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CLINICAL AND SURGICAL FOUNDATIONS OF REGENERATIVE MEDICINE WITH AUTOLOGOUS FAT

FUNDAMENTOS CLÍNICOS E CIRÚRGICOS DA MEDICINA REGENERATIVA COM GORDURA AUTÓLOGA

FUNDAMENTOS CLÍNICOS Y QUIRÚRGICOS DE LA MEDICINA REGENERATIVA CON GRASA AUTÓLOGA

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ABSTRACT

Autologous fat grafting is both a reconstructive operation and a biologically active tissue transfer. Its clinical value depends on the survival of transplanted adipose parcels, the response of the recipient bed, and the behavior of stromal, vascular, extracellular-matrix, and immune components that accompany mature adipocytes. This narrative review examines the biological basis, surgical technique, indications, safety, evidence quality, and regulatory boundaries of regenerative medicine using autologous fat. PubMed/MEDLINE, major professional statements, and regulatory guidance were reviewed through September 2026, prioritizing mechanistic studies, consensus documents, randomized trials, systematic reviews, meta-analyses, and large clinical series. Conventional fat grafting is distinguished from microfat, nanofat, microfragmented adipose tissue, stromal vascular fraction, cell-assisted lipotransfer, and culture-expanded adipose-derived stromal cell products. Graft survival is governed by diffusion before revascularization, recipient-site vascularity, parcel size, atraumatic harvest and processing, and the avoidance of excessive local pressure. No single donor site or processing system is universally superior. Clinically, the strongest and most established uses are restoration of soft-tissue volume and contour in breast and craniofacial reconstruction, with additional but heterogeneous evidence for radiated tissue, scars, burns, chronic wounds, and selected functional disorders. Musculoskeletal injections and fresh adipose treatment of fistulas remain emerging and should not be presented as established stem-cell therapies. Complications range from undercorrection, oil cysts, fat necrosis, infection, and contour irregularity to rare catastrophic vascular events, including blindness, stroke, and pulmonary fat embolism. Safe practice requires precise anatomical planning, low-pressure delivery of small aliquots during cannula withdrawal, strict subcutaneous placement in gluteal grafting with real-time ultrasound, staged treatment when

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recipient capacity is limited, and coordinated oncologic surveillance in breast reconstruction. Manipulated cellular products may trigger substantially different regulatory requirements from conventional structural fat transfer. Autologous fat is therefore best understood as a living surgical graft with regenerative potential—not as a uniform drug or an unqualified source of stem cells.

Keywords: Adipose Tissue. Autologous Transplantation. Fat Grafting. Regenerative Medicine. Stromal Vascular Fraction.

RESUMO

O enxerto de gordura autóloga é, simultaneamente, um procedimento reconstrutivo e uma transferência de tecido biologicamente ativo. Seu valor clínico depende da sobrevivência das porções de tecido adiposo transplantadas, da resposta do leito receptor e do comportamento dos componentes estromais, vasculares, da matriz extracelular e imunológicos que acompanham os adipócitos maduros. Esta revisão narrativa examina as bases biológicas, a técnica cirúrgica, as indicações, a segurança, a qualidade das evidências e os aspectos regulatórios da medicina regenerativa com gordura autóloga. As bases de dados PubMed/MEDLINE, os principais posicionamentos profissionais e as diretrizes regulatórias foram analisados até setembro de 2026, priorizando-se estudos mecanísticos, documentos de consenso, ensaios randomizados, revisões sistemáticas, metanálises e grandes séries clínicas. O enxerto de gordura convencional distingue-se do microfat, nanofat, tecido adiposo microfragmentado, fração vascular estromal, lipotransferência assistida por células e produtos de células estromais derivadas do tecido adiposo expandidas em cultura. A sobrevivência do enxerto é determinada pela difusão antes da revascularização, pela vascularização do sítio receptor, pelo tamanho das porções de gordura, pela coleta e processamento atraumáticos e pela prevenção de pressão local excessiva. Não existe um sítio doador ou sistema de processamento universalmente superior. Clinicamente, as aplicações mais robustas e estabelecidas são a restauração de volume e contorno de tecidos moles na reconstrução mamária e craniofacial, havendo evidências adicionais, porém heterogêneas, para tecidos irradiados, cicatrizes, queimaduras, feridas crônicas e distúrbios funcionais selecionados. Injeções musculoesqueléticas e o tratamento de fístulas com tecido adiposo fresco permanecem como abordagens emergentes e não devem ser apresentados como terapias estabelecidas com células-tronco. As complicações variam desde subcorreção, cistos oleosos, necrose gordurosa, infecção e irregularidades de contorno até eventos vasculares catastróficos raros, incluindo cegueira, acidente vascular cerebral e embolia gordurosa pulmonar. A prática segura exige planejamento anatômico preciso, aplicação de pequenas alíquotas sob baixa pressão durante a retirada da cânula, posicionamento estritamente subcutâneo em enxertos glúteos com auxílio de ultrassom em tempo real, tratamento em etapas quando a capacidade do leito receptor é limitada e vigilância oncológica coordenada na reconstrução mamária. Produtos celulares manipulados podem acarretar exigências regulatórias substancialmente diferentes daquelas aplicáveis à transferência estrutural de gordura convencional. Portanto, a gordura autóloga é mais bem compreendida como um enxerto cirúrgico vivo com potencial regenerativo — e não como um fármaco uniforme ou uma fonte genérica de células-tronco.

Palavras-chave: Tecido Adiposo. Transplante Autólogo. Enxerto de Gordura. Medicina Regenerativa. Fração Vascular Estromal.

RESUMEN
El injerto de grasa autóloga constituye tanto una intervención reconstructiva como una transferencia de tejido biológicamente activo. Su valor clínico depende de la supervivencia de los fragmentos de tejido adiposo trasplantados, de la respuesta del lecho receptor y del comportamiento de los componentes estromales, vasculares, de la matriz extracelular e inmunitarios que acompañan a los adipocitos maduros. Esta revisión narrativa examina las bases biológicas, la técnica quirúrgica, las indicaciones, la seguridad, la calidad de la evidencia y los marcos regulatorios de la medicina regenerativa mediante el uso de grasa autóloga. Se revisaron PubMed/MEDLINE, las principales declaraciones de sociedades profesionales y las normativas regulatorias hasta septiembre de 2026, priorizando estudios mecanísticos, documentos de consenso, ensayos aleatorizados, revisiones sistemáticas, metaanálisis y grandes series clínicas. El injerto de grasa convencional se distingue de otras modalidades como el microfat, el nanofat, el tejido adiposo microfragmentado, la fracción vascular estromal, la lipotransferencia asistida por células y los productos de células estromales derivadas del tejido adiposo expandidas en cultivo. La supervivencia del injerto está condicionada por la difusión previa a la revascularización, la vascularidad del sitio receptor, el tamaño de los fragmentos, la obtención y el procesamiento atraumáticos, así como por evitar una presión local excesiva. No existe un sitio donante ni un sistema de procesamiento que sea universalmente superior. Desde el punto de vista clínico, las aplicaciones más sólidas y consolidadas son la restauración del volumen y el contorno de los tejidos blandos en la reconstrucción mamaria y craneofacial; existe evidencia adicional, aunque heterogénea, para su uso en tejidos irradiados, cicatrices, quemaduras, heridas crónicas y determinados trastornos funcionales. Las inyecciones musculoesqueléticas y el tratamiento de fístulas con tejido adiposo fresco siguen siendo enfoques emergentes y no deben presentarse como terapias establecidas con células madre. Las complicaciones abarcan desde la corrección insuficiente, los quistes oleosos, la necrosis grasa, la infección y las irregularidades en el contorno, hasta eventos vasculares catastróficos poco frecuentes, como ceguera, accidente cerebrovascular y embolia grasa pulmonar. Una práctica segura requiere una planificación anatómica precisa, la infiltración de pequeñas alícuotas a baja presión durante la retirada de la cánula, una colocación estrictamente subcutánea en los injertos glúteos (con guía ecográfica en tiempo real), tratamientos escalonados cuando la capacidad del lecho receptor es limitada y una vigilancia oncológica coordinada en la reconstrucción mamaria. Los productos celulares manipulados pueden conllevar requisitos regulatorios sustancialmente diferentes a los de la transferencia de grasa estructural convencional. Por consiguiente, la grasa autóloga debe entenderse como un injerto quirúrgico vivo con potencial regenerativo, y no como un fármaco uniforme ni como una fuente genérica de células madre.

