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International Expert Panel Consensus on Fat Grafting of the Breast

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Background: Autologous fat grafting has broad applications in reconstructive and aesthetic breast surgery as a natural filler and for its regenerative purposes. Despite the widespread use of fat grafting, there remains no shared consensus on what constitutes the optimal fat grafting technique and its oncological safety. For this reason, the authors of this study have organized a Survey and an International Consensus Conference that was held at the Aesthetic Breast Meeting in Milan (December 15, 2018).

Methods: All studies on fat grafting, both for breast aesthetic and reconstructive purposes, were electronically screened. The literature review led to 17 "key questions" that were used for the Survey. The authors prepared a set of 10 "key statements" that have been discussed in a dedicated face-to-face session during the meeting.

Results: The 10 key statements addressed all the most debated topics on fat grafting of the breast. Levels of evidence for the key statements ranged from III to IV with 2 statements (20%) supported by a level of evidence III and 6 statements (60%) by level of evidence IV. Overall consensus was reached for 2 statements (20%) with >75% agreement reached for 7 statements.

Conclusions: The survey demonstrated a diversity of opinion and attitude among the panelists with regard to technique. Clear recommendations for evidence-based clinical practice for fat grafting use both in aesthetic and reconstructive breast surgery could not be defined due to the scarcity of level 1 or 2 studies. *(Plast Reconstr Surg Glob Open 2019;7:e2426; doi: 10.1097/GOX.0000000000002426; Published online 28 October 2019.)*

INTRODUCTION

Autologous fat grafting is a well-accepted and useful adjunct for reconstructive and aesthetic breast surgery. Its role as a natural filler material has demonstrated success for volume enhancement, contour correction, and regenerative capability.[1] Its efficacy to improve the quality of damaged skin following radiation therapy has been especially noteworthy and has demonstrated predictability and reproducibility in properly selected patients.[2]

Despite the widespread acceptance and utility of autologous fat grafting, there is tremendous variability in the harvesting, processing, and injection techniques

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without strong level of evidence (LoE) to support one technique over another.[3] Although efficacy has been demonstrated in the majority of studies, concerns about oncological safety remain due to discrepancies reported in experimental and clinical studies.[4] In addition, potential complications of autologous fat grafting include fat necrosis, calcifications, and oil cyst formation all of which can potentially interfere with the detection of breast cancer and the surveillance of patients with a history of breast cancer.[5]

The heterogeneity associated with these studies is further complicated by assessing outcomes using nonstandardized and subjective methods.[6]

As a result of these shortcomings, the authors created a survey and organized an International Consensus Conference at the Maurizio Bruno Nava (MBN) 2018 Aesthetic Breast Meeting that was held in Milan, Italy, on December 15, 2018.[7] The participants included plastic surgeons, breast surgeons, and radiation oncologists from around world who perform autologous fat grafting or evaluate patients on a regular basis. The intent of the consensus conference was to assess and understand the different attitudes toward fat grafting for aesthetic and reconstructive surgery of the breast to produce a consensus statement that was agreed upon and approved by all the international experts.

MATERIALS AND METHODS

The principle organizers (M.B.N., N.R., G.C.) performed an electronic search of MEDLINE (1997 to June 2018), EMBASE (1985 to June 2018), and the Cochrane Central Register of Controlled Trials (CENTRAL) with the launch of a specific search strategy ("Fat transplantation" or "Fat augmentation" or "Fat graft" or "Fat grafting" or "Lipotransfer" or "Lipoaspirate" or "Lipofilling" or "Autologous Fat Graft" or "Autologous Fat Filler" or "Autologous Fat Grafting" or "Autogenous Fat Graft" or "Autologous Fat Transplant" or "Autologous Fat Transplantation" or "Autogenous Fat Transplantation" or "Autogenous Fat Filler" or "Autogenous Fat Transfer" or "Adipose Harvest" or "Adipocyte Graft" or "Adipose Cell Transfer" or "Adipose Cellular Transplantation" or "Fat harvesting" or "Fat injection" or "Fat reinjection" or "Fat processing" or "Centrifugation" or "Decant" or "Decantation" or "breast surgery" or "breast" or "breast reconstruction" or "cosmetic breast surgery" or "aesthetic breast surgery").

