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# Lipofilling and Breast Reconstruction after Partial or Total Mastectomy

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## Abstract

**Background:** To describe the fat harvesting, applications and outcomes of autologous fat grafting in breast reconstruction and to explore this promising technique with new breast reconstruction applications.

**Methods:** Literature review of publications on fat grafting.

**Results:** Lipofilling has become increasingly popular. Several modifications have been made to the procedure. The "wet" method involves fluid injection at the donor site, facilitates lipoaspiration and appears to minimize ecchymosis. Low-speed centrifugation is preferred to high-speed centrifugation, sedimentation or filtration. Fat grafting is not only good filler but also improves the cutaneous trophicity. Complications of lipofilling are minimal and include pain, infection, ecchymosis on the donor site and necrosis and calcifications on the sample site. Several systematic reviews and meta-analyses have also confirmed its oncological safety. Initially used to improve breast implant or flap reconstruction, this technique is currently being extended to exclusive immediate or delayed breast reconstruction.

**Conclusion:** Adipose tissue is an ideal filler because it is readily available, easily obtained with low donor site morbidity, repeatable, inexpensive, versatile and biocompatible. The simplicity of the surgical technique and equipment required, and the high satisfaction rate confirm that lipofilling should be included in the panel of choice of breast reconstruction techniques.

**Keywords:** Lipofilling; Breast cancer; Mastectomy; Reconstruction

## Introduction

The fat transfer or autologous fat grafting (AFG) or lipofilling (technique known since 1998) has a great impact on the breast surgery results.

A better quality of life has been described after reconstruction in patients who have had a mastectomy compared to patients who have not. However, the number of mastectomy patients asking for breast reconstruction is quite low: about 55% in United States and 35% in France [1]. This low rate can be explained by the age of patient, the difficulty to access to plastic surgery, the apprehension of a heavy surgery. This new lipofilling since the 2000s has been increasingly and change the approach to breast reconstruction [2].

This fat transfer was initially used as an adjuvant in breast reconstruction for total autologous latissimus dorsi, implant reconstruction, breast asymmetry to correct or improve the aesthetic outcome. In recent years, it has also been used for exclusive breast reconstruction.

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The aim of this work was to describe the lipofilling technique, its new indications, its limitations, its oncological safety, its complications, its results and to review the current literature on the subject.

## Role of Lipofilling

### 1. To improve tissue trophicity as shows in figure 1

Particularly in post irradiation patients, Debald and colleagues [3] found an improvement in tissue quality with mean post-radiation skin scores from 2.40 ± 0.89 to 1.21 ± 0.76 in 68 patients.

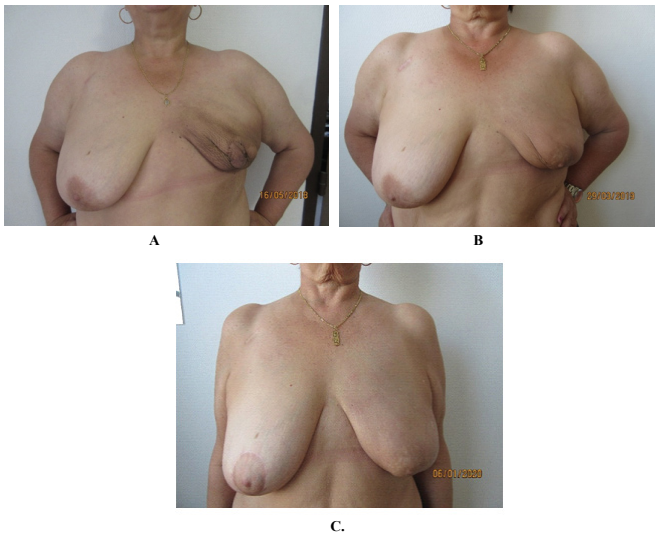

**Figure 1:** **A.** after IBR by latissimus dorsi and radiotherapy before surgery. **B.** after one lipofilling in 2018(472cc) **C.** after second lipofilling in 2019 (521cc)

### 2. To obtain a breast autologous volume

Lipofilling is a way to achieve breast reconstruction in different situation such as before with a breast implant, to complete breast implant reconstruction or flat reconstruction (Figure 2) or to use adipocyte cells as an exclusive reconstruction without an implant or flap.

It must be taken into account that the transferred fat is partially resorbed during the first three months after fat grafting as described by Ho Quoc et al. [4]. The fat resorption seems to be between 30 to 80% and the experimental studies register a variation between 50 and 90%. Ho Quoc studied in retrospective analysis 32 reconstructed breasts by total autologous latissimus dorsi flap with an average fat volume transferred of 291 cc. The volumetric study showed that intramuscular volume on the third day was measured at 284 cc and at the third month about 223 cc with an intramuscular resorption. These results suggest that muscle is an excellent receptive matrix for fat tissue.

Del Vechio et al. [5] has also estimated that about sixty percent of volume maintenance can be expected per session influencing by many factors as graft of capacity ratio, radiation, scarring, and quality of processing.

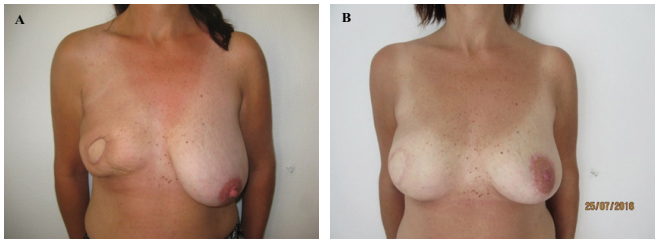

**Figure 2:** **A.** after RMI by latissimus dorsi and adiotherapy before surgery. **B.** after two lipofilling and left pexy (first 320 cc lipofilling

### 3. To get more natural consistency

Piffer et al. [6] in 2022 have shown that autologous reconstruction allowed more natural reconstruction by patients and surgeons.

### 4. To limit scars

The scar ransom is quite minimal by only 5 mm scars for liposuction compared to long flap scars.

