Thesis

FAT GRAFTING IN PLASTIC SURGERY
a systematic literature review of its state-of-the-art applications

submitted by

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Graz, 30.06.23

Declaration of Academic Integrity

I hereby confirm that the present diploma thesis is the result of my own independent scholarly work. I also confirm that in all cases, where material from the work of others (in books, articles, essays, dissertations, and on the internet) is acknowledged, quotations and paraphrases are clearly indicated. No material other than that cited in the reference list has been used. I have read and understood the Medical University's regulations and procedures concerning plagiarism.

Graz, 30.06.23 *Adrian Georg Mogl eh.*

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Zusammenfassung

Hintergrund: Bei der Eigenfetttransplantation handelt es sich um eine chirurgische Behandlung, bei der Fettgewebe aus einer Körperregion entnommen und als freies Transplantat in eine andere Körperregion eingebracht wird. Eigenfett verfügt über eine Reihe von Eigenschaften, die es zu einem wirksamen Füllmaterial machen. Da das Fettgewebe aus dem eigenen Körper des*der Patienten*Patientin stammt, besteht kein Risiko einer anaphylaktischen Reaktion oder immunbedingten Abstoßung, und ausreichende Mengen sind bei den meisten Patient*innen leicht verfügbar. Aufgrund dieser Eigenschaften wird es in der plastischen Chirurgie für ein breites Spektrum an rekonstruktiven und kosmetischen Zwecken eingesetzt.

Ziel: Da sich die Techniken der Eigenfetttransplantation in der klinischen Medizin und der medizinischen Forschung ständig weiterentwickeln, ist es das Ziel dieser Arbeit, einen aktuellen und umfassenden Überblick über die Anwendung von Fetttransplantationen in der plastischen Chirurgie zu geben.

Methoden: Es wurde eine systematische Literaturrecherche in der Datenbank MEDLINE der National Library of Medicine unter Verwendung von PubMed als Suchmaschine durchgeführt. Weiterhin wurde die Suche auf englischsprachige" Publikationen beschränkt, die nach 2010 veröffentlicht wurden. Die Suchergebnisse wurden anhand des Titels oder des Abstracts manuell auf Artikel überprüft, die sich auf Anwendungen von Fetttransplantationen in der plastischen Chirurgie konzentrieren. Schließlich wurden die für jede Anwendung am besten geeigneten Artikel auf der Grundlage ihrer Zusammenfassungen abgerufen und in ihrer Gesamtheit überprüft, bevor sie auf der Grundlage ihrer jeweiligen Anwendungen katalogisiert wurden.

Ergebnisse: Mit Hilfe der vorgegebenen systematischen Suchstrategie wurden aus den 1 649 Veröffentlichungen, die nach den ursprünglichen Suchkriterien gefunden wurden, 28 Artikel gefunden. Aus diesen Veröffentlichungen wurden 21

verschiedene Anwendungen extrahiert, die dann jeweils ausführlich beschrieben wurden.

Diskussion: Die systematische Suche ergab eine Reihe von verschiedenen Anwendungen für Eigenfetttransplantationen, die in früheren Übersichten über Fetttransplantationsanwendungen nicht behandelt wurden. Einige der Anwendungen basieren jedoch auf einigen wenigen Eingriffen, und es sind weitere Forschungen und kontrollierte Studien erforderlich, um sie im Bereich der plastischen Chirurgie zu etablieren. Obwohl die Fetttransplantation in der Mehrzahl der Fälle zu hervorragenden Ergebnissen geführt hat, müssen einige Aspekte wie Komplikationen, onkologische Sicherheit und unterschiedliche Retentionsraten berücksichtigt werden.

Schlussfolgerung: Mit Hilfe einer systematischen Literaturrecherche wurde eine gründlichere Übersicht über Fetttransplantationsanwendungen in der plastischen Chirurgie erstellt als bisher verfügbar.

Abstract

Background: Fat grafting is a surgical procedure that involves harvesting adipose tissue from one region of the body and then reintroducing it as a free graft to another region of the body. Autologous fat possesses a number of characteristics that make it an effective filler. Since the adipose tissue is obtained from the patient's own body, there is no risk of anaphylactic reaction or rejection, and sufficient quantities are readily available in the majority of patients. Because of these properties, it is currently commonly employed in plastic surgery for a wide range of reconstructive and cosmetic purposes.

Aim: Because techniques in clinical medicine and medical research are continually developing, the aim of this thesis is to give an up-to-date and comprehensive overview of fat grafting applications in plastic surgery.

Methods: A systematic literature search was conducted on the National Library of Medicine's MEDLINE database using PubMed as a search engine. Furthermore, the search was limited to "English" publications released after 2010. The search results were manually screened for articles concentrating on applications of fat grafting in plastic surgery based on title or abstract. Finally, the most suitable articles for each application, chosen based on their abstracts, were retrieved, and reviewed in their entirety before being cataloged based on their respective applications.

Results: Using the specified systematic search strategy, 28 articles were retrieved from the 1,649 publications the initial search yielded. From those publications, 21 distinct applications were extracted, each of which was then thoroughly detailed.

Discussion: The systematic search yielded a number of different applications for autologous fat grafting that were not addressed in previous overviews of fat grafting applications. Some of the applications, however, are based on very few procedures, and further research and controlled studies are required to establish them in the field of plastic surgery. Although fat grafting generated excellent results in the

majority of instances, some issues, such as complications, oncological safety, and varying retention rates, need to be taken into account.

Conclusion: A more thorough review of fat grafting applications in plastic surgery than previously available was developed using a systematic literature search strategy.

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Abbreviations

ASPS	American Society of Plastic Surgeons
NLM	National Library of Medicine
ADSC	adipose-derived stem cell
IGF	insulin-like growth factor
FGF	basic fibroblast growth factor
VEGF	vascular endothelial growth factor
PDGF	platelet-derived growth factor
PALF	percutaneous aponeurotomy and lipofilling
RFF	radial forearm flap
STSG	split-thickness skin graft
FTSG	full-thickness skin graft
POSAS	Patient and Observer Scar Assessment Scale
HIV	Human Immunodeficiency Virus
GMG	genio-mandibular groove
IBR	implant-based reconstruction
ADM	acellular dermal matrix
TRAM	transverse rectus abdominis myocutaneous
DIEP	deep inferior epigastric perforators
BMI	body mass index

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1 Introduction

Fat grafting, autologous fat transplantation, or lipofilling all describe a surgical procedure where adipose tissue is removed from a certain area of the body and then reintroduced as a free graft to a different body location (1). In general, it can be approached in two different ways (2). In the first approach, appearing as a liquid state, fat is harvested through liposuction and subsequently it is processed, modified, and injected into the recipient site (2). This is the way most commonly used, although the post-procedure resorption has to be kept in mind (2). The second approach of autologous fat transplantation involves removing a composite block of adipose tissue to be implanted as a whole at the recipient site (2). However, there are only few publications that mention this technique, but low post-procedure resorption rates make this second approach also very useful in some cases (2).

Autologous fat has a lot of qualities that make it an excellent filler. Since the adipose tissue is obtained from the patient's body, there is no potential for allergic reactions or rejection response, as well as being readily available in adequate amounts in the majority of patients. Additionally, the extraction of adipose tissue typically involves a straightforward process with minimal negative impact on the donor site, resulting in low morbidity and provides long-lasting, likely permanent outcomes. (1)

Because of these characteristics, fat grafting has gained widespread acceptance in the field of plastic surgery for a variety of reconstructive and aesthetic applications (1). Most existing reviews of applications focus on the most common and established applications of fat grafting. Because procedures in clinical medicine and medical research are constantly evolving, the objective of this systematic review is to offer an updated and more complete overview of these applications of autologous fat transplantation in plastic surgery, by also looking into applications that are not particularly well-known yet.

History

Autologous fat has been used for reconstructive and aesthetic procedures since the late nineteenth and early twentieth century. In 1893, Neuber (3) was the first one to perform a fat graft to a concave facial scar and two years later, Czerny (4) described transplanting a large buttock lipoma to correct a patient’s postmastectomy contour

deformity (1,5). Then, in 1912, Eugene Hollander (6) reports the use of adipose tissue to treat patients with facial lipoatrophy (7).
Additional small series were published over the next several decades, but the procedure did not gain widespread acceptance due to inconsistent outcomes. However, the implementation of liposuction in the 1980s rekindled interest, and surgeons started to describe their experiences with reinjecting aspirated fat for breast augmentation. (1)
Following a statement from the American Society of Plastic Surgeons (ASPS) in 1987 opposing the use of fat grafting for breast surgery due to concerns that it could be obstructive in the detecting breast cancer, surgeons were reluctant to perform the procedure as part of breast surgery (1,8,9). However, after multiple studies found no oncological or radiological to fat grafting to the breasts, the ASPS revised their standpoint in the year 2009, acknowledging that lipofilling, or fat grafting, could be deemed appropriate for a diverse array of indications (8,10).
When Coleman (11) described an innovative advanced method that aimed to minimize the traumatic manipulation of fat during liposuction and resulted in a substantial decrease in complications and enhanced survival of the grafts in 1997, lipofilling started becoming increasingly popular (12). Although some technical modifications were made over time, Coleman's technique is still the gold standard for liposuction and lipofilling (13).

Fat Grafting Technique

The process of adipose tissue transplantation, according to Abu Ghname and colleagues, may be categorized into five essential components, including donor site selection, recipient site preparation, graft harvesting, graft processing, and graft delivery. Furthermore, it can be categorized into three groups, based on the harvested volume. These include small volumes (less than 100ml), which are usually used for regenerative or rejuvenation purposes, large volumes (100 to 200ml), which are primarily used for breast and body contouring, and finally mega volumes (more than 300ml), which are mainly used for breast reconstruction, breast augmentation, or gluteal augmentation. (12)

Donor Site Selection and Preparation

The selection of the donor region for fat harvesting is typically based on two primary factors: the availability of an ample amount of fat and the ease of technical execution during the procedure. Common sites include the thighs, flanks, and abdomen for supine-positioned patients (1).

The authors Li et al. conducted a study comparing fat grafts obtained from six women, utilizing different donor sites. These donor sites included the lateral thigh, inner thigh, upper abdomen, lower abdomen, as well as the flanks. The objective of the study was to assess and compare the quality and outcomes of fat grafts obtained from these various donor regions. The results of their study indicated that there were no significant variations in volume, weight, or histological attributes observed among the different donor regions. Consequently, the authors recommended that when selecting a donor site, factors such as accessibility and patient preference should be taken into account, as these factors have a greater influence on the decision-making process. (12,14)

The donor site can be prepared in a multitude of manners, encompassing no pretreatment or injection of varying quantities of local anesthetic combined with epinephrine. Injections of 10–30cc of 1% lidocaine with 1:100,000 epinephrine may help minimize donor area bleeding and pain for small-volume fat grafting. Lidocaine and epinephrine injections in larger volumes have been shown to be helpful in liposuction and can additionally be used to prepare the donor site for lipofilling. Studies examining the effects of these pretreatments on the viability of fat cells within grafts have revealed that they do not adversely affect cell survival. In fact, there is evidence to suggest that they might enhance the overall survival of the transplanted fat cells. (1)

Recipient Site

In the process of preparing the graft for harvesting, it is crucial to assess the capacity of the recipient site, taking into account its volume and mechanical compliance. The palm-and-pinch method is commonly employed to estimate these factors, where pinching the tissue provides an approximation of its laxity and thickness, while using the palm measures the surface area. Numerous studies have highlighted the significance of external volume expansion in achieving successful large-volume

autologous fat transfers. This technique has been shown to stimulate adipogenesis, enhance tissue vascularity, and augment both the capacity and mechanical compliance of the recipient site. By employing external volume expansion, the recipient site is adequately prepared to accommodate and support a larger volume of fat during the transfer process. (12)

Harvesting

It has been demonstrated that less traumatic methods of fat harvesting result in improved viability of adipocytes and increased graft survival. Multiple methods for fat harvesting have been suggested, and the literature is divided on which approach produces more viable and usable adipocytes. Syringe or vacuum aspiration, and surgical excision, however, are the most common procedures. (13)

Despite the fact that various writers recommend different negative pressure values, it is widely agreed upon that low vacuum pressure for vacuum or manual aspiration is less traumatic and improves graft viability (12).

Processing

Processing of the aspirated tissue is required for multiple reasons. The lipoaspirate, which comprises adipocytes along with collagen fibers, blood, and debris, has the potential to induce inflammation at the recipient site of the fat graft. Blood, moreover, can accelerate the deterioration of the fat that has been transplanted. Furthermore, as the debris within the lipoaspirate is gradually absorbed by the body within a few hour, its injection gives an incorrect impression of the transplanted amount. Sedimentation, filtering, washing, and centrifugation are the most popular techniques for preparing fat grafts. There were no major differences in the weight or architecture of fat grafts produced, using centrifugation, filtration, or sedimentation methods in animal experiments. In comparison, studies in patients have shown that centrifugation, rather than gravity separation, produces better results. Coleman's approach to isolating fat by centrifuging the aspirated tissue at 3000rpm for 3min, has gained popularity and is now used in many clinical fat-transfer protocols. The lipoaspirate is separated into three distinct layers following centrifugation. The lipids are in the first layer, adipose tissue is in the second, and tissue fluids, blood, and local anesthetic are in the third. For the purpose of fat grafting, only the middle layer,

made up of fatty tissue and including the vascular stromal faction and adipocyte-derived stem cells, is commonly used. (13)

Delivery

Despite the extensive clinical use and advancements in fat transfer procedures, a consensus has yet to be reached regarding the optimal method and long-term outcomes. However, the primary focus of fat delivery concepts revolves around ensuring optimal vascularity at the recipient site to enhance the survival of the fat graft. The fat graft is typically inserted into the targeted anatomical area through a skin incision that matches the diameter of the cannula. often created during the injection process using various access points, with the fat being injected in a "fanning-out" pattern as the cannula is withdrawn. (13)

The use of small gauge "blunt tip" cannulas is believed to minimize recipient site damage, reducing the risk of bleeding, hematoma formation, and inadequate oxygen diffusion to the graft (12,13). As revascularization of the graft begins at the periphery, the central region of the graft experiences a longer ischemic period (13). As a result, several sessions of small-volume fat delivery are favored over a single large-volume injection (13).

2 Material and methods

In this chapter, all stages of the process that led to the creation of this systematic review will be described. All steps are explained in detail, from the search for literature to the final selection of the papers.

Systematic Review

A systematic review is a comprehensive and unbiased summary of available literature on specific topics at a particular moment, presenting the existing scientific knowledge on the subject. This particular systematic review on the applications of autologous fat transplantation in the realm of plastic surgery was performed on the base of the PRISMA checklist (15) for systematic reviews of 2020.

Research Strategy

The research objective was to identify and summarize possible applications of fat grafting in plastic surgery, which was accomplished by conducting a systematic literature search on the National Library of Medicine's (NLM) MEDLINE database using PubMed as a search engine. Since the aim of this research made it necessary to find as many relevant applications as possible, a "Recall-oriented" search was performed in May 2022 using Boolean algebra with the following search terms:

"**plastic surgery**" AND ("**autologous fat transplantation**" OR "**fat grafting**" OR **lipofilling** OR **lipomodelling** OR "**fat transplantation**" OR "**adipose tissue transplantation**")

Table 1: search terms

Furthermore, to reduce the number of results, the search was restricted to language "English" and published after 2010. Subsequently, the remaining 1,218 search results were manually screened based on title or abstract to identify all papers focusing on one or more applications of fat grafting in plastic surgery. Excluded were papers whose title or abstract suggested that they were either: not specifically about the field of plastic surgery, not specifically about fat grafting, or not about application but other aspects of fat grafting (i.e.: safety, efficacy). This resulted in 172 papers, though multiple papers still focused on the same application or only a subset of a larger application (For example, only concentrating on periorbital rejuvenation, in the application of facial rejuvenation). To eliminate papers that focus on the same application, those 172 papers were screened again and classified by their respective field of application. The result of this classification is visualized in **table 2**. Finally, the most suitable papers for each application were selected based on their abstracts, resulting in 28 papers for this systematic review. Furthermore, a flow chart (**Figure 1**) was created for optimal representation of the literature selection process.

The included papers were then retrieved and read in their entirety before being cataloged in an excel chart using Microsoft Excel Version 2016 in accordance with their specific applications.

