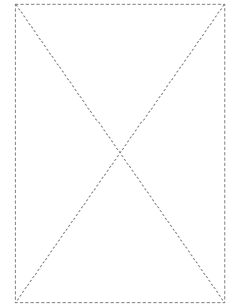


## Fat Graft in Prosthetic and Autologous Breast Reconstruction

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**Nowadays autologous fat transplant represents an effective cell therapy, due to the fact that a fraction of the lipoaspirate consists of adipose-derived adult stem cells. In this study we retrospectively report the two-year experience of 41 patients treated with autologous fat transplant to repair different breast-related problems. A postoperatively 3 months interval follow-up was performed in association to imaging follow-up, using ultrasound as first step. According to the grading scale, we report the results assisted by the plastic surgeons and the patients. A total of 68 breasts were treated in 65 operations. 38 patients were treated unilaterally and 15 patients bilaterally. In the follow-up we evaluate the clinical outcome using a grading scale consisted of 5 crescent grades, from 1 to 5, based on the patient's satisfaction and on the clinical evidence of the achievement of the desired target. A percentage of 70.7% are classified with a grade over 3. Among 12 patients, one developed small liponecrotic lesion. We confirm that placing small aliquots of fat in the recipient site strongly reduce the phenomenon of liponecrosis on sonography. Thus, our experience confirms that this procedure is an easy, safe, effective and reliable surgical procedure also in the breast.**

**Key Words:** Breast reconstruction, Graft, Subcutaneous fat, Fat necrosis

### I. INTRODUCTION

Autologous fat transplant, also known as lipofilling or fat graft, represents an attractive and widely used surgical procedure to correct contour deformities of the face and the body. In 1893 Neuber was one of the first to report the use of fat graft for treatment of facial contour defect, even if his experience was unsuccessful. In 1926 Miller published his experience in fat graft injected with cannula, with interesting results. Only in early 80's, first Illouz and then Fournier described an alternative technique to harvest the fat from donor sites,

using cannulas or needles. In the following years, Illouz and Ersek in 1991 published works that could have marked the end of lipofilling, as they showed their disappointment in the long-term results.<sup>1,2</sup> It was Coleman that reported interesting results with his technique, publishing two important articles on lipofilling in 1995 and 1997. Now, his three step procedure (harvesting, centrifugation and injection) is widely used.<sup>3</sup> Although there are many reports on the use of lipofilling for contouring defects in the face, hand and body, only a few numbers of papers reported the use of lipofilling for breast contouring.<sup>4</sup> This is also due to a well-know prejudice on breast fat injection that would interfere with the imaging diagnosis of malignant breast lesions.<sup>4</sup> The recent reports about the therapeutic properties of the autologous fat transplant for the treatment of

### 보형물과 자가조직을 이용한 유방재건에서 지방이식

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radiation damage open new horizons in breast surgery.<sup>5</sup>

Nowadays, autologous fat transplant represents an important surgical therapy, based on the potential therapeutic properties of a part of its content, the adipose-derived stem cells.<sup>5,6</sup> In this study we report the two years experience of the first author(M.S.) in autologous fat transplant for the correction of contour defects in the breasts reconstructed by either prosthetic or autologous methods and to repair other breast-related problems.

## II. PATIENTS AND METHODS

Retrospectively, we review 41 patients treated with autologous fat transplant, from October 2006 to June 2008. The youngest case treated was 20 years old, the oldest 65 years old, with an average age of 36.7 years old. The patients were treated after they have expressed their informed agreement. It was showed them the potential complications and risks that could occur after this surgery. It was explained that, the eventual discovery of a breast nodular lesion under self-palpation should be examined according to the guidelines for the management of breast cancer. The evaluation of negative findings from mammography represented an important pre-operative assessment for the patients treated.

The indications for the autologous fat transplant were: mammary defects after prosthetic reconstruction(27 patients) of whom 1 patient was reconstructed using a TDAP flap(thoracodorsal artery perforator flap) and implant, breast defects after QUART(quadrantectomy, axillary lymphadenectomy, radiotherapy)(5 patients) of whom 1 patient was reconstructed using a TDAP flap, mammary defects after autologous flap breast reconstruction(5 patients), radical mastectomy prior to receiving an eventual prosthetic reconstruction(2 patients), mammary defects in Poland Syndrome with bilateral prosthetic breast augmentation(1 patient), depressed scar in superior medial quadrant of the right breast after bone biopsy(1 patient, Table I).