### Technique

Breast reconstruction is carried out by experienced hospital doctors specializing in oncological and reconstructive breast surgery (prosthesis, flap, lipofilling…). The advantages and disadvantages of each technique are explained to the patients and final decision is made after discussion. The final choice of technique was made after discussion with the patient and according to her wishes and morphology.

**The harvesting technique** is the same to improve results or to get exclusive reconstruction.

If lipofilling is chosen, donor sites for the first lipofilling session is determined at the time of the preoperative consultation based on the patient's morphology and preference.

There are several natural fat deposits in the body and the surgeon should identify the most suitable area after a thorough examination of the patient. The abdomen is the most common site for fat harvesting following by is the trochanteric region (saddlebags) and the inside of the thighs and knees.

It is necessary not to remove twice from the same area as post-operative fibrosis makes liposuction difficult.

Patients were positioned in the dorsal decubitus position with arms crossed or along the body.

Surgical procedure was performed under general anesthesia. The procedures started with infiltration of the donor site ("wet" method) with adrenaline saline (1 mg of adrenaline for 1 L of saline) or sometimes without infiltration ("dry" method). The technical set-up consists of two conventional suction tubes to connect the sampling cannula

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to a Redon bottle, itself connected to a wall aspiration. Erdim et al. [7] and Kirkham et al. [8] found that the use of larger liposuction cannulas led to improved fat graft retention and quality, which further facilitated clinical outcomes.

The fat is collected by liposuction in the Redon and then distributed in syringes of 10 mL which were centrifuged for 1 min at 1000 to 3000 rpm. The purified fat obtained is separated from the liquid phase, which is eliminated.

Simonacci et al. [9] published those comparative studies investigating the effects of fat processing with centrifugation, washing, and filtration showed no significant differences in fat retention; however, filtration resulted in nodules, whereas centrifugation did not. In addition, higher centrifugation speeds were correlated with increased fluid content, decreased injectable tissue volume, and increased oil portion, which are associated with adipocyte damage.

## The fat reinjection technique

The patient is placed in a semi-seated position for the reinjections: the purified fat is reinjected through a metal cannula (3 to 5 mm).

Several small incisions are made using a needle with a blunt tip so as not to damage the tissue or the implant, and reinjection is performed in a retrograde and radial fashion in the different planes (pectoral and subcutaneous).

As revascularization starts at the periphery, the ischemic time in the center of the graft is longer [9]. Therefore, fat reinjection in multiple small volume sessions is preferable to a single injection.

Except in the case of immediate breast reconstruction, it is very important to perform fasciotomies in order to obtain a kind of skin expansion to shape the breast before and during the fat reinjection; in the case of secondary reconstruction, the skin must be freed from the breast by these multiple fasciotomies.

This is the essential condition to re-expanding the inframammary fold. In the case of immediate fat reconstruction, the first fat reinjection is made into the pectoral muscle and it is interesting to preserve the prepectoral fascia during the mastectomy in order to consolidate the injection site. For subsequent injections, the two plans (subcutaneous and pectoral) are used.

After the fat was re-injected, a fat-containing dressing was applied. Depending on the aesthetic result, further sessions could be offered at 3-to-6-month intervals. In many teams, patients were then seen in consultation after 15 days, 3 months, and then every 6 months as part of the breast cancer follow-up.

## Indications

### 1-Fat grafting in total autologous latissimus dorsi

It can be used to complete a flap-based breast reconstruction to avoid breast implant as described by Sinna [10].

In figure 3 and 4 lipofilling has been done some months after latissimus dorsi to improve breast volume.

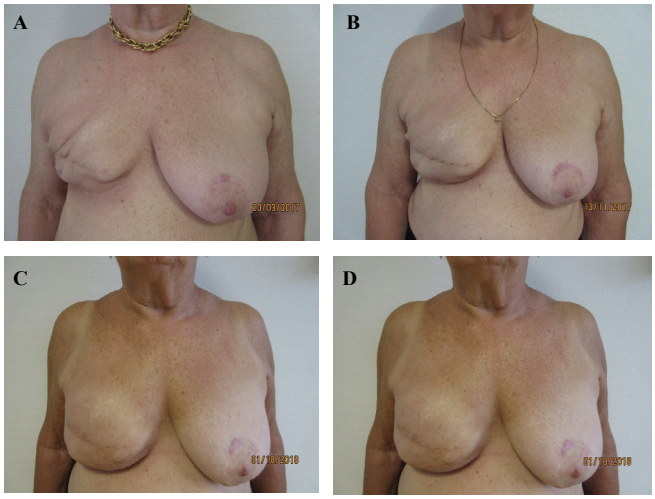


**Figure 3: A.** after mastectomy and radiotherapy. **B.** after left breast reduction. **C.** after right latissimus dorsi flap. **D.** after one lipofilling(320cc)

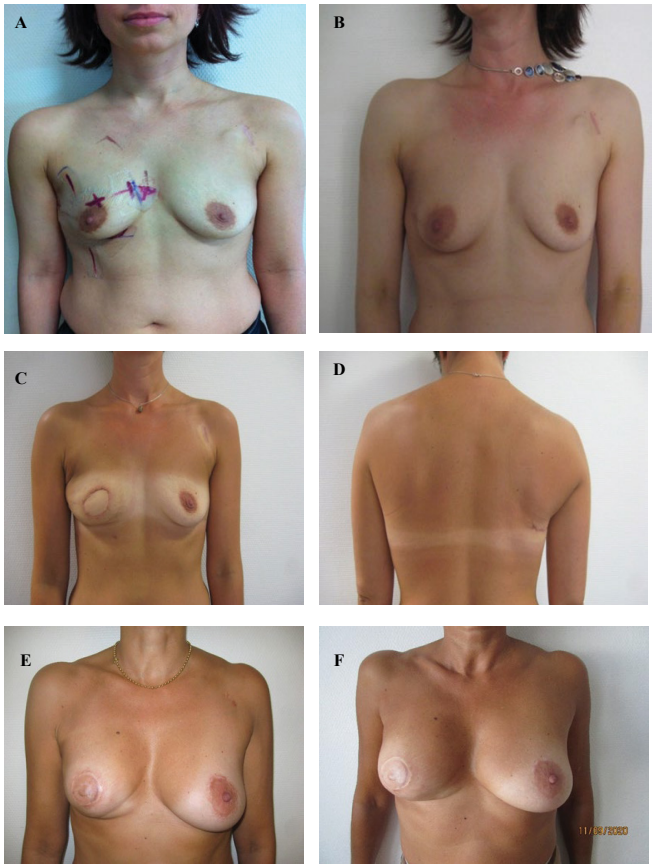


**Figure 4 A.** Chemotheray and radiotherapy before mastectomy **B.** After radiotherapy **C.** After right mastectomy and IBR by autologous **D.** Dorsi scar latissimus dorsi after chemo and radiotherapy E. After one lipofilling **F.** After second lipofilling

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In figure 5, fat grafting has two goals: the first is to improve tissue trophicity and the second to obtain more breast volume.