Application	**Number of papers**
Aesthetic breast surgery	10
Breast reconstruction	26
Burn injuries	5
Craniofacial deformities	2
Facial surgery	55
Female genital surgery	4
Gluteal augmentation	7
Hand surgery	4
Lower leg augmentation	4
Neuropathic pain	13
Pedal fat pad atrophy	6
Pediatric patients	8
Radiation damage	3
Reviews	3
Scars and fibrosis	21
Tenolysis	1
TOTAL	172

Table 2: classification of identified papers

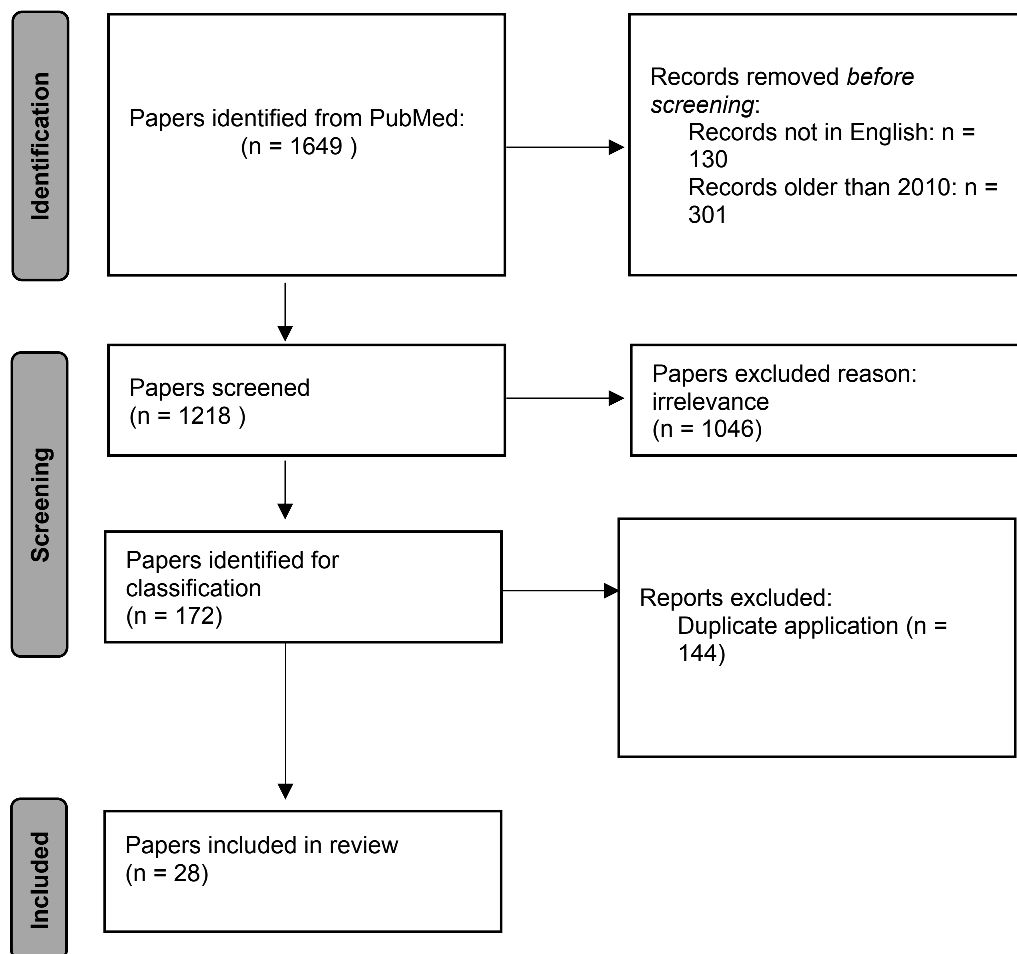

Figure 1: Flow chart depicting the organization of search results

3 Results

3.1 Search Results

By using the systematic search method described in the previous chapter, 28 papers could be extracted from the 1,649 papers resulting from the search terms, illustrated in **table 1**.

All the papers that were included can be found in **table 3.** From those publications, 21 distinct applications were extracted, each of which will be described in detail.

Authors:	Title:
Abu-Ghname, A., Perdanasari, A. T. & Reece, E. M.	Principles and Applications of Fat Grafting in Plastic Surgery
Cihantimur, B. & Herold, C.	Genital beautification: A concept that offers more than reduction of the labia minora
Conlon, C. J. et al.	Fat Grafting for Hand Rejuvenation
Damgaard, O. E. & Siemssen, P. A.	Lipografted tenolysis
Davis, M. J. et al.	Application of Fat Grafting in Cosmetic Breast Surgery
de Gast, H., Specialist, P., Torrensma, B., Fitzgerald, E. & Stevens, H.	The Treatment of Chronic Neuropathic Pain
Delay, E. & Guerid, S.	The Role of Fat Grafting in Breast Reconstruction
Egro, F. M., Coleman, S. R. & Rubin, J. P.	Fat Grafting for Treatment of Secondary Facial Deformity
Fredman, R., Edkins, R. E. & Hultman, C. S.	Fat grafting for neuropathic pain after severe burns
Fredman, R., Katz, A. J. & Hultman, C. S.	Fat Grafting for Burn, Traumatic, and Surgical Scars
Guaraldi, G. et al.	Surgical correction of HIV-associated facial lipoatrophy
Huang, S. H. et al.	Micro-Autologous Fat Transplantation for Treating a Gummy Smile
Khouri, K. S., Beidas, O., Coleman, S. & Rubin, P.	Is Fat Grafting a Viable Treatment Option for Chronic Neuropathic Pain
Khouri, R. K. & Khouri, R. K.	Current clinical applications of fat grafting
Klinger, M. et al.	Autologous fat graft in scar treatment
Longo, B., Sorotos, M., Laporta, R. & Santanelli di Pompeo, F.	Aesthetic improvements of radial forearm flap donor site by autologous fat
Marten, T. J. & Elyassnia, D.	Fat grafting in facial rejuvenation
O’Neill, R. C. et al.	The Role of Fat Grafting in Buttock Augmentation
Ranganathan, K. et al.	Fat grafting for thermal injury: Current state and future direction

Ribak, S., Vasconcelos, A. L. & Oliveira, R. K.	Fat Grafting for Esthetic Correction of the Muscle Atrophy Secondary to Ulnar Nerve Lesion
Ruane, E. J., Minteer, D. M., Wyse, A. J., Gusenoff, B. R. & Gusenoff, J. A.	Volumetric Analysis in Autologous Fat Grafting to the Foot
Schultz, K. P. et al.	Fat Grafting for Facial Rejuvenation
Shih, L. et al.	Applications of Fat Grafting in Pediatric Patients
Simonacci, F., Bertozzi, N., Grieco, M. P., Grignaffini, E. & Raposio, E.	Procedure, applications, and outcomes of autologous fat grafting
Skorobac Asanin, V. & Sopta, J.	Lower Leg Augmentation with Fat Grafting, MRI and Histological Examination
Turner, A. et al.	Fat Grafting in Breast Reconstruction
Vogt, P. M., Herold, C. & Rennekampff, H. O.	Autologous fat transplantation for labia majora reconstruction
Williams, E. A. & Thaller, S. R.	The role of fat grafting in the treatment of keloid scars and venous ulcers

Table 3: Papers included in the systematic review

3.2 Applications

Cellular Effects

Adipocytes and Cell Survival

The process of adipocyte remodeling and regeneration in a recently transplanted environment is a constantly changing and dynamic process. Its success and outcomes are influenced by the proximity of the adipocytes to a nutritional supply. Up until now, the "cell survival theory" has been widely accepted in the literature regarding adipocyte transplantation. This theory proposes that the number of adipocytes initially transplanted into a wound bed directly influences the overall volume of fat that develops in the area. Nevertheless, there have been recent updates to this concept that highlight the importance of adipose-derived stem cells (ADSC) and mesenchymal cells in the process of adipocyte transplantation. These cells release factors that have been found to significantly influence the wound bed. Adipocytes make up about 20% of all cells in the subcutaneous tissue and assist cells to regenerate and proliferate in the wound environment. (7)

Eto and colleagues have identified and categorized three distinct zones of healing within the recently grafted adipose tissue. These zones are referred to as the surviving zone, regenerating zone, and necrotic zone. Whereas all cells die in the

necrotic zone, adipose-derived stromal stem cells continue to live in the regenerating zone and are necessary to replace dead adipocytes with new ones. Within the peripheral surviving zone, both adipose-derived stromal stem cells and adipocytes survive. Hence, it is not solely the initial volume of adipocytes that determines the final volume of the graft, but rather the intricate interactions among various cell types within the graft site. These cell types include necrotic adipocytes, viable adipocytes, and adipose-derived stromal stem cells. The retention of a specific volume is influenced by these interactions and is ultimately determined by the composite of tissue initially transplanted into the wound bed. (17)

Adipose-Derived Stem Cells

Previously, it was believed that the presence of healthy adipose tissue could hinder the healing process of burn injuries because adipocytes are susceptible to necrosis and cell death if they do not receive adequate blood flow within four days after grafting. However, the detection of ADSCs within the stromal vascular areas of a fat graft has raised doubts on this concept in the context of burn injury and many studies have concluded that the stromal fat graft's vascular section has proangiogenic capabilities similar to bone marrow-derived stem cells. (7)

Numerous researchers have examined the angiogenic capacity of ADSCs through mouse models and uncovered that these stromal cells secrete substances that stimulate angiogenesis and inhibit apoptosis by integrating into the preexisting vasculature. After recognizing the apparent role of mesenchymal and ADSCs in promoting tissue revascularization, scientists began to explore their potential in treating conditions such as radiation-induced tissue damage, ischemia, dermatitis, erythema, desquamation, edema, and radionecrosis. Consequently, research involving lipoaspirates that contain ADSCs demonstrates enhanced angiogenesis and, subsequently, an improved ability to heal devitalized tissue. (7)

Furthermore, Sultan et al. confirm these findings in their studies utilizing a murine model, ultimately concluding that autologous fat transplantation diminishes inflammation in cases of acute radiation-induced tissue damage (18). Thus, the inclusion of adipose-derived stem and stromal cells is essential for tissue healing in thermal injuries, owing to their innate regenerative capabilities (7).

The Regenerative Capacity of Adipose-Derived Stem Cells

The regenerative capacity of fatty tissue and its derived stem cells is a highly compelling and clinically significant attribute of these tissues (7). An example of the regenerative potential of ADSCs is their ability to be utilized in the development of human skin substitutes, as demonstrated by Trottier et al. Notably, this can be achieved in the absence of scaffolds or synthetic factors, with the cooperation of keratinocytes (19). Furthermore, "in vitro experiments using mouse models have shown that an epidermal differentiation system that induces the development of a stromal compartment is initially created, catalyzing the formation of epidermis" (7). A trilaminar structure is formed as a result of this process, consisting of the epidermis, dermis, and hypodermis layers, which are critical for simulating the protective role of the skin. This regenerative potential, especially the development of epidermis and dermis, makes this method particularly useful in burn reconstruction. (7)

Levels of Growth Factors in Fat Grafts

The endocrine qualities of transplanted tissue, both inside the graft and in the surrounding tissue, were only recently discovered by surgeons. The presence of growth factors in the transplanted graft influences the angiogenic capacity of the transplanted adipose tissue, and by promoting cellular growth and blood vessel formation, they contribute to a successful graft take. Angiopoietins, insulin-like growth factor (IGF), basic fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF) have all been shown to improve transplant viability. Moreover, these growth factors help the adipose graft develop by complementing each other. (7)

According to Pallua et al., lipoaspirate transplants contain significant quantities of IGF-1 and basic FGF, while the levels of VEGF and PDGF are relatively lower. Importantly, the high levels of naturally occurring growth factors present in pretransplanted adipose grafts remain unchanged after the transplant (7,20). Moreover, researchers have found that the addition of basic FGF to the transplanted cells enhances their viability. Additionally, VEGF has been shown to improve the viability of the transplanted tissue by inducing the formation of a vascular network, benefiting both the transplant and the surrounding tissue. PDGF promotes cell

proliferation, as well as decreasing cell death and adipocyte survival is improved by IGF-1. (7)

Overall, “high levels of these four growth factors in the transplanted lipoaspirate provide a nourishing medium for transplant viability [and] [t]hus, one would expect fat transfer functions to provide not only volume but also growth factors to improve the burn wound niche” (7).

Scars and Fibrosis

Rigotti and colleagues published a paper in 2007 that discusses the use of autologous fat grafts to treat radiation-induced skin lesions and demonstrated that autologous fat grafts can, in fact, improve the local tissue environment in humans. They theorized that adipose-derived stem cells within the lipoaspirate were responsible for regeneration. (25)

Since then, autologous fat transplantation’s uses have become more versatile, and lipofilling has come to be recognized as a flexible medium with beneficial regenerative and mechanical properties (5).

In particular, fat grafting has recently been shown to be an effective treatment for patients that suffer from retractile and painful scars that are interfering with their usual daily activities or the mobility of their affected joints. Indeed, lipofilling has emerged as a regenerative option that can be used as an alternative to other surgical techniques. It can not only be employed to fill atrophic scars but also to reduce scar contracture. (13)

The authors Khouri et al. state that the soft tissue counterpart for a fibrous scar is fat. The fibrous scar is transformed into a recipient matrix by skillful lipofilling. The loose supportive fibrous scaffold for fat grafts is created from what was formerly a dense fibrous scar. According to the cicatrix-to-matrix theory, the fat grafting process can transform tight and stiff into loose and flexible. (26)

They were the first to introduce the concept of cicatrix-to-matrix, which elucidates how lipofilling has the ability to transform tight fibrous tissue into a more lax recipient matrix. This novel method presents a promising substitute to flap surgery for the treatment of scar contractures and fibrous tissue, offering a promising regenerative approach (12,26).

Klinger and colleagues used fat grafting to address scarring in a total of 694 individuals, where they noticed an increase in the quality of all scars that underwent treatment, both in terms of aesthetics and functionality. The first effects were seen fourteen days after the procedure, whereas after three months pain reduction and improved scar elasticity were observed, and all patients maintained these improvements until the one-year follow-up. The skin may become smoother, more flexible, and extensible due to the lipofilling, and the color often looks comparable to the surrounding unaffected skin. Another benefit from fat grafting is scar release, both superficial and deep, resulting in the increased movement capability of the affected body area, especially the affected eyelids, mouth, joints, and nasal valve, and the potential of partial facial expression restoration for the patient. Furthermore, scar release also fills volume deficits in patients with severe skin depression, resulting in excellent aesthetic outcomes and a positive impact on the patient's body image. (27)

Scar Contractures

As an alternative regenerative option to flap surgery, percutaneous aponeurotomy and lipofilling (PALF) has emerged for the treatment of scar contractures. The cicatrix is expanded into a fat-filled matrix by injecting fat and percutaneously meshing the restrictive scar, the resulting microcavities are widened in the treatment of scar contractures. To ensure proper three-dimensional release in areas where restrictive fibers hinder expansion, it is necessary to stagger the nicks in multiple planes and directions. Khouri et al. label this procedure “Rigottomy”, according to its creator Rigotti. This technique of percutaneous meshing extends the restrictive block of scar tissue, creating a larger three-dimensional recipient scaffold that is suitable for fat grafting. As the grafted scar tissue loosens, it undergoes a transformation, becoming softer and resembling the normal surrounding adipose tissue. Additionally, performing the procedure again after a few months leads to substantial volume gain in the tissue, ultimately replacing the scar with normal fat. (26)

Scars and defects in various parts of the body, including the face, trunk, extremities, and breasts have all been treated with this technique (12). Moreover, PALF has shown success in treating various conditions such as burn scar contractures, posttraumatic scars, breast agenesis, and Dupuytren's contracture (26).

When utilizing PALF for the treatment of Dupuytren's contracture, it is important to highlight the significance of exercising caution to prevent damage to the neurovascular structures. This involves ensuring a strong digital extension while releasing the cord. The cords are tensed before the neurovascular structures, allowing the needle to selectively cut the restrictive fibers during the expansion. Furthermore, research has shown that abdominal adipose tissue inhibits Dupuytren's fibroblasts. (12)

Overall, when transplanting fat into scarred tissue to correct a volume deficit, the Rigottomy is an effective procedure, since it can convert a cicatrix into a regenerative matrix (26).