Palabras clave: Tejido Adiposo. Trasplante Autólogo. Injerto de Grasa. Medicina Regenerativa. Fracción Vascular Estromal.

1 INTRODUCTION

Autologous fat grafting transfers living adipose tissue from a donor site to a recipient site in the same patient. Initially developed as a method of restoring volume, it now occupies a broader position at the intersection of reconstructive surgery, aesthetic surgery, wound repair, and regenerative medicine. The graft provides immediate structural replacement, but its longer-term behavior reflects cell survival, ischemia, inflammation, revascularization, extracellular-matrix remodeling, and interaction with the recipient tissue.[1-5]

The biological interest in adipose tissue increased after the identification of multipotent stromal populations within lipoaspirate. Adipose tissue contains mature adipocytes, vascular and lymphatic structures, pericytes, fibroblasts, immune cells, endothelial cells, extracellular matrix, and heterogeneous progenitor populations. These components may support angiogenesis, modulate inflammation, influence fibrosis, and facilitate repair through paracrine signaling. Their presence, however, does not mean that every fat-grafting procedure is a stem-cell therapy or that clinical benefit results from differentiation into replacement tissue.[2,4]

Terminology has expanded faster than standardization. Macrofat, microfat, nanofat, microfragmented adipose tissue, stromal vascular fraction, adipose-derived stromal cells, and cell-assisted lipotransfer differ in composition, intended function, degree of manipulation, delivery technique, evidence base, and regulatory status. Treating these products as interchangeable obscures both surgical principles and patient risk.[4,5,7]

Clinical results are technique-dependent. A graft survives only if transferred parcels are sufficiently small and sufficiently close to a vascularized recipient interface to receive oxygen and nutrients before neovascularization. Traumatic harvest, prolonged exposure to air, blood and free oil contamination, high-pressure injection, pooling, excessive recipient tension, and poor vascularity all reduce predictability. Volume retention therefore cannot be separated from surgical design.[3,5,6]

The enthusiasm surrounding adipose-based regeneration must be balanced against variable evidence and distinctive hazards. Most published studies are small, use heterogeneous processing methods, lack blinded assessment, or report short follow-up. At the same time, intravascular facial injection can cause blindness or stroke, and deep gluteal injection can produce fatal pulmonary fat embolism. Clinical governance, informed consent, and anatomical discipline are as important as cellular biology.[19-22]

2 OBJECTIVES

The primary objective was to review the clinical and surgical foundations of regenerative medicine using autologous fat. Secondary objectives were to define adipose-based products, explain graft survival and proposed regenerative mechanisms, synthesize evidence for major indications, describe patient selection and operative technique, identify preventable complications, examine oncologic and imaging considerations, and distinguish conventional fat transfer from regulated cellular products.

3 METHODS

A structured narrative review was performed using PubMed/MEDLINE and official publications from professional and regulatory organizations. The search was updated through September 2026. Search concepts included autologous fat grafting, lipofilling, adipose tissue, graft survival, stromal vascular fraction, adipose-derived stromal cells, cell-assisted lipotransfer, nanofat, microfragmented adipose tissue, breast reconstruction, facial reconstruction, radiation injury, scars, wounds, burns, osteoarthritis, perianal fistula, fat embolism, blindness, minimal manipulation, and homologous use.

Priority was given to mechanistic human studies, consensus definitions, evidence-based statements, randomized clinical trials, systematic reviews, meta-analyses, and large clinical series. Foundational experimental studies were retained when they explained clinically relevant graft behavior. Reports were included when they informed product definition, preparation, efficacy, retention, complications, oncologic safety, functional outcomes, or regulation. Isolated promotional claims and uncontrolled commercial descriptions were excluded from the central synthesis.

Evidence was organized by study population, intervention, comparator, outcomes, and principal limitations. Particular attention was paid to heterogeneity in harvest and processing, lack of standardized volume measurement, variable follow-up, confounding by indication, concurrent procedures, absence of placebo control, inconsistent definitions of complications, and the distinction between structural tissue transfer and isolated or culture-expanded cellular products. No original meta-analysis was performed.

Recommendations in this review are interpretive and are intended to support specialist clinical judgment. Device authorization, tissue regulation, scope of practice, and permitted processing vary by jurisdiction and must be checked locally. The review does not replace

patient-specific multidisciplinary assessment, operative training, or institutional safety protocols.[27-29]

4 RESULTS AND DISCUSSION

Thirty principal publications were selected to represent biological foundations, technical variables, clinical outcomes, safety, and regulation. Table 1 summarizes the evidence base and the interpretation used in this review; it should not be read as implying equal methodological quality across indications. [1-30]

