Fat Ful'fill'ment: A Review of Autologous Fat Grafting

For more than a century, clinicians have attempted to utilise fat for the treatment of tissue deficiencies and contour abnormalities. Autologous fat transplantation for soft-tissue augmentation has become increasingly popular in recent years. The popularity of tumescent liposuction has brought renewed interest and accessibility of fat for transplantation. Newer techniques and approaches to augmentation have provided more predictable and reproducible results. Fat augmentation has become an effective, safe and reliable method for restoring volume and correcting the atrophy that accompanies senescence. In this review, the authors have described their approach to fat transplantation.

KEYWORDS: Autologous fat grafting, autologous dermal fillers, fat transplantation

INTRODUCTION

Dermal fillers are an important tool in the armamentarium of an aesthetic dermatologist in the management of ageing skin. A surge in the use of fillers has been witnessed owing to increasing awareness among people, easy availability of fillers and increased enthusiasm amongst the Dermatologists and plastic surgeons to use this modality. Fat has the potential to be the ideal soft-tissue filler because it is abundant, easily accessible, inexpensive, host compatible and because it can be harvested repeatedly. It also offers a similar long-term durability with a low-cost compared to dermal fillers.[1]

A large array of indications have been reported previously: Cosmetic enhancement and rejuvenation, body contour improvement and reconstruction of scarred sites, periocular rejuvenation, fat atrophy in human immunodeficiency virus positive patients, Parry-Romberg syndrome and radiation-damaged sites, among others. Multiple contributions and discoveries have also been made in this field and tumescence anaesthesia is the pillar of all these fat graft surgeries.[2] Use of platelet rich plasma for longer survival of grafts and the realization that fat contains stem cells are few of the new concepts that have gained importance nowadays.[3]

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Even though, fat grafting has become widely used by plastic surgeons, most surgeons choose their method of fat grafting based almost entirely on anecdotal evidence. As more and more scientific studies appear in the literature, we now may have a more objective, scientific evidence to support the use of specific techniques. This paper focuses on the evolution of autologous fat grafting and giving a rationalised approach to it in present times.

HISTORICAL PERSPECTIVE

Autologous fat transplantation has been attempted for over a century with varying degrees of success. During this time, it has been alternately embraced and abandoned Table 1 shows the historical contributions made in the field of Autologous fat grafting.

In the early 2000s, appreciation of the potentials of adipose tissue and its related stromal elements, led to examination of the adipose-derived adult mesenchymal stem cell content.[2,17,18] Evidence has clearly shown the key importance of the progenitor cells, stromal vascular fraction and extracellular matrix as integral contributors to the tissue maintenance and healing processes.[3]

TECHNIQUE

Pre-operative planning is critical when performing fat

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Table 1: Historical contributions to the field of autologous fat grafting

Year	Name of the contributor	Contribution
1893	Neuber	1st documented use of AFG. He transplanted multiple 1-cm fat grafts from the arm to fill soft-tissue depressions of the face caused by tuberculosis[4]
1909	Lexer	Grafted fat from the abdomen to treat a depression of the malar infraorbital area and to augment a receding chin[5]
1911	Tuffier	Studied the histopathology of transplanted fat and made note that large portions of fat were absorbed and replaced with fibrous tissue. Furthermore in that year, Brunings used fat for the correction of postrhinoplasty deformities[6]
1950	Peer	Determined that approximately 45% of the volume of transplanted fat was absorbed after 1 year[7]
1977	Illouz	Demonstrated that it was possible to extract fat by suction rather than by the previous rudimentary methods[8]
1982	Bricoll	The first formal presentation of lipo injection for facial re contouring was made[9,10]
1989	Fournier	Coined the term liposculpture to describe a procedure by which adipose tissue was removed with liposuction and selectively injected to areas with contour irregularities and also demonstrated that fat could be extracted using a 13-gauge needle while using local anaesthesia[11]
1986	Ellenbogen	Used free "pearl" fat autographs of between 4 min and 6 mm in diameter for treatment of acne scarring, facial atrophy and rhytides[12]
1987	Klein	Introduction of the tumescent anaesthesia.[13]
1993	William Coleman III	"Lipocytic dermal augmentation"-mechanically processed fat when injected intradermally stimulated new collagen synthesis as a result of fibrosis at the recipient site[14]
1997	Sidney Coleman	He believed that by using large volumes of fat, he was able to achieve maximum aesthetic results[15]
2000	Carpeneda	Believed that there was improved survival and longevity of the transplanted fat[16] when small volumes of fat, less than 3 mm in diameter, were implanted