Keloid Scars

Patients affected with keloid scars are often subjected to major clinical and psychosocial burdens. A range of treatments, including compression therapy and surgical excision, have been explored and documented for various conditions. However, it is unfortunate that a significant proportion of patients do not respond favorably to these interventions. As a result, the utilization of fat transplantation has emerged as a novel therapeutic approach to facilitate scar maturation and enhance aesthetic outcomes in individuals suffering from hypertrophic and keloid scars. While research on the application of autologous fat grafting in the treatment of keloid scars is limited, preliminary findings indicate a positive impact on scar improvement. In summary, lipofilling shows promise as a valuable additional therapy in the management of keloids. It carries minimal procedural risks and has the potential to enhance patient satisfaction. (28)

Scleroderma/Systemic Sclerosis

According to studies conducted by Magalon et al. and Sautereau et al., subcutaneous perioral microfat injection has shown effectiveness in addressing various symptoms associated with systemic sclerosis. These include facial handicap, skin sclerosis, limited mouth opening, sicca syndrome, and facial pain. (29,30)

The effects on hand scleroderma are also remarkable (26). After 10 to 15mL of fat was injected into the hand, patients with Raynaud’s phenomenon experienced

subjectively improved function, fewer ulcerations, enhanced skin and soft tissue quality, fewer cold attacks, as well as less discomfort (31). As per the protocol outlined by Bank et al. in their study, it is recommended to distribute the fat between specific areas, including the spaces on the back and palm sides of the hand, the hollow area between the tendons of the thumb and index finger (snuffbox), and the shallow blood vessel network on the palm side (superficial palmar arch). Due to the absence of notable alterations in blood flow, the specific mechanism by which the intervention operates remains unclear. (32)

Burn Injuries

A burn injury is a serious form of trauma that affects the entire body, and even though survival rates have improved, it continues to present a significant challenge in the context of healing wounds on the skin (13). Each year, the American Burn Association approximates that there are more than 500,000 burn injuries of clinical significance, requiring medical treatment (16).

If deep burns are allowed to heal without intervention, the skin tends to develop fibrotic scars that exhibit reduced elasticity and have an uneven appearance in terms of color and texture. This fibrotic scarring causes substantial physical deformity and also frequently has a negative impact on function. (7).

Approximately 75% of white patients with third-degree burns experience the development of hypertrophic burn scars. These scars pose challenges due to both cosmetic and functional considerations. Moreover, there are concerns regarding the impact on the patient's social and psychological well-being. As a result, achieving satisfactory outcomes in the treatment of burn injuries remains a significant challenge. Patients with extensive burn injuries often face a shortage of viable skin to cover their burns. Unfortunately, the currently available options for cutaneous replacements and cultured epithelial autografts can be inefficient and ineffective in addressing this issue. (13)

In this context, surgeons have shown a keen interest in utilizing fat for surgical procedures, primarily due to its autologous nature. Fat is derived from the patient's own body, making it readily available and easily manipulated for use in these procedures. Tissue engineering has put a greater focus on the use of adipose tissue as a regenerative medium over the last decades. Many methods have recently been

used to minimize skin damage and the resulting deformity, including silicone gels, corticosteroids, pressure dressings, and finally, autologous fat grafting. (7)

Burn scars, including those that have aged over time, cannot be characterized as “quiescent” scars, according to Bruno et al.'s immunohistochemical analysis, since they show a hypervascularized and proinflammatory status and their maturation is limited (21). Lipofilling allows for a significant improvement in this status, bringing the tissue closer to that of healthy tissue histologically (13).

Brongo and colleagues describe their experience using lipofilling to treat burn scars in another study, in which they used a questionnaire, as well as physical and histopathological examinations, to assess the scars' evolution one year after treatment. All patients indicated an enhanced clinical condition at the one-year follow-up. The histological results suggested tissue regeneration, by showing neoangiogenesis, dermal hyperplasia, and new collagen deposition. Clinically, the treated skin's elasticity, softness, texture, thickness, and color improved, and scar retraction was reduced. (22)

On the contrary, Gal et al. conducted a study where they treated eight pediatric patients with burn injuries using a single session of fat grafting. They observed minimal differences in scarring compared to a control group that received saline injections (23). The authors of the study proposed that the limited impact of the fat grafting on scar improvement could be attributed to the fact that they only performed a single session of autologous fat transplantation, as a series of fat grafting sessions may be needed to enhance scarred recipient sites, according to Strong et al. (23,24). Intense tissue engineering, with the production of 3D scaffolds or matrices, as well as enhanced preconditioning cell therapies and optimized culture conditions, are critical for improving the therapeutic effect following stem cell treatment in burns patients (13).

Based on multiple case reports and studies, autologous fat transplantation has shown promise as a treatment for addressing various issues commonly associated with thermal injuries. These issues include hypoplasia, asymmetry, soft tissue thinning, and poor quality of the affected site's skin. (7)

Radiation Damage

Radiation therapy is effective in destroying cancer cells, but it also has the drawback of damaging or killing adipose-derived stem cells. These stem cells, which are

abundant in liposuctioned fat, play a crucial role in tissue maintenance and engraftment. Although engraftment may initially be challenging due to the hostile environment caused by radiation therapy, the small amount of graft that successfully takes place in the first round can make subsequent grafting attempts easier. As the process of grafting is repeated, the benefits tend to grow exponentially. With each subsequent grafting session, the transplanted tissue becomes richer in normal cells and gradually starts to resemble nonirradiated tissue more closely. (26)

Rigotti et al. made a significant discovery by demonstrating that fat transplantation has the potential to reverse the damage caused by radiation therapy, which has resulted in the field of autologous fat transfer for radiation damage reversal (25,26). Since it helps to minimize fibrosis and soothe the inflammation, autologous fat grafting is best done right after radiation therapy, when the tissues are still inflamed and before fibrosis develops (26).

For instance, in a study conducted at an average follow-up of 40 months after fat grafting, patients who had undergone radiation therapy for head and neck cancers and experienced radiation-induced injuries reported significant improvements in various aspects. These improvements included enhanced phonation, swallowing, and breathing. These results could be backed up by speech therapists and surgeons who worked with these patients. The irradiated area, in particular, was shown to have improved laryngeal mobility, improved skin appearance, decreased perilaryngeal fibrosis, and enhanced capacity to articulate the jaw. (7)

Radiation dermatitis is a condition that occurs when the skin is exposed to ionizing radiation for an extended period of time. It has an impact on individuals receiving radiation treatment, whether or not they are also receiving additional chemotherapy. Acute radiodermatitis, chronic radiodermatitis, and eosinophilic, polymorphic, and pruritic eruption associated with radiotherapy are the three types of skin inflammation that can occur after exposure to radiotherapy. (13)

The transfer of fat tissue incorporating adult ADSCs, according to Rigotti et al., is a highly successful treatment option for degenerative, chronic lesions caused by oncologic radiation treatments. The capillary bed usually is significantly reduced in the radio-damaged tissue, as shown through ultrastructural analysis. Fat grafting disrupted a harmful sequence of events involving damaged blood vessels, reduced blood flow, excessive permeability, and tissue scarring. This interruption led to improved blood flow and the formation of a network of small blood vessels alongside

an appropriate balance of fat cells and capillaries. The release of angiogenic factors by ADSCs played a crucial role in this process. Furthermore, these alterations result in the formation of new microscopic blood vessels, which boosts blood flow. Rigotti and colleagues describe the chain of events contributing to tissue mesemchymalization as follows: first, damaged areas are targeted by stem cells, followed by the release of factors, then formation of new vessels occurs, and lastly oxygenation. This process would favor stem cell maturation into mature adipocytes, as well as the formation of a new microcirculation to replace the current, severely damaged one. Additionally, they stress the significance of administering multiple injections in order to attain consistent enhancement in the area affected by radiation damage. This is crucial because certain damaged blood vessels may still be present in areas of fibrosis that persist even after the procedure. Moreover, they describe a linear correlation between the number of transplants and clinical improvement. This is likely attributed to the fact that the healing of tissue microangiopathy improves proportionally with the total quantity of stem cells present. (25)

Aesthetic Improvement of Radial Forearm Flap Donor Site

Since it was introduced in 1981, the radial forearm flap (RFF) has gained extensive popularity due to its reliability, versatility, and outstanding outcomes in terms of covering defects. Despite the fact that it has become a crucial resource for plastic surgeons, the undesirable look of the donor site remains a problem that needs to be addressed further in order to improve the aesthetic results of the forearm. A split thickness or full-thickness skin graft (STSG/FTSG) is commonly used to repair a donor site defect, however, there is a significant incidence of postoperative complications associated with this procedure, including issues such as unsatisfactory cosmetic outcomes, delayed healing of wounds, adhesion of tendons, partial loss of skin grafts, and limited range of motion. In addition, it is important to note that primary closure and the use of local skin flaps for closure of the RFF donor site can only be considered when the defect size is small enough and the surrounding tissue elasticity is sufficient. Although FTSGs can be utilized to enhance outcomes by providing increased thickness and better coverage, it is important to acknowledge that primary closure is seldom achieved, and the use of tissue expanders and local skin advancement flaps is limited and accompanied by

inherent challenges. As a result, patients may still express dissatisfaction with the overall results. (33)

In a 2018 study, Longo and colleagues describe using lipofilling to enhance the aesthetic and functional outcome following skin graft RF donor site reconstruction. After autologous fat transplantation, ultrasonic measurements of forearm soft tissue thickness revealed a noteworthy enhancement in the thickness from the epidermal layer to the hypodermal layer on the RFF donor site. However, when compared to the corresponding area on the opposite side of the forearm, there were still discernible differences in tissue thickness. In all patients, the RFF donor site's cutaneous sensibility was preserved and remained intact, though it was decreased when compared to the contralateral arm. Overall, there was an improvement in the quality of scars at the end of the treatment in all cases, with higher postoperative scores on the Patient and Observer Scar Assessment Scale (POSAS) for both patients and observers. Except for discrete swelling and ecchymosis during the early postoperative period, which resolved uneventfully, no postoperative donor or recipient site complications, like hematoma or infection, occurred. In general, while the retention of fat grafts may vary, Longo et al. advocate for this procedure due to its effectiveness in providing filling and rejuvenating properties. (33)

Chronic Neuropathic Pain

"Neuropathic pain manifesting as complex regional pain syndrome is difficult to manage because of its intermittent and severe nature as well as its, often refractory, response to typical medication" (34). The International Association for the Study of Pain defines neuropathic pain as pain that affects the somatosensory system and is characterized by symptoms such as burning, stabbing, pins and needles, shooting, and electric pain (35). Its causes vary and include nerve trauma or compression, infection, autoimmune disease, drugs, and abnormal healing of surgical or traumatic cutaneous wounds (36).

Chronic neuropathic pain syndromes can be classified into two categories depending on whether the nervous system lesion is located in the central or peripheral nervous system, although most forms of neuropathic pain are likely to persist due to mechanisms in both the peripheral and central nervous systems. At present, it is believed that peripheral neuropathic pain occurs due to an abnormal

healing process of the affected nerve, leading to changes in nerve conduction, the formation of neuromas, and the occurrence of spontaneous nerve signals. When a peripheral nerve is injured, a cascade of neuroinflammation-related events is triggered, which often maintains or worsens the original injury. Medications are commonly used to treat neuropathic pain, but only about half of the patients experience sufficient pain relief, whereas the required drugs have a long list of side effects. (36)

Given the ineffectiveness of drug therapy in providing long-term pain relief, some researchers are investigating the widespread utilization of ADSCs as a treatment alternative (34). The use of autologous fat transplantation, focusing on regeneration and immunomodulation, provides an alternative approach (36). As mentioned before, adipose-derived stem cells have been shown to divide into a variety of cell lineages, including adipogenic, chondrogenic, cardiomyogenic, osteogenic, and neurogenic, which all may contribute to repairing damaged tissue (36). Some published in-vivo studies have suggested peripheral nerve regeneration after ADSCs were applied. Moreover, the neuroinflammatory cascade has also been shown to be immunomodulated by ADSCs (36).

Furthermore, to avoid the reappearance of scar contracture and maintain the alleviation of neurogenic pain, it is possible to enhance the improvement by placing fat grafts around the affected nerve (13).

The authors Khouri et al. report the case of a 34-year-old woman that was admitted to the Department of Plastic Surgery at the University of Pittsburgh for treatment of chronic cranial neuralgia and headaches. She had been experiencing daily episodes of intermittent, intense, shooting, and piercing pain in the face after hardware removal following a craniotomy. Conventional pain medication could only provide minimal relief, but she observed a substantial reduction in pain after one procedure with 25ml of lipofilling to the central scalp concavities and left scalp. She had sustained relief in the areas where the fat had been transplanted after six months and requested further treatment in areas that had not yet been grafted. Consequently, additional areas of nerve irritation were discovered in the occipital region of her head using Tinel's sign as a guide and after another session of lipofilling, she once more showed significant improvement. Overall, the patient was pleased with the outcome and contour. (34)

Additionally, in their case series, de Gast and colleagues describe the treatment of two female patients who had developed painful scars from aesthetic surgical procedures, the pain was initially managed pharmacologically in accordance with the World Health Organization Analgesic Ladder (37), but had failed to deliver sufficient relief. In order to reduce the stiffness of the scar tissue, provide cushioning, and alleviate the ongoing pain, fat grafting was carried out in the affected regions. In both cases a rapid, sustained improvement was observed after one or two treatments of lipofilling and the women would recommend the treatment to other patients. (36)
Although there is a limited availability of large-scale randomized controlled clinical trials, the expanding body of literature and the outcomes obtained thus far indicate that lipofilling is a safe and innovative therapy for neuropathic pain syndromes. Additionally, it holds promise as a potential treatment option for various other chronic pain syndromes (34,36).

Postmastectomy Pain

Research has demonstrated that fat injections can provide relief to patients experiencing Arnold Neuralgia as well as post-mastectomy pain syndrome, assisting them in managing their pain effectively (34).
Postmastectomy pain syndrome refers to the presence of chronic pain in the shoulder, axilla, or chest wall on the same side as the patient's surgery. This pain is neuropathic in nature and persists beyond the expected healing period of three months, occurring either intermittently or continuously. While the extended use of pharmaceutical substances is not well-received due to limited tolerance, conventional treatment methods involve utilizing topical patches containing lidocaine, anticonvulsant medications, or cyclic antidepressants. Numerous studies have concluded that, due to the adipose tissue remodeling scars, fat transplantation is an effective way of treating postmastectomy pain syndrome. It is proposed that the nerve entrapment that may cause the patient’s pain, might be prevented by fat grafting, and the morbidity for this procedure, similar to that of liposuction, has been found to be minimal. (38)
As reported by Papadopoulos et al., autologous fat transplantation can lower the severity of capsular contractures and provide pain reduction, which, according to the authors, may be credited to tissue differentiation and softening reducing nerve

entrapment. Typically, the treatment necessitates multiple fat grafting sessions over an extended duration. (38,39)

Chronic Neuropathic Pain Following Burn Injuries

Despite a scarcity of literature, reports claim that up to 29% of burn patients experience chronic neuropathic pain. A burn scar can cause neuropathic pain through a variety of mechanisms. The etiology of burn scar neuropathy involves the trapping of nerves inside the scar tissue and the development of neuromas (40). According to research, burn patients with chronic pain exhibit an elevation in nociceptive nerve fibers within their burn scars. The research also revealed comparable findings in nerves located in non-injured areas, suggesting the existence of a systemic mechanism that is activated by dermal injury. The primary reason behind long-lasting nerve-related pain following burn injuries can be attributed to the interplay between the initial injury, the healing process, and the restructuring that occurs at the boundary between the skin and underlying subcutaneous tissues. Moreover, electrical injuries might also cause peripheral nerve damage, as well as the destruction of somatosensory end organs in the cutis and inferior structures. (40)

After conducting initial follow-up and monitoring for one year after the surgeries, Fredman et al. observed that out of seven patients who underwent lipofilling treatment, six experienced a noticeable enhancement in neuropathic pain, as assessed by the surgeon. The estimated fat graft volume extracted ranged from 60% to 80% in all fourteen procedures, as evidenced by the enhanced flexibility of the burn scars. One year after lipofilling, fat placed in between skin grafts and muscle fascia, or periosteum was healthy and displayed no indications of atrophy. In contrast to the presence of Tinel signs in all patients prior to the operation, the examination conducted after the procedure revealed the absence of Tinel signs in all seven patients. While two patients did not report improvement in their neuropathic pain, all seven patients experienced significant enhancements in texture, scar pliability, color, and pruritus. The intense surgical pain felt at the donor and fat injection locations diminished quickly and lasted for a maximum of two weeks. Moreover, at their donor sites, no patients experienced chronic pain. (40)

Only a single adverse event was reported, a minor, asymptomatic donor-site seroma at the umbilical port site in one patient, which did not require any treatment. Donor-

site irregularity, infection, wound breakdown, dehiscence, fat necrosis or liquefaction, or wound necrosis did not occur in any of the patients. (40)
Overall, autologous fat transfer can be seen as a potential solution for patients with burn injuries where nerve decompression, occupational therapy, laser therapies, and pharmacologic regimens have failed, particularly if symptoms impede resuming work or school and disrupt their daily activities (40).