Two authors (N.R. and G.C.) independently reviewed the abstracts and selected all manuscripts that met the criteria for inclusion based on the LoE. Selected manuscripts were scored from LoE I to V (according to Oxford criteria).[8] Inter-reviewer discordance was resolved with arbitration with a third author (M.B.N.).

Following the literature review, prominent areas of controversy and clinical uncertainty were identified and 17 key questions (Table 1) were asked in a survey format and distributed to the international experts.

The international experts (Table 2) were invited according to semiquantitative criteria that included:

- Coverage of different aspects of fat grafting (cosmetic and reconstructive issues, oncological issues, and radiological issues);
- Surgical skills (renowned experience in breast cosmetic and reconstructive breast surgery and fat grafting use);
- Representatives from Europe and the Americas (North- and South-America);
- Authorship of peer-reviewed papers in the field of fat grafting for breast aesthetic and reconstructive purposes in high impact factor journals.

Questions for the survey were sent via e-mail to the panelists 3 months preceding the conference, requesting their evidence-based answers. There were opportunities to suggest other relevant topics not already covered by the formulated questions.

Distribution of answers was calculated and graphically presented at the face-to-face session at the MBN2018 Aesthetic Breast Meeting. For each topic addressed in the key questions, the organizers produced a "Key Statement" with its LoE based on the highest LoE among the reviewed topic-specific studies (Table 3).

This led to 10 "Key Statements" with corresponding LoE. The panelists discussed and expressed their opinion on each key statement in the face-to-face session through a dedicated bespoke web-based survey. The panelists were invited to record their agreement, disagreement, or abstention for each key statement directly from their electronic devices (tablets, smartphones, or PC). This led to minor amendments of some key statements regarding their wording. Agreement of 75% or more with the statement was considered as consensus among the panelists. Agreement from >50% to 74% was considered as a simple majority.

There was a further round of sharing of the key statements in the month following the event with full accordance with the final version of the key statements.

Table 1. Key Questions for the Survey

What is your favorite infiltration technique before fat harvesting?
Which are your decisional drivers for donor site choice?
What is your favorite harvesting technique?
What is your favorite method for fat processing?
Do you use any additional processing step to isolate, prepare, and store adipose stem cells?
Do you use any method of fat enrichment?
What is your favorite method for fat reinjection?
Do you use frozen fat?
Is there a significant correlation between fat grafting technique and clinical outcomes?
Which are the outcomes you consider when evaluating the results of your fat grafting procedures?
How do you measure your outcomes?
Is your opinion in fat grafting rate predictable?
Do you consider fat grafting to be a safe procedure after breast-conserving treatment for breast cancer?
Do you consider fat grafting a safe procedure following mastectomy for breast cancer treatment?
Would you consider fat grafting use in BRCA-mutated patients?
What is your opinion in the role of fat grafting in aesthetic breast surgery?
What is your opinion in the impact of fat grafting procedures on breast cancer detection and surveillance?

BRCA, breast cancer.

Table 2. Expert Panel Members

Name	Nation	Specialty
Phillip Blondeel	Belgium	Plastic and Reconstructive Surgeon
Giovanni Botti	Italy	Plastic and Reconstructive Surgeon
Francesco Casabona	Italy	Plastic and Reconstructive Surgeon
Giuseppe Catanuto	Italy	Breast Oncoplastic Surgeon
Mark Warren Clemens	United States	Plastic and Reconstructive Surgeon
Domenico De Fazio	Italy	Plastic and Reconstructive Surgeon
Roy De Vita	Italy	Plastic and Reconstructive Surgeon
James Grotting	United States	Plastic and Reconstructive Surgeon
Dennis Clyde Hammond	United States	Plastic and Reconstructive Surgeon
Paul Harris	United Kingdom	Plastic and Reconstructive Surgeon
Paolo Montemurro	Italy/Sweden	Plastic and Reconstructive Surgeon
Alexandre Mendonça Munhoz	Brazil	Plastic and Reconstructive Surgeon
Maurice Nahabedian	United States	Plastic and Reconstructive Surgeon
Stefano Pompei	Italy	Plastic and Reconstructive Surgeon
Alberto Rancati	Argentina	Plastic and Reconstructive Surgeon
Gino Rigotti	Italy	Plastic and Reconstructive Surgeon
Marzia Salgarello	Italy	Plastic and Reconstructive Surgeon
Gianfranco Scaperrotta	Italy	Breast Radiologist
Andrea Spano	Italy	Plastic and Reconstructive Surgeon
Constantin Stan	Romania	Plastic and Reconstructive Surgeon