Fat was harvested, treated and injected according to Coleman's technique.<sup>3</sup> The donor sites were infiltrated with the superwet technique with a solution made of saline 0.9%, epinephrine(1:1,000,000) and xylocaine (1:50,000). The harvesting site were chosen according to the quantity of fat needed, aesthetic implications,

patient desires, but also to the evidence from our experience that some donor sites seems to have a "better" fat than the others, as subcutaneous tissue from the medial knee, the lateral and medial aspect of upper thigh. A needle with a sharp lancet-shaped tip(NoKor needle; BD Admix Needle Nokor<sup>TM</sup> 16G, Becton, Dickinson, NJ, USA) was used to dissolve the fibrous adherences in the dermis and the subcutaneous fat in those cases where a scar retraction was present at the recipient site. The 17 gauge Coleman needle was introduced to transplant the fat. A maximum of 0.2 mL of fat was multi-directionally placed, from muscle or deep subcutaneous to the subdermal layer, in the recipient site as the blunt cannula was withdrawn. This reduces the risk of intravascular fat injection and allows a more detailed placement of fat. The multi-directional placement of the fat was performed till the achievement of the desired contour. Patients were examined one week post-operatively and asked to return for follow-up after 3 months. Breast ultrasonography(US) was chosen as first diagnostic step to evaluate complication rate of cystosteatonecrotic lesions. All the patients received one sonographic assessment before the first surgery and are scheduled for postoperative US after 3-6 months. The presence of any suspicious lesions from patient's self-assessment, clinical observation and US represents the indications for mammography and MRI. Further suspect may be solved performing biopsy of the lesion.

In the follow-up we report the time from the last operation and the evaluation of the clinical outcome using a grading scale. This consists of 5 crescent grades, from 1 to 5, based on the patient's satisfaction and on the clinical evidence of the result achieved. Grade 1 stands for no result obtained, Grade 2 stands for poor improvement, Grade 3 signifies visible result, Grade 4 stands for a good result that almost satisfied the volume and result planned. Grade 5, as excellent result, is attributed when the desired outcome was achieved. These results are considered at least 8-12 weeks postoperatively, when the local edema is resolved.

## III. RESULTS

A total of 68 breasts were treated in 65 operations. Fat was transplanted unilaterally in 38 cases and 15 times bilaterally. One to 4 operations for each patient

**Table I.** Patients Treated with Autologous Fat Transplant in Breast

Patient (Age)	Previous Surgery	Date	Qt.(cc)	N° Cent.	Donor site	Recipient Site	Xrt	NoKor Needle	F-up T,Gr
1(27)	L Mast	12/07	64	2	MThigh + knee	L breast	Yes	No	6m, 3
2(56)	B Mast + B IPrRec	01/07	35	1	MThigh + knee	B breast	No	No	3m, 3 12m, 3
		01/08	107	3	MThigh + knee	78cc R IQ 29cc L breast	No	No	3m, 3 T : 15m, 3
3(50)	R SSM + R IPrRec	05/08	89	3	LThigh + knee	R breast	Yes	No	Scheduled
4(52)	R Mast + R DPrRec	11/07	60	2	MThigh + knee	L breast	Yes	No	3m, 3
		02/08	82	3	MThigh + knee	L breast	Yes	No	6m, 3 T : 9m, 3
5(41)	B ScMast + B IPrRec	11/06	19	1	LowAbd	10cc L breast 9cc R breast	Yes	No	3m, 2 8m, 2
		07/07	97	3	LowAbd	43cc L breast 54cc R breast	Yes	No	3m, 2
		11/07	127	4	MThigh + knee	50cc L breast 77cc R breast	Yes	No	3m, 2 T: 15m, 2
6(37)	B Mast + B IPrRec	12/06	20	1	LThigh	R breast	No	No	3m, 4
		03/07	40	2	MThigh + flanks	R breast	No	No	3m, 4 6m, 4
		10/07	70	3	MThigh + flanks	R breast	No	No	3m, 4
		04/08	45	2	Flanks	R breast	No	No	3m, 4 T : 19m, 4
7(58)	B ScMast + B IPrRec	03/08	107	4	LThigh + knee	50cc R SQ 57cc L SQ	No	No	Scheduled
8(57)	L Mast + TRAM rec	04/07	49	1	MThigh	L breast	No	No	3m, 3 6m, 3
		10/07	87	3	MThigh + knee	L breast	No	Yes	3m, 3 T : 9m, 3
9(40)	R SSM + R IPrRec	03/07	19	1	LowAbd	R breast	No	No	3m, 3
10(41)	B SSM + B IPrRec	12/06	39	1	LowAbd + MThigh	B breast	Yes (left Breast)	No	3m, 4
		03/07	60	3	MThigh + knee	B breast	Yes (left Breast)	No	3m, 4 8m, 4
		11/07	77	2	Flanks	B breast	Yes (left Breast)	No	3m, 4 T : 14m, 4
11(33)	R Mast + TRAM rec	03/08	25	1	LThigh	SMQ R breast	Yes (previous QUART)	No	Scheduled
12(38)	R BreastAug	05/08	14	1	Flanks	IMQ R breast	No	No	Scheduled
13(44)	L SSM + L IPrRec	01/07	27	1	knee	L breast	Yes	No	1m, 4
		02/07	141	4	LThigh	L breast	Yes	No	3m, 4 Stop for expander rupture T : 5m, 5
14(46)	L Mast + DIEP rec	10/07	60	3	LThigh + MThigh + knee	R breast	Yes	No	3m, 4
		04/08	77	2	LThigh	R breast	Yes	No	3m, 4 T : 9m, 4
15(65)	R Mast + TRAM rec	02/08	103	3	MThigh + knee	45cc R SubClv 58cc R axilla	Yes	Yes	3m, 4
16(47)	L SSM + L IPrRec	02/07	21	1	LowAbd	L breast	No	No	3m, 2 5m, 2
		07/07	20	1	LowAbd	L breast	No	No	3m, 2 T : 8m, 2
17(46)	B Mast + R TDAP rec + B IPrRec	03/08	66	3	LowAbd	R breast	Yes (right breast)	No	3m, 4
18(65)	R QUART SLQ	04/08	52	2	LThigh + knee	52cc SLQ	Yes	Yes	3m, 4
19(39)	R SMQ (Scar due to biopsy)	12/07	25	1	LowAbd + knee	R SMQ	No	Yes	3m, 4
20(45)	R SSM + R IPrRec	07/07	57	2	LowAbd	R breast	No	No	3m, 5