As a result of technical difficulties and variable survival of the implanted fat, fat transplantation fell out of favour. It is of interest to note that during the early part of the 1900s, numerous medical specialties attempted to employ fat transplantation. However, Autologous fat grafting was rediscovered in the 1970s-1980s

transplantation. During the pre-operative consultation, medications and allergies are reviewed, with specific concern given to medications that interfere with lidocaine metabolism. Patient is instructed to stop all medications that interfere with the platelet function, 2 weeks prior to surgery and can restart them 1 week after the procedure. Contraindications [Table 2][19] to fat transplantation should be noted and the procedure avoided in certain patients. Appropriate laboratory tests are obtained approximately 1 week before the procedure. Patient is instructed to take 500 mg of Cefadroxil the evening before and continue twice daily to 1 week after the procedure. In cases with a history of previous herpes labialis infection, 400 mg of acyclovir was given in the morning of the procedure and then twice daily for 1 week). Diazepam may be given to any anxious patient, approximately, 1 hr before the procedure.

More recently, the atraumatic technique has been popularized and known to many surgeons. This technique emphasises on atraumatic method of fat harvesting, proper centrifugation and injection aimed at maximising nutrition and structural integrity at the recipient site.[20] This basic fat grafting procedure was arbitrarily divided into four parts: Donor site selection, harvesting, processing and placement.

Donor site selection

Studies by Rohrich *et al*.[21] and Ullmann *et al*.[22] have shown that there is no evidence of a favourable donor site for the harvest of fat grafts. According to these two studies, the viability of lipocytes within the fat grafts from different donor sites may be considered

Table 2: Contraindications for the procedure

Absolute	Consider additional discussion or a waiting period	May necessitate medical clearance
Haematologic abnormalities	Unrealistic expectations	Diabetes
Anticoagulant medication such as aspirin or clopidogrel	Body dysmorphic disorder	Cardiac disease
Allergy to lignocaine		Chronic liver disease

equal. However, adipose tissue has recently been identified as a source of processed lipoaspirate cells or adipose-derived stem cells (ADSCs).[23] Padoin *et al*. evaluated that lower abdomen and inner thigh have higher concentrations of these processed lipoaspirate cells and the inner thigh and lower abdomen may be the better donor sites of adult ADSCs compared with other common donor sites.[24] Hence, fat grafts may not only serve as fillers, but also improve the quality of aged and scarred skin.

With what we know about the potential role of ADSCs in autologous fat grafting, the lower abdomen and inner thighs should; therefore, be chosen as the better donor sites for fat transplantation. We prefer using the thigh as a donor site as in the Indian setting, women usually wear saris and accidental asymmetry of the lower abdomen would be unacceptable. These donor sites are not only easily accessible by the surgeons with a patient in the supine position, but also scientifically sound because they have a higher concentration of stem cells than other donor sites as long as patients have an adequate amount of adipose tissue in those areas.[25]

Once the donor site is decided, the surgeon should also estimate approximate amounts that will be transplanted into each area so that the appropriate amount of fat is harvested. The area for liposuction is marked with a patient in the standing position after a sterile preparation. Often in a thinner patient, several areas have to be prepared and marked in order to accomplish the full harvest.

Method of harvest

In our series, all patients were given short general anaesthesia as this helps to reduce anxiety and pain as per our experience. Then area to be suctioned was infiltrated with 500 ml of ringer lactate with 0.5cc of adrenaline. If small infiltrate is required then the procedure can be carried out under tumescent anaesthesia and in larger areas, tumescent anaesthesia with sedation is given [Table 3]. Once the area is infused, it is best to wait 15 min in order to allow epinephrine to take full effect and for the anaesthesia to infuse evenly through the tissues. If one suctions too quickly, the area tends to give an extract that has a greater percentage of tumescent fluid and is blood-tinged. There are various methods as options for harvesting the fat; Most of these comprehensive studies consistently support that the atraumatic technique for the harvest of fat grafts is superior to conventional liposuction.[26] We prefer using blunt atraumatic fat grafting cannulas since they are considered superior to the conventional liposuction as a preferred method of choice for fat graft harvesting.[27] Comparison between the cannula and syringe harvesting is given in Table 4.[27,28]

The next question to tackle is, what is the proper size of the cannula and syringe favourable for aspiration to harvest fat grafts? A comprehensive study (Viable cell count, a cell proliferation assay, an enzyme assay and Oil Red O stain) conducted by Gonzalez *et al*. conclude that the viability of fat grafts is significantly better when fat graft is harvested by 2 mm diameter cannula with a blunt tip and several side holes connected to a 10cc syringe as compared with a 3 mm diameter blunt tipped cannula connected to a 60cc syringe.

