Structural Fat Grafting: More Than a Permanent Filler

Sydney R. Coleman, M.D.
New York, N.Y.

Summary: Grafted fat has many attributes of an ideal filler, but the results, like those of any procedure, are technique dependent. Fat grafting remains shrouded in the stigma of variable results experienced by most plastic surgeons when they first graft fat. However, many who originally reported failure eventually report success after altering their methods of harvesting, refinement, and placement. Many surgeons have refined their techniques to obtain long-term survival and volume replacement with grafted fat. They have observed that transplanted fat not only adjusts facial and body proportion but also improves surrounding tissues into which the fat is placed. They have noted not only the improvement in the quality of aging skin and scars but also a remarkable improvement in conditions such as radiation damage, chronic ulceration, breast capsular contracture, and damaged vocal cords. The mechanism of fat graft survival is not clear, and the role of adipose-derived stem cells and preadipocytes in fat survival remains to be determined. Early research has indicated the possible involvement of more undifferentiated cells in some of the observed effects of fat grafting on surrounding tissues. Of particular interest is the research that has pointed to the use of stem cells to repair and even to become bone, cartilage, muscle, blood vessels, nerves, and skin. Further studies are essential to understand grafted fat tissue. (*Plast. Reconstr. Surg.* 118 (Suppl.): 108S, 2006.)

Grafted fat exhibits many of the qualities of an ideal filler. It is autologous and completely biocompatible, in most patients available in sufficient quantities, naturally integrated into the host tissues, removable if necessary, and, by all indications, potentially permanent. Because of these characteristics, in the last decade fat grafting has become increasingly popular in aesthetic and reconstructive surgery as a primary procedure and as an adjunct to other procedures.

In 1912, Eugene Holländer (1867–1932) from Berlin published photographic documentation of natural appearing changes after infiltration of fat into two patients with lipoatrophy of the face.[1] In 1926, Charles Conrad Miller wrote about his experiences with infiltration of fatty tissue through cannulas.[2] He described 36 cases of correcting cicatricial contraction on the face and neck with only "moderate shrinking of the fat." He observed that the shape of the nose improved over months after fat implantation. Miller also claimed to treat "two cases of very persistent parotid fistula. . .which defied all other methods of treatment—with excellent results" which he followed over 5 years. However, his technique never became widely used.

In the early 1980s, liposuction provided plastic surgeons with a valuable byproduct: semiliquid fat that could be grafted with relative ease using a needle or small cannula. Although Illouz's early publications described great results for iatrogenic liposuction deformities and facial lipodystrophies,[3] his later reports were discouraging and claimed that grafted fat had a survival similar to that of injectable collagen.[4,5] As with many new techniques, the initial experimentation yielded variable results and many failures. For instance, Ersek[6] advocated a technique in which the fat was "agitated with a wire whisk

Structural fat grafting is an autologous tissue transfer in which the fat is removed and then infiltrated at the same procedure. This type of procedure is not regulated by the FDA.

From the New York University School of Medicine.
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. . . then rinsed repeatedly. . .then suspended in physiologic solution." His article in *Plastic and Reconstructive Surgery* included a photograph of the "cleansed fat" being forced through a strainer. After using this traumatic technique, he reported that fat grafting had a low survival rate. This article set an unusual precedent in the plastic surgery literature whereby a surgeon developed a new surgical technique and then proceeded to report on its failure in his first published article on the topic. Carson Lewis[7] responded vehemently to Ersek's negative article, insisting that Ersek and those surgeons who were experiencing poor results "must be doing something different from other surgeons."