Table I. Continue

Patient (Age)	Previous Surgery	Date	Qt.(cc)	N° Cent.	Donor site	Recipient Site	xrt	NoKor Needle	F-up T,Gr
21(50)	R SSM + R IPrRec	02/08	90	3	Flanks	47cc L breast 43cc R breast	No	Yes	3m, 2
22(49)	R SSM + R IPrRec	04/07	30	1	knee	R breast	No	No	3m, 3 5m, 3
		09/07	87	3	MThigh + knee	R breast	No	No	3m, 3 T : 8m, 3
23(58)	R QUART SLQ	11/07	118	4	MThigh + knee	110cc R Breast 8cc R axilla	Yes	Yes	3m, 3
		03/08	127	5	LThigh + LowAbd	R breast	Yes	Yes	3m, 3 T : 7m, 3
24(47)	B SSM + R IPrRec	02/08	83	3	MThigh + knee	40cc R SLQ 43cc L SLQ	No	Yes	3m, 3
25(44)	L BreastAug	03/07	135	4	MThigh	L breast	No	No	3m, 3
		06/07	21	1	knee	L breast	No	No	3m, 3 6m, 3
		12/07	50	2	LThigh + MThigh	L breast	No	No	3m, 3 T : 12m, 3
26(40)	L SSM + L IPrRec	03/07	91	3,5	LThigh	L breast	No	No	2m, 3
		05/07	50	2	MThigh + knee	L breast	No	No	Scheduled
27(58)	L Mast + L IPrRec	11/06	19	1	LowAbd	L breast	Yes	No	3m, 3
28(44)	L ScMast + L IPrRec	06/07	41	2	knee	L Breast	No	No	8m, 3
29(45)	QUART L ILQ	06/07	40	2	knee	L breast	Yes	Yes	3m, 4
		09/07	40	2	MThigh	L breast	Yes	Yes	3m, 4 T : 6m, 4
30(39)	R ScMast + L SSM + B IPrRec	10/07	50	2	MThigh + knee	L breast	No	Yes	3m, 3
31(38)	Poland S, B PrRec	10/06	25	1	LowAbd	SQ + SubClv	No	No	3m, 2 14m, 2
		02/08	59	3	MThigh + knee	SQ + SubClv	No	No	3m, 3 T : 19m, 3
32(20)	B BreastAug (Tuberous Breasts)	05/08	94	3	LThigh	33cc L LQ 61cc R LQ	No	Yes	2m, 4
33(50)	QUART L IMQ	02/08	78	3	MThigh + knee	L MQ	Yes	Yes	3m, 4
		05/08	88	3	LThigh + knee	L MQ	Yes	Yes	3m, 5 T : 6m, 5
34(58)	B ScMast + B IPrRec	04/08	113	4	Lthigh	30cc L breast 83cc R breast	No	No	3m, 4
35(65)	L QUART + TDAP rec	12/07	34	1	UppAbd	L SQ	Yes	No	Scheduled
36(55)	R SSM + R IPrRec	03/08	122	4	LThigh	R breast	No	No	Scheduled
37(54)	R ScMast + R IPrRec L Mast + TRAM rec	10/07	115	4	LThigh	100cc L breast 15cc R breast	Yes (left breast)	No	2m, 2
		12/07	108	4	LThigh + MThigh + knee	80cc L breast 28cc R breast	Yes (left breast)	Yes	3m, 2
		03/08	112	4	LThigh + MThigh + knee	82cc L breast 30cc R breast	Yes (left breast)	No	3m, 2 T : 20m, 2
38(42)	R Mast	01/07	20	1	MThigh + knee	R breast	No	No	3m, 4 4m, 4
		05/07	40	3	MThigh + knee	R breast	No	No	3m, 4 T : 7m, 4
39(50)	L Mast + L IPrRec	04/08	63	2	LThigh + knee	B breast	No	No	Scheduled
40(45)	R SSM + R IPrRec	05/07	25	1	LowAbd	R breast	No	No	3m, 3
41(49)	L Mast + L DPrRec	07/07	26	1	LowAbd	L breast	No	No	12m, 4