RESULTS

The systematic review of the literature identified 1,253 peer-reviewed publications (**see figure, Supplemental Digital Content 18,** which displays literature review flow diagram, *http://links.lww.com/PRSGO/B214*). After duplicates removal and exclusion of reviews, editorials, and commentaries, we assessed the LoE for 1,150 studies with only 5 (0.4%) LoE I studies addressing key topics on fat grafting.[9–13] One hundred three studies (9%) were assessed as LoE II, 624 (54.2%) as LoE III, 348 (30.3%) as LoE IV, and 70 (6.1%) as LoE V.

This review led to the identification of the key questions for the survey on fat grafting, with questions on (a) surgical technique; (b) regenerative purposes of fat grafting; (c) clinical outcomes; (d) oncological safety of fat grafting; (e) the impact of fat grafting on breast cancer detection and surveillance; (f) fat grafting and aesthetic breast surgery.

The results of the survey and the distribution of the panelists' answers are presented in Supplemental Digital Content. Question #1. What is your favorite infiltration technique before fat harvesting? (**See figure, Supplemental Digital Content 1,** which displays survey results, *http://links.lww.com/PRSGO/B197*). Question #2. Which are your decisional drivers for donor site choice? (**See figure, Supplemental Digital Content 2,** which displays survey results, *http://links.lww.com/PRSGO/B198*). Question #3. What is your favorite harvesting technique? (**See figure, Supplemental Digital Content 3,** which displays survey results, *http://links.lww.com/PRSGO/B199*). Question #4. What is your favorite method for fat processing? (**See figure, Supplemental Digital Content 4,** which displays survey results, *http://links.lww.com/PRSGO/B200*). Question #5. Do you use any additional processing step to isolate, prepare and store adipose stem cells? (**See figure, Supplemental Digital Content 5,** which displays survey results, *http://links.lww.com/PRSGO/B201*). Question #6. Do you use any method of fat enrichment? (**See figure, Supplemental Digital Content 6,** which displays survey results, *http://links.lww.com/PRSGO/B202*). Question #7. What is your favorite method for fat reinjection? (**See figure, Supplemental Digital Content 7,** which displays survey results, *http://links.lww.com/PRSGO/B203*). Question #8. Do you use frozen fat? (**See figure, Supplemental Digital Content 8,** which displays survey results, *http://links.lww.com/PRSGO/B204*). Question #9. Is there a significant correlation between fat grafting technique and clinical outcomes? (**See figure, Supplemental Digital Content 9,** which displays survey results, *http://links.lww.com/PRSGO/B205*). Question #10. Which are the outcomes you consider when evaluating the results of your fat grafting procedures? (**See figure, Supplemental Digital Content 10,** which displays survey results, *http://links.lww.com/PRSGO/B206*). Question #11. How do you measure your outcomes? (**See figure, Supplemental Digital Content 11,** which displays survey results, *http://links.lww.com/PRSGO/B207*). Question #12. Is your opinion in fat grafting rate predictable? (**See figure, Supplemental Digital Content 12,** which displays survey results, *http://links.lww.com/PRSGO/B208*). Question #13. Do you consider fat grafting to be a safe procedure after breast-conserving treatment for breast cancer? (**See figure, Supplemental Digital Content 13,** which displays survey results, *http://links.lww.com/PRSGO/B209*). Question #14. Do you consider fat grafting a safe procedure following mastectomy for breast cancer treatment? (**See figure, Supplemental Digital Content 14,** which displays survey results, *http://links.lww.com/PRSGO/B210*). Question #15. Would you consider fat grafting use in BRCA-mutated patients? (**See figure, Supplemental Digital Content 15,** which displays survey results, *http://links.lww.com/PRSGO/B211*). Question #16. What is your opinion in the role of fat grafting in aesthetic breast surgery? (**See figure, Supplemental Digital Content 16,** which displays survey results, ***http://links.lww.com/PRSGO/B212***). Question #17. What is your opinion in the impact of fat grafting procedures on breast cancer detection and surveillance?(**See figure, Supplemental Digital Content 17,** which displays survey results, *http://links.lww.com/PRSGO/B213*). An overview about the panelists' attitude toward different technical aspects of fat grafting is reported in Table 4.

