical oncologist), who confirmed the diagnosis of breast cancer and prescribed the treatment plan.

Procedure

(1) Group (A)/the mastectomy incision was marked on the skin using either skin-sparing, nipple-sparing, or skin-reducing techniques with or without a separate incision for axillary clearance. In addition, the donor area for the fat was marked and the mastectomy was performed.
(2) The donor area was infiltrated with a tumescent solution (1 mg epinephrine in 500 ml saline).
(3) An atraumatic 3–4 mm suction cannula was inserted through a 4 mm incision. With a 10 mL luer-lock syringe adapted to the cannula. The amount of fat aspirated was slightly greater than necessary to compensate for the loss during preparation.

Preparation of the fat

(1) The aspirated fat was processed in the syringes, washed with normal saline, and placed in a rack for sedimentation for 15 min Sedimentation allows the formation of three layers in the syringe: oily upper layer, bloody lower layer with the infiltration solution. And a central layer containing purified fat. The central layer was transferred to a 3 ml syringe, and the others were discarded.
(2) Fat transfer was performed directly with a 1–3 ml syringe specially adapted to a 2 mm diameter cannula. Fat grafting was performed from a deep to a superficial level to realize a three-dimensional pattern in the skin flap and

increase its thickness. The amount of fat transplanted varied from patient to patient with a mean of 131.36±11.85 ml of fat grafted per breast

(3) The tissue expander was inserted in the prepectoral plane and inflated with normal saline to achieve an acceptable size compared with the normal breast without stretching the suture line.

(4) Group (B): These patients underwent the same procedure as group (A) without (AFT)

(5) Patients in both groups received postoperative radiotherapy with a dose of 45–50 Gy in 15–25 fractions using three-dimensional conformal external beam radiotherapy.

(6) All patients were followed up at 15 days, 3 months, and 6 months. Photographs were taken at each consultation. Follow-up examinations were used to detect postoperative complications.

(7) Cosmetic outcome was evaluated by both independent reviewers and the patient herself using a four-point Likert scale.

(8) Patients who received (AFT) were subjected to two breast CT examinations to assess the volume of fat, the baseline CT 1week after surgery and the second one after 3 months of surgery.

(9) CT examinations were performed with the Siemens Emotion 16 detector. The patients were lying in a prone position with the chin on the pillow and the abdomen on the lower leg pillow. This position allowed the breast to rest freely without wrinkling or compression. The following CT protocol constants were used as shown in Table 1.

(10) After examination, all images were processed and reconstructed in multi-planner views. Volume calculations were performed using a freehand technique to estimate the volume of adipose tissue. Attenuation of mixed soft tissue was used (300 to −300). The percentage of fat retention is measured based on the calculation.

$$\frac{\text{Volume of breast on } 2^{nd} \text{ examination - volume of expander}}{\text{Volume of breast on } 1^{st} \text{ examination - volume of expander}} \times 100$$

Statistical analysis of the data

Data were fed into the computer and analyzed using the software package IBM SPSS version 20.0 (Armonk, NY: IBM Corp). Qualitative data were described with numbers and percentages. The Kolmogorov-Smirnov test was used to check the normality of the distribution. Quantitative data were described with mean±standard deviation. *F*-test (ANOVA) for normally distributed quantitative variables. The significance of the obtained results was assessed at the 5% level.

Result

20 patients were divided into two groups. Group (A) consisted of 10 patients (one bilateral and 9 unilateral).

Table 1 Computed Tomography protocol

Slice thickness	1 mm
tube rotation	0.6
Collimation	0.6 mm
Pitch	1
Gap	no gap
Peak kilovoltage (PKV)	120
Milliampere (MA)	100–200
Scan field	Neck root-upper liver