Qt. (cc), amount of fat transplanted in milliliter; N° Cent, number of centrifugation cycle, each cycle is referred for 6 syringe of 10 mL; previous xrt, previous radiotherapy; F-upT, follow up time(m, month); G(grade of clinical result achieved); R, right; L, left; B, bilateral; Mast, radical mastectomy; SSM, skin sparing mastectomy; ScMast, subcutaneous mastectomy; QUART, quadrantectomy, axillary lymphadenectomy and radiotherapy; SLQ, superior lateral quadrant; ILQ, inferior lateral quadrant; SMQ, superior medial quadrant; IMQ, inferior medial quadrant; PrRec, prosthetic reconstruction (I, immediate; D, delayed); TRAM rec, reconstruction with TRAM flap; DIEP rec, reconstruction with DIEP flap; TDAP rec, reconstruction with TDAP flap; BreastAug, breast augmentation; Poland S, Poland Syndrome; MThigh, medial aspect of upper thigh; LThigh, lateral aspect of upper thigh; knee, medial aspect of knee; LowAbd, lower abdomen; UppAbd, upper abdomen; R, right; L, left; breast, wall breast; SQ, superior quadrants; IQ, inferior quadrants; SLQ, superior lateral quadrant; ILQ, inferior lateral quadrant; SMQ, superior medial quadrant; IMQ, inferior medial quadrant; SubClv, sub-clavicular.

were performed, on the base of the amount of the contour defects to remodel and the type of indication. We performed a single procedure on 23 cases, two treatments in 13 patients, three procedures in 4 patients and 1 received a four-time treatment. A number of 27 patients are scheduled for further fat transplantations and for 14 patients the treatment is considered finished. In the 65 operations, we used 5 main harvesting sites. The knee bilaterally and the medial and lateral aspect of upper thigh represents the main harvesting sites. The abdomen and flanks were the following ones. In 69.1% of the treatments, the donor sites were lateral and/or medial aspect of upper thigh and/or medial knee. The patients were classified in reference to: age, indications, number of operations, quantity of fat transplanted, cycles of centrifugation needed, fat donor sites, recipient sites, previous radiotherapy, need of NoKor Needle to release the fibrous adherence in the recipient site.

A number of 17 patients presented tissue damage after radiation therapy for cancer treatment, of whom 52.9%(9 patients) showed signs of improvement. Patient 4 and 5 showed a softening of the implant contracture at clinical examination. Patient 13, 15, 17, 18, 23 and 33 presented clinical improvement of the radiation-damaged soft tissue. Patient 29, who inserted an implant in an irradiated site, did not present any implant contracture after 2 fat transplants. At now, for 8 patients is not possible to evaluate the therapeutic effect of the fat transplanted. Patient 2, not irradiated, presents clinically a softening of the implant contracture, also referred under self-assessment. The 16 gauge NoKor needle was used one time in 9 patients and two times in 2 cases. For each patient we scheduled a regular follow-up per 3 months. The minimum period of post-operative control was 2 month and the maximum 20 months, with an average of 7.5 months. Eight patients underwent fat transplant recently and they are scheduled for the next first follow-up. In one patient the controls were stopped because of a complication due to tissue expander rupture. The evaluation of the results was done using the grading scale described above. A percentage of 70.7%(29 patients) are classified with a grade over 3 of whom 34.1%(14 patients) were grade 3, 31.7%(13 patients) grade 4 and 4.9%(2 patients) grade 5. Four patients were classified with grade 2 and