In the early 1990s, many positive reports of fat grafting were published.[7–11] Despite these successes, the negative effects of Ersek's initial report and the dramatic title of the article, "Transplantation of Purified Autologous Fat: A 3-Year Follow-Up Is Disappointing," lingered and captured the attention of the fat grafting world for over 15 years. Even today, Ersek's article is possibly the most cited article on fat grafting technique in the literature, appearing not only in the plastic surgery literature but also in tissue engineering, ophthalmologic surgery, otolaryngology, dermatology, oral, maxillofacial surgery, and even basic science publications with alarming frequency. Almost never cited are Ersek's later positive experiences with fat grafting, when he subsequently altered his technique to a method similar to the one that I have advocated and experienced long-term survival of grafted fat.[12] Ellenbogen also went through a similar cycle. He first published an enthusiastic initial report on fat grafting,[13] which he later denounced,[14,15] and then, years later like Ersek, he described a technique similar to that described in this article in which he obtained good results.[16,17] Nevertheless, the world continues to dwell on the early failures of fat grafting rather than on the eventual successes.

My experiences with fat grafting have confirmed the efficacy and permanence of grafted fat, provided that it is handled atraumatically and that proper harvesting and grafting technique is followed. I have been reporting on my findings since 1988 at the American Society for Aesthetic Plastic Surgery annual meeting in San Francisco, when I presented cases of fat grafting to the nasolabial folds that maintained correction at 1 year. In 1995, these same patients demonstrated continued correction 7 years after one procedure.[18] My consistent observation is that fat grafting can result in long-term corrections.[19–23]

In the mid 1990s, I began to observe other attributes of fat. I noted that the quality of the skin under which grafted fat was placed improved, not only as an effect of the fullness but also with gradual improvement in the quality of the skin. Wrinkles softened, pore size decreased, and pigmentation improved over the first year. There also appeared to be an improvement in the quality of the tissues into which fat is grafted. Around 1995, I noted that fat grafted under depressed scars not only relieved the depression but also seemed to soften or even completely eliminate the scar, making it look like normal skin.[21] The effect of grafted fat seems to be much more than a long-term filling. Now, with reports of the clinical efficacy of fat grafting for the treatment of radiation damage,[24–26] breast capsular contracture,[25] damaged vocal cords,[27] chronic ulceration,[28–30] and even the regrowth of calvarial bone,[31] we need to look at grafted autologous fat with a different eye and as much more than just a filler.

MATERIALS AND METHODS

Harvesting

The technique of structural fat grafting has been previously described in detail.[22,32] Current studies have not indicated increased viability from any one donor site,[33,34] so harvesting sites are chosen for ease of accessibility and to improve the patient's body contours. Through 3-mm incisions, a two-hole Coleman harvesting cannula with a blunt tip is attached to a 10-ml Luer-Lok syringe. The cannula is pushed through the harvest site as the surgeon uses digital manipulation to pull back on the plunger of the syringe and create a gentle negative pressure. A combination of slight negative pressure and the curetting action of the cannula through the tissues allows parcels of fat to move through the cannula and Luer-Lok aperture into the barrel of the syringe. When filled, the syringe is disconnected from the cannula and replaced with a plug that seals the Luer-Lok end of the syringe. The plunger is removed from the syringe before it is placed into a centrifuge.

Refinement and Transfer

Centrifugation separates the denser components from the less dense components to create layers. The upper level is the least dense and consists primarily of oil. The middle portion is primarily fatty tissue. The lowest layer is blood, water, and any aqueous element (lidocaine). For sterility, a smaller centrifuge with a central rotor and sleeves that can be sterilized is preferred. The recommended centrifugation speed is 3000 rpm for 3 minutes. Larger centrifuges can create significantly more gravitational force at 3000 rpm than the smaller centrifuges commonly used in offices. After the oil layer is decanted, the Luer-Lok plug is removed to release the densest liquid layer. Absorbent material can be used to wick off any remaining oil. The refined fat is then transferred into a 1- or 3-ml Luer-Lok syringe.