Table 1

Principal publications informing the biological, clinical, surgical, safety, and regulatory synthesis.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Coleman, 2006[1]	Technical review of structural fat grafting.	Harvest, parcel placement, contour restoration, and graft behavior.	Atraumatic handling and placement of small parcels in multiple tissue planes form the operative basis of predictable structural grafting.
Zuk et al., 2001[2]	Laboratory characterization of cells isolated from human lipoaspirate.	Adherence, expansion, and multilineage differentiation in vitro.	Adipose tissue contains stromal populations with multilineage potential, creating a biological rationale for investigation but not proving clinical efficacy.
Eto et al., 2012[3]	Experimental analysis of nonvascularized fat graft fate.	Early adipocyte death, viable peripheral tissue, and regeneration.	Grafts develop survival, regenerative, and necrotic zones; recipient diffusion distance and revascularization are central determinants of retention.
Bourin et al., 2013[4]	Joint IFATS/ISCT consensus statement.	Definitions and phenotypic criteria for stromal vascular fraction and culture-expanded adipose stromal cells.	Fresh heterogeneous SVF and culture-expanded stromal cells are distinct products and require precise terminology.
Strong et al., 2015[5]	Comprehensive review of harvest, processing, and injection methods.	Effects of cannula, suction, preparation, and delivery variables.	Many techniques are clinically workable; no single protocol is universally superior, and reporting should be standardized.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Gir et al., 2012[6]	Evidence-based review of harvest, processing, reinjection, and storage.	Cell viability, contamination, and retention across techniques.	Low-trauma transfer and removal of contaminants are rational, whereas prolonged storage and excessive manipulation add uncertainty.
Tonnard et al., 2013[7]	Basic and clinical description of mechanically emulsified nanofat.	Histology, cell content, and skin-quality applications.	Nanofat has little volumizing capacity but retains stromal elements; proposed regenerative uses require indication-specific evidence.
Kølle et al., 2013[8]	Randomized placebo-controlled trial of ex vivo expanded adipose-derived stromal cell enrichment.	Graft retention after experimental fat transplantation.	Cell enrichment improved retention in a controlled model, but culture expansion changes regulatory status and limits routine translation.
Hanson et al., 2022[9]	Prospective randomized comparison of clinical fat-processing techniques.	Retention and clinical outcomes after alternative processing methods.	Common processing techniques produced broadly comparable results, supporting technique consistency over claims of universal superiority.
Botti et al., 2011[10]	Clinical facial fat-grafting trial comparing washed/filtered with centrifuged fat.	Volume persistence and adverse effects.	Both approaches were usable; processing choice should minimize contaminants and trauma while fitting the target tissue.
Li and Chen, 2021[11]	Systematic review and meta-analysis of cell-assisted versus conventional breast lipotransfer.	Volume retention and complications.	Cell-assisted transfer may improve retention, but heterogeneity, cost, processing, and regulatory concerns prevent routine universal adoption.
Gutowski et al., 2009[12]	American Society of Plastic Surgeons task-force review.	Applications, techniques, complications, and evidence gaps.	Fat grafting is versatile, but outcomes depend on indication and technique; standardized reporting and long-term follow-up are required.
Nava et al., 2019[13]	International expert-panel consensus on breast fat grafting.	Technique, oncologic safety, surveillance, and indications.	Breast lipofilling is accepted for selected reconstructive and aesthetic uses when performed with appropriate imaging and oncologic coordination.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Krastev et al., 2018[14]	Systematic review and meta-analysis after breast-cancer treatment.	Local recurrence and oncologic outcomes.	Observational evidence did not show increased locoregional recurrence, although residual confounding and subgroup uncertainty remain.
Rigotti et al., 2007[15]	Clinical series of fat grafting for radiotherapy-damaged tissue.	Tissue quality, healing, and histologic changes.	Clinical improvement supported investigation of regenerative effects in irradiated beds, but uncontrolled design limits causal inference.
Abu Alqam et al., 2024[16]	Systematic review and meta-analysis of post-traumatic and post-burn scars.	Patient and observer scar scores.	Scar outcomes generally improved, but protocols, scar types, concurrent treatments, and follow-up were highly heterogeneous.
Brown et al., 2020[17]	Multicenter randomized, blinded, internally placebo-controlled scar trial.	Objective and patient-reported scar quality.	Fat and saline-treated sites both improved, illustrating the importance of controls and the uncertainty of a specific regenerative effect.
Abouzaid et al., 2022[18]	Randomized study in acute superficial and deep dermal burns.	Healing, hospitalization, pain, graft requirement, and early scarring.	Results favored an adipose-based protocol, but single-center design and combined interventions restrict generalizability.
Krastev et al., 2018[19]	Systematic review and meta-analysis of facial reconstructive fat transfer.	Patient and surgeon satisfaction, volume restoration, and complications.	Facial reconstruction showed high satisfaction and low reported routine morbidity, with heterogeneous and mostly nonrandomized evidence.
Mofid et al., 2017[20]	International surgeon survey and mortality analysis of gluteal grafting.	Fatal and nonfatal pulmonary fat embolism.	Deep intramuscular injection and unsafe cannula orientation were associated with catastrophic risk; deep placement must be avoided.
Del Vecchio and Kenkel, 2022[21]	Multisociety-informed practice advisory on gluteal fat grafting.	Anatomy, technique, surgeon fatigue, and real-time imaging.	Fat should remain in the subcutaneous plane, and ultrasound improves continuous confirmation of cannula position.
Mortada et al., 2022[22]	Systematic review and meta-analysis of ophthalmic complications after facial fat injection.	Vision loss, ophthalmoplegia, cerebral events, and recovery.	Ophthalmic embolization is rare but often irreversible; prevention is more reliable than rescue.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Finnoff et al., 2021[23]	Sports-medicine position statement on responsible regenerative practice.	Terminology, evidence appraisal, ethics, and patient communication.	Orthobiologic use requires accurate product description, transparent uncertainty, adverse-event monitoring, and avoidance of unsupported claims.
Baria et al., 2024[24]	Randomized trial comparing microfragmented adipose tissue with platelet-rich plasma for knee osteoarthritis.	Pain and Knee injury and Osteoarthritis Outcome Score through 12 months.	Both groups improved without a significant between-group difference; equivalence to an active comparator does not establish superiority to placebo.
Barfod et al., 2025[25]	Blinded randomized placebo-controlled trial with two-year follow-up in knee osteoarthritis.	Patient-reported pain and function.	A single microfragmented adipose injection was not superior to saline, arguing against routine first-line use.
Dige et al., 2019[26]	Prospective pilot study of freshly collected adipose injection for perianal Crohn fistulas.	Fistula healing and adverse events in 21 patients.	Complete healing occurred in a proportion of patients, but small uncontrolled data support investigation rather than established practice.
Malik et al., 2020[27]	Systematic review of autologous fat therapies for acute and chronic wounds.	Healing, closure, pain, and safety.	Signals of benefit were reported, but evidence quality was low and methods were insufficiently standardized.
Lovell-Badge et al., 2021[28]	ISSCR international guideline update.	Standards for research, translation, oversight, and communication.	Stem-cell interventions require rigorous preclinical rationale, independent oversight, transparent consent, and controlled clinical evaluation.
U.S. FDA, 2020[29]	Regulatory guidance on human cells, tissues, and cellular and tissue-based products.	Minimal manipulation and homologous-use criteria.	Processing and intended use can move an adipose product outside the lower-risk tissue pathway; jurisdiction-specific review is essential.
Largo et al., 2014[30]	Systematic review of autologous fat grafting to healthy breast tissue.	Efficacy, imaging changes, complications, and patient satisfaction.	Breast grafting can achieve high satisfaction, but variable retention and fat necrosis require counseling and surveillance.

4.1 CONCEPTUAL FRAMEWORK AND TERMINOLOGY

Conventional autologous fat grafting is a structural tissue-transfer procedure. Lipoaspirate is harvested, prepared to reduce unwanted fluid, blood, and disrupted lipid, then implanted as viable parcels. The intended function is usually cushioning, contour, filling,

gliding, or tissue separation. Its biological activity is intrinsic to the transplanted tissue, but the clinical product remains structurally recognizable adipose tissue.[1,5,6]

Macrofat and microfat are pragmatic surgical terms rather than universally standardized products. Macrofat generally contains larger lobules suitable for deeper volumization, whereas microfat contains smaller clusters that can pass through narrower cannulas for more superficial or precise placement. Their actual composition depends on the harvest aperture, processing device, transfer system, and injection cannula; brand names should not substitute for a reproducible method description.[5,6]

Nanofat is produced by mechanical emulsification and filtration. This process disrupts most mature adipocytes, so nanofat should not be expected to provide durable three-dimensional volume. Its proposed effect is related to stromal, vascular, matrix, and signaling components used for skin-quality and scar applications. Calling nanofat a concentrated stem-cell preparation is inaccurate because cell number, viability, phenotype, and potency vary, and the product is not equivalent to isolated stromal vascular fraction.[4,7]

Stromal vascular fraction is the heterogeneous nonadipocyte cell fraction obtained from adipose tissue. It may include endothelial cells, pericytes, immune cells, fibroblastic cells, and adipose-derived stromal populations. Enzymatic isolation, mechanical isolation, point-of-care processing, and culture expansion generate materially different products. Culture-expanded adipose-derived stromal cells are more homogeneous by consensus criteria but entail manufacturing, quality-control, and regulatory requirements that conventional fat grafting does not.[4,28,29]

