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Breast Augmentation: The Current Landscape

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Abstract

Primary breast augmentation is one of the most common surgeries performed by plastic surgeons. Breast augmentation, since its inception in 1895, has become a multimillion-dollar industry. Today, the two most common methods include implant-based and fat graft augmentation. Implant-based augmentation includes the use of silicone or saline prosthesis to enhance breast volume or shape. With fat grafting, a patient's fat is harvested, processed, and injected into the breast to achieve the desired result. This thesis aims to outline the current literature on both methods of breast augmentation, review patient reported outcomes, as well as a proposed clinical trial to gain further understanding into fat grafting to address the current deficiencies in the literature.

Keywords

Breast augmentation, Breast Implants, Fat grafting, BreastQ, cosmetic breast surgery, reconstructive breast surgery.

Summary for Lay Audience

Patients undergo breast surgery for either cosmetic or reconstructive (breasts removed due to cancer or for lack of normal breast development) indications. Breast augmentation is one of the most common procedures performed by plastic surgeons. Breast implants have been a standard option for breast augmentation for the past 60 years. However, in the past decade a large group of patients are requesting a more 'natural' option to enhance their breast, with no prosthetic implant.

Fat grafting provides an option for breast enhancement using the patient's own tissue. The fat grafting procedure involves liposuction to the abdomen, thighs, or buttocks. The harvested fat is then processed and prepared for injection into the breast. During surgery the fat is injected into the breast, balancing the desired result and limitations of injectable volume. This procedure can produce great initial results; however, long-term fat graft survival can be unpredictable. The injected fat, over time, may not survive. This can result in the body breaking down the non-viable fat, creating hard and painful nodules, and ultimately losing a volume of the injected fat. This has limited the widespread adoption of this technique.

In this thesis the current data is reviewed on the above methods, as well as patient satisfaction surveys. Secondly, a proposed clinical trial looking into fat grafting. This will give us more knowledge on how to treat the fat during surgery, to increase the amount of fat survival after surgery.

List of Acronyms

ADM – Acellular dermal matrix
ADSC – Adipose derived stem cell
AFG – Autologous fat grafting
ASPS – American society of plastic surgery
BEQ – Breast evaluation Questionnaire
BIA-ALCL – Breast Implant associated - Anaplastic Large Cell Lymphoma
BII – Breast Implant Illness
BIS – Breast Implant sickness
BMI – Body mass index
BRASSQ - Breast reduction assessed severity scale questionnaire
CC – Capsular contracture
CI – Confidence Interval
CT – Computerized tomography
DIEP – Deep inferior epigastric perforator
FDA – Food and Drug Administration
IMF – Infra mammary fold
IQR – Inter quartile range
ISAPS – International society of Aesthetic Plastic Surgeons
LAP – Lumbar artery perforator
LHSC – London health sciences center
LOI – Letter of Information
MINORS - Methodological Index for Non-Randomized studies
MRI – Magnetic Resonance imaging
NAC – Nipple areolar complex
NR – Not reported
PAP – Profunda artery perforator
PET – Positron emission tomography
PRISMA - Preferred Reporting Items for Systematic Reviews and Meta- Analysis
PROM – Patient reported outcome measure
PRP – Platelet rich plasma
PRSJ – Plastic and Reconstructive surgery journal
QOL – Quality of Life
RCT – Randomized controlled trial
REB – Research ethics board
RR – Relative risk
SD – Standard deviation
SVF – Stromal vascular factor
TE – Tissue expander
TRAM – Transverse rectus abdominus muscle

Co-Authorship Statement

Chapter 1 –Kathryn Minkhorst and Katrina Jackzul are credited for their help with the database search. Drs. Simpson, DeLyzer, Symonette and Yazdani contributed their guidance and review of the manuscript.

Chapter 2 – Literature search and data extraction were done by Kathryn Minkhorst and Katrina Jackzul. The statistical analysis was completed by a statistician, Leonardo Guizzetti. Drs. Appleton, DeLyzer and Yazdani are credited for their guidance and review of the manuscript.

Chapter 3 – Drs. DeLyzer and Yazdani are credited for their guidance and review of the trial. Kalan Lynn was also instrumental in her help and support with the Research Ethics submission.

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Thesis Outline

In Chapter 1, a literature review of available data and information on breast augmentation is performed. Particularly, addressing concerns with prosthetics and their associated complications. The review will further highlight current surgical recommendations and best practice guidelines. Finally, the review highlights fat grafting, including current techniques, analysis, pathophysiology, and theories associated with fat survival.

In Chapter 2, the thesis addresses breast augmentation satisfaction from the patients' perspective. The comprehensive meta-analysis of qualitative data available in the literature from patient reported outcome measures is evaluated. The thesis will compare the two most popular methods of breast augmentation, implants, and fat grafting to gain further understanding regarding the patient's quality of life.

In Chapter 3, the lack of information truly known regarding fat grafting, retention, survival, and best surgical practice are highlighted. The thesis further proposes a randomized controlled trial to help address current deficiencies in our knowledge, to help guide future practice, increase patient safety and satisfaction.

1 Breast Augmentation – A literature review

Breast Augmentation is a popular surgical procedure that is well described in the surgical literature. The most common method of surgical augmentation relies on alloplastic implants and in fact these are one of the most common surgical prosthetic devices in North America. This chapter will broadly outline the currently available breast implant categories (silicone and saline), surgical adjuncts, surgical techniques, and complications. This review will also highlight alternative methods of breast augmentation, particularly, fat grafting. Outlining what is currently understood regarding the pathophysiology and survival of fat, current surgical recommendations, fat enhancers, fat analysis and finally, future trends.

This chapter has been modified from a manuscript for the purpose of this thesis. The manuscript is currently pending submission to the European Journal of Plastic Surgery.

1.1 Introduction

1.1.1 Anatomy

Anatomically, the breast extends from the second rib to below the sixth rib and spans from the mid-axillary line to the sternum laying over top of pectoralis major, with most of the tissue situated in the upper outer quadrant. (1,2) The skin is the most superficial layer, and it merges with the superficial fascia that envelopes the breast

parenchyma with the deep fascia. This is particularly important as the convergence of superficial and deep layers create the infra-mammary fold. (2) The nipple is located at the level of the fourth intercostal space and contains 15-20 lactiferous ducts. It is surrounded by the areola which has visible sebaceous glands and smooth muscle fibers for nipple erection. (1,2) The blood supply to the breasts is via branches from the axillary, internal thoracic, and intercostal arteries. (1,2) Venous drainage follows the arterial supply through the internal mammary vein, tributaries of the axillary vein, and intercostal veins. (2) The lymphatic drainage of the deep parts of the breasts is through the axillary (75%) and internal thoracic lymph nodes. The superficial layer of the breast is drained by Sappey's plexus. (1,2) Sensory innervation to the breast is through the lateral cutaneous branch of the sixth intercostal nerves and the nipple-areola complex (NAC) itself is innervated by the fourth intercostal nerve. (2)

1.1.2 Rationale

A patient's decision to undergo a breast augmentation is multi-factorial, but the primary three reasons include cosmesis, reconstruction, and correction of congenital deformities. (3) An individual's decision and rationale are often complex and may include a multitude of personal, social, and cultural contexts. (4) Several reasons an individual may choose to undergo breast augmentation is to improve self-esteem, self-acceptance, sexual interest, and to better express an individual's gender identity. Regarding the reconstructive population, it can reduce stress, anxiety, restore wholeness and well-being in patients who have gone through their breast cancer journey. (5,6)

Cosmetic breast augmentation is growing in popularity and has seen a 41% increase since 2010 and is one of the most common procedures in North America. (7,8) In the United States in 2017, there was over 300,000 breast augmentation surgeries performed, and 299,715 surgeries in 2019. (7,8) Data from the international association of aesthetic plastic surgeons (ISAPS) from 2019 (pre-pandemic), showed that breast augmentation was the most common procedure internationally with 1,795,551 surgeries performed. This was followed by liposuction at 1,704,786 procedures internationally. (7,8) The two most common methods for cosmetic breast augmentation are fat grafting and implant-based augmentation procedures, with implants being significantly more popular overall (29% vs 71%). (7) The majority of patients who undergo breast augmentation, according to North American data, are Caucasian, female, middle to upper socioeconomic status, married, between the ages of 20 to 40 years old, with children. (9,10)

The objective of this review is to evaluate the currently available literature, describe the most popular techniques and assess current trends.

1.2 Breast Implants

1.2.1 Historical Overview

Breast implants date back to 1895 when Vincenz Czerny used a lipoma to correct a breast defect after a mastectomy. (3,11) In the early 1900's breast implants were experimental, taking the form of glass balls, ground rubber, polyvinyl alcohol-

formaldehyde polymer sponges, and polyether foam sponges, and by 1954, breast augmentation was performed using adipose tissue and omentum to augment the breast. (3,12) Polyurethane, polytetrafluoroethylene (Teflon), epoxy resin, shellac, beeswax, paraffin, rubber, petroleum jelly, and liquefied silicon became popular materials used in breast implantation. (3) In 1961, the first modern breast implant was made as a silicone gel implant, and saline implants followed in 1965. (3) Silicone implants gained popularity in the 1980s, however in the early 1990's an ever-growing subset of patients experienced implant ruptures. The ruptured silicone led to multiple lawsuits from patients, associating the silicone with connective tissue disorders, such as Sjogren's, Scleroderma, Rheumatoid arthritis, as well as melanoma and stillbirths. The long list of lawsuits, as well as the growing public demand at the time, led the FDA (Food and Drug administration, USA) to ban the use of silicone implants in 1992. The leading manufacturer of silicone implants at the time, Dow Corning, filed for bankruptcy in 1995. (PMC1676088).

A landmark paper, published by the institute of medicine in 1999, showed that there was no evidence to associate the above conditions with silicone implants (www.iom.edu/CMS/3793/5638.aspx). The growing body of medical literature, along with clinical data from countries still using silicone at the time of the ban, showed that silicone implants were safe. The reassuring clinical data allowed the FDA to approve the use of silicone implants from Allergan and Mentor in 2006. Silicone implants are now the most popular type of breast implant, with FDA approval for cosmetic and reconstructive purposes in patients over the age of 22. (3,7,9,11)

1.2.2 Implant Properties

The two main types of material used to fill implants are silicone and saline. Silicone breast implants are by far the most common type of material used in cosmetic breast augmentation (90% vs 10%). (13,14) Silicone is more expensive but has a more natural feel and is offered in a greater variety of shapes. (7,11) The volume and density of the gel inside the implant will ultimately affect how natural it will feel. (15) Although, in endoscopic trans-axillary and trans-umbilical breast augmentation, saline implants are the only option for minimally invasive surgery. (16)

Saline implants pose a five-time higher risk of rupture in the short term (2.5% vs 0.5%), and it may feel less ‘breast like’ given the lower density of saline compared to natural breast tissue. (17) If a silicone implant ruptures, it does not always require surgery for removal. The ‘ruptured’ content is typically contained in the capsule, this would therefore not affect the overall cosmetic appearance. In certain cases, when the person is symptomatic, or the rupture has affected the cosmetic outcome, a second surgery would be needed to replace the implant. (18)

Breast implants come in two main shapes, round and anatomical. (3) An external texture is a requirement of anatomical implants as it is thought to increase friction and avoid unwanted movement and rotation. Anatomical implants (tear-drop shaped, flattened on the aspect that lies against the chest wall) offer a more natural shape, but they are more expensive and have a higher risk of malrotation. This occurs when the implant moves within the pocket and causes the breast to look abnormally shaped. (19) Round implants inherently give a fuller look in the upper pole, which leads to the

potential of having an un-natural result. This must be considered in the pre-operative assessment. (20)

Projection is affected by the base diameter and height of the implant, as well as the total volume. (21) Maximal projection is defined as the distance between the lower aspect of the implant to the maximal distance the implant protrudes away from the body, typically below the midline of the implant, which may change when the patient is prone versus supine. (22,23) There is a huge variety of projections available to choose from. The choice of projection is made between the surgeon and patient balancing patient desire for post-augmentation/reconstruction breast shape and surgeon experience with post-operative appearance and skin envelope capacity. (23)

Smooth implants are supple and can mimic the feel and movement of a natural breast. (18) The textured surface, however, stabilizes the implant, disrupts the formation of a capsule in a subpectoral plane augmentation, and help prevent certain post-operative complications, including malrotation, which is only associated with anatomical implants, as they have an asymmetric form-factor. (17,18) Breast animation causes movement of the implant when pectoralis is engaged, causing an un-natural movement of the overlying skin and nipple-areolar complex (NAC). (18,19)

A form of saline implant, known as tissue expanders (TE), are provided empty and gradually filled with saline. (8,11) This offers a wider possibility of staging procedures. This method creates a pocket and is slowly expanded during clinic visits to accommodate the requested implant size. This is needed in two main situations, firstly, when the breast tissue envelope, in its current state will not accommodate the required

implant size and secondly, when then surrounding breast tissue requires further surgery or radiation. (11,13)

In the first case, the tissue expander is inserted in a similar manner as a permanent breast implant. The TE is filled to an appropriate volume intra-operatively to minimize tension on the wound and breast tissue. During subsequent clinic visits, the TE, and more importantly the injection port, can be identified with a magnet. This allows the clinician to gradually inflate the tissue expander, over time, to achieve the desired size. (8,13,15) Secondly, TE's are commonly used as a temporary measure to maintain the implant pocket. (3,8,11) This is most notable when the breast tissue will be undergoing radiation post-operatively. The fibrosis caused by the radiation, not only thickens, and discolors the skin, however, also causes a similar and more severe effect to the capsule around the implant, which results in tightening of the pocket. (3,8) This can result in both a cosmetically unacceptable breast placement, as well as pain. Although TE's are a great method in achieving certain results, there are several downsides. The use of TE's will require frequent clinic visits and inherently, a second surgery. (8,11) The frequent needling can be a source of infection and if not done properly, cause the TE to rupture. Certain newer TE's, such as the BECKER implant (Mentor worldwide LLC, Irvine, California, USA) has an external filling port, away from the expander, on the skin surface, to avoid the above-mentioned complications.

Intra-operatively when there is insufficient tissue for coverage or support of the implant. Acellular dermal matrices (ADMs) can be considered. In most cases the implant is placed below the breast tissue, fascia, or muscle. (26,28) If the pocket is not adequate to accommodate the implant, ADMs can be used to cover the exposed part of the implant

and facilitate the formation of the capsule and therefore placement of the implant. ADMs are a soft connective tissue mesh, from either human or animal origin. They are decellularized to avoid an immune reaction, however, the structural matrix is preserved. Surgical techniques will be discussed later in this chapter. (26,27,28,29)

1.2.3 Implant Surgical Technique

A major factor that affects the long-term outcome of breast augmentation, is the location in which the implant is placed. Three main anatomic pockets: sub-muscular, sub-fascial and sub-glandular, as well as combinations of these, known as ‘dual-plane’, exist. The major contributing factor in the decision of implant placement is dependent on several factors including patient anatomy, surgeon preference, implant size, the soft tissue envelope, patient characteristics and surgical approach. (24,25,30)

The more superficial planes, due to the weight of the implant and natural physiology, are more susceptible to ptosis (the drooping of breast tissue from a more youthful position, ideally with the NAC above the level of the IMF). (30) The deeper planes, are more robust structures, attached to a bony component, therefore, more resistant to mechanical drooping, as well as providing more tissue coverage to avoid palpation of the implant. (24,25) The deeper pockets involve muscle dissection and are therefore more painful and require a slightly longer recovery for patients. The muscle being more superficial to the implant can also lead to certain deformities, known as animation (breast implant movement when pectoralis is engaged) and window-shading

(crease or dimple formed at the lower medial aspect of the breast when pectoralis is engaged). (24,25,30)

There has been a significant amount of research published to decrease peri-operative complications and increase patient safety. Research has shown that to reduce the risk of infection, patients should receive IV antibiotics 30-60 minutes before skin incision and an antibiotic solution to irrigate the pocket and allow it to rest there for at least 5 minutes prior to the implant being inserted. (7,32) More so, before touching the implant, all individuals involved in the surgery should change into a new set of sterile gloves to minimize contamination. (7) Implants should be irrigated in the opened packaging to minimize the risk of infection, using triple-solution (Cefazolin, Gentamicin and Bacitracin in normal saline). (32) Breast implants should ideally not be handled. To help maintain sterility, the no-touch technique has been described in the literature, which uses a plastic sleeve provided or a reverse glove sleeve using a latex-free glove to insert the implant after being bathed in a betadine and/or antibiotic solution. (32,38)

To further reduce the risk of infection, various methods have been created to protect patients against the most common pathogens, *Staphylococcus epidermidis* and *Staphylococcus aureus*. (39) The povidone-iodine solution has been shown to be the most effective at reducing staphylococcus stains and Gram-positive bacteria but may weaken the shell of silicone implants. (39) Triple-antibiotic saline irrigation is used after washing the breast pocket with povidone-iodine and has demonstrated inconsistent benefits to preventing implant infections but does not significantly reduce the risk of capsular contracture or the overall risk of bacterial contamination. (39,40,41)

1.2.4 Implant Related Complications

Early complications, within the first 30 days, after breast augmentation include hematoma, seroma, infection, implant extrusion, and asymmetry. (31) Later complications, past 30 days, include late seroma, double-capsule formation, and chronic pain. (31) Physiologically, when an implant is inserted, the body begins to form a fibrous capsule of tissue around the prosthetic. In most cases, this does not cause patients to experience symptoms. However, in a certain subset of patients, they can experience complications, including implant immobilization, pain, and discomfort, secondary to this fibrous capsule contracting around the implant. This is known as a capsular contracture (CC). There have been several classifications and staging systems proposed, however, there is poor inter-observer reliability and they do not provide any specific treatment algorithms. This highlights one of the main disadvantages of implants, and slightly more so silicone implants, as they have an increased risk of capsular contracture, with an incidence of approximately 5% compared to 2.8% for saline implants. (14) If a patient is diagnosed with a capsular contracture, the resulting treatment, is operative removal of the prosthetic implant, along with the complete or partial removal of the fibrous capsule. This not only exposes patients to more operative time, to replace the implant, there is still a possibility of getting a capsular contracture again with the new implants. (32,34)

The most common and least understood complication is capsular contracture (CC) (ranging from 4-17%) which, as described earlier, can be painful and distort the shape and volume of the breast, ultimately affecting the cosmetic result of the breast and the patient’s quality of life. (31) It tends to occur within the first year after surgery, but can

occur at any time post-operatively. (31,32,34) Capsular contracture has been associated by several factors; a bacterial infection, and more specifically the formation of a sub-clinical staphylococcal biofilm has shown a very strong correlation with a clinically symptomatic capsular contracture. (32,33,34) The literature has shown that a sub-glandular placement of the implant has been associated with a higher risk of CC. On the other hand, a textured implant has been thought to make it more difficult for thick scar tissue to adhere around the implant, thus reducing the risk. Drain placement and patient factors have also been associated with the formation of CC, however, the overall evidence is inconclusive. (3,33,34)

Aside from CC, infection around a prosthetic device can cause several issues, including a superficial cellulitis, chronic wounds, implant failure, and sepsis, indicating the great importance of maintaining a sterile field and minimizing any potential sources of contamination. (7,32) Another important risk factor to consider in the reconstructive and cancer population, is adjuvant radiation therapy. Radiation poses an increased risk for a patient developing CC, with a rate up to 30%. (33) This is due to the increased amount of fibrosis, which, would also affect the capsule around the implant. It is, therefore, a relative contraindication for patients receiving implant-based augmentation. (33) The staging of procedures, as mentioned above, or the use of autologous methods of augmentation are recommended. (3,7)

1.2.5 Breast Implant Sickness and Lymphoma

Breast Implant Sickness (BIS) or illness (BII) have been described since the 1960s. It was first described as Human adjuvant disease (1964), then renamed silicone-induced human adjuvant disease in 2011, then silicone implant incompatibility syndrome in 2013, and is now known as BIS or BII. (35) BIS is an assumed autoimmune disease that arises after the surgical implantation of a silicone prosthesis in the breast. (35) A large part of BIS is yet to be fully understood. The presenting symptoms are extensive and non-specific, some of the most reported symptoms include, fatigue, muscle pain, headaches, hair loss, dry mucous membranes, poor memory, depression, and anxiety. The current treatment recommendation is implant and capsule removal. In most cases, surgery has resulted in the resolution of patient symptoms. (35)

The literature describes a second, more serious disease in a small subset of patients who have been exposed to Allergan BIOCELL breast implants being 18 times (one in 2,832) more likely to develop a condition known as ‘Breast Implant-Associated’ Anaplastic Large Cell Lymphoma (BIA-ALCL), which is a T-cell lymphoma. (6,35,36,37) This is a systemic cancer which is now understood to be associated specifically with the BIOCELL implants. Symptoms, are however, more specific, they include breast enlargement, pain, swelling, hardening, a fluid collection, and possibly lymph node involvement. These are typically noticed at least one year post-operatively and on average after 8-10 years. Patients can also experience general B-symptoms associated with cancer, including fatigue, weight loss and night sweats. (7,36,37)

If a patient is thought to have BIA-ALCL, this should be worked up, similar to any other systemic cancer. Initial steps should include diagnostic imaging with a CT (Computerized tomography) or PET (Positron emission tomography) scan to assess the extent, and stage the disease. The involvement of an oncology service is strongly recommended. From a surgical perspective, the removal of the implant, along with the capsule is recommended. Surveillance with imaging is recommended for two years post-implant removal. Once resolved, disease recurrence has not been documented. (36,37)

Due to this association between textured implants and lymphoma, there has understandably, been a huge shift from patients to either exchange their current textured implants or avoid implants altogether. This has not only put pressure on surgeons, to comply with patient requests, but also manufacturers to subsidize the cost. There has been extensive litigation over this matter, and the Allergan BIOCELL implant has since been recalled. Of note, smooth implants, and textured implants from other manufacturers have not been associated with BIA-ALCL. (36,37)

1.2.6 Summary

The use of breast implants remains the gold standard option in breast augmentation. The choice of implant, procedure staging, and surgical technique are important factors every surgeon should consider. Understanding patient goals and counseling them on expectations, potential complications and anticipated outcomes is crucial. Despite the popularity of implants, an ever-growing subset of patients are

requesting a ‘no implant’ augmentation, which has given rise to more autologous surgeries, most notably, fat grafting.