Placement

The instruments used for placement of fatty tissue are dramatically different from those used for harvesting: the placement cannulas are of a much smaller gauge, with only one hole at the distal end. Like the harvesting cannula, the proximal end of the infiltration cannula has a hub that will fit into a Luer-Lok syringe. The most useful size of cannula for placement in the face is 17 gauge. However, larger bore cannulas can be used for corporal fat grafting and smaller gauges may be appropriate in areas such as in the lower eyelids. For various situations in the face and body, cannulas with different tip shapes, diameters, lengths, and curves can be used.[32] The use of blunt cannulas allows placement of the fat parcels in a more stable, less traumatic manner. However, less blunt cannulas may give the surgeon more control for placement in the immediate subdermal plane, in fibrous tissue, and in scars. A cannula with pointed or sharp elements can be used to free up adhesions.

Through 2-mm incisions, the infiltration cannula is inserted and advanced through the recipient tissues into the appropriate plane. Fatty tissue should be injected only as the cannula is withdrawn—this deposits the fatty tissue in the pathway of the retreating blunt cannula. As the cannula is withdrawn, the deposited fatty tissue parcels fall into the natural tissue planes as the host tissues collapse around them.

Accuracy of the initial placement of fat is important because it is difficult to manipulate the infiltrated fatty tissue afterward. If a clump forms accidentally, digital manipulation can sometimes flatten minor irregularities. However, the tissue should never be placed with the idea that digital pressure can change the shape after placement. In the face, the largest amount of tissue that should be placed with each withdrawal of a cannula is 1/10th ml, but in some areas, such as the eyelid, the maximum placed should be closer to 1/30th or even 1/50th ml per withdrawal. The endpoint of placement varies widely between anatomical areas. In the lateral malar cheek and mandibular border, the appearance at the conclusion of infiltration of fat will be similar in shape and even size to the final outcome. In contrast, areas such as the lips or eyelids will be grossly distorted and not resemble the desired outcome for weeks after placement.

Safety

Fat grafting procedures have a reputation for being relatively safe, but as with any surgical procedure, complications can occur. Fortunately, the complication rate with fat grafting is extremely low compared with the rate associated with most open surgical techniques, and the incidence of problems decreases dramatically with the surgeon's experience. This is a brief summary of complications; a more exhaustive list of potential and experienced complications can be found elsewhere.[32]

Most patients find the removal of fat and the body contouring performed at the same time to be desirable, yet even a surgeon who is facile at liposuction may experience liposuction deformities. Furthermore, some patients simply do not have donor sites adequate to accomplish the desired corrections. This is especially true in thin patients or patients who have already had liposuction.

Although infection is uncommon with fat grafting, sterile technique should be observed at all times. Even a blunt cannula when inserted for removal and placement of fat can damage underlying structures such as nerves, muscles, glands, and blood vessels when this technique is used; however, permanent injuries are extremely rare. In 1926, Conrad Miller warned of the dangers of intraarterial injection of fillers.[2] No intravascular injections have been reported using a blunt cannula, but caution should always be exercised with any injection or infiltration to avoid the creation of intravascular emboli.[35]

The most common complications of fat grafting are related to aesthetics, such as the placement of too much or too little fat in a specified area. The next most common problem is the presence of irregularities, which can be caused by the intrinsic nature of the patient's body, from the technique used for placement, and from migration after placement. Irregularities after fat grafting diminish significantly as the surgeon gains experience with the technique. A rare reported aesthetic complication is the overgrowth of fat grafts with or without weight gain.[36,37]

The placement of fatty tissue in the manner described above may create remarkable swelling

Fig. 1. This 34-year-old woman presented with chronic acne scarring of the cheeks and expanded polytetrafluoroethylene strips in her lips (*second row*). She was treated with fat grafting in one session, with release of buccal adhesions and removal of the expanded polytetrafluoroethylene strips. (*Above*) Markings demonstrate the placement of fat, with *green* representing areas of significant placement and *orange* delineating the limits of placement (where no fat was placed). The patient returned at 11 months (*third row*) and at 3 years 7 months (*below*). The fat grafting resulted in a lip that is more everted centrally to create an attractive pout. The upper lip is fuller and more natural appearing, with less upper incisor show. A healthy fullness has been restored to the buccal cheeks, with significant ablation of the acne scarring. The deepest linear scar located on the patient's left anterior lower cheek has practically disappeared, as have many of the other scars. The patient noted that the quality of her skin had improved between 11 months and 3 years 7 months. She felt her lip and even her cheeks had become fuller over the 3 years, without weight gain.