Cell-assisted lipotransfer combines fat with an additional stromal or cellular fraction in an attempt to improve retention or tissue response. Although controlled studies and meta-analyses suggest a possible retention advantage, dose, processing, safety surveillance, and legal classification are inconsistent. It should therefore be described by its exact components and not marketed generically as enhanced regenerative fat.[8,11]

Table 2

Practical distinctions among adipose-derived surgical and cellular products.[4,5,7,28,29]

Product	Biological composition	Typical intended role	Clinical and regulatory caution
Conventional fat / macrofat	Intact adipocytes and relatively large lobules with stromal and vascular elements.	Deep volume restoration, contour correction, cushioning.	Parcel size must match recipient vascularity; pooling increases central necrosis.
Microfat	Smaller adipose clusters produced with smaller harvest/transfer systems or size reduction.	Fine contouring, face, hands, superficial defects.	Narrower delivery does not eliminate intravascular risk or guarantee greater survival.
Nanofat	Mechanically emulsified and filtered tissue with few viable mature adipocytes; stromal/matrix components remain.	Skin-quality, dyschromia, fine scars; generally not volumization.	Evidence is heterogeneous; avoid labeling it an isolated stem-cell product.
Microfragmented adipose tissue	Mechanically processed small tissue clusters retaining variable matrix and perivascular niche.	Investigational orthobiologic and selected soft-tissue applications.	Composition is device-dependent; clinical efficacy must be indication-specific.
Stromal vascular fraction	Heterogeneous nonadipocyte nucleated fraction obtained mechanically or enzymatically.	Research and selected regulated clinical protocols.	Isolation method, dose, sterility, and regulatory category must be explicit.
Culture-expanded adipose stromal cells	Cells expanded ex vivo and characterized by consensus criteria.	Clinical trials and regulated advanced-therapy pathways.	Not equivalent to routine same-session grafting; requires manufacturing oversight.
Cell-assisted lipotransfer	Conventional fat supplemented with an additional stromal/cellular fraction.	Proposed improvement in graft retention.	Benefits are not uniform; processing and cell manipulation may alter regulation.

4.2 BIOLOGY OF GRAFT SURVIVAL

A nonvascularized fat graft is abruptly separated from its native circulation. During the initial period, survival depends on diffusion of oxygen and nutrients from the recipient bed. Cells near the graft-host interface have the highest probability of survival; cells farther from that interface experience more severe ischemia. Revascularization must occur before irreversible injury extends through the parcel.[3]

The three-zone model describes an outer survival zone, an intermediate regenerative zone, and a central necrotic zone. Some peripheral adipocytes survive directly. In the intermediate region, mature adipocytes may die while more ischemia-resistant stromal cells persist and participate in repair and adipogenesis. In the center, prolonged ischemia leads to liquefaction, oil cysts, calcification, inflammation, or fibrosis. The model explains why many small deposits have a greater vascular interface than one large bolus of the same total volume.[3]

Recipient-site capacity is finite. A compliant, well-vascularized tissue bed can support more graft than a thin, scarred, tense, infected, or heavily irradiated bed. Overfilling raises interstitial pressure, reduces perfusion, compresses adjacent parcels, and converts potentially viable graft into necrotic material. Staging is therefore a biological strategy, not merely a logistical inconvenience.[1,3,5]

Inflammation has a dual role. Controlled macrophage recruitment and matrix remodeling contribute to clearance and repair, whereas excessive tissue injury, blood contamination, free oil, infection, or large necrotic volumes prolong inflammation and fibrosis. The clinical objective is not to eliminate the early inflammatory response but to limit preventable injury and support orderly revascularization.[3,5]

Long-term volume reflects surviving adipocytes and newly generated tissue, not the immediate injected volume. Early postoperative fullness includes edema, tumescent fluid, and transient overcorrection. Weight change can enlarge or shrink surviving adipocytes, so postoperative body-weight stability is important for interpreting retention and avoiding late hypertrophy.[1,5,30]

4.3 REGENERATIVE MECHANISMS: WHAT IS ESTABLISHED AND WHAT IS INFERRED

Adipose tissue is richly vascularized and contains perivascular and stromal populations that release angiogenic, antiapoptotic, immunomodulatory, and matrix-remodeling signals in experimental systems. Vascular endothelial growth factor, hepatocyte growth factor, insulin-like growth factors, interleukins, extracellular vesicles, and other mediators have been proposed as contributors. These pathways are biologically plausible but vary with tissue injury, donor factors, processing, oxygen tension, and the local immune environment.[2-4]

Paracrine signaling is a more defensible explanation for many clinical observations than direct multilineage replacement. Stromal cells may recruit host endothelial cells, influence macrophage phenotype, support neovascularization, and modulate fibroblast and

myofibroblast activity. Direct differentiation can occur in experimental settings, but the magnitude and durability of lineage replacement in routine human grafting are uncertain.[2-4]

The extracellular matrix provides mechanical support and biochemical cues. Mechanical fragmentation may preserve portions of the perivascular niche even when adipocytes are disrupted, whereas aggressive enzymatic digestion isolates cells from that structural context. Consequently, equal injected volumes of fat, nanofat, microfragmented tissue, and isolated cells cannot be assumed to deliver equal biological doses.[4,7]

Clinical improvement in texture, pliability, pain, or radiation fibrosis may arise from several simultaneous effects: scar release by cannula passage, physical separation of tethered planes, increased padding, new vascular interfaces, wound-healing responses to needling, volume restoration, and adipose-derived signaling. Controlled trials are needed to separate the specific effect of the graft from the effect of the operation itself.[15-17]

For these reasons, the term regenerative potential is preferable to a categorical claim that transplanted fat regenerates an organ. Outcomes should be expressed in measurable clinical domains—volume retention, pliability, perfusion, pain, range of motion, epithelialization, or validated patient-reported function—rather than inferred from the presence of putative stem cells alone.[23,28]

4.4 PATIENT SELECTION AND PREOPERATIVE PLANNING

Appropriate selection begins with a defined clinical objective. Volume restoration, scar release, tissue-quality improvement, functional cushioning, and experimental orthobiologic treatment are different indications and require different products, endpoints, and consent. The clinician should document the defect, the expected number of stages, alternative treatments, likely resorption, donor-site trade-offs, and the possibility that no regenerative effect will occur.[12,23]

History should address weight stability, smoking and nicotine exposure, diabetes, vascular disease, immunosuppression, coagulation disorders, thromboembolic risk, prior liposuction, previous grafting, radiation, infection, malignancy, implanted devices, antithrombotic therapy, and expectations. Examination should assess donor availability, skin quality, recipient vascularity and compliance, scars, anatomic danger zones, and the relationship of the defect to bone, muscle, vessels, ducts, glands, and nerves.[5,12]

Active infection, uncontrolled systemic disease, severe uncorrected coagulopathy, unstable oncologic status, and unrealistic expectations are reasons to postpone or reconsider

treatment. Heavy nicotine exposure and poorly controlled diabetes impair wound healing and may reduce graft reliability. A thin or heavily irradiated recipient bed is not an absolute contraindication, but it often requires smaller sessions, careful release, and realistic counseling.[5,12,15]

Breast grafting after cancer treatment requires review of pathology, oncologic treatment, surveillance imaging, current symptoms, and the reconstructive plan. New masses, unexplained skin changes, or incomplete cancer evaluation should be investigated before grafting. Baseline imaging should follow age-, risk-, and treatment-appropriate protocols rather than an indiscriminate additional test for every patient.[13,14]

Standardized photography and objective measurements should be obtained before surgery. Depending on the indication, these may include three-dimensional surface imaging, magnetic resonance imaging, ultrasound, scar scales, range of motion, pain scores, functional instruments, or wound area. Without a prespecified outcome, postoperative impressions are especially vulnerable to expectation and observer bias.[16,19,23]

