

Fat grafting: A historical review

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Abstract

Fat grafting is a popular procedure that provides a physician with a range of aesthetic, reconstructive, and regenerative clinical applications. It involves the harvest of fat tissue from one region of the body and transfer to another. The indications and techniques of fat grafting have undergone dramatic changes over time. This review revisits the important milestones in the historical evolution of fat grafting.

Key words

Fat graft; Autologous fat graft; Lipofilling; Lipoinjection; Graft harvest; Adipose derived stem cell; Centrifuge; Regenerative medicine.

Introduction

Fat grafting is a popular procedure in which fat tissue is transferred from one part of the body to another. Fat tissue was once considered an organ of energy storage and was discarded as a cosmetically unnecessary tissue, but over time, it attained the position of a safe tissue filler to enhance the body contours. Currently, it is regarded as a valuable source of adult stem cells with an abundance of progenitor cells, some of which can differentiate into diverse lineages. This transformation of concepts and understanding has occurred over the last three centuries, and this history can be broadly divided into three distinct phases,¹ as depicted in **Figure 1**.

1. The open-air period when adipose tissue was harvested by open surgical excision
2. The non-purified or unrefined or traumatic period, marked by the introduction of liposuction.

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3. The purified or refined or atraumatic period that started in 1990's with Coleman's work and continues till this day.

The objective of this article is to give a broad overview of the significant turning moments in the historical development of fat grafting.

Methods

A comprehensive literature review was carried out using the keywords "fat graft," "autologous fat graft," "history of fat graft", and "lipofilling" in electronic databases like PubMed, SciSpace, ResearchGate, SEMANTIC SCHOLAR, Saudi Digital Library, and Scopus. Individual keywords were used in the search together with a boolean logic (AND) combination. No specific dates were selected, and articles published in the English language were analyzed. References in other languages, with the translation of the full text or else an elaborate abstract, were utilized.

Discussion

1 Open-Air Period (1889-1975) The initial attempts at fat tissue grafting took place during

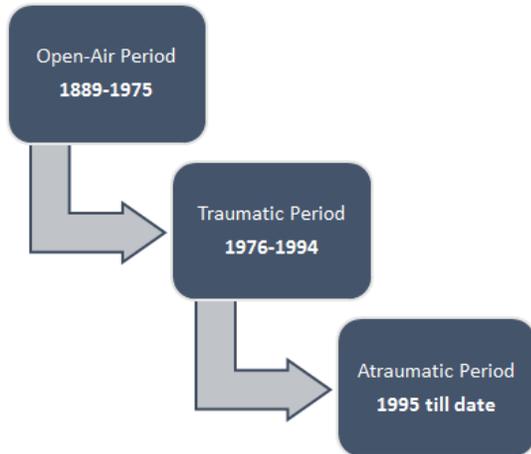


Figure 1 Distinct evolutionary phases in the history of fat grafting.

the ‘open-air phase’, when tissue was harvested by open surgical excision.¹ It was an era of innovations and failures. The first attempt at transferring autologous adipose tissue was reported by Meulen and Richard in 1889, when they treated a diaphragmatic hernia by placing an omental fat (epiploon) between the liver and diaphragm.² However, the first transfer of adipose tissue that may be truly recognized as a fat graft was reported in 1893 by a German surgeon, Gustav Neuber. He employed tiny forearm fat grafts to augment facial volume to correct a depressed scar following chronic osteomyelitis. The result was not satisfactory, however, and it was noted by him that the failures were related to the size of the grafts. He found that avoiding large grafts and transferring only small graft pieces increased the possibility of graft survival.³⁻⁴ Viktor Czerny reported the first use of autologous fat in breast reconstruction just two years later, in 1895. He filled a lumpectomy-induced breast deformity with fat from a lipoma located over the dorsal region, thereby restoring symmetry.⁵

In the latter years of the nineteenth century, reconstruction of depressions, asymmetries, and contour abnormalities was nevertheless mostly achieved by injection of paraffin, despite these

early accounts of successful fat transfer.¹ In that era, a saddle nose deformity secondary to congenital syphilis was a fairly common disorder requiring cosmetic treatment, in addition to abnormalities resulting from injuries. Filling with paraffin presented a viable option because the material seemed inert and the procedure was fairly straightforward.¹ However, it was not unusual to end up with severe adverse consequences like repeated infections, chronic inflammation, skin necrosis, foreign body granulomas, and the worsening of cosmetic abnormalities.¹ Hence, in the early 20th century, the idea of a more natural and readily available filler in the form of fat as an alternative to paraffin gained some popularity, with its use extending to indications including craniofacial and breast reconstruction and enhancement of joint mobility after surgical release for ankylosis. The procedures involved two incisions: i) donor site incision to harvest the fat graft en-bloc, often along with the dermis (the so-called dermal fat graft), and ii) recipient site incision to insert the graft into the area to be reconstructed.