in the recipient tissues. This depends primarily on the amount of fat placed and the anatomical location to which it is grafted. Patient care after fat transplantation is directed at minimizing swelling and avoiding migration. Elevation, cold therapy, and external pressure with elastic tape help pre-

Fig. 2. This 23-year-old man presented 15 years after radical local excision of a rhabdomyosarcoma of his left masseter followed by irradiation (*left*). Seven months after one procedure, the volume correction is obvious. Not only is the skin is softer and healthier appearing but the beard also appears denser in the buccal region. The position of the ear has changed radically and appears to be more normally supported. No subcutaneous fullness could be pinched; only thin supple skin over the newly supported area (*below*, *second from right* and *right*). The grafted tissue felt completely integrated into the recipient tissues.

vent swelling. The patient is asked to avoid heavy pressure on the grafted areas for 7 to 10 days to avoid migration of the grafted fat.

CASE REPORTS

Case 1

A 34-year-old woman (Fig. 1) presented for treatment of chronic acne scarring in her cheek, and a lip deformity created by the placement of expanded polytetrafluoroethylene strips. The patient had undergone a carbon dioxide laser treatment of her entire face 8 years earlier, and had expanded polytetrafluoroethylene strips placed into her upper and lower lips 4 years earlier. Otherwise, she had no other procedures or fillers to her face. Only one fat grafting procedure was performed, during which fat harvested from the abdomen and lateral thigh was infiltrated in the following quantities: 15.2 cc over the right cheek and lower eyelid and 18.2 cc over the left cheek and lower eyelid; and 3.1 cc into each nasolabial/marionette fold and 4 cc into the chin. In the buccal cheek only, a double pointed V-dissector was used after the fat placement to release adhesions from the acne scarring. To minimize the possibility of intraoral contamination, the lip procedure was performed last. After infiltration of 3 cc of fat

Fig. 3. The patient in case 3 is a 45-year-old woman who presented for panfacial rejuvenation and also requested larger cheeks and a stronger mandibular border. Fat was grafted to her brow, temples, upper and lower eyelids, cheeks, nasolabial folds, lips, chin, and border of mandible. Eleven days after the procedure (*above*, *center*) she returned swollen, but with resolution of most of the bruising. At 5 weeks (*above*, *right*) she looks presentable, but still slightly swollen. The volume at 12 weeks (*center*, *left*) appears similar to six months (*center*, *center*) and 10 months (*center*, *right*). However, there were subtle changes even between six months and ten months. When she returned at 4 years 8 months (*below*, *left*), she had no apparent loss of volume of the transplanted fat in comparison to the earlier photo. Even at 8 years (*below*, *center*) the grafted areas maintained their correction. At 11 years and 7 months after only one fat grafting and no other procedures or fillers, the patient still had considerable maintenance of her volume correction.

Fig. 4. Close-up periorbital view of the patient in case 3. Before the procedure, her upper eyelids and brow are asymmetric, with her left upper eyelid being markedly hollow (*above*, *left*). At 12 weeks (*above*, *right*), the placement of fat into the upper eyelids resulted in a decrease in the left palpebral show but a slight increase in the palpebral show on the right. The fullness in both upper eyelids, however, now appears more symmetric. The increased fullness of the temple supports more lateral eyebrows so that more eyebrow is exposed. From 12 weeks (*above*, *right*) to 6 months (*center*, *left*), there continues to be a remodeling of the lower eyelid, with flattening of the fullness in the tear trough region (see also Fig. 3). There is little change from 6 months (*center*, *left*) to 4 years 8 months (*center*, *right*). The superior temple shows signs of atrophy by 8 years (*below*, *right*), but the upper eyelids remain full. The upper eyelids show some signs of atrophy by 11 years 7 months. The areas of infiltration in the lower eyelids are becoming obvious as they persist and as the surrounding areas atrophy.