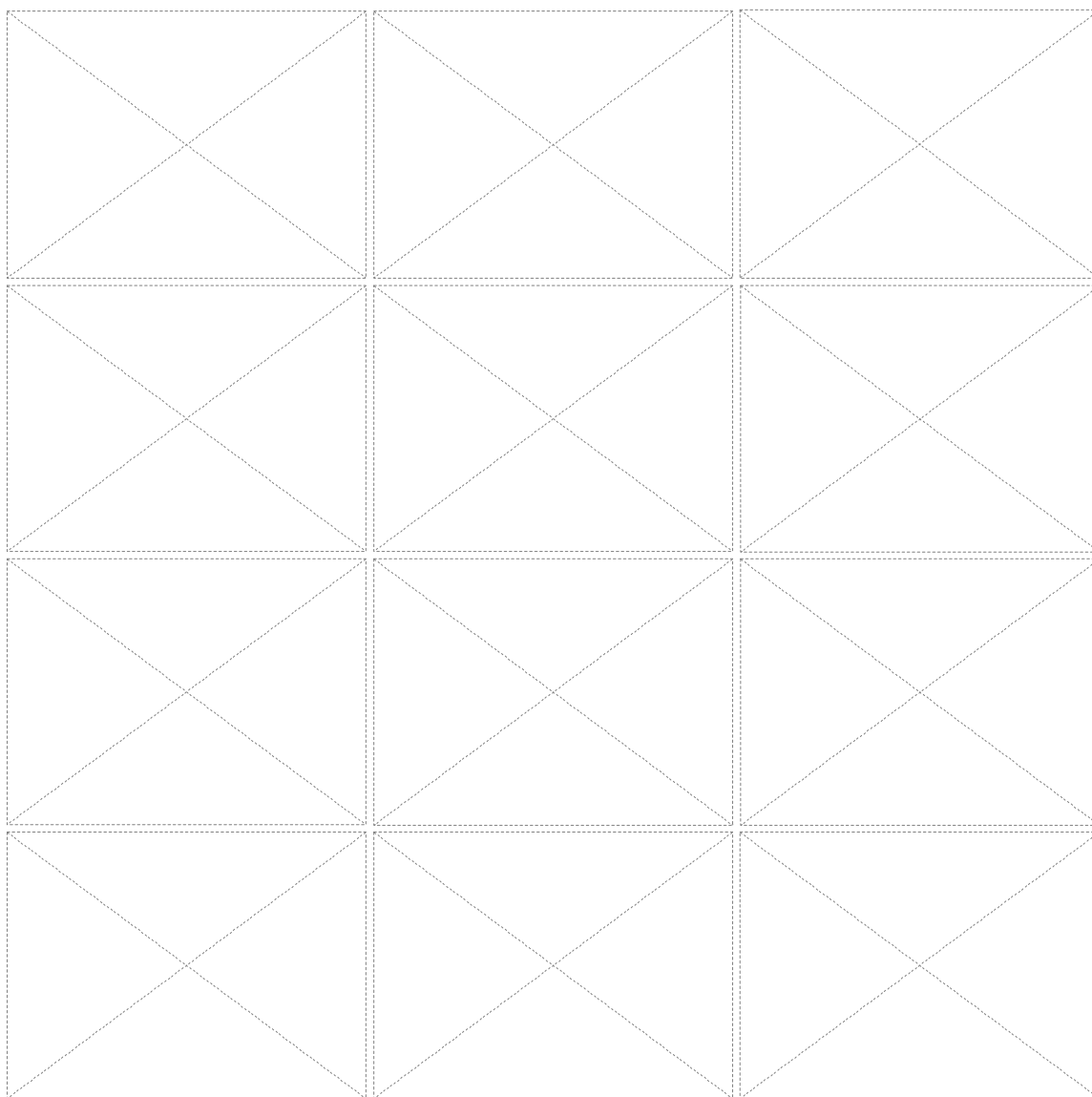
no patient was classified with grade 1. For 8 patients there aren't available results yet(Fig. 1-3). There were 2 complications in 65 treatments. Patient 8 reported a seroma after the fourth treatment. This may be due to the use of NoKor needle. Patient 13 had a rupture of skin expander during the phase of transplant. All the patients underwent a sonographic and mammographic assessment preoperatively and a regular ultrasound follow-up was planned.

At moment, a total of 12 patients(patient 2, 4, 9, 10, 14, 16, 17, 18, 20, 22, 24, 29) returned with US assessment. In one case(patient 4, 8,3 % on 12 patients) it was diagnosed an anechoic little lesion of liponecrosis, about 60 days after the second fat transplant. This patient was negative for fat necrosis when assessed after 3 months from the first fat transplant of 60 cc.

#### IV. DISCUSSION

Autologous fat transplant is an attractive and widely used surgical procedure. Fat graft represents natural filler requiring a more complex surgical procedure for transplantation compared with the artificial ones. Moreover, it holds important therapeutic potential, due to the high quantity of adipose-derived stem cells involved.<sup>5,6</sup> Each gram of fat tissue contains up to 350,000 preadipocytes and 5,000 adipose-derived stem cells. The large quantity of fat tissue available for harvesting, the demonstration that adipose tissue contains the highest percentage quantity of adult stem cell, even more than bone marrow, and the easiness to harvest this tissue, leads to consider it as an important source of adult stem cells. For this reason, it is more appropriate to call this procedure as autologous fat transplant instead of others used name such as fat graft, lipofilling, fat injection that seem to be more appropriate to identify only a filler surgery.

One of the most controversial aspect is how to achieve long-term results. The influence of the different techniques widely used in harvesting and purifying fat, seems to be not significant on the long-term survival of the transplanted fat.<sup>7</sup> Furthermore, Rohrich et al. in 2004<sup>8</sup> and the year after Ullmann et al., published experimental works that demonstrated no significant differences of three donor sites, thigh, abdomen and breast, in influencing fat viability. On the base of