4.5 DONOR-SITE SELECTION AND ANESTHESIA

The abdomen, flanks, thighs, and hips are common donor sites. Selection is primarily determined by adequate accessible tissue, patient position, contour priorities, prior scars, and the volume required. Laboratory differences among sites have not established a universally superior donor region for clinical graft survival. A site that permits controlled, symmetric harvest with low morbidity is usually preferable to a biologically fashionable but technically unfavorable site.[5,6]

Local, regional, monitored, or general anesthesia may be used according to volume, recipient site, comorbidity, and procedural complexity. Tumescent infiltration facilitates analgesia and hemostasis, but excessive fluid can dilute the harvest and distort donor and recipient assessment. The formula, infiltrated volume, vasoconstrictor dose, and interval before harvest should be documented.[5,6]

The donor plan is part of the reconstructive plan. Aggressive harvest from a limited zone can create depressions, waviness, seroma, sensory change, or skin compromise. Broad, layered, crossing passes and attention to pre-existing asymmetry reduce contour morbidity. The quantity harvested should include anticipated processing loss without encouraging unnecessarily extensive liposuction.[5,12]

4.6 HARVEST, PROCESSING, AND TRANSFER

Harvest should minimize mechanical injury while maintaining procedural control. A blunt multiport cannula connected to a syringe or a regulated low-pressure system is commonly used. Excessive negative pressure, very small apertures, repeated high-shear passage, or uncontrolled power may increase cell and matrix disruption. The ideal cannula depends on whether the final product is intended for macrostructural filling, fine facial placement, or further mechanical processing.[5,6]

Processing aims to concentrate useful tissue and remove excess infiltration fluid, blood, cellular debris, and free oil. Sedimentation and decantation are simple but may leave more fluid. Centrifugation separates layers efficiently but can impose mechanical forces if excessive. Washing and filtration may improve cleanliness and workflow while introducing device-specific effects. Randomized clinical comparisons have not identified a universally dominant technique, so reproducibility and appropriate handling matter more than proprietary claims.[5,6,9,10]

Free oil should be removed because it reflects ruptured adipocytes and may contribute to inflammation. Blood and residual anesthetic solution add volume that is not graft and may interfere with interpretation. Conversely, excessive drying, repeated transfers, vigorous agitation, prolonged manipulation, or forceful filtration can damage viable tissue. The preparation should match the required particle size while preserving sterility and minimizing time outside the body.[5,6]

Closed or functionally closed transfer systems reduce handling and opportunities for contamination. Syringes and connectors should be clearly labeled, and sharps, cannulas, drugs, and graft material should remain distinguishable throughout the procedure. When additives, enzymatic digestion, cell isolation, or culture expansion are used, sterility assurance, traceability, dose characterization, and regulatory authorization become more demanding.[4,28,29]

4.7 RECIPIENT-SITE PREPARATION AND INJECTION

Recipient preparation begins with a three-dimensional map of the deficit and the structures that must be avoided. Fibrotic adhesions may be released through limited subcision or cannula tunneling, but release itself can injure vessels and create dead space. The surgeon should reassess compliance after release rather than assume that a stiff bed will accept the planned volume.[1,5]

The central injection principle is deposition of small aliquots during cannula withdrawal through multiple tunnels and, when anatomically safe, multiple planes. The cannula should move freely without force. Injection into a stationary cannula, large bolus delivery, high resistance, sudden pain in an awake patient, or an uncertain tip position should prompt immediate cessation and reassessment. Aspiration before injection does not reliably exclude intravascular placement and cannot replace anatomical control.[1,5,22]

Parcel size should decrease as the target becomes thinner or more superficial. Fine facial compartments require small syringes, low pressure, limited aliquots, and precise knowledge of vascular pathways. Deep structural defects can accept larger parcels, but each parcel still requires contact with a vascularized interface. The endpoint is even distribution without blanching, excessive tension, pooling, or forced overcorrection.[1,5,19,22]

Scarred or radiated sites are often treated in stages. The first session may prioritize release, vascular interfaces, and tissue quality rather than full volume correction. Subsequent sessions should be delayed until edema has resolved and retention can be judged. Reinjecting too early risks overcorrection and confuses stable graft with postoperative swelling.[15]

The operative record should include donor sites, infiltration, harvest device and pressure, processing method, net prepared volume, cannula dimensions, recipient planes, injected volume by side or subunit, adjunctive procedures, and intraoperative complications. This level of detail is essential for safety review and meaningful comparison of outcomes.[5,23]

Table 3

Operative workflow for reproducible and risk-controlled autologous fat grafting.[1,5,6,20-22]

Stage	Required action	Principal risk controlled
1. Define the endpoint	Specify structural, functional, scar, wound, or investigational objective; establish baseline measures.	Vague regenerative claims and unmeasurable success.
2. Select patient and sites	Assess oncologic status, vascularity, infection, comorbidity, donor sufficiency, anatomy, and expectations.	Operating in an unstable, infected, poorly evaluated, or unsuitable field.
3. Harvest	Use broad, layered, atraumatic passes and controlled negative pressure; preserve donor contour.	Adipose trauma, bleeding, donor irregularity, and excessive harvest morbidity.
4. Process	Remove excess aqueous fluid, blood, and free oil with a validated, reproducible method.	Contamination, excessive manipulation, nonviable tissue, and inconsistent composition.

Stage	Required action	Principal risk controlled
5. Prepare recipient	Map danger zones, release adhesions selectively, and reassess tissue compliance and capacity.	Unrecognized vessels, dead space, pressure, and overestimation of capacity.
6. Inject	Place small aliquots during withdrawal through multiple controlled tunnels at low pressure.	Pooling, necrosis, intravascular injection, embolization, and contour nodules.
7. Verify and document	Confirm plane and symmetry; use real-time ultrasound for gluteal grafting; record volumes and technique.	Unknown cannula position, poor traceability, and inability to audit complications.
8. Follow up	Monitor early complications and assess stable retention after edema resolves; stage additional treatment if needed.	Premature re-grafting, delayed diagnosis, and unrecognized weight-related change.

4.8 POSTOPERATIVE CARE AND OUTCOME ASSESSMENT

Postoperative care should protect the recipient from excessive pressure, shear, infection, and thermal injury while permitting donor-site management. Compression garments may benefit liposuction areas but should not compress a newly grafted recipient unless specifically intended. Analgesia, mobilization, venous-thromboembolism prevention, and wound care should reflect procedural extent and patient risk.[5,12]

Early swelling, bruising, firmness, and asymmetry are common and should not be interpreted as final retention. Follow-up should distinguish expected inflammation from expanding hematoma, infection, ischemia, neurologic symptoms, respiratory compromise, or compartment-like pressure. Sudden visual change, focal neurologic deficit, hypoxemia, chest pain, or cardiovascular collapse after injection is an emergency.[20-22]

Stable volume is usually assessed after several months, with the interval adapted to site and indication. Serial standardized photographs are the minimum. Three-dimensional imaging, magnetic resonance imaging, ultrasound, or displacement methods can improve volumetric assessment but each has limitations. Reoperation volume is not a pure measure of resorption because it also reflects staged planning, patient preference, and evolving asymmetry.[9,19,30]

Regenerative endpoints require validated measures. Scar studies should use instruments such as the Patient and Observer Scar Assessment Scale, pain and pruritus scores, pliability measures, and range of motion. Wound studies should report time to epithelialization, proportion healed, recurrence, infection, and need for reconstruction.