1.3 Fat Grafting

1.3.1 Cell Biology

White adipose cells are a normal component of the subcutaneous tissue, found all over the body. The distribution and quantity of adipose cells, varies significantly from person to person and relies on a multitude of genetic, social, and environmental factors. (46,48)

Each white adipose cell is composed of mainly lipids (80%), and 90% of the lipid component is made up of six triglycerides (linoleic, myristic, oleic, palmitic, palmitoleic and stearic acid). The remainder of the adipose cell is made up of cholesterol, free fatty acids, mono- and di- glycerides. Each cell contains a large central vacuole, as this expands to accommodate the above contents, the cell nucleus and organelles are pushed to the periphery. This gives adipose cells the classical ‘signet ring’ appearance under the microscope. The size of each individual cell varies from 30 to 230 microns. (46,47,48)

Adipose cells, and in turn fat, are the main energy reservoir in humans. Fat is mainly derived from excess consumption in an individual’s diet. Foods high in lipid content, provide lipids that are easily used or stored. Other nutrients, in excess, such as

carbohydrates and proteins, can undergo a conversion in the liver to fat for storage. (46,48)

Historically, fat was only considered useful for insulation, energy storage, thermal regulation, and mechanical protection. However, fat is much more complex, participating in a multitude of interactions with the cardiovascular, endocrine, and neurovascular systems. Fat is composed of both adipose and stromal cells, which most notably include adipose tissue-derived stem cells (ADSCs). ADSCs have the ability to differentiate into cells with a mesenchymal origin, such as chondrocytes, osteocytes, myocytes and in the case of fat grafting, adipocytes. The conversion of ADSCs to adipocytes is known as adipogenesis, which is a normally occurring process to increase the amount of fat, when current stores are insufficient. This process is quite sensitive and certain factors such as radiation, not only significantly dampen the proliferative abilities of ADSCs but also increase local apoptotic cells, causing fat loss. (46,47,48)

1.3.2 Historical Overview

Autologous fat grafting (AFG) was first described in 1893 by Neuber as a method of reconstructing soft tissue defects. (42) In 1919 and 1920, the first textbooks describing fat grafting to the breast were published by Lexer and Pennisi, respectively. A landmark paper published by Mel Bircoll in 1987 described his long experience with fat grafting, despite his early success with fat grafting, the calcific nodules (which is caused as a result of fat necrosis) raised concern, as radiological imaging at the time, was not able to differentiate calcific nodules caused by fat necrosis and cancerous lesions with certainty. This raised oncological concerns with the procedure and that same year, the American

society of plastic surgeons (ASPS) took an unprecedented stance and banned fat grafting to the breast for the next two decades. (42)

In 2001, Sydney R. Coleman published his methods of fat grafting, which have since been termed, ‘the Coleman technique’, this was centered around the gentle handling of fat to improve the purification of alive adipocytes. Multiple other publications and clinical trials followed over the next several years. Following the overwhelming data on efficacy and safety, the ASPS reversed its decision on fat grafting to the breast in 2009, declaring it “effective with no significant risk”. (42,43,44) Today, fat grafting is an incredibly popular technique used by plastic surgeon to correct defects and augment volume in any part of the body. More so, data over the past decade has emphasized the safety and effectiveness of the procedure (43,44,45)

1.3.3 Pathophysiology

Autologous fat grafting (AFG) consists of three main steps. Liposuction of the fat from areas of excess, processing of the harvested fat, and re-injection of the processed fat into the desired region. Common areas of harvest include the abdomen, flanks, and thighs, as they are common areas of excess. AFG involves the avascular transfer of fat; therefore, the donor cells must revascularize from the surrounding tissue to survive. (46) Currently, there are three main theories of fat graft survival after avascular implantation.

First, Peer et al. described their theory of graft survival, which hypothesizes that grafts survive differently in the short and long term. Initially, the avascular, grafted fat

survives by diffusion, through the direct contact with the surrounding vascularized tissue. Later, the fat stimulates an inflammatory reaction, which in turn stimulates a molecular cascade which initiates vasculogenesis and angiogenesis to support long term survival. (47) Therefore, smaller volume grafts achieve increased survival as they are better suited to achieve nutrient supply through complete diffusion until complete neovascularization occurs. (48) More recently, the graft replacement theory was described, in which very few grafted adipocytes are thought to survive and instead are replaced by ADSCs that are transferred with the fat. (49) ADSCs are collected and concentrated intra-operatively. They are a natural component of lipo-aspirate, in which, using commercially available devices are concentrated into a serum, which can be added to the harvested fat, for injection.

As such, recent studies have focused on investigating the enrichment of fat grafts with ADSCs, as well as stromal vascular fraction (SVF). SVF is a collection of cells (mesenchymal stem cells, endothelial cells, T-cells, M2 macrophages and preadipocytes), that are isolated from the lipo-aspirate. They have emerged as a desirable source of cells with anti-inflammatory and regenerative potential. They have been correlated to increased graft retention. (49,50)

Lastly, the host replacement theory postulates that no grafted cells survive and instead necrose and are replaced by new fat cells, fibrous tissue, and new blood vessels. (49) It is likely that the true mechanism of avascular fat grafting includes aspects from all three of these theories. The underlying principles of all theories have emphasized the health of the donor adipose cells with smaller volume grafts, to increase direct contact with the surrounding vascularized tissue. (48)

This is encompassed by the three-zone survival theory that states when fat is transferred, it can be divided into cellular zones. (50,51) As described by the Coleman technique, the current recommendation is to inject the fat in thin strands, with a fan like pattern, over multiple sessions to achieve the desired result. This allows for a larger surface area to be in direct contact with the surrounding vascularized tissue. The injected fat, as a whole, is divided into zones. The most peripheral zone, which is 0.3 mm thick, includes cells that directly survive, as they have direct contact with the surrounding tissue. (51) The middle zone, which is 0.6 mm – 1.2 mm thick, is the regenerative zone, where ASCs survive and are regenerated into new adipocytes. (50,51) And lastly, the central zone is known as the necrotic zone, where no cells can survive and are either resorbed or replaced with fibrotic tissue. (51) The bulk of this process of survival, neovascularization and regeneration is thought to occur in the first three months; however, it can take up to a year for the areas of necrosis and fluid to be fully resorbed, and a stable volume is attained. (46,50)

1.3.4 Retrieval of the fat

Fat harvest involves two steps: first, the injection of tumescent fluid, and second, liposuction of the fluid and fat from the donor area. Tumescent fluid is a combination of a crystalloid with low concentrations of epinephrine and lidocaine, which is injected into the donor area at two to three times the desired extraction volume; the exact formula and volume are variable depending on surgeon preference. (52,53) This process helps to develop the adipose plane and decrease blood loss due to vasoconstriction from the epinephrine. (52) For the purpose of fat grafting, there has been some debate as to the

effect of lidocaine and epinephrine on fat survival. However, studies conducted on animal models have shown no effect on fat survival in the use of tumescent fluid versus normal saline. (54,55) To maximize cell survival, care must be taken in the technique of harvesting through liposuction. In-vitro studies have found that minimizing cellular trauma and using larger, blunt-tipped cannulas can increase graft viability. (56,57) Lastly, utilizing lower pressures during aspiration has been shown to increase adipocyte survival. (58) Coleman was one of the first surgeons to describe a minimally traumatic technique using a 3mm blunt-edged two-hole cannula connected to a 10-mL syringe with the operator manually holding negative pressure. Overall, this knowledge has led to the use of tumescent fluid, with a small bore blunt-tipped cannula under low-pressure lipo-aspiration as the standard method of harvest in AFG procedures. (59)

1.3.5 Fat Processing

Fat processing is a crucial step in AFG that involves techniques to remove as much fluid, blood, and oil from the aspirated fat before injecting it to the targeted site. If not removed, these factors can increase inflammation and increase degradation of the fat graft. (60) The simplest method allows gravity to separate the harvested material and decant off the liquid component. (61) The Coleman technique involves centrifuging the fat for 3 minutes at 3000 rpm sterilely to separate the harvested fat from blood, tumescent, and oil. (62) However, more recent studies have proposed that higher centrifugal forces can cause damage to fat cells, and lower forces have comparable outcomes to the decantation method. (63) Fat processing devices have also been developed in an attempt to refine the fat even further. Many of these devices on the

market are closed systems that use a combination of gravity and washing. (61) Although these new devices have shown promising results for decreasing oil, fluid and blood products while maintaining a high adipocyte viability, there is a lack of clinical data showing significantly increased retention and survival of cells in the breast once injected. (59)

1.3.6 Fat injection

In the case of breast augmentation, the target site is the breast, and the fat is commonly injected in the subcutaneous, pre-pectoral and subpectoral planes to increase the overall volume of the breast. (59) Based on the principles of fat survival, Coleman proposed the use of a 17-gauge blunt cannula, injecting small amounts in a retrograde (Inject while withdrawing the cannula) fashion to decrease trauma and increase surface area contact with recipient vascular beds. (62) Care must be taken when injecting to do so in layers, and often surgeons will use a fan-like pattern to avoid creating any larger pockets of fat graft, which will be more likely to necrose. (57) Furthermore, the volume of fat injected into the breast should not be overly large for the tissue envelope, which increases the pressure and can be detrimental to the graft. (46) A recent systematic review of AFG to the breast showed that the range of injected volume was 20 cc to 607 cc per session. (70) However, there is no maximum recommended volume of injection, this varies from person to person and mostly relies on the amount of harvested fat available, as well as the breasts' skin laxity and ability to accommodate the volume. Therefore, in AFG breast augmentation, the increase in size may be limited or require multiple sessions to achieve the desired effect. (64) However, unlike implant augmentation, the surgeon

can contour the breasts in a precise fashion to give the patient a more natural shape and address specific areas of the breast. (62)

1.3.7 Fat Enhancers

In an attempt to increase the volume retained following AFG, in-vitro studies have evaluated the potential enrichment of fat grafts with a variety of factors, including SVF, ADSCs, or platelet-rich plasma (PRP). These studies are based on the fat survival theory that regeneration may play a large role in fat survival. (46) Studies involving enrichment with ADSCs have shown promising results with 1.5-fold increase in retention compared to no enrichment. (65) However, enrichment with ADSCs is expensive, and culturing cells for clinical use is subject to strict regulatory requirements. (66) Comparatively, SVF cells do not require the same extensive laboratory setup as ADSCs; however, clinical data has not shown any significant increase in retention compared to controls. (66) PRP has also been studied as a possible enhancement to AFG. PRP (The extracted plasma layer from an individual's blood following centrifugation) contains both nutrients and growth factors, which could support the graft during the avascular stage and help to promote neovascularization. (67) Furthermore, compared to ADSCs, it is relatively easy, safe, and inexpensive. (67) Animal models have shown increased fat survival when grafts were enriched with PRP; however, clinical data has not shown significantly increased retention rates. (68,69)

1.3.8 Fat Grafting Complications

1.3.8.1 Recipient Site

The overall rate of complications after AFG is low regardless of the processing technique. (70) The most common minor complication is the presence of palpable nodules in the breast, which is a consequence of necrotic fat (6.2%). (70,71) Other minor complications include infections (0.85%), cysts (oil, simple) (4.5%), seroma (<0.1%), granuloma (<0.1%), dysesthesia, lymphadenopathy, pain and hematoma. (70,71,72) Aesthetic complications may occur as patients weight fluctuates, the grafted fat has memory, and acts similar to fat from the harvest site. This can lead to the overgrowth or resorption of fat grafts proportional to the original site. (73,73) Major complications are defined as complications that require surgical intervention. (71) Additional major complications include unsatisfactory volume, shape, or breast asymmetry. (71) Additionally, the greater the volume in the amount of fat injected, the higher the risk of a patient developing fat necrosis. (70,72) AFG poses a small risk of pneumothorax (collapse of the lung due to the needle being inserted into the thoracic cavity), fat emboli (the entry of adipose cells into the vascular system, causing an obstruction) and septicemia (Contamination of the injected fat, causing a systemic bacterial infection). (70,71,72)

Lesions such as calcifications and cysts may however complicate breast cancer screening and follow-up, with possible increased rates of false positives. Follow-up imaging and/or biopsy for definitive diagnosis is recommended for all palpable breast nodules. (72) In patients who previously had breast cancer, the rate of re-occurrence ranges from 0-12%, which is equivalent to the normal population. (70,71)

1.3.8.2 Donor Site

The site in which the fat is collected, has its own set of surgical complications. Fat can be harvested from nearly any site of excess. Complications can occur with the tumescent fluid, during the fat harvest and in the early or late post-operative phase. Tumescent fluid can vary; however, most published formulations contain lidocaine and epinephrine, both of which must be calculated pre-operatively to avoid toxicity. If not, this could lead to cardiac and neurological events, including arrythmias and seizures, respectively.

As the procedure is performed without direct visualization of the subcutaneous structures, there is a risk of nerve and vessel damage. If adipose cells enter the vascular system, this could lead to a fat embolus. More so, in the case of abdominal fat harvests, intra-abdominal injuries are a possibility. Either from entering the abdominal cavity with a cannula or injuring an undiagnosed hernial sac. Post-operatively, early complications, within the first 30 days, include hematoma, seroma, and superficial infections. Later complications include contour irregularities, skin laxity and dysesthesia.

1.3.9 Fat Survival and Analysis

On average, the post-operative fat loss ranges from 25-70% and only a percentage of injected fat cells will survive after one year. (75) As mentioned above, fat survivability is heavily influenced by the harvesting method as any damage to the adipocytes will reduce the survival rates of the cells. (75,76) It has however been demonstrated that there is no difference in fat survivability when it is harvested from the abdomen, lateral thigh,

inner thigh, and flank. (77) In order to promote fat viability, it is best to inject it at a slow rate to reduce the shear stress. (77,78) To optimize the survivability of the fat, it is best to place it in areas of high vascularity, typically in the periphery, in a “fanning-out” pattern. (78,79) Due to the low rates of fat survivability, it may be more beneficial to observe fat grafting as a percent augmentation versus a percent survival. (79) This would also be beneficial with patient counselling, advising them that a certain percentage of fat will survive, therefore, a larger volume would need to be injected, compared to referring to a specific volume.

The gold standard method for assessing fat viability is histologic analysis to assess for fibrosis, intact nucleated fat cells, mitochondrial function, and apoptosis. (80) Magnetic resonance imaging (MRI) can reliably assess breast volume; however, this is not a cost-effective or time efficient assessment method. (81) The most practical and validated method currently available to monitor and assess fat survivability is three-dimensional (3D) image analysis. (77,82) There are many 3D scanners available, but the most accurate and reliable tool available to assess breast volume is the VECTRA 3D imaging system (Canfield, NY, USA). (81)

1.3.10 Future Trends

At present, breast implants remain the primary option for the majority of augmentations, future trends will need to focus on further improving the physical implant. Particularly, minimizing the rates of capsular contracture and mitigating any oncological risk. (83) The focus of new breast implants should also favor optimizing

minimally invasive surgical techniques and improving patient understanding regarding recall, replacement, and long-term risks. (83)

In fat grafting, future advancements should focus on reducing inflammation and improving the design of adipose extraction and processing to ultimately help improve outcomes and fat survival. (84,85) As fat grafting is also a relatively newer technique used by this generation of surgeons, there will be a greater shift in helping to clarify inconsistencies in study results and methodology in human studies, to better understand ideal patient selection criteria to ensure optimal results in patients seeking fat grafting to improve previous surgeries as well as those selecting fat grafting as a primary augmentation method. (85)

With current advances in fat grafting and its current success, it is predicted that fat grafting could replace the need for implant-based breast augmentation in a significant subset of the patient population. (86) Fat grafting offers numerous benefits. It's non-immunogenic, versatile, bio-compatible, and readily available. More so, it's relatively minimally invasive, with no large incisions. (86) Fat grafting advances will also help the development of other cosmetic procedures as this technique is also currently being used for facial and body contouring, wound healing, and the treatment of inflammatory conditions. (87)

At present, fat retention, predictability and analysis remain the most complicated aspects. It is difficult to guarantee certain volumes post-operatively, however, the literature has demonstrated that several sessions of fat grafting are safe, if, the above pathophysiology of fat survival is respected. The first session also demonstrates the

amount of fat survival to be expected in each patient, allowing for relatively more predictable future sessions.

1.4 Autologous Breast Reconstruction

A subset of patients undergoing breast augmentation have had previous surgery due to breast cancer. Patient factors in these circumstances are more nuanced when assessing the appropriate method of reconstruction and augmentation. Implants and fat grafting can be used in tandem, initially, to create the optimal size and then contour post-operatively with fat grafting. However, certain patients would not be amenable to implants or fat grafting, as the tissue loss from cancer is too large and/or patients require or have received radiation as part of their cancer treatment that has fibrosed the recipient site and altered the micro-environment, as well as the regional capacity for neovascularization.

These patients may instead be advised to undergo more elaborate reconstruction using local, regional, or free flaps to bring healthy, non-radiated tissue into the breast recipient site as a partial or total replacement of breast tissue. Autologous reconstructions (to replace partial or total breast volumes lost to cancer surgery) differ from fat grafting in that the total tissue with its own blood supply is harvested from one site and relocated to the breast area. While outside of the scope of discussion for this thesis aimed at evaluating fat grafting techniques, a review of the current gold standard of free flap reconstruction along with alternatives is attached. (Appendix 1).

1.5 Conclusion

Currently, patients can choose whether they prefer to receive implant-based or fat grafting breast augmentation. Patient selection and thorough understanding of both procedures is critical. Future directives should include focusing on comparing patient outcomes and satisfaction for patients who undergo implant-based augmentation and fat grafting. More human studies should focus on improving techniques to optimize fat retention and survival factors. This will allow for the implementation of best-practice guidelines regarding patient selection and operative techniques for fat grafting.

CHAPTER 1 – REFERENCES

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2 Fat Grafting vs. Implants: Who's Happier? A systematic review and meta-analysis

This chapter is an altered version of a manuscript pending submission to the plastic and reconstructive surgery journal (PRS). Following from the above chapter, the review addresses the two common methods of breast augmentation from the patient's perspective. To date, this is the most comprehensive qualitative meta-analysis assessing primary breast augmentation.