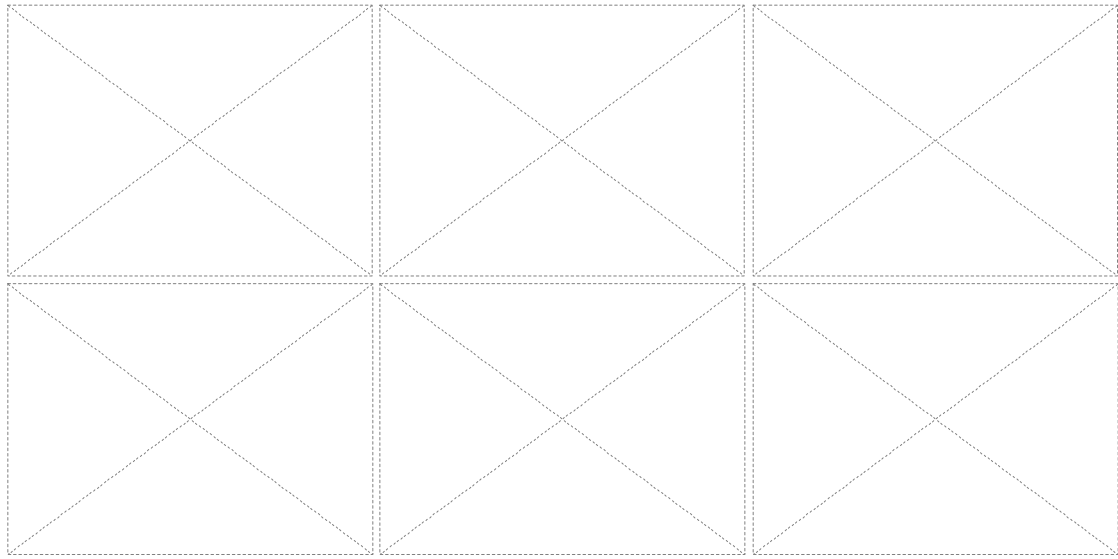
**Fig. 1.** (Above) Patient 6, 37 years old, after right immediate prosthetic breast reconstruction for skin sparing mastectomy. It is evident the contour defect in the superior quadrants of the right breast. (Center, above) A 4 month result after a 20 mL fat transplant in the right superior breast quadrants. A reconstruction of the nipple areolar complex was performed. The drawings show the area to be transplanted. (Center, below) Postoperatively result after the injection of further 40 mL of fat (second transplant). (Below) After 6 months the patient has undergone a third fat transplant of 70 mL in the medial upper quadrant of the right breast. A good result is showed with evident clinical improvement of the breast contour and scar healing (grading 4).

evidence from our experience, fat harvested from donor site with a more complex histoarchitecture, as subcutaneous tissue from medial knee and from the lateral and medial aspect of thigh, seems to favour the survival of the transferred cells. Further follow-up and studies are needed to statistically prove this assertion.

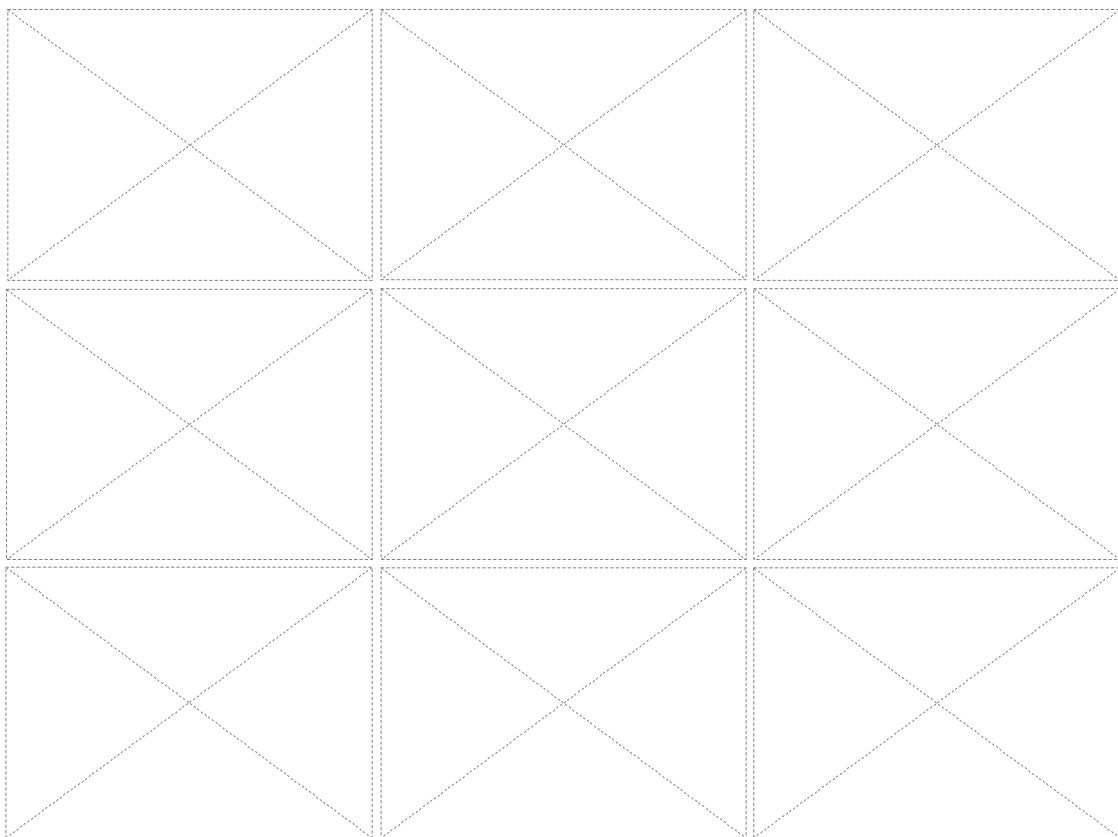
The blood supply to the injected cells in the recipient site represents an important factor that may influence

the long-term survival of the fat transplanted. In 1987 Bircoll presented his results in fat grafting with the use of 1 - 3 cc fat microinjection, advancing the well-know Coleman's Lipostructure.<sup>3</sup> Placing small aliquots of fat allows a better interaction with the recipient site, playing an important role on the transplant trophism and its survival.<sup>4</sup>