Table 2 Demographics data

	Group A (*n*=10) Number (%)	Group B (*n*=10) Number (%)	*P*
Age (years)			
≤40	7 (70.0)	6 (60.0)	^{FE}P=1.000
>40	3 (30.0)	4 (40.0)	
Min. – Max.	31.0–58.0	29.0–43.0	0.444
Mean±SD.	39.40±8.19	37.0±5.16	
BMI (kg/m^2)			
≤30	3 (30.0)	4 (40.0)	^{FE}P=1.000
>30	7 (70.0)	6 (60.0)	
Min. – Max.	29.0–40.0	26.0–41.0	0.852
Mean±SD.	33.0±2.98	32.70±4.03	
Cup size			
C	8 (80.0)	7 (70.0)	^{MC}P=0.436
D	1 (10.0)	3 (30.0)	
D+	1 (10.0)	0	
DM	1 (10.0)	1 (10.0)	^{FE}P=1.000
Smoking	1 (10.0)	2 (20.0)	^{FE}P=1.000
Chemotherapy	9 (90.0)	8 (80.0)	^{FE}P=1.000

Group (B) consisted of 10 patients (one bilateral and 9 unilateral), the average patient age in Group (A) was 39.40±8.19 and in Group (B) 37.0±5.16. Patient characteristics and comorbidities are listed in Table 2.

The types of oncologic resection are detailed in Table 3. The average operative time in the group (A) was 132.50±17.68 min and in group (B) was 119.50±8.32.

Mean follow-up was 6 months (Fig. 1), Complication rates in group (A) versus group (B) were as follows: surgical-site infection, 0% versus 9.1%; Superficial mastectomy flap necrosis, 9.1% versus 18.2%; wound dehiscence, 0% versus 9.1%; minor capsular contracture grade 1 2, 36.4% versus 54.5%; major capsular contracture grade 3 4 0% versus 18.2%; Radiation dermatitis 9.1% versus 27.3%; no hematoma, Seroma, Full-thickness mastectomy flap necrosis nor extrusion in both groups Table 4.

Table 3 Oncologic resection types

Type of mastectomy	Group A (*n*=11) Number (%)	Group B (*n*=11) Number (%)
Nipple sparring	0	3 (27.3)
Nipple sparring with skin reduction	5 (45.5)	0
Skin sparing	5 (45.5)	8 (72.7)
Skin sparing with skin reduction	1 (9.1)	0

In group (A) 9 (90%) patients were satisfied with breast shape (4 of them highly satisfied) while it was only 7 (70%) in group (B) (none of them highly satisfied) (Fig. 2). While reviewers' opinion was good result about breast shape in 10 (100%) cases of group (A) (3 of them excellent result) while it was only 6 (60%) in group (B) (Fig. 3).

The average amount of injected fat was 131.36 ±11.85 ml ted/breast with an average retention percent of 74.82±4.21 after 3 months from PMRT. (Fig. 4).

Discussion

Treatment options for breast cancer continue to improve, and as such, there is growing emphasis on the quality of life of breast cancer survivors Martin and colleagues [25]. In the past decade, there has been a steady rise in the use of PMRT along with an increase in implant-based breast reconstruction Martin and

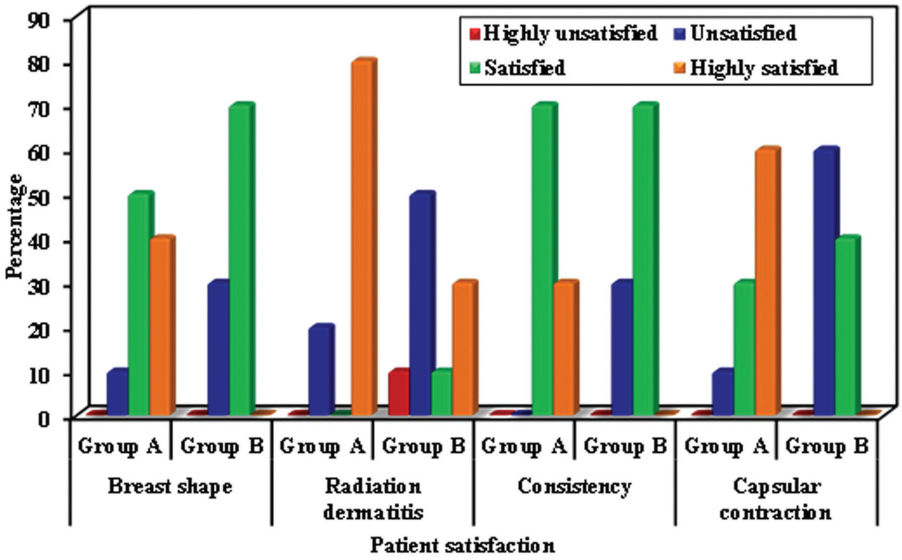
Figure 1

Skin sparing mastectomy on right side with injection of 150 ml of autologous fat and insertion of prepectoral 400 cc expander then PMRT and chemotherapy ((a) Preoperative, (b) Early Postoperative, (c) Immediate After radiotherapy, (d) 6 months after radiotherapy).