2.1 Background

2.1.1 Breast Augmentation

Breast implants were first introduced in the 1960s in Texas and have long been used for reconstructive and cosmetic surgery and have since created a multi-million-dollar industry. (1,2,3,4) Breast implants are the most common mode for breast reconstruction and accounted for 72.3% of breast augmentation procedures in 2016. (5) Breast implants now come in many different shapes, sizes, and materials for patients to achieve the best possible result based on their wants and needs. (2,6) Implant-based breast procedures carry several risks of complications, including capsular contracture, breast animation, implant failure, breast implant-associated

anaplastic large cell lymphoma (BIA-ALCL), and possible consequences to psychological well-being. (4,5,6)

Fat grafting, otherwise known as fat transfer, lipoagumentation, liposculpture, or lipomodeling, has created a shift in the field of plastic and reconstructive surgery in the approach to patient care. (4,7) Fat grafting was first introduced in 1897 by Czerny for reconstructive surgery. (7) In 1987, the American Society of Plastic Surgeons condemned fat grafting procedures with concerns for oncological safety but have since been proven to have no additional risk, and in 2009, fat grafting was revisited and approved as a technique that could be used in plastic and reconstructive surgery. (1,8) Since the year 2000, fat grafting accounts for a 29% increase in breast reconstruction and a 25% increase in cosmetic breast surgery. (1) In cosmetic surgery for primary augmentation, it provides an advantage of breast augmentation without a prosthetic device which eliminates the possibility for rippling and other cosmetic concerns and complications seen with breast implants. (1,4) This procedure is best suited to patients who would like a moderate increase in their breast volume, typically seen in patients who underwent significant weight loss or post-pregnancy or in reconstructive patients such as in post-breast cancer reconstructive surgery.

2.1.2 Patient reported outcome measures (PROM)

In cosmetic and reconstructive patients, it is important to assess a patient's perception of their quality of life (QoL) to determine the impact on a patient's appearance, functional and mental health. (9) By assessing QoL in patients in a valid, systematic, and reliable way, it can help influence future decision-making for patients

and physicians. (10) However, when using the patient's perspective on their quality of life and outcomes, it is subjected to many biases, and the response rate can be heavily influenced by motivation, health, age, and socioeconomic status. (11)

The importance of PROMs, particularly in the field of plastic and reconstructive surgery, where we aim improve form, just as much as function cannot be overstated. A patient will, in most cases, negate the surgical results if their quality of life remains poor. PROMs can be broken down by generic, specialty, or procedure specific. A 2019 review by Sharma et al. highlighted the currently available instruments available to assess PROMs in plastic and reconstructive surgery. For the breast, they highlighted three instruments. BreastQ, Breast evaluation questionnaire (BEQ) and Breast reduction assessed severity scale questionnaire (BRASSQ). Of note, BreastQ and BEQ are the only two breast specific instruments that are validated to assess breast augmentation. They concluded that BreastQ is currently the most well-validated breast specific PROM instrument available, with the added benefit of having a pre-operative and post-operative component.

2.1.3 BreastQ

BREAST-Q is an example of a patient-reported outcome measure (PROM) as it is a standardized form completed by patients. (9) The BREAST-Q questionnaire was developed in 2009 and can be used for various cohorts of patients, including augmentation, reduction, and reconstructive patients. It aims to investigate topics known as modules such as psychosocial, physical, sexual well-being, satisfaction of care, and satisfaction of breasts. (9,10,12) Since its introduction, BREAST-Q has

become the gold standard for assessing quality of life and patient satisfaction for patients undergoing breast surgery. (12) (Appendix 4)

The BREAST-Q module for women who undergo breast augmentation is a rigorously developed PROM that is comprised of 9 independently functioning scales. (9) It has undergone extensive psychometric evaluation and its developers report that it may be used like interval-scale data. Scores from these instruments are scaled to range from 0 to 100.

This review aims to highlight the importance of PROMs when considering various surgeries. There have been several observational and assessment tools to compare cosmetic outcomes. However, to use a relatively objective scale to assess how satisfied a person is with their initial objective, in this case augmentation, is valuable. The use of blinded surgeons to evaluate before and after images only gives us one perspective. Arguably, a surgeon's visual assessment of an outcome is important, however, as surgeons, we are sometimes biased with varying levels of expectations post-operatively compared to patients.

The main outcome in this study is PROMs using BREAST-Q. This systematic review and meta-analysis aim to compare patients 'quality of life outcomes using BREAST-Q to assess if patients who undergo fat grafting or implant-based primary augmentations are more satisfied.

2.2 Methods

2.2.1 Search Strategy

Prior to commencing the review, the PROSPERO database was searched, and no similar review was found. The study methodology was then designed and was registered in the PROSPERO database (CRD42022297860). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline was used (Appendix 2). The search strategy was designed by the lead author and two reviewers (K.M. and K. J.). The search strategy included search terms related to primary breast augmentation, the two methods of interest, and terms related to the primary outcome, Breast-Q. The full search strategy, including terms used can be seen in Appendix 2.

Five bibliographic databases were searched: PubMed®, Cochrane Library®, EMBASE®, MEDLINE® and Scopus ®. The search was conducted on November 4, 2021. References were manually screened by the lead author and two reviewers from relevant review articles to identify if there were any studies that were not captured in the initial search. However, no additional sources were identified in this process.

2.2.2 Inclusion and Exclusion Criteria

Inclusion and exclusion criteria were determined *a priori*. We included prospective studies, retrospective studies and randomized controlled trials written in English or French, published in peer reviewed journals over the past ten years from the date of the search. As autologous fat grafting was approved in 2009, a range from 2011-2021 would allow us to capture similar data from both groups. Only studies that

included patients who underwent primary breast augmentation using either implants or fat grafting for aesthetic purposes were included. Studies reporting on augmentation with a combination of implant and fat grafting, or breast reconstruction were excluded. Patients who have had a previous mastectomy were excluded due to them having undergone a previous breast surgery which may skew their score. We excluded patients undergoing gender affirmation surgery as they would be unable to complete the pre-operative BreastQ survey. Patients who have had massive weight loss have been excluded from the study as their surgeries are multifactorial and would not be eligible for fat grafting as they would typically require skin removal. We excluded patients who have had multiple sessions of fat grafting, as we are assessing the primary surgery in this review. All studies must report at minimum post-operative Breast-Q data as a study outcome to be included. Single case reports, reviews, animal studies, conference proceedings, abstracts, inaccessible manuscripts, editorials and articles not reporting BreastQ were excluded. (Table 1).

Parameters	Inclusion	Exclusion
Journal Characteristics	Prospective, Retrospective or Randomized controlled trial Peer Reviewed English	Editorial, Case Report, Abstract, Presentation, Poster Non-Peer Reviewed Non-English Published prior to 2011
Sample characteristics	Human N >1 Primary breast augmentation patients	Non-human Breast Reconstruction patients (mastectomy) Gender confirmation surgery Massive weight loss
Methods	Primary Implant augmentation (Any type of implant) Primary fat grafting augmentation	Combination implant and fat grafting augmentation Revision of previous augmentation (ex. Implant exchange, implant removal and fat grafting, secondary fat grafting session)
Outcomes	Primary: BREAST-Q Secondary: common complications • Fat necrosis • Implant rupture • Hematoma • Seroma • Infection	Does not report BREAST-Q

Table 1. Inclusion and Exclusion Criteria.

2.2.3 Study Selection

Studies extracted were analyzed, and duplicates were eliminated. The primary investigator extracted the studies which then underwent screening by two independent reviewers (K.J. and K.M.) using Rayyaan platform to organize and manage the articles for a systematic review (Rayyaan Systems Inc., Cambridge, MA, USA). For the primary screen, titles and abstracts were reviewed. Selected articles underwent full-text review for the secondary screening. The principal investigator functioned as an independent arbitrator (K.A.) and was available for any conflict disputes. The Methodological Index for Non-Randomized studies (MINORS) score was used to assess the quality of all articles selected for the review and meta-analysis. Papers that failed to achieve a benchmark score of 60% or higher were excluded. (Appendix 2)

2.2.4 Data Extraction

The two independent reviewers (K.J and K.M) extracted data using the Google Sheet platform (Google, Mountain View, CA, USA). Any possible errors were reviewed and discussed with the principal investigator (KA) to ensure correctness. Study type, number of patients, average age and BMI, type of augmentation, augmentation characteristics and surgical technique, pre- and post-operative Breast-Q data, and common complication rates were extracted. Attempts were made to contact the authors of any study that had incomplete Breast-Q data or mentioned conducting Breast-Q but where the Breast-Q data was not reported in their paper.

2.2.5 Statistical analysis

Statistical and meta-analysis was conducted by a contracted statistician. Cohen's kappa coefficient was calculated to assess for inter-rater reliability for article selection, with values 0.41-0.60, 0.61-0.80 and 0.81-1.00 representing moderate agreement, substantial agreement, and perfect agreement respectively. Studies that reported multiple patient groups using the same augmentation technique were pooled to create a single summary for that study.

Mean scores from the Breast-Q instruments were meta-analyzed using random-effects models with the empirical Bayes between-study variance estimator.[13] As pre-operative scores were not consistently available, the primary outcome measure was the post-operative mean Breast-Q score, and whether the pooled average was different between breast augmentation methods, either using implants or fat grafting. Therefore, post-op mean scores were stratified by surgical method as the main factor of interest. Inferences about the differences in pooled subgroup means were performed using meta-regression, which is well-known as a form of subgroup analysis. Reported demographics in the pre-op period (age, BMI) were used to explore possible sources of heterogeneity by meta-regression.

Between-group heterogeneity was characterized using the random-effects heterogeneity parameter (τ^2), and I^2, which describe the absolute or relative degree of between-study heterogeneity. For the meta-regression models, the adjusted R^2 statistic was used to assess the proportion of variance between studies, which could be attributed to the covariates. Publication bias was assessed by funnel plots, as well as Egger's regression test. Galbraith plots (also known as radial plots) with the same

random-effects model were assessed to examine between-study heterogeneity and to identify potential outlier studies.

Bivariate meta-regression of scores were used to corroborate whether and to what extent were potential differences in pooled estimates of post-op scores between surgical methods confounded by the few available pre-op scores. These models included surgical method as the only factor and were fit using a random-effects model restricted maximum likelihood estimator. A conservative value of 0.2 was assumed for the within-study correlation between pre-op and post-op scores.

All analyses were performed in Stata 17 (StataCorp LLC, College Station, TX).

2.3 Results

2.3.1 Study Characteristics

The search strategy identified a total of 1398 articles and an additional 5 were added from relevant reviews discovered in the search. After duplicates were removed, a total of 597 articles were screened using title and abstract. A total of 57 articles were selected for full text review, and 22 fit the inclusion criteria and were deemed suitable by both reviewers and independent arbitrator for data extraction. The Cohen's Kappa scores were 0.87 for primary screen and 0.88 for secondary screen. All studies included received a MINORS Score of 60% or higher. Of these 22 studies, 14 included data that could be pooled for a meta-analysis, which included two fat grafting studies, ten implant studies and two studies that included data from both methods (Figure 1). Total number of

patients included in this study was 1616, with 81 in the fat grafting group and 1535 in the implant group.

2.3.2 Post-operative satisfaction score

Two small studies (Brault and Tenna) reported on both fat grafting and implant augmentation methods. The mean satisfaction score for implants was 12.9 points greater than with fat grafting (95% CI: -0.6, 26.5, p=0.061; Figure 1), with only moderate heterogeneity (Q=2.68, p=0.11).

	Fat grafting		Implant	
Study label	Size (N)	Post-op score mean (SD)	Size (N)	Post-op score mean (SD)
Brault (2017)	22	71.4 (21.8)	15	51.6 (8.6)
Tenna (2017)	22	78.0 (22.0)	16	72.0 (11.0)

Table 2. Studies comparing satisfaction scores for both augmentation methods (N=2)

Abbreviations: SD, standard deviation

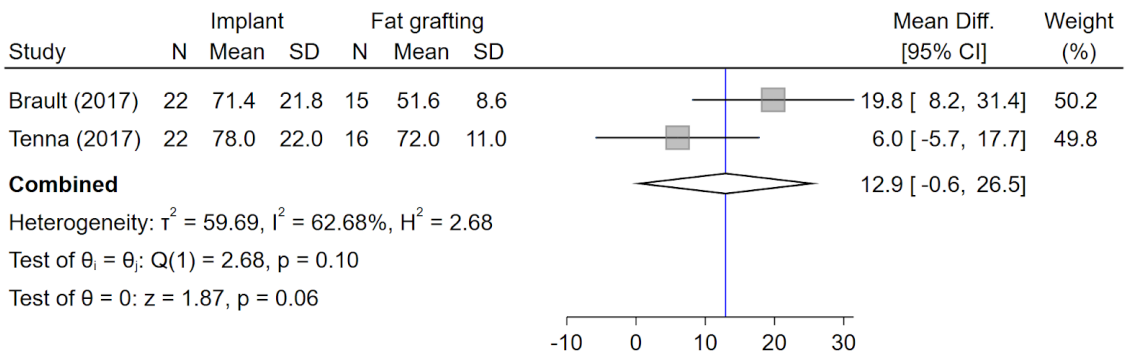

Figure 1. Forest plot of mean difference in post-op satisfaction score between augmentation methods.

There were 14 studies that reported post-operative satisfaction scores that could be pooled, and infrequently reported pre-op scores (Table 3). Mean post-op scores were pooled for each method of augmentation, and overall (Figure 2) there was no evidence of publication or small study bias, but the relative heterogeneity within augmentation groups was high.

Study	Method	Size (N)	Pre-op score mean (SD)	Post-op score mean (SD)
Overschmidt (2018)	Implant	72	20.6 (15.1)	85.3 (12.3)
Overschmidt (2018)	Implant	13	19.3 (18.2)	87.2 (14.1)
Randquist (2018)	Implant	22	n.r.	69.2 (14.8)
Guo (2019)	Fat grafting	8	16.8 (16.5)	50.4 (16.6)
Xu (2006)	Implant	70	14.7 (11.0)	64.9 (5.6)
Deschler (2020)	Fat grafting	42	23.8 (20.8)	62.8 (13.3)
Diaz (2017)	Implant	150	n.r.	80.6 (15.1)
McCarthy (2012)	Implant	41	27.0 (18.0)	70.0 (23.0)
Bracaglia (2020)	Implant	70	29.6 (13.3)	85.5 (6.6)
Xiao (2020)	Implant	57	30.3 (6.1)	55.8 (7.8)
Xiao (2020)	Implant	66	29.6 (6.3)	55.4 (8.6)
Gryskiewicz (2014)	Implant	670	n.r.	76.0 (16.6)
Faure (2021)	Implant	40	n.r.	71.8 (18.5)
Li (2021)	Implant	65	22.5 (12.1)	76.6 (11.8)
Li (2021)	Implant	155	16.1 (10.3)	60.8 (19.3)
Brault (2017)	Fat grafting	15	n.r.	51.6 (8.6)
Brault (2017)	Implant	22	n.r.	71.4 (21.8)
Tenna (2017)	Fat grafting	16	n.r.	72.0 (11.0)
Tenna (2017)	Implant	22	n.r.	78.0 (22.0)

Table 3. Reported Pre-op and post-op satisfaction scores (N=14 studies)

Abbreviations: n.r., not reported; SD, standard deviation

For analysis, groups were pooled within studies if the same augmentation method was used.

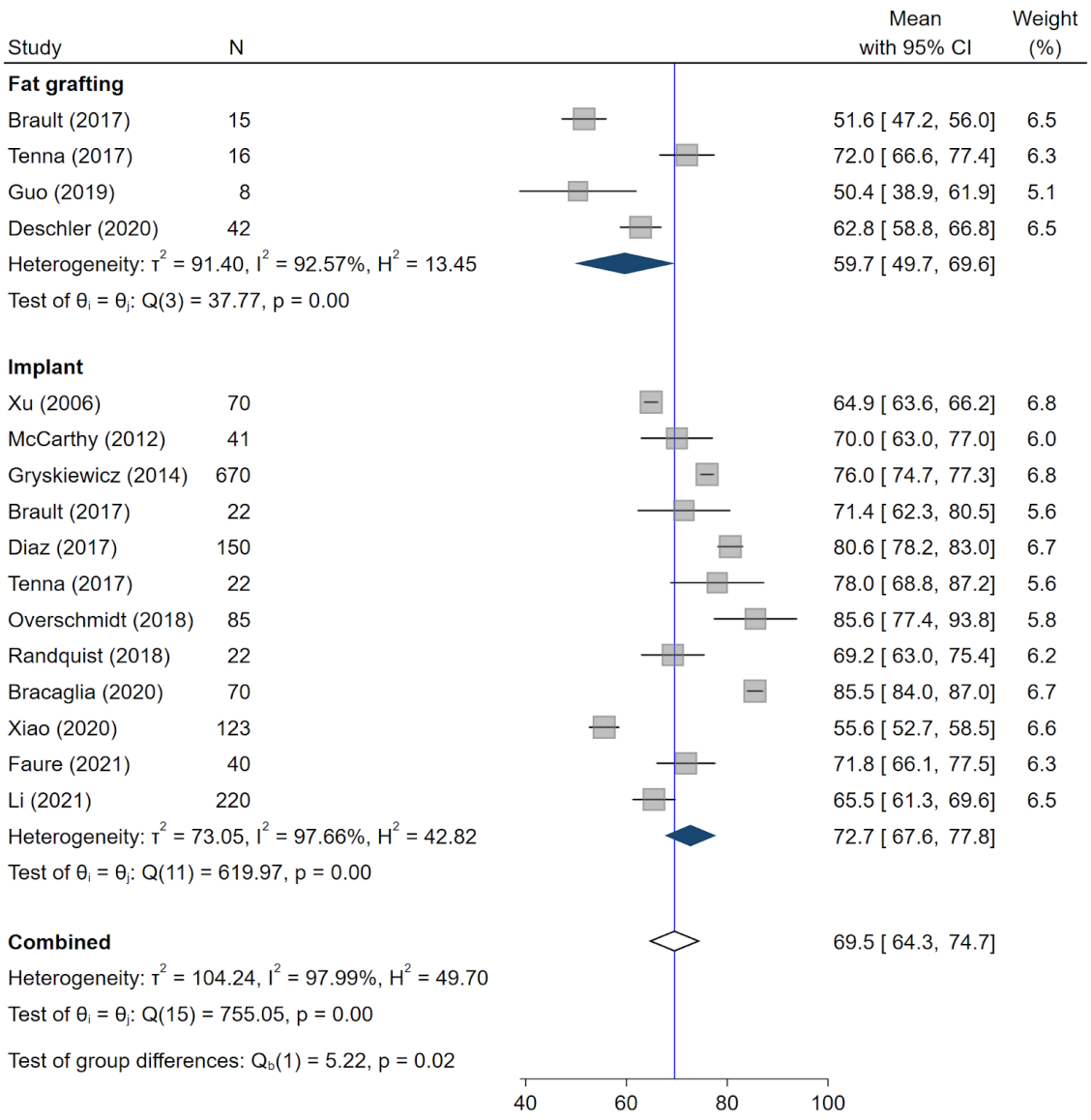

Figure 2. Forest plot of post-op satisfaction scores, stratified by augmentation method (raw mean).

The pooled mean in the implant group is statistically greater than in the fat grafting group (**Figure 2**). Based on meta-regression, the estimated difference in mean post-op satisfaction scores is 13.0 (95% CI: 2.4 to 23.5; p=0.016). Augmentation method explained 26.4% of observed variation.

Factor	**Studies**	**Mean**	**95% CI**	**p-value**	***R²* (%)**	***I²* (%)**
Age, mean	13	0.86	(-0.15, 1.86)	0.094	14.2	97.7
BMI, mean	8	2.83	(-1.02, 6.68)	0.149	14.5	97.9

Table 4. Univariable meta-regression of post-op satisfaction score on baseline characteristics.

Table 4 shows univariable meta-regression of post-op satisfaction scores on mean post-op age and BMI. Despite some studies failing to report demographic details, both age and BMI were strongly associated with greater post-op satisfaction scores. Both factors explained about 20% of observed variation among the subset of reporting studies.