Adipose-derived stem cells may play either an im-



**Fig. 2.** (Left) Patient 20, 45 year old after right immediate prosthetic breast reconstruction for radical mastectomy. The mastectomy scar in the right breast is dystrophic. (Center) Planning of the site to be transplanted. (Right) A 3 month result after surgical scar revision and 57 mL of fat transplanted. The improvement of breast contour and scar is evident. It has been classified as Grading 5.



**Fig. 3.** (Above) Patient 33, 50 years old, after QUART in medial inferior quadrant in left breast. (Center) The 3 month result after a transplant of 78 mL of fat is shown. The planning of the further fat transplant has been drawn. (Below) Fifteen day result after the second transplant of 88 mL of fat. The progressive improvement of the breast contour and of the radiodamaged skin is shown. Grading 5.

portant role in the fat viability and being a source for the cell therapy. Adipose-derived stem cells are more resistant than adipocytes to mechanical trauma due to harvesting and purification of the lipoaspirate. Furthermore, their features allow them to be more resistant than mature adipocyte to the local metabolic stress due to transplantation. Comparing to adipocytes, these cells can survive with no nutrition for a longer time and they also present a minor oxygen consumption rate. It's important to minimize the mechanical stress. Its excess during harvesting and centrifugation may damage intact adipocytes and adipose-derived stem cells.<sup>7,9</sup> Kurita et al. "tentatively recommend" to use a 1200 rpm centrifugal force to reduce the cell damage. This may favour good short and long-term results in fat transplant.<sup>9</sup> The therapeutic properties of the stromal-vascular cell fraction of adipose tissue are multipotentiality, angiogenesis and vasculogenesis potential<sup>5,6</sup> and immunomodulation that may reduce the local inflammation in the recipient site. According to Rigotti et al, these bring first to a phenomenon of mesenchymalization and then to a maturation of the fetal-like tissue in a normal mature adipose tissue with its new formed microcirculation.<sup>5</sup> This explains the therapeutic potential of autologous fat transplant in radiation tissue disease and probably in others dystrophic soft-tissue damages.

The large availability of subcutaneous tissue and the significant technical confidence of plastic surgeons in using fat graft make autologous fat transplant an ideal source of stem cell for cell therapy.<sup>6</sup> The transplantation following the principles of Coleman's Lipostructure<sup>®</sup> in association to a less traumatic harvesting and purification step, seems to have a positive influence on long-term survival of the transplanted fat. Further prospective studies will be necessary to better define these factors.

Fat graft has a fascinating and effective role in breast surgery. Micromastia, tuberos breast, defects and complications after prosthetic breast augmentation and prosthetic breast reconstruction in capsular contracture and soft tissue deformities,<sup>4,5</sup> defects from autologous breast reconstruction(as soft tissue defects), defect after conservative treatment plus radiation damage<sup>5</sup> are indications for autologous fat transplantation. Its first report in breast dates back to 1987 when Bircoll performed breast augmentation using fat graft. Maillard first and in 1999 Castello described their experience with fat

injection in the breast reporting the development of cyst of fat necrosis. Later, Spear et al.<sup>10</sup> in 2005, Coleman and Saboeiro<sup>4</sup> in 2007 and Zheng et al.<sup>11</sup> in 2008, published encouraging results in autologous fat.

Local and systemic complication may occur with this surgery. Sepsis and fat embolism represent very rare events. Combination of epinephrine-induced vasoconstriction from local anaesthesia and the use of blunt cannula in harvesting and transferring the fat reduce the chance of intravascular dissemination of it. The local complications are described more frequently, such as haematoma(due to vessels damage in the donor and in the recipient site), seroma, local traumatic lesions. Eremia and Newman reported the complication of hematoma in 3.3% of 116 patients evaluated.<sup>12</sup>

On a total of 41 patients, we experienced 2 complications; one seroma and one tissue expander rupture. We did not experience any case of local inflammation, either in the donor and recipient site. This may be due to the immunomodulation effect of the adipose-derived stem cells. Aesthetic local complications are also widely experienced. Among them: donor site deformities from liposuction(more frequent in slim patient and in those that had already received liposuction), under or over target transplanted amount of fat, soft tissue irregularities, and fat overgrowth in the recipient site with no significant relation to weight gain are the most reported ones. At the recipient site is common the presence of local edema, little hematoma and discomfort. These normally resolve in few days and are not considerable complications.<sup>12</sup> In the first 10 postoperative days it has to be avoided strong pressure on the recipient site because it may favour migration of transplanted fat.