Secondary Craniofacial Deformity

Craniofacial deformities can have traumatic, oncological, or congenital origins and can cause functional impairment as well as psychological distress. Restoring normal craniofacial morphology is essential for patients to regain their ability to engage in regular activities and successfully reintegrate into society. Furthermore, improving the quality of injured soft tissues is critical to enhancing facial movement and preventing sequelae such as wound breakdown and worsening fibrosis. (41)
Autologous fat grafting has emerged as a viable treatment option for craniofacial deformities. Applying this method to craniofacial abnormalities appears to be simple, but various elements complicate the transplantation process, leading to challenging outcomes due to uncertain rates of resorption. For one, scarring and fibrosis in the facial recipient area have diminished its ability to provide sufficient blood flow and elasticity required for successful fat graft integration. Moreover, the effectiveness of graft retention is influenced by the quality of the harvested fat cells and the extent of adipocyte necrosis resulting from damage during the various stages of harvesting, processing, and transplantation. It is advisable to refrain from using large quantities of infiltration in patients with a scarred and noncompliant facial bed, as they are at a higher risk of experiencing complications such as fat necrosis, contour irregularities, or oil cysts. Additionally, the underlying injury site is often lined with mesh or another avascular foreign material, that reduces the vascular supply to the recipient bed, consequently affecting the success of engraftment. (41)
To minimize contour irregularities and improve the survival of the fat graft, it is recommended to inject the fat in a uniform manner using a radial, fan-like technique at different tissue depths. This should be done by using small amounts of fat at a time. While fat transfer in the intradermal or subdermal layers improves skin quality, it can cause skin tears and superficial contour defects. In order to mitigate the

possibility of unintentional intravascular injection and embolization, it is crucial for the surgeon to exercise caution regarding the depth and location of the blood vessels, as well as to avoid areas known to be danger zones. (41)

Even though many of these secondary deformities require reconstructive approaches, it is important for the surgeon to incorporate fundamental facial aesthetic principles in order to improve symmetry and contour. Moreover, the surgeon should take into consideration the quality and texture of the skin, the extent of underlying scarring, and the level of tissue compliance. Due to the aforementioned factors, there will be limitations on the amount of fat that can be safely transferred. As a result, the surgeon may need to carry out the reconstruction in multiple sessions, ensuring a gradual and careful approach to achieve optimal results while maintaining patient safety. (41)

Despite the limited amount of literature available on the utilization of lipofilling for correcting craniofacial deformities caused by trauma or surgery, current research indicates that using a person's own fat for transplantation is a secure procedure. It has been shown to have minimal complications, high levels of patient satisfaction, and positive aesthetic outcomes. (41)

A recent prospective cohort study conducted by Bourne et al. examined the safety and efficacy of fat grafting as a treatment for craniofacial deformities resulting from trauma or surgery. The results of the study demonstrate the safety of lipofilling, with no significant adverse events. The study reported an average volume retention of 63% at the nine-month mark, with the three-month measurement serving as a strong predictor for the final outcome. Enhancements were observed in the overall quality of life concerning one's physical appearance, social connections, and social functioning, leading to increased satisfaction in these aspects. The authors' conclusion emphasizes that autologous fat grafting for craniofacial deformities is an exceptional alternative due to its reduced invasiveness and enhanced safety compared to traditional reconstructive options. The procedure demonstrates volume stabilization within three months and yields positive outcomes as reported by the patients. (41,42)

In conclusion, lipofilling has transformed the treatment of secondary deformities, moving away from invasive and complicated procedures and toward a less invasive and more practical treatment (41).

Human Immunodeficiency Virus Associated Lipodystrophy

In lipodystrophy associated with Human Immunodeficiency Virus (HIV), there is a redistribution of fat, where fat deposits are relocated. Specifically, there is an increase in subcutaneous fat in the breasts, cervical and dorsal regions, and an accumulation of visceral fat in the abdomen , as well as fat wasting in the arms, legs, face, and buttocks. Numerous theories have been proposed to explain the cause of lipodystrophy, particularly in relation to HIV treatment. The prevailing theories primarily emphasize the harmful impact on mitochondria and the disruption of adipocyte development due to nucleoside reverse transcriptase inhibitors and protease inhibitors. However, lipodystrophy has also been described as a form of specific neuropathy. (13)

"Facial lipoatrophy is characterized by loss of the buccal and/or temporal fat pads, leading to facial skeletonization with concave cheeks, prominent nasolabial folds, periorbital hollowing, and visible facial musculature" (43), altering the healthy, youthful, convex facial curves into pathologic, aged, and concave contours (43).

The risk of facial fat loss rises with cumulative exposure to highly active antiretroviral therapy, and it may happen as early as the first year of treatment. Since the appearance of the face is commonly viewed as a manifestation of health and cannot be concealed behind clothing, facial lipoatrophy is a stigmatizing characteristic of HIV-related lipodystrophy. The data on beneficial effects of certain medications for lipoatrophy, such as uridine, pravastatin, rosiglitazone, or pioglitazone has not been confirmed conclusively either. (43)

Coleman's extensive experience and expertise in facial lipofilling for cosmetic purposes have established lipofilling as a highly dependable procedure for augmenting the subcutaneous layer of the face. Unfortunately, not all patients are suitable candidates for lipofilling due to inadequate subcutaneous tissue in the lower abdominal region, which is typically the area with the highest concentration of fat. (13)

Facial Rejuvenation

Facial aging is a dynamic and complicated process, which is caused by changes in the bone structure, subcutaneous soft tissue, and skin. In order to properly bring back attractive, juvenile, and natural facial features with rejuvenation procedures, it

is important to understand these changes. As a person ages, the midface rotates clockwise in relation to the cranial base, resulting in enlargement of the orbital aperture, posterior displacement, and increased size of the maxilla, as well as reduced mandible size in both horizontal and vertical planes. These procedures result in the reduction of fat compartments in specific areas of the face, leading to the emergence of loose skin and noticeable creases around the eyes, jawline, and the lines running from the nose to the mouth. Additionally, they cause the displacement of the ligaments and soft tissues that support the surface of the face. (44)

Due to the fat's important role as structural support to the face, age-associated tissue changes require not only the removal of abundant tissue and resuspension of ptotic tissue but especially volume augmentation. Surgeons should have an accurate anatomical understanding of the distinct facial fat compartments, to ensure a precise preoperative analysis and to successfully rejuvenate the face. By considering these principles, the lift-and-fill face lift has revolutionized the surgical method for enhancing the appearance of an aging face in a more aesthetically pleasing way. The procedure begins with lipofilling, which involves filling both the deep and superficial layers of fat compartments. Next, the superficial musculoaponeurotic system and platysma are manipulated. Finally, fat is injected into specific areas that require additional volume, such as the chin, oral commissure, tear trough, temples, and forehead. Unlike nonautologous injectables, the process of fat grafting to these areas involves using the patient's own fat, which seamlessly integrates with the facial tissues. This results in a smoother, more natural-looking contour that can last for a longer duration of time. Additionally, ADSCs' ability to regenerate can reduce scars and sun damage and enhances the quality of the overlying tissue. (44)

Upper Third

As individuals age, the appearance of the upper third of the face undergoes noticeable transformations, primarily affecting the upper eyelids, temples and brows. The youthful brow and upper eyelid area exhibit characteristics such as being prominent, curved, and seamlessly blending with the surrounding temple region. It also contains a lateral arch. (44)

The process of aging is associated with a reduction in the volume of the fat pads in the temporal area, leading to the development of hollowed regions on the sides of the forehead and a downward descent of the outer brow. The use of lipofilling, which involves transferring fat to the temples and forehead, can be an effective method to restore a more youthful contour in the temporal area. This procedure can also lift the lateral brow, resulting in a more natural appearance compared to a surgical brow lift that primarily focuses on elevating the inner brow. Injecting fractioned fat after blepharoplasty can increase the volume of the upper eyelid, as well as stimulate dermal regeneration. (44)
Lipofilling the hollowed upper orbit can provide rejuvenation to the upper eyelid, effectively eliminating the appearance of an unnaturally sunken and aged look often described by patients as "nursing-home" or "owl eyes" (45).

Middle Third

The lower eyelid, tear trough, and malar area are the most prominent features of the midface (44).
Transferring fat to the infraorbital region provides a comprehensive solution for addressing the hollowing that occurs with age, which can contribute to an unhealthy appearance. This procedure not only fills in the hollow area but also reduces the visible length of the lower eyelid and creates a seamless transition from the lower eyelid to the cheek. These results are typically difficult to achieve with traditional lower eyelid surgery methods. (45)
Given the challenge of distinguishing the precise boundaries between the infraorbital, tear trough, and cheek regions, it is often necessary to treat these areas simultaneously in most patients. The treatment areas tend to overlap to a certain extent, similar to other regions of the face. (45)
The presence of a deep tear trough deformity can be attributed to multiple factors that occur with aging. These include hollowing of the infraorbital area, which refers to a loss of volume in the area beneath the lower eyelid, laxity of the orbital retaining ligament, and a decrease in volume in the front portion of the cheek. In cases where patients have fat herniation at the inferior orbital rim, it may be necessary to perform blepharoplasty, a surgical procedure targeting the lower eyelid, to address this specific issue. Overall, fractionated fat grafting is the optimal way to blend the lid-cheek junction and correct orbital hollowing. (44)

When it comes to increasing the volume of the cheek area, there are four important sections that need to be considered. These sections consist of the inner portion of the cheek (medial compartment), the deeper region between the nose and cheeks (deep nasolabial malar compartment), the upper outer part of the cheek (high lateral superficial malar compartment), and the middle outer part of the cheek (middle superficial malar compartment). To ensure optimal results, surgeons should begin by focusing on the deep malar compartment. Afterward, they should proceed to address the superficial high and middle malar compartments. (44)

In the case of the cheek, lipofilling has the potential to improve the facial proportion and shape similarly, and in some cases even better, than the improvements obtained from cheek implants (45).

Existing imbalances in the cheek area can be effectively corrected. Additionally, it is important not to overlook the significance of the buccal fat pad in maintaining a youthful midface. After performing the augmentation procedure, it is crucial to recreate the buccal fat pad in a way that complements the malar region. This is essential to prevent the appearance of sunken or hollowed cheeks. (44)

Lower Third

Key elements of the lower third of the face are the nasolabial fold, prejowl sulcus/genio-mandibular groove (GMG), lips, labiomental sulcus, labiomandibular fold, and chin (44).

Lipofilling makes an ideal and effective addition to treating the nasolabial fold for patients receiving facelifts (45). Nevertheless, it is essential that the surgeon sets realistic goals and limits the injected fat volume to an appropriate amount, since overfilling the nasolabial region can change the patient's appearance by altering the posture of the patient's mouth and smile shape (45). To avoid overcorrection, the malar fat compartments should be filled prior to any nasolabial augmentation, for the deepening of the nasolabial fold is connected to the loss of cheek volume, and filling it effectively already lifts the nasolabial fold (44).

By performing lipofilling in the GMG area, an uninterrupted and strong aesthetic line from the mental region to the posterior mandible can be achieved, similar to the result of a prejowl implant. It is not possible to create this solely by lifting the jowl and it produces a highly attractive enhancement on both the female and the male face. (45)

As the mandibular border shrinks with aging, the facial appearance can become frail and atrophic. The facial shapes and the overall facial proportions of patients can be improved, broadened, and strengthened, similar to the results acquired with mandibular border and mandibular angle implants, by transplanting fat to the jawline. This results in a more attractive, youthful, and fit appearance and works as a powerful addition to a facelift, which in turn usually worsens the feeble and deficient mandibular contour if performed by itself. Lipofilling to the mandible is, furthermore, particularly useful in patients with longer faces in general, looking for enhancement and rejuvenation. Finally, since the two regions overlap in the majority of cases, the jawline is usually treated together with the GMG. (45)

The lips tend to thin with age and lose their crispness along the philtral columns (44). Marten and colleagues point out that lipofilling the lips has apparent advantages and disadvantages, but a successful procedure and adequate graft take means patients can be spared repeated filler treatments and numerous problems associated with lip implants and other variations of lip grafts and therefore less inconvenience and discomfort (45).

Fat grafting, in addition to providing a gentle and authentic improvement, typically achieves a slight moderation that can be considered ideal and suitable for individuals undergoing a standard facelift procedure. Unfortunately, it shows the disadvantage of producing a substantial amount of slow-resolving swelling and varying graft takes between patients. Also, according to Marten et al., by using fat it is usually impossible to produce the highly stylized “fashion magazine cover-girl” lip look, for which nonautologous fillers are better options. (45)

Conventional methods of skin resurfacing, including peels, lasers, and dermabrasion, often fail to adequately address perioral pucker lines in patients. This is due to the fact that these procedures solely focus on treating the skin and fail to restore the loss of subcutaneous fat in the perioral area caused by the aging process. Fat transplantation, on the other hand, can enhance outcomes by replenishing fat that is normally located between the skin and the orbicularis oris muscle near the vermillion-cutaneous junction. Furthermore, combining perioral fat grafting and laser resurfacing or dermabrasion, indicates that healing and the overall results are superior and go beyond the improvement achieved by mere additional volume, which can be attributed to the effect of the ADSCs. (45)

In most cases, the treatment of the chin area is typically performed in conjunction with the GMG, as these two areas often exhibit overlap or interconnection. Lipofilling, or the process of using fat grafting to enhance the chin, offers multiple benefits for individuals experiencing various chin-related issues. These include the loss of chin projection, decreased vertical chin height, and the natural loss of chin volume associated with aging. In certain situations, lipofilling can even yield outcomes comparable to those achieved with small chin implants. Additionally, this procedure has the ability to widen and strengthen the chin while addressing any atrophic or feeble impressions that may arise as the chin diminishes in size due to the aging process. This can be accomplished by filling in the labiomental and submental sulcus if necessary. (45)
Overall, because the best uses for fat transplantation to the chin are small changes, larger augmentations usually require chin implants, otherwise resulting in a less sculptured and globular appearance (45).

Rhinoplasty

Patients who are considering augmentation rhinoplasty commonly express concerns regarding a low dorsum and a nose that appears shorter than desired. While both synthetic implants and autologous grafts can produce satisfactory rhinoplasty results, synthetic implants are generally linked to higher complication rates, with displacement and extrusion. (13)
When conducting structural fat grafting, Coleman emphasizes the significance of precisely delivering small amounts of fat to areas that have thin skin, such as the periorbital region (46,47). Due to the nasal dorsum's thin skin and limited space, the placement of large fat parcels is more prone to causing problems such as nodulation, implant dislodgement and skin irregularities (13). As a result, lipofilling is often used to improve the nose's profile (13).