In 1910, the use of autologous adipose tissue in aesthetic surgery for the expansion of malar areas and the filling of facial creases and lines in order to mitigate the visible signs of aging was first introduced by a German maxillofacial surgeon named Erich Lexer.⁵ In 1911, Brunning pioneered the use of a syringe for fat grafting when he injected autologous fat into subcutaneous space. To improve the aesthetic results of rhinoplasty, he used tiny pieces of adipose tissue. He did, however, make the point that, over the course of time, graft reabsorption can lead to the loss of positive effects.⁶⁻⁷

Around the same time, Eugene Hollander from Germany also adopted the use of fat instead of paraffin but soon encountered the issue of reabsorption. To mitigate the reabsorption issue,

he combined the adipose tissue from patients with a tougher version of fat derived from rams. He attained satisfactory results and, in 1912, published photographic documentation of improvement in two cases of lipoatrophy of the face. However, his technique did not enjoy wide acceptance and was hence phased out due to its limited clinical application.⁸

A tremendous task of reconstructing facial injuries of terrifying nature and in great numbers was brought on by World War I, which lasted from 1914 to 1918. At the hospital of Val-de-Grace in Paris, Hippolyte Morestin served as the chief surgeon. His division experimented with and created a number of surgical methods for reconstructing the face, including autoplasties that used cartilaginous and adipose grafts.⁹⁻¹⁰

In the meantime, the experiences of Erich Lexer related to fat grafting accumulated over the course of time, and in 1919, he released an important, two-volume book titled "Die freien Transplantationen" (Free Transplantations), in which he analyzed all of the different kinds of free grafts that were available at that time.⁵ The greater than 300 pages devoted specifically to fat grafting covered a staggering array of clinical applications, including the correction of contour deformities for ramifications of facial injuries, hemifacial microsomia, microgenia, breast asymmetry, post-traumatic hand stiffness, and restoration of tendon mobility in Dupuytren's contracture. The lateral thigh was typically employed as a donor for autologous adipose tissue, though occasionally the abdomen was also employed. In one case of chronic cystic mastitis, he excised all the glandular tissue of the breast and filled the defect with fatty tissue from the axilla. In his detailed analysis of fat graft survival, he found that tissue shouldn't be destroyed either during collection or implantation in order to have a positive outcome. Furthermore, he also reported the use

of fat in conjunction with local flaps and cartilage grafts in facial reconstruction.^{5,11}

In 1926, Charles Conrad Miller reported his experiences with the correction of scar contraction over the face and neck by infiltration of fat grafts through the cannulas.⁵ In 1941, Billings and May¹¹ presented a case of bilateral breast reconstruction with an autologous fat graft (AFG) on one side and a fascia-fat autograft on the other. He believed that fascia could preserve adipose tissue, reduce the absorption of grafted fat, and reduce its absorption.

World War II from 1938–1942 brought in new challenges and inspired innovations. It is also known that during that war, Salvat injected fat to alter the looks of spies. He employed homologous fat for short-term effects and autologous fat for results that would last.¹² After World War II, many surgeons enthusiastically reported the encouraging results of fat grafts in breast and facial reconstruction. These include Boering,¹³ Sawhney,¹⁴ Grandin,¹⁵ Bames,¹⁶ and Scorcher.¹⁷

However, as experience grew, it was discovered that unpredictable reabsorption and the onset of fibrosis made the initially extremely encouraging results from fat grafting worse over time. In fact, Peer accurately investigated the eventual outcome of autologous fat grafts for one year and, in 1950, demonstrated that about half of the grafted adipocytes ruptured to get replaced by fibrosis. Cells that did not rupture continued to survive long-term and constituted the remaining adipose tissue.¹⁸ As a result, concerns about the efficacy of fat grafting were raised, slowly contributing to its decline and making it a nearly obsolete technique.¹