The insufficient nutrition of the transferred fat may lead to a secondary local inflammation of the poorly vascularized fat, resulting in aseptic necrotic cysts and calcifications.<sup>4,11,13</sup> In their review on 66 patients treated with autologous fat transplant in the breast, Zheng et al.<sup>11</sup> reported a percentage of this event in the 16.7% of the patients, with an average follow-up of 37 months.

In our experience, on 12 patients with an average follow-up of 6 months, evaluated with US, only in one case(patient 4, 8.3% on 12 patients) we found presence of a fat necrosis lesion. This was about 60 days after the second fat transplant. The patient was negative for fat necrosis when assessed after 3 months from the first



fat transplant of 60 cc. The low incidence of liponecrosis represents an encouraging result. This is enforced on the base that 10 patients(83% on 12 patients) received more than 50 mL of fat, of whom in 5 patients(41% on 12 patients) there were transplanted more than 100 mL of fat. A sonographic assessment of all the patients is in progress. This will lead to report a more significant result in the next future.

We agree that multiple microinjections of a maximum of 0.2 mL of fat may allow a sufficient nutrition to the fat transplanted because it maximize the surface area of contact between the transplanted cells and the recipient site. This allows a trophic support to the host cells and it may strongly reduce the possibility of fat necrosis. Furthermore, the structural and metabolic features of preadipocyte and adipose-derived stem cells make these cells more resistant to mechanical trauma and metabolic stress than mature adipose cells. An association of a lipoaspirate rich in viable preadipocytes and adipose-derived stem cells with the lipostructure<sup>®</sup> may influence positively the long-term volume results and may strongly reduce fat necrosis. In literature, cystic lesions represent the primary long-term complication.<sup>11</sup> They may interfere with breast cancer image detection. It represented a diffused prejudice that strongly limited the use of fat in breast surgery for the past twenty years.<sup>4</sup>

On the other hand, the interference in breast cancer detection due to liponecrotic cyst and calcifications is possible with any breast surgery, varying up to 50% of patients in the two postoperative years.<sup>14</sup> Now, radiologist have the possibility to distinguish new malignant mass and local tumor recurrence from cystosteatonecrosis phenomena.<sup>14,15</sup> In patient that underwent a breast surgery or reconstruction for breast carcinoma, the presence of any suspicious lesion must be approached with the intent to exclude a neoplasm recurrence. Cystosteatonecrotic lesions have different clinical and imaging patterns.<sup>13</sup> Moreover, a regular clinical and imaging control allow to follow the development of these lesions. Breast US appear to be more effective than mammography in the differentiation of a cystic lesion from a solid one after fat transplant.<sup>12</sup> Fat necrosis may present different US patterns.<sup>13</sup> Furthermore, sonography is a low-cost and not invasive diagnostic exam, even if it presents the limit of subjectivity. This brings to consider ultrasound as first diagnostic approach in fat

necrosis. Mammography may be not sufficient to distinguish malignancy from benign lesions. Using MRI is possible to detect malignancy by revealing neoangiogenesis and an early stage gadolinium chelate capitation. It also allows to follow the survival of the transplanted fat by monitoring necrotic cyst and calcifications due to fat necrosis. The capability with imaging to detect a malignancy and the possibility of the formation of suspect lesions with breast surgery lead to strongly advice these patients regular self-examinations and screening controls.

Fat injection can play an important role after breast cancer therapy. Autologous fat transplant represents an innovative therapeutic strategy in patients that underwent a breast conservative therapy. In fact, it allows either an autologous reconstruction of the defect and represents a cell surgical therapy for the radio-damaged skin. Fat transplant represents the only therapeutic approach in irradiated lesions, when the autologous reconstruction is unreasonable. Furthermore, this helps to avoid the complications associated to the eventual prosthetic reconstruction(Authors' unpublished data). After prosthetic breast reconstruction, fat transplant allows to fill the contour deformities, mostly seen in the upper quadrants. The artificial shape of the prosthesis may not perfect fit the personal and unique profile of each patient and/or the defects from mastectomy. Fat transplant is a natural filler solution and can also be used as surgical cell therapy for capsular contracture and prosthesis-associated deformities. After the autologous breast reconstruction, fat transplant plays a role of filler and represents a source for cell therapy to treat irradiation tissue damage.

## V. CONCLUSIONS

In the last twenty years fat injection has been limited from prejudicial belief that it may strongly interfere in the breast cancer detection. On the base that any breast surgical procedure brings to the formation of cystosteatonecrosis lesions that may interfere with breast tumor detection, and based on the capability of the radiologist to distinguish between benign and malignant lesions, autologous fat transplant is considerable as safe and reliable, as any breast surgical procedure. Furthermore, our experience shows that the multiple micro-

injection of a maximum of 0.2 mL strongly reduce the rate of liponecrosis. Thus, this may bring to consider this procedure not to be the main breast surgery responsible of imaging interference. Self-examination and regular imaging screening of breast is strongly recommended to these patients. For our experience, autologous fat transplant represents a natural, attractive, safe and reliable surgical cell therapy for breast reconstruction. It has to be considered either as a complementary procedure or, in some cases, as a unique surgery in breast reconstruction.

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