Factor	Mean	95% CI	p-value	
Implant method	10.45	(-5.59, 26.49)	0.202	
Age, mean	1.01	(-0.32, 2.35)	0.137	
BMI, mean	3.51	(0.16, 6.87)	0.040	
Joint test of coefficients, p-value				0.044
80.36				
R^2 (%)				45.7
I^2 (%)				94.3
Studies				8

Table 5. Multivariable meta-regression of post-op satisfaction score.

Meta-regression of post-op scores on age, BMI and method substantially reduced the between-study heterogeneity parameter (τ^2), reduced (I^2), and increased the proportion of explained variance (R^2). The implant method is still associated with a greater score than fat grafting after adjusting for age and BMI. Overall, these three factors appear to account for much of the between-study heterogeneity (**Table 5**).

To support the claim that differences in post-op mean scores between methods are not confounded by pre-op scores, a bivariate meta-regression was conducted to account for pre-op scores, using method as the only covariate. Using bivariate meta-regression, the mean change in the implant group was grater in magnitude, but not statistically significant, from the change in the fat grafting group 12.4 (95% CI: -4.9 to 29.6; p=0.160). That this difference was similar in magnitude corroborates that pre-op scores did not differ between groups. Following bivariate meta-analysis, heterogeneity was reduced in post-op scores (I^2=74.4%).

2.3.3 Post-operative sexual well-being score

Two small studies reported on both fat grafting and implant augmentation methods (**Table 6**). The mean sexual well-being score was similar in both implant and fat grafting groups (difference = -0.4, 95% CI: -16.9, 16.0, p=0.96; **Figure 3**), with moderate heterogeneity (Q=3.41, p=0.06).

	Fat grafting		**Implant**	
		Post-op score		**Post-op score**
Study label	**Size (N)**	**mean (SD)**	**Size (N)**	**mean (SD)**
Brault (2017)	22	65.7 (24.4)	15	56.8 (19.3)
Tenna (2017)	22	74.0 (14.0)	16	82.0 (18.0)

Table 6. Studies comparing sexual well-being scores for both augmentation methods (N=2)

Abbreviations: SD, standard deviation

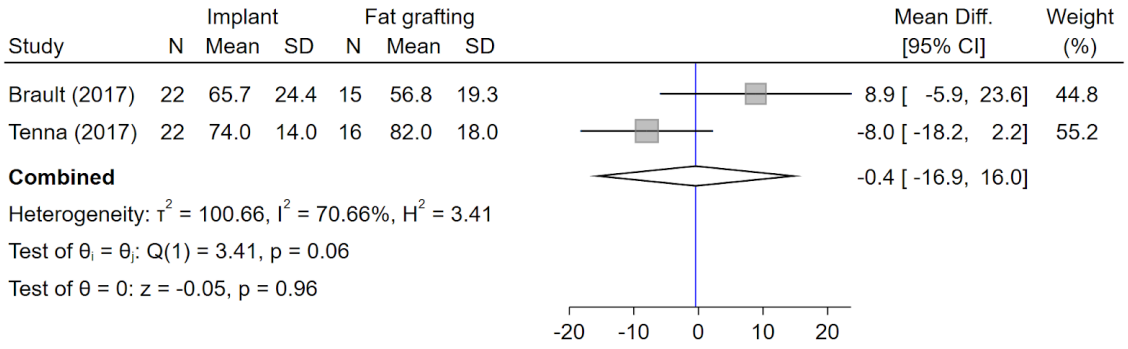

Figure 3. Forest plot of mean difference in post-op sexual well-being score between augmentation methods.

There were 13 studies that reported post-operative sexual well-being scores that could be pooled (**Table 7**). Mean post-op scores were pooled for each method of augmentation, and overall (**Figure 4**). There was no evidence of publication or small study bias, but the relative heterogeneity within augmentation groups was high.

Study	**Method**	**Size (N)**	**Post-op score mean (SD)**	**Post-op score mean (SD)**
Overschmidt (2018)	Implant	13	36.2 (20.8)	95.1 (7.8)
Overschmidt (2018)	Implant	72	36.7 (18.2)	90.4 (13.5)
Randquist (2018)	Implant	22	n.r.	80.0 (22.7)
Guo (2019)	Fat grafting	8	25.6 (16.9)	75.4 (12.3)
Xu (2006)	Implant	70	16.1 (9.3)	83.9 (8.5)
Deschler (2020)	Fat grafting	42	40.4 (18.0)	57.1 (17.6)
Diaz (2017)	Implant	150	n.r.	88.0 (17.8)
McCarthy (2012)	Implant	41	35.0 (19.0)	72.0 (29.0)
Bracaglia (2020)	Implant	70	35.4 (25.7)	91.6 (6.5)
Xiao (2020)	Implant	66	35.6 (6.7)	51.0 (8.3)
Xiao (2020)	Implant	57	36.2 (8.8)	52.8 (9.3)
Faure (2021)	Implant	40	n.r.	62.4 (17.4)
Li (2021)	Implant	65	29.4 (9.7)	61.5 (14.6)
Li (2021)	Implant	155	30.5 (10.4)	62.4 (25.5)
Brault (2017)	Fat grafting	15	n.r.	56.8 (19.3)
Brault (2017)	Implant	22	n.r.	65.7 (24.4)
Tenna (2017)	Fat grafting	16	n.r.	82.0 (18.0)
Tenna (2017)	Implant	22	n.r.	74.0 (14.0)

Table 7. Reported Pre-op and post-op sexual well-being scores (N=13 studies)

Abbreviations: n.r., not reported; SD, standard deviation

For analysis, groups were pooled within studies if the same augmentation method was used.

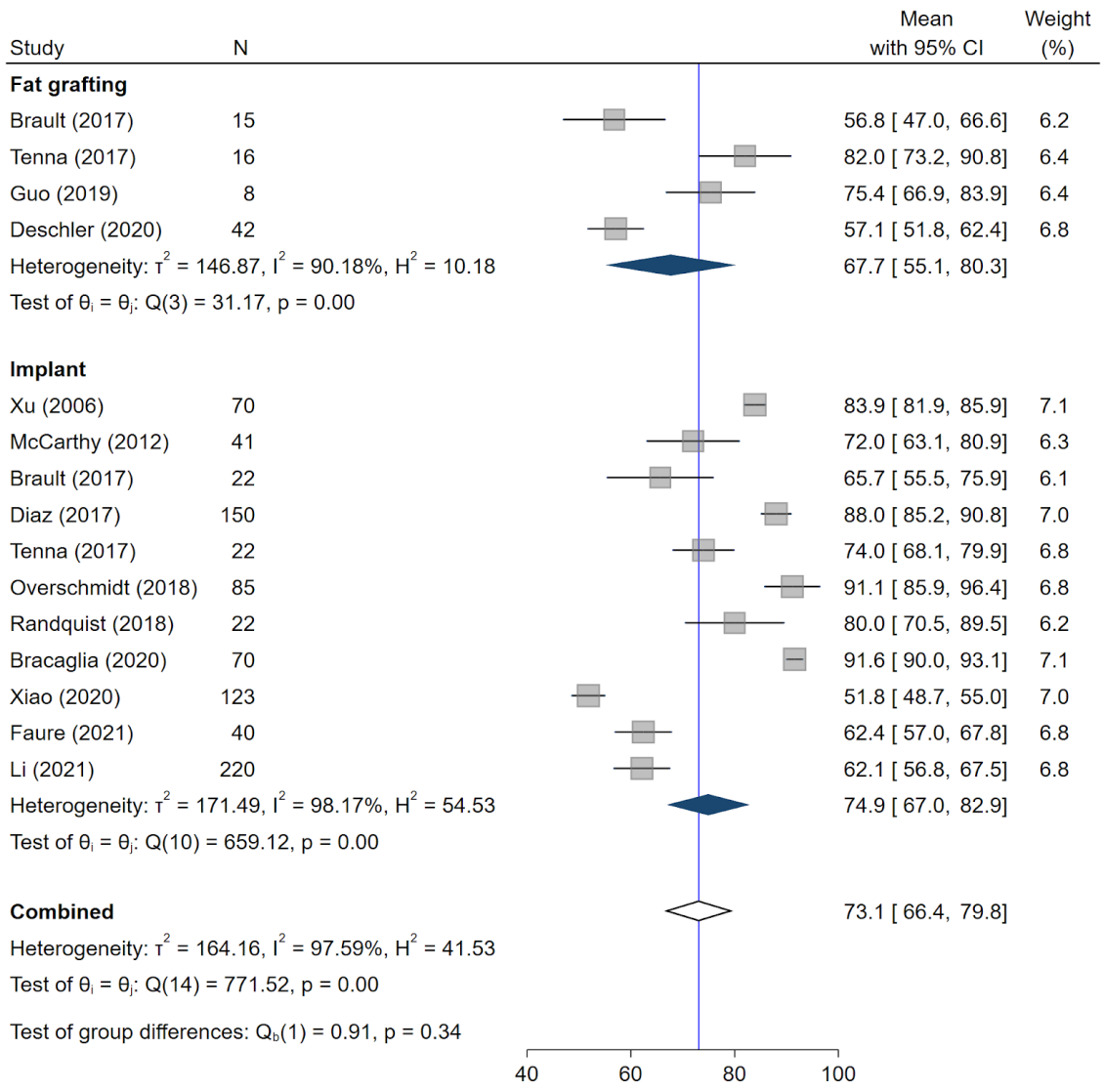

Figure 4. Forest plot of post-op sexual well-being scores, stratified by augmentation method (raw mean).

2.3.4 Post-operative psychosocial well-being score

Two small studies reported on both fat grafting and implant augmentation methods (**Table 8**). The mean sexual well-being score was similar in both implant and fat grafting groups (difference = -2.8, 95% CI: -3.1, 8.6, p=0.35; **Figure 5**), with no heterogeneity (Q=0.96, p=0.33).

	Fat grafting		**Implant**	
		Post-op score		**Post-op score**
Study label	**Size (N)**	**mean (SD)**	**Size (N)**	**mean (SD)**
Brault (2017)	22	63.0 (22.8)	15	67.2 (23.4)
Tenna (2017)	22	83.0 (8.0)	16	79.0 (12.0)

Table 8. Studies comparing sexual well-being scores for both augmentation methods (N=2)

Abbreviations: SD, standard deviation

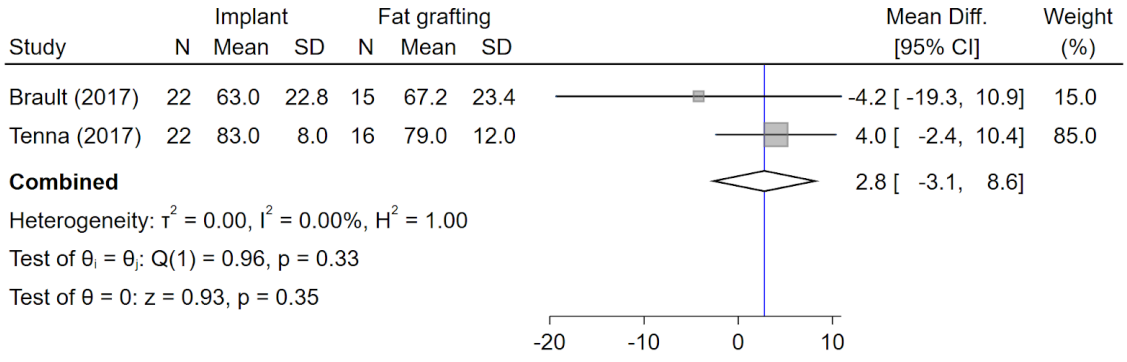

Figure 5. Forest plot of mean difference in post-op psychosocial well-being score between augmentation methods.

There were 13 studies that reported post-operative sexual well-being scores that could be pooled (**Table 9**). Mean post-op scores were pooled for each method of augmentation, and overall (**Figure 6**).

Study	**Method**	**Size (N)**	**Post-op score mean (SD)**	**Post-op score mean (SD)**
Overschmidt (2018)	Implant	72	49.5 (18.1)	91.0 (12.9)
Overschmidt (2018)	Implant	13	48.2 (14.1)	93.2 (12.7)
Randquist (2018)	Implant	22	n.r.	84.0 (21.0)
Guo (2019)	Fat grafting	8	37.1 (12.7)	55.1 (11.7)
Xu (2006)	Implant	70	10.2 (13.1)	78.9 (10.1)
Deschler (2020)	Fat grafting	42	43.1 (22.8)	63.5 (16.4)
Diaz (2017)	Implant	150	n.r.	89.1 (16.5)
McCarthy (2012)	Implant	41	45.0 (19.0)	78.0 (24.0)
Bracaglia (2020)	Implant	70	44.3 (10.9)	89.9 (8.7)
Xiao (2020)	Implant	57	36.5 (5.1)	48.5 (9.2)
Xiao (2020)	Implant	66	35.8 (5.5)	47.4 (6.9)
Faure (2021)	Implant	40	n.r.	64.7 (16.7)
Li (2021)	Implant	65	40.7 (13.4)	67.6 (17.8)
Li (2021)	Implant	155	41.4 (14.1)	71.9 (21.0)
Brault (2017)	Fat grafting	15	n.r.	67.2 (23.4)
Brault (2017)	Implant	22	n.r.	63.0 (22.8)
Tenna (2017)	Fat grafting	16	n.r.	79.0 (12.0)
Tenna (2017)	Implant	22	n.r.	83.0 (8.0)

Table 9. Reported Pre-op and post-op psychosocial well-being scores (N=13 studies)

Abbreviations: n.r., not reported; SD, standard deviation
For analysis, groups were pooled within studies if the same augmentation method was used.

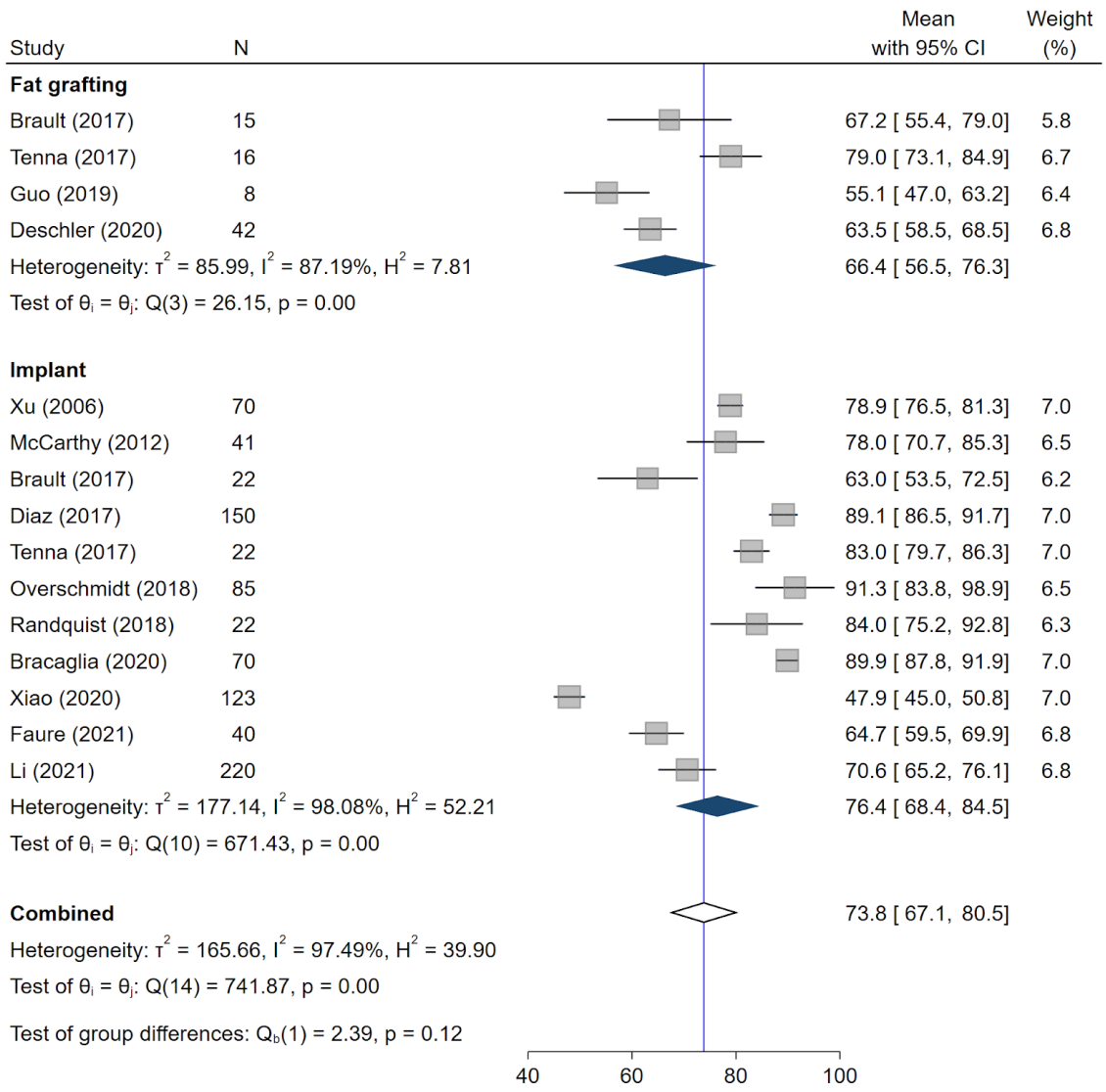

Figure 6. Forest plot of post-op psychosocial well-being scores, stratified by augmentation method (raw mean).

The pooled mean in the implant group showed no statistically significant difference than in the fat grafting group (**Figure 6**). Based on meta-regression, the estimated difference in mean post-op psychosocial well-being scores is 10.1 (95% CI: -4.8 to 25.1; p=0.184). Augmentation method explained 5.4% of observed variation. The study by Xiao et al (2020) is an apparent outlier based on a Galbraith plot. Excluding this

study resulted in a more precise estimate of the difference between methods, in which the average implant group had a significantly higher score than fat grafting by 13.1 (95% CI: 1.2 to 25.1; p=0.031). The variation explained by method also increased to 24.1%.

Factor	**Studies**	**Mean**	**95% CI**	**p-value**	***R²* (%)**	***I²* (%)**
Age, mean	11	1.49	(0.57, 2.41)	0.001	52.1	89.4
BMI, mean	7	-0.24	(-5.81, 5.32)	0.931	0.0	97.9

Table 10. Univariable meta-regression of post-op psychosocial well-being score on baseline characteristics. * Excluding the study by Xiao (2020).

Table 10 shows univariable meta-regression of post-op psychosocial well-being scores on mean pre-op sex and BMI. Despite some studies failing to report demographic details, both age and BMI were strongly associated with greater post-op psychosocial well-being scores. Both factors explained about 20% of observed variation among the subset of reporting studies.

Factor	**Mean**	**95% CI**	**p-value**	
Implant method	12.13	(2.19, 22.06)	0.017	
Age, mean	1.25	(0.48, 2.03)	0.002	
Joint test of coefficients, p-value				0.000
36.93				
R² (%)				71.4
I² (%)				82.9
Studies				11

Table 11. Multivariable meta-regression of post-op satisfaction score.

Meta-regression of post-op scores on age and method substantially reduced the between-study heterogeneity parameter (τ^2), reduced (I^2), and increased the proportion of explained variance (R^2). BMI was not associated with post-op score in univariate regression and was not included in this model. The implant method is still associated with a greater score than fat grafting after adjusting for age, and excluding the single outlier study by Xiao (2020) (**Table 11**)

2.3.5 Post-operative physical well-being score

There were no studies that provide direct comparison of the physical well-being scores. There were 8 studies that reported post-operative sexual well-being scores that could be pooled (**Table 12**). Mean post-op scores were pooled for each method of augmentation, and overall (**Figure 7**).

Study	Method	Size (N)	Post-op score mean (SD)	Post-op score mean (SD)
Randquist (2018)	Implant	22	n.r.	86.1 (13.4)
Xu (2006)	Implant	70	87.1 (10.4)	85.2 (11.7)
Deschler (2020)	Fat grafting	42	90.1 (15.0)	90.4 (10.6)
Diaz (2017)	Implant	150	n.r.	86.7 (13.5)
Bracaglia (2020)	Implant	70	92.1 (10.2)	89.9 (9.0)
Xiao (2020)	Implant	57	92.8 (6.7)	92.8 (8.0)
Xiao (2020)	Implant	66	93.1 (7.1)	92.4 (7.0)
Faure (2021)	Implant	40	n.r.	22.9 (17.1)
Brault (2017)	Fat grafting	15	n.r.	85.6 (12.2)
Brault (2017)	Implant	22	n.r.	79.9 (20.1)

Table 12. Reported Pre-op and post-op physical well-being scores (N=8 studies)

Abbreviations: n.r., not reported; SD, standard deviation
For analysis, groups were pooled within studies if the same augmentation method was used.