The 10 key statements addressed the most debated topics related to autologous fat grafting of the breast. Statements 1–5 address technical issues; statement 6 defines the role of stem cells in fat grafting; statement 7 defines the need of core outcome set use and standardized meth-

Table 3. Key Statements on Fat Grafting of the Breast

	Key Statements	LoE	Agreements	Disagreements	Abstentions
1	No high LoE data about fat grafting are available in literature despite the great increase in fat grafting use over the past 20 years. No evidence supports any specific procedural standardization (optimal donor site selection, infiltration, fat harvesting, fat processing, injection, fat storage). Randomized controlled trials are required to understand which factors may significantly impact on fat grafting outcomes.	—	86%	14%	—
2	The available evidence does not support any infiltration technique above another. No significant effects of local anesthesia or epinephrine on fat graft have been demonstrated but local anesthetics may modulate isolated preadipocytes viability rates. Epinephrine/local anesthesia use should be based on pain relief and bleeding control rather than fat cell viability.	IV	86%	14%	—
3	The available evidence does not support any harvesting technique above another. Low-pressure suction (<250 mm Hg) appears to increase adipocyte viability.	IV	79%	7%	14%
4	The available evidence does not support any processing technique above another. When centrifugation is used, several studies suggest that forces >3,000 rpm cause more cellular damage.	IV	79%	7%	14%
5	a. Additional processing steps to isolate, prepare, and store adipose stem cells have not been sufficiently explored in a clinical setting. We actually do not know the viability of the respective cell types (mature fat cells, adipose-derived stem cells, fibroblasts, and endothelial cells) between the various fat harvesting and processing techniques. b. The respective roles that the different cell types play in fat graft take are not known. In particular, there is no definitive evidence about any relationship between the number of adipose stem cells in the transferred fat and the fat grafting outcomes.	IV	93%	—	7%
6	The actual evidence reports that frozen fat can be used for autologous fat transfer. The addition of a cryoprotective agent and the methodology of freezing/defreezing could significantly impact on cell viability.	IV	43%	7%	50%
7	A core outcome set for fat grafting has been recently identified. It is recommended for researchers to use the core outcome set to choose appropriate and standardized outcomes when conducting clinical trials on fat grafting, with the aim of reducing reporting bias and facilitating data synthesis. There is a primary need for identifying appropriate methods for objective and standardized outcome assessment	—	93%	7%	—
8	Fat grafting is a useful tool in aesthetic breast surgery in association to implants (composite/hybrid breast augmentations) or for minor refinements. Fat grafting could be also considered as an alternative to implants for breast augmentation with adequate patient information about the achievable results and the number of sessions needed	IV	93%	7%	—
9	a. Oncological concerns have risen with the use of fat grafting for breast reconstruction. There is an evident contradiction between experimental and clinical findings about the oncological safety of fat grafting. The very complex interplay "in vivo" is not simulated in "in vitro" studies. b. Fat grafting could be considered a safe procedure after breast-conserving treatment and mastectomy for breast cancer treatment with an adequate postoperative surveillance. Prospective clinical trials with adequate follow-up are awaited to definitely confirm the safety of fat grafting in BRCA-mutated patients (both following risk-reducing surgery and surgery for the treatment of breast cancer).	III	100% 93%	— 7%	—
10	Fat grafting is a safe procedure when considering the impact on breast cancer detection and surveillance if a proper technique is used and the surveillance is granted by dedicated breast imaging specialists.	III	100%	—	—

LoE, level of evidence.

ods for outcome assessment in fat grafting studies; statement 8 addresses the use of fat grafting in aesthetic breast surgery; statement 9 underlines current evidences on fat grafting oncological safety; and statement 10 defines the safety of fat grafting in terms of breast cancer detection and surveillance.