Gummy Smile

The appearance of a smile is influenced by the different features of the mouth. The condition commonly referred to as a "gummy smile" or "horse smile" occurs when the upper lip is excessively retracted, resulting in the exposure of the incisors and a noticeable portion of the gums in certain individuals. What is considered

aesthetically appropriate for gingival showing in a smile varies. A gummy smile, however, is typically characterized by the excessive exposure of more than 2 mm of the gums when a person smiles. Skeletal, gingival, muscular, and iatrogenic etiologic factors may all be present on their own or in combination. Several studies have been published on the treatment of skeletal issues such as vertical maxillary excess and gingival problems associated with delayed passive eruption (48). When the “levator labii superioris”, “levator labii superioris alaeque nasi”, “levator anguli oris”, “zygomaticus major”, “zygomaticus minor”, and “depressor septi nasi” muscles are hyperfunctional, they have the ability to elevate the upper lip, leading to excessive gingival display or gummy smile. Since the late 1970s, botulinum toxin has been clinically investigated for the treatment of extreme cases associated with intense pain or muscle contraction. In the case of treating a gummy smile, a non-surgical option like botulinum therapy can be advantageous. This treatment aims to reduce muscle hyperfunction, which is responsible for the excessive gingival display, by injecting botulinum toxin into the relevant muscles. Due to the limited long-term effectiveness of botulinum toxin, repeated therapy sessions are often necessary. (48)

In their study, Huang et al. present positive long-term outcomes when utilizing fat grafting as a corrective technique for addressing the gummy smile. The authors report that all their patients showed less than 2 mm of gingival display after the lipofilling procedure. Additionally, the individuals under their care were monitored for an average duration of thirteen months. During this time, no significant issues such as skin tissue death, infection, abnormal growths, hardening, damage to blood vessels, or unevenness were recorded. However, there was mild to moderate swelling in the treated regions, which subsided within a week to ten days. All of the patients were subjectively pleased with the result. (48)

Breast Reconstruction

Utilizing fat grafting for breast augmentation and reconstruction has become increasingly significant in the century since the first reported case (38). As a result of its suspected interference with cancer surveillance, along with the suspected oncogenic potential for breast cancer, the ASPS recommended caution using fat grafts in 1987 (9). Due to the research by Coleman and Saboeiro, who describe

benign postoperative findings in mammograms subsequent to autologous fat transplantation, this statement could later be retracted (38,49).
Additional studies could further alleviate initial concerns regarding the interference with tumor surveillance of autologous fat transplantations and their oncogenic potential. In addition, surgeons have been able to successfully employ fat transfers for various applications by establishing explicit guidelines and improving the techniques for fat grafting procedures to the breast. Lipofilling is becoming increasingly popular among eligible patients as a reconstructive option because it can create a breast that looks and feels natural, providing both a realistic appearance and a soft texture. Autologous fat transplantation offers significant versatility due to its wide range of potential applications in breast reconstruction. (38)

Fat Grafting in Implant-Based Breast Reconstruction

The most common procedure for reconstructing the breasts, the two-stage implant-based reconstruction (IBR), profits in a number of ways from fat grafting. In the past, fat has been utilized to conceal step-off deformities, which arise from a distinct contrast between the natural chest wall and the implant. In numerous instances, the transplantation of fat is carried out concurrently with implant placement, typically after tissue expansion. During this process, the fat is strategically positioned in the subcutaneous plane just above the implant capsule. This delayed fat placement, after tissue expansion, carries multiple advantages, like allowing time for a maximal dermal matrix vascularization, facilitating the development of contour irregularities, and giving away areas with thin skin and rippling to be targeted during autologous fat transplantation. Prior to the ultimate placement of the implant, lipofilling can also be performed as an interim procedure over the tissue expander. This allows for additional volume and contour adjustments before the final implant is placed. Advocates of this approach propose that the regenerative properties of injected adipose tissue can be advantageous for patients who have undergone radiation therapy or have thin mastectomy flaps. These factors can potentially compromise the integrity of the soft tissue envelope, and the regenerative capacity of adipose tissue may help improve the overall outcome in such cases. Autologous fat transplantation is thought to not only increase chest wall healing but also reverse soft tissue damage by providing stability during tissue expansion. (38)

Submuscular Breast Reconstruction

For breast reconstruction, implants were usually positioned in the subpectoral pocket. Submuscular implants or expanders can be suspended with synthetic or bioprosthetic materials at the inferior pole or can be placed with total muscular coverage. During implant exchange, in IBR, fat can be injected into various areas such as the midline plane, the edge of the implant, and the upper poles of the breast. This is done to camouflage rippling, reduce the visibility of the implant, and create a more natural and anatomically pleasing contour in the upper pole of the breast (38). Furthermore, to augment volume, autologous fat transplantation can be performed directly into the pectoral muscle. (38)

In a prospective cohort study conducted by Qureshi et al. in 2017, the authors aimed to assess patient satisfaction with cosmetic outcomes in two groups: those who underwent direct implant placement and those who received implants after tissue expansion. The study concluded that incorporating autologous fat transplantation as an adjunct to conventional implant placement techniques yielded favorable aesthetic results, as reported by both the patients and the surgeons involved in the study. (38,50)

Prepectoral Breast Reconstruction

Prepectoral implants have reappeared as an effective alternative for IBR in recent years. Due to the high risks of mastectomy flap necrosis, capsular contracture, and implant migration necessitating its removal, prepectoral implant placements have previously been discarded, They could be revisited and valued for their relative reduction in the patient’s muscular impairment and pain, after analyzing intraoperative flap perfusion, developing fat transplantation principles, and optimizing surgical skills. Compared to submuscular breast reconstruction, lipofilling could potentially serve as a more effective additional technique for prepectoral IBR. The reason for this is that lipofilling depends on a smaller layer of soft tissue to provide support and coverage for the implant. By using fat grafting to the upper pole, rippling or step-off deformities, which are repeatedly observed in patients with prepectoral implants and a diminutive skin envelope, can be minimized. (38)

In 2015, the authors Hammond et al. were the first to propose applying the fat graft to the plane between the overlying skin flap and an acellular dermal matrix (ADM). This new technique allowed the authors to camouflage deformities, restore flap

thickness, and improve the overall volume of the breast. In the beginning, the procedure involved inserting a tissue expander beneath the muscle and using an ADM over the pectoralis major muscle. After the tissue expander was removed and the implant was placed, the ADM had developed enough blood supply, allowing for the placement of fat between the ADM and the skin flap above it. This helped increase volume and hide any deformities caused by the implant. (38,51)

Implant to Fat Conversion

For patients with implant failures who suffer from recurring prosthetic-associated infections or who cannot undergo prolonged tissue flap procedures, lipofilling has been suggested as the next best option. The authors Panettiere and colleagues, for instance, describe achieving excellent cosmetic outcomes with lipofilling, subsequent to implant failure in a patient with comorbidities who cannot tolerate general anesthesia (38,52). According to Khouri et al., it is advised to conduct the fat transfer right after removing the implant due to the gradual loss of maximum tissue looseness and flexibility over time (26,38).

Moreover, the process of fat grafting begins in the immediate subdermal layer next to the implant. Following the removal of the implant through a lateral thoracic incision, autologous fat transplantation is performed in the subcapsular plane. Although the overall outcome might result in a more natural-looking shape compared to that of IBR, implant-to-fat conversion might produce a smaller or similar-sized breast, depending on the surgical technique. (38)

Fat Grafting in Autologous Breast Reconstruction

Latissimus Dorsi Reconstructed Breasts

The authors Delay and colleagues describe breast reconstruction without implants using a latissimus dorsi flap as the gold standard technique, since it produces a more natural breast and does not have complications related to implants. However, in some cases the reconstructed volume might be insufficient. An efficient solution to this was to place an implant beneath the flap but then reconstruction was no longer autologous. In other cases, while the overall results may be satisfactory, a missing projection or a localized defect stopped the outcomes from being excellent. Using autologous fat transplantation to a reconstructed breast has a number of benefits, including symmetry, natural consistency and appearance of the breast,

cost-effectiveness, autologous reconstruction, reproducibility, and even treating the fat deposits in the donor areas. Delay et al. describe the latissimus dorsi flap as their first choice for autologous breast reconstruction when combined with lipofilling, since due to its highly vascularized nature, the latissimus dorsi flap is the best one to receive fat. Furthermore, their experience shows that a significant amount of fat (up to 500 mL per breast) can be transferred in a single session with an excellent outcome. The fat transplantation starts at the bone plane and progresses to the pectoralis major muscle, the reconstructed breast, and finally the subcutaneous plane. Patients fully comprehend the technique's effectiveness and principle and are thus extremely happy with the procedure. (53)

TRAM or DIEP Reconstructed Breasts

The deep inferior epigastric perforators (DIEP) and transverse rectus abdominis myocutaneous (TRAM) flaps are considered excellent options for breast reconstruction by many surgeons. However, certain shape and volume defects may be visible. Intrapectoral and intraflap lipofilling is performed during the second stage of surgery, primarily on those areas that lack volume. Furthermore, fat transplantation is in some cases used to increase the overall volume of a flap. Since the TRAM and DIEP flaps are less vascularized than a latissimus dorsi flap, it is necessary to transplant less fat to them. Finally, another benefit of lipofilling after a TRAM or DIEP flap is the possible improvement to the abdominal and flank contour. (53)

Fat Grafting for Whole Breast Reconstruction

Although autologous fat transplantation is, in the case of breast reconstruction, usually an adjunctive procedure to implants and tissue flaps, recent studies describe successful primary reconstructions solely using fat grafting. This process requires an external expansion for six to twelve hours for up to two months. Since adipocytes take two to three months to mature, fat transfer procedures, following expansion, should be performed in three- to six-month intervals, with the final result being a breast that feels soft and natural in its proportions. (38)

The authors Stark et al. report that, with an estimated volume loss of 60% per procedure, at least two sessions of primary fat transfer, subsequent to a nipple-sparing mastectomy, are necessary to restore the soft tissue deficiency (38,54).

Following principles akin to that of injecting into the breast tissue, fat is first injected into the pectoralis muscle, the lateral thoracic fascia, and the base of the mastectomy flaps. The desired aesthetic result is usually accomplished after five or six lipofilling sessions. (38)

Khouri et al. present expansion and fat grafting as a less invasive, affordable, and secure option for autologous breast reconstruction. They utilized an average of 225 mL of fat grafting per session, conducted over a period of eight to fourteen weeks. Each session produced a retention volume of between 27 and 52%. (38,55)

Fat Grafting in Breast Conservation Therapy

In the case of breast conservation therapy, fat grafting can be utilized to reduce scarring, achieve breast symmetry, and increase volume (38). Van Turnhout and colleagues report that in a prospective maintained database, individuals who received fat grafting after undergoing radiation therapy and breast-conserving surgery exhibited noticeable improvements in volume, symmetry, shape, and scarring during the six months following the operation (38,56). Despite the excellent aesthetic outcomes linked to autologous fat transplantation following breast conservation therapy, its oncological safety and tumor surveillance are still subjects of controversy due to the lack of conclusive evidence in the literature (38).

Thoracic Malformations

Poland Syndrome

“Poland syndrome is a rare congenital condition characterized by the unilateral absence or underdevelopment of the chest wall muscles and associated limb deformities, including syndactyly or brachydactyly, on the ipsilateral side”. While the exact cause of Poland syndrome is currently not known, it is believed to be associated with a disruption in the blood flow to the embryonic tissues that supplies the chest wall and hand. Common clinical findings include an underdeveloped breast and anomalies of the thorax, such as hollowing of the subclavicular area, an anterior axillary and pectoralis major muscle malformation. On the affected side, breast, cartilage, skin, subcutaneous tissue, long bones, and the rib cage may all be malformed. The biggest issue for males is usually chest wall asymmetry, whereas in females breast asymmetry is a major problem since the breasts are also

irregular in both position and size. To address volume and contour abnormalities in patients, particularly females, with various degrees of Poland syndrome, fat grafting has been commonly employed alongside traditional reconstructive methods like free or pedicled flaps and customized chest wall implants. This combination approach, sometimes involving tissue expansion, has proven beneficial in achieving the desired outcomes. Autologous fat transplantation as a standalone procedure can be a viable and efficient treatment choice for small contour and volume irregularities, eliminating the need for implants or complex reconstructive surgeries. In conclusion, lipofilling might lessen the need for implants or work in conjunction with other chest wall reconstruction techniques to enhance muscle and breast shape. Nevertheless, utilizing fat transplantation as the sole method for addressing Poland syndrome has proven to yield high levels of patient satisfaction and effectively avoids complications commonly associated with the use of external substances or tissue flaps. (57)

Pectus Excavatum

"Pectus excavatum is a deformity characterized by depression of the anterior chest wall due to overgrowth of the rib cage" (57). Frequently, the restoration of pectus excavatum primarily results in noticeable irregularities in the contour of the chest wall (57).

Subsequent to minimally invasive pectus excavatum repair, Facchini et al. describe how lipofilling can be utilized for addressing remaining deficiencies and improving the shape of the chest. After the procedure, the average satisfaction score improved from 1.8 to 2.7 (0. unacceptable, 1. acceptable, 2. good, 3. very good, 4. excellent), indicating that autologous fat transplantation can be advantageous in enhancing the appearance of the chest wall following pectus excavatum surgery. (57,58)

Furthermore, lipofilling has been used to treat these patients' breast asymmetry, achieving natural-appearing outcomes, and high patient satisfaction. Although the outcomes appear promising, it is important to acknowledge that performing lipofilling in the sternal area can present difficulties. This is primarily due to the presence of numerous ligaments and limited subcutaneous tissue, which can result in inadequate survival of the transplanted graft. The two-case series studying autologous fat transfer for pectus excavatum management involved a

combination of pediatric and adult patients and it was concluded that fat grafting is a useful treatment alternative for pectus excavatum patients. (57)

Oncological Safety

Initially, concerns about autologous fat transplantation revolved around its possible negative impact on tumor detection and its potential to promote cancer development. However, subsequent research has demonstrated that the rates of distant, regional, and local recurrences in breast reconstruction procedures involving fat grafting are comparable to those without the use of fat grafts. (12,38) Moreover, previous concerns about impaired tumor surveillance could be alleviated because, due to technological advances, radiologists are capable of properly identifying the differences between neoplastic calcifications and post-fat grafting necrosis. Overall, several authors agree that autologous fat transplantation alone does not reduce the ability to detect recurrence on imaging or raise the risk of cancer recurrence. (38)

Complications

Complications from autologous fat transplantation are relatively rare and include infection, oil cysts and fat necrosis. Ultrasound is used to detect these complications, whereas to differentiate masses from cysts and respectively definitely detect recurrence, mammography is used. While the imaging of recurring lesions may resemble the original cancerous lesion, with pleomorphic calcifications and irregular masses seen on mammography, oil cysts, and fat necrosis have clear imaging characteristics, such as coarse calcifications, for which a biopsy is hardly ever necessary. Furthermore, while fat necrosis and fibrosis typically won't demonstrate a rapid uptake of contrast, with few exceptions showing gradual uptake, breast cancer will usually demonstrate the former. The occurrence of complications in autologous fat transplantation heavily relies on the recipient site and reflects the level of compliance in that area. In general, major complications in breast reconstruction using this method are relatively rare. However, the rates of complications tend to be higher in patients who have undergone radiation therapy following a modified radical mastectomy or a skin-sparing mastectomy. In patients who have received radiation therapy after a modified radical mastectomy or a skin-

sparing mastectomy, the recipient sites tend to have reduced compliance and increased fibrosis. As a result, these patients often require additional sessions of fat transfer to achieve the desired results. When aiming to overcorrect the recipient site with volumes of fat transplantations exceeding 10%, surgeons should anticipate higher rates of oil cysts and subsequent calcifications in patients without irradiated breasts. It is important to note that even with maximum compliance, the recipient's site has a limited capacity for accommodating additional volume. (38)

Aesthetic Breast Surgery

The important role of an aesthetic breast appearance has been highlighted in recent trends in both cosmetic and reconstructive breast surgery. Annual breast reconstruction procedures have increased by more than 29% since 2000, while annual augmentation mammaplasty procedures have increased by 48%. Approximately 25% of all cosmetic surgeries performed annually are related to cosmetic breast procedures. However, despite the increasing number of these surgeries, there has been slow progress in the development of new techniques. One notable exception is lipofilling, which stands out as a method that can enhance patient satisfaction and overall aesthetic outcomes. Additionally, lipofilling addresses many of the limitations associated with traditional breast surgery methods. It can be used for primary breast augmentation without the use of prosthetic devices, volume reconstruction following implant removal, and as an adjunctive procedure alongside breast implant placement to address issues such as rippling and visible deformities, particularly in slim patients or those with subglandular implants. (59)

A wide range of lipomodelling techniques for the breast is reported in the current literature. Intraoperative methods have been described to vary based on the surgeon’s choice, and technical developments are pushing the limits of what can be done with fat grafting in terms of aesthetic improvements. According to Davis and colleagues, lipomodelling in aesthetic breast surgeries appears to be a relatively safe technique with increasing popularity and high patient satisfaction rates. However, further research is needed to explore the technique in more detail and assess any potential risks associated with it. (59)