Orthobiologic studies require blinded patient-reported outcomes, functional testing, rescue treatment, and adequate placebo or active controls.[16-18,23-25,27]

4.9 BREAST RECONSTRUCTION AND AESTHETIC BREAST SURGERY

Breast fat grafting is established as an adjunct for contour defects, implant rippling, upper-pole deficiency, asymmetry, lumpectomy deformity, and refinement after autologous flap reconstruction. It can also contribute to total breast reconstruction in selected programs, but this typically requires multiple high-volume sessions and meticulous recipient-capacity management. Fat transfer does not reproduce the reliability or projection of every flap or implant reconstruction.[12,13,30]

The breast is particularly sensitive to parcel distribution. Large deposits or overcorrection increase fat necrosis, oil cysts, palpable nodules, and calcification. Imaging findings are usually distinguishable by experienced breast radiologists, but any new or suspicious lesion must be assessed according to oncologic principles rather than presumed to be benign graft change.[13,30]

Oncologic safety data are broadly reassuring. Meta-analyses of mainly observational cohorts have not demonstrated a significant increase in locoregional recurrence after fat grafting following breast-cancer treatment. Nevertheless, selection bias, timing, tumor biology, adjuvant therapy, and follow-up differ across studies. The most defensible conclusion is that appropriately selected grafting has not shown an excess recurrence signal, not that every oncologic subgroup has been proven risk-free.[13,14]

Clinical decisions should be coordinated with the breast and oncology teams when cancer history is relevant. The indication, interval from treatment, disease status, surveillance plan, and management of palpable changes should be documented. Informed consent should address variable retention, repeated sessions, fat necrosis, possible biopsy, and the limits of current long-term evidence.[13,14]

Cell enrichment is not required for conventional breast lipofilling. Although meta-analysis suggests that cell-assisted transfer can improve volume retention, the incremental benefit must be weighed against product variability, added operative steps, cost, sterility requirements, and regulatory classification. Routine use should not precede validated protocols and transparent patient counseling.[8,11,29]

4.10 CRANIOFACIAL RECONSTRUCTION AND FACIAL REJUVENATION

Facial fat grafting is used for congenital and acquired asymmetry, trauma, postoperative contour defects, hemifacial atrophy, human immunodeficiency virus-associated lipoatrophy, and age-related volume loss. Its advantages include biocompatibility, the ability to treat broad three-dimensional deficits, and potential improvement in skin quality. Systematic review data report high patient and surgeon satisfaction, but most studies are nonrandomized and use inconsistent retention measures.[19]

The face is also a high-consequence vascular territory. Anastomoses among branches of the facial, ophthalmic, and internal carotid circulations create pathways by which retrograde arterial injection under pressure can reach the retina or brain. The forehead, glabella, nose, temple, and periorbital region demand exceptional anatomical precision. Blindness and cerebral infarction may occur immediately and can be irreversible.[22]

Risk reduction includes slow low-pressure injection, very small aliquots, continuous cannula motion and withdrawal, avoidance of force against resistance, limited syringe size, and use of an appropriate blunt cannula where suitable. No maneuver, including aspiration, makes an unsafe plane safe. The operator must know both the expected vessel course and how prior surgery, trauma, or scarring may displace it.[5,22]

Patients should be informed explicitly that catastrophic visual or neurologic injury is rare but possible and that no consistently effective reversal agent exists for fat embolization. Emergency planning should include immediate recognition, cessation of injection, ophthalmologic and stroke pathways, and rapid transfer; it should not create false confidence that prevention can be replaced by rescue.[22]

4.11 RADIATION INJURY, FIBROSIS, AND SCARS

Clinical reports describe improved softness, mobility, pain, ulcer tendency, and reconstructive readiness after grafting irradiated tissue. Proposed mechanisms include new vascular interfaces, paracrine signaling, matrix remodeling, and replacement of deficient subcutaneous padding. The landmark clinical series demonstrated striking tissue changes, but the absence of a randomized control means that magnitude and mechanism remain uncertain.[15]

Scar treatment often combines cannula release with fat placement, making the procedure both mechanical and biological. Systematic reviews and meta-analyses suggest improvement in validated scar scores, pliability, pain, and appearance across burn and

traumatic scars. However, studies mix hypertrophic, adherent, depressed, painful, and irradiated scars and use different products, volumes, intervals, and co-interventions.[16]

A randomized, blinded, internally placebo-controlled trial found improvement in both fat-treated and saline-treated scar segments without a clear specific advantage for fat. This finding does not prove that fat is ineffective; it shows that subcision, needling, fluid injection, natural maturation, and expectation can produce important changes. Future trials must isolate these effects and prespecify clinically meaningful outcomes.[17]

In practice, the best candidates have a defined structural problem—tethering, loss of padding, contour depression, or restricted glide—where volume and release have an independent rationale. Claims that nanofat or stromal cells erase scars should be avoided. Multiple sessions may be needed, and hypertrophic or keloid biology may require additional established therapies.[7,16,17]

4.12 BURNS AND CHRONIC WOUNDS

Adipose-based treatments have been studied in acute burns, burn scars, pressure injuries, diabetic ulcers, radiation wounds, and other chronic defects. Potential benefits include vascular support, cushioning, matrix remodeling, and modulation of inflammation. A randomized acute-burn study reported favorable healing and early scar outcomes with a protocol combining fat injection and topical nanofat, but the bundled intervention and single-center design make the independent effect of each component uncertain.[18]

The systematic review of acute and chronic wounds found encouraging healing signals but low overall evidence quality, inconsistent preparation, small samples, and inadequate controls. Autologous fat should therefore be considered an adjunct or investigational option, not a substitute for debridement, revascularization, pressure off-loading, glycemic control, edema management, infection treatment, or durable soft-tissue coverage.[27]

Injection into an infected, ischemic, or undebrided wound bed risks graft loss and worsening inflammation. Before treatment, clinicians should define perfusion, bacterial burden, pressure and mechanical causes, exposed structures, malignancy risk in chronic wounds, and whether flap or graft reconstruction is indicated. Trials should report complete closure and recurrence, not only short-term changes in surface area.[23,27]

4.13 MUSCULOSKELETAL APPLICATIONS

Intra-articular and peri-tendinous adipose products are often promoted as stem-cell treatments, although microfragmented adipose tissue is a heterogeneous tissue product rather than a purified or potency-tested cell dose. Proposed actions are anti-inflammatory and trophic rather than proven regeneration of durable hyaline cartilage. Product composition varies by device and patient, complicating comparison among studies.[4,23]

Randomized evidence in knee osteoarthritis is mixed. In one trial, microfragmented adipose tissue and platelet-rich plasma produced similar improvement through 12 months, with no significant between-group difference. This demonstrates comparability with an active orthobiologic in that population but does not prove a specific adipose effect.[24]

A later blinded placebo-controlled trial with two-year follow-up found that a single microfragmented adipose injection was not superior to saline. Differences in selection, processing, comparators, rehabilitation, and outcome timing may explain some inconsistency, but the placebo-controlled result argues against presenting the treatment as established first-line care or as proven cartilage regeneration.[25]

Responsible use requires a correct diagnosis, discussion of exercise therapy, weight management, analgesic and anti-inflammatory options, established injection therapies, and surgical alternatives. The exact product, regulatory status, cost, uncertainty, and conflicts of interest should be disclosed, and treatment should ideally occur within registries or controlled studies when evidence is limited.[23,25,28,29]