The pooled mean in the implant group showed no statistically significant difference compared to the fat grafting group (**Figure 7**). Based on meta-regression, the estimated difference in mean post-op physical well-being scores is -10.4 (95% CI: -46.0 to 25.3; p=0.569).

The study by Faure et al (2021) was identified as an outlier based on Galbraith and funnel plots. Excluding this study resulted in making estimates of mean scores in each augmentation group more similar, with a difference in means of -1.0 (95% CI: -7.2 to 5.3; p=0.762) (**Figure 8**).

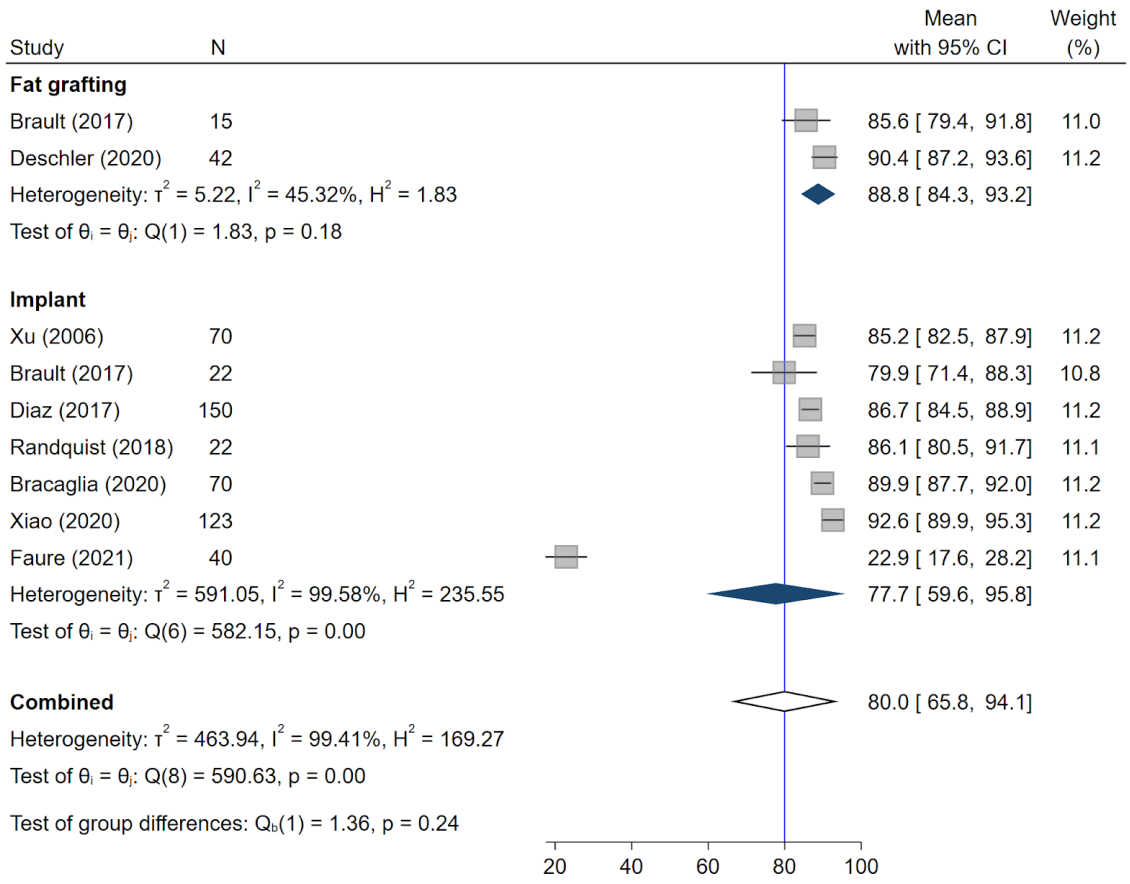

Figure 7. Forest plot of post-op physical well-being scores, stratified by augmentation method (raw mean).

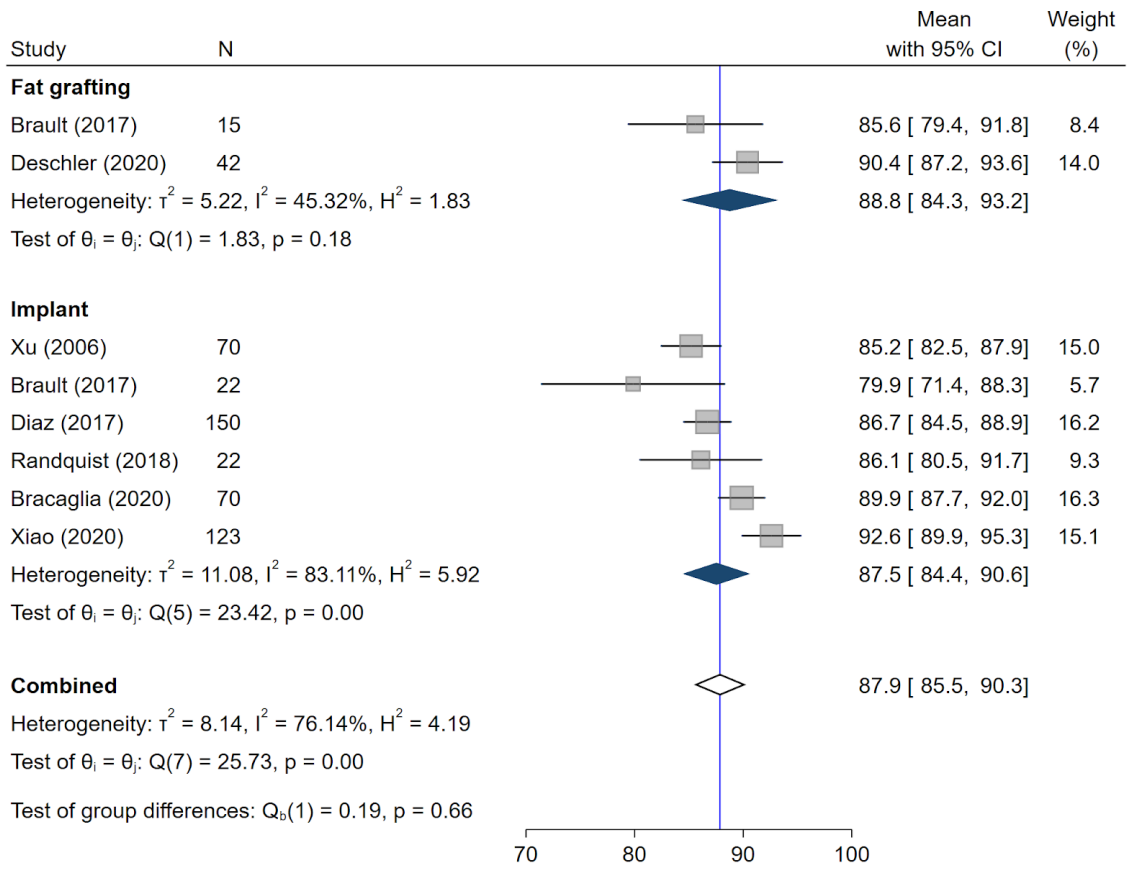

Figure 8. Forest plot of post-op physical well-being scores, stratified by augmentation method (raw mean), excluding outlier.

2.4 Discussion

BREAST-Q is a validated tool that can be used to evaluate patient-reported QoL in post-operative breast augmentation patients. (17) This meta-analysis investigated the QoL using BREAST-Q in patients who underwent cosmetic breast augmentation with either fat grafting or breast implants. To our knowledge, there has been no other study that compared breast augmentation using breast implants exclusively or exclusively fat grafting for cosmetic breast augmentation.

Overall, in this review the results demonstrated that patients who received implant-based breast augmentation reported a higher overall satisfaction score than those who received fat grafting. The results show no difference amongst both groups in terms of sexual well-being, physical well-being, and psychosocial well-being scores in the BREAST-Q modules. One possible explanation for the higher overall satisfaction, is that implant augmentation is one of the most common cosmetic procedures, and surgeons have developed standardized methods to give an overall more reliable and predictable result in size and shape of the breasts, leading to increased satisfaction. (18) In comparison, fat grafting for breast augmentation, is a much newer procedure, and lacks standardized surgical methods. The major limitations of fat grafting are the limit of volume increase that can be reliably achieved, and the degree of fat resorption, which can be up to 60% of fat injected. (19) However, there are advantages, as the lack of a foreign body may decrease long term complication rates, and re-operation rates. (20) More long-term follow-up studies are needed to determine the satisfaction of patients over their lifetime post-augmentation.

In this study, there were two major outliers. One implant study reported lower physical well-being scores; this is likely because it was a tuberous breast study (Faure et al., 2021). A possible explanation of these results is that patients who undergo breast augmentation with tuberous breasts, who sometimes require several surgical procedures during their primary procedure, often suffer from physical post-operative symptoms including bruising and swelling, which may impact patient quality of life. (21) The second outlier was in the psychosocial well-being scores with a study from the implant group (Xiao et al., 2020). This study was conducted in China and may demonstrate cultural differences in what different groups define as psychosocial well-being. BREAST-Q was originally written in English with standardized questions and has since been translated to many languages to eliminate the need for patients to be English-speaking. Another limitation with the BREAST-Q is that it was created in North America and with each translation, the questionnaire is not adapted to accommodate for cultural differences thus creating a bias to the Western societies. Therefore, this study as an outlier may be more reflective of the need to not only ensure adequate translation of the modules but also to ensure that the modules are adapted to account for cultural differences when being disseminated to patients outside of North America.

It is difficult to answer the question “who is happier?” when comparing patients who underwent cosmetic fat grafting and those who received implant-based breast augmentation. There were very few differences between the groups, and solely due to the overall satisfaction score being slightly higher in the implant group does not mean that all patients will be happier in all aspects of their life receiving implant-

based breast augmentation. Therefore, the external validity of this study cannot be certain based on the results of this systematic review. In addition, based on the lack of demographic data, it is uncertain if patients of all ages, BMI ranges, socioeconomic statuses, ethnic backgrounds, and other demographic characteristics were represented in this data; therefore, this data may not apply to all populations. (23)

In the context of the current practice, most breast augmentation is implant-based augmentation, which explains why more studies are focused on breast implants. (5) Worldwide, there is also significant variability in terms of surgical techniques and types and shapes of implants used, leading to a lack of standardization when using studies from around the world. (24) Additionally, fat grafting is not as common worldwide as it is in North America and is specifically not used very frequently in Latin America and Asia due to concerns about cost, safety, and the possibility of needing further procedures. (24)

This study included data from 1616 patients and 14 studies; 2 of those studies investigated fat grafting, 10 investigated implants, and 2 investigated both. This study has several limitations. There was a lack of randomized control studies, likely due to the challenges with ethical and logistical concerns patients receiving cosmetic breast augmentation. (25) Additionally, there was a lack of standardization between each paper. Not all studies reported both pre-operative and post-operative BREAST-Q data, and there was variable reliability in reporting this data, although our analysis revealed there was not an association between pre- and post-operative scores. Many articles did not provide extensive demographic data, which posed a challenge in

comparing the studies. Finally, there was a small sample size of patients, and there were more papers in the implant group than in the fat grafting group.

Our study selection was blinded to help minimize potential biases. However, none of the contacted authors replied with their BREAST-Q data, which may introduce presence of publication bias in this study. As the included studies were primary studies, there is a potential risk of bias; however, all the papers received a passing score based on the MINORS criteria. (26)

In the future, it would be beneficial to investigate other ways to improve fat grafting techniques and improve outcomes in fat grafting patients. Additionally, larger studies comparing breast implant patients to fat grafting patients with matched cohort data would be helpful to draw more accurate conclusions on the true difference in QoL outcomes between the two groups.

2.4.1 Limitations

Although this study aims to assess patient satisfaction with a similar goal, breast augmentation. The two surgical methods are incredibly different, with different patient expectations and goals. The much smaller patient population in the fat grafting group was a major obstacle in this review. BreastQ is non-specific to breast augmentation, however, it is the most accurate PROM instrument available, and the data still represents deficiencies in fat grafting, that need to be addressed.

We did not have enough pre-operative data to accurately measure the change in breast score across both groups. A bivariate meta regression showed that the difference in

available pre-operative scores was not statistically significant when assessing method of breast augmentation.

The studies did not provide sufficient surgical data, regarding implant placement or fat grafting technique. Patient dissatisfaction with a certain aspect of their care, could confound their post-operative scoring. Particularly considering that over 10% of patients in the implant group, will have some form of capsular contracture in the long term.

2.5 Conclusion

Overall, our study represents the first meta-analysis using Breast-Q scores to compare patient satisfaction with implant versus fat grafting techniques for primary breast augmentation. We found that there was a mean 13-point higher mean satisfaction score in the implant group, although there was no statistically significant difference in the other QoL parameters evaluated by the Breast-Q score. More research using standardized methodology and longer term follow up is needed to further characterize patient satisfaction with augmentation method. However, currently our review suggests, those who undergo implant augmentation are ‘happier’ with their results.

2.6 Future Implications

The above data does show that patients who have undergone fat grafting augmentation, are still incredibly satisfied with their results. The deficiencies can be

accounted for by the lack of standardized surgical techniques, as well as PROMs comparing two widely different surgeries.

A major obstacle to the widespread adoption of fat grafting is standardized surgical guidelines to help improve fat survival and ultimately, patient outcomes. Particularly, given the unpredictable percentage of fat survival and need for multiple fat grafting sessions. The next chapter will outline a proposed clinical trial which is designed to contrast two common methods of fat processing, to help create more standardized methods to establish clinical guidelines.

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3 The fat analysis trial (FAT): A Double Blinded Prospective Randomized Controlled Trial

This chapter is a proposed randomized controlled trial publicly available on clinicaltrials.gov (NCT05318716) and submitted to the trials journal for publication. With this trial, the aim is to evaluate methods of processing lipoaspirate, as well as patient reported outcome measures (PROM), surgical outcomes and fat incorporation.

3.1 Background

Fat grafting is a technique used commonly in plastic surgery that has gained popularity in breast augmentation and breast reconstruction. (1,2) This technique involves harvesting fat using liposuction from donor sites, processing the extracted fat and re-injecting it back into the breast for the desired volume and shape. (3,4) Fat grafting has gained popularity due to its resulting natural appearance and feel. This technique can also be used in conjunction with implant reconstruction to achieve a more natural contour and symmetry. (4,5) However, the main issue is an unreliable rate of fat retention, which, based on the literature, is only an average of 60% of the volume of fat injected. (6,7) Furthermore, there are very few clinical studies studying the long-term clinical survivability of the grafted fat. Therefore, care must be taken in setting patient expectations, and sometimes multiple sessions are required to achieve the desired results. (8,9)

Using a meta-analysis (chapter 2) to contrast fat grafting to implant based augmentation suggested an improved patient satisfaction with implant over fat grafting. This is speculated to be a result of variations in techniques leading to a lack of standardization and therefore less predictable cosmetic outcomes.

Although the use of fat for augmentation has been around since 1893, the relatively recent reemergence of its popularity has led to a multitude of harvesting and processing techniques, with varying levels of success. (6) The overall gentle handling of adipocytes with minimal disruption has been the general consensus. However, newer technologies, such as power assisted liposuction have proven to be equally effective. (1) Fat can be collected from any area of excess adiposity. (6) Once collected, several products and processing solutions have been developed in recent years, including the Revolve advanced adipose system (AbbVie/Allergan, USA), which is currently used at our institution. (10)

Revolve is a device that has an inner filter basket where lipoaspirate is deposited and an outer canister that collects the filtered fat after it has been separated from the tumescent fluid, and the adipose tissue is irrigated using a Lactated Ringer's solution. (22,23) In animal studies, when compared to decantation, it has been demonstrated that it has less blood debris and free oil as well as a higher percentage of adipose tissue and retention and lower fat necrosis and need for revision. (22) (Figure 1)

Decantation is one of the most frequently used methods for fat processing and is advantageous due to the simplicity and reproducibility of the technique relative to other fat processing methods that exist. (19,20) Decantation for fat processing involves the use

of gravity to separate the fat. (21) Retention rates of decantation range from 20% to 90%. (18)

Figure 1. Revolve device connected as an intermediary to the liposuction cannula and lipoaspirate collection container.

Over the past decade, simple decantation of fat by gravity (figure 2) or centrifugation were the most common processing methods. (10,11) However, due to damage to fat during processing and lower retention rates in the literature, centrifugation has largely been abandoned as a processing method. (6,11) However, there is no standard method of donor fat harvest or processing, and there is a lack of well-defined prospective clinical studies comparing popular, more modern techniques in the current literature, particularly in the long term. Additionally, the amount of fat injected and patient factors such as previous radiation can affect the amount of fat retention.

Figure 2. Lipoaspirate following decantation. Top layer of oils, middle layer of adipose cells, bottom layer is a serosanguinous mixture of blood and tumescence.

In order to assess the rate of fat retention in the breast, volumetric imaging tools have been validated in the literature. (12) One of the most popular techniques is 3D body surface scans. (3,4,5,13) These can be taken easily, quickly, and cost-effectively for volume assessment at various time points pre and postoperatively. (12) Comparatively, MRI imaging has a much higher upfront, operating and interpretation cost, it's more time-consuming, and therefore not practical for frequent follow-up. Furthermore, as 3D imaging becomes more accessible, cost-effective, and portable, its use could become more common in clinical practice for preoperative planning and objective assessment of outcomes. (14) A validation study done by Killaars et al. have shown that although MRI is the current gold standard for volumetric analysis, 3D imaging systems, particularly the VECTRA, were less accurate per independent measurement, however, with subsequent measures, 3D imaging systems were comparable to MRI with excellent reliability.

Currently, there is a lack of prospective clinical studies directly comparing the rate of fat graft retention between processing techniques. The purpose of this clinical trial is to evaluate two popular methods of fat processing; decantation and the Revolve system. The primary outcome will assess long term fat survival and incorporation using volumetric analysis and ultrasonographic imaging. The secondary outcomes include comparisons of PROMs using BreastQ, operative time, surgical complications and outcomes.

This trial is currently under review with Western Ontario's research ethics board (REB #11811) and is publicly available on www.clinicaltrials.gov (NCT05318716).

3.2 Methods

3.2.1 Patient eligibility

All patients presenting for fat grafting to four of our local breast surgeons will be eligible to join this study. The treating surgeon will approach their patients undergoing fat grafting for breast augmentation or reconstruction. Patients will need to consent for 3D imaging instead of standard 2D photography, pre-operatively and post-operatively, at the standard follow-up imaging timepoints for this procedure to be eligible for participation in this study. At any point in the study, patients will be permitted to withdraw from participation in the study.

Inclusion criteria will include any patient above the age of 18 undergoing fat grafting from any donor site to the breast for cosmetic or reconstructive purposes. The exclusion criteria will include patients who are unable to consent to the study or are

undergoing a repeat fat grafting procedure after a previous unsatisfactory result. Patients who have undergone autologous breast reconstruction, including regional and free flaps will be excluded. Patients who undergo multiple breast surgeries in the same sitting will also be excluded (i.e., augmentation and mastopexy).

3.2.2 Recruitment

With our proposed prospective randomized controlled trial, we aim to recruit patients already scheduled to undergo fat grafting to the breast for reconstruction or cosmetic augmentation. A power analysis based on published image-based prospective trials showed a minimum number of 22 patients. We will initially aim to recruit 100 patients into each of the cosmetic and reconstructive group, with a total of 200.

Each arm of patients will be divided further into high and low volume fat grafting, this will leave us with enough power within each subgroup, which is above the current standard in the literature for studies with statistical significance(15) (16). Based on the clinical practice of the multiple breast surgeons who perform fat grafting at both our centers, this would take 12-14 months to recruit enough patients.

