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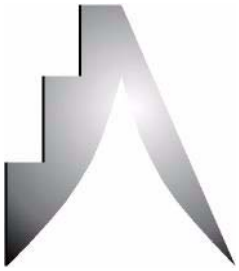

Australian Safety and Efficacy Register of New Interventional Procedures-Surgical

Systematic Review

Autologous Fat Transfer for Cosmetic and Reconstructive Breast Augmentation

September 2010

Australian Safety & Efficacy Register of New Interventional Procedures – Surgical

The Royal Australasian College of Surgeons

Autologous fat transfer for cosmetic and reconstructive breast augmentation

ISBN 978-0-9806299-7-2

Published September 2010

This report should be cited in the following manner:

Leopardi D, *et al.* Systematic review of autologous fat transfer for cosmetic and reconstructive breast augmentation. ASERNIP-S Report No.70. Adelaide, South Australia: ASERNIP-S, September 2010.

Copies of these reports can be obtained from:

ASERNIP-S
PO Box 553,
Stepney, SA 5069
AUSTRALIA
Ph: 61-8-8363 7513
Fax: 61-8-8362 2077
E-Mail: asernips@surgeons.org
http://www.surgeons.org/asernip-s

The Systematic Review of

Autologous fat transfer for cosmetic and reconstructive breast augmentation

Was ratified by the ASERNIP-S Advisory Committee on

18 June 2010

Approved by the Research Audit and Academic Surgery Board on 5 July 2010

Received by the Professional Development and Standards Board on 4 August 2010

Noted by the Council of the Royal Australasian College of Surgeons on 27 August 2010

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Executive Summary

Objective

To assess, through a systematic review of the literature, the safety and efficacy of autologous fat transfer for:

- cosmetic breast augmentation in comparison with saline and cohesive silicone gel implants
- reconstructive breast augmentation in comparison with autologous tissue transfer and tissue expanders with breast implants.

Methods

Search strategy – Studies were identified by searches of Current Contents, The York Centre for Reviews and Dissemination, The Cochrane Library, Entrez-PubMed and Ovid EMBASE from January 2001 to January 2009. Date limitations were necessary to obtain literature published since the original ASERNIP-S systematic review of autologous fat transfer for cosmetic breast augmentation was conducted in 2002.

Study selection – Included in the review were case series studies and single-arm data obtained from randomised controlled trials of comparator procedures. The outcomes examined included complication rates, durability of enhancement, reoperation rates and patient satisfaction.

Data collection and analysis – Data from the included studies was extracted by an ASERNIP-S researcher using standardised extraction tables created a priori and checked by a second researcher. Overall complication rates were calculated as a means of indirectly comparing the safety of autologous fat transfer with the nominated comparator procedures.

Results

Thirty five studies were included in this systematic review. Nine studies were randomised controlled trials from which data from 12 single arms were extracted, and 26 were case series studies, 11 of which reported outcomes for autologous fat transfer. Overall, the literature available for inclusion in this review was of poor quality. In particular, the complete lack of comparative evidence necessitated indirect comparisons to be made which made the findings of this review less reliable. It was also difficult to draw comparisons between autologous fat transfer and its cosmetic and reconstructive comparator procedures given the differences in volume achievable using prostheses or autologous tissue transfers compared with fat injections alone.

Fat necrosis, calcification and cysts were the most commonly reported complications associated with autologous fat transfer; however, these complications only occurred

in a small proportion of patients. There was no data linking the presence of these complications with long-term mammographic and cancer-related outcomes; therefore, the safety of autologous fat transfer in regards to interference with cancer detection could not be determined by this review. Complications, such as skin/flap necrosis, occurred at a similar frequency in patients undergoing breast reconstruction with gluteal and abdominal flaps. In addition, there were a variety of serious complications related to some of the comparator procedures that were not associated with autologous fat transfer (including hernia and capsular contracture).

The efficacy of autologous fat transfer could not be compared with that of prostheses augmentation procedures or breast reconstruction using autologous tissue due to the variability of outcomes reported in these studies. Patient satisfaction following autologous fat transfer, as well as reconstructions using tissue expanders with breast implants and abdominal flaps, was high. However, patient satisfaction with breast reconstruction using gluteal flaps and latissimus dorsi flaps was generally higher than that of autologous fat transfer. For autologous fat transfer the limited breast volume increase was the main complaint associated with the procedure. Where patients desire a moderate to large increase in breast volume, the use of autologous fat transfer as an adjunct to prostheses or autologous tissue transfer is feasible. Results suggest that autologous fat transfer can be safely and effectively used in conjunction with other augmentative procedures.

Fat reabsorption occurred following autologous fat transfer to varying degrees, usually in the short-term (12- month) follow-up period. As a result, additional fat transfer procedures were often necessary to obtain the desired outcome. Flap loss occurred following autologous tissue reconstruction in some cases, but it was uncommon.

Classifications and recommendations

On the basis of the evidence presented in this systematic review, the ASERNIP-S Review Group agreed on the following classifications and recommendations concerning autologous fat transfer for cosmetic and reconstructive breast augmentation:

Classifications

Evidence rating

The evidence base in this review is rated as poor, limited by the quality of the available evidence. Specific limitations of the evidence include absence of studies comparing autologous fat transfer to the nominated comparator procedures, as well as a lack of standardised reporting of outcomes.

Safety

Autologous fat transfer for cosmetic and reconstructive breast augmentation is considered to be at least as safe as the nominated comparator procedures. It is

important to note that this rating is based on indirect comparisons that have been made using overall complication rates. Important safety data examining the effect of microcalcifications following autologous fat transfer on subsequent breast cancer detection were not reported in the studies included in this review; therefore, safety in regards to this outcome cannot be determined.

Efficacy

The efficacy of autologous fat transfer cannot be determined from the literature included in this review. Efficacy outcomes reported in the included autologous fat transfer studies varied from those reported for the nominated comparator procedures; therefore, it was not possible to compare efficacy. However, the inability of autologous fat transfer to achieve a volume increase comparable to that of prostheses or autologous tissue augmentation suggests that it is less efficacious than these comparator procedures.

Clinical and research recommendations

There is a need for controlled trials (ideally randomised), assessing the effects of microcalcifications following autologous fat transfer on immediate and long-term breast cancer detection, to be conducted. Studies to determine the maximal breast volume increase reliably achieved by autologous fat transfer would also be useful in order to define the patient population who would benefit most from the procedure, as well as which breast indications should be treated using autologous fat transfer.

The ASERNIP-S Classification System

Evidence rating

The evidence for ASERNIP-S systematic reviews is classified as Good, Average or Poor, based on the quality and availability of this evidence. High quality evidence is defined here as having a low risk of bias and no other significant flaws. While high quality randomised controlled trials are regarded as the best kind of evidence for comparing interventions, it may not be practical or ethical to undertake them for some surgical procedures, or the relevant randomised controlled trials may not yet have been carried out. This means that it may not be possible for the evidence on some procedures to be classified as good.

Good

Most of the evidence is from a high quality systematic review of all relevant randomised trials or from at least one high quality randomised controlled trial of sufficient power. The component studies should show consistent results, the differences between the interventions being compared should be large enough to be important, and the results should be precise with minimal uncertainty.

Average

Most of the evidence is from high quality quasi-randomised controlled trials, or from non-randomised comparative studies without significant flaws, such as large losses to follow-up and obvious baseline differences between the comparison groups. There is a greater risk of bias, confounding and chance relationships compared to high quality randomised controlled trials, but there is still a moderate probability that the relationships are causal.

An inconclusive systematic review based on small randomised controlled trials that lack the power to detect a difference between interventions and randomised controlled trials of moderate or uncertain quality may attract a rating of average.

Poor

Most of the evidence is from case series, or studies of the above designs with significant flaws or a high risk of bias. A poor rating may also be given if there is insufficient evidence.

Safety and Efficacy Classification

Safety

At least as safe compared to comparator* procedure(s)
This grading is based on the systematic review showing that the new intervention is at least as safe as the comparator.

Safety cannot be determined
This grading is given if the evidence is insufficient to determine the safety of the new intervention.

Less safe compared to comparator* procedure(s)
This grading is based on the systematic review showing that the new intervention is not as safe as the comparator.

Efficacy

At least as efficacious compared to comparator* procedure(s)
This grading is based on the systematic review showing that the new intervention is at least as efficacious as the comparator.

Efficacy cannot be determined
This grading is given if the evidence is insufficient to determine the efficacy of the new intervention.

Less efficacious compared to comparator* procedure(s)
This grading is based on the systematic review showing that the new intervention is not as efficacious as the comparator.

Research recommendations

It may be recommended that an audit or a controlled (ideally randomised) clinical trial be undertaken in order to strengthen the evidence base.

Clinical recommendations

Additional recommendations for use of the new intervention in clinical practice may be provided to ensure appropriate use of the procedure by sufficiently qualified/experienced centres and on specific patient types (where appropriate).

* A comparator may be the current 'gold standard' procedure, an alternative procedure, a non-surgical procedure or no treatment (natural history).

The ASERNIP-S Review Group

ASERNIP-S Director

Professor Guy Maddern
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069

Protocol Surgeon

Mr Norman Olbourne
Sydney Institute of Plastic Surgery
Chatswood NSW 2067

Advisory Surgeon

Mr Keith Mutimer
Brighton Plastic Surgery Centre
Brighton VIC 3186

ASERNIP-S Researcher

Ms Deanne Leopardi
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069

ASERNIP-S Researcher

Dr Prema Thavaneswaran
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069

Conflict of Interest

None of the authors declared a conflict of interest.

Introduction

Objective

To assess, through a systematic review of the literature, the safety and efficacy of autologous fat transfer for:

- cosmetic breast augmentation in comparison with saline and cohesive silicone gel implants
- reconstructive breast augmentation in comparison with autologous tissue transfer and tissue expanders with breast implants.

Background

Breast augmentation

Female breast augmentation is a commonly requested surgical procedure whereby breast size and shape is altered. Since the late 1800s foreign substances have been injected or implanted into breasts to augment or reconstruct them (Bondurant et al 1999). Use of autologous tissue for breast augmentation began in 1887 with part of a patient's healthy breast tissue being transferred on a pedicle to reconstruct the other breast, and continued in 1895 with transplantation of a lipoma from a patient's hip to repair the patient's breast (Bondurant et al 1999). Experimentation with paraffin injections for breast augmentation was first reported in 1889 (Bondurant et al 1999). Despite the complications associated with paraffin injections, which included infection and lump formation, this procedure remained popular throughout the first half of the twentieth century (Erguvan-Dogan 2006). Early experimentation with breast augmentation saw many different materials implanted into the breasts, including ivory, glass balls, ground rubber and ox cartilage, all of which led to varying levels of complications (Bondurant et al 1999). For example, in 1949, synthetic sponges (composed of materials such as polyvinyl) were implanted into breasts; however, they generally shrank and hardened within a year and were prone to infection (Renwick 1996). In the 1950s and 1960s subglandular silicone injections were used, which led to many complications, including chronic inflammation, infection and lumps (Collis et al 2004). Soon after this in 1964, the first silicone implants were developed and refined until 1992, when they were withdrawn from use due to safety concerns (Renwick 1996). In 1992, only saline breast implants were allowed to be used for breast augmentation. Soybean oil implants were developed in 1987 and marketed to surgeons in 1995 while there was concern surrounding traditional silicone based breast prostheses; however, their use was short lived, as it was found that they contained a filler that was toxic when broken down by the body (Kirkpatrick et al 2002). In 2001, a manufacturer of a newer range of silicone breast implants was able to satisfactorily demonstrate their quality, safety and efficacy, and as a result silicone implants were re-approved by the Therapeutic Goods

Administration (TGA) and placed on the Australian Register of Therapeutic Goods (TGA 2004). Currently in Australia, saline and cohesive silicone are the only breast implant fillers used. Polyurethane-covered breast prostheses are also available in Australia.

Indications for breast augmentation

Cosmesis

Over time, an increasing number of women have opted to undergo breast surgery for cosmetic reasons alone (Didie et al 2003). From 2006 to 2007, a total of 7,755 augmentation mammaplasty procedures were carried out in Australia, 7,089 of which were bilateral augmentation not following mastectomy (Australian Institute of Health and Welfare 2008). The number of procedures of this kind has increased by 34% from both 2000 to 2003 and 2003 to 2006. The overall increase in the number of bilateral augmentation mammaplasty procedures not related to mastectomy from 2000 to 2006 was 56%.

Literature on the indications for cosmetic breast augmentation is limited, but anecdotal evidence suggests that one of the motivations for this surgery may be linked with female identity and how it is focused on physical appearance and breast size and shape. Many studies reported that women undergoing cosmetic surgery have a heightened dissatisfaction with a specific feature, in this case their breasts, rather than a global dissatisfaction with their entire body (Didie et al 2003). Interpersonal factors may also influence a woman's decision to elect breast augmentation, for example some studies suggest that breast augmentation patients have poorer interpersonal and romantic relationships (Didie et al 2003).

In Australia, breast augmentation for cosmetic indications is not covered by the Medicare Benefits Schedule (MBS) unless it can be demonstrated that surgery is required to treat a significant breast deformity (MBS 2008).

Reconstruction

For women, reconstruction following breast cancer or disease resulting in breast deficits is believed to provide a sense of overcoming the disease (Bondurant et al 1999). Breast cancer is the most common cause of cancer and the second most common cause of death in women (Makhoul et al 2006). One study stated that at present breast cancer accounts for the highest prevalence of malignant disease in women from industrialised countries (Ziswiler-Gietz et al 2008). In 2006 in Australia 12,614 women were diagnosed with breast cancer, accounting for 28% of all new cancer cases that year (AIHW 2009). From 2007 to 2008, 5,187 hospitalisations (4.9% of all breast cancer-related hospitalisations) took place for the performance of simple mastectomy (AIHW 2009). The aims of breast reconstruction are both functional and aesthetic. Reconstructive mammaplasty is performed to restore body symmetry and achieve the closest to normal breast contour possible, without compromising immediate or subsequent cancer treatment (Andrews et al 1999).