into the upper lip and 5 cc into the lower, the expanded polytetrafluoroethylene strips were removed through vertical incisions. More fat was then added for contouring of the lip, for a total placement of 4.9 cc into the upper lip and 8 cc into the lower lip. She returned at 11 months after fat grafting (Fig. 1, *center*) enthusiastic about the appearance of her lips, but was especially delighted by the virtual disappearance of the scars of her anterior buccal region. When she returned at 3 years 7 months (Fig. 1, *below*), she felt that her scars had continued to improve, as did the general quality of her skin over the infiltrated areas.

Case 2

A 23-year-old man (Fig. 2) underwent radical excision of a rhabdomyosarcoma of the masseter muscle, followed by radiation, at the age of 8 years. This left him with a significant mandibular and buccal deficiency of both the bone and soft tissues. As a result of the radiation damage, the skin was thin and friable, with scattered alopecia of his beard. One hundred fifteen cubic centimeters of refined fat harvested from the abdomen and anterior thighs was infiltrated over the left mandibular, buccal, and mastoid regions. The placement was limited by the lack of supple soft tissue into which fat could be implanted and adhesions along the mandible and anterior buccal regions. A double-pointed cannula was used to release adhesions in the anterior buccal region and mandible. He had no postoperative problems and there was no evidence of nerve injury or damage to any underlying structures. When he returned at 7 months for the next stage, a significant volume had been restored. The skin over the implanted fat was much softer and more pliable, and his beard hair had grown into some of the areas of alopecia (Fig. 2). Even with this significant volume change, the cheek, mandible, and mastoid did not feel fat but felt like the normal tissues in his face.

Case 3

A 45-year-old woman (Figs. 3 and 4) presented for rejuvenation of her periorbital region. She also requested the larger cheeks and square jaw of her youth. The only prior operation on her face was a rhinoplasty 20 years previously. The procedure was performed in one session. Using only a completely blunt infiltration cannula, the patient had diffuse infiltration of fat to her face that was harvested from the thighs and flanks. Onto the temple, brow, and upper eyelids, 26.5 cc was placed. That placement extended caudally to 4 mm below the eyebrow and posteriorly and superiorly to the hairline. In the glabella, nasion, and nasal dorsum, 2.25 cc was placed. Into the cheeks from the infraorbital rim to the buccal cheek and back to the sideburns, 22 cc was placed on the right and 18.75 cc on the left; 7.5 cc was placed into the nasolabial fold/marionette region on the right and 6 cc on the left; 20 cc was placed diffusely over the entire chin down past the border of the mandible. Along the mandibular border, 27 cc was place along the right and 17.5 cc along the left; 6 cc was placed into the lower lip and 4.5 cc into the upper lip. Finally, 40 cc was suctioned from her submentum. No excisional or suspension procedures were performed.

The patient had an uneventful postoperative course, with no complications. No lymphatic drainage, massage, electromagnetic therapy, laser, or any other topical treatments were performed on her face. Approximately 1 year after the procedure, she intentionally lost 10 pounds over a 1-year period, and her weight remained stable after that point. She used only over-the-counter skin care products and has never had a chemical peel or laser treatment. She was extremely pleased for the first 8 years but then began to notice a slight deterioration in her appearance, especially with atrophy of the areas that had not been grafted with fat (Figs. 3 and 4).