Applications

Lipofilling is used in a variety of ways in the area of cosmetic breast surgery. Fat grafting to the medial chest will enhance cleavage appearance by reducing the intermammary distance. Additionally, in situations where there is a significant difference in breast size due to tuberous breast deformity, the technique of fat transplantation can be employed on one side to increase the volume of the underdeveloped breast. Lipofilling of the breast, like other body parts, may be used to fill contour defects. In cosmetic breast surgery, the use of fat transplantation as a standalone procedure for primary breast augmentation has emerged as a popular and widely utilized method. This procedure has the advantage of giving the breasts a natural look and feel without the complications of implant-based breast augmentation, such as the need for implant exchanges, implant rupture, or the development of capsular contracture. It is important to note that adipose tissue is not an expander when using it for augmentation. (59)

Hence, prior to transferring the fat, it is necessary to enhance the capacity of the recipient site to accommodate the augmentation, particularly in cases where patients have tight skin envelopes or relatively small breasts. The suggestion of external volume expansion prior to grafting is commonly made, as it has shown remarkable and consistent outcomes. Lipofilling for breast augmentation has demonstrated great cosmetic results in recent years, with high patient satisfaction in terms of breast mound size, shape, and texture. (12)

Lipofilling can be used to enhance the appearance of implant-based breast augmentation by smoothing and concealing the edges of the implant. This process creates a more seamless and realistic transition between the natural breast tissue and the augmented area, which is especially beneficial in cases of subglandular breast augmentation and individuals with thin skin. On the flip side, lipofilling can also be beneficial for patients who opt to have their breast implants removed by restoring some of the volume that was lost. Additionally, lipofilling is often utilized as a complementary procedure in combination with other commonly performed breast surgeries like mastopexy and reduction mammoplasty. This approach aims to enhance the aesthetic results and enhance overall patient contentment. (59)

Complications

Despite the high overall success rates of aesthetic lipofilling procedures to the breast, these surgeries are not without risk. The most commonly observed negative effects linked to lipofilling involve the occurrence of minor irregularities in the shape and noticeable firm areas. The development of breast striae, inflammation, oil cyst formation and calcification, fat necrosis, hematoma formation, and persistent pain at the injection site are other known complications. Regional deformation has also been described at the donor site. (59)

Groen and colleagues published a systematic analysis in 2016 that looks at the results and complications of autologous fat transplantation for aesthetic breast augmentation. More than 35,000 patients were included in the review, which included 22 articles, and observed a 17.2% complication rate, with the most common complication being indurations, followed by persistent pain and hematoma. Furthermore, microcalcifications and macrocalcifications could be detected on mammograms. (59,60)

Hand Rejuvenation

The appearance of someone's hands can often reveal their true age. According to studies, people can roughly guess a person's age by looking at their hands. Dermatoheliosis and photoaging, which cause irregular pigmentation and wrinkles in the form of telangiectasia, seborrheic keratosis, actinic keratosis, punctuate hypopigmentation, solar purpura, and solar lentigines are examples of extrinsic effects on the hand. As a result of dehydration and a decrease in collagen, the aging process often leads to intrinsic effects such as the gradual loss of volume under the skin and tissue atrophy. This causes dorsal skin wrinkles and makes the extensor tendons more visible, as well as making subcutaneous veins look bluer and more tortuous. (13)

The procedure of lipofilling to the hand was initially introduced in 1988. During this treatment, a fat bolus was placed on the proximal dorsum of the hand's side, followed by massaging to achieve the desired contour. After that, a wave of new concepts followed, and lipofilling and laser resurfacing were first combined in 1989. In 1990, hand rejuvenation with microlipoinjection was introduced for age-related aesthetic enhancement, while in 1992, the first patient series was published with

excellent patient satisfaction. In general, utilizing a person's own fat for transplantation to the hand proves to be an effective remedy for age-related loss of volume, which leads to the increased visibility of blood vessels and tendons. Moreover, it also improves the texture and firmness of the skin and soft tissues on the back of the hands, thanks to its regenerative properties. (31)

Procedure

Low pressure, low speed, and low volume fat distribution to the hand by several tunnels and planes are the principles of fat grafting to the hand. During injection, the emphasis must lie on delivering the smallest amount of fat to the desired planes in an even manner at low pressure. (31)

In order to reach the outer layer of the hand and the upper part of the back of the hand, it is required to make an incision closer to the body, below the extensor retinaculum. Alternatively, a comparable outcome can be accomplished by making an incision in the area between the first and second metacarpal bones. By choosing to make incisions in the remaining web spaces, it is possible to gain access to the inner layers of the hand and the lower part of the back of the hand, while minimizing the appearance of scars. Furthermore, in order to minimize scarring to an even greater extent, certain surgeons recommend making a solitary incision between the third and fourth metacarpal bone. What laminae are best suited for fat deposition is still a source of debate,yet there is widespread consensus on the reliability and effectiveness of fat injections only into the superficial lamina. There are no essential structures in the superficial lamina, and the fat graft protects the tendons and underlying blood vessels. The dorsal veins, however, are located in the intermediate lamina, which some surgeons recommend avoiding in order to prevent injecting fat into the vascular system. While some people advocate for injecting fat into this specific layer to enhance the effectiveness of treatment without significant safety concerns, there are differing opinions. Additionally, certain experts propose using fat grafting in the deeper layer (deep lamina) to address concavity between the metacarpal bones. On the other hand, some argue that performing lipomodelling at such a deep level in the hand is unnecessary. Certain surgeons recommend overcorrection as a preemptive measure, anticipating some loss of the graft. In contrast, other surgeons highlight that apparent graft loss is primarily caused by the extended resolution of swelling and discourage overcorrection. (31)

Complications

After undergoing autologous fat transplantation, edema is the primary complication that frequently occurs. However, certain surgeons argue that edema is a normal aspect of the hand's healing process following fat grafting. Therefore, they suggest that it should not be regarded as a genuine complication since it typically resolves on its own. Compression dressings worn for multiple days will facilitate the management of postoperative edema. Two additional complications that resolve on their own after autologous fat transplantation are ecchymoses and paresthesia. These complications are believed to arise from minor injuries to small blood vessels and nerves, respectively. Infections of the hand pose a greater risk as severe complications, although abscesses after hand rejuvenation procedures have only been recorded in a few cases. To minimize the risk, cephalosporin-based antibiotic prophylaxis has been used. (31)

Female Genital Reconstruction and Beautification

Reconstruction

While numerous reports and procedures outline the process of reducing the labia minora, there is a scarcity of literature discussing the augmentation of the labia majora. Vogt et al. report a case where autologous fat transplantation was used to address a deformity in the labia majora that resulted from both oncologic treatment and unsuccessful reconstructive procedures. The patient had undergone resection of a significant tumor as part of the initial treatment for Bowen's disease. Reconstruction with a pudendal thigh fasciocutaneous flap, also known as Singapore flap, was previously attempted, but it failed due to partial skin necrosis, although some fat tissue managed to survive. To provide adequate coverage, the patient required an additional local skin flap, which improved the contour of the area but did not completely meet the patient's expectations. After the tumor resection, the patient’s left labium majus experienced a significant reduction in volume, resulting in the exposure of her clitoris, which caused considerable pain. Local flaps can provide skin restoration for the deformity, thus autologous fat transplantation is a great way to enhance the fullness of the labia majora by softening the scars from flap reconstruction. (61)

For the first two weeks after each operation, there was a mild amount of self-limited swelling. Furthermore, there were no signs of a hematoma or infection, the sutures could be extracted on the 10th day after the surgery, and the rest of the healing process went uneventfully. The patient registered a significant reduction in her clitoris and labia minora irritation symptoms, according to the author. Also, her labia majora pain subsided, and she retained normal sensation. Four months after the operations, the patient requested another fat grafting procedure because of the moderate degree of volume. The patient claimed that her local discomfort and soreness had subsided eight months following this second injection. The clitoris was protected, and she experienced no adverse consequences. (61)

In general, after undergoing ablative labial surgery, fat grafting emerges as a minimally invasive alternative for restoring volume and enhancing aesthetics. This approach shows promise, especially when compared to traditional reconstructive surgery using flaps, that may not consistently achieve equally effective or efficient results. Furthermore, for that patient, the required liposuction was a convenient additional benefit. (61)

Beautification

Autologous fat transplantation for vaginal rejuvenation enhances ablative procedures by adding augmentative surgeries to the extensive array of cosmetic procedures for female genital enhancement. These procedures include reducing the size of the labia minora, brightening the labia through laser treatments, and tightening the vaginal area. The augmentation of the labia majora is a common approach, although lipofilling alone would not be able to hide major hypertrophy of the labia minora. (62)

In 2013, Cihantimur and colleagues used lipofilling, among other techniques, to perform genital beautification. The total amount of transplanted fat was adjusted to the specific needs of each patient. According to the authors, they were able to achieve vulva closure by rejoining the augmented labia majora using this technique. Moreover, during the process of obtaining the fat graft, liposuction was utilized to address the issue of an excessively large mons pubis. (62)

In conclusion, each patient's original labial volume must be taken into account when lipofilling to the labia majora is performed. Although the labia have a good blood supply, it is still crucial to adhere to fundamental principles of fat transplantation.

This includes avoiding the injection of large amounts of fat at once and overfilling the recipient area, as these principles remain important for successful outcomes. (62)

Gluteal Augmentation

The technique of using fat grafting for buttock augmentation initially gained popularity in Brazil and has since gained significant recognition worldwide (63). According to information published in 2018 by the ASPS, there has been a significant increase in the number of lipomodelling-based gluteal augmentations performed. Since 2017, there has been a 19% rise, and since 2014, there has been a substantial 61% increase. Furthermore, the data reveals that over 99% of buttock augmentations have been carried out on female patients aged between eighteen and fifty years. (64,65)

In addition, the data indicates that in 2018 fat grafting was the chosen method for 94% of buttock augmentation procedures, while implant-based augmentation accounted for the remaining percentage (65). At present, fat grafting for gluteal augmentation is widely regarded as the preferred and most commonly accepted method (63).

The author Toledo published one of the first studies in the United States on fat transplantation for buttock augmentation in 1987. Back then, the only method of buttock augmentation that was widely accepted, was using silicone implants. During a time when many surgeons were cautious about injecting more than 10mL of fat in a single operation for gluteal augmentation, the author of the statement took a more daring approach. They were injecting up to 450mL of fat into each buttock, surpassing the conservative limits set by their peers. (63,66)

As a consequence, due to concerns about the safety and cosmetic result after graft reabsorption, he was vehemently criticized. It wasn't until the 1990s that autologous fat transplantation gained widespread popularity in the field of body contouring. This period laid the foundation for its current status as the standard treatment approach in this field. (63)

An hourglass figure with a “waist-to-hip ratio”, which is measured by dividing the circumference of the waist at its narrowest point by the circumference of the thigh at the level of maximum gluteal projection, of about 0.7 has been described as the

most desirable figure for a woman. Nevertheless, as a result of the impact of social media and the influence of celebrities, the concept of the "ideal ratio" might have shifted towards a more exaggerated proportion of 0.6 or 0.5 in recent times. Autologous fat transplantation enables the shaping and sculpting of the buttocks, as well as enhancing the overall body shape, while also providing the advantage of extracting fat and contouring the donor site. Lipofilling is used in gluteal augmentation to shape and augment the buttocks in ways that silicone implants cannot achieve, including the potential to attain the recently popularized more exaggerated waist-to-hip ratios. (63)

The final outcome of buttock augmentation and body contouring through autologous fat transplantation is primarily influenced by factors such as body shape, the presence of excess skin, and the amount of fat available for the procedure. Most patients are suitable for this method, but these specific factors play a significant role in determining the ultimate result. The amount of fat in the body can be assessed by the body mass index and the body fat percentage. The best possible candidates for lipomodelling are patients with a BMI between 20 and 30 kg/m^2, or alternatively a body fat percentage between 20 or 30%, since the excess fat can be extracted from the unwanted area and injected into the gluteal region, improving the overall body contour. On the other hand, patients with a body mass index (BMI) below 20 kg/m^2 or a body fat percentage below 20% are not ideally suited for this procedure, since there is an insufficient amount of donor fat to augment the buttocks in a significant manner. Similarly, patients with a BMI above 30 kg/m2 or a body fat percentage above 30%, usually possess too much adipose tissue to significantly change the shape or appearance of their gluteal region. (63)

In the case of skin excess, the authors Mendieta and Sood categorize multiple variations of buttock ptosis, as well as no-ptosis classes A to C, which show no volume or skin below the infragluteal fold, but a lack of volume in the lower buttocks (63,67).

Since the operation will help in lifting and reshaping the gluteal area, the best-suited candidates for autologous fat grafting are those with either no ptosis or grade I ptosis. Less ideal candidates are patients who show “moderate-to-severe skin excess”, characterized by grade II or III ptosis, are considered less suitable candidates for fat transplantation alone. This is because fat transplantation alone cannot effectively address the issue of skin sagging and provide adequate lifting

and redraping of the skin. In such cases, additional procedures, such as surgical skin tightening or a combination of fat transplantation and skin removal, may be necessary to achieve the desired aesthetic outcome. The body shapes of patients typically do not eliminate the possibility of using lipofilling for gluteal augmentation, but they do limit the potential for achieving optimal results. These body shapes are an important factor to take into account when managing patients' expectations. A widely recognized gluteal classification system categorizes body shapes based on the relationship between the upper lateral hip, lateral thigh, and lateral midbuttocks. This system identifies four main shapes: A, V, square (H), and round. Individuals with V- or square body shapes often experience more challenging outcomes when it comes to achieving the desired waist-to-hip ratio of 0.7. These body shapes can make it more difficult to attain the optimal ratio, which may result in poorer outcomes for gluteal augmentation procedures. Patients with an A-shaped body or a round body shape, on the other hand, generally make more suitable candidates because it is easier to adjust, their natural curvature resulting in desirable buttocks with an ideal waist-to-hip ratio. (63)

In addition to carefully selecting suitable candidates, it is crucial to have a clear understanding of the patient's goals for lipofilling and to establish realistic expectations. This approach significantly increases the likelihood of the patient being satisfied with the final results. (63)

Procedure

To start off, fat is taken out from the regions surrounding the buttocks until a sufficient quantity is acquired. Next, in order to create an hourglass shape with an enhanced buttock, the extracted fat is relocated to specific regions of the buttock (63). “Anatomically, this encompasses the area between the lateral border of the sacrum, iliac wing, and femoral neck, the area overlying the gluteus maximus, and the region between the maximus, medius, and tensor fascia lata” (63).

By combining the process of extracting fat from the surrounding areas of the buttocks and transferring it through lipofilling to the buttocks, a synergistic effect is achieved. This approach emphasizes the hourglass figure and enhances the augmentation of the buttocks. The transition region, which is anatomically determined by the “iliac crests” and “intergluteal cleft apex”, lies between these two areas and should be left untouched. It is advisable to avoid the triangular area

extending from the apex of the infragluteal cleft to the medial third of the lower buttocks, as it contains the primary gluteal neurovascular structures. Moreover, this particular region is characterized by dense fascial and ligamentous attachments, which require vigorous manipulation during the procedure. Such aggressive manipulation poses an increased risk of cannula misdirection into deeper planes and potential harm to major structures. Multiple incisions have been described for the purpose of utilizing lipofilling for body contouring and gluteal augmentation. The ideal incision for this procedure is one that is minimally noticeable while still providing adequate access to the gluteal region that require the most augmentation. The "intergluteal cleft apex", the region inferior to the "iliac crest", and the upper and lower lateral buttocks are frequently used locations for making surgical cuts. Studies have demonstrated that these incision sites can enhance both the aesthetic outcome and the safety of the patients. Numerous surgeons advocate for a fan-like injection pattern to ensure even fat distribution and achieve a smooth and natural contour without abrupt transitions. Additionally, it is crucial to avoid directing the cannula medially, as this increases the risk of inadvertently targeting important structures in deeper layers. The specific injection site may also vary depending on the expert's preference and the desired amount of fat to be injected. While some surgeons have historically distributed fat both within the muscle and under the skin, several publications explicitly discourage injecting fat into deep muscular planes. (63)

Guerrerosantos et al.'s 1996 study, which finds that intramuscular fat injection lowers fat resorption, influenced these techniques (63,68).