In Australia, reconstructive breast augmentation is covered by the MBS. Table 1 specifies the criteria in order for Medicare benefits to be payable to patients undergoing breast augmentation, along with the number of claims made per annum for each item from 2005 to 2008 (MBS 2008; MBS Statistics 2008).

Table 1: Breast augmentation procedures covered by the MBS

Item Number	Descriptor	Fee/Benefit*	Number of Claims
45524	MAMMAPLASTY, AUGMENTATION, for significant breast asymmetry where the augmentation is limited to 1 breast	Fee: $700.95 Benefit: $525.72	2005: 266 2006: 336 2007: 302 2008: 400 2009: 411
45527	MAMMAPLASTY, AUGMENTATION, (unilateral), following mastectomy	Fee: $700.95 Benefit: $525.75	2005: 222 2006: 226 2007: 219 2008: 248 2009: 281
45528	MAMMAPLASTY, AUGMENTATION, bilateral, not being a service to which Item 45527 applies, where it can be demonstrated that surgery is indicated because of malformation of breast tissue (excluding hypomastia), disease or trauma of the breast (other than trauma resulting from previous elective cosmetic surgery)	Fee: $1,051.30 Benefit: $788.50	2005: 39 2006: 31 2007: 22 2008: 31 2009: 36
45559	TUBEROUS, TUBULAR OR CONSTRICTED BREAST, where it can be demonstrated, correction of by simultaneous mastopexy and augmentation of (unilateral)	Fee: $1,074.40 Benefit: $805.80 or $1,005.30	2005: 0 2006: 1 2007: 40 2008: 88 2009: 128

*at July 2010

Conventional procedures

Cosmetic mammaplasty

Cosmetic breast enhancement surgery is often, but not always, performed under general anaesthesia and involves an incision on or near the breast so that a prosthesis, or implant, can be inserted (TGA 2008). The three most common types of incision are inframammary incisions (below the breast where the breast tissue meets the chest wall), periareolar incisions (in the areola) or transaxillary incisions (in the armpit) (TGA 2008). The implant is either inserted behind the breast tissue but in front of the muscles and fibrous tissues that line the front of the ribs and chest wall (subglandular), or behind the breast tissue and partially or fully under the pectoral and other chest muscles (submuscular) (Mladick 1993). The most common types of implants used for cosmetic breast augmentation are prefilled silicone gel filled prostheses or silicone shells which are filled with saline at the time of surgery.

Saline implants

Saline implants are composed of a dense-walled silicone elastomer envelope that is filled with sodium chloride (saline) solution (TGA 2008). The surface of the envelope may be textured or smooth. The benefits of saline-filled silicone implants are that saline is found naturally in the body, and is therefore easily absorbed in the case of

implant rupture or leak. Saline implants may also be inserted empty and filled with the desired volume of saline once they are in place, which means a smaller incision is required and scarring may be reduced.

Cohesive silicone gel implants

Like saline breast implants, silicone implants are composed of a dense-walled silicone elastomer envelope, which may be textured or smooth, but the envelope is prefilled with a specific volume of silicone. Silicones are complex man-made plastics or 'polymers', which are considered to be the most compatible synthetic material available for implantation in the human body (TGA 2008). A cohesive silicone gel has been developed so that in the event of implant rupture the silicone would not permeate into the surrounding tissues as readily as the more liquid gels of previous times (TGA 2008). The benefit of silicone implants is that the gel content can be manipulated to feel similar to normal breast tissue, which saline filled implants can not do.

Both types of implants are associated with complications of various clinical and aesthetic significances. Handel et al (1995) monitored complications in 1,655 breast implants, both silicone- and saline-filled, over 15 years, and found that common complications included capsular contracture, skin wrinkling and low rates of infection and even rupture. Other adverse events associated with breast implants, but not necessarily caused by them, include axillary adenopathy, haemorrhage at the operative site, peri-implant haematoma or seroma, rashes, swelling, implant extrusion, misplacement, shifting, pain, changes in skin sensation, chest wall skeletal changes, pneumothorax, calcification, lactation and galactocele (Institute of Medicine 1999). Complications specific to saline implants include deflation, implant filler port or valve leakage and rippling, while complications specific to silicone implants include gel migration, silicone granuloma, and silicone exudation through the skin or nipple (Institute of Medicine 1999).

Reconstructive mammaplasty

Conventional reconstructive breast augmentation is almost always performed under general anaesthesia and may utilise either the patient's own tissue from another region of the body or tissue expanders and implants to reconstruct the breast (Bassiouny et al 2005). The different procedures that can be used for breast reconstruction are detailed below.

1. Autologous reconstruction

Transverse rectus abdominis myocutaneous (TRAM) flaps

TRAM flaps are taken from the abdomen and utilise some of the rectus abdominis muscle as a carrier for the overlying skin and fat. They may be pedicled on the superior epigastric system, or raised as free flaps, pedicled on the inferior epigastric vessels with microvascular anastomosis at the recipient site to re-establish blood flow (Ziswiler-Gietz et al 2008). The first TRAM flaps were described in 1982 by Hartrampf, and were pedicled (DellaCroce et al 2007). Before long this procedure

was recognised as the 'gold standard' reconstructive procedure for breasts (Andrews et al 1999).

The benefits of pedicled TRAM flaps are that they are reliable, easy to harvest and do not require special instruments, or surgeons with microvascular experience (Bassiouny et al 2005). The benefits of free TRAM flaps are that they can provide a larger skin volume with reduced donor site morbidity, and they can be easily contoured for a pleasing aesthetic result (Bassiouny et al 2005). The disadvantages of both types of TRAM flaps are that they are more invasive than prosthetic breast reconstruction procedures, and because they utilise skin, fat and muscle from the donor site, they are associated with potential donor site morbidity, such as abdominal hernia, as well as a prolonged hospital stay (Fathi et al 2008).

Perforator flaps

Perforator flaps were pioneered in Japan by Koshima in 1989, and utilise the patient's own skin and fat, as in a TRAM flap, without the underlying muscle tissue (Sananpanich et al 2008). The flap is isolated on a vascular pedicle from the donor site and circulation is re-established at the recipient site, which requires skills in microvascular surgery. Different perforator flaps include:

Deep inferior epigastric perforator (DIEP) flaps

DIEP flaps comprise skin, fat and a perforator vascular pedicle taken from the abdomen. The selected perforator is traced inferiorly to the point where the external iliac vessels branches. A long vascular pedicle is taken based on the inferior epigastric vessels and anastomosed to the mammary or thoracodorsal vessels (Howard et al 2005).

An advantage of this procedure is that the rectus abdominis muscle is not compromised. This is because the vessel taken from the abdomen is carefully dissected through the muscle fibres leaving the rectus abdominis virtually intact. The patient is not left with a weak abdominal area reducing the risk of some of the potential complications of the TRAM flap. In addition, the benefit of closing the incision in the muscle where the flap was harvested is a flatter abdomen, as the tendency to pseudohernia development is reduced producing results similar to that of abdominoplasty (Howard et al 2005). The major disadvantage of this procedure is that it is time consuming due to the need to carefully dissect the vessels through the rectus muscle without causing damage to the pedicle.

Superficial inferior epigastric artery (SIEA) flaps

Free SIEA flaps were first applied to breast reconstruction in the early 1900s (Fathi et al 2008). Like DIEP flaps, SIEA flaps utilise skin and fat from the abdomen, except the vessel dissected from the muscle to vascularise the flap of tissue lies closer to the surface of the flap, which allows the flap to be taken from a relatively superficial dissection. However, the pedicle is often smaller and less reliable.

The advantages of this procedure are similar to that of DIEP in that the patient experiences similar results to an abdominoplasty with a reduced risk of vessel injury

due to the superficiality of the donor vessels (Fathi et al 2008). The disadvantages of this procedure are inconsistent vascular pedicle anatomies and shorter and smaller diameter vascular pedicles (Fathi et al 2008). SIEA is also not appropriate in many patients due to the unsuitability of their superficial vessels.

Superior gluteal artery perforator (SGAP) flaps

Perforator flaps taken from a gluteal donor area can be used in women who have inadequate abdominal tissue or whose abdomen is not suitable due to scarring from previous laparotomy, caesarean section, abdominoplasty or liposuction (De Frene et al 2006). SGAP flaps utilise skin and fat from the buttock (Howard et al 2005). A perforator vessel emerges from the gluteus maximus between the posterior iliac spine and the greater trochanter (Howard et al 2005). This vessel is traced and carefully dissected through the gluteus maximus to develop a length of the vessel as long as possible (Howard et al 2005).

The advantage of this procedure is that there is often an abundance of adipose tissue in the buttock even in thin patients and the scar left from the removal of the flap is well hidden (Howard et al 2005). A disadvantage of this procedure is that the perforator is often not long enough to reach the axilla when transplanted onto the chest and can only be easily used when the internal mammary artery is available for the anastomosis (Howard et al 2005). It is possible to lengthen the vascular pedicle with vein graft but this is time consuming and increases the risk of failure due to vascular compromise. As well as this, breast reconstruction using gluteal perforator flaps is a technique that is not widely taught; therefore, experience in this area is less widespread than abdominal flap techniques (Howard et al 2005).

Inferior gluteal artery perforator (IGAP) flaps

Much like SGAP flaps, IGAP flaps are comprised of skin and fat taken from the gluteal area, with the exception of the use of perforating vessels from the inferior gluteal artery rather than the superior gluteal artery (Howard et al 2005). The flap is also taken from the lower buttock crease.

The advantages and disadvantages of this procedure are the same as that of SGAP; however, IGAP flaps have longer vascular pedicles than SGAP flaps, and can often reach the axilla (Howard et al 2005).

Latissimus dorsi flaps

This procedure was first described by Iginio Tansini in 1897 to cover a chest wall defect resulting from breast amputation (Kim et al 2007). In 1912, Stefano d'Este performed a variation of this procedure to reconstruct a breast following mastectomy (Kim et al 2007). The donor site in this case is the back of the chest wall (Kim et al 2007). This tissue is dissected free and its vascular pedicle isolated in continuity, the flap is then passed under the skin of the axilla and brought forward to reconstruct the breast (Kim et al 2007). Its functionality depends on the integrity of the axillary vessels and nerves that vascularise and innervate the latissimus dorsi muscle.

The main benefit of this procedure is that microsurgical experience is not required. The limitation of the procedure is that the donor area (back) generally has very little adipose tissue available and may not sufficiently provide the desired breast volume. Consequently, implants are often used to augment the latissimus dorsi flap, which brings into consideration the limitations and risks associated with prosthetic breast augmentation. Despite the little functional deficit resulting from latissimus dorsi breast reconstruction, the scar on the back from closure of the donor site can be associated with wound healing problems and seroma, as well as being a cosmetic issue.

2. Tissue expanders and breast implants

Following mastectomy the remaining skin and subcutaneous tissue is often thin and there is an increased risk of capsular contracture or prosthesis exposure if a breast implant is placed in the subcutaneous pocket (Yano et al 2007). Therefore, a submuscular location for the prosthetic reconstruction is preferable. To do this the pectoralis major muscle may be detached from its sternal origin to create a sufficiently sized pocket to accommodate a tissue expander (Yano et al 2007). Once in place the tissue expander is gradually inflated by injection of physiological saline to as much as 20% over the desired breast volume (Yano et al 2007). Three to six months after surgery the tissue expander is removed and replaced with a silicone implant (Yano et al 2007). The overexpansion is accommodated to the definitive prosthesis, giving a more natural droop to the breast and potentially reducing the incidence of breast capsule contraction.

The benefit of breast reconstruction using a prosthesis is that it is a more simple procedure than breast reconstruction using autologous tissue transfer, with a shorter operation time and hospital stay. It does not cause extra scarring or donor site morbidity (Abdalla et al 2006). The disadvantages of this type of reconstruction includes the risk of implant failure, most commonly in the form of infection, rupture, capsular contracture or extrusion, and the inability to withstand radiotherapy should it be required (Abdalla et al 2006). Another disadvantage is the need for a second operation to replace the expander with a definitive prosthesis and repeated attendances to progressively inflate the tissue expander.

Autologous fat transfer

Concerns regarding the efficacy of silicone breast implants have motivated the search for an alternative transplant material for many years (Bircoll et al 1987). The first clinical fat transplantation was performed in 1893 by Neuber, who filled out depressed scars with small pieces of autogenous fat. Fat transplants were tried either as free grafts or as injections but could only persist as small pieces of tissue, since problems with revascularisation would inevitably lead to necrosis of large transplants of fat with cyst formation and reabsorption.

A breast enhancement technique described by Bircoll et al involved the collection of fat using standard liposuction techniques (Bircoll et al 1987; Bircoll 1987). The fat

was then mixed with insulin and reinjected using a 16-gauge needle and a small syringe. Fat was injected into multiple submammary pockets in the breast in very small quantities to minimise the risk of absorption or necrosis. Today, autologous fat transfer is often performed under local anaesthesia using fat aspirated from a donor site where it is abundant. Multiple procedures are often employed with a small amount of fat transplanted at intervals in an attempt to obtain the most aesthetically pleasing and durable result. Re-injecting amounts of fat is thought to achieve maximal augmentation with minimal reabsorption.