3.2.2.1 Reconstruction (sub-group 1)

This group of patients would be undergoing fat grafting to correct contour irregularities following implant-based reconstruction. Fat grafting would typically occur for breast contouring 3-6 months following their initial implant-based reconstruction procedure. On the day of their fat grafting appointment, the primary surgeon will provide

them with the verbal information and answer their questions, as well as a letter of information (LOI) (appendix 3). Pre-operative 3D imaging with volumetric analysis of the patient's breast will be done. This group will be analyzed based on injected volume (<200 cc or <50% of pre-op breast volume and >200 cc or >50% of pre-op breast volume) as well as subgroup analysis based on adjuvant chemo or radiation therapy to minimize heterogeneity.

3.2.2.2 Cosmetic (sub-group 2)

This group of patients will be undergoing a primary or secondary augmentation for cosmesis. They will be included if this is a primary augmentation using fat grafting or a secondary augmentation (previous implant-based augmentation, now undergoing fat grafting for further augmentation) with no history of fat grafting to the breasts. Patients will undergo volumetric breast analysis similar to the above group.

3.2.3 Volume based analysis

Each of the above groups will be stratified based on baseline pre-treatment breast volume, as well as injected volume. Each group will be divided into low volume, which will be less than 200cc of injected fat or 50% of breast volume (whichever is lower) needing replacement or augmentation. The high-volume group will include volumes greater than 200cc or 50% of breast volume (whichever is higher) needing replacement or augmentation.

3.2.4 Imaging

A Vectra H2 (Canfield medical, NJ) will capture a 3D image in place of our traditional 2D imaging, for both pre-operative and post-operative photos. A volumetric analysis will be performed using the proprietary software. With a pre-operative baseline volume, we will be able to track fat survival between the two-methods post-operatively during follow up visits. We will include a bedside ultrasound image of the breast tissue at 3 months, to assess fat incorporation and the amount of oil and oil cysts. The ultrasonographic image will be independently evaluated by a blinded assessor.

3.2.5 Randomization and Blinding

If a patient is included in the study, they will be randomized into either the Decantation or Revolve group. A validated method of randomization will be used. When the patients check in at the reception desk, they will be assigned a ticket with a 0 or 1 sequentially. This will be collected by the surgeon, and they will be able to set up for either decantation or revolve. Group 0 patients will receive Decantation, and group 1 will receive Revolve. The surgeon will make no mention of processing techniques in the operative note. The surgeon will keep a log of their patients and processing technique used on a secure shared file (file-safe, LHSC). The patient will be consented in the regular manner as there are no additional risks with one method over the other.

Photography (VECTRA H2 imaging system) will be done by a separate research assistant/coordinator that will be recruited for the project. The person will be responsible for imaging patients, as well as conducting the volumetric analysis following training by

the software manufacturer. This person will be blinded to which fat processing technique was used. Photos will be kept on a secure network drive accessed in the research office, as is standard practice for patient photographs in the department. Demographic data will be collected, including patient age, weight, smoking status, radiation status (if applicable), and reason for fat transfer to the breast. In addition, standard intraoperative data will be taken, including length of procedure, volume of tumescent fluid injected, volume of lipoaspirate, and volume of fat injected into each breast. 3D imaging will be used to analyze the change in volume.

During subsequent follow ups, the patient will be assessed in the regular manner with 3D volumetric imaging, in place of the standard 2D photography.

The surgeon, assistants and nurses will not be able to be blinded as they are responsible for using the device in the operating room. All assessors will be blinded.

3.2.6 Standardized fat collection

The donor areas previously agreed on by the patient and surgeon for fat harvesting will be injected with a pre-standardized formulae (Klein formulae for tumescent fluid – 500mg Lidocaine, 1mg Epinephrine and 12.5 mEq sodium bicarbonate per one liter of 0.9% normal saline) and volume of tumescent fluid. Fat will be extracted using a standardized harvesting method between surgeons. Once the fat is collected. It will then be processed in one of two ways depending on the patient's group, using a Revolve system or via decantation. Fat will then be injected into the breast using a 10 or 20cc syringe in the standard retrograde manner to achieve the desired size and shape. A

standard gauze-based dressing will be applied post-operatively for 24 hours with no compression. The patient will be allowed to shower and remove the dressing on post-operative day one and followed up in clinic two weeks following the procedure.

Post-operative follow up will be at two weeks (3D image), six weeks (3D image and BreastQ), three months (3D image and Ultrasound), six months (3D image and BreastQ), one year (3D image) and two years (3D image and BreastQ).

3.2.7 Statistical Analysis

Statistical analysis will be done by a contracted statistician for this study. The level of significance for all statistical tests will be set at $p < 0.05$, with multiple comparisons adjusted using Bonferroni coefficient. All analyses will be performed according to the intention-to-treat principle. As appropriate, differences in dichotomous outcomes will be assessed using the chi-square test or Fisher exact test. Differences in continuous outcomes will be assessed using the independent-samples t-test or the Mann–Whitney U test, as appropriate. Dichotomous outcomes will be reported as relative risks (RRs) with corresponding 2-sided 95% confidence intervals (CIs). Continuous outcomes will be reported as means with standard deviations (SDs) or as medians with interquartile ranges (IQRs), depending on the data distribution. All statistical analysis will be done using SPSS (IBM corporation, Armonk, NY).

3.3 Conclusion

This RCT aims to explore the differences in the outcomes for patients who undergo fat grafting using either Revolve or Decantation for fat processing. In this trial, patients will be followed for up to 2 years post-operatively, which will provide an ample amount of time for the fat to be incorporated, as well as assess the longevity of the injected fat volume.

Fat grafting for breast augmentation is becoming increasingly more popular, and it now poses the question of what processing method will achieve the most optimal results for patients? (17) The goal of processing the fat is to remove contaminants, infiltration solution, blood, cell fragments, and free oil to optimize the amount of active fat constituents being transferred. (17,18) When the breast tissue is imaged at 3 months, the echogenicity of the image will highlight how well the fat has incorporated, which could ultimately predict better long-term results and volume stability.

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4 Discussion

4.1 Introduction

Breast Augmentation remains the most popular cosmetic procedure performed by plastic surgeons around the world with current trends showing that this popularity is ever growing. Patients have access to an extensive amount of information using the internet, this, along with popular patient forums of social media, have caused a shift toward a 'no-implant' augmentation. Since 2009, there has been a steady upwards trend of autologous, non-implant-based augmentation proving to be a viable and more so, desirable alternative, this creates massive potential for surgical innovation and creativity.

More so, fat grafting has proven to be more than an adjunct procedure. Given the right circumstances, patients can achieve their desired augmentation result, with larger fat volumes in a single session. Fat grafting has also proven itself with no long-term adverse events, and high levels of patient satisfaction.

4.2 Patient selection

As we outlined earlier, choosing the right patient for fat grafting is critical. These days, patients are highly informed regarding their possible choices for primary breast augmentation. A large portion of these patients are turning away from the use of prosthetics. Opting for an autologous, and there for a more 'natural' augmentation. Patients who are well informed regarding the post-operative course and possible pitfalls

following fat grafting are excellent candidates if they are physically able to undergo fat grafting.

Patients undergoing fat grafting must meet certain criteria, physically. There must be enough excess fat to be harvested, taking into consideration the possibility of multiple sessions. The breast itself, must have minimal ptosis with good quality skin. The breast itself must have the ability to stretch to accommodate the required amount of grafted fat.

4.3 Operative Considerations

Preparation for surgery requires several considerations. Particularly regarding fat harvesting. Popular harvest sites include the abdomen, thighs, and flanks. These areas typically provide sufficient, high-quality fat for grafting. Equal attention should be paid to contouring these areas during the harvest, to avoid post-operative asymmetry, seroma, and hematoma formation. However, excess liposuction is discouraged, as to avoid excess skin laxity. The current literature is inconclusive regarding the optimal sites to harvest fat, however, there is weak data to suggest peri-umbilical fat to be slightly inferior.

Pre-operative photos of both the harvest and donor areas must be well documented. As outlined in Chapter 3, the use of 3D imaging with volumetric analysis is recommended. This would provide a quantifiable method of analysis and tracking post-operatively.

There have been a multitude of techniques and devices described for fat harvesting. Manual syringe aspiration, power assisted, water assisted, and radiofrequency

or ultrasound assisted liposuction, each with their own benefits. Power assisted liposuction is much more efficient in harvesting larger volumes with no evidence to suggest a superior harvesting method.

At present the options for processing the lipo-aspirate, include centrifugation, decantation, and industry-devices, such as Revolve. Each with their own set of benefits, and associated cost. At present, there is a community preference towards decantation and industry-devices in place of centrifugation. The proposed RCT in chapter 3 should shed more light on this important aspect of fat grafting. However, in-vitro studies have shown a slight increase of viability of adipocytes processed with industry-devices, this has not been reproduced clinically, to date.

Lastly, planning operative time and cost. An implant-based augmentation will require 60-90 minutes of operating time, as well as the cost of the prosthetics. Fat grafting is a longer process. Certain considerations include time for tumescence, time for fat harvesting and fat processing. Patient positioning will also need to be considered, depending on harvest sites. More so, many community centres do not have access to liposuction devices or a limitation due to the cost of disposables. Therefore, manual aspiration will take significantly longer and may not yield enough fat for larger augments.

Intra-operatively, there are considerably more surgical steps and two or more surgical sites. Secondly, fat grafting requires a visual analysis and approach towards breast volume and contouring by the surgeon. This requires the surgeon to add a significant volume of fat to structurally enlarge the breast, while maintaining ideal breast contour and shape.

At present, implant-based augmentation still accounts for a large majority of breast augmentation. Certain barriers are preventing the widespread adoption of fat grafting augmentation. Primarily, the inability to ‘guarantee’ a reliable breast size post-operatively due to unpredictable fat necrosis. As well as a surgeon’s level of experience, comfort and hesitation with augmenting and contouring a breast using fat. Humans are a creature of habit; surgeons have gotten excellent results using implants for the past 60 years. These results are reproducible and as demonstrated in chapter 2, patients are incredibly satisfied, more so than fat grafting.

The unpredictability of fat retention and analysis have been the toughest barrier. More structured research into every step of fat harvesting, processing and injection must be studied, as well as patient factors that may affect fat retention. Fat is autologous, and inherently, will always have a certain amount of unpredictability compared to its synthetic counterparts.

With implant-based augmentation, the data and evidence are quite clear regarding the best surgical techniques and precautions to ensure the highest level of patient safety and satisfaction. On the other hand, there are no standardized methods of fat harvesting, processing, or injection. Moreover, there are no practical methods of assessing fat survivability, particularly, in the longer term. Therefore, this method relies strongly on patient selection and pre-operative counselling.

A comprehensive literature review regarding the current available evidence on fat grafting showed inconsistencies regarding surgical technique and the pathophysiology of fat survival. Although studies have demonstrated no significant differences with fat

harvesting, the consensus has aligned with the gentle extraction of adipose tissue. The processing of fat, however, has remained slightly more controversial. Previously, centrifugation was considered standard practice to separate the layers of extracted fat for injection, similar to other methods used for autologous injectables, such as platelet rich plasma treatments. Over the past few years, centrifugation has been considered damaging to fat cells and phased out of practice. At present, the predominant technique used is the simple decantation of fat using gravity.

During decantation the adipose cells along with oils, tumescent fluid and blood separate depending on their density. Injecting oils are particularly concerning as this can create subcutaneous pockets of oil, which could be a source for infection. Newer industry devices are processing and irrigating the fat to eliminate the aforementioned layers and providing a 'purer' adipose product for injection. The literature is in disagreement and no standardized clinical trials have been conducted to assess fat processing. Our proposed RCT not only assesses the two methods of fat processing, but it also assesses surgical outcomes, and PROMs as well. We also assess the fat incorporation within the breast tissue itself at 3 months. This is significant, as we are assessing whether the volume is from true fat retention or oil cysts. The long-term follow-up period of two years should yield incredible qualitative and quantitative data regarding the fat grafting experience.

During the qualitative meta-analysis, we were able to see that the implant-based augmentation group were 'more satisfied' than the fat grafting group post-operatively. This is based on a significantly smaller cohort of fat grafting patients, where the data can be easily skewed by outliers. The drastically different procedures and post-operative recovery between the two methods of augmentation can also explain the difference.

Where in most cases, implant-based augmentation continually improves from the immediate post-operative period, that is not the case with fat grafting. As the fat settles in, it can get hard and ‘cystic’ before it is ultimately incorporated to the surrounding tissue. Fat grafting results are ultimately, in the long term, softer and more natural than implants. Therefore, a longer follow up period might prove the inverse of what was found in this meta-analysis.

However, the meta-analysis did show that in most recorded aspects on the BreastQ questionnaire, there were no significant difference between the two methods of augmentation from the patients’ perspective. However, they were overall, less satisfied. This highlights the need for more high-quality data and studies regarding fat grafting.

4.4 Limitations

Overall, breast augmentation is an incredibly broad topic, particularly when reviewing two popular surgical techniques. Although both fat grafting and implant-based augmentation have a similar goal, they are incredibly different. The literature review attempts to highlight the current knowledge and trends with both procedures, however, there is still more to cover outside the scope of the review on implant selection, surgical adjuncts, combination procedures and complications. Moreso, chapter one reviews the current knowledge on adipose cell biology and the importance of adipose derived stem cells, however, there are significant gaps in our knowledge and much that is unknown.

The meta-analysis, although attempting to answer a simple question, had limitations with minimal pre-operative BreastQ data and the large discrepancy between patient numbers. Although this did not affect the analysis, a larger fat grafting cohort

might yield a different outcome, highlighting the need for more patient reported outcomes and clinical research into fat grafting.

Although the randomized controlled trial is the first of its kind, there are still obstacles due to the inherent nature of autologous tissue and clinical resources. The trial addresses two popular methods of processing currently available at our centre, however, we do not address centrifugation or ‘closed system’ fat grafting devices due to surgeon preference and cost barriers. The trial also aims to assess fat grafting following one session; however, a large percentage of patients would require multiple session to achieve their desired result. This will inevitably result in earlier endpoints for certain patients and their ineligibility to re-join the trial for the subsequent fat grafting session (due to the exclusion criteria).

4.5 Conclusion

As we have established, the literature is saturated with data regarding various methods of implant-based augmentation. Comparably, fat grafting data is relatively sparse and inconsistent.

The popularity of fat grafting is expected to continue growing. It has proved itself as a safe procedure, with good patient outcomes. However, more standardized methods and clinical guidelines need to be established. The above trial could be a major step towards more clinical evidence to the fat grafting body of knowledge. The implications of this trial could influence both patients’ and surgeons’ decision, in the commonest performed cosmetic surgery in the world

APPENDIX 1 – Breast Reconstruction Article

This manuscript is submitted for publication to the plastic and reconstructive surgery journal (PRS).

"Alternatives to the gold standard: The profunda artery perforator and lumbar artery perforator flaps compared to the deep inferior epigastric perforator flap for breast reconstruction a systematic review"

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Short Running Head:

PAP and LAP vs DIEP for breast reconstruction

Abstract

INTRODUCTION:

Breast reconstruction with the deep inferior epigastric perforator (DIEP) flap is the current gold-standard autologous option. The profunda artery perforator (PAP) and lumbar artery perforator (LAP) flaps have been described as alternatives for patients who are not candidates for a DIEP flap. The aim of this review was to compare the survival and complication rates of PAP and LAP to DIEP flaps.

METHODS:

A literature search was conducted using PubMed, MEDLINE, EMBASE, BIOSIS, Web of Science, and Cochrane databases. Papers were screened by title and abstract, and full texts reviewed by three independent blinded reviewers. Quality was assessed using MINORS criteria.

RESULTS:

Sixty-three studies were included, for a total of 745 PAP, 62 Stacked PAP, 187 LAP and 23748 DIEP flap breast reconstructions. The PAP (98.3%) had comparable success rate to DIEP (98.4%), and the Stacked PAP (88.7%) and LAP (92.5%) success rate was significantly lower ($p<0.0001$). The PAP and LAP groups had a significantly lower incidence of fat necrosis, compared to the DIEP group ($p<0.01$ and $p=0.02$). However, revision rate for the LAP group was significantly higher than the DIEP group ($p<0.0001$). The PAP group also had a significantly higher rate of donor site wound dehiscence ($p<0.0001$).

CONCLUSION:

In conclusion, PAP, stacked PAP and DIEP flaps demonstrated similar overall survival. LAP flap had a high survival rate, but lower than DIEP. This review highlights that PAP flaps are a safe alternative for autologous breast reconstruction and may be a preferred choice to LAP.

Introduction

The deep inferior epigastric perforator (DIEP) flap is a well-established autologous technique for breast reconstruction[1–4]. Originally designed as an alternative to the transverse rectus abdominus myocutaneous (TRAM) flap, DIEP flaps preserve the integrity of the rectus abdominis muscle, and results in decreased donor site morbidity[1,5]. However, the lack of adequate donor site tissue or previous abdominal surgery can make some patients unsuitable candidates for a DIEP flap.

Two new flaps, the profunda artery perforator (PAP) flap and the lumbar artery perforator (LAP) flap have gained popularity as alternatives for autologous breast reconstruction. The PAP flap harvests donor tissue from the posterior thigh[6]. Commonly, patients have redundant tissue in this area, and benefits include a thigh contouring effect and a easily hidden scar[6,7]. However, there is typically smaller tissue volume available, and therefore may be ideal for women desiring a smaller reconstruction[7]. Alternatively, to achieve a larger volume two PAP flaps may be used for unilateral breast reconstruction[8,9]. Although technically challenging, stacked PAP flaps have been used with promising post-surgical survival and aesthetic outcomes[9].

The LAP flap harvests tissue from the lower back, ‘love handle’ region, another common area of redundant tissue[10]. This flap is larger than PAP flap and comparable in size to a typical DIEP flap[11]. There is minimal donor site morbidity and the scars are easily hidden. The main challenge is positioning. The LAP flap must be harvested in the prone or lateral decubitus position, and necessitates a position change to supine for microvascular anastomosis and flap inset[12]. While this may lead to increased ischemia

time and technical challenges, initial studies have shown promising results for LAP-based breast reconstruction[11–13].

Presently, the DIEP flap is the gold standard for post-mastectomy autologous tissue-based reconstruction. However, PAP and LAP flaps are promising alternatives. They are especially useful for reconstruction in women with insufficient volume of abdominal tissue, previous donor site surgery, previously failed reconstruction, poor perforators, or patient preference for a non-abdominal flap. Survival outcomes and complications associated with the PAP and LAP flaps have been reported, however, no systematic review has been conducted comparing the outcomes or complications between the DIEP flap and these two alternatives. The purpose of this review was to compare breast reconstruction with PAP and LAP flaps to DIEP flaps, with the focus on flap survival and complications.

Methods

Data Sources and Search Strategy

For this review, the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline was used (Figure 1). The PROSPERO database was reviewed, and no similar review was found. The study was registered in the PROSPERO database, number CRD42021238660. The search strategy was designed by two reviewers (K.M. and V.C.). The search was conducted in two groups, the first for DIEP papers and the second for the LAP and PAP papers. The search strategy included search terms related to the flaps of interest, the region of interest, and terms related to the primary outcomes and the secondary outcomes. Primary outcome was flap survival and secondary

outcomes were common complications. Within each block items were combined with the Boolean operator “OR”, and the three blocks were combined by the Boolean operator “AND” to obtain the final search results. The search strategy is provided in Appendix 1.

To include the largest number of studies investigating breast reconstruction using the autologous tissue flaps of interest, we systematically searched a total of six bibliographic databases: BIOSIS®, PubMed®, Cochrane Library®, EMBASE®, MEDLINE® and Web of Science®. The DIEP studies were searched on two dates, February 17, 2021, and July 24, 2021. The search for PAP and LAP articles was conducted on June 7, 2021.

In addition, we manually screened references from relevant review articles to identify pertinent studies that escaped our search strategy.

Inclusion and Exclusion Criteria

Inclusion and exclusion criteria were determined *a priori*. Due to the anticipated large number of DIEP studies available compared to PAP and LAP, we developed two sets of inclusion and exclusion criteria. We included prospective studies, retrospective studies and randomized controlled trials written in English or French, published in peer reviewed journals. For the DIEP papers we included studies published in 2012 or later with an N >/=10 flaps. For the LAP and PAP papers we included studies published in 2012 or later with N>1 flaps. Of these studies, we included those that reported outcome measures involving flap survival. Case reports, reviews, animal studies, conference proceedings, abstracts and editorials were excluded. We also excluded any study that

non-randomly selected a specific subset of breast reconstruction patients from a larger dataset (Table 1 and 2).