Other authors have detailed their preferred technique for distributing fat during gluteal augmentation. They advocate starting with the superficial muscular layer and continuing the injections in a superficial manner until the desired size of the buttocks is achieved. The cannula must be kept angled superiorly and parallel to the gluteal muscle to control the injection level; this approach helps prevent accidental fat injection into the profound muscular plane, which could result in an injection into the main gluteal vessels. According to a systematic review, it was found that among the nineteen studies examined, 46% of them utilized a combination of subcutaneous and intramuscular injections, 27% exclusively reported using intramuscular injections, and another 27% described solely subcutaneous and/or subfascial

injections. In order to minimize the risk of fat embolism, many surgeons have chosen to avoid injecting fat intramuscularly in recent times. (63)
To mitigate the risk associated with intramuscular injections, Frank et al. have recently developed two formulas, one for males and another for females. These formulas are designed to determine the thickness of subcutaneous fat in the gluteal region. High BMI and increased age were also found to have statistically significant associations with increased subcutaneous fat thickness in this study. (63,69)
According to a systematic review, tunneling, which involves creating tunnels with a cannula before applying suction during fat grafting procedures, is performed by a smaller number of surgeons. Furthermore, a lot of surgeons only utilize retrograde injections to ensure the blood vessels' safety. The injection of excess fat or overcorrection as a means to compensate for potential fat resorption remains a topic of debate among surgeons, and there is no consensus on the matter. Although some surgeons advocate for a 50 to 100% overcorrection, others oppose it due to concerns about graft viability because of the increased pressure within the buttocks. (63)
Overall, according to patient satisfaction surveys, gluteal augmentation with lipofilling showed a 97.1% satisfaction rate, with 6 to 10% of patients requiring further procedures to reach the augmentation level they wished for (63).

Complications

Autologous fat transplantation for gluteal augmentation is associated with a complication rate ranging from 7 to 10%. It is important to note that severe adverse events occur in less than 1% of all procedures (63).
The chance of fat emboli has been a major topic of debate when it comes to lipofilling for gluteal augmentation. When a small number of fat cells enter the bloodstream, it can result in the formation of microemboli. These microemboli have the potential to cause pulmonary fat emboli or fat embolism syndrome. This syndrome is characterized by microscopic inflammatory occurrences that are initiated by tiny fat emboli, leading to a widespread inflammatory response throughout the body. In contrast, if large fat particles manage to enter the bloodstream and become trapped in the right side of the heart, it leads to a condition known as macroembolism. This condition causes sudden mechanical heart failure, characterized by a significant impairment in the heart's ability to function properly. Differentiating between micro

and macro fat emboli can be done based on the timing of symptom onset. Micro fat emboli typically manifest within the initial few days following surgery, while macro fat emboli tend to occur either during or shortly after a lipofilling procedure. (63)
The Aesthetic Surgery Education and Research Foundation Task Force examined a group of 692 plastic surgeons who collectively performed 198,857 lipofilling procedures to the buttocks. From this analysis, they identified only 135 instances of pulmonary fat emboli, out of which 32 cases resulted in fatalities. According to the findings of the Task Force, the estimated prevalence of pulmonary fat emboli following gluteal fat grafting was approximately 1 in 1,030 cases, equivalent to 0.08%. Fatal cases were observed at a rate of 1 in 3,448 cases, while nonfatal cases occurred at a rate of 1 in 1,449 cases, both accounting for approximately 0.03% of the total cases. (63,70)
Furthermore, deaths from gluteal fat grafting have been documented around the world, with thirteen deaths in Mexico over the course of ten years and nine deaths in Colombia over the course of fifteen years, that were all linked to fat embolization. Gluteal fat grafting has a higher risk of fatal complications than any other cosmetic surgery, with a rate of around 1 in 55,000. Moreover, it is important to note that the reported rates mentioned above are likely to underestimate the true risk of fat emboli following gluteal fat grafting. This underestimation could be attributed to factors such as a reluctance to disclose serious complications and the fact that the study's survey population consisted exclusively of board-certified plastic surgeons. Fat embolism is the most severe risk associated with lipofilling for gluteal augmentation, but surgeons face plenty of other complications subsequent to this surgery. However, the risks mentioned above are not as frequent as those linked to gluteal enhancement using implants, that have been found to result in complications in approximately 30% of all cases. Minor complications such as seroma, erythema, pain, uneven contours or asymmetry, fat necrosis, temporary numbness in the sacral area, and cellulitis are frequently observed. Fat necrosis can pose a significant problem if it solidifies and is mistakenly diagnosed as a malignant condition, potentially subjecting the patient to invasive or unnecessary procedures. The most frequently documented severe complications include anemia, septic shock fat embolism, as well as symptomatic hypovolemia. Furthermore, sciatic nerve injuries have been described, with symptoms ranging from acute to permanent bilateral foot drop making the use of a wheelchair necessary.

Intramuscular fat injection has the highest complication rate with 28.7%, compared to a 4% complication rate for subcutaneous fat grafting, according to one study. With a higher BMI and with increasing volumes of injected fat, complication rates rise. For optimal safety during the procedure, it is advised to carefully select the appropriate patients, avoid injecting into the muscles, and avoid the triangular area extending from the apex of the infragluteal cleft to the medial third of the lower buttocks. It is also recommended to use a blunt cannula and inject in a retrograde manner parallel to the buttocks. Having accurate knowledge of the anatomy of the gluteal region is crucial for ensuring the best possible safety outcomes. Most significantly, only skilled, board-certified plastic surgeons should undertake fat grafting for buttock augmentation. (63)

Lower Leg Augmentation

Harmonious legs are characterized by their length, width, and curves and are regarded as one of the most notable beauty features in women. Generally, liposuction of fatty areas has been used to improve the appearance of the lower legs, while muscle hypotrophy has been corrected with implants. In addition to muscle-associated corrections, there presently is a growing demand for contouring the entire lower leg. As a result, adipose tissue has emerged as a viable choice for this procedure for several reasons. It is readily available in ample supply within the body, and it can be easily implanted in various areas of the leg. Adipose tissue also possesses a low potential for triggering immune reactions, making it biologically compatible with the recipient. Furthermore, using adipose tissue as an implant option minimizes the negative impact on the donor, reducing the associated morbidity. Moreover, conducting an anthropological analysis of the leg's shape and harmonizing it with the overall body proportions is essential for this technique to effectively contour and enhance the legs. The mathematically specified optimal proportions of the lower leg by Cuenca-Guerra serve as a fundamental reference for devising an operative strategy to enhance the lower leg. These measurements encompass various aspects such as the length, diameter, and curvature of both the medial and lateral lines. (71)

Von Szalay recommends 33–36cm as an optimal diameter for the widest portion of the calf, while Benslimane mentions angles between the femur's central axis and the tibia's central axis (71,73,74).
In addition to the surgeon's artistic abilities, defining anthropological measures is a basis for further fine contouring. The shape of the leg is influenced by several factors, including the orientation of the lower leg's central axis in relation to the upper leg. Additionally, the fullness provided by the soleus muscle and the distinct contributions of the medial and lateral heads of the gastrocnemius muscle play a role in shaping the leg's appearance. Furthermore, the amount and distribution of subcutaneous fat also contribute to the overall contour and shape of the leg. (71)
From the 48 patients, on which Skorobac Asasin et al. performed lipofilling to the lower leg, eleven patients were not satisfied with the initial result and requested additional augmentation, which subsequently was done six months after the first operation, when volume retention and percentage of fat survival could be determined. Also, compared to inserting sub-fascial or sub-muscular implants, there were no major complications, such as capsular contracture, postoperative hematomas, compartment syndromes, seromas, or double contours. (71)
Indeed, augmenting the lower leg with adipose tissue is a beneficial technique as it can enhance the overall contour of both the leg and the underlying muscles. This approach allows for a comprehensive improvement in the aesthetic appearance of the lower leg region. Moreover, fat grafting for lower leg contouring is considered a minimally invasive procedure, which offers advantages in terms of reduced surgical invasiveness and associated risks. Due to its relatively low risk of complications, fat grafting may become a preferred choice for treating patients with muscle dystrophies or traumatic injuries, providing them with a viable option for achieving desired leg contouring outcomes. (71)

Pediatric Patients

Although fat grafting is mainly discussed in relation to adults, it has also been employed in children for various reconstructive and functional objectives. Such applications encompass the management of congenital anomalies such as cleft lip and palate, as well as addressing secondary soft tissue defects linked to congenital conditions like Poland syndrome and Parry-Romberg syndrome. Furthermore,

autologous fat transplantation has proven beneficial in addressing functional deficiencies associated with velopharyngeal insufficiency. The literature regarding fat grafting in pediatric patients is currently limited, and there is a scarcity of data concerning long-term outcomes and graft survival rates. However, existing studies on pediatric autologous fat transplantation have demonstrated high levels of effectiveness, patient satisfaction, and safety. (57)

Craniosynostosis

Craniosynostosis is a condition present at birth that involves the premature fusion of one or more sutures in the skull. This abnormal fusion can lead to significant craniofacial asymmetry and distortion of the skull shape. Remodeling of the cranial vault is the standard method for treating patients with craniosynostosis. Despite successful correctional surgery of cranial sutures, some patients may still experience small deformities in the contour after the operation. (57)

To address these issues, lipofilling has been identified as a potential solution. In a 2018 case series conducted by Castro-Govea et al., they examined the asymmetry in post-craniosynostosis repair among patients with an average age of six years. The authors utilized autologous fat grafts enriched with adipose-derived stem cells to improve facial appearance and correct the asymmetry. This approach resulted in high satisfaction levels among the patients and their families. (57,75)

Moreover, autologous fat transplantation has been employed in the enhancement of craniofacial aesthetics among adult individuals suffering from unrepaired craniosynostosis. Kalantar-Hormozi et al. conducted a study involving fifteen patients, both pediatric and adults, with an average age of nineteen years, who had not undergone prior craniosynostosis repair. The study provided evidence supporting the effectiveness and safety of lipofilling as a treatment for anterior plagiocephaly. There were few complications, and the majority of patients had their cranial deformities corrected adequately. (57,76)

While there is a lack of research on the long-term effects of fat graft retention in this specific context, the available limited case series suggest that the use of autologous fat transplantation in pediatric patients with craniosynostosis yields positive overall outcomes (57).

Craniofacial Microsomia

"Craniofacial microsomia commonly involves hemifacial hypoplasia affecting facial bones and overlying soft tissue" (57).

In 85% of cases, craniofacial microsomia occurs unilaterally, resulting in an asymmetrical face. While there has been extensive research conducted on treatment options for mandibular defects related to craniofacial microsomia, there has been relatively limited investigation into surgical interventions specifically targeting the soft tissue deformities that occur above the affected area. Procedures, like mandibular distraction osteogenesis for instance, may effectively improve mandibular deformities but are often insufficient to correct facial asymmetry. Lipofilling has been recognized as a surgical adjunct for patients with craniofacial microsomia, aiming to enhance contour and promote the symmetry of the face. (57)

A systematic review conducted in 2019 examined 38 published papers to evaluate the surgical approaches used to treat soft tissue defects observed in individuals with craniofacial microsomia. While microvascular free flaps offer the advantage of greater volume augmentation and require fewer overall procedures, structural lipofilling can achieve a higher level of facial symmetry with significantly lower rates of complications. According to Sinclair et al., fat transplants were used alone and in combination with other procedures such as surgeries to bony structures on patients from all Pruzansky groups. According to the authors, it is important to note that achieving sufficient volume augmentation and facial symmetry often requires multiple sessions. The extent of the soft tissue defect determines whether or not serial lipofilling can be used. Autologous fat transplantation alone may treat mild to moderate soft tissue deficiencies, but more serious deficiencies usually necessitate transfer of free tissue followed by contouring with lipofilling. (57,77)

In conclusion, although certain studies have highlighted the advantages of using lipomodelling for correcting soft tissue deformities in children suffering from craniofacial microsomia, it is important to note that the available literature on this topic remains scarce (57).

Parry–Romberg Syndrome

"Parry–Romberg syndrome is a rare congenital disorder characterized by the progressive atrophy of soft tissue on one side of the face followed by spontaneous remission and stabilization of soft tissue volume" (57).

Hemifacial atrophy frequently leads to significant facial asymmetry and an unfavorable aesthetic appearance. While microsurgical free flap reconstruction has traditionally been the standard approach for treating soft tissue atrophy in individuals with Parry-Romberg syndrome, recent studies have shown that autologous fat grafting can yield comparable results. Furthermore, fat grafting is a less invasive procedure and is associated with reduced donor site morbidity and shorter operative time compared to free flap reconstruction. It is typically recommended to restore volume in the affected area after a stabilization of the soft tissue atrophy. This allows for more accurate surgical planning to correct the volume loss and helps minimize the need for repeated grafting procedures. Due to the time it takes for the soft tissue atrophy in Parry-Romberg syndrome to stabilize, individuals with this condition often undergo fat grafting as adults. This is because the condition can take several years to reach a point of stability where surgical interventions, such as fat grafting, can be more effectively performed. According to a systematic review of 31 articles, lipofilling has shown to produce positive cosmetic outcomes while having fewer adverse events, lower expenses, reduced donor site morbidity, and shorter operation time compared to reconstructive techniques using free tissue transfer. Overall, lipofilling has emerged as a dependable and effective approach for restoring volume in individuals diagnosed with Parry-Romberg syndrome. (57)

Cleft Lip

Even after successful primary correction of cleft lip, patients often continue to exhibit deficiencies in nasolabial tissue. These deficiencies can manifest as indistinct vermillion border and philtral columns, as well as a flattened upper lip. Traditionally, secondary revision techniques such as V-Y advancement flap or z-plasty have been employed to address the mentioned deficiencies in nasolabial tissue after cleft lip treatment. However, these surgical procedures often result in additional scarring on the face and rely on adjacent regions that already have insufficient soft 55issuee volume. Following cleft lip revision, autologous fat transplantation has been utilized as a method to restore nasolabial volume while circumventing the limitations associated with other treatments. This technique involves injecting volumes ranging from 1 to 3 mL for a single area or from 7 to 10 mL for multiple areas. The most commonly targeted regions to address tissue defects in cleft lip revision are the alar base, upper lip vermillion, and the philtral column bordering the repaired lip.

Numerous studies have demonstrated the safety and long-term effectiveness of lipofilling in addressing residual defects after cleft lip repair. This technique has been shown to improve contour, fullness, and overall cosmesis of the upper lip, resulting in enhanced aesthetic outcomes (57). Although the results are promising, the data on lipofilling after cleft lip reconstruction is still scarce. (57)

Functional Velopharyngeal Insufficiency in Cleft Palate

In individuals with cleft palates, lipofilling can be employed as a primary treatment option to assist with velopharyngeal insufficiency (57). "Velopharyngeal insufficiency is characterized by hypernasality and an audible nasal air emission during phonation due to inadequate velum closure of the posterior pharyngeal space" (57). Velopharyngeal insufficiency can occur both before and after cleft palate reconstruction. The extent of speech impairment is typically influenced by the size of the velopharyngeal gap. While there is no universally agreed-upon optimal method for treating velopharyngeal insufficiency, fat grafting has gained popularity as a viable option. This technique involves using autologous fat to augment the posterior wall of the pharynx, aiming to reduce the size of the velopharyngeal gap and improve velopharyngeal function. (57)

Studies have shown positive speech outcomes when fat is injected into various regions within the velopharyngeal space. These regions include the posterior and lateral walls of the pharynx, as well as the soft palate (57,78).

Several case studies, furthermore, describe that autologous fat augmentation of the posterior pharyngeal wall improves speech outcomes. Lipofilling, when combined with surgical procedures like z-plasty and sphincter-pharyngoplasty, has been shown to improve several aspects of velopharyngeal function. These include reducing air escape, enhancing the quality of speech, and improving velar mobility. However, there are also some risks with using fat transplantation to treat velopharyngeal insufficiency. Injecting fat into the posterior or lateral pharyngeal wall carries risks, including the possibility of fat embolization. In rare cases, this can lead to the unintended injection of fat into the internal carotid arteries, potentially resulting in a stroke or even patient death. For that reason, Shih and colleagues advise against pharyngeal wall injections. Graft hypertrophy, which can cause airway obstruction and serious obstructive sleep apnea, is another major risk. (57)

While this particular adverse event is usually uncommon, Phua et al. indicate that individuals with hypotonia-related syndromes might have a higher vulnerability to this rare but severe complication (57,79).