For the purpose of clarity, 2 statements have been split (statements 5 and 9). Levels of evidence for the key statements ranged from III to IV with 2 statements (20%) supported by LoE III and 6 statements (60%) by LoE IV. Two statements (ie, 1 and 7) are not associated to LoE because they do not present data deriving from the analysis of published papers but general information about the quality of the evidence on fat grafting of the breast and the published core outcome set.

Overall consensus was reached for 2 statements (20%) with >75% agreement reached for 7 statements. The lowest level of agreement was related to fat storage and frozen fat use (43% agreement, 7% disagreement, and 50% abstention).

CONCLUSIONS

The survey on fat grafting of the breast demonstrated a diversity of attitudes among the panelists with a great heterogeneity in the outcomes considered to evaluate the results of the performed procedures and in most cases subjective nonstandardized methods for outcome assessment.

Tumescent technique using the Klein Solution (saline, lidocaine 0.1%, epinephrine 1/1,000,000) was the most commonly used technique for infiltration before fat harvesting and was the preferred technique for 39% of the panelists.

Some authors investigated the effect of epinephrine and lidocaine on human fat viability, concluding that the use of epinephrine and lidocaine did not have a significant effect on cell attachment in culture, cell morphology, proliferation, or adipocyte metabolic activity.[14,15] These findings were confirmed by other authors who investigated fat cell viability with different epinephrine doses.[16] Contrary to these findings, some researchers examined isolated preadipocytes from fat and found that cell viability was reduced with lidocaine, ropivacaine, and prilocaine.[17] They demonstrated that local anesthetics significantly impaired preadipocyte differentiation into mature adipocytes, with the exception of bupivacaine.[18] With this knowledge in mind before the consensus meeting, some panelists (11%) preferred to use a modified Klein solution without local anesthetics whereas others chose not to use epinephrine (6%).

According to the survey results, fat availability was the main driver for donor site choice (57% of the panelists), followed by the patient's preference (30%). Some panelists chose the closest site to the receiving area based on the notion of "similarity" of the closest fat (7%). No significant differences in terms of cell viability have been demonstrated in relation with the area (abdomen, flank, thigh, and medial knee) where the fat is grafted.[19] Some authors have demonstrated an increased concentration of adipose stem cells in fat harvested from the knees compared with other anatomical locations. The same authors also demonstrated that the superficial fat (ie, the fat situated above the fascia superficialis) was richer in stem cells when compared with the fat below the fascia superficialis.[20]

The panelists underscored the importance of preserving the abdominal donor site in reconstructive patients as autologous flaps from the abdomen (ie, DIEP flap) can be considered in the event of a failed implant-based breast reconstruction.

Table 4. Fat Grafting Technique: The Panelists' Attitude

What Is Your Favorite Technique for:	
Infiltration	Tumescent Klein Solution 39%
	Super wet technique 17%
	Tumescent without local anesthetics 11%
	Power-assisted techniques 11%
	Tumescent without epinephrine 6%
	No infiltration 6%
Harvesting	>3-mm cannulas 29%
	Low-pressure pump assisted 25%
	Manual aspiration with 10–50 ml syringe 25%
	<3-mm cannulas 11%
	Power assisted 4%
Fat processing	Decantation 39%
	Wash and filter (closed sterile devices) 22%
	Wash and filter (no closed sterile devices) 17%
	Filtration (closed sterile devices) 6%
	Centrifugation (various rpm and timings) 6%
Reinjection	1- to 2-mm cannulas and 10 cm^3 syringes 33%
	12/14 G needles and 10 cm^3 syringes 22%
	12/14 G needles and 1–3 cm^3 syringes 15%
	1- to 2-mm cannulas and 1–3 cm^3 syringes 11%
	19/23 G needles and 1–3 cm^3 syringes 7%
	Assisted fat delivery (Celbrush, etc.) 4%

Data are from the MBN 2018 Survey on fat grafting.