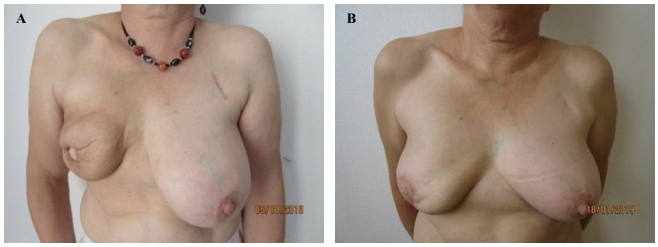

**Figure 5:** **A.** after right post radiotherapy mastectomy and IBR by autologous latissimus dorsi. **B.** After two lipofilling and left 290g reduction

## 2-Fat grafting before implant placement in irradiated chest wall

Fat grafting to the irradiated chest wall prior to implant placement might be an alternative to flap reconstruction for patients who are not suitable or who refuse this option. Sarfati and al. [11] show that the mean number fat grafting sessions was 2.3, the mean volume injected per session was 115 mL (70-275), and the mean volume of breast implants was 300 mL (185-400).

One implant explanation (1.47%) was described and the mean cosmetic result was 4.5/5.

So the pre-treatment of irradiated skin with fat grafting prior to implant-based reconstruction was evaluated positively as shown in figure 6.

**Figure 6:** **A.** Patient after bilateral mastectomy in 2004. **B.** 4 months after the first 450 cc fat grafted **C.** In 2015 Implants 250 cc right, 275 cc left **D.** 2018 inframammary field fixation and 125 cc fat grafting

Irani Y et al. [12] published that autologous fat grafting in radiated tissue prior to breast reconstruction is a safe and reliable technique. They studied 25 patients who had undergone a modified radical mastectomy followed by radiotherapy were retrieved. The mean refined fat injected volume was 160 cc and the mean number of total surgical procedures was 2.5 per patient. Prosthetic reconstruction was achieved in 23 cases and there was only two failures treated with a latissimus dorsi flap with implant. Quality of reconstruction was judged as good by both physicians and patients.

In a multicenter retrospective study published by K Razzouk and A Fitoussi [13], 136 patients who underwent mastectomy and external chest wall radiotherapy between 2014 and 2018 were selected for chest wall lipofilling and silicone implant placement were chosen. Patients were assessed for skin trophicity, thickness, and mobility and were allowed to undergo several lipofilling sessions prior to implant placement. No patient had >3 lipofilling sessions (58% received only 1 session). The reconstruction failure rate was 2.2%. The average satisfaction score was 4.7 out of 5 as evaluated by patients, 4.8 out of 5 by surgeons, and 4.8 out of 5 for nurses.

In selected cases, primary lipofilling can achieved a simple prosthetic reconstruction avoiding a flap procedure.

## 3-Fat grafting to improve breast implant reconstruction (Figure 7 and 8)

Outcomes and patient satisfaction have also been evaluated with BREAST-Q after breast implant reconstruction by Cogliandro [14]. The role of lipofilling after breast implant reconstruction showed a significant satisfaction in terms of quality of life after average number of 2.2 lipofilling with a mean follow-up of 2.5 years After further analysis of the Breast Q. questionnaire, they found that patients in group A (with secondary lipofilling had significantly better postoperative results than patients from group B (without lipofilling) regarding the following items: the ability to wear more fitted clothing; the reconstructed breast softness; symmetry (breasts of equal size relative to the other); reconstructed breast appearance and feel; amount of implant rippling perceived by the patients; and psychosocial well-being and physical well-being: chest and upper body.

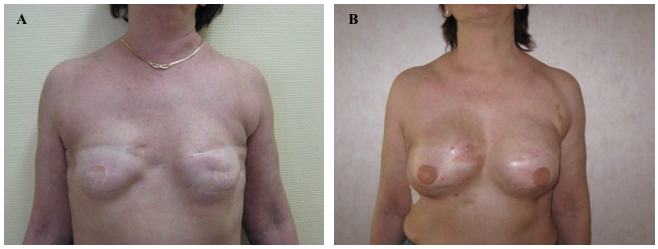

**Figure 7:** **A.** Before bilateral fat grafting (420 ml) **B.** After bilateral fat grafting (420 ml)

## 4-Fat grafting to improve breast asymmetry after conservative breast treatment

Lipofilling is being performed either as a part of oncoplastic technique or alone by itself to correct defects and asymmetry after oncological breast cancer surgery by Hamza et al [15].

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**Figure 8: A and B**: 2014 Nipple sparing mastectomy (1200g) reconstructed with implant 500 ml C. After right fat grafting (190 cc) and left reduction (360g)

Di Summa [16] over a 13-year period (2006-2018) compared breast implant surgery and fat grafting for asymmetry in terms of number of operations to achieve symmetry, complications and overall patient satisfaction.

Thirty-five patients underwent breast implant surgery, requiring an average 2.1±1.6 operations to achieve symmetry, with a major complication rate (requiring secondary procedures) of 26% (n=9). Again, 26% (n=9) were converted to lipofilling due to either implant removal or unsatisfactory results. Thirty (86%) patients underwent fat transfer alone to achieve symmetry and no major complications were recorded.