4.14 PERIANAL FISTULAS AND OTHER EMERGING INDICATIONS

Fresh autologous adipose tissue has been injected around perianal Crohn fistulas after tract preparation and internal-opening management. In a 21-patient pilot study, complete healing was reported in 57%, sometimes after repeated injections. The study demonstrated feasibility and an acceptable short-term safety signal but lacked a control group and was too small to establish comparative effectiveness.[26]

Perianal Crohn disease requires multidisciplinary control of luminal inflammation, sepsis, abscesses, setons, anatomy, continence risk, and medical therapy. Fresh fat, isolated autologous cells, culture-expanded products, and approved allogeneic cell products are not interchangeable. A favorable result with one product cannot be extrapolated to another.[4,26,28,29]

Other emerging applications include painful scars, neuropathic interfaces, hand conditions, vulvovaginal disorders, vocal-fold insufficiency, and systemic-sclerosis-related soft-tissue changes. Many have promising small series but insufficient controlled evidence. Use outside established reconstructive indications should have a clear mechanistic rationale, independent oversight where appropriate, and explicit consent regarding uncertainty.[12,23,28]

Table 4

Evidence-informed clinical status of major autologous adipose applications.[12-19,23-27,30]

Indication	Evidence profile	Practical status	Critical caution
Breast contour and reconstruction	Moderate; broad observational evidence and consensus, limited randomized data.	Accepted in selected reconstructive settings.	Variable retention, fat necrosis, imaging findings, repeated sessions, oncologic coordination.
Facial reconstruction / rejuvenation	Low to moderate; many series and systematic reviews, few controlled trials.	Established for selected structural indications.	Vascular anatomy, blindness/stroke risk, small aliquots, conservative pressure.
Radiated tissue	Low to moderate; consistent clinical signals but mostly uncontrolled evidence.	Adjunct in specialized reconstruction.	Staging, recipient capacity, oncologic status, uncertain mechanism.
Scars	Low to moderate and heterogeneous; meta-analyses positive, controlled trial mixed.	Selected structural/tethered scars; not universal.	Separate subcision effect from graft effect; use validated scar outcomes.
Burns / chronic wounds	Low; small studies, mixed products, limited controls.	Adjunctive or investigational.	Do not replace perfusion, debridement, infection control, off-loading, or coverage.
Knee osteoarthritis	Conflicting randomized evidence; placebo-controlled trial negative.	Investigational / non-first-line in most settings.	Accurate product description, cost, regulation, and transparent uncertainty.
Perianal Crohn fistula	Early pilot evidence for fresh fat; separate evidence exists for other cell products.	Investigational and multidisciplinary.	Control sepsis and disease; do not extrapolate between products.
Cell-enriched applications	Possible retention benefit; highly variable protocols.	Regulated research or validated programs.	Cell dose, sterility, manipulation, manufacturing, and authorization.

4.15 COMPLICATIONS AND THEIR PREVENTION

Donor-site complications include ecchymosis, pain, edema, seroma, hematoma, infection, sensory change, pigmentation, skin laxity, and contour irregularity. Risk increases with aggressive focal harvest, superficial passes, poor compression strategy, bleeding tendency, and excessive overall liposuction. The donor site should be consented and followed as an operative field, not treated as a negligible source of tissue.[5,12]

Common recipient problems are undercorrection, resorption, asymmetry, overcorrection, nodules, fat necrosis, oil cysts, calcification, infection, and contour irregularity. These are often consequences of insufficient recipient capacity, pooling, large parcels, contamination, or imprecise plane selection. Small asymptomatic areas may be observed; persistent or suspicious masses may require imaging, aspiration, biopsy, or excision according to site and oncologic context.[12,13,30]

Facial vascular occlusion is uncommon but catastrophic. Fat entering an artery under pressure may travel retrograde and then forward into ophthalmic or cerebral branches. Sudden visual loss, severe ocular pain, ophthalmoplegia, ptosis, altered consciousness, or focal neurologic deficit requires immediate emergency activation. Unlike hyaluronic acid, fat has no dissolving enzyme with established rescue effectiveness.[22]

Gluteal fat embolism results when fat enters injured gluteal veins, especially after intramuscular or deeper injection. Deep muscle injection, downward cannula direction, small cannulas, and loss of awareness of the tip have been associated with mortality. Current safe practice is strict subcutaneous-only placement, use of a large blunt cannula appropriate to the procedure, injection only with the cannula in controlled motion and withdrawal, and real-time ultrasound visualization of the cannula throughout graft delivery.[20,21]

Ultrasound is a positioning safeguard, not permission to exceed recipient capacity or inject rapidly. The operator must be trained to maintain an interpretable image, identify the fascial boundary, and stop whenever the tip cannot be continuously located. Surgeon fatigue, excessive daily case volume, and poorly coordinated assistants are system hazards that should be addressed in institutional policy.[21]

Systemic complications also include venous thromboembolism, fluid shifts, anesthesia events, local-anesthetic toxicity, and infection. Their likelihood reflects the combined operation, not the graft alone. Large-volume harvest and grafting require appropriate facility accreditation, perioperative monitoring, thromboprophylaxis, and postoperative observation.[12,20,21]

Table 5

Major complications, preventive measures, and initial response.[12,13,20-22,28-30]

Complication	Mechanism / risk	Prevention	Response
Donor contour injury	Excessive focal or superficial harvest.	Broad crossing passes, conservative endpoint, symmetric assessment.	Document and observe; compression, staged correction, or secondary contour treatment as indicated.
Fat necrosis / oil cyst	Large parcels, pooling, high pressure, poorly vascularized bed.	Small dispersed deposits, staging, avoid overfilling.	Clinical assessment; ultrasound or other imaging; biopsy/excision if suspicious or symptomatic.
Infection	Contamination, devitalized tissue, active recipient infection.	Asepsis, closed handling, careful selection, minimal necrotic load.	Culture, antibiotics, drainage, and debridement when required.
Undercorrection / asymmetry	Expected resorption, uneven placement, changing edema.	Preoperative mapping, symmetric volumes, delayed stable assessment.	Observe to stability; staged grafting or alternative reconstruction.
Facial blindness / stroke	High-pressure intra-arterial injection with retrograde embolization.	Anatomic planning, tiny aliquots, low pressure, continuous controlled withdrawal; never rely on aspiration alone.	Stop immediately; activate ophthalmic/stroke emergency pathways; prognosis often poor.
Pulmonary fat embolism	Gluteal intramuscular/deep injection into injured veins.	Subcutaneous-only injection with real-time ultrasound and continuous tip awareness.	Emergency resuscitation and critical care; prevention is paramount.
Breast diagnostic concern	Fat necrosis, calcification, palpable mass, or unrelated neoplasm.	Baseline risk assessment, oncologic coordination, standard surveillance.	Evaluate new findings according to breast-imaging and biopsy protocols.
Cell-product harm	Unvalidated processing, contamination, undefined dose, inappropriate indication.	Regulatory review, manufacturing controls, trial governance, exact consent.	Report adverse events; involve regulatory and institutional oversight.