The advantages of autologous fat transfer for breast augmentation include being able to avoid prosthesis usage and the associated complications, a more realistic breast feel, and the avoidance of large incision scars, both at the donor site and on the breast. Its major disadvantage is the need for repeated surgical procedures and the unpredictable survival of the injected fat.

Breast augmentation by fat injection was condemned by the American Society of Plastic and Reconstructive Surgeons (ASPRS) and others in 1987 for potentially obscuring carcinoma of the breast, necessitating many biopsies to assess the numerous false positives that may arise (Dixon 1988a). Although mammographic evaluation of breasts augmented by more conventional means (including implants) may be difficult, alternative imaging methods such as MRI potentially overcome these problems (Huch et al 1998). Some have argued that conventional breast augmentation via prosthesis presents as serious a challenge to mammography as fat injection, a view that has not gone unchallenged (Fox 1988; Dixon 1988b). By 2007 the American societies of plastic and aesthetic plastic surgeons issued a joint caution against fat injection of the breast (Chan et al 2008). Despite this, both societies 'strongly support the ongoing research efforts that will establish the safety and efficacy of the procedure' (Chan et al 2008). In the most recent Guiding Principles released by the American Society of Plastic Surgeons in January 2009, it is stated that autologous fat transfer should be administered with caution in patients at high risk of breast cancer and that physicians should provide appropriate informed consent for each patient prior to treatment.

Critics have also maintained that much of the injected fat will not survive (ASPRS 1987). Proponents of fat transfer for breast augmentation claim up to 80% fat survival for injections into the breast, whilst noting that different sites in the body have differing fat reabsorption rates (Bircoll 1988). However, others have reported complete reabsorption of fat injected into the breast over a 12-month period, using fat suctioned from the thighs (Illouz 1990).

Various complications have also been associated with fat transfer to the breast. Castello et al (1999) reported a case of a giant liponecrotic pseudocyst following breast augmentation by fat injection, which necessitated lumpectomy and subsequent treatment of the surgical defect with a gel-filled prosthesis. They suggest that their findings '…should completely exclude fat injection as a technique for breast

augmentation'. Likewise, Maillard (1994) reported a case in which fat directly injected into the breast resulted in painful calcified capsules which required removal via a subcutaneous mastectomy. He stated, 'This case clearly warns against augmentation using fat taken from liposuction'.

Summary

Breast augmentation by autologous fat transfer remains controversial, and there are still doubts about the safety of this procedure. The systematic review conducted by ASERNIP-S in February 2002 on autologous fat transfer for breast augmentation for cosmetic indications found that, at that time, because of the lack of evidence regarding patient benefit from the procedure, coupled with the theoretical dangers of obscuring radiological diagnosis of carcinoma of the female breast, the Royal Australasian College of Surgeons could not endorse the collection of data within Australia for the procedure (Chapman et al 2002). Since then, with advances in imaging techniques, it has become evident that it may be possible to distinguish between the calcifications sometimes caused by autologous fat transfer and actual early stage breast cancer, potentially making autologous fat transfer a viable technique for breast augmentation for both cosmetic and reconstructive indications. Thus, the aim of this review is to assess the safety and efficacy of autologous fat transfer, compared with conventional cosmetic and reconstructive breast augmentation procedures in light of new technology and evidence arising since the original review was conducted in 2002.

It is important to note that although autologous fat transfer has been compared with numerous cosmetic and reconstructive procedures in this review, the outcomes that can be achieved using prostheses and autologous tissue augmentations vary from those that can be achieved using fat transfer alone.

Research questions

The specific research questions that will be addressed in this review are as follows:

1. Is autologous fat transfer for breast augmentation (cosmetic and reconstructive) as safe as saline implants, cohesive silicone implants, autologous tissue transfer or tissue expanders and implants?
2. Is autologous fat transfer for breast augmentation (cosmetic and reconstructive) as effective as saline implants, cohesive silicone implants, autologous tissue transfer or tissue expanders and implants?
3. Is one intervention (autologous fat transfer, saline implant or cohesive silicone implant) superior to the others for cosmetic breast augmentation?
4. Is one intervention (autologous fat transfer, autologous tissue transfer or tissue expanders and implants) superior to the others for reconstructive breast augmentation?

Methodology

Literature search protocol

Inclusion criteria

Articles were selected for inclusion in this systematic review on the basis of the following criteria:

Population

Adult women undergoing breast augmentation for cosmetic or reconstructive indications.

Index intervention

Autologous fat transfer, in the form of injectable fat, used as the sole technique for breast augmentation or used in conjunction with or adjunct to a comparator intervention (see below).

Comparator interventions

Cosmetic comparators

Saline or cohesive silicone gel implants, with either smooth or textured walls.

Reconstructive comparators

Perforator flaps (including DIEP flaps, SIEA flaps, SGAP flaps and IGAP flaps), TRAM flaps (free or pedicled), latissimus dorsi flaps or breast implants (saline and cohesive silicone gel) facilitated by the use of tissue expanders.

Outcomes

Studies were included if they contained information on at least one of the following outcomes:

- **Perioperative and postoperative morbidity of patients**[1] which included, but was not limited to:
  - capsular contracture
  - implant rupture
  - infection
  - leakage
  - skin wrinkling
  - deflation
  - haemorrhage or bleeding complications.

- **Perioperative and postoperative mortality of patients**

1 The occurrence of a postoperative event which is common to all surgical procedures, particularly of this nature, will be extracted but not considered a complication. Such events are generally transient and include inflammation, bruising/ ecchymosis and pain. Only those events that are not considered to be a normal part of the postoperative course will be reported as a complication.

- **Perioperative and early postoperative outcomes for patients** which included, but were not limited to:
  - operation time
  - early re-intervention
  - readmission.

- **Perioperative and postoperative effectiveness of the procedure** which included, but was not limited to:
  - mammographic issues
  - psychosocial effects, including patient satisfaction
  - effectiveness of enhancement, including
    - measures of fat re-absorption
    - scarring
    - durability of enhancement
  - failure of operation.

- **Convalescence of patients** which included, but was not be limited to:
  - length of hospital stay
  - healing time.

- **Cost/resource use**

Types of studies

Where possible all systematic reviews[2], randomised controlled trials (RCTs) and non-randomised comparative studies comparing autologous fat transfer (AFT) for cosmetic or reconstructive breast augmentation with any of the comparator procedures were eligible for inclusion in the review. Case series for autologous fat transfer were also eligible for inclusion.

In the absence of comparative evidence, single arm or case series evidence was included for each comparator procedure. Due to the wealth of literature available for cosmetic and reconstructive breast augmentation using the comparator techniques, the following inclusion criteria was applied to these studies alone:[3]

- For comparator procedures with more than five level II studies, benchmark data were collated only from the study arms of RCTs where the comparator procedure was compared to another treatment (not AFT).

[2] Systematic reviews were defined as those studies with a focused clinical question, explicit search strategy, use of explicit, reproducible and uniformly applied criteria for article selection, critical appraisal of the included studies, and qualitative or quantitative data synthesis (Cook et al 1997).

[3] Single arm benchmark data were not obtained from level III studies due to the large number available and time constraints. Case series data were included when high-quality comparative evidence (RCTs) was not available or where it did not meet the inclusion criteria, due to their generally longer follow-up and larger patient numbers, as well as their tendency to report important safety outcomes.

- For comparator procedures with fewer than five level II studies and more than 10 level IV studies, benchmark data were collated only from case series with at least 100 patients and a minimum of 2 years follow-up.
- For comparators with fewer than five level II and 10 level IV studies, benchmark data were collated from all case series studies that were eligible for inclusion.
- Level III comparative evidence were not included.
- Case reports were not included.

The level II studies must have fulfilled the following criteria to be included in the review. Those level II studies that did not fulfil these criteria were excluded and case series evidence substituted.

- Use of the word random to define patient allocation.
- Use of some form of blinding (patient or assessor) throughout the immediate follow-up period.
- Less than 10% of patients lost to follow-up.[4]
- Greater than 1-year follow-up.

Additional information

Where appropriate, additional relevant published literature, in the form of letters, conference material, commentary, editorials and abstracts, was included as background information.

Publication date

In order to encompass all of the literature regarding autologous fat transfer and its cosmetic comparators which has become available since the initial review (Chapman et al 2002) was conducted, searches for this update review were date limited (for level IV evidence only, as this was the only level of evidence included in the original review) to retrieve articles published from January 2001 to 14 January 2009. Literature pertaining to reconstructive breast augmentation using autologous fat transfer, or the reconstructive comparators, were not date limited as this literature was not assessed in the earlier review.

Language restriction

Searches were conducted without language restriction. Non-English language articles were excluded unless they appeared to provide additional information in a higher level of evidence than the English language articles.

Literature search strategies

In order to obtain recent literature for autologous fat transfer for cosmetic breast augmentation and all literature for autologous fat transfer for reconstructive breast augmentation, two separate searches were conducted and the final results combined.

[4] Where the occurrence of losses to follow-up was not reported or unclear it was assumed they did not occur.

Databases searched

For cosmetic breast augmentation, the following databases were searched from January 2001 to 14 January 2009:

- Current Contents
- The York (UK) Centre for Reviews and Dissemination (CRD)
- The Cochrane Library
- Entrez-PubMed
- Ovid EMBASE.

For reconstructive breast augmentation, the same databases were searched with no date limitation.

Search terms used

The search terms used can be seen in Appendix B.

Clinicaltrials.gov, Current Controlled Trials and the Australian and New Zealand Clinical Trials Registry were also searched using the search terms listed in Appendix B for trials in progress.

Literature database & exclusions

Articles were retrieved if they were judged to possibly meet the inclusion criteria based on their abstracts. Two ASERNIP-S researchers independently applied the selection criteria and any differences were resolved through discussion. Full publications that did not meet the inclusion criteria were excluded and the reasons were documented. The bibliographies of all publications retrieved were manually searched for relevant references that may have been missed in the database search (pearling).

Studies were excluded if they represented multiple publications of the same series or if they were isolated case reports. Papers reporting the effect of silicone on human tissue or the association between systemic disease and implants were also excluded. Specific types of breast enhancements including hydrogel implants and non-cohesive silicone gel implants are also beyond the scope of this review.

Data extraction and assessment of study quality

Data from all included studies were extracted by one researcher and checked by a second using standardised data extraction tables that were developed a priori.

Table 2 contains the guidelines that were used to assess the level of evidence of the studies to enable the filtering and inclusion of studies. Critical appraisal was conducted by one researcher and checked by a second and any differences were resolved through discussion. The RCTs that were used to collect case series data for the comparator interventions were not critically appraised as it is unrealistic to assess

the methodological quality of these studies using standard RCT checklists because comparative data were not extracted. Case series appraisal methods also do not apply.

Case series studies were evaluated in respect to the following factors:

- Were the inclusion and exclusion criteria clearly described?
- How were patients selected to undergo the procedure (i.e. consecutive versus non-consecutive recruitment)?
- Was the sample size sufficient (≥20 patients)?
- Were the outcomes reported objective?
- Was the duration of follow-up sufficient (≥1 year)?
- Were the number of patient who withdrew or dropped out of the study reported, and the characteristics of these patients described?

Table 2: National Health and Medical Research Council Hierarchy of Evidence (NHMRC 2000)

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

Data analysis

If the data were suitable for statistical pooling, meta-analyses of the main outcomes would be performed. Formal statistical pooling (meta-analysis) could only be performed if two or more RCTs addressed the same comparison, with data available for comparable outcomes. A test for statistical heterogeneity would then be performed, with $P<0.10$ chosen to indicate the presence of statistical heterogeneity. Relative risks (random effects model) with 95% confidence intervals would then be calculated for dichotomous outcomes. Otherwise, data for the main outcomes would be reported narratively.

Overall occurrence rates for safety outcomes were calculated where appropriate. Calculation of complication rates only occurred when it was clear what the unit of analysis (breast or patient) and denominator (number of patients or number of breasts) were. When the occurrence of losses to follow-up was not reported, overall rates could not be calculated because the denominator was not known. Where

possible, overall rates were calculated as the total number of breasts of patients experiencing a complication over the total number of breasts being augmented. In studies where the number of breasts was not reported, the rate was calculated as the total number of breasts of patients experiencing a complication over the total number of patients undergoing the augmentation procedure. Where authors reported actual complication rates in their studies, it was not necessary to calculate the complication rate manually.

Studies included in the review

From the search strategy, 532 potentially relevant articles were identified, of which 155 were retrieved for appraisal. A total of 35 studies were found to be eligible for inclusion and are listed in Appendix C. Excluded studies plus the reasons for exclusion are listed in Appendix D. There were no systematic reviews identified from which useful data could be derived for this review, and level III studies were not eligible for inclusion.

Of the 35 included studies, nine were level II evidence from which 12 'single arms' of data on the comparator interventions could be derived (Table 3). Twenty-six studies were level IV case series evidence, of which 11 studies reported outcomes for the intervention of interest, autologous fat transfer, and had been published since the search end date of the previous ASERNIP-S review (Chapman et al 2002). The remaining 15 studies reported data on IGAP flaps, SGAP flaps, SIEA flaps, DIEP flaps and tissue expanders with breast implants. Fewer than five level II studies and 10 level IV studies were retrieved for IGAP, SGAP and SIEA flaps; therefore, all of their available level IV evidence was included. The remaining comparator procedures, tissue expanders with breast implants and DIEP flaps, had less than five level II studies and greater than 10 level IV studies retrieved, and thus were subject to the inclusion criteria of greater than 100 patients and greater than 2 years follow-up.

Data extraction tables for all included studies are presented in Appendix E in alphabetical then date order.