In figure 9 and 10 after one lipofilling, breast softness and volume is restored. Figure 10C shows an inflammatory reaction probably related to the increased invasion of T lymphocytes, mast cells, and CD163+ (M2 polarized) macrophages indicates that these immune cells participate in remodeling scar and skin towards normal skin as published Spiekman M et al [17].

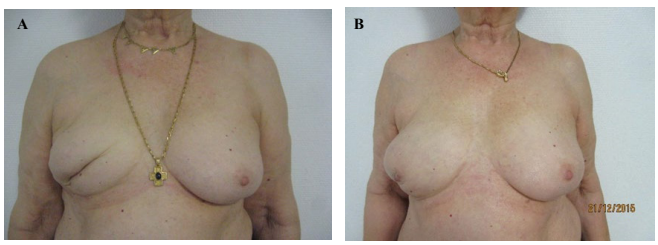


**Figure 9: A.** 2 January 2015 after breast conservative surgery **B.** December 2015 after one 295 cc lipofilling

## 5- Implant to fat conversion (Figures 11 and 12)

Tahseen et al. [18] show that implant-to-fat conversion is a good option for complicated breast implant cases, with

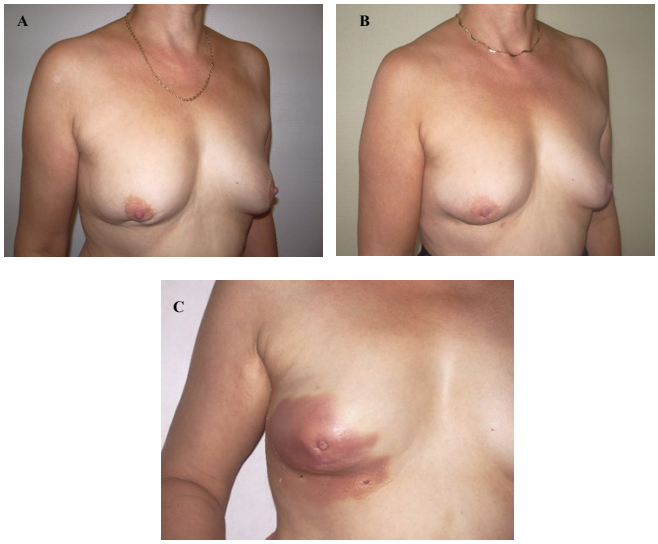


**Figure 10: A.** After breast conservative right surgery **B.** 6 months after one 220 cc lipofilling **C.** 10 days after lipofilling with usual and banal inflammatory reaction

good long-term results and excellent patient's satisfaction as verified by the BREAST-Q. The size of the implants removed ranged from 200 -350 $cm^3$ (average of 310). The volume of fat injected ranged from 300 to 550 ml (average of 430).

Fabiocchi et al. [19] from January 2010 to September 2018 performed 253 breast reconstruction procedures on 100 patients. The reverse expansion technique consists of autologous fat tissue transplantation which requires the combined use of a skin expander and multiple lipofilling sessions. Fifty-six breast reconstructions were performed after skin-sparing mastectomy and 44 after nipple-sparing mastectomy. An average of 661.5 $cm^3$ of fat per session was harvested and an average of 305.3 $cm^3$ per breast was injected. The average number of sessions to achieve breast

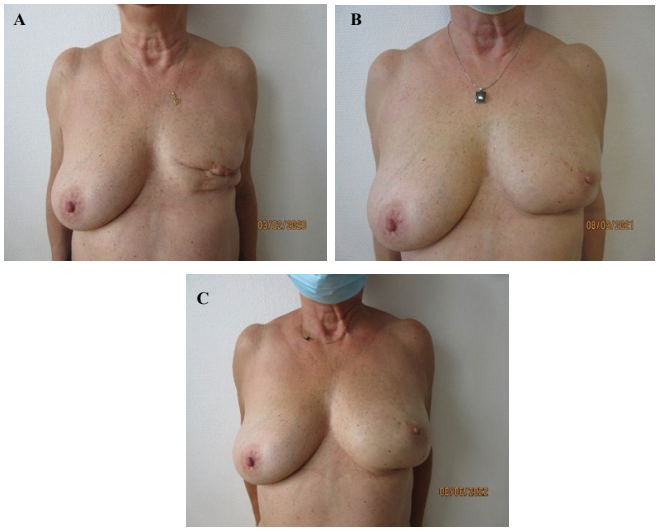


**Figure 11: A.** After 295 cc implant ablation and first 270 cc **B.** After second 208 cc lipofilling **C.** After third 283 cc lipofilling with a total of 941 cc

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reconstruction was 2.53. Four complications after 253 procedures (1.5%) were reported: one donor site bleeding due to genetic lack of coagulation factors, and three surgical site infections.

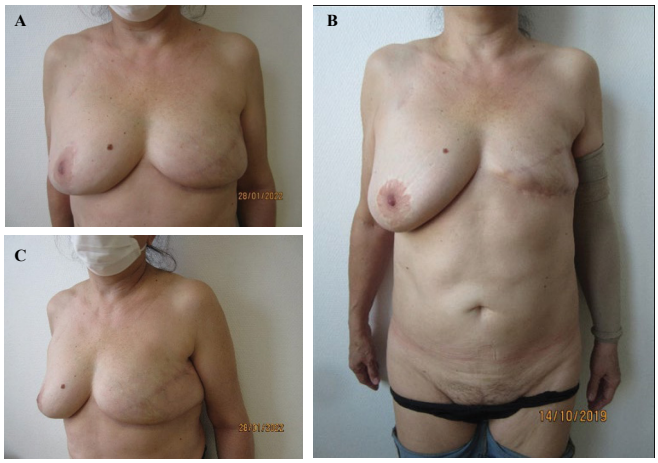


**Figure 12: A.** 2011 after RMI par 220 cc left implant **B.** 2012 with 305 cc implant replacement **C.** 2019 after implant ablation and 2 lipofilling 208 cc and 244 cc