RESULTS

These three patients illustrate the types of discoveries that are being made worldwide from short-term and long-term observations of patients after fat grafting. The patient in case 1 demonstrates the potential of fat to correct depressions associated with scarring and treatment of a deformed, scarred lip. Fat grafting has been described frequently for the treatment of depressed traumatic, acne, or iatrogenic scars,[8,11,21,38–40] sometimes with release of adhesions,[41] as in the patient in case 1. Observation over time demonstrates more than just filling of the scars. In some instances, such as the patient in case 1, there appears to be remodeling of the scar over time to the point that an obvious scar can become imperceptible.[21]

The patient in case 2 demonstrates that the use of fat grafting not only provides a structural improvement in a remarkable bone and soft-tissue deficiency but also results in an improvement in the quality of skin damaged by radiation and in the recovery of beard hair follicles. The patient in case 3 illustrates my consistent long-term experience with grafted fat. The volume of fat seems to stabilize at 3 to 4 months, but there may be a subtle decrease in volume for even up to 1 year after the procedure. After that, the volume remains constant, with the surrounding tissue losing significantly more fullness than the grafted areas. In this patient, as in the others I have followed for extended periods, enough deterioration in fullness occurs between 8 and 12 years that they may desire additional treatment. However, even at 11 years 7 months after the one fat grafting procedure there is still a significant volume correction.

In all three patients, the transplanted fatty tissues did not feel like isolated collections of fat. Over the past 15 years, I have consistently observed a remarkable integration or blending of the newly grafted fat into the recipient sites.[18–20] The fat placed next to bone seemed to feel like bone, the fat placed directly under skin felt like thicker skin, and the fat placed into muscle felt like muscle. Patients with significant augmentation of their facial elements returned complaining that the grafted fat must have all died because they could not feel the fat. Because of this high level of integration of the grafted fat with the surrounding tissues, I realized that meticulous photography was essential for evaluation of results from fat grafting. Without accurate photography in many views to demonstrate three-dimensional correction, grafted fat is so natural feeling that many patients (and physicians) think that the correction from the fat is gone.

DISCUSSION

Harvest and Refinement

Recent studies have demonstrated that fat harvested using a blunt cannula and refined by centrifugation as described above has a greater than 90 percent survival rate according to histologic studies[42–44] and near normal adipose cellular enzyme activity.[42,43,45,46] In vivo studies are still needed to determine actual survival rates; however, one clinical study observed increased survival of grafted fat after centrifugation.[47]

Immediately after harvesting, the suctioned aspirate can be composed of as little as 10 percent fat and as much as 90 percent fat. The amount of nonliving components in the suctioned aspirate depends on the quantity of liquid injected by the surgeon, the amount of blood in the harvested specimen, and the release of lipids from ruptured cells. To obtain predictable results, these nonliving elements should be removed so that the surgeon knows how much fat is being infiltrated. We need continued studies to determine in a more scientific and reproducible fashion whether the best method of refinement is cell isolation through centrifugation[48] or by other means.[49]

A problem we face with studying fat grafting is the difficulty of comparing different techniques for grafting fat. Even if the experimenters claim to be using a certain technique, often they are not. The instruments used, leaving out one step, or adding a step may influence the viability and make one study not comparable to another. Even plastic surgeons that claim to use the Coleman technique often skip a step or reverse a portion of the technique. For instance, von Heimburg claims to use the Coleman technique for harvesting fat to use in his freezing experiments, but on careful examination of his article, he did not use the harvesting cannula for removing the fat. Instead, he used the much smaller cannula intended for infiltration of the fat to harvest the fat.[43] Therefore, he is harvesting fat for his study with a much smaller cannula than the technique describes. It is essential that experiments describe in detail each step and the exact instruments used such that the studies are comparable and understandable. This is rarely done.

Method of Placement

The factors that lead to survival of transplanted fat continue to perplex us, but I believe that the most important consideration in fat grafting is the method of placement. The early suggestions by Bircoll of placing fat in small aliquots[35] were met with disdain. His critics claimed that placing fat in increments as small as 1 cc per pass (130 cc in 130 passes) was "ludicrous."[50] However, most descriptions of successful fat grafting involve the purposeful placement of a miniscule volume of fat with each pass.[25,27,44,51–54] Diffuse infiltration with multiple passes and the placement of extremely small amounts with each pass, and attempting to separate the newly grafted fat parcels from each other, is one of the keys to successful fat grafting.