Table 4 Complication incidence

Complication	Group A (*n*=11) No. (%)	Group B (*n*=11) No. (%)	*P*
Hematoma	0	0	–
Seroma	0	0	–
Infection	0	1 (9.1)	
Wound dehiscence	0	1 (9.1)	
Skin-flap necrosis			
Superfascial flap necrosis	1 (9.1)	2 (18.2)	^{FE}P=1.000
Full-thickness flap necrosis	0	0	–
Capsular contraction			
Minor grade 1 2	4 (36.4)	6 (54.5)	0.392
Major grade 3 4	0	2 (18.2)	^{FE}P=0.476
Expander removal	0	0	–
Radiation burn	3 (27.3)	4 (36.4)	^{FE}P=1.000
Radiation dermatitis	1 (9.1)	3 (27.3)	^{FE}P=0.586

Figure 2



Comparison between the two studied groups according to patient satisfaction.

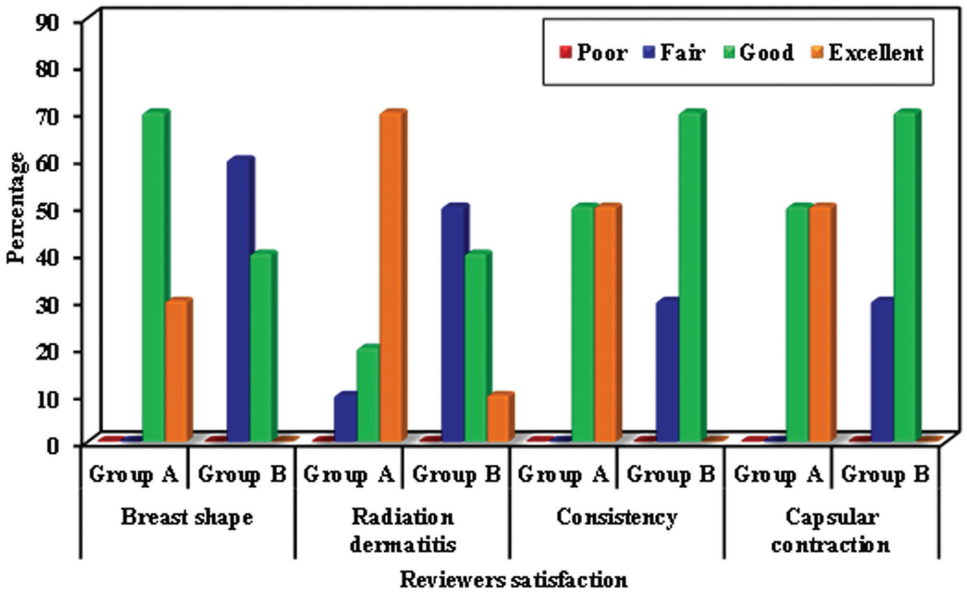
colleagues [25]. Contrary to previous recommendations for delayed autologous reconstruction when radiotherapy is planned, advances in mastectomy, reconstruction, and radiation have led to an increasing number of patients opting for immediate implant-based reconstruction Razdan and colleagues [26].

PMRT has been shown to increase the risk of complications in prosthetic reconstruction and negatively impact cosmetic outcomes, which is largely due to the microvascular damage and fibrosis of the breast soft-tissue envelope Nelson and Disa, Momoh, and colleagues [10,11].

This issue may have several partial remedies, according to reports. The main disadvantage of Kronowitz and Robb [27] delayed-immediate breast Reconstruction is the use of autologous tissue (on a radiated area). By allowing PMRT on the permanent implant, the fast-track expander exchange approach put forward by Cordeiro and colleagues [14] should reduce problems. However, there are still issues leading to extrusion, and time for expansion is frequently insufficient.