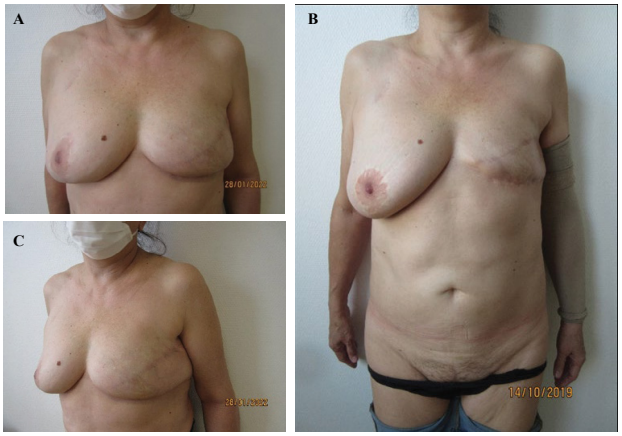


**Figure 12 ABC:** After 3 lipofilling in delayed breast reconstruction after mastectomy and radiotherapy (October 2019 304cc, July 2020 245cc, July 2021 250cc)

## 6 Breast Reconstruction by Exclusive Lipofilling after Total Mastectomy

A multicenter retrospective study was published by M Herly [20]. Breast reconstruction with fat grafting is a new alternative to prosthetic implants and flaps for women with breast cancer. In this study, they conducted a meta-analysis of the effectiveness of fat grafting for breast reconstruction.

Twenty-one studies were included in the meta-analysis. The studies comprised 1011 breast reconstructions in 834 patients. The estimated numbers of treatments to complete a reconstruction were 2.84-4.66 in the mastectomy groups. The number of fat grafting sessions needed to complete a breast reconstruction was significantly higher for the irradiated patients than for the no irradiated patients: 4.27 (95% CI 3.27–5.28) vs. 2.84 (95% CI 2.69–2.98) ($p = 0.01$) for modified radical mastectomy and 4.66 (95% CI 3.12–6.19) vs. 2.93 (95% CI 2.25–3.61) ($p = 0.04$) for skin-sparing mastectomy.

There was no significant difference in the number of fat grafting sessions needed to complete a breast reconstruction after a modified radical mastectomy (MRM) versus a skin-sparing mastectomy (SSM)when the patients were stratified by whether they received radiotherapy or not ($p > 0.05$).

### In secondary reconstruction:

Before beginning the exclusive breast reconstruction, it is necessary to evaluate:

+ If the west has been irradiated

+ If the donor's sites are sufficient in relation to the volume to be reconstructed. If donor sites appear a bit limit, the patient should be informed that an implant may be proposed if the reconstructed volume is insufficient. In this case, the result will be better than without lipofilling because the implant will be smaller and will be recovering in a softer and thicker way.

+ If the infra mammary fold is visible

+ If the patient is ready to accept about 3 to 4 lipofilling

+ If the tissue is quite flexible

*Particularities of the technique in secondary reconstruction:*

In secondary breast reconstruction and especially if the chest has been irradiated, scar adhesions need to be treated by needle band release.

A 16-gauge needle is used to release these adhesions. When the fibrotic adhesions have been released, there is less tension and the skin can be reextended easier by the fat and can be allowed to restore the shape.

This is the way to recover an infra mammary fold (Figures 12, 13 and 14).

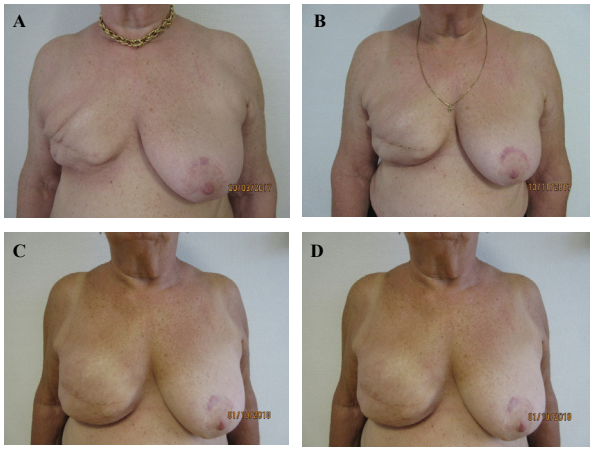


**Figure 13: A** After 1 right fat grafting (370 cc) and left reduction **B:** After second fat grafting ( 310cc)

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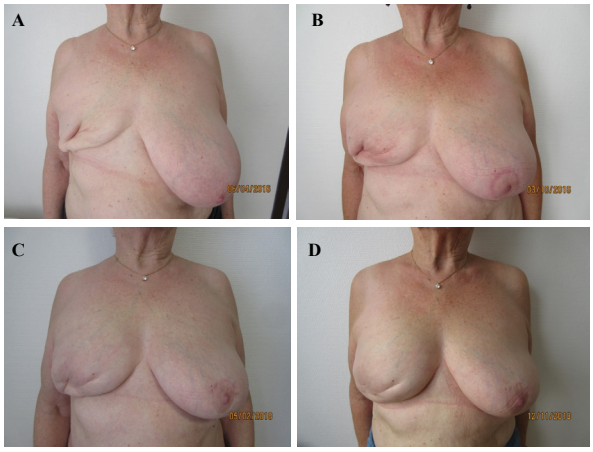


**Figure 14 ABCD:** Delayed breast reconstruction without radiotherapy and after three lipofilling and fasciotomy (380 cc, 402cc and 280cc

Longo B et al. [21] have also defined a fat grafting protocol to achieve successful reconstruction following nipple sparing mastectomy in irradiated and non-irradiated patients. Twenty-one patients were prospectively enrolled and stratified in Group-A (11 non-irradiated) and Group-B (10 irradiated) NSMs to compare clinical and aesthetic outcomes. Volume, shape, position of the breast mound and scar location subscales obtained high score evaluations with no significant difference between the groups ($p > 0.05$), whereas the skin texture subscale showed a lower score evaluation in Group-B than in Group-A ($p = 0.001$). Although there was a significant difference for total subscales in favor of Group-A ($p = 0.001$), the global score had a high-rate evaluation in both groups ($p = 0.132$).