4.16 ONCOLOGIC SAFETY AND SURVEILLANCE

Concern about oncologic safety arises because adipose stromal and immune components can secrete signals relevant to angiogenesis, inflammation, and tumor biology in experimental models. The clinical question, however, is whether grafting after adequate cancer treatment increases recurrence in humans. Current meta-analyses of breast-cancer cohorts have not identified an increased locoregional recurrence signal.[13,14]

These data should be interpreted within their design. Most studies are observational and can be affected by selection of healthier survivors, delayed grafting, exclusion of active disease, differences in tumor subtype, and incomplete long-term follow-up. Safety evidence is strongest for standard structural grafting in appropriately selected patients and cannot automatically be extended to cell-enriched, culture-expanded, or highly manipulated products.[11,14,29]

Fat necrosis can generate palpable and radiologic findings. Experienced radiologists can often recognize benign oil cysts and calcifications, but graft history must not lower the threshold for appropriate evaluation of a suspicious lesion. Operative documentation should be available to the imaging and oncology teams, and surveillance should continue according to the patient's cancer and age-related risk.[13,30]

4.17 CELL ENRICHMENT, ADJUNCTS, AND EVIDENCE LIMITS

The desire to increase graft retention has produced cell enrichment, platelet-rich plasma supplementation, growth-factor strategies, hypoxic preconditioning, extracellular-vesicle preparations, and biomaterial scaffolds. Many are supported by compelling laboratory studies, but clinical products differ in composition and potency. A positive result with one protocol does not validate the category as a whole.[8,11,23]

Ex vivo expanded stromal cells improved fat retention in a randomized placebo-controlled experimental clinical model. Translation to routine surgery is limited by expansion time, manufacturing controls, dose characterization, cost, and regulation. Meta-analysis of cell-assisted breast lipotransfer suggests improved retention, but between-study heterogeneity and inconsistent adverse-event surveillance remain important.[8,11]

Platelet-rich plasma is itself heterogeneous and should not be assumed to synergize with fat without an indication-specific controlled trial. Adding more biologically active material can increase cost and complexity without overcoming the fundamental limits of diffusion and recipient capacity. Surgical distribution remains essential even when an adjunct is used.[5,23]

Commercial language may blur transplantation and drug development. Terms such as stem-cell facelift, stem-cell joint regeneration, or regenerative breast therapy imply a characterized mechanism and efficacy that conventional lipoaspirate has not established. Accurate consent identifies the material, processing, intended function, evidence level, alternatives, and regulatory status.[23,28,29]

4.18 REGULATORY, ETHICAL, AND QUALITY CONSIDERATIONS

Regulation depends on jurisdiction, degree of manipulation, intended use, combination with other substances or devices, and whether the proposed function is homologous to the tissue's normal role. In the United States, the concepts of minimal manipulation and homologous use help determine whether an adipose-derived product may qualify for regulation solely under the lower-risk human-cell-and-tissue framework or requires drug, biologic, and device pathways. Clinical teams must obtain current local advice rather than assume that autologous origin makes every use exempt.[29]

Enzymatic dissociation, culture expansion, substantial cell selection, and nonhomologous therapeutic claims commonly raise additional regulatory requirements. Mechanical processing is not automatically minimal manipulation, and same-day use is not automatically permissible. The exact device instructions, institutional tissue policies, sterility controls, and national rules must be reviewed.[4,29]

The ethical requirements for innovative care include a credible biological rationale, proportional risk, independent review when appropriate, transparent consent, prospective outcome collection, adverse-event reporting, and separation of clinical payment from exaggerated promises. ISSCR guidance specifically opposes premature commercialization of unproven stem-cell interventions and emphasizes rigorous translation.[28]

Quality improvement should track indication, product definition, donor and recipient sites, processing, volume, complications, reoperation, patient-reported outcomes, and long-term follow-up. A registry can reveal learning curves and uncommon harms that single-surgeon series miss. Serious vascular or systemic events require prompt institutional review and reporting through applicable safety systems.[12,21,23,28]

4.19 A PRACTICAL DECISION FRAMEWORK

First, define whether the problem is structural. A measurable deficiency in volume, contour, padding, or tissue glide provides a direct rationale for conventional fat grafting. If the

proposed benefit is exclusively cellular or paracrine, the evidence and regulatory requirements should be scrutinized more closely.[1,4,29]

Second, characterize the recipient environment. Vascularity, compliance, scar, radiation, infection, pressure, and oncologic status determine capacity. A compromised bed favors conservative parcel size, smaller total volume, and staging. When perfusion or infection is inadequate, these problems take priority over grafting.[3,15,27]

Third, select the least manipulated product capable of the intended function. Intact fat is appropriate for structural filling; smaller clusters support fine placement; nanofat may be considered for selected surface-quality protocols but not as volume; isolated or expanded cells should be reserved for authorized protocols with appropriate evidence.[4,5,7,28,29]

Fourth, design the operation around recipient capacity and hazard anatomy. Choose a donor method that preserves contour, process reproducibly, place small aliquots under low pressure, and use real-time ultrasound whenever required to confirm the safe plane, particularly in gluteal grafting. Stop when tissue capacity or tip certainty is lost.[1,5,20-22]

Fifth, measure what was promised. Structural treatment should report stable volume and contour; scar treatment should report symptoms, pliability, and function; wound treatment should report durable closure; orthobiologic treatment should report validated pain and function against an appropriate comparator. Biological vocabulary is not an outcome.[16,17,23-25,27]

Finally, treat uncertainty as a consent obligation. Patients should understand likely benefit, evidence strength, number of sessions, costs, alternatives, common morbidity, rare catastrophic events, and the possibility of no durable improvement. A technically feasible injection is not automatically a clinically justified regenerative treatment.[23,28]

4.20 RESEARCH PRIORITIES

Future studies need consensus reporting of donor site, infiltration, harvest aperture and pressure, processing, particle size, time to implantation, cannula, plane, aliquot size, recipient preparation, and postoperative management. Product composition should be measured when mechanistic claims depend on cell populations. Without this information, studies with the same label may evaluate different interventions.[4,5,23]

Randomized trials should use credible comparators. Saline, needling, subcision alone, platelet-rich plasma, standard reconstruction, or rehabilitation may each answer a different question. Blinded outcome assessment and core outcome sets are essential in scar, wound,

pain, and orthobiologic research, where expectation and natural history strongly influence results.[17,23-25,27]

Long-term registries are needed for oncologic subgroups, large-volume breast reconstruction, gluteal safety, delayed hypertrophy, repeat-session burden, and uncommon vascular complications. Imaging and three-dimensional measurement should be validated against clinically meaningful endpoints rather than used as isolated surrogate outcomes.[13,14,20,21,30]

Mechanistic research should connect a characterized product to a reproducible biological signal and then to a patient-centered outcome. Demonstrating stromal markers or growth factors is insufficient unless dose, viability, delivery, safety, and clinical effect are established. This sequence is necessary to move adipose regenerative medicine from plausible biology to dependable therapy.[4,8,28]

5 CONCLUSION

Autologous fat is a living structural graft with regenerative potential. Its success depends less on a single proprietary preparation than on correct indication, recipient vascularity, atraumatic handling, meticulous distribution, respect for tissue capacity, and objective follow-up. The most established role is restoration of soft-tissue volume and contour, especially in breast and craniofacial reconstruction. Evidence for radiated tissue and selected scars is promising but heterogeneous, while chronic wounds, osteoarthritis, fistulas, and cell-enriched interventions remain investigational or indication-dependent.[1,5,12-19,23-27,30]

Safety must shape every technical decision. Small low-pressure aliquots, continuous control of the cannula tip, conservative staging, coordinated breast surveillance, and strict subcutaneous ultrasound-guided gluteal injection reduce preventable harm. Catastrophic embolic events are rare but demand explicit consent and prevention-focused systems.[13,20-22]

Finally, conventional fat grafting must be distinguished from stromal vascular fraction, cell-assisted transfer, and culture-expanded cell therapy. Accurate terminology protects patients, improves science, and clarifies regulation. The appropriate clinical question is not whether adipose tissue contains regenerative cells, but whether a precisely defined product, delivered by a reproducible operation, improves a meaningful outcome with acceptable risk.[4,23,28,29]

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