With regard to the technique for fat harvesting, manual aspiration with 3–4 mm diameter cannulas and 10–50 cm^3 syringes was the most commonly performed technique (29% and 25%, respectively), followed by low-pressure pump-assisted techniques (25%). The panelists also emphasized the importance of the diameter of the fenestrations within the aspiration cannula as larger diameter fenestrations are associated with less mechanical trauma to the fat and improved fat retention and outcomes.

Several authors studied the impact of the harvesting technique on fat grafting outcomes. Comparisons among various cannulas, needles, suction pressures, external ultrasound, and the utility of preoperative massage on cell viability was studied and demonstrated >10% damage when a −700 mm Hg vacuum was used.[21] Additional studies have compared syringe liposuction to pump-assisted liposuction and demonstrated no differences in terms of cell viability or cell metabolic activity.[22] When comparing cannula diameter, studies have demonstrated increased cell viability using a 4-mm cannula compared with a 2- or 3-mm cannula.[23,24] Pu et al.[25] compared the Coleman technique to conventional liposuction and demonstrated significantly higher adipocyte viability in the Coleman cohort.

Decantation is the most frequently used technique for fat processing by the panelists (39%), followed by washing and filtration using closed sterile devices (22%). Most of the panelists using decantation commented on the benefits of simpler techniques for fat processing after trying different techniques without finding any difference in the final outcome. Only 6% of the panel preferred centrifugation for fat processing using the modified Coleman techniques.[13,17–28]

In a randomized controlled trial that compared centrifuged versus noncentrifuged fat, the centrifuged cohort demonstrated a significant advantage based on fat retention at 5 months.[13] Rohrich et al.[19] disputed these findings demonstrating no significant differences in cell viability between centrifuged (500*g* for 2 minutes) and noncentrifuged samples.[26] Ferraro et al.[27] compared the Coleman technique (3,000 rpm for 3 minutes), their personal technique (1,300 rpm for 5 minutes) and simple decantation of fat, demonstrating a significantly higher intake rate with their own technique. Others have compared different timing of centrifugation at 50*g* (2, 4, 6, and 8 minutes) and demonstrated that centrifugation beyond 2 minutes did not increase the number and proportion of viable adipocytes.[28] Other studies have compared centrifugation (1,500 rpm for 5 minutes) to an open method using a cotton towel,[29] and demonstrated no differences in fat grafting weight and volume after 16 weeks when injected into nude mice. Rose et al.[30] compared adipocyte viability using different methods of fat processing (washing, centrifugation, or sedimentation) and demonstrated that intact adipocytes and nucleated adipocytes were significantly greater in samples processed by sedimentation. Other researchers investigated the effects of centrifugation on liposuction aspirates (various *g* forces for 3 minutes or noncentrifuged) and demonstrated that the optimal centrifugal force is 1,200*g* (3,000 rpm).[31] Condé-Green et al.[32] studied the influence of decantation, washing, and centrifugation (3,000 rpm for 3 minutes) on adipocyte and adipose stem cells content of aspirated adipose tissue, concluding that adipocyte counts were significantly greater in decanted lipoaspirates compared with centrifuged lipoaspirates.

With regard to injection cannulas and syringe volume, the panelists showed a preference (33%) toward 1–2 mm Coleman cannulas and 10 cm^3 syringes for fat reinjection with 22% preferring to use 12/14 gauge needles (diameter 2.06 and 1.63 mm, respectively) and 10 cm^3 syringes. only 7% of the panel preferred using assisted fat delivery systems (Celbrush, Cytori Therapeutics Inc.).

Few studies have investigated the different methods of fat reinjection. Ozsoy et al.[23] compared 3 different Coleman-type cannulas of variable diameter and demonstrated increased adipocyte viability with 2.5 mm diameter cannula compared with the smaller diameters (1.6 or 2 mm). Erdim et al.[24] compared 3 needles based on variable diameters for reinjection (14, 16 and 20 gauge) and found no significant differences between needle gauge and cell viability.