Fitoussi and Razzouk [22] realized for fifteen patients requiring a radical mastectomy fat transfer for immediate reconstruction. Previous breast irradiation was not a contraindication. A mean of 3 (2-6) lipofilling procedures were required to achieve total breast reconstruction. They reported only 2 minor complications (1 hematoma and 1 abscess) not impairing results. After a mean follow-up of 26 months the results were considered by the patients and surgeon as highly satisfactory even in previously irradiated breast.

Ahmed et al. [23] show that immediate lipofilling as a volume replacement technique in BCS is a safe and simple technique without major complications in 54 patients. It has a locoregional recurrence rate similar to BCS alone, with an acceptable fat resorption rate and high postoperative patient satisfaction.

Particularities of the technique in immediate reconstruction:

If the patient desires a natural-feeling reconstruction without a dorsal skin scar and without an implant, a primary important volume flat graft can be used.

It is also important to evaluate:

- The adequacy between the breast volume to be obtained and the donor site.
- The fact that radiotherapy could be might be prescribed after NSM

The skin incision is often made with a periareolair extended in extern direction. This way offers a good exposure for mastectomy and hemostasis without skin damage if a desepidermisation is carried out at the same time and if the tension exerted by the retractors is not too high (Figure 15).

**Figure 15:** Hemiperiareolar incision

Dissection is also done by scissors with serum infiltration with or without adrenalin.

When the hemostasis is achieved, the removed and centrifugal fat is injected in the pectoralis major (Figure 16A). More often, about 100 to 150 cc can be injected into the pectoralis major, depending on the capacity of the recipient site.

Then if the skin is not too thin (Figure 16 B), the injection can be made in intradermal basin (about 80 cc) especially in the inner superior quadrant because of the well vascularized major pectoral close proximity.

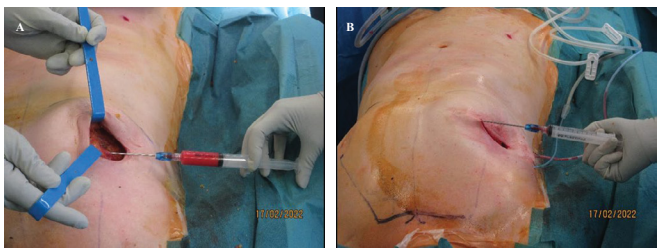


**Figure 16: A.**Intrapectoral fat injection **B.** Intradermic fat injection

As with the other indication, 4 to 6 months are required prior to proceeding with the next procedure. The next procedure is done with the being to inject as much fat is tolerated by the site.

In this example (Figure 17 A and B), no radiotherapy has been given after surgery and the results appeared to be stable over time.

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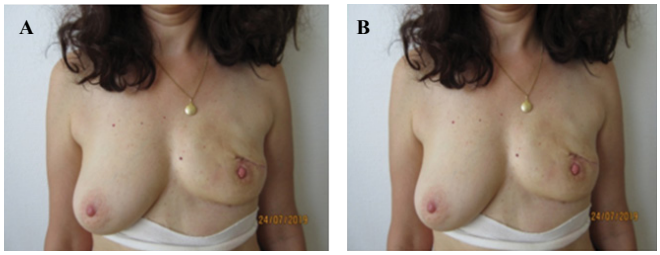


**Figure 17: A.** 2019 mastectomy 195 g with 180g lipofilling **B.** 2020 After Second 310g immediate grafting

In this case (Figure 18A, B and C) radiotherapy has been done after lipofilling on the right side and the results look also quite stable in 2021.

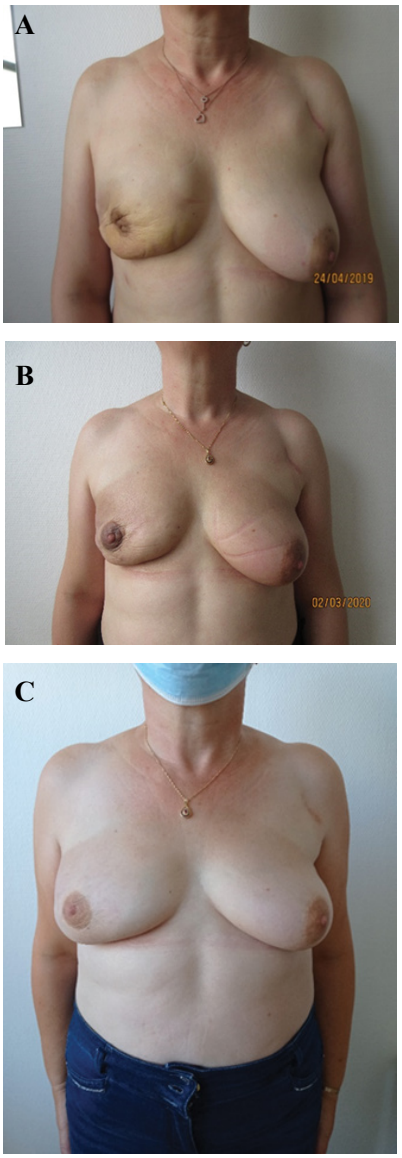


**Figure 18: A.** In 2018 right and left sentinel nodes then neoadjuvant chemotherapy for metastasis node and HER amplification and in 2019 total right mastectomy (300 g) and lipofilling immediate reconstruction (265 cc) **B.** 2020 Bilateral radiotherapy **C.** 2021 after a second right 310 cc lipofilling

## Oncological safety

Petit et al. [24] published a large retrospective study of 513 patients submitted to lipofilling after breast cancer, in which 370 women underwent mastectomy, and the local regional recurrence rate was 1.38% with a mean follow-up of 19.2 months after lipofilling.

Consistent with this data, Silva-Vergara et al. [25] reported a case-controlled study of 205 patients who underwent mastectomy followed by lipofilling and 410 without lipofilling in delayed breast reconstruction. No relapse or mortality differences were found between the lipofilling and control groups. The total number of recurrences for the lipofilling and control groups was 14 (6.8%) and 32 (7.8%) patients, respectively, leading to comparable cumulative incidence curves ($P$ = 0.526). They observed a cumulative LRR incidence for 7 lipofilling patients (3.4%) and 16 control group patients (3.9%) during the follow-up period. No statistically significant difference was detected in the univariate analysis ($P$ = 0.525, Kaplan-Meier, log-rank test) and the cumulative relapse rate was 3.4% and 4.2% in the cases and controls groups, respectively.