2 Traumatic Period (1976-1994) The second phase in the history of fat grafting is called the

“traumatic”, “unpurified”, or “unrefined” period because the adipose tissue was obtained by aspiration and then reinjected without any specific purification or preparation, causing trauma. This phase started as interest in fat grafting was rekindled after Italian father-and-son cosmetic surgeons Arpad Fischer and Giorgio Fischer introduced modern liposuction in 1976.¹⁹ They inserted a suction source-attached blunt hollow cannula into the patient and demonstrated the removal of adipose tissue using the criss-cross suctioning technique with three 5 mm incisions. Fischer's method was revised by Illouz and made very popular. In order to lessen the trauma associated with the liposuction procedure and decrease damage to nerves, blood vessels, and lymphatics, he redesigned the machinery and added blunt cannulas with lower diameters.²⁰

He pioneered the use of lipoaspirate as a filling product and introduced the concept of fat grafting without donor or recipient incisions. However, liposuction was still traumatic and would, on occasion, cause bleeding, bruises, ecchymosis, or else result in cosmetically unsightly contour deformities with pits and depressions. One option suggested was the return of lipoaspirate using a syringe, though it was frequently seen that the reinjected material underwent complete or nearly complete reabsorption within a few weeks.

For the treatment of breast hypoplasia and asymmetry following surgical management of cancer, Bircoll was the first to employ autologous fat and liposuction procedures in 1987. He suggested administering small amounts of fat injections in series across several sessions.²¹⁻²² In 1995, Hang-Fu introduced an innovative tool termed liposuction fat-fillant implants for breast reconstruction.²³ These were impermeable or semi-permeable membrane prostheses filled with autologous adipose tissue.

They asserted to avoid all the drawbacks of direct injection of fat. In 1986, Ellenbogen described the effective use of free autogenous fat grafts ranging from four to six millimeters to treat acne pits, depressed nasolabial folds and eyelids, facial atrophy and wrinkles, and atrophic scars. Luiz Toledo from Brazil presented his series in 1988, in which he made use of commonly available disposable syringes of various sizes to aspirate fat grafts.²⁵ The method offered was to measure collected fat tissue volumes precisely and accurately, as well as to make it possible to inject that fat more delicately.

In addition, Fournier offered many iterations of a similar approach for infiltration of adipose tissue, referring to it by various names, including lipofilling, micro-lipoextraction, and micro-lipoinjection.²⁶ However, the need for overcorrection and the unpredictability of results did not allow it to gain any popularity. Jeffrey A. Klein recommended an entirely novel method known as the tumescent technique, in which, before the graft harvest, the donor site is injected with a crystalloid fluid known as Klein's solution that contains very low amounts of lignocaine and epinephrine.²⁷⁻²⁸ Following this, fat is aspirated with the use of suction using small-calibre aspiration cannulae. This technique eliminated the need for general anesthesia and reduced bleeding to a great extent, thereby improving the overall safety of large-volume liposuction.

3 Atraumatic Period (1995 till date) The 1990s saw the most significant transformation in the history of fat grafting when Coleman modified the methods of his predecessors and set up protocols for atraumatic harvesting, processing, and reinjection of fat.²⁹⁻³⁰ This phase in the history of fat grafting is hence termed the “purified”, “refined” or “atraumatic” period, and Coleman named his technique 'Lipostructure'.³⁰

He emphasized the significance of fat parcels remaining intact for adequate fat graft survival. His method entailed the insertion of a 3-mm blunt two-hole extraction cannula through which fat was aspirated from several donor regions using a 10-cc Luer-Lok syringe under low negative pressure. The lipoaspirate was subjected to centrifugation, resulting in the separation of pure fat from unrequired entities. Subsequently, the purified fat was placed in minuscule (less than 0.1 ml) aliquots with each withdrawal of the infiltrating cannula. The small volume makes it possible for the graft to hold on to the recipient tissue and ensures its proximity to capillaries. In contrast, the fat injected as a bolus in pre-Coleman methods would form a clump, and only the adipocytes lying peripherally would get nourishment to survive. Coleman's ground-breaking discoveries greatly increased fat graft survival and made widespread application more practical.³¹⁻³²