Table 3: Tumescent anaesthesia

1 L of 0.9% sodium chloride solution
0.50 mg epinephrine 1:1000
500 mg lignocaine (25 cc 2% lidocaine) for a 0.05% solution
Bicarbonate (8.4%) in 1:10 dilution with lignocaine

Table 4: Comparison of a traumatic harvesting techniques[27,28]

Cannula (2 mm)	Syringe (10cc)
Are comparatively more traumatic	Are more atraumatic
They maintain the cellular function much better	Cellular function may be compromised
Yield a higher ratio of viable adipocytes	Ratio is comparatively lower
Difficult to maintain the required negative pressure	Easier to maintain the required negative pressure better

To start with the harvesting, once the cannula attached to 10cc syringes is ready, the left hand makes a fold on the extraction site and the needle is pushed through the skin in the middle of the adipose tissue. The left hand is then placed flat on the extraction zone and will stay that way throughout the procedure. The right hand pulls out the syringe plunger completely and the surgeon begins the extraction [Figure 1]. Throughout the procedure, the plunger has to be kept in the same position; hence, syringe locks available in the market can be used for same. At different levels back and forth movements are made in a fan shape almost the length of the cannula. Four or five of these are made in one direction before going to neighbouring region, without taking out the cannula, which must remain under the skin. This process is then repeated with multiple syringes until the required amount of fat is harvested.

Method of process

Most surgeons believe that fat grafts harvested with syringe aspiration or conventional liposuction need to be processed in some way in order to limit the blood or oil within the lipoaspirates so that only pure fat as a soft-tissue filler will be used for injection. However, this has become a highly controversial issue and currently there is no agreement among surgeons in terms of which is the best method for processing fat grafts. Three primary methods (Sedimentation by gravity, filtering technique and centrifugation) have been used clinically to process fat grafts. Many experimental studies designed to compare these three refinement techniques were evaluated only by a single measurement selected by the investigators and thus, which method is better still remains debatable. Although comprehensive studies have now proved that centrifugation, may be more aggressive on adipocytes, but it clears the fat from most blood remnants are able to possibly maintain the highest concentration of stem cells within the processed lipoaspirates.[29] Since stem cell or angiogenic growth factor may play a role in fat graft survival, centrifugation at 3000 rpm (about 1289 g) for 3 min appears to offer more benefits and should be a better method of choice for processing fat grafts.[30,31] After the centrifugation, layers are seen in the syringe, yellow supernatant and blood stained infranatant, this blood stained fluid collected in the lower layer is wicked away prior to injection [Figure 2]. We prefer using a manual centrifuge since it is not too harsh on the adipocytes and also gives a fairly good separation of blood and fat. In this centrifuge machine, the surgeon

rotates the lever and this leads to desirable separation of the fat in approximately 5 min. Sedimentation technique relies mainly on gravity and is time consuming. It can be used when adjunct procedures are planned. Washing of grafts and filtration can also be carried out with commercially available systems.

Anaesthesia of recipient site and method of placement of graft

For recipient site anaesthesia, the entry sites are anaesthetised and a regional nerve block is given. A standard 18 gauge needle is used to create the entry site and local anaesthesia is infiltrated with a blunt cannula. Now, a 10cc syringe full of adipose tissue is used and the injection begins. Approximately, 0.1cc is injected with every pass. This is carried out in an intermittent retrograde pattern while constantly verifying the evacuation of the syringes contents by its graduated scale. This fan shaped reinjection should be carried out at various different levels to obtain a harmonious result and restore the previous anatomy of the site [Figure 3]. This technique also makes sure that fat grafts have a maximal amount of contact with the vascularised tissue in the grafted area for better survival.[32] The placement of fat grafts in different tissue planes was also studied by Karacaoglu *et al*. in a rabbit face model. By measuring transplanted fat grafts morphometrically and histologically, the results reveal the survival of fat grafts is significantly higher if they are placed in supra muscular layer than in subcutaneous or submuscular layer. The findings of the study support the placement of fat grafts indifferent tissue planes to achieve a better result clinically.[33] We prefer, injecting the fat in the subcutaneous layer as the author feels the survival of the grafts is better in this layer.

POST-OPERATIVE

Oedema varies from one patient to another. There are rarely ecchymoses and patients do not mention any pain or discomfort. Patients have a normal appearance after 3-5 days. However, the extraction zones take longer to return to normal. They have oedema and are indurated for several weeks.