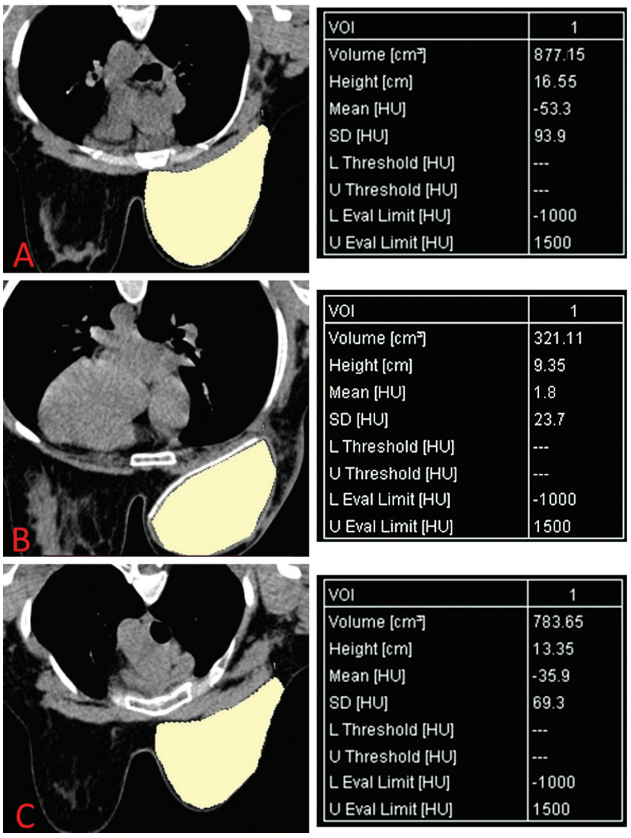
Some surgeons suggest RT first, then expander deflation and reinflation. Once more, research has shown that this is harmful to the cutaneous blood supply Celet Ozden and colleagues [28]. In the context of PMRT, the use of acellular dermal membranes has also been suggested as a way to lessen difficulties with prosthetic reconstructions Basu and Jeffers [29]. The main focus of the activity, however, is capsular contracture rather than tissue thinning and ulceration. Additionally, several

Figure 3



Comparison between the two studied groups according to reviewers' opinion.

Figure 4



(a) Volume of the breast after 1 week from the operation before PXRT (b) volume of the tissue expander c) Volume of the breast after 3months.

studies show a significant incidence of postoperative seromas, which eventually result in infection and higher expenditures Butterfield [30].

AFT offers a potential solution to prevent radiation complications. Far from inert, fat has regenerative potential, which is thought to be a function of its adipose stem cells Khouri and Khouri [31]. The AFT's regenerative potential has been found to promote angiogenesis and peripheral nerve regeneration and enhance dermal thickness and elasticity Khouri and Khouri [31]. Critically, fat grafting has also shown promise in reversing radiation-associated dermal fibrosis and improving pain and breast sensation when used to treat capsular contraction Papadopoulos and colleagues [32].

The findings of our investigation indicate clinical differences in the occurrence of complications in patients with IBBR receiving radiation whether or not AFT is used. The validity of these findings will need to be confirmed by other studies including larger number of patients.

Conclusion

Radiation-induced tissue damage is a challenge for the reconstructive surgeon, especially in the setting of IBBR. There is increasing evidence that fat grafting has beneficial effects on radiated tissue.

Based on the available evidence, AFT is a powerful tool that offers a simple technique, with low donor site morbidity and very few complications.

Our study demonstrated encouraging results when AFT was used for the reduction of radiation

complications in IBBR, expanding the choices for IBBR to a lot of cases that need PMRT. Such an approach is an accepted surgical approach from the oncologic and cosmetic aspects for women having immediate breast reconstruction.

Additional follow-ups and a larger number of patients are required to assess the long-term benefits and complications.

Also, according to our study Fat survival after radiation did not differ from survival in nonradiated breast.

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Conflicts of interest
There are no conflicts of interest.

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