This method of placement attempts to separate the parcels of fat, one from the other. Because the newly grafted fat is not in contact with other grafted fat, it means that more of the fat will be in contact with the new recipient tissue. This large surface area of contact between the host tissues with its capillaries and the newly grafted tissue promotes nutrition and respiration. In addition, this large surface area of contact stabilizes placed fat to deter migration and integrates the fat so that it feels like generalized fullness rather than discrete collections of fatty tissue.

Relatively pure fat should be placed into the recipient site to encourage uniform survival, stability, and integration into the surrounding tissues. However, it is not enough to graft fat so that it merely survives; the grafted fat must make a positive change in the recipient sites. The surgeon should become familiar with not only the levels of placement (e.g., subdermal, intramuscular, supraperiosteal) but also the amounts necessary at each level to accomplish desired change. This varies with each part of the face and body and from patient to patient.[21,32,51,53] Clinical studies demonstrate the obvious: variations in technique determine the clinical outcome.[44,55] We need better studies aimed at improving our clinical experience with free fat grafts.

Fat Graft Survival Theories

In 1923, Neuhof and Hirshfeld[56] examined grafted fat under a microscope and observed that that the fat grafts were dominated for 2 or 3 months by "degenerative phenomena." Beginning in the second month, they noted that some regeneration began to occur as "wandering cells undergo characteristic changes into embryonal fat cells," which eventually became adult fat tissue. At the end of 5 months, they felt that the regeneration was complete, and newly "metaplastic fat" assumed the appearance of normal fatty tissue. They also observed that on occasion, instead of becoming normal-appearing fat, the grafted tissue became permeated with connective tissue. They concluded that transplanted fat completely died and was replaced by fibrous tissue or newly formed metaplastic fat. This came to be known as the "host cell replacement theory" of fat grafting. Thirty years after Neuhof and Hirshfeld, Lyndon Peer took an even closer look at fat grafts and concluded that not all of the adipocytes died.[57,58] Instead, after being cut into small pieces and transplanted into donor sites, approximately 50 percent of the fat tissue survived intact. It is possible that a combination of these two theories about the survival of fat grafts is true, but recently scientists have also considered the influence of undifferentiated cells normally found in fatty tissue.

Looking at the physical characteristics of adipose-derived stem cells and preadipocytes will help us understand transplanted fat. These cells are more resistant to trauma than adult adipocytes, probably because of the significant differences between the two types of cells with regard to size, metabolic rate, and intracellular content of lipid. The fragile, lipid-filled adipocytes are more easily damaged by harvesting than are preadipocytes,[42] and they are much less hardy in the donor site. If the adult fat cells survive the trauma of transplantation, within 4 to 8 days after implantation they must obtain nutrition by a method such as inosculation.[59–61] Preadipocytes are more resilient to the trauma of liposuction, so they are more likely to survive harvesting and refinement. It is equally important that they are able to survive without nutrition much longer[42] and have a much lower oxygen consumption rate than mature adipocytes.[43] Because adipose-derived stem cells are so much more tenacious than lipid-filled adult adipocytes, some researchers believe that a major effect of fat tissue transplantation is caused by the survival of adipose-derived stem cells in the stromal cell fraction.[25,42] Preadipocytes and adipose-derived stem cells might be the only tissue that survives transplantation, and the variability of these cells between individuals may be one of the reasons for the observed variability of survival of fat grafts.

Even though surgeons have come to acknowledge the potential of grafted fat to survive over a long period,[12,16,40,62–64] fat grafting has proven to be unpredictable in the hands of many surgeons. They find that sometimes too much fat survives and at other times not enough appears to persist. Further research will possibly help us to better understand the survival of grafted fat.