Fat storage and frozen fat were not routinely used by any member of the panel despite literature alluding to fat storage as a viable option. Matsumoto et al.[33] compared cell viability of adipose tissue in different storage temperatures and observed that preservation for 4 hours at room temperature significantly damaged adipocytes but that adipose stem cells remained unchanged. Adipose stem cell yield from cryopreserved fat was decreased compared with fresh isolated aspirated fat. The authors concluded that aspirated fat could be transported to a cell-processing center for cell isolation on the day after harvesting and for subsequent tissue banking if it is kept at 4°C. The methodology for freezing significantly impacted the process. Other authors demonstrated no significant difference between fat graft mixed with cryoprotective agents and fresh graft in terms of adipocyte viability.[34] All available studies have concluded that frozen fat can be used for autologous fat transfer but the addition of a cryoprotective agent and a strict methodology of freezing could improve cell viability.

The large majority (88%) of the panel did not use any method to isolate, prepare, and store adipose stem cells and only 8% of the panelists use fat-enrichment techniques. Some authors have described the technique used for enrichment as a "self-enrichment," mixing the fat of the deep layer (under the fascia superficialis) with the superficial fat, potentially richer in stem cells.[20]

Only 7% of the panel considered fat grafting retention rate to be completely predictable with the majority of panelists (53%) agreeing that retention of grafted fat was not completely predictable and was dependent on patient characteristics and comorbidities, adjuvant therapies, and fat grafting technique.

The majority of the panel (69%) agreed that there was a significant correlation between the fat grafting technique and clinical outcomes.

There was significant variability among the panelists with regard to outcome assessment following autologous fat grafting. The breakdown is listed below:

- fat intake/survival (30%);
- aesthetic outcome of the recipient site (shape/volume/symmetry) (22%);
- regenerative effects on damaged tissues (19%);
- patients' satisfaction levels and quality of life (QoL; 11%);
- aesthetic outcomes of the donor site (8%);
- fat necrosis in the recipient site (8%).

Methods for measuring outcomes reported by the panelists are distributed as follows:

- clinical assessment (35%);
- preoperative/postoperative standard pictures (30%);
- preoperative/postoperative magnetic resonance imaging (10%);
- preoperative/postoperative 3-dimensional pictures (10%);
- nonvalidated questionnaires for satisfaction level and QoL assessment (10%);
- Lent-Soma Scale for radiation damage (5%).

A core outcome set for fat grafting has been recently identified with a strict methodology, listing oncological (rate of locoregional cancer recurrence), clinical (all complications assessed with Clavien-Dindo grading), aesthetic (surgeon assessed), functional (EQ-D5, BREAST-Q), patient-reported (BREAST-Q), process (number of fat grafting sessions need to get optimal result), and radiological outcomes (incidence of radiological abnormalities, interference with mammography) as key outcome to consider when evaluating the results of fat grafting procedures.[6]

It is recommended for researchers to use the core outcome set to choose appropriate and standardized outcomes when conducting clinical trials on fat grafting,[35] with the aim of reducing reporting bias and facilitating data synthesis among different studies.

The panelists emphasized the importance of identifying objective and standardized methods for outcome assessment, going beyond simple clinical assessment, preoperative/postoperative standard pictures or nonvalidated questionnaires for satisfaction level, and QoL assessment.

Oncological concerns have risen about the safety of fat grafting after breast cancer surgery. A recent systematic review[4] reported data deriving from 18 clinical studies,[36–53] showing locoregional recurrence rates (LRR) between 0% and 3.9% per year following breast-conserving treatment and mastectomy plus fat grafting. LRR per year between 0% and 1.62% has been reported following mastectomy plus fat grafting and between 0% and 3.9% following breast-conserving treatment plus fat transfer. Some of the included studies considered a matched control group finding no significant difference between cases and controls with the exception of a subgroup of patients with in situ breast carcinoma.[38]

These concerns derive from the potential interaction between adipose-derived mesenchymal stem cells within the transferred fat and primary breast cancer cells in after breast cancer surgery. Several adipokines have been reported to potentially promote tumor initiation and growth, but clinical studies did not show any significant increase in LRR in patients receiving fat grafting after breast cancer surgery.