Study Selection

Studies extracted underwent two levels of screening by three independent reviewers (K.F., K.M and V.C) using Rayyaan and Covidence platforms (Rayyaan Systems Inc., Cambridge, MA, USA and Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). For Level 1 screening, studies titles and abstracts were reviewed. Selected articles underwent full-text review. Assessment of quality was conducted for all non-randomized studies selected using the Methodological Index for Non-Randomized studies (MINORS) score. Papers that failed to achieve a score of 60% or higher were excluded. Reasons for exclusion were documented and reported in the PRIMSA flowchart (Figure 1). All conflicts were resolved between reviewers, and an independent arbitrator (K.A.) was available for any disputed conflicts.

Data Extraction

Data was extracted using the Google Sheet platform (Google, Mountain View, CA, USA), and reviewed by two additional independent reviewers (E.L. and K.J) for errors. Disagreements were discussed with both sets of reviewers to resolve conflicts. Data extracted included study information, number of patients, demographic characteristics, flap characteristics, and primary and secondary outcomes.

Statistical Analysis

Statistical analysis was conducted using SPSS and GraphPad Prism 9 software (IBM, Armonk, NY, USA and GraphPad Software, Inc., San Diego, CA). Descriptive statistics were calculated for demographic data with weighted means, and standard deviation. Chi-square with Yate's continuity correction test was used to analyze primary and secondary outcomes. Cohen's kappa coefficient was calculated to assess for inter-rater reliability for article selection, with values 0.41-0.60, 0.61-0.80 and 0.81-1.00 representing moderate agreement, substantial agreement, and perfect agreement respectively[14].

Results

Study Characteristics and Demographics

The search strategy identified 2430 articles, and an additional 6 were added from other sources. After removal of duplicates, 1448 articles were screened using title and abstract and 166 articles underwent full text review (Figure 1). In total, 61 full-text articles were included for data extraction, representing a total of 24742 free-flaps for breast reconstruction. Fourteen of the studies were PAP focused[7,8,15–25], six were LAP[12,13,26–29] focused and forty-one DIEP focused[2,12,15,30–66]. Of the PAP focused papers, three included outcomes from stacked PAP flaps for unilateral breast reconstruction[8,16,20]. Cohen's Kappa coefficient was 0.87 between K.M. and V.C. for the DIEP studies, and 0.89 between K.F. and V.C. for the PAP and LAP study selection. Table 2 summarizes the characteristics of articles included in this review. Data was extracted from a total of 745 PAP flap, 62 Stacked PAP flap, 177 LAP flap and 23748 DIEP flap breast reconstructions.

Patient demographic data for age, BMI and flap weight was extracted for each flap group (Table 4). Weighted mean and standard deviation were calculated using the number of flaps in each study reporting demographics as the frequency variable. Average age 46.7 +/- 2.9 and 48.5 +/- 3.2 for PAP and LAP respectively compared to 50.4 +/- 2.0 for DIEP (Table 4). The PAP and LAP groups also had lower average BMI, 24.2 +/- 2.2 and 23.9 +/- 1.4 respectively, compared to the DIEP group, 27.1 +/- 2.4 (Table 4). For flap weight, the DIEP flap average was the highest, at 628.7 +/- 97.4g, the LAP average was 533.2 +/- 56.8g and single PAP flaps were the lowest average at 374.4 +/- 55.6g. Of the three stacked PAP papers one reported the average combined flap weight as 420+/- 164.8g[8].

Primary Outcomes

Primary outcomes were analyzed in two ways. First, we compared flap survival and loss, between the PAP, stacked PAP, LAP and DIEP groups (Table 5). Flap survival was defined as flaps reported as full and partial survival. All flaps had high survival rates, with 98.4% for DIEP, 98.3% for PAP, 88.7% for stacked PAP and 92.5% for LAP. Table 5 shows there is no significant difference between flap survival for PAP ($p=0.8$) compared to DIEP. However, the stacked PAP and LAP groups had significantly lower survival rate compared to DIEP ($p<0.001$).

Second, we analyzed full flap loss and partial flap loss rates. There was no significant difference in complete flap loss for PAP ($p=0.8$) compared to DIEP (Table 6). There was a significantly higher rate of complete flap loss for the stacked PAP and LAP flap ($p<0.0001$). Interestingly, the PAP group had a significantly lower partial loss rate,

0.3% compared to the DIEP group, 1.1% (p=0.05). The LAP partial flap loss rate was 0.6% (p=0.8).

Of the LAP flaps reported, 171 (96.6%) used artery and vein interposition grafts (Table 7). Table 7 shows the operative positioning and vein graft usage, as well as corresponding ischemia time and operative time.

Secondary Outcomes

Secondary outcomes included fat necrosis, revision surgery and donor site wound dehiscence. Revision surgery was defined as any report of re-operation for complications, most commonly for microvascular compromise. Other causes included hematoma, fat necrosis, and wound dehiscence. Revision for aesthetics was not consistently reported, and therefore was excluded from analysis.

Table 8 shows reconstruction with a single PAP flap resulted in significantly lower rates of fat necrosis, 2.6% compared to DIEP, 7.7% ($p<0.01$). There were no reported cases of fat necrosis in the LAP flap group (p=0.2).

The PAP group had a comparable rate of revision surgery, 3.3%, compared to 5.2% to the DIEP group (p=0.2). There was a significantly higher rate of revision of 16.1% in the LAP group ($p<0.0001$). Revision of stacked PAP flaps was not reported.

Incidence of donor site wound dehiscence was 9.1% of cases in the PAP group, which was significantly higher than 3.4% in the DIEP group ($p<0.001$). There was no significant difference in donor wound dehiscence rate for LAP flaps compared to DIEP (Table 8).

Two PAP papers reported the rate of revision for solely aesthetic reasons. Hupkens et al. 2016, reported a 30% rate of secondary fat grafting, while Tielemans et al. 2021 reported a rate of 67.8%. Wade et al. reported a liposuction/lipofilling rate of 11.6% in unilateral and 10.3% in bilateral breast reconstruction with DIEP flaps.

Discussion

Our study demonstrates that the PAP flap is comparable to the gold standard DIEP flap for reconstructive surgery after mastectomy. The LAP flap had significantly higher rates of failure compared to the DIEP flaps. This is the first systematic review directly comparing the outcomes of breast reconstruction with PAP and LAP flaps to DIEP.

As reported previously, our review found patients chosen for PAP and LAP flap reconstruction were generally younger and had a lower BMI than DIEP patients[11,67]. The PAP and LAP flap reconstruction offer benefits in situations where patients are not ideal candidates for a DIEP flap, due to previous abdominal surgery or lack of redundant abdominal tissue, or who do not want an abdominal scar[7,9]. One patient group who may benefit from a PAP or LAP reconstruction is gene mutation carriers high-risk for breast cancer, such as BRCA-positive patients, desiring prophylactic mastectomy and autologous reconstruction. These patients are commonly younger and slimmer than typical breast cancer patients, and therefore may not be ideal DIEP candidates[11,12]. Therefore, depending on the breast size desired, a bilateral PAP or LAP-based reconstruction may be an alternative.

Patients undergoing mastectomy for unilateral breast cancer may be another candidate group. Currently, the role of concurrent contralateral prophylactic mastectomy for non-gene mutation carrier patients is controversial[68]. When undergoing DIEP reconstruction all abdominal tissue must be removed[50]. Therefore, if patients develop breast cancer on the contralateral side, or a recurrence, they will no longer have tissue for a DIEP reconstruction. This could lead patients to consider undergoing prophylactic mastectomy and bilateral DIEP reconstruction unnecessarily. Having viable alternatives may give patients more options and peace of mind for possible future reconstructive options.

We reported an overall flap failure rate of 1.7% in the PAP group and 1.6% in the DIEP group. Two previous reviews reported a failure rate of 2.67% for DIEP flaps, and 1% for PAP flaps[69,70]. Additionally, we found that PAP flap reconstructions had lower rates of partial failure than DIEP flaps, a complication that can result in the need for revision surgery, and a poorer aesthetic outcome[69]. The major downside of the PAP flap is the size. This can be overcome by using two PAP flaps can be combined to reconstruct a single breast, for a 'stacked PAP' reconstruction. Our review found higher rates of failure in the stacked PAP group, however one paper accounted for six out of seven total failures.

Comparatively, the LAP flap had a failure rate of 7.5%, which was significantly higher than the DIEP flap. The main advantage of the LAP flap is its size, favorable donor site quality of tissue and aesthetic outcome. We reported a mean flap weight of 533.2g, consistent with analysis done in previous literature that it is comparable to the size of a DIEP flap[39]. Slim patients, or those who have undergone abdominoplasty, often

have redundant tissue in the flank area, and the LAP flap has the simultaneous advantage of giving a buttock lift effect.

One factor possibly contributing to the higher rate of failure in LAP flaps include the use of interposition grafting. The LAP flap typically has a shorter pedicle and smaller vessel diameter, with three studies reporting averages of 4.5cm, 5.25cm and 6cm mean pedicle length[12,26,28]. Opsomer et al. describe that although a pedicle length of up to 7cm is possible, their group no longer pursues this length to avoid a deep dissection around the transverse process that can lead to nerve root damage and neurapraxia of the leg[11]. We found the majority of LAP flap reconstructions used artery/vein interposition grafts, which requires two anastomoses and can increase the risk of vessel thrombosis[12]. Indeed, Peters et al. noted that of the six flaps they had to take-back to the operating room, in five flaps the vein had thrombosed at the site of the vein graft and pedicle anastomosis[26].

The LAP flap is a logistically challenging flap, that requires intraoperative position change. The majority of flaps were harvested in prone positioning and anastomosed in supine, necessitating donor site closure and patient repositioning in between[12,13]. Additionally, the surgeon also has to anastomose the graft to the pedicle. Both these factors can increase ischemia time. Increased ischemia time can increase the risk of ischemia reperfusion injury and has been correlated with increased failure rates in DIEP flaps[53,71]. One LAP study reported mean ischemia time of 65 minutes without a graft, compared to 131 minutes when a graft was used[26]. This prolonged ischemia time has led some surgeons to not attempt simultaneous bilateral LAP flap reconstruction. One study included bilateral LAP flap reconstruction with 15 patients, and experienced two flap losses[13]. Although this is promising that the ischemia time was not prohibitive, the

procedure was completed by two experienced microsurgeons preforming simultaneous harvest[13].

In terms of complications, PAP and LAP reconstruction demonstrated low rates of fat necrosis, however the LAP group had increased revision rates, and PAP had increased donor site wound dehiscence compared to DIEP. Factors affecting ischemia, such as flap size and number of perforators predict fat necrosis, and patient factors that affect perfusion such as smoking status, previous abdominal surgery and radiation history are believed to contribute to its development[72]. The PAP flap is a smaller flap than DIEP, and therefore the lower rate of fat necrosis is expected. There are also confounding variables such as smoking and radiation that was not consistently reported and could explain this result. In both PAP and LAP groups, revision surgery was significantly higher than DIEP. For the PAP group this may be due to the increased rate of lipofilling done, which one study reported was done in up to 67.8% of PAP flap reconstructions[24]. Donor site wound dehiscence was most prevalent in the PAP group at 9.1% compared to 3.4% for DIEP and 2.9% for the LAP groups. This is likely due to strain placed on the donor site wound from sitting. Improved post-operative wound care and patient education for ideal positioning may be needed to achieve comparable surgical outcomes in this area.

Limitations to this study include the discrepancy in sample size between DIEP flap and PAP and LAP flap reconstructions extracted from the literature. Specifically, for the LAP and stacked PAP group, the sample size is such that the outcomes from one study can influence the overall result reported in this review. Furthermore, the majority of studies did not report their definition of partial flap loss, and of those that did report, the definition ranged from greater than twenty to fifty percent flap necrosis. Similarly the

data for fat necrosis was based on inconsistent definitions, most commonly greater than 2cm palpable mass, however some reported as greater than 1cm, or with ultrasound detection. Therefore, these results may be biased based on the authors definition. Additionally, confounding factors for surgical outcomes such as smoking status and use of adjuvant chemotherapy or radiation was not consistently reported. Patient satisfaction and aesthetic outcome data was also lacking. Importantly, most data published from the PAP and LAP flaps come from a relatively small group of surgeons who do a high volume of these alternative flaps and therefore, there is likely a learning curve associated, and the failure rates may be higher for surgeons with less experience in these flaps.

Conclusion

Although the DIEP flap remains the gold standard for autologous breast reconstruction, our systematic review presents the PAP flap as the favorable alternative over the LAP flap. The major advantage of the PAP flap is its high success rate comparable with DIEP. The disadvantages remain the flap size, as well as increased donor site complication rates. The advantages of the LAP flap identified were the size and donor site outcomes. However, the LAP flap has a significantly higher rate of failure and therefore inferior as an alternative reconstructive option compared to the PAP flap.

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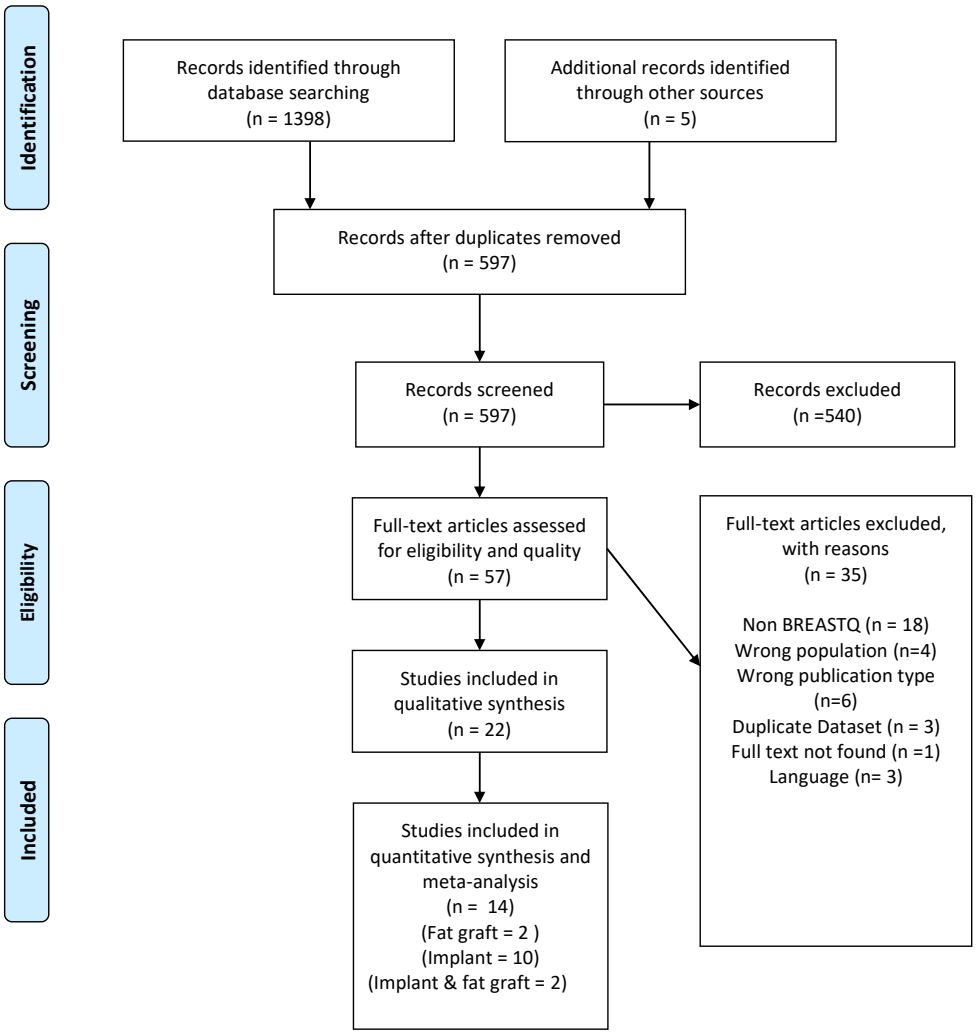
APPENDIX 2 – Search Strategy

A. Search terms

(((“Fat” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“adipose” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“adipocyte” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“lipo” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“autologous” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“autologous” AND “Fat” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“homologous” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“homologous” AND “Fat” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“autogenous” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR (“autogenous” AND “Fat” AND (“transplant*”OR “graft*” OR “transfer” OR “autograft*” OR "autologous transplant*" OR “sculpt*” OR “inject*”)) OR “Autograft*” OR “soft tissue augmentation” OR “autotransplant*” OR "adipose tissue/transplantation" OR (“adipose” AND “tissue” AND “transplant*”) OR “lipostructur*” OR “lipoinfiltr*” OR “lipomodel*” OR “lipotransf*” OR “lipo-transf*” OR “lipofill*” OR “lipo-fill*” OR “lipoinfil*” OR “lipo-infil*” OR “lipoaugmen*” OR “lipo-augmen*” OR “fat-augmen*” OR “lipoplasty” OR "lipectomy" OR “liposculpt*” OR “lipoinject*” OR “lipo-inject*” OR “fat fill*” OR “microlipoinjection*” OR “lipoaspirate*” OR “lipotransplant*” OR

“microlipofill*” OR “micro-lipofill*”) OR ((“breast” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR (“mamma*” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR (“silicon*” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR (“saline” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR (“gel” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR (“alloplast*” AND (“implant*” OR “prosthes*” OR “endoprosthesis”)) OR “smooth implant*” OR “textured implant*” OR “Structured saline implant*” OR “Gummy bear implant*” OR “round implant*” OR “teardrop implant*” OR “Silicone gel implant*” OR “Internal Breast Prosthes*” OR “breast implant surgery”)) AND (“Breast augment*” OR “augmentation” OR “mammaplast*” OR “mammoplast*” OR “breast enlargement” OR “breast enhanc*” OR “Augmentation mammaplasty” OR “augmentation mammoplasty” OR “cosmetic breast augment*” OR “aesthetic breast augment*” OR “aesthetic breast enhanc*” OR “cosmetic breast enhanc*”) AND (“BREAST-Q” OR “Breastq” OR “breast questionnaire*” OR “Breast-Q questionnaire”)

B. PRISMA diagram for records screened, and final papers included in data extraction and analysis.



C. MINORS score template

The revised and validated version of MINORS Methodological items for non-randomized studies Score.

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies and 24 for comparative studies.

	Score
1. A clearly stated aim: the question addressed should be precise and relevant in the light of available literature	
2. Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion)	
3. Prospective collection of data: data were collected according to a protocol established before the beginning of the study	
4. Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. Also, the endpoints should be assessed on an intention-to-treat basis.	
5. Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise, the reasons for not blinding should be stated	
6. Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events	
7. Loss to follow up less than 5%: all patients should be included in the follow up. Otherwise, the proportion lost to follow up should not exceed the proportion experiencing the major endpoint	
8. Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes Additional criteria in the case of comparative study	
9. An adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data	
10. Contemporary groups: control and studied group should be managed during the same time period (no historical comparison)	
11. Baseline equivalence of groups: the groups should be similar regarding the criteria other than the studied endpoints. Absence of confounding factors that could bias the interpretation of the results	
12. Adequate statistical analyses: whether the statistics were in accordance with the type of study with calculation of confidence intervals or relative risk	
Total	

APPENDIX 3 – Letter of Information

LETTER OF INFORMATION and CONSENT

The Fat Analysis Trial (FAT): The Impact of Lip-aspirate Processing on Fat Resorption in Autologous Fat Grafting to the Breast: A Randomized Controlled Trial

Principal investigator

Tanya Delyzer, MD, FRCSC

Co-investigators

Arjang Yazdani, MD, FRCSC

Khalifa AlGhanim, MD

Introduction

You are being invited to voluntarily participate in this study because you will be scheduled to have fat grafting for breast augmentation and/or reconstruction. Before you decide to participate, it is important for you to know why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your family, friends, and/or your doctor as you wish. There may be words or statements

that you do not understand. Ask your study doctor or study staff to explain anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

In this consent document, "you" always refers to the study participant. If you are a substitute decision maker (SDM) (i.e. someone who makes the decision of participation on behalf of a participant), please remember that "you" refers to the study patient. If an SDM is needed for this study, you will be asked to review and sign this consent form on behalf of the participant.