Kronowitz et al. [26] confirmed the overall safety of this method in a matched controlled study with 719 women. K Wang et al. [27] collected five basic science studies and 26 clinical studies, involving a total of 10,125 patients. In the basic science studies, adipose-derived stem cells promoted breast cancer growth, but fat grafting and adipose-derived stem cells plus fat grafting were not associated with breast cancer growth. An overall analysis of the clinical studies showed that autologous fat grafting did not increase the risk of breast cancer recurrence. Subgroup analyses showed that autologous fat grafting did not increase the risk of breast cancer recurrence in Asian or Caucasian patients, in patients who underwent breast-conserving surgery or modified radical mastectomy, in patients with in situ carcinomas or invasive carcinomas, or in patients undergoing postoperative radiotherapy.

Jiale S et al. in 2022 [28] selected a total of 11 studies. Eight studies reported local-regional recurrences (LRR) and five studies reported disease-free survival (DFS) in 5,886 patients. The meta-analysis of all included studies for survival outcomes showed that autologous fat grafting was not associated with increased LRR (local recurrence rate) and DFS (disease free survival). The pooled hazard ratios (HRs) (95% CIs) for LRR and DFS were 1.26 (0.90-1.76) and 1.27 (0.96-1.69), respectively.

**Goncalves et al. in 2022 [29]** reviewed the literature published up to 2021. Outcomes were overall survival (OS), disease-free survival (DFS), and local recurrence (LR). They included studies that evaluated women with breast cancer who underwent surgery followed by reconstruction with

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AFG. Fifteen studies evaluating 8541 participants were included. Hazard ratios (HR) could be extracted from four studies, and there was no difference in OS between the AFG group and control (HR 0.9, 95% CI 0.53 to 1.54, p = 0.71, $I^2$ = 58%, moderate certainty evidence), and publication bias was not detected. The HR for DFS could be extracted from six studies, and there was no difference between the AFG group and the control group (HR 1.01, 95% CI 0.73 to 1.38, p = 0.96, $I^2$ = 0%, moderate certainty evidence). The HR for LR could be extracted from ten studies, and there was no difference between the AFG group and the control group (HR 0.86, 95% CI 0.66 to 1.12, p = 0.43, $I^2$ = 1%, moderate certainty evidence).

Ho Cuoq and Piat [30], from September 1999 to November 2017, identified 18 BRCA carriers with no history of breast cancer who underwent bilateral prophylactic mastectomy, followed by breast reconstruction with lipofilling. A total of 36 lipofilling procedures were performed following an implant or latissimus dorsi flap, or as an exclusive fat grafting breast reconstruction. The average number of lipofilling sessions was 1.4 with a mean volume of 108.8cc per breast. The median follow-up was 33.0 months after mastectomy and 24.5 months after the last lipofilling procedure; no patients were diagnosed with breast cancer during follow-up.

In France [31], the consensus recommendation for lipofilling in BRCA patients with a history of breast cancer presents some strict indications and lipofilling should be performed with a minimum of two years' delay.

Currently, lipofilling does not appear to increase breast cancer incidence in patients with a germline BRCA mutation who have previously undergone breast prophylactic mastectomy as published by Ho Quoc [32] with a mean follow-up of 26.2 months after breast prophylactic mastectomy and lipofilling and Kronowitz [26] with a mean follow-up of 36 months after breast prophylactic mastectomy and lipofilling.

Current evidence suggests that fat transfer is a safe technique for breast reconstruction in patients who have undergone breast conservating surgery and does not affect OS (overall survival), DFS, or LR (local recurrence).

## Failure complications and limitations

Kellou et co [33] performed a retrospective study in Normandy analyzing cases of secondary breast reconstruction by exclusive lipofilling after radical mastectomy, from January 2006 to December 2016. They compared a group of patients who completed exclusive lipofilling breast reconstruction (n=22) with a group of patients who underwent other techniques of breast reconstruction (n=16).

The failure rate of breast reconstruction by exclusive lipofilling was 32.6% the need to place an implant. The need of adjuvant chemotherapy treatment was associated with a higher failure rate of exclusive lipofilling breast reconstruction (81.2% vs. 45.5%, P<0.05). Patients were significantly older when reconstruction failed (45.2 vs. 50.9 years mean age, p<0.05). The need of adjuvant radiotherapy treatment was not associated with a higher failure rate than exclusive lipofilling breast reconstruction.

Sorotos et al. [34] show in three groups, group A (25 irradiated), group B (21 smokers), or group C (71 controls) that the global score had a high evaluation rate in all groups and propose fat transfer to smokers with comparable clinical and aesthetic results.

The main complications were skin burns due to the cannula and hematoma at the donor site (11/22) and breast hematoma (11/22). Each step in fat grafting, harvesting, processing, and grafting, is important, but the viability of the harvested fat cells is crucial. The chances of survival are higher the less the fat graft is manipulated and the faster it is re-injected as published by Smith et al. [35]. Donor site complications appear to be minimal and related to the liposuction technique. According to Delay et al. [36] potential complications include bruising, swelling, hematoma formation, paresthesia or donor-site pain, infection, hypertrophic scarring, contour irregularities, and damage to the underlying structures for example due to the intraperitoneal or intramuscular penetration of the cannula.

Lipofilling of the breast could cause in the recipient site fat necrosis, oil cyst formation and calcification if large volumes of fat are injected into a single area or if fat is injected into poorly vascularized areas. These changes lead to failure of "graft take" and lead to palpable masses due to fat necrosis. These masses can be difficult to distinguish clinically from local recurrence in breast cancer patients and lead to a need for additional imaging and needle biopsy in 3%-15% of patients. Post-lipofilling calcifications can be found on mammograms in 0.7%-4.9% of patients [37]. Agha et al. [38] in a review of 24 studies reported 207 complications, 7.3% of 2832 treated breasts. Fat necrosis accounted for 62% of all complications and occurred in 17 of the 24 studies.