Table 3: Number of included studies and study arms

Procedure type	Number of studies	Number of study arms
Autologous fat transfer	11	11
Comparator procedures		
Saline implants	2	4
Cohesive silicone implants	5	6
TRAM flaps	1	1
DIEP flaps	4	4
SIEA flaps	3	3
SGAP flaps	4	4
IGAP flaps	2	2
Latissimus dorsi flaps	1	1
Tissue expanders and breast implants	2	2
TOTAL	**35**	**38**

TRAM: transverse rectus abdominis myocutaneous; DIEP: deep inferior epigastric perforator, SIEA: superficial inferior epigastric artery; SGAP: superior gluteal artery perforator; IGAP: inferior gluteal artery perforator.

Appraisal of study methodology

Autologous fat transfer studies

Eleven case series for autologous fat transfer, reporting outcomes in 1,341 patients, were considered eligible for appraisal and inclusion in this systematic review. In these

studies autologous fat transfer was either used alone (Fulton 2003; Yoshimura et al 2008; Zheng et al 2008) or in conjunction with another procedure (Spear et al 2005; Missana et al 2007) to achieve cosmetic or reconstructive augmentation. Five studies utilised autologous fat transfer both alone and in conjunction with other procedures in a single patient population (Coleman and Saboerio 2007; Rigotti et al 2007; Pinsolle et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009) and four of these studies did not stratify their results accordingly; therefore, it was not possible to separate the evidence of autologous fat transfer according to its use (i.e. alone or adjunct) in the results section of this review.

Two studies (Rigotti et al 2007; Yoshimura et al 2008) reported detailed inclusion and exclusion criteria (Table 4). The remaining studies either reported inclusion criteria alone (Fulton 2003; Spear et al 2005; Carvajal and Patino 2008; Pinsolle et al 2008; Zheng et al 2008; Illouz and Sterodimas 2009) or no criteria (Coleman and Saboerio 2007; Missana et al 2007; Zocchi and Zuliani 2008). When studies report clear inclusion and exclusion criteria it is easier to explain unexpected results by linking them with potentially obvious preoperative patient characteristics, defined by these criteria. It is also easier to describe expected results in a particular patient population dependent on their preoperative characteristics, which are also defined by the inclusion and exclusion criteria. In the study by Fulton (2003), patients were highly selected, that is only healthy patients without severe breast ptosis, and with adequate areas of donor fat and realistic expectations for the procedure were selected to undergo the procedure. Patients with these characteristics are likely to have favourable outcomes; thus the results of this study are likely to be biased.

The inclusion of consecutive patients reduces selection bias by ensuring physicians could not have only selected patients whom they felt would produce favourable results. In the included autologous fat transfer case series, only two patient populations were selected in this manner (Rigotti et al 2007; Illouz and Sterodimas 2009).

The majority of included case series reported outcomes in patient samples with ≥20 individuals; two studies had a smaller number of patients than this (Coleman and Saboerio 2007 n=17; Pinsolle et al 2008 n=6). Ideally, an analysis of statistical power should be used to determine the number of patients or breasts required to detect change to a desired level of statistical significance; however, this is very rarely found in case series. When comparing small patient groups it is difficult to determine if the lack of a statistically significant outcome is a true effect or the result of inadequate power caused by the small sample sizes. However, most of the autologous fat transfer case series had ≥20 patients.

Duration of follow-up should also be sufficiently long to maximise the ability to detect late complications or treatment failures, and to allow reasonable long-term conclusions to be made. Ten studies (Fulton 2003; Spear et al 2005; Coleman and Saboerio 2007; Missana et al 2007; Rigotti et al 2007; Carvajal and Patino 2008;

Yoshimura et al 2008; Zheng et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009) reported follow-up greater than 1 year and one study (Pinsolle et al 2008) did not report the length of their follow-up period.

Losses to follow-up were only reported in two studies, where 0% and 18% of patients were lost, respectively (Spear et al 2005; Illouz and Sterodimas 2009). In the study where losses occurred, the authors did not report the characteristics of the patients lost. Unless reasons for losses to follow-up are reported, the conclusions may not reflect true patient outcomes. A summary of the methodology used in autologous fat transfer case series can be seen below in Table 4.

Table 4: Summary of included autologous fat transfer studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n≥20 patients	Follow-up ≥ 1 year	Losses to follow-up
Fulton, 2003 IV/case series	65	Inclusion criteria only	Prospective	Yes	Yes	Unclear
Spear et al 2005 IV/case series	37	Inclusion criteria only	Retrospective	Yes	Yes	None
Coleman and Saboerio 2007 IV/case series	17	None	Retrospective	No	Yes	Unclear
Missana et al 2007 IV/case series	69	None	Prospective	Yes	Yes	Unclear
Rigotti et al 2007 IV/case series	20	Inclusion and exclusion criteria	Prospective, consecutive	Yes	Yes	Unclear
Carvajal and Patino 2008 IV/case series	20	Inclusion criteria only	Retrospective	Yes	Yes	Unclear
Pinsolle et al 2008 IV/case series	6	Inclusion criteria only	Retrospective	No	NR	Unclear
Yoshimura et al 2008 IV/case series	40	Inclusion and exclusion criteria	NR	Yes	Yes	Unclear
Zheng et al 2008 IV/case series	66	Inclusion criteria only	Retrospective	Yes	Yes	Unclear
Zocchi and Zuliani 2008 IV/case series	181	None	NR	Yes	Yes	Unclear
Illouz and Sterodimas 2009 IV/case series	820	Inclusion criteria only	Consecutive	Yes	Yes	n=150 (18%)

NR: not reported.

Description of studies providing comparator data

The comparator procedures which fulfilled the criteria for use of 'single arm' data from RCTs were saline implants, cohesive silicone implants, TRAM flaps and latissimus dorsi flaps. Although a set of selection criteria were used to ensure that only good quality RCTs were included, these studies were essentially used as a source of case series data and could not be critically appraised as either study type. Instead, a

brief description of the study methodology and reporting of each of the 12 included RCTs is provided below.

Cosmetic mammaplasty

Saline implant studies

Two RCTs compared smooth-surfaced saline implants with textured-surfaced saline implants (Tarpila et al 1997; Fagrell et al 2001). In both cases these were within-patient comparisons, that is, breasts rather than patients were randomised for implant (smooth-surface or textured-surface) allocation. For the purposes of this review both arms from each study were extracted.

Patient numbers were small in the RCTs included for this comparator procedure. Both studies were also only single blind (patients); in these cases the assessor was aware of implant allocation when evaluating the patients' outcomes. Table 5 below summarises these details.

Table 5: Summary of included saline implant studies (RCT single-arm data)

Level of evidence/ study design	n	Study comparisons	Blinding	Follow-up
Tarpila et al 1997				
II/randomised controlled trial	21 (42 breasts) **Unit of analysis:** breast	Smooth-surface implants (n=21 breasts) versus textured-surface implants (n=21 breasts) (both arms included)	Single blind (patient)	**Duration :** maximum 2 years **Losses:** n=2 (9%)
Fagrell et al 2001				
II/randomised controlled trial	20 (40 breasts) **Unit of analysis:** breast	Smooth-surface implants (n=20 implants) versus textured-surface implants (n=21 breasts) (both arms included)	Single blind (patient)	**Duration:** mean 7.5 years (range, 5 years 11 months to 8 years 4 months) **Losses:** n=2 by 6 and 12 months follow-up (10%)

Cohesive silicone implant studies

Five RCTs reported the use of silicone implants for cosmetic breast augmentation in 158 patients (Coleman et al 1991; Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Malata et al 1997; Niechajev et al 2007). Four of these studies compared smooth-surfaced silicone implants with textured-surfaced silicone implants (Coleman et al 1991; Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Malata et al 1997), and the remaining study compared two brands of textured silicone implants. Of the four studies comparing smooth- and textured-surface implants, one study reported short-term (12-month) outcomes for a patient sample receiving either implant type (Coleman et al 1991), and another study provided mid-term (3-year) outcomes for the same patient sample (for textured implants only) (Malata et al 1997). Mid-term data for smooth implants was also reported in this study; however, losses to follow-up in that arm exceeded 10%, preventing these data from being included in the review. Of the other two studies that compared smooth- and textured-surfaced

implants, one reported short-term (12-month) data for a second patient population (Hakelius and Ohlsen 1992), and the other provided extended (5-year) follow-up in these patients (Hakelius and Ohlsen 1997).

All of the RCTs included in this review for the use of cohesive silicone breast implants were double blinded (Table 6). In the RCTs conducted by Hakelius and Ohlsen the unit of analysis was the breast, whereas in the remaining three studies it was the patient (Coleman et al 1991; Malata et al 1997; Niechajev et al 2007).

Table 6: Summary of included cohesive silicone implant studies (RCT single-arm data)

Level of evidence/ study design	n	Study comparisons	Blinding	Follow-up
Coleman et al 1991; Malata et al 1997				
II/randomised controlled trial	53 (106 breasts) **Unit of analysis:** patient	**Coleman et al 1991** Smooth-surface implants (n=26 patients) versus textured-surface implants (n=27 patients) (both arms included) **Malata et al 1997** Smooth-surface implants versus textured surface implants (n=27 patients) (in Malata et al textured-surface arm included only)	Double blind (patient and assessing surgeons)	**Duration:** 12 months (short-term), 3 years (mid-term) **Losses:** **Smooth-surface implants** 12 months: n=2 (8%) **Textured-surface implants** 12 months: n=1 (4%)
Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997				
II/randomised controlled trial	25 (50 breasts) **Unit of analysis:** breast	**Hakelius and Ohlsen 1992** Smooth-surface implants (n=25 breasts) versus textured-surface implants (n=25 breasts) (both arms included) **Hakelius and Ohlsen 1997** Smooth-surface implants (n=25 breasts) versus textured-surface implants (n=25 breasts) (both arms included)	Double blind (patient and assessors)	**Duration:** 1 year (short-term); 5 years (long-term) **Losses:** **Smooth-surface implants** 6 weeks: n=2 (8%); 12 weeks: n=1 (4%); 36 weeks: n=2 (8%) **Textured-surface implants** 6 weeks: n=2 (8%); 12 weeks: n=1 (4%); 36 weeks: n=2 (8%)
Niechajev et al 2007				
II/randomised controlled trial	80 (160 breasts) **Unit of analysis:** patient	McGhan Style 410 implant (n=40 patients) versus Eurosilicone Vertex implant (n=40 patients) (both arms included)	Double blind (patient and assessing surgeon)	**Duration:** median 5 years (range, 4 to 6 years) **Losses:** Did not see surgeon or complete questionnaire: n=10 (8%)

Reconstructive mammaplasty

TRAM flap studies

One study reporting outcomes for TRAM flap breast reconstruction was included (Temple et al 2006). This study aimed to determine whether innervation of the free TRAM flap improved the sensation of reconstructed breasts, and for the purposes of this review, patients who underwent the procedure using non-innervated TRAM flaps were included as this is the more conventional form of the procedure (Temple et al 2006).

This RCT had a patient population of less than 20 individuals (Temple et al 2006 n=12) and the unit of analysis was patient, not breast. It was unclear if losses to follow-up did or did not occur; therefore, it is assumed they did not.

Table 7: Summary of included TRAM flap studies (RCT single-arm data)

Level of evidence/ Study design	n	Study comparisons	Blinding	Follow-up
Temple et al 2006 II/randomised controlled trial	12 **Unit of analysis:** patient	Innervation of free TRAM flap versus non-innervation (12 patients) of free TRAM flap (non-innervated arm included only)	Single blind (examiner)	**Duration:** mean 16 months **Losses:** unclear

TRAM: transverse rectus abdominis myocutaneous.

DIEP flap studies

Of the four case series reporting outcomes for DIEP flap breast reconstruction (Keller 2001; Gill et al 2004; Guerra et al 2004c; Hofer et al 2007), inclusion and exclusion criteria were reported in detail in one. The remaining studies did not report their selection criteria. Selection of consecutive patients was most apparent in this comparator with three out of four studies reporting outcomes in consecutive patients, reducing potential selection bias. In addition, all of the studies had patient samples greater than 20 individuals and follow-up of at least 1 year. The occurrence of losses was not reported in any of the included case series. Table 8 briefly describes these findings.

Table 8: Summary of included DIEP flap studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n ≥ 20 patients	Follow-up ≥ 1 year	Losses to follow-up
Keller, 2001 IV/case series	108	Inclusion and exclusion criteria	Consecutive	Yes	Yes	Unclear
Gill et al 2004 IV/case series	609	None	Retrospective	Yes	Yes	Unclear
Guerra et al 2004c IV/case series	140	None	Retrospective, consecutive	Yes	Yes	Unclear
Hofer et al 2007 IV/case series	131	None	Consecutive	Yes	Yes	Unclear

SIEA flap studies

Three case series studies were included for SIEA flaps (Arnez et al 1999; Wolfram et al 2006; Holm et al 2008). Two of the three studies did not report any inclusion or exclusion criteria; one study reported inclusion criteria alone. None of the included case series reported outcomes in consecutive patients. One study had patient population greater than 20 individuals and one study had follow-up greater than 1 year. Losses to follow-up were not reported in any of the studies; therefore, it is not possible to determine whether drop outs occurred. Table 9 below summaries the methodological aspects of the included SIEA flap case series.

Table 9: Summary of included SIEA flap studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n≥20 patients	Follow-up≥ 1 year	Losses to follow-up
Arnez et al 1999 IV/case series	5	None	NR	No	No	Unclear
Wolfram et al 2006 IV/case series	11	None	Non-consecutive	No	Yes	Unclear
Holm et al 2008 IV/case series	25	Inclusion criteria only	NR	Yes	NR	Unclear

NR: not reported.

SGAP flap studies

Four case series studies were included for SGAP flaps (Blondeel 1999; Guerra et al 2004a; Guerra et al 2004b; DellaCroce and Sullivan 2005). In general, inclusion and exclusion criteria were not reported, or were reported in little detail. One of the four studies recruited their patients consecutively and only two studies had ≥20 patients enrolled. The duration of follow-up was not reported in three of the included studies, and in the remaining study follow-up was greater than 1 year. One study reported losses to follow-up in 0% of patients and the other studies did not report whether any losses occurred. This is summarised below in Table 10.

One of the included studies had a particularly small sample size and undertook the first four procedures a substantial time earlier (1994-1996) than the final two (2003-2004). This split study period may influence the complications experienced as experience and technology would have advanced since the time the initial procedures were performed (Guerra et al 2004b). Another of the included studies selected their patient population for low incidence of comorbidity and general good heath, potentially biasing their results for positive outcomes (DellaCroce and Sullivan 2005).

Table 10: Summary of included SGAP flap studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n ≥ 20 patients	Follow-up ≥ 1 year	Losses to follow-up
Blondeel, 1999 IV/case series	16	None	Prospective	No	Yes	None
Guerra et al 2004a IV/case series	142	None	NR	Yes	NR	Unclear
Guerra et al 2004b IV/case series	6	Inclusion criteria only	Consecutive	No	NR	Unclear
DellaCroce and Sullivan 2005 IV/case series	20	None	NR	Yes	NR	Unclear

NR: not reported.

IGAP flap studies

Two case series studies were included for IGAP flap reconstruction (Allen et al 2006; Beshlian and Paige 2008), neither of which reported inclusion and exclusion criteria or whether patients were selected consecutively (Table 11). One study had greater

than 20 patients enrolled but less than 1 year follow-up. The other study reported outcomes in less than 20 patients and follow-up duration was not reported. Losses to follow-up were also not reported in either study. A summary of this can be seen below in Table 11.

Table 11: Summary of included IGAP flap studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n≥20 patients	Follow-up ≥1 year	Losses to follow-up
Allen et al 2006						
IV/case series	24	No	NR	Yes	No	Unclear
Beshlian and Paige 2008						
IV/case series	14	No	Retrospective then prospective	No	NR	Unclear

NR: not reported.

Latissimus dorsi flap studies

One study reporting outcomes for latissimus dorsi flap breast reconstruction was included (Daltrey et al 2006). This study reported the incidence of symptomatic seroma formation in patients receiving latissimus dorsi flap breast reconstruction, using one of two types of donor site wound closure methods (the experimental method was quilted closure) (Daltrey et al 2006). Patients undergoing the conventional (non-quilted) wound closure method were included.

Daltrey et al 2006 randomly assigned patients to receive either latissimus dorsi procedure, instead of breasts. Table 12 below summarises the methodology employed in this study.

Table 12: Summary of included latissimus dorsi flap studies (RCT single-arm data)

Level of evidence/ study design	n	Study comparisons	Blinding	Follow-up
Daltrey et al 2006				
II/randomised controlled trial	54 **Unit of analysis:** patient	Quilted wound closure versus non-quilted (n=54 patients) wound closure (non-quilted arm included only)	Single blind (patient)	**Duration:** maximum 3 years **Losses:** n=2 (4%)

Tissue expanders and breast implant studies

Two studies were included for tissue expanders with breast implants (Cordiero and McCarthy 2006; Wright et al 2008). Both studies reported inclusion and exclusion criteria. One case series reported detailed inclusion and exclusion criteria and the other reported inclusion criteria alone. Sample size and the duration of follow-up were considered adequate in both studies and losses to follow-up were reported in one study. In this study, 7% of patients were lost to follow-up; reasons for this were not recorded. The remaining study did not report if losses occurred in their patients. A summary of these findings can be seen below in Table 13.

In one of the included studies selection bias may have influenced the outcomes obtained, particularly complication rate, because the authors stated that women with

poor prognosis due to locally advanced disease may have been discouraged from immediate reconstruction or neoadjuvant chemotherapy, two procedures which ordinarily hold a greater risk of complication, even in healthy subjects (Wright et al 2008). Similarly in the other included study, patients with a history of irradiation were of a 'highly select' group, that is, they were offered expanders for reconstruction based on favourable preoperative assessment of their skin quality and the presumed ability to perform successful skin-sparing mastectomy in them (Cordiero and McCarthy 2006).

Table 13: Summary of included tissue expander and breast implant studies

Level of evidence/ study design	n	Detailed inclusion and exclusion criteria	Data collection/ Patient selection	n≥20 patients	Follow-up ≥1 year	Losses to follow-up
Cordiero and McCarthy 2006						
IV/case series	315	Inclusion criteria only	Retrospective	Yes	Yes	Unclear
Wright et al 2008						
IV/case series	104	Inclusion and exclusion criteria	Retrospective	Yes	Yes	n= 7 (7%)

Results

The limitation of an evidence base consisting only of case series is that comparisons must be made between studies, often by different authors, rather than within a single study where patients are generally well-matched at baseline and there is a consistent study methodology. The safety and efficacy outcomes for the relevant comparators were extracted and tabulated from primary studies in order to reflect the current trends for these procedures in the published literature. It was not the purpose of this review to assess the safety and efficacy of the various comparators for autologous fat transfer. Therefore, the data presented on the safety and efficacy of comparator interventions are not definitive and are only intended as a guide for general reference in comparing autologous fat transfer with the various comparator procedures.

In regards to the research questions outlined for this review, the current evidence base precludes the evaluation of the questions relating to a superior cosmetic or reconstructive augmentation procedure, and does not allow adequate assessment of the safety and efficacy of autologous fat transfer compared with the comparator procedures.

Safety

Autologous fat transfer

Ten of the included autologous fat transfer case series reported safety outcomes (Fulton 2003; Spear et al 2005; Coleman and Saboeiro 2007; Missana et al 2007; Carvajal and Patino 2008; Pinsolle et al 2008; Yoshimura et al 2008; Zheng et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009). One study did not report complications; it is unclear if this was because no complications occurred or if safety was simply not the authors' main focus (Rigotti et al 2007).

Two of the ten studies reporting safety outcomes reported the use of autologous fat transfer for cosmetic indications (Fulton 2003; Yoshimura et al 2008), and three studies reported the use of autologous fat transfer for reconstructive indications (Spear et al 2005; Missana et al 2007; Pinsolle et al 2008). Four studies reported safety outcomes for both cosmetic and reconstructive indications (Coleman and Saboerio 2007; Zheng et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009). In one study it was not clear if the indication for use was cosmetic, reconstructive, or both (Carvajal and Patino 2008) (Table 14).

In the study by Fulton (2003), most outcomes were reported qualitatively. The only outcome reported quantitatively in this study was striae, which was considered a minor complication and occurred in 3% of patients (2/65 patients). The extent of the striae in these patients improved with daily application of tretinoin. Bruising and pain were reported as 'minimal' during immediate follow-up. Lumps and cyst formation were apparent in the study by Yoshimura et al (2008), as was bleeding which was

reported qualitatively. Expected adverse events such as bruising/ecchymosis and inflammation were also common in patients undergoing autologous fat transfer for cosmetic reconstruction.

In general, complications were considered to be major and commonly included breast lumps, fat necrosis and cysts. Despite the serious nature of many of these complications, in some cases patients were asymptomatic, and therefore unaware of these abnormalities, until mammographic imaging took place. Surgical intervention, such as drainage or lumpectomy, was often utilised to remove fat necrosis and breast lumps. None of these 'lumps' were found to be malignant or led to subsequent malignancy of any kind.

Table 14: Complication rates following autologous fat transfer procedure

	Fulton	Spear et al	Coleman & Saboerio	Missana et al	Rigotti et al	Carvajal & Patino	Pinsolle et al	Yoshimura et al	Zheng et al	Zocchi & Zuliani	Illouz & Sterodimas
Study design	Case series	Case series	Case series	Case series	Case series	Case series	Case series	Case series	Case series	Case series	Case series
n	65	37	17	69	20	20	6	40	66	181	820
Mean follow-up	NR	15 months	62.2 months	11.7 months	30 months	34.5 months	NR	NR	37 months	NR	11.3 years (n=230)
Minor complication											
Haematoma	0%	-	-	-	-	-	0%	-	-	-	1%
Pain	NA	-	-	-	-	-	-	-	-	-	-
Bruising	NA	-	-	-	-	-	-	-	-	44%	-
Striae	3%	-	-	-	-	-	-	-	-	-	4%
Infection	-	2%	3%	0%	-	-	0%	-	-	-	<1%
Inflammation	-	-	100%	-	-	-	0%	-	-	100%	-
Bleeding	-	-	-	-	-	-	-	NA	-	-	-
Ecchymosis	-	-	-	-	-	-	-	-	-	-	9%
Major complications											
Fat emboli	0%	-	-	-	-	-	-	-	-	-	-
Lumps	-	7%	8%	0%	-	-	0%	3%	8%	-	-
Fat necrosis	-	5%	5%	7%	-	10%	17%	-	8%	1%	-
Calcification	-	-	-	-	-	23%	-	-	-	4%	-
Cysts	-	-	-	-	-	20%	-	5%	NA	2%	-
Dysesthesia	-	-	-	-	-	-	-	-	-	8%	-

Note: multiple complications may have occurred per patient.
NR: not reported; NA: not applicable, e.g. the outcome was reported qualitatively in the study.

Cosmetic mammaplasty

Saline implants

All of the included studies describing the use of saline implants reported safety outcomes (Tarpila et al 1997; Fagrell et al 2001).

All of the complications which occurred were considered major; the most common complication occurring across the studies was capsular contracture (Table 15). The smooth- and textured-surface arms of the studies reported a slight increase in the number of patients with capsular contracture over time (Tarpila et al 1997; Fagrell et al 2001). Tarpila et al (1997) reported contracture at 6 and 12 months and Fagrell et al (2001) reported contracture at 1 and 7.5 years. Despite the trend seen in Fagrell et al (2001), Tarpila et al (1997) reported that 90% of capsular contracture occurs in the first 12 months of follow-up, supporting the duration of follow-up employed by this study.

Table 15: Complication rates following saline implant procedure

	Tarpila et al (smooth-surface)	Tarpila et al (textured-surface)	Fagrell et al (smooth-surface)	Fagrell et al (textured-surface)
Study design	RCT	RCT	RCT	RCT
n	21	21	20	20
Mean follow-up	NR	NR	7.5 years	7.5 years
Minor complications				
Haematoma	0%	0%	-	-
Infection	0%	0%	0%	0%
Major complications				
Capsular contracture	6 months: 32% 12 months: 38%	6 months: 26% 12 months: 29%	12 months: 20% 7.5 years: 30%	12 months: 5% 7.56 years: 20%
Implant perforation	-	-	5%	-
Bleeding	-	-	5%	5%

RCT: randomised controlled trial; NR: not reported.

Cohesive silicone implants

All five studies reporting on the use of silicone implants for cosmetic breast augmentation reported safety outcomes (Coleman et al 1991; Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Malata et al 1997; Niechajev et al 2007).

The majority of complications were considered major and commonly included capsular contracture and other implant related problems, such as skin wrinkling and implant rotation (Table 16). In all of the studies reporting outcomes for both smooth-surfaced and textured-surfaced silicone implants, capsular contracture occurred more frequently in breasts augmented with smooth-surfaced implants (Coleman et al 1991; Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Malata et al 1997).

Several studies noted that capsular contracture grading systems, including the Breast Augmentation Classification (BAC) system and the Baker Classification system (see Appendix A), were relatively subjective and in some cases were not sensitive enough to detect small changes in capsular contracture rate (Coleman et al 1991; Hakelius and Ohlsen 1997; Malata et al 1997). In particular, in the patient series reported by

Hakelius and Ohlsen, BAC was not sensitive enough to detect a modest increase in contracture rate from 1- to 5-year follow-up.

Other prostheses-related complications include implant rotation, which does not appear to be affected by the positioning of the implant, as rotation occurred in three implants positioned subglandularly and one submuscularly (Niechajev et al 2007). Both skin wrinkling and breast hardness occurred in smooth- and textured-surfaced implants, but to a greater degree in smooth implants (Hakelius and Ohlsen 1997). Haematoma occurred in a small number of patients and was generally considered a minor complication, with the exception of one study where haematoma proved to be a major complication requiring reoperation (Coleman et al 1991).

Table 16: Complication rates following cohesive silicone implant procedure

	Coleman et al (smooth-surface)	Coleman et al; Malata et al (textured-surface)	Hakelius & Ohlsen (smooth-surface)	Hakelius & Ohlsen (textured-surface)	Niechajev et al (McGhan)	Niechajev et al (Eurosilicone)
Study design	RCT	RCT	RCT	RCT	RCT	RCT
n	26	27	25	25	40	40
Follow-up	12 months	12 months; 3 years	12 months; 5 years	12 months; 5 years	Median 5 years	Median 5 years
Minor complications						
Infection	0%	0%	0%	0%	1%	0%
Haematoma	-	-	4%	8%	-	-
Skin wrinkling	-	-	24%	4%	-	-
Major complications						
Haematoma*	2%	-	-	-	-	-
Capsular contracture	54%	12 months: 7% 3 years: 6%	4%	0%	18%	19%
Breast hardness	-	-	68%	4%	-	-
Seroma	-	-	-	-	1%	1%
Implant rotation	-	-	-	-	4%	1%
Bleeding	-	-	-	-	0%	1%

*defined in the study as a major complication.
RCT: randomised controlled trial.

Reconstructive mammaplasty

TRAM flaps

There were no safety outcomes reported in the one study included in the review for the use of TRAM flaps (Temple et al 2006). It is unknown if this was because no complications occurred in their patient population or simply if safety was not the main focus of the study.

DIEP flaps

Safety outcomes were reported in all four case series included for the use of DIEP flaps for breast reconstruction (Keller 2001; Gill et al 2004; Guerra et al 2004c; Hofer et al 2007). Among these studies fat necrosis, seroma and wound dehiscence occurred commonly. Vascular complications, such as arterial and venous occlusion or insufficiency, were also reported commonly, in comparison to other breast reconstructive procedures. Major adverse events including deep vein thrombosis and/or pulmonary embolism were reported in three studies in a total of two and six patients, respectively (Keller 2001; Guerra et al 2004c; Hofer et al 2007).

Table 17: Complication rates following DIEP flap procedure

	Keller	Gill et al	Guerra et al	Hofer et al
Study design	Case series	Case series	Case series	Case series
n	108	609	140	131
Mean follow-up	28.9 months	13.2 months	14.6 months	1.8 years
Minor complications				
Donor site weakness	3%	-	-	-
Infection	-	3%	-	-
Haematoma	-	2%	-	5%
Bleeding	-	NA	NA	-
Abdominal complications	-	-	-	15%
Flap complications	-	-	-	9%
Scarring	-	-	-	3%
Major complications				
Infection	<1%	-	<1%	-
Fat necrosis	7%	13%	13%	6%
Hernia/bulge	1%	<1%	1%	4%
Pulmonary embolism	<1%	-	-	3%
Pneumothorax	0%	-	-	-
Seroma	-	5%	11%	<1%
Venous occlusion	-	4%	-	-
Arterial occlusion	-	<1%	-	-
Abdominal complication	-	14%	-	6%
Flap complication	-	-	-	10%
Dehiscence	-	-	8%	10%
Venous thrombosis	-	-	1%	-
Wound drainage	-	-	NA	-
Venous congestion	-	-	<1%	-
Acute ischemia	-	-	<1%	-
Deep vein thrombosis	-	-	<1%	<1%
Cancer recurrence	-	-	1%	-
Flap necrosis	-	-	-	9%
Skin necrosis	-	-	-	3%
Arterial insufficiency	-	-	-	1%
Venous insufficiency	-	-	-	2%
Arterial & venous insufficiency	-	-	-	<1%
Abscess	-	-	-	<1%

NA: not applicable, e.g. the outcome was reported qualitatively in the study.

SIEA flaps

Safety outcomes were reported in all three case series included for the use of SIEA flaps for breast reconstruction (Arnez et al 1999; Wolfram et al 2006; Holm et al 2008). Given the variable anatomy of the superficial inferior epigastric artery, in each of these studies SIEA flap reconstruction was only undertaken after investigation of the artery revealed its viability. Where the artery diameter or length was too small an alternate reconstructive procedure (either DIEP or muscle-sparing TRAM) was employed. This makes it difficult to ascertain if the results obtained were due to SIEA, DIEP or TRAM flap reconstruction.

Common complications included flap necrosis and haematoma (Table 18). Most cases of haematoma were minor, with the exception of one which required reoperation and was considered major (Wolfram et al 2006).

Table 18: Complication rates following SIEA flap procedure

	Arnez et al	Wolfram et al	Holm et al
Study design	Case series	Case series	Case series
n	5	11	25
Mean follow-up	7 months	23 months	NR
Minor complications			
Haematoma	20%	-	-
Major complications			
Flap necrosis	-	8%	4%
Seroma	-	8%	-
Haematoma	-	8%	-

NR: not reported.

SGAP flaps

A total of four case series were included for the use of SGAP flaps in breast reconstruction, all of these reported safety outcomes (Blondeel 1999; Guerra et al 2004a; Guerra et al 2004b; DellaCroce and Sullivan 2005) (Table 19).

The need for blood transfusion appears to be a common occurrence among the studies reporting the use of SGAP flaps. Two studies reported that blood transfusion was required in approximately 36% of patients and 50% of patients, respectively (Guerra et al 2004a; Guerra et al 2004b). One study reported that no patients required blood transfusion (DellaCroce and Sullivan 2005).

Donor site morbidity also appeared to be common following reconstruction with SGAP flaps. The types of complications experienced at the donor site included seroma, dehiscence and haematoma, which may be associated with the position of the donor site and the difficulty in avoiding movement and pressure in that area. Pneumonia occurred in one patient across all of the included studies (Blondeel 1999).

Table 19: Complication rates following SGAP flap procedure

	Blondeel	Guerra et al[a]	Guerra et al[b]	DellaCroce & Sullivan
Study design	Case series	Case series	Case series	Case series
n	16	142	6	20
Mean follow-up	11.1 months	NR	NR	NR
Minor complications				
Pain	0%	-	-	-
Haematoma	-	2%	8%	-
Bleeding	-	NA	NA	-
Delayed healing	-	-	8%	-
Major complications				
Lumps	5%	-	-	-
Flap necrosis	5%	4%	-	5%
Fat necrosis	5%	-	-	-
Seroma	35%	2%	-	3%
Dehiscence	10%	-	8%	-
Pneumonia	5%	-	-	-
Blood transfusion	-	37%	50%	0%
Vascular complications	-	6%	-	-
Venous thrombosis	-	-	8%	-

[a] Guerra et al 2004a
[b] Guerra et al 2004b
NR: not reported; NA: not applicable, e.g. the outcome was reported qualitatively in the study.

IGAP flaps

Each of the studies reporting outcomes of breast reconstruction with IGAP flaps provided safety outcomes (Allen et al 2006; Beshlian and Paige 2008) (Table 20).

Overall, wound dehiscence and seroma occurred commonly in patients receiving IGAP flaps, at both the donor site and the breast. In the study by Beshlian and Paige (2008), healing complications were very common at 42% and it is likely this rate encompasses other complications that were reported independently, including wound dehiscence. As well as this, Beshlian and Paige (2008) performed muscle harvest in some but not all of their patients, which would confound complication rates as muscle sparing procedures result in less donor site morbidity. Two different recipient vessels were also employed in this patient population and not stratified in the results.

Table 20: Complication rates following IGAP flap procedure

	Allen et al	Beshlian & Paige
Study design	Case series	Case series
n	24	14
Mean follow-up	NR	NR
Minor complications		
Haematoma	3%	-
Pain	3%	-
Major complications		
Dehiscence	10%	5%
Bleeding	NA	-
Flap necrosis	-	11%
Seroma	-	37%
Healing complications	-	42%
Thrombocytosis	-	5%

NR: not reported; NA: not applicable, e.g. the outcome was reported qualitatively in the study.

Latissimus dorsi flaps

Daltrey et al 2006 reported safety outcomes (Table 21). The majority of the complications associated with breast reconstruction using latissimus dorsi flaps were considered major complications. Infected seroma in two out of four patients became loculated and required reoperation (Daltrey et al 2006). Pain appeared to be minor and should be considered an expected event rather than a complication. Pain and subsequent analgesic usage decreased from week one to week two.

Table 21: Complication rates following latissimus dorsi flap procedure

	Daltrey et al
Study design	RCT
n	54
Mean follow-up	NR
Minor complications	
Pain	NA
Analgesic usage	NA
Major complications	
Infection	11%
Skin necrosis	19%
Seroma	96%
Haematoma	2%

RCT: randomised controlled trial; NR: not reported; NA: not applicable, e.g. the outcome was reported qualitatively by the study.

Tissue expanders and breast implants

Both case series included for the use of tissue expanders and breast implants reported safety outcomes (Cordiero and McCarthy 2006; Wright et al 2008). In the study by Wright et al (2008), 5% of patients died in the follow-up period. Four of these deaths occurred as a result of metastatic cancer and one occurred as a result of an unknown cause.

Capsular contracture rate was high. In the study by Cordiero and McCarthy (2006) patients who had undergone previous radiation had a higher rate of capsular contracture than patients who had not (P=0.092). Patients who underwent radiation subsequent to exchange to a permanent prosthesis also had a higher rate of capsular contracture compared to patients without radiation; however, this difference was significant (P<0.001). Implant deflation (major complication) and skin wrinkling (minor complication) also occurred commonly (Cordiero and McCarthy 2006).

The type of filler utilised in the permanent implant used (saline or silicone) did not influence the severity of the skin wrinkling encountered (P=0.814); however, silicone implants were encouraged in slender patients in whom skin wrinkling was thought to be of concern (Wright et al 2008). A BMI>30kg/m^2 was associated with a significantly lower wrinkling severity (P<0.001).

Table 22: Complication rates following tissue expander and breast implant procedure

	Cordiero & McCarthy	Wright et al
Study design	Case series	Case series
n	315	104
Follow-up	Mean 36.7 months	Median 64 months
Minor complications		
Skin wrinkling	52%	-
Major complications		
Capsular contracture	18%	-
Skin wrinkling (severe)	<1%	-
Implant deflation	2%	-
Biopsy proven distant metastasis	-	14%
Contralateral breast cancer	-	7%
Subsequent non-breast cancers	-	3%

Effectiveness

Autologous fat transfer

Mammographic outcomes

Eight studies reported outcomes relating to mammographic issues as a result of autologous fat transfer, including the masking or compression of breast tissue, the detection of calcifications and palpable masses (Fulton 2003; Spear et al 2005; Coleman and Saboerio 2007; Missana et al 2007; Carvajal and Patino 2008; Yoshimura et al 2008; Zheng et al 2008; Illouz and Sterodimas 2009). Table 23 below summarises the mammographic outcomes reported in each study.

Mammographic issues, particularly microcalcifications, occurred in 5-27% of patients. In general these calcifications were classified as benign or probable benign findings, requiring no intervention other than further monitoring in some cases.

Table 23: Mammographic outcomes following autologous fat transfer

Study	Outcome	n/N	%/qualitative result
Fulton 2003	Masking or compression of breast tissue	0/65	0% patients
	Benign calcifications	NR	9% patients
	Small speculated calculi	0/65	0% patients
Spear et al 2005	Palpable mass with signs of fat necrosis	2/3	67% masses
Coleman and Saboeiro 2007	**Mammographic findings** *(15/17 patients underwent mammography)*		
	Normal	8/17	47% patients
	Breast cancer	2/17	12% patients
	Benign	4/17	24% patients
	Nodules	3/17	18% patients
Missana et al 2007	Malignancy	NA	'no cases of microcalcifications suggestive of malignancy'
Carvajal and Patino 2008	**Mammographic findings (BI-RADS)[a]**		
	Grade 2	NR	85% breasts
	Grade 3	NR	15% breasts
Yoshimura et al 2008	Microcalcifications	2/40	5% patients
Zheng et al 2008	Palpable masses	11/66	17% patients
	Calcifications	7/66	11% patients
Illouz and Sterodimas 2009	**ACR BI-RADS[a] (6 months)**		
	Grade 0	NR	10% patients
	Grade 1	NR	41% patients
	Grade 2	NR	23.5% patients
	Grade 3	NR	25.5% patients
	Grade 4	NR	0% patients
	Grade 5	NR	0% patients
	ACR BI-RADS[a] (12 months)		
	Grade 0	NR	4.5% patients
	Grade 1	NR	47% patients
	Grade 2	NR	31% patients
	Grade 3	NR	17.5% patients
	Grade 4	NR	0% patients
	Grade 5	NR	0% patients

[a] American College of Radiology Breast Imaging Reporting and Data System = grade 0: incomplete. Additional imaging or comparison with outside films required; grade 1: negative. Routine screening needed; grade 2: benign finding. Only routine screening required; grade 3: probably benign findings. Short-interval mammographic follow-up suggested to observe stability; grade 4: suspicious finding. Biopsy recommended; grade 5: highly suggestive of malignancy. Biopsy required.
NR: not reported; NA: not applicable; BI-RADS: breast imaging reporting and data system, ACR: American College of Radiology.

Patient and surgeon satisfaction

Five studies reported patient and surgeon satisfaction with the procedure (Fulton 2003; Coleman and Saboerio 2007; Missana et al 2007; Yoshimura et al 2008; Zheng et al 2008) (Table 24). From these studies it appears that in general both patients and surgeons were satisfied with the procedure. Patients tended to be happiest with the softness and natural feel of their augmented breasts, and in some cases patients were pleased they were able to avoid having a prosthesis. One drawback of the procedure that was repeatedly reported was the limited volume increase achievable with fat transfer alone; this is represented by the proportion of patients in Table 24 who were dissatisfied with the procedure. However, in many cases, both cosmetic and reconstructive autologous fat transfer was successfully used in conjunction with other augmentative techniques capable of obtaining a desired volume, to improve breast contour and symmetry.

Table 24: Patient and surgeon satisfaction with autologous fat transfer

Study	Outcome	n/N	%/qualitative result
Fulton 2003	Patient satisfaction	NA	Subjective remarks from 3 patients, all 3 patients reported 'favourable results'
Coleman and Saboeiro 2007	Patient satisfaction	NA	'patients reported enlargement of breasts and improvement in surface contour' 'all patients pleased with results'
Missana et al 2007	**Surgeons satisfaction**		
	Good to very good	64/74	86% breasts
	Moderate	10/74	14% breasts
Yoshimura et al 2008	Patient satisfaction	NA	'all patients satisfied with texture, softness, contour and absence of foreign material, despite limit in size increase'
Zheng et al 2008	**Patient satisfaction**		
	Very satisfied	27/66	41% patients
	Satisfied	26/66	39% patients
	Dissatisfied	13/66	20% patients

NA: not applicable.

Durability

Six studies reported outcomes for the durability of autologous fat transfer, often measured by fat reabsorption following the procedure (Fulton 2003; Coleman and Saboerio 2007; Missana et al 2007; Yoshimura et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009) (Table 25). The general consensus among these studies was that fat reabsorption occurred frequently during the early postoperative period (particularly the first postoperative month) and continued throughout the following 2 to 6 months to a lesser extent, after which time the residual augmented breast volume remained relatively constant, with the exception of changes due to weight and menstrual cycle. The mean residual augmented volume after stabilisation of fat reabsorption was reported in two studies to be 73% (at an unknown point in time) and 55% at one year follow-up (Fulton 2003; Zocchi and Zuliani 2008).

Table 25: Durability of enhancement following autologous fat transfer

Study	Outcome	n/N	%/qualitative result
Fulton 2003	Mean residual augmented volume	NA	73%
	Volume reduction during first 60-90 days	NA	20-30%
	Volume reduction after 90 days	NA	Constant (except for changes with weight and menstrual cycle)
Coleman and Saboeiro 2007	Fat reabsorption	NA	'volume stabilised after 4-6 months and little reduction occurred thereafter'
Missana et al 2007	**Implant volume changes**		
	Following AFT and implant	NR	36% cases
	Following AFT and latissimus dorsi and implant	NR	62% cases
Yoshimura et al 2008	Fat reabsorption	NA	Fat gradually absorbed during first 2 months (especially first month). Minimal change thereafter
Zocchi and Zuliani 2008	Mean volume of fat persistent at 1 year	NA	55% volume (maximum 70%)
Illouz and Sterodimas 2009	Fat reabsorption	NA	'fat graft reabsorption was observed in our series'

NA: not applicable; AFT: autologous fat transfer; NR: not reported.

Reoperation

Five studies reported the need for reoperation to achieve desired breast volume or for treatment of fat necrosis complications (Spear et al 2005; Coleman and Saboeiro 2007; Missana et al 2007; Pinsolle et al 2008; Zheng et al 2008) (Table 26). A second injection was required in 8-18% of patients (reported in three studies) and a lesser proportion of patients required a third injection (3% in two studies). The mean number of fat transfer sessions required in conjunction with either prosthetic or autologous tissue reconstruction, in order to achieve a desired volume, did not appear to vary greatly. Two studies reported the need for reoperation in order to resolve a complication (drain fat necrosis) and this occurred in 17% and 3% of patients respectively (Pinsolle et al 2008; Zheng et al 2008;).

Table 26: Need for reoperation following autologous fat transfer

Study	Outcome	n/N	%/value
Spear et al 2005	Reoperation (2nd injection)	3/37	8% patients
	Reoperation (3rd injection)	1/37	3% patients
Coleman and Saboeiro 2007	Reoperation (2nd injection)	3/17	18% patients
Missana et al 2007	Reoperation (2nd injection)	9/66	14% patients
	Reoperation (3rd injection)	2/66	3% patients
	Number of sessions (adjunct implant)	NA	Mean 1.04
	Number of sessions (adjunct latissimus dorsi and implant)	NA	Mean 1.17 (range, 1-2)
	Number of sessions (adjunct latissimus dorsi)	NA	Mean 1.2 (range, 1-2)
	Number of sessions (adjunct TRAM)	NA	Mean 1.67 (range, 1-2)
	Number of sessions (adjunct conservative treatment)	NA	Mean 1.56 (range, 1-3)
Pinsolle et al 2008	Reoperation (to drain fat necrosis)	1/6	17% patients
Zheng et al 2008	Reoperation (to drain fat necrosis)	2/66	3% patients

NA: not applicable.

Aesthetic outcomes

Aesthetic outcomes including contour and volume improvement were reported in five studies (Spear et al 2005; Yoshimura et al 2008; Zheng et al 2008; Zocchi and Zuliani 2008; Illouz and Sterodimas 2009) (Table 27). Overall, autologous fat transfer was generally responsible for a slight to moderate improvement in breast contour at approximately 12 months follow-up. A considerable proportion of patients had no improvement in breast contour or long-term asymmetry, which is likely to be due to fat reabsorption during the postoperative follow-up period.

Table 27: Aesthetic outcomes following autologous fat transfer

Study	Outcome	n/N	%/qualitative result
Spear et al 2005	**Contour improvement (panel judged)**		
	Substantial	10/47	21% breasts
	Moderate	30/47	64% breasts
	None	7/47	15% breasts
Yoshimura et al 2008	Aesthetic outcome (6 months)	NA	All patients had breast circumference increased by 4-8cm or 2-3 cup sizes. Corresponds with 100-200mL volume increase per breast
Zheng et al 2008	**Breast contour (12 months)**		
	Slightly improved	28/66	42% patients
	Improved	24/66	36% patients
	Not improved	14/66	21% patients
Zocchi and Zuliani 2008	**Patient rating of aesthetic result**		
	Insufficient	5/181	3% patients
	Fair	10/181	6% patients
	Good	128/181	71% patients
	Excellent	38/181	21% patients
	Surgeon rating of aesthetic result		
	Insufficient	10/181	6% patients
	Fair	25/181	14% patients
	Good	123/181	68% patients
	Excellent	23/181	13% patients
Illouz and Sterodimas 2009	Long-term asymmetry	34/820	4% patients

NA: not applicable.

Other outcomes

Other outcomes including operative time (Missana et al 2007; Yoshimura et al 2008) and LENT-SOMA grades (Rigotti et al 2007), which were used as a means of measuring symptom improvement following reconstruction, were also reported. Missana et al (2007) reported autologous fat transfer adjunct to conventional reconstructive procedures to improve final contour and volume. Total mean operative time was 115 minutes (range, 60 to 165 minutes). Yoshimura et al (2008) also reported mean operative time, at 257.1 minutes (SD, 39.1 minutes).

Rigotti et al (2007) reported LENT-SOMA grades, where Grade 0 indicated no symptoms and grade 4 indicated severe symptoms. For patients with a baseline grade of 4 (n=11), 36% (4/11 patients) improved to grade 0, 45% (5/11 patients) improved to grade 1, 9% (1/11 patients) improved to grade 2 and 9% (1/11 patients) had no improvement. For patients with baseline grade 3 (n=9), 44% (4/9 patients) improved to grade 0 and 44% (4/9 patients) improved to grade 1.

Cosmetic mammaplasty

Saline implants

Reoperation

Two studies reported reoperation rate in both study arms; however, patients in only one of these studies required reoperation (Tarpila et al 1997; Fagrell et al 2001) (Table 28). Indications for reoperation included postoperative bleeding, of which the origin was unknown, and implant exchange due to perforation of a smooth implant. No patients underwent reoperation to exchange their implant for the alternative surface type or to treat capsular contracture.

Table 28: Need for reoperation following saline implant procedure

Study	Outcome	n/N	%
Tarpila et al 1997 (smooth-surface)	Reoperation	0/21	0% patients
Tarpila et al 1997 (textured-surface)	Reoperation	0/21	0% patients
Fagrell et al 2001 (smooth-surface)	Reoperation	2/20	10% patients
	Readmission	1/20	5% patients
Fagrell et al 2001 (textured-surface)	Reoperation	1/20	5% patients

Breast consistency

Breast consistency, measured by tonometry, was reported by both studies (Tarpila et al 1997; Fagrell et al 2001). Generally tonometric impression was similar in smooth- and textured-surface implants and did not illustrate a pattern in breast firming or softening over time (up to 7.5 years follow-up). The mean change in tonometric impression from 6- to 12-month follow-up for both studies was 1 cm^2.

Patient opinion

Both studies reported patients' opinions of their augmented breasts with smooth- versus textured-surface implants (Tarpila et al 1997; Fagrell et al 2001) (Table 29). The breast which was classified by the patient to feel harder varied between the smooth- and textured-surfaced implant. One study asked if the patient could feel their implant and the rate at which they answered yes to this question was the same for both implant surface types (Tarpila et al 1997). Patient preference for implant surface types was also similar, except in one study in which approximately twice as many patients preferred smooth-surfaced implants (Fagrell et al 2001). Fewer patients wanted to change their textured implant for smooth; however, pain was only reported in textured-surfaced implants.

Table 29: Patient opinion of saline implant procedure

Study	Outcome	n/N	%
Tarpila et al 1997	**Patient opinion**		
(smooth-surface)	Thought smooth implant was harder	4/21	19% patients
	Could feel smooth implant	12/21	57% patients
	Preferred smooth implant	6/21	29% patients
	Wanted to change smooth implant	3/21	14% patients
	Had pain in smooth implant	0/21	0% patients
Tarpila et al 1997	**Patient opinion**		
(textured-surface)	Thought textured implant was harder	7/21	33% patients
	Could feel textured implant	12/21	57% patients
	Preferred textured implant	6/21	29% patients
	Wanted to change textured implant	1/21	5% patients
	Had pain in textured implant	2/21	10% patients
Fagrell et al 2001	**Patient opinion**		
(smooth-surface)	Thought smooth implant was harder	8/20	40% patients
	Preferred smooth implant	8/20	40% patients
	Wanted to change smooth implant	3/20	15% patients
	Had pain in smooth implant	0/20	0% patients
Fagrell et al 2001	**Patient opinion**		
(textured-surface)	Thought textured implant was harder	6/20	30% patients
	Preferred textured implant	5/20	25% patients
	Wanted to change textured implant	2/20	10% patients
	Had pain in textured implant	3/20	15% patients

Results from this table are read as follows: in the study by Tarpila et al (1997) 19% (4/21) of patients thought their smooth-surfaced saline implant was harder than their textured-surfaced saline implant, 57% (12/21) of patients could feel their smooth-surface saline implant etc.

Cohesive silicone implants

Reoperation

Four studies reported the need for reoperation following the silicone breast implant procedure (Coleman et al 1991; Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Malata et al 1997) (Table 30).Coleman et al (1991) reported the need for reoperation in a similar proportion of patients receiving either smooth- or textured-surface implants. Conversely, Hakelius and Ohlsen (1992) reported a considerably higher reoperation rate in patients with smooth-surface implants compared with textured-surface implants.

Common reasons for reoperation included the patient's request to treat firmness and capsular contracture, or to adjust inadequately positioned implants. From these two studies, reoperation appeared to be closely linked to patient preference and capsular contracture rate.

Table 30: Need for reoperation following cohesive silicone implant procedure

Study	Outcome	n/N	%
Coleman et al 1991 (smooth-surface)	Reoperation	1/26	4% patients
Coleman et al 1991; Malata et al 1997 (textured-surface)	Reoperation	2/27	7% patients
Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997 (smooth-surface)	Reoperation	29/25*	116% patients
Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997 (textured-surface)	Reoperation	2/25	8% patients

*Some patients underwent greater than one reoperative event.

Breast consistency

Three studies reported breast consistency outcomes (Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997; Niechajev et al 2007). These studies measured breast consistency both subjectively in the form of patient preference and BAC scores and objectively using applanation tonometry. Results generally showed that breasts implanted with smooth implants appeared to experience more firmness and deformation, although not severe, than breasts implanted with textured implants. One study measured tonometric area and found smooth implants to have a considerably smaller mean area, supporting the idea smooth-surfaced implants are associated with breast firmness (Hakelius and Ohlsen 1992). Breast consistency does not appear to change over time (from 2 weeks follow-up to 1 year follow-up) in a uniform manner, except for a slight increase in softness after immediate follow-up (2- or 6-weeks) which is likely to be due to the subsiding of inflammation, which is expected during the early postoperative period.

Other outcomes

Niechajev et al (2007) was the only study to report breast skin and nipple sensitivity postoperatively. An average of 74% of patients had normal breast skin sensitivity postoperatively, 3% had increased sensitivity and 23% had a slight loss in sensitivity at 4-6 years follow-up. Nipple sensitivity at the same time was normal in an average

of 85% of patients, increased in 7%, slightly lost in 7% and nonexistent in 1%. Hakelius and Ohlsen (1992) reported that mean bilateral operative time was 40 minutes (range, 30 to 50 minutes).

Reconstructive mammaplasty

TRAM flaps

Effectiveness outcomes were reported in the one study reporting outcomes following breast reconstruction using TRAM flaps (Temple et al 2006).

Temperature discrimination at the nipple, areola and peripheral breast skin was measured and it was found in all cases that the ability to discriminate temperature decreased postoperatively (nipple: 0.625 to 0; areola: 0.625 to 0.125; skin: 0.5 to 0.065). Two-point discrimination was also tested for the nipple, areola and breast skin. The ability to distinguish between two points improved postoperatively, although the distance between the two points became only marginally smaller (nipple: 1 to 0.75cm; areola: 1.2 to 1cm; skin: 1 to 0.75cm), which may indicate slightly increased sensitivity in these areas. It is important to note that Temple et al (2006) reported temperature discrimination and two-point discrimination tests graphically; therefore, all of the values reported were taken visually from these graphs and are estimates.

DIEP flaps

Reoperation

Reoperation occurred at the same rate in three of the four studies reporting this outcome (Keller 2001; Gill et al 2004; Guerra et al 2004c; Hofer et al 2007) (Table 31). Hofer et al (2007) reported an elevated reoperation rate compared to the other studies.

Table 31: Need for reoperation following DIEP flap procedure

Study	Outcome	n/N	%
Keller 2001	Reoperation	6/108	6% patients
	Readmission	1/108	<1% patients
Gill et al 2004	Reoperation	45/758	6% flaps
Guerra et al 2004c	Reoperation	9/140	6% patients
Hofer et al 2007	Reoperation	29/131	22% patients

Operative time

All four studies reported operative time (Keller 2001; Gill et al 2004; Guerra et al 2004c; Hofer et al 2007) (Table 32). Operative time appeared to be consistent between the studies.

Table 32: Operative time for DIEP flap procedure

Study	Outcome	n/N	Value
Keller 2001	Operative time	NR	Range, 6-14 hours
Gill et al 2004	Operative time (unilateral)	NR	4.6 hours
	Operative time (bilateral)	NR	7.3 hours
Guerra et al 2004c	Operative time	NR	Mean 7.3±1.4 (SD) hours (range, 5-12 hours)
Hofer et al 2007	Operative time (unilateral)	NR	Mean 7.1±1.9 (SD) hours
	Operative time (bilateral)	NR	Mean 10.1±2 (SD) hours (range, 6-16 hours)

NR: not reported; SD: standard deviation.

Length of hospitalisation

All of the included studies reported mean length of hospitalisation (Keller 2001; Gill et al 2004; Guerra et al 2004c; Hofer et al 2007) (Table 33). Length of hospitalisation was consistently short across the studies, with the exception of Hofer et al (2007). The mean length of hospitalisation reported by Hofer et al was 10.1 days (SD, 7.3 days), with a maximum of 54 days hospitalisation in one patient. This is likely to represent the occurrence of a major complication requiring further intervention and recovery time. This is consistent with the safety results reported by Hofer et al (2007).

Table 33: Length of hospitalisation following DIEP flap procedure

Study	Outcome	n/N	Value
Keller 2001	Length of hospitalisation	NR	Mean 3.5 days (range, 3-7 days)
Gill et al 2004	Length of hospitalisation	NR	Mean 3.86 days
Guerra et al 2004c	Length of hospitalisation	NR	Mean 3.9 days (range, 2-9 days)
Hofer et al 2007	Length of hospitalisation	NR	Mean 10.1±7.3 (SD) days (range, 4-54 days)

NR: not reported; SD: standard deviation.

Failure (flap loss)

Failure of the procedure, in the form of total flap loss, occurred in two of the studies at a very small rate (Keller 2001; Gill et al 2004), and in Hofer et al (2007) at a considerably higher rate (Table 34). Partial flap loss occurred in a slightly higher proportion of patients in two of the included studies, but can still be considered an uncommon outcome.

Table 34: Flap failure following DIEP flap procedure

Study	Outcome	n/N	%
Keller 2001	Failure (total flap loss)	1/148	<1% flaps
Gill et al 2004	Failure (total flap loss)	4/758	<1% flaps
	Partial flap loss	19/758	3% flaps
Guerra et al 2004c	Failure (total flap loss)	0/280	0% flaps
	Partial flap loss	5/280	2% flaps
Hofer et al 2007	Failure (total flap loss)	15/175	9% flaps

SIEA flaps

Reoperation

Reoperation rate was reported in two studies (Wolfram et al 2006; Holm et al 2008). Both of these studies reported considerably high reoperation rates. Indications for reoperation included haematoma and seroma. Reoperation rate in the study by Wolfram et al (2006) was 18% (2/11) of patients and in the study by Holm et al (2008) it was 12% (3/25) of patients.

Other outcomes

Arnez et al (1999) reported 100% flap survival in its small sample of five patients and that all patients graded their results as excellent (on a scale of excellent, good, fair, poor). Wolfram et al (2006) reported a mean hospitalisation length of 11 days, while Holm et al (2008) reported a mean operative time of 5.83 hours (range, 4.17-8 hours). Failure of the procedure did not occur in any of the included studies, suggesting that when the procedure is appropriate, it is generally effective.

SGAP flaps

Reoperation

Reoperation occurred in all studies reported, at a median rate of 10.5% (range, 5% to 17%) (Blondeel 1999; Guerra et al 2004a; Guerra et al 2004b; DellaCroce and Sullivan 2005).

Operative time

Three studies reported operative time (Blondeel 1999; Guerra et al 2004b, DellaCroce and Sullivan 2005). As expected bilateral operative time (mean 11 hours and 6 minutes) was approximately twice as long as unilateral operative time (mean 5 hours and 23 minutes) (Blondeel 1999). Mean operative time as reported by Guerra et al (2004b) was 9.5 hours and as reported by DellaCroce and Sullivan (2005) was 7 hours and 47 minutes. DellaCroce and Sullivan also reported mean bilateral flap harvest time as 3 hours and 28 minutes.

Failure (flap loss)

Failure as a result of flap loss was uncommon in SGAP breast reconstruction, occurring in only 2% (3/142) of patients in one of the three studies that reported this outcome (Guerra et al 2004a). The remaining studies reported 0% failure rate (Guerra et al 2004b; DellaCroce and Sullivan 2005).

Other outcomes

In the study by Blondeel (1999), one patient (6%) had two zones of benign microcalcification noted on routine mammogram at one year postoperative. Scar hypertrophy and gluteal depressions were noted in 5% and 20% of flaps and buttocks, respectively. Mean hospitalisation was 8.2 days (range, 4-13 days) and all patients were reported to be able to perform the same tasks after surgery as before; however, this was not quantified, therefore it is unknown how long was needed before patients could resume normal activity.

Guerra et al (2004a) narratively reported patient satisfaction with their breast and donor site as 'excellent'. In this same study donor site contour deformity was apparent in 4% of patients (6/142 patients). In the study by DellaCroce and Sullivan (2005), mean hospital stay was 4 days and no flaps were lost.

IGAP flaps

Reoperation

Reoperation rate ranged from 13% to 14% (Allen et al 2006; Beshlian and Paige 2008). Reoperation was required to rectify wound healing issues and venous insufficiency.

Operative time/length of hospitalisation

Both studies reported mean operative time and mean length of hospitalisation (Allen et al 2006; Beshlian and Paige 2008). IGAP flap reconstruction appears to be a long surgical procedure; most likely due to deficiency with vessel harvest. The mean hospitalisation duration ranged from 4 days to 4.2 days, and mean operative time ranged from 5.3 hours to 9 hours and 7 minutes.

Failure (flap loss)

Failure due to flap loss occurred in both studies at a rate of 4% and 14%, respectively. Complete flap failure occurred secondary to venous thrombosis in the early postoperative period in one study (Allen et al 2006) and in two patients with previous irradiation in the other study (Beshlian and Paige 2008). In both post-irradiation failure cases vein grafts were used in an attempt to salvage the flaps after primary revascularisation failed.

Other outcomes

Neither study reported quantitative patient satisfaction data. In the study by Allen et al (2006) patient satisfaction was narratively reported to be 'very high' and in the study by Beshlian and Paige (2008) most patients were reported to be 'very satisfied'. In addition, Beshlian and Paige (2008) reported delayed healing in 7% of patients (1/14 patients).

Latissimus dorsi flaps

Daltrey et al (2006) reported reoperation in two patients (4%) due to infected seroma 3 months after the procedure and a median hospital stay of 5.1 days.

Tissue expanders and breast implants

One study reported effectiveness outcomes (Cordiero and McCarthy 2006). In this study, reoperation took place in 4% of patients after exchange to permanent implants. Reoperation to replace existing implants was indicated for implant deflation/leakage, capsular contracture or volume adjustments. A large proportion of patients reported satisfaction with their procedure (95%), with 89% (279/315 patients) grading their aesthetic outcome as good, very good or excellent. Only 5% of patients (16/315 patients) were unsatisfied with their procedure. Ninety-one percent of patients (288/315 patients) would undergo the same procedure again.

Of the patients who classified themselves as dissatisfied, 75% (12/16 patients) graded their overall aesthetic result good to excellent.

Discussion

Limitations of the evidence

Thirty five studies published between 1991 and 2009 were identified as eligible for inclusion in this systematic review. Of these, nine studies were RCTs from which data from 12 single arms were extracted, and 26 were case series, 11 of which reported outcomes for autologous fat transfer.

The greatest limitation of the evidence available for this review was the absence of studies comparing outcomes of autologous fat transfer with outcomes for other cosmetic and reconstructive procedures, which necessitated indirect comparisons of safety and efficacy to be made. Comparing patient outcomes between different studies was challenging due to differences in patient selection criteria, performance of the procedure, postoperative management, and the types of outcomes reported.

It was also difficult to make comparisons between autologous fat transfer and its cosmetic and reconstructive comparator procedures given the differences in volume achievable using prostheses and autologous tissue transfers compared with fat injections alone.

Many of the case series studies included in this review lacked clear and detailed inclusion and exclusion criteria, reported non-consecutive patient selection, and had small sample sizes and short follow-up periods. Of the 11 case series included for autologous fat transfer, potential selection bias proved to be the most common limitation of the validity of the findings, because inclusion and exclusion criteria were generally not reported and patients were not selected consecutively. Patient population size was generally appropriate in these studies, with several studies having more than 50 patients and a few studies having more than 100 patients, while one study by Illouz and Sterodimas (2009) had 820 patients The duration of follow-up in the autologous fat transfer studies was generally adequate, with the majority of studies reporting follow-up periods of approximately 12 months. Follow-up did not exceed 3 years in any of these studies; this may be due to a fall in the number of procedures being undertaken following the 1987 ASPRS caution regarding its use and the possible obscuring of malignancies. It was not until 2007 that the caution was modified to support continued research into the use of autologous fat transfer.

Similar methodological deficiencies were encountered in the four case series studies included on the use of DIEP flaps, the three case series studies on the use of SIEA flaps, the four case series studies on the use of SGAP flaps, the two case series studies on the use of IGAP flaps, and the two case series studies on the use of tissue expanders and breast implants.

Overall, the methodological quality of the available literature was poor, with particular weaknesses including potential selection bias (non-consecutive recruitment and unclear inclusion/exclusion criteria), chance variance (small sample size), and attrition bias.

Autologous fat transfer

Autologous fat transfer studies generally reported low complication rates. Fat necrosis is considered the most detrimental complication associated with autologous fat transfer, due to the potential role it may play in masking malignant lesions in the breast during mammographic examination. From the literature included in this review, at short-term follow-up, fat necrosis, calcification and fat cyst formation occurred in eight out of 11 autologous fat transfer studies at a generally low rate of 5-17%. The exact pathogenesis of liponecrotic cysts is unknown; however, it is thought that they develop secondary to an inflammatory response of the host tissue to the fat grafts that degenerate due to inadequate blood supply. To reduce the risk of fat necrosis following autologous fat transfer, the injection of large amounts of vascular fat into one region of the breast is avoided; this supports the suggested use of small aliquots of fat over several treatment sessions to achieve desired breast volume from fat transfer (Pinsolle et al 2008). Given the improved technologies available for breast imaging it is less likely a malignant breast tumour would be masked by, or mistaken for, a benign lesion resulting from autologous fat transfer (Illouz and Sterodimas 2009). Despite this, it is important to obtain preoperative mammographic images to serve as a baseline for postoperative mammographic monitoring, and in the case of uncertainty, tumour biopsy should be undertaken to ensure early detection of cancerous breast tumours (Carvajal and Patino 2008).

Patient satisfaction was reported in the majority of autologous fat transfer studies, and patients were generally satisfied with their procedure, with the only complaint being the limitation in volume increase achievable. It is important to note that autologous fat transfer is disadvantaged by its limitations in volume increase, particularly in patients requiring cosmetic augmentation, as breast enlargement is the main outcome required. Similarly, fat transfer alone has no role in complete breast reconstruction. The main purpose of fat injection in reconstructive augmentation is to improve contour following other forms of reconstruction.

Reoperation, in the form of a second fat injection, in order to obtain the patient's desired breast volume was reported in three studies in approximately 8-18% of patients (total n=15), and a third injection was required in two studies in 3% of patients each (total n=3). Reoperation to drain fat necrosis was apparent in another two studies in 3% and 17% of patients (total n=3).

Cosmetic mammaplasty

Prostheses

The safety and efficacy outcomes of saline implants and cohesive silicone implants can be grouped together as a collective 'prostheses' group. A large quantity of literature was available for comparator procedures utilising prostheses, including high-quality level II studies. Despite the abundance of literature pertaining to breast augmentation using prostheses, there was a lack of studies comparing autologous fat transfer with prostheses.

Complications that occurred following prostheses implantation included capsular contracture, implant rotation, implant perforation/leakage and skin wrinkling/rippling. The most common implant-related complication was capsular contracture, which occurred in 0% to 54% of patients at 12 months follow-up. The occurrence of fat necrosis or calcification was not reported in any of the prostheses studies.

Reoperation following breast augmentation with prostheses was generally required in order to correct a complication or convert from one implant type to another. Breast consistency outcomes were reported and in general breasts implanted with smooth implants were firmer and appeared to experience more deformation, although not severe, than breasts implanted with textured implants.

Reconstructive mammaplasty

Abdominal flaps

TRAM flaps, DIEP flaps and SIEA flaps can be grouped together as 'abdominal flaps' because they each utilise skin, fat and in some cases muscle from the abdomen to reconstruct the breast.

Complications which occurred following breast reconstruction using abdominal flaps included hernia or abdominal bulge and vascular complications, including vascular congestion, occlusion and deep vein thrombosis.

Patient satisfaction was reported in SIEA flap studies, but not in TRAM and DIEP flap studies. Patients considered the outcomes of SIEA flap reconstruction to be very good to excellent.

The proportion of patients who underwent DIEP flap reconstruction and required reoperation was the same in all of the studies reporting this outcome (6%), with the exception of one DIEP study, which reported a reoperation rate of 22% (Hofer et al 2007). In this study, some procedures were carried out using TRAM flaps instead of DIEP flaps and results were not separated accordingly. The most likely cause of increased reoperation rate in this case was more difficult DIEP flap procedures.

In DIEP flap studies, complete flap loss did occur, but was rare. Hofer et al (2007) reported the highest complete failure rate of all of the DIEP flap studies, which again is likely to be linked with more difficult DIEP flap cases. SIEA flap studies reported a 0% failure rate.

It is not possible to raise a SIEA or DIEP flap on