Nevertheless, despite the potential complications mentioned earlier, lipofilling represents a minimally invasive procedure that can be utilized to address velopharyngeal insufficiency in certain patients presenting with small localized closure gaps. Transferring fat exclusively to the velum has fewer health risks and lower chances of complications compared to traditional surgical approaches such as pharyngoplasty, pharyngeal flaps, synthetic implants, and palatoplasty. Although conventional surgical treatment options may have a higher likelihood of complications, they generally yield better functional results and are typically recommended for severe cases of velopharyngeal insufficiency. In conclusion, lipofilling is considered a safe, dependable, and low-risk alternative for individuals with mild cases of velopharyngeal insufficiency. (57)

Concerns and Complications

Although lipofilling can lead to adverse events in both adults and children, including unpredictable fat resorption and the risk of fat embolism, performing fat grafting in pediatric patients presents unique challenges. An example of this is that children and adolescents in the stage of puberty often experience ongoing weight gain and growth, which can impact the integration and proliferation of the graft. As a result, accurately predicting the volume correction becomes more challenging in these cases. Unfortunately, no research has been conducted to determine and measure the true effect of puberty on autologous fat transplants so far. Furthermore, pediatric patients with congenital disorders like Parry–Romberg syndrome can have a higher rate of resorption than the general population. Compared to adults, children's fat stores are also smaller, potentially limiting the number of available donor sites. (57)

Aesthetic Correction of the Muscle Atrophy Secondary to Ulnar Nerve Lesion

Injuries to the ulnar nerve are highly prevalent and result in both sensory and motor abnormalities within the hand. The ulnar nerve can suffer damage or compression, either in the region of the elbow or at the forearm level. Notably in the area between

the fingers, one can observe the weakening and shrinkage of the hand's internal muscles, leading to noticeable changes in appearance. The medical literature mentions only a limited number of procedures for cosmetically correcting muscular atrophies. These procedures include the use of silicone implants, dermal grafts, or other synthetic materials. However, it is important to note that these procedures are frequently associated with complications. In their study, Ribak and colleagues discuss the utilization of an adipose tissue block to address the aesthetic concerns resulting from muscle atrophy in the first interdigital space. They applied this approach to fifteen patients, eleven of whom had ulnar nerve injury and four with ulnar nerve compression at the elbow. (2)

Procedure

In case of late ulnar injuries, nerve grafts were used to treat those at first, and in instances where the ulnar nerve is compressed in the cubital tunnel, neurolysis was used. Fat grafts could be collected from the proximal forearm or the elbow’s medial side during the same operation, using the same incision. The amount of adipose tissue needed was approximated to fill the first commissure adequately. Afterward, the fatty tissue transplant was carefully removed, and a solution of physiological saline was employed to cleanse the graft. Then, the transplant was inserted into the weakened adductor muscle through a minor incision on the back, specifically in the middle area of the initial junction. Potential complications included edema, undercorrection, pain, scar hardening, infection, and a restricted flexibility and mobility. In the Ribaks et al.’s case, only edema was observed. Following the surgery, the functional and aesthetic outcomes of the grafted hand were satisfactory for fourteen out of fifteen patients. However, one patient experienced a higher level of graft resorption and did not express the same level of satisfaction as the others. (2)

Venous Ulcers

Chronic wounds pose a significant public health challenge in the "western world," impacting approximately one to two percent of the population. Among all chronic wounds, venous ulcers constitute 70% of the cases. Individuals with venous ulcers experience insufficient wound healing, which is accompanied by the development

of hyperkeratosis, lipodermatosclerosis, and edema. Chronic inflammation, fibrosis, cell senescence, and decreased blood flow are all consequences of their elevated venous pressure. All of these factors obstruct the appropriate healing mechanisms and play a role in the development of persistent venous ulcers. (28)

Although surgical intervention is frequently employed to treat chronic venous ulcers, many individuals may not meet the criteria for this approach and instead require less invasive treatment options. Since cytokines, surface proteins, and differentiation abilities, expressed in ADSCs, can induce wound tissue renewal and regeneration, autologous fat grafting can be an effective, less invasive treatment alternative for chronic vascular wounds. In fact, lipofilling has been used successfully as an adjunct treatment for persisting vascular wounds, including venous ulcers, in recent years. The success of fat as a treatment for various conditions can be attributed to its numerous metabolic and regenerative properties. These properties include its ability to promote neovascularization and regeneration. Additionally, the 3D projection created by fat transplantation contributes to enhancing the contour of affected extremities, further contributing to its positive outcomes. (28)

According to Konstantinow et al., patients with multiple coexisting ulcers who received treatment with stromal vascular fraction (SVF), obtained through liposuction from abdominal adipose tissue and directly applied to the venous ulcers, exhibited complete epithelization of their ulcers within a period of 71 to 174 days following the surgical procedure (28,80). Lipofilling, when used in individuals who have received skin grafts as a treatment for chronic ulcers, can enhance the success of graft integration and reduce the risk of additional wound breakdown (28). In a case report conducted by Bartisch et al., a patient with a chronic lower extremity ulcer who underwent a skin graft demonstrated a notable and clinically significant enhancement in the subcutaneous volume over the grafted area (28,81). In conclusion, autologous fat transplantation to the site of an ulcer has been linked to better patient outcomes, and it is likely to be proven more beneficial as more research is conducted (28).

Pedal Fat Pad Atrophy

Forefoot fat pad atrophy is a common condition, affecting approximately 30% of patients over the age of 60 years. The condition is potentially caused by factors such

as obesity, unusual foot mechanics, collagen vascular disease, or the use of steroids. However, it is primarily associated with the aging process. The presence of bony protrusions in the foot, often accompanied by painful skin lesions, can be attributed to the displacement or degeneration of the fat pad in the area. Fat pad atrophy can cause severe pain or a compensatory gait, which can lead to ulceration or callus formation. While there have been different techniques proposed to enhance atrophied fat pads, many of these methods have not shown long-term improvements in tissue thickness. (82)
The authors Ruane et al. describe performing autologous fat grafting on seventeen patients, suffering from fat pad atrophy. Patients reported experiencing postoperative bruising at the donor site and in their feet, along with soreness and discomfort. However, no cases of infections, hematomas, seromas, or oil cysts were reported, and there were no significant adverse effects or unexpected events documented during the procedure. Although no visible changes in the foot's appearance were observed at the six-month postoperative mark, significant improvements were noted in terms of pain reduction, enhanced ability to engage in work and leisure activities, improved performance of daily tasks, and increased participation in sports. In general, additional research is necessary to determine whether the increased volume of fat pads following lipofilling is sustained over a longer period and to explore whether qualitative changes in the fat pads are also involved. However, it has been observed that lipofilling leads to a significant augmentation of the metatarsal fat pad volume. This increase is associated with improved functionality, reduced pain, and lower forces and pressures exerted on the foot. (82)

Tenolysis

Tendon adhesion is a common complication following tendon damage or surgical repair. Patients with an adherence of tendons frequently have reduced function, which affects their work and everyday lives. If regular physiotherapy fails to mobilize these adhesions, the surgeon should consider tenolysis. However, despite undergoing a tenolysis procedure, a notable number of individuals may experience a relapse, with some returning to their preoperative condition. To mitigate the occurrence of such complications, various strategies have been developed. These

include the implementation of steroid injections, the use of physical barriers, and the application of autologous fat transplantations, such as omentum flaps. In standard tenolytic procedures, approximately 20 to 25% of patients do not experience any improvement and, in some cases, their condition may even worsen. However, the majority of the remaining patients show varying degrees of improvement in their condition. (83)

Damgaard et al. published a case report, in which they describe using autologous fat transplantation to treat a 54-year-old female patient with considerable scar fibrosis and conglomerated “tibialis anterior” and “extensor hallucis longus” tendons, after suffering from a crushing injury to the back side of her left foot. They describe performing tenolysis by using the Coleman lipofilling technique. Although the procedure effectively alleviated the contractions and restored normal, unimpaired walking, the woman continued to experience a sensation of tightness around the scar. As a result, fourteen months after the initial fat injection, the patient underwent a second treatment that included scar release, tenolysis, and fat grafting. When the woman was examined another fourteen months later, the scar was found to be soft and pliable with no indications of adhesion. Additionally, the patient reported being able to engage in everyday activities and long walks without experiencing any pain or discomfort in the foot. (83)

In conclusion, Damgaards and colleagues’ case suggests that adding fat transplantation to the tenolytic procedure can reduce the incidence of readhesions, with little morbidity, simple post-operative care, and no need for foreign-body implants (83).

4 Discussion

Summary of Main Results

In this systematic literature review, 1,218 papers were screened from which 28 were chosen that contain qualitative information about the various applications of autologous fat transplantation in plastic surgery. While the chosen articles include three previous reviews on fat grafting, none of them were conducted in a systematic manner. Furthermore, because they did not just focus on the applications, but also on other aspects, the mentioned applications were mostly only briefly described.

A variety of different applications for autologous fat grafting in plastic surgery could be identified through the systematic search, which were not mentioned in the existing overviews of fat grafting applications. However, some of the applications are based on only a few procedures, and more research and controlled studies are needed to establish them in the field of plastic surgery.

Potential Bias

Potential bias in the review process was minimized as much as possible by employing a methodical search strategy and deferring the manual selection of the papers, which was unavoidable, to the final step. Although the search strategy was designed to return as many results as possible, some relevant articles may have been overlooked due to not identifying them through their title, being published in a language other than "English," not appearing with the used search terms, or being registered in a different database. The search terms were chosen with the goal of bringing up as many relevant papers as possible. While MeSh Terms were being considered, trial runs revealed that by using them, many relevant papers were not displayed.

Although there are systematic literature reviews on a specific application (for example, composite breast augmentation) or a specific aspect of the procedure (for example, complications), to the author's knowledge, there are currently no systematic literature reviews on fat grafting applications.

Safety and Complications

Although fat grafting produced excellent results in the majority of cases, some concerns must be addressed.
The survival of the collected fat cells is crucial, and every stage of the fat grafting procedure - including collection, preparation, and transplantation - holds significance. The greater the minimization of fat processing and the swiftness of reinjection, the greater the chances of the fat graft's viability. (13)

Safety and complications must be considered in all procedures, but most current research shows that lipofilling is a relatively safe procedure with low complication

rates when performed properly. While fatal complications are possible, they are extremely rare, and protocols to prevent them exist for more dangerous applications, such as gluteal augmentation. Rare occurrences of adverse events at the donor site are typically associated with the liposuction procedure. Several potential side effects can arise from liposuction at the donor site, including swelling, bruising, hematoma formation, paresthesia pain, infection, hypertrophic scars, contour irregularities, and damage to underlying tissues. (13)

The primary risks linked to fat grafting for facial rejuvenation are often associated with the placement of fat cells in specific areas prone to complications, such as the nasolabial folds and the glabella. Fat grafts have been known to cause thrombosis in the cerebral or ophthalmic artery, increasing local pressure and allowing fat to backflow into the internal carotid and ophthalmic arteries. To mitigate these risks and reduce the chances of complications, several precautions are recommended during fat grafting procedures. Firstly, using a blunt-tipped cannula instead of a sharp one helps minimize trauma and decreases the likelihood of damaging blood vessels. Secondly, injecting the fat graft gently with low pressure reduces the risk of fat embolism and related severe consequences. It is also essential to ensure that no blood flows back into the syringe before injection, as this confirms proper placement and minimizes the risk of injecting into a blood vessel. When using lipofilling to correct the nasal bridge, surgeons should exercise caution to avoid increasing local pressure, as it could potentially push a fat packet in an upstream direction toward the ophthalmic artery. If a fat packet were to block the central retinal artery, it could result in vision loss or even blindness. (13)

The oncological safety of autologous fat transplantation for breast reconstruction must be kept in mind, and even though research suggests the procedure's safety, experts should continue to investigate its long-term safety.
The injection of large volumes of fat cells into a single region or areas with insufficient blood supply during breast lipofilling can lead to various complications. These include the formation of fat necrosis, oil cysts, and calcifications at the recipient site. These changes can hinder the acceptance of the fat graft and result in the development of palpable lumps caused by fat necrosis. Furthermore, distinguishing these palpable lumps resulting from fat necrosis in breast lipofilling

from local cancer recurrence can be challenging in clinical practice. As a result, additional imaging studies and needle biopsies may be necessary in up to 15% of cases. (13,84)
Calcification may be seen on mammograms after lipofilling in up to 4.9% of patients (84). Finally, because the retention rates of the applied grafts vary, predicting how much volume truly remains after the transfer is difficult. As a result, multiple sessions are frequently required to achieve the desired result.

Future Applications

The regenerative potential of ADSCs, as well as the relative ease with which they can be obtained, has prompted plenty of studies into their reconstructive potential. ADSCs have shown potential for differentiation and paracrine activity not only in the restoration of skin nerves but also in tissue engineering applications. While their effectiveness in mesenchymal tissues such as bone, cartilage, and adipose tissue is well-established, the complete therapeutic potential of their differentiation abilities is still a topic of debate. While certain scientists maintain that ADSCs manifest their therapeutic capabilities by transforming into specific cell types within the intended tissue, opposing viewpoints suggest that even though the newly generated target cells display phenotypic changes, they do not possess full functionality. There is still a need for thorough investigation and establishment of various aspects related to the technique, including the seeding process, vascularization, the use of a biocompatible scaffold, and determining whether ADSCs should be utilized alone or combined with other types of as well as whether they should be differentiated or undifferentiated. To address the main challenge of vascularization after in vivo implantation, several methods have been proposed to establish a functional and organized vascular network. These include applying mechanical stimulation, utilizing 3D cell printing techniques, and employing biomaterials that possess beneficial angiogenic properties. Contrarily, some studies have demonstrated that ADSCs can facilitate tissue regeneration through the secretion of various cytokines and growth factors, especially in hypoxic environments. This has led some researchers to shift their focus towards exploring the therapeutic potential of ADSCs' paracrine activity. (12)

Current State and Outlook

Fat grafting is ranked third on Rohrich et al.'s list of the most significant advancements in cosmetic surgery (13,85). In a recent systematic review and meta-analysis on this subject, Agha et al. show the effectiveness of this method when it comes to six outcome categories, including clinical, oncological, aesthetic, functional, patient-reported, procedural, and radiological (86). Their goal is to create a core outcome set (COS) for breast augmentation with autologous fat, which would improve how autologous fat grafting research is conducted and reported, reduce outcome and reporting bias, standardize endpoints, increase transparency, increase reproducibility, and increase external validity, while also helping with evidence synthesis and future clinical decision-making (13,87).

As with the aesthetic aspect of plastic surgery, most people would probably associate fat grafting with the most prominent applications seen in the media, like body contouring through breast or buttock enlargement while concurrently generating a smaller waist, skinnier thighs, and so on. Although, as seen in this review, the applications are significantly more varied and are not confined to simple volume addition.

This can be problematic if physicians or other surgeons who do not work in the field of plastic surgery are faced with an issue that can be improved by fat grafting but do not consult a plastic surgeon about it because they only associate fat grafting with cosmetic surgery.

This review may serve to highlight lesser-known fat grafting applications and demonstrate that they are significantly more diverse than those commonly shown in the media.

Finally, this systematic literature review can be used as a guide for surgeons considering fat grafting for a specific surgery and want to know if it has been done before. Furthermore, it can be used as a starting point for future application research, either to transfer the described application to a similar field of use or to further investigate a specific application.

The applications demonstrate that autologous fat transfer has multiple uses, including enhancing soft tissue and restructuring it through various techniques such

as expanding its volume externally, aligning its fibers, and expanding them like a mesh. The fat acts as an adhesive similar to epoxy, penetrating and cementing the altered supportive fibrovascular structure, allowing for the effective reshaping of tissue. In essence, this process empowers practitioners to become "true plastic surgeons," as described by Dr. Khouri. (26)

5 Conclusion

This systematic literature review examined the literature on the applications of autologous fat grafting in plastic surgery, a procedure with a wide range of potential applications. The review uncovered several applications that had not previously been mentioned in fat grafting overviews.

While fat grafting is commonly thought of as a way to add volume to fill deficits or contour the body, future research may look into more ways to use autologous fat as a therapeutic option, since the regenerative potential of the ADSC it contains enable it to be used for a variety of purposes in reconstruction.

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