When the filling is carried out in an ambulatory basis without general anaesthesia, the whole operation can be completed in 1.5-2 hrs. Antibiotics and

Figure 1: Harvesting of fat grafts seen from the inner thigh

Figure 3: Placement of the fat grafts in the recipient site

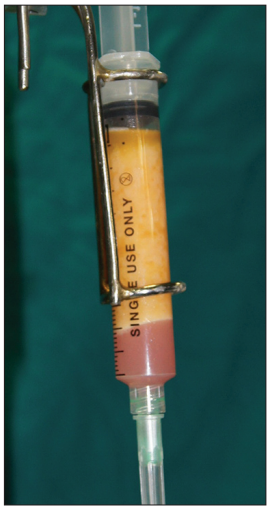

Figure 2: Layers of supernatant yellow fat and infranatant blood-tinged fluid seen post-centrifugation

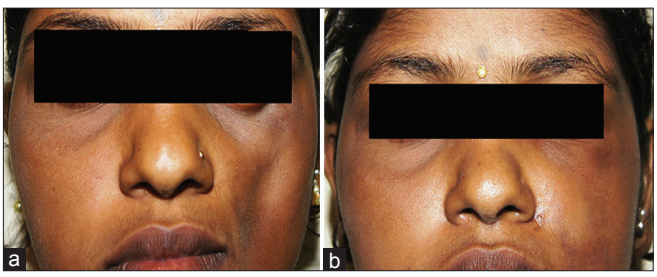

Figure 4: (a) Hemifacial atrophy seen on the left side of the face. (b) Defect is filled post-operatively giving clinically acceptable symmetry

anti-inflammatories are prescribed post-operatively, analgesics are not required [Figures 4a and b].

COMPLICATIONS

Fat transplantation is a relatively safe procedure with a low complication rate. Fat allows a patient to benefit from autologous tissue without risk of allergy, rejection or possible transmission of viral infection. The most common complication of fat transplantation is absorption of fat; this can be avoided by some overcorrection [Figures 5a and b] as per the author's preference. Unintentional overcorrection is also frequently encountered. This is particularly problematic in the infra orbital area where visible nodules may develop. Other complications are:

1. Superficial nodules can also result from the injection of an extremely large bolus of fat too superficially.[34]
2. Other common complications that may occur include post-operative erythema, oedema, bleeding and ecchymosis.
3. Infections following augmentation have been reported.[35] During the pre-operative period, the physician needs to screen for and if necessary, treat active, chronic or recurrent infections, particularly of adjacent facial areas such as sinus, dental or ocular regions. There are reports of the centrifuge serving as a source of infection with *Pseudomonas*. It is recommended that sterile centrifuge sleeves be utilized to decrease the chance of transmission.
4. Vascular occlusion or the development of emboli is the most serious complication associated with fat transplantation. A case of blindness following transplantation in the glabellar region was reported by Dreizen.[36] In addition, occlusion of the middle cerebral artery and ocular fat embolism has occurred following transplantation of fat in the face.[37] There was a report in the literature of an acute fatal stroke immediately following autologous fat transplantation in the face.[38] Vascular compromise is often indicated by dramatic blanching of the skin. In the rare event that this does occur, it is suggested that the patient be placed in the trendelenburg position, apply nitroglycerin paste and massage the area until blanching resolves.[39] It is believed that sharp instrumentation and 10-cc syringes with high injection pressures were involved in the majority of cases with vascular involvement. Coleman reports that the use of a blunt-tipped cannula with initial withdrawal prior to injection will decrease the risk of vascular penetration.[40] To safeguard against intravascular injections, it has also been suggested that physicians use1-cc syringes as well as epinephrine in the anaesthesia so as to promote vasoconstriction. Other recommendations postulated to decrease the risk of fat embolisation include slow injections of small aliquots of fat using low injection pressures. Furthermore, avoidance of fat injection into pre-traumatised tissue[41] is recommended.
5. Fat hypertrophy following weight gain may occur after augmentation. This may require surgical revision to correct.[42]
6. Depressions, asymmetries and bulges may occur.
7. Fat necrosis may lead to contour irregularities. A case, in which a growing liponecrotic pseudocyst developed in the submandibular area, 6 months following fat injection to the cheek and mandibular area was described.[43] In this scenario, it was suggested that the lesion should be excised as aspiration may cause leakage of contents and possible further granulomatous reactions.

Graft survival

Since overall take rate of fat grafting by even more experienced surgeons ranges from about 50-90%,[44]

Figure 5a: Patient with bilateral loss of facial contour

Figure 5b: Post-operative oedema and overcorrection seen

additional procedures are always necessary to achieve an optimal result. However, there is no scientific study, which has addressed the timing of subsequent fat grafting. So far, only "expert" opinion has been mentioned in the literature regarding this specific issue.[45] In our experience, fat survival is for 6-8 months and a repeat procedure is required then.

CONCLUSION

This paper gives a brief review on autologous fat grafting, from evolution to current times. The often abundant supply of this autologous material in our patients requiring aesthetic correction following disease or intrinsic aging behoves us to refine our knowledge of this valuable technique. Furthermore with the new discovery of adipose-derived mesenchymal stem cells, there is added scientific interest now in this procedure. It is hoped that this article will help those new to the field of autologous fat grafting, like cutaneous surgeons, to better understand the procedure.

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