There are a clear discrepancy and contradiction between experimental and clinical findings with regard to the oncological safety of autologous fat grafting. It is evident that there is a very complex interplay that occurs "in vivo" that may not be accurately duplicated with the "in-vitro" studies. The role and impact of radiotherapy and systemic therapies cannot be simulated with "in vitro" studies.[54]

The majority of panelists consider fat grafting a safe procedure after breast-conserving surgery (69%) and mastectomy (86%) for breast cancer treatment. Fat grafting was also considered safe in patients with the BRCA mutation (71%), as long as adequate postoperative follow-up is maintained.

The safety and effectiveness of fat grafting of the breast have also been questioned with regard to the development of fat necrosis, calcifications, and oil cysts, all of which can potentially interfere with the detection of breast cancer and surveillance of patients following surgery for breast cancer. However, there is ample evidence that supports the safety and effectiveness of fat grafting of the breast in terms of breast cancer detection and surveillance.[55–64]

The majority of the panelists (75%) stated that fat grafting represents a safe procedure when considering the impact on breast cancer detection and surveillance if a proper technique for grafting is used and the follow-up is granted by dedicated breast imaging specialists. Twenty-five percent of the panelists consider fat grafting safe in terms of breast cancer detection and surveillance, with the need of informing the patient about the possibility of higher second level examination rates (magnetic resonance imaging/biopsies).

Fat grafting use has been also described as an alternative to implants or in association to implants for composite/hybrid procedures for breast augmentation, or as a useful tool for minor refinements following breast augmentation with implants. Forty peer-reviewed articles have been published investigating the use of fat grafting for cosmetic breast augmentation.[59,65–103] Most studies showed a low LoE, with only 1 level II study[103] in only 10 patients. Indications for fat grafting were mostly aesthetic augmentations (92.4%) and corrections of congenital malformations (7.6%).

The majority of the panelists consider fat grafting to be a useful tool in aesthetic breast surgery in conjunction to implants (composite/hybrid augmentations) (41%) or for minor refinements (41%). Only 19% considered fat grafting to be a reliable alternative to implants for breast augmentation. The important factors included adequate patient information about the achievable results and the need for multiple procedures.

In particular, Rigotti et al.[104] presented and discussed a new minimally invasive approach toward breast aesthetic surgery, called biological morphogenetic surgery that exploits the physiological mechanisms of tissue repair and the interaction between the transferred fat and the host tissue to reach a shape enlargement or reduction depending on the patient's surgical needs and requests, following a mild surgical injury.

In summary, the consensus conference demonstrated high levels of agreement among panel of experts with >75% being in agreement for 9 of 10 statements. The only statement that demonstrated a lack of consensus was in regard to fat storage with only a 43% agreement and a 50% abstention rate. The explanation for the high abstention rate was based on the lack of experience with frozen fat as the majority had never utilized fat storage.

Our consensus conference presents some limitations, as the literature behind each key statement has not been assessed with a standardized methodology (ie, GRADE method),[105] but only the LoE according to Oxford Criteria[8] has been evaluated. Thus our conclusions only remain the expression of the opinion of a group of experts on some statements on fat grafting of the breast, not being guidelines for clinical practice. Another limit is represented by choice of the panel that could be not representative of the entire world, in particular with the absence of experts coming from Asia, where fat grafting is widely used.[106]

Clear recommendations for evidence-based clinical practice for fat grafting use both in aesthetic and reconstructive breast surgery could not be defined due to the scarcity of good quality and high LoE studies addressing technical issues related with fat grafting.

The panelists concluded that higher quality and LoE studies, better if randomized controlled trials, are strongly awaited to support procedural standardization in terms of optimal donor site selection, infiltration technique, fat harvesting, fat processing, injection and storage, and to

better understand which factors may significantly impact on fat grafting outcomes.

Prospective studies, better if randomized controlled trials, with adequate follow-up are also awaited to definitively confirm the oncological safety of fat grafting following breast cancer surgery in particular in BRCA-mutated patients and to further approve the safety of fat grafting in terms of breast cancer detection and surveillance.

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