Before agreeing to participate in this study, it is important that you know about the study. This document describes the purpose, procedures, benefits, discomforts, and risks associated with this study, as well as your rights if you decide to participate in this study.

Why is this study being done?

Fat grafting is a commonly used technique that involves harvesting fat using liposuction, processing the fat, and then injecting it into the breast for augmentation or reconstruction. There is currently no standard method for fat processing. The downside of fat grafting is the fact that fat can get reabsorbed into the body after surgery. This can often be unpredictable and can lead to undesired cosmetic results.

The goal of this study is to compare two common fat processing methods to determine if one is better than the other at reducing the amount of fat that is reabsorbed into the body from the breasts after surgery.

How many people will take part in the study?

200 patients will participate in this study at London Health Sciences Centre and St. Joseph's Hospital (100 patients will be scheduled for fat grafting for the purposes of breast reconstruction and the other 100 will be scheduled for fat grafting purely for cosmetic breast augmentation).

What is involved in the study?

If you choose to take part in this study, you will be randomly selected to be part of one of two groups:

1) Decantation Group – The use of gravity to separate the different layers of the fat prior to injection.
2) Revolve Group – The use of a medical device, which will collect the fat and suction off the fluid and oils, leaving the fat behind, to be injected.

For each group, the following will be done:

- Breast volume will be measured before and after surgery using a non-invasive 3D imaging technique.
- BreastQ questionnaire will be filled in before the procedure

At the post-surgery check-up:

- Breast volume will be measured using a non-invasive 3D imaging technique.

Three months after surgery:

- BreastQ will be completed again.
- A non-invasive ultrasound of the breast tissue will be done in clinic.

How long will I be in the study?

If you choose to take part in this study, you will have your regular follow up appointments, up to two years following the procedure.

Are there benefits to taking part in the study?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will help guide plastic surgeons in the future and will ultimately increase patient satisfaction in the future.

What are the risks of the study?

There are risks associated with the procedure, however, there are no additional risks if you take part in this study.

What about privacy and confidentiality?

All data that will be collected from this study will be considered confidential. We will maintain your confidentiality by using a unique identifier number (a study ID) on all documents instead of your name. A separate secure document will contain the linkage between your name and study ID to minimize the possibility of a privacy breach. This list will be kept in a secure place, separate from your study file. Your research records will

be stored in a locked cabinet in Dr. Delyzer's office and kept in electronic format in a password protected file behind the hospital firewall. Any data that we collect for this study will not include identifying information other than your study ID in order to protect your confidentiality. If the results of the study are published, your name will not be used and no information that discloses your identity will be released or published without your explicit consent.

By signing the consent form, you hereby consent to participation in this study. By consenting to this study, you agree to allow us to confidentially collect this data. If you do not consent to this data collection, then you cannot participate in this study. Representatives of Western University Health Sciences Research Ethics Board and the Lawson Health Research Institute's Quality Assurance and Education Program may contact you or require access to your study-related records to monitor the conduct of the research.

The study doctor will keep any personal health information about you in a secure and confidential location for a minimum of 15 years as required by Lawson Health Research Institute policy.

If, during the course of this study, new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by your study doctor.

What are my rights as a research participant?

Your participation in this study is voluntary. You may refuse to participate, refuse to answer any questions, or you may withdraw from the study at any time with no effect on your future care. If you decide not to participate or if you withdraw from the study before it is completed, the alternative procedures or courses of action will be explained to you by your doctor.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. If the results of the study are published, your name will not be used. If you would like to receive a copy of the overall results of this study, please put your name and address on a blank piece of paper and give it to the Clinical Research Associate.

What are the costs?

You will not be paid for taking part in this study.

In the case of research-related side effects or injury, medical care will be provided by your study doctor or you will be referred for appropriate medical care. No funds have been set aside to compensate you in the event of injury or illness related to the study treatment or procedures. You do not waive any of your legal rights by signing the consent form.

Whom do I call if I have questions or problems?

If you have questions about this study, you can talk to your doctor. You can also talk to the doctor who oversees the study at this institution

Dr. Tanya Delyzer

If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Patient Relations Office at LHSC at (_____ ext. ___)

24 hour contact number - LHSC at _____ [Plastic surgery resident on call]

If a medical emergency arises, proceed to your local Emergency Department.

A copy of this letter will be made for you to keep.

London Health Sciences Centre
London Regional Cancer Program

St JOSEPH's HEALTH CARE LONDON

LAWSON HEALTH RESEARCH INSTITUTE

CONSENT FORM

The Fat Analysis Trial (FAT): The Impact of Lip-aspirate Processing on Fat Resorption in Autologous Fat Grafting to the Breast: A Randomized Controlled Trial

I have read the accompanying letter of information and have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction. Upon signing this form, I will receive a copy.

_____ _____

Signature of Participant Date

_____

Name of Participant

_____ _____

Signature of Person Conducting Date

The Informed Consent Discussion

_____

Name of Person Conducting

The Informed Consent Discussion

□ The person signing below acted as a translator for the participant during the consent process and attests that the study as set out in this form was accurately translated and has had any questions answered.

_____ _____

Signature of Interpreter Aiding Date

The Informed Consent Discussion

_____ _____

Name of Interpreter Aiding Language

The Informed Consent Discussion

APPENDIX 4 – BREASTQ

BREASTQ			
Scale	**Scale Component**		
APPEARANCE-RELATED PSYCHOSOCIAL DISTRESS	Instruction		Circle only one answer for each statement. These phrases may be used by people to describe themselves. Regarding your appearance - To what extent do you disagree or agree with each statement:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree
	Item		1. I feel sad about how I look.
	Item		2. I feel nervous about how I look.
	Item		3. I feel frustrated about how I look.
	Item		4. I feel anxious when people look at me.
	Item		5. I fear that my appearance is not normal.
	Item		6. I am afraid of being ugly.
	Item		7. I tend to avoid staying among people.
	Item		8. I have little interest in doing things.

EXPECTATIONS	Instruction		Circle only one answer for each statement. These phrases people may use to describe how their lives will change after a cosmetic surgery. Regarding your appearance - To what extent do you disagree or agree with each statement:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree

	Item		1. I will look great.
	Item		2. People will tell me how great I look.
	Item		3. People closest to me will be proud of my appearance.
	Item		4. I got to change.
	Item		5. Good things will happen to me.
	Item		6. I will feel as if my condition is right.
	Item		7. My close relationships will improve.
	Item		8. New people will try getting to know me.

BODY IMAGE	Instruction		Circle only one answer for each statement. Regarding your body - and considering the last week - To what extent you disagree or agree with each statement:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree
	Item		1. I feel positive about my body.
	Item		2. My body is not perfect, but I love it like this.
	Item		3. I am happy with my body.
	Item		4. I am proud of my body.
	Item		5. I see I have an attractive body.
	Item		6. I feel good about my body when I get naked.
	Item		7. I have the body I wish.

SOCIAL FUNCTION	Instruction		Circle only one answer for each statement. Regarding your body - and considering the last week - To what extent you disagree or agree with each statement:
	Response option		Never agree

	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree
	Item		1. I feel comfortable in social gatherings with people I know.
	Item		2. People listen to what I have to say.
	Item		3. I feel accepted by people.
	Item		4. I feel integrated in social situations.
	Item		5. I leave a good first impression.
	Item		6. Take part in life instead of being humble.
	Item		7. It is easy for me to make new friends.
	Item		8. I feel confident when I am at events with gatherings (such as: meetings).
	Item		9. I feel comfortable around people I don't know well.
	Item		10. I feel confident when entering a room full of people, I don't know.

PSYCHOLOGICAL FUNCTION	Instruction		Circle only one answer for each statement. Regarding your body - and considering the last week - To what extent you disagree or agree with each statement:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree
	Item		1. I trust myself.
	Item		2. I am proud of myself.
	Item		3. I feel happy.
	Item		4. I love myself.
	Item		5. I am a deeply emotional person.
	Item		6. I feel being able to control my life.

	Item		7. I feel confident.
	Item		8. I feel self-acceptance.
	Item		9. I am at peace with myself.
	Item		10. I feel proud of myself.

PHYSICAL FUNCTION	Instruction		Circle only one answer for each question. Regarding your bod - and considering the past week - how often have you had a problem with:
	Response option		Always
	Response option		frequently
	Response option		Sometimes
	Response option		Never
	Item		1. Getting out of bed?
	Item		2. Bending from side to side?
	Item		3. Walking or moving?
	Item		4. Bending over (for example: to tie your shoes)?
	Item		5. Do moderate-Intensity exercises (for example: jogging)?
	Item		6. Going up or down stairs?
	Item		7. Standing for a long period of time?

PHYSICAL SYMPTOMS	Instruction		Circle only one answer for each question. Regarding your body - and considering the last week - How many times this has happened to you:
	Response option		Always
	Response option		frequently
	Response option		Sometimes
	Response option		Never
	Item		1. Feeling tired throughout the day?
	Item		2. Back pain?

	Item		3. Joint pain?
	Item		4. Leg pain or discomfort?
	Item		5. Feeling unbalanced?
	Item		6. Feeling weak?
	Item		7. Shortness of breath with light exercise?
	Item		8. Swollen feet?
	Item		9. rash or skin infection?
	Item		10. Excessive sweating?

SEXUAL FUNCTION	Instruction		Circle only one answer for each statement. Regarding your own body - To what extent do you disagree or agree with each statement:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		Somewhat agree
	Response option		Definitely agree
	Item		1. Sex is satisfactory to me.
	Item		2. I am comfortable taking off my clothes in front of my life partner.
	Item		3. I am satisfied with my sexuality.
	Item		4. I feel comfortable if the lights are on during sex.
	Item		5. I feel sexy attractive if I am without clothes

SATISFACTION WITH ABDOMEN	Instruction		Circle only one answer for each question. Considering your belly (any abdomen or stomach area) - over the last week - How satisfied or dissatisfied are you with the following:
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied

	Item		1. How well your clothes fit your belly?
	Item		2. The size of your belly?
	Item		3. The shape of your belly from the side (the side view)?
	Item		4. The shape of your belly?
	Item		5. What does your belly look like in a swimsuit?
	Item		6. What do your stomach muscles look like?
	Item		7. What shape is your belly when you are naked?

SATISFACTION WITH BACK	Instruction		Circle only one answer for each question. Considering your back - over the last week - How satisfied or dissatisfied are you with the following::
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. How smooth is your back?
	Item		2. What does your back look like from different angles?
	Item		3. The shape of your back muscles?
	Item		4. The shape of your back when you are naked?

SATISFACTION WITH BODY	Instruction		Circle only one answer for each question. Considering your whole body - over the last week - How satisfied or dissatisfied are you with the following::
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. What does your body look like while you are dressed?
	Item		2. How well your clothes fit your body?

	Item		3. The size (any weight) of your body?
	Item		4. Your body shape?
	Item		5. What is your body like in pictures?
	Item		6. Your body shape from behind?
	Item		7. What is your body shape from the side (the side view)?
	Item		8. The shape of your body in summer clothes (such as shorts and t-shirts)?
	Item		9. What does your body look like in a swimming suit?
	Item		10. What is your body shape on the mirror without clothes?

SATISFACTION WITH BUTTOCKS	Instruction		Circle only one answer for each question. Considering your buttocks in mind - over the last week - How satisfied or dissatisfied are you with the following:
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. The size of your buttocks?
	Item		2. The shape of your buttocks from the side (from the side view)?
	Item		3. The shape of your buttocks?
	Item		4. How smooth is your buttocks?
	Item		5. The appearance of the buttocks skin?

CHEST MODULE - SATISFACTION WITH CHEST	Instruction		The following questions ask about the appearance of your breast (breast area). Note: If your chest (breast area) has a different shape on both sides, answer questions about which side you are less satisfied with. Looking at your chest (breast area) - over the last week - How satisfied or dissatisfied are you with the following:
	Response option		Completely dissatisfied

	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. The shape of your chest (breast area) in a baggy T-shirt?
	Item		2. The shape of your chest (breast area) when you lie on your back?
	Item		3. How flat is your chest (breast area) when you stand upright?
	Item		4. How muscular is your chest (breast area)?
	Item		5. The shape of your chest (breast area) while you are in motion (for example: running or jumping)?
	Item		6. What does your chest (breast area) look like in soft T-shirts?
	Item		7. The shape of your chest (breast area) without clothes?
	Item		8. What does your chest (breast area) look like when you are bent?
	Item		9. Is your chest (breast area) shaped from the side (from the side view) and you are without clothes?
	Item		10. The shape of your chest (breast area) on the mirror while you are without clothes?
	Item		If you had surgery in your chest (breast area), please answer the following question:
	Item		1- What are the scars resulting from surgery?

CHEST MODULE - SATISFACTION WITH NIPPLES	Instruction		The following questions ask about the shape of your nipples. Note: If your chest (breast area) has a different shape on both sides, answer questions about which side you are less satisfied with. Looking at how your nipples looked over the last week, How satisfied or dissatisfied are you with the following:
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. The shape of your nipples?
	Item		2. The size of your nipples?
	Item		3. How flat are your nipples?

	Item		4. How soft do your nipples appear from your T-shirt?
	Item		5. Your nipples shape without clothes?

SATISFACTION WITH UPPER ARMS	Instruction		Circle only one answer for each question. Considering your upper arms - over the last week - How satisfied or dissatisfied are you with the following::
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. The size of your upper arms?
	Item		2. How soft are your upper arms?
	Item		3. The shape of your upper arms?
	Item		4. The skin appearance on your upper arms?
	Item		5. How aligned are your upper arms?
	Item		6. What did your upper arms look like when you lifted them up?
	Item		7. What does your upper arms look like when they are not covered (for example: wearing a sleeveless shirt)?

SATISFACTION WITH INNER THIGHS	Instruction		Circle only one answer for each question. Considering your inner thighs - over the last week - How satisfied or dissatisfied are you with the following::
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. How soft are your inner thighs?
	Item		2. The appearance of your inner thighs skin?
	Item		3. How aligned are your inner thighs?
	Item		4. The appearance of your inner thighs when you are naked?

SATISFACTION WITH HIPS AND OUTER THIGHS	Instruction		Circle only one answer for each question. Considering your outer hips and thighs - over the last week - How satisfied or dissatisfied are you with the following:
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. The size of your outer hips and thighs?
	Item		2. The shape of your outer hips and thighs?
	Item		3. The appearance of your outer hips and thighs skin?
	Item		4. How soft are your outer hips and thighs?
	Item		5. The appearance of your outer hips and thighs on the back side?

APPRAISAL OF EXCESS SKIN	Instruction		Circle only one answer for each question. Considering excess sagging - over the last week - how bothered you are:
	Response option		Severe discomfort
	Response option		Moderate discomfort
	Response option		Slight discomfort
	Response option		I'm not upset at all
	Item		1. Increased sagging makes you look bigger than you are (meaning gaining weight)?
	Item		2. Do you need to wear clothes to hide excess sagging?
	Item		3. Your inability to wear certain clothes due to excess sagging?
	Item		4. The extent of excess sagging hanging from you?
	Item		5. How much sag you have?
	Item		6. Seeing people lose your excess sagging?
	Item		7. What does your excess sagging look like when you are naked?

APPRAISAL OF STRETCH MARKS	Instruction		Circle only one answer for each question. Consider your wrinkles - over the last week - how bothered you are:
	Response option		Severe discomfort
	Response option		Moderate discomfort
	Response option		little discomfort
	Response option		I'm not bothered at all
	Item		1. Are you unable to wear certain clothes due to wrinkles?
	Item		2. How wide are your wrinkles?
	Item		3. Do you need to wear clothes to hide wrinkles?
	Item		4. The length of your wrinkles?
	Item		5. Where are your wrinkles (places on your body)?
	Item		6. How old are you looking like due to your wrinkles?
	Item		7. How can you observe your wrinkles?
	Item		8. How many wrinkles do you have?
	Item		9. People can see your wrinkles?
	Item		10. How is the look of your wrinkles up close?

APPRAISAL OF BODY CONTOURING SCARS	Instruction		Circle only one answer for each question. Consider your scars - over the last week - how bothered are you:
	Response option		Severe discomfort
	Response option		Moderate discomfort
	Response option		Slight discomfort
	Response option		I'm not bothered at all
	Item		1. Do you need to wear clothes to hide your scars?
	Item		2. How wide are your scars?
	Item		3. Where are your scars located?
	Item		4. The length of your scars?

	Item		5. How noticeable are your scars?
	Item		6. The color of your scars?
	Item		7. How thick are your scars (i.e. bumpy or streaked)?
	Item		8. The shape of your scars curled (not straight in shape)?
	Item		9. People can see your scars?
	Item		10. What do your scars look like when they're not covered by clothing?

SATISFACTION WITH INFORMATION	Instruction		Circle only one answer to each question. These questions inquire about information you have received from your medical team (for example: your surgeon, nursing, and staff) regarding your last surgery. How satisfied or dissatisfied are you with the information you have received regarding the following:
	Response option		Completely dissatisfied
	Response option		Somewhat dissatisfied
	Response option		Fairly satisfied
	Response option		Fully satisfied
	Item		1. Quality of answers to your questions?
	Item		2. How much information have you received written so that you can read it?
	Item		3. Activities that you should avoid during the recovery period?
	Item		4. How to perform the surgery?
	Item		5. The length of time required for convalescence and recovery?
	Item		6. Options for how to perform the surgery?
	Item		7. The nature of the complications that may occur?
	Item		8. The experience of other patients after having the same operation?
	Item		9. How long will it take to fully recover?
	Item		10. How much pain will you feel while recovering?

	Instruction		Circle only one answer for each question. These questions ask about the surgeon who performed your last operation. Did you feel that he / she:

SATISFACTION WITH DOCTOR/ SURGEON	Response option		Never agree
	Response option		Somewhat disagree
	Response option		I somewhat agree
	Response option		I definitely agree
	Item		1. Behave in a professional manner?
	Item		2. Speak to you in an easy-to-understand way?
	Item		3. All your inquiries answered?
	Item		4. Treat you with respect?
	Item		5. Made you feel comfortable?
	Item		6. Involve you in making decisions about your treatment?
	Item		7. Listen to you and understand your concerns?
	Item		8. Help you determine what works best for you?
	Item		9. Was there to reassure your concerns?
	Item		10. Spend enough time with you?

SATISFACTION WITH MEDICAL TEAM	Instruction		Circle only one answer for each question. These questions ask about members of the medical team other than your surgeon (for example: nurses and other physicians) who participated in your last surgery. Did you feel that they:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		I somewhat agree
	Response option		I definitely agree
	Item		1. Take care to protect your privacy?
	Item		2. They treated with kindness and affection?
	Item		3. Treat you with respect?
	Item		4. They answered all your inquiries?
	Item		5. Was it easy to talk to them?

	Item		6. Have they met your needs?
	Item		7. You were distinguished by accuracy?
	Item		8. Work together as a team?
	Item		9. Have the required experience?
	Item		10. Were there to reassure your concerns?

SATISFACTION WITH OFFICE STAFF	Instruction		Circle only one answer for each question. These questions inquire about members of the administration staff (for example: secretaries, receptionists) who helped you during your last surgery. Did you feel that they:
	Response option		Never agree
	Response option		Somewhat disagree
	Response option		I somewhat agree
	Response option		I definitely agree
	Item		1. Treat you with respect?
	Item		2. They made you feel comfortable?
	Item		3. Were they aware?
	Item		4. Did they fulfill your desires?
	Item		5. You were distinguished by accuracy?
	Item		6. Work together as a team?
	Item		7. They welcomed you at the front desk?
	Item		8. Were they interested?
	Item		9. They answered all your inquiries?
	Item		10. Were there to reassure your concerns?

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Curriculum Vitae

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Honors and Awards:	Western Graduate research Scholarship (WGRS) 2020-2021 LRCP Catalyst Grant for translational cancer research (25,000 CAD) – 2020 National Surgical Skills competition - RCSI winner & National Finalist – 2015 and 2016
Related Work Experience	Resident Physician – Plastic and Reconstructive surgery The University of Western Ontario 2021 – Present Assistant Registrar – Plastic Surgery/ General Surgery Department of Surgery, Jaber Al-Ahmed Hospital, Kuwait 2019- 2020 Intern Physician (Surgical) Kuwait Institute of Medical Specializations 2018 - 2019

Publications:

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