Even though fat graft was initially used as a filler to enhance volume, over the last two decades, researchers gradually realized that adipose tissue is not only the main energy storage of our body but a dynamic connective tissue that contains a pool of mesenchymal stem cells with the potential to divide endlessly and produce different cellular lines. This understanding opened the doors for a progressively greater field of application in regenerative medicine and tissue engineering.^{33,34}

Accordingly, Rigotti *et al.* conducted a prospective study to evaluate purified lipoaspirate with respect to the presence of adipose-derived adult stem cells and the clinical effectiveness of its transplantation in the management of patients with cutaneous adverse effects of radiotherapy.³⁵ Twenty patients with severe symptoms or irreversible function damage were enrolled, and 60cc to 120cc of

purified autologous lipoaspirates obtained from healthy donor sites were administered by serial low-invasive computer-assisted injections. The results were incredibly positive. Clinically, all of the patients who were assessed showed a considerable improvement, and histological analysis revealed progressive regeneration, including neo-vessel formation and improved hydration.³⁵ Inspired by these results, Klinger *et al.* tried fat injection in severe burns.³⁶ They attained excellent clinical results, and histologic examination of the treated skin showed a tendency towards tissue regeneration with features of neo-collagen deposition, local hypervascularity, and dermal hyperplasia. Klinger *et al.* extended the application of autologous fat graft to scars and hard-to-heal wounds of widely differing etiologies and demonstrated its capability to induce architectural remodeling and tissue regeneration.³⁷⁻³⁸

In the last two decades or so, autologous fat grafting (AFG) has demonstrated its safety and potential to promote healing across a wide range of indications. Khouri and Del Vecchio reported success in breast reconstruction by fat grafting, preceded by pre-expansion of the recipient area.³⁹⁻⁴⁰ According to Wnger *et al.*,⁴¹ if an alloplastic breast reconstruction is preceded by fat grafting, patients with breast cancer who are otherwise unsuitable for the procedure may be rendered suitable. Toyserkani *et al.*⁴² reported lipotransfer in the axillary region of a case of breast cancer-related lymphedema and the patient reported a significant improvement in daily symptoms and limb volume with a reduction in the need for compression therapy.

In patients with erectile dysfunction (ED) after radical prostatectomy, Haahr *et al.*⁴³ reported the effectiveness and safe profile of intracavernous administration of autologous adipose-derived regenerative cells. Huang *et al.*⁴⁴ investigated the

role of autologous fat grafts in the management of complex anorectal fistulas, enrolling 52 patients, including cases of inflammatory bowel disease. The majority of the subjects had failed with the more commonly applied surgical procedures, including endorectal advancement flaps or ligation of the intersphincteric fistula tract (LIFT). In 64% of the cases, all fistula tracts were completely closed, and 81% of the cases reported significant improvement in their symptoms. A relapse was observed in 40%, and complications such as perianal abscesses and mild bleeding occurred in roughly 15% of cases. The study concluded that autologous fat grafting can be offered in conjunction with other therapies safely and economically in complex anal fistulae. Recently, Klinger *et al.*⁴⁵ described the successful use of fat grafting as part of an integrated approach along with percutaneous scar release by needles and local flaps for the revision of secondary deformities acquired after cleft lip correction surgeries. Similarly, Cervelli *et al.*⁴⁶ demonstrated the success of lipofilling in patients with maxillo-mandibular malformations.

Besides the expansion of the list of indications, advances are being made in the quality and variety of armaments. Energy-assisted liposuction devices, including ultrasound-assisted and tissue-liquefaction liposuction, computer-assisted injections, etc., have also been introduced for the harvest of fat grafts, and various studies have been conducted to compare these devices with respect to adipocyte survival and long-term fat retention. Similarly, more refinements in techniques to make fat grafting safer and more effective are being proposed by different institutions around the world. The “3L3M” technique is one such step in that direction, and it calls for the application of liposuction at low pressure, centrifugation at low speed, and injection of low volume at multi-points, in multi-planes, and through multi-

tunnels.⁴⁷

Given the volume of research being done in this area of study right now, the future appears to be fairly promising for fat grafting. It has come a long way since it was established about three centuries ago.

Conclusion

Fat grafting is one of the most commonly performed procedures in aesthetic surgery and regenerative medicine. Over the course of nearly three centuries, the concepts and techniques relating to this modality have evolved. This modality continues to be a crucial topic for research, and more evidence-based studies are still needed to fully understand its therapeutic indications.

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