Adipose-Derived Stem Cells

What is a stem cell? A basic working definition is that these cells have both a self-renewing capacity and the ability to produce daughter cells that have a more specialized function.[65] Human adipose tissue has emerged as an important source for stem cells.[66] Recently, we have discovered that fatty tissue has the highest percentage of adult stem cells of any tissue in the body, with as many as 5000 adipose-derived stem cells per gram of fat compared with 100 to 1000 stem cells per milliliter of bone marrow.[67] In addition, one study showed that as many as 350,000 preadipocytes can be isolated from 1 g of adipose tissue.[42]

These more primitive cells can clearly differentiate into adipose tissue, but recent studies have demonstrated the ability of adipose-derived stem cells to undergo multilineage differentiation,[68–74] not just into fat but also into bone, cartilage, skeletal muscle, cardiac muscle, blood vessels, nerves, and skin. This happens not only in vitro but also in animal models[75–81] in vivo. Perhaps even more important, recent studies have demonstrated that adult, lipid-filled adipocytes can dedifferentiate into stem cells and redifferentiate into other tissues such as bone.[78] What really happens when fatty tissue is transplanted into humans has yet to be confirmed. As we discover more about the role of adipose-derived stem cells and preadipocytes and their abilities to change or repair tissue, we will probably understand the changes we are observing after fat grafting.

Fully differentiated epidermis can form from adipose-derived stem cells in vitro,[82] and we now have evidence that skin repair under normal physical conditions may involve stem cells.[83] Studies will delineate the role of adipose-derived stem cells in the repair of damaged skin both in normal physiologic conditions and after free transplantation of fat.

Effect on Surrounding Tissue

Recently, plastic surgeons have had remarkable clinical experiences with the effect of fat on surrounding tissues. Gino Rigotti[25] has successfully treated end-stage radiation dermatitis and breast capsular contracture with fat grafting. Others have successfully treated chronic ulcerations with fat grafting.[29] A recent report by Cantarella, an otolaryngologist working with Mazzola in Milan, shows remarkable improvement in the medialization of vocal cords after injection of fat using the Coleman technique.[27] Similar improvements were not noted with fillers or even fat grafted by other methods. Now, Drs. Mazzola and Cantarella are researching the effect of vocal cord tissue regeneration mediated by mesenchymal stem cells in adipose tissue. They are currently using animal models of damaged vocal cords to investigate the effect that adipose-derived stem cells have in the repair of damaged vocal cords.

Stem cells may provide an explanation for the apparent healing effects seen with fat grafting. However, we do not have a great deal of insight into the mechanisms of these effects. Some of the studies point to interaction that the grafted fat is having on neighboring tissue to be repair of the surrounding tissues either directly or through angiogenesis or vasculogenesis.[79,84] Other studies emphasize the plasticity between preadipocytes and macrophages, so that some or all of the healing effect may be secondary to enhanced immune response[85,86] or removal of dying or defective cells, leading to permanent tissue remodeling.[87] Other factors may potentially be involved, such as the release of hormones, cytokines, or a growth factor.

CONCLUSIONS

Fat can fill large and small soft-tissue defects of the face and body, with every indication of permanence. However, fat grafting does not seem to work equally for every technique, for every area of the body, for every patient, or for every surgeon. The experiences of Ersek and Ellenbogen demonstrated clearly that, as with any surgical procedure, the technique used, the execution of the technique, and the experience of the surgeon affect the outcome. There is no doubt that surgeons can kill fat in the process of transplanting it[6,14]; and the same surgeons with a different technique can experience great survival of the grafted tissue.[12,16,17] The literature reports large numbers of clinical successes with fat grafting but few objective data to explain the successes or the failures.

Fat grafts have other potential attributes that we are just beginning to realize. Fat as a living, free graft does more than just fill the area into which it is placed. Grafted fat affects the tissue into which it is placed in many ways for the life of the patient. It can improve the quality of aged and scarred skin and heal radiation damage and chronic ulcers. Just how grafted fat causes these changes remains unanswered. We know that fat can perform amazing feats in a glass tube and in some animal models, but we have little insight into what happens to fat when it is grafted from one part of the human body to another part. The focus of the near future should be research to explain and expand on our clinical successes.

Sydney R. Coleman, M.D.
New York University School of Medicine
44 Hudson Street
New York, N.Y. 10013
lipostructure@yahoo.com

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DISCLOSURE

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