If fat tissue is not supplied with blood, it can die, leading to necrotic cysts and even calcification, but this complication can occur with any breast surgery.

## Quality of live

Homsy et al. in 2023 [39] presented detailed patient-reported outcomes of total breast reconstruction with lipofilling. Most of the patients reported a reasonable similarity in the three physical characteristics between their two breasts. Sensitivity of the reconstructed breast was also reported to be close to normal. MRI volume data were consistent with the self-perceived volume symmetry, with the reconstructed breast achieving a median of 76% of the contralateral breast volume.

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## Discussion

Lipofilling has become established as a standard technique for contour enhancement following breast reconstruction. However, there is a paucity of current literature on the use of this technique for complete reconstruction as an alternative to conventional techniques, such as expander or flap-based procedures.

Lipofilling seems to be quick and easy alternative to other classical breast reconstruction techniques, which are often associated with serious complications. More and more patients have heard about this technique and are asking for it. In fact, some patients are put off autologous free flap reconstruction because of the invasiveness and recovery time associated with this type of reconstruction. The scarring is minimal and in the event of failure, it is possible to try another reconstruction method.

## Several factors could influence the results of this new exclusive autologous breast reconstruction:

***1-Radiotherapy and autologous breast reconstruction:*** The influence of pre-operative irradiation on successful reconstruction has been examined by Heine N et al. [40]. The authors describe their experience with successful fat injection in pre-radiated breasts compared to non-pre-radiated patients. A total of 47 lipofilling procedures were performed in 12 non-irradiated patients (14 breasts) and 48 procedures were performed in 14 irradiated women (also 14 breasts). Per session, approximately 297 ± 112 cc of adipose tissue was grafted in group A (no radiotherapy) and approximately 259 ± 93 cc was grafted in group B (radiotherapy).

This team estimated the number of treatments required for complete reconstruction to be 2.84 (95% CI 2.69–2.98) for the non-irradiated modified radical mastectomy group, 4.27 (95% CI 3.27–5.28) for the irradiated modified radical mastectomy group, 2.93 (95% CI 2.25–3.61) for the non-irradiated skin-sparing mastectomy group, 4.66 (95% CI 3.12–6.19) for the irradiated skin-sparing mastectomy group. 71% of breast reconstructions limited to lipofilling only showed permanent fat grafting with a successful reconstructive outcome, while only 21% of patients with pre-radiated breasts showed complete breast reconstruction with a permanent fat grafting.

Preoperative radiotherapy significantly hinders the successful completion of breast reconstruction planned using autologous fat transfer alone. Patients should be selected individually and carefully for complete breast reconstruction using lipofilling alone.

In one of the largest series of breast lipofilling, Khouri et al. [41] demonstrated a higher complication rate and more necessary procedures in case of previous radiation.

M Sorotos et al. [34] confirmed the efficacy of their fat transfer protocol in both irradiated and non-irradiated nipple-sparing mastectomy patients and propose its indication to smokers with comparable clinical and aesthetic results.

One of the most crucial factors for reliable ingrowth of fat tissue after lipofilling is the quality, perfusion and elasticity of the recipient tissue.

In the future, it would be interesting to predict the reaction of irradiated skin after fat transfer.

***2-Donor site:*** Exclusion criteria for some authors were a BMI lower than 22 [40] in view of lipofilling exclusive reconstruction.

***3-Number of sessions:*** The main limiting factor of this technique is the repetition of the surgical procedure which may discourage both the patient and the surgeon. Indeed, in the literature the number of sessions spread over a period approximately 15 months [42-4].

Son et al [45] discuss the feasibility of cryopreservation of adipose tissue and ADSC (adipose-derived stem cells) leading to a new era in fat grafting and ADSC-related tissue regeneration therapy in breast surgery.

The aim of the pilot study by Massiah et al. [46] was to find out a feasible method of cryopreserving adipose tissue, to avoid repeated liposuctions. Lipoaspirates samples have been harvested from 10 women and preserved by three methods: (1) the first one, using 10% $Me_2SO$ (dimethyl sulfoxide) and 20% human albumin from human plasma as cryoprotective agents; (2) the second one, adding 5% $Me_2SO$ as cryoprotective agent; (3) the last one, without any cryoprotective agent. Fresh and cryopreserved fat samples, obtained through the aforementioned processes, have been analyzed ex vivo. Lipoaspirates stored at -196 °C for 3 months, after thawing, retained comparable adipocyte viability and histology to fresh tissue and no significant differences were found between the three methods used.

Ohashi et al. [47] performed lipofilling for aesthetic purpose on 54 women who underwent breast augmentation using cryopreserved adipose tissue at -196 °C by slow freezing, adding a commercial cryoprotective solution without dimethyl sulfoxide ($Me_2SO$), resulting in a full patient satisfaction and absence of complications with a follow-up of about 2 years.

## Perspective fat transfer trend

Some teams such as Ahmed [48] have published on the feasibility of immediate lipofilling as a volume replacement technique in breast conservative surgery (BCS) in terms of the volume of fat graft resorption after radiotherapy, patient satisfaction, and oncological safety.

The members of the Senology Commission [49] agree with the conclusions of the HAS working group, in particular

that lipofilling should not be used "without cautionary periods", excessively, or in cases of high risk of relapse, and recommend clear, detailed information to patients before undergoing lipofilling, and the need for postoperative follow-up. The creation of a national registry could address most questions regarding both the oncological safety of this procedure and the modalities of patient follow-up.

## Conclusions

Initially limited to the correction of contour deformities following breast reconstruction, fat grafting should be included in the panel of breast reconstruction techniques because of the simplicity of the surgical technique with an easy learning curve, the simplicity of the equipment required, the lack of need for a specialized surgical team, the low complication rate, the oncological safety and the high satisfaction rate with a natural appearance of the breast shape and the soft consistency of the breast grafted tissue.

## Author contributions

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Formal analysis: Catherine Bouteille

Validation: Catherine Bouteille, Gilles Houvenaeghel

Investigation: Catherine Bouteille

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All authors have read and agreed to the published version of the manuscript.

## Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Paoli Calmettes Institute.

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The authors declare no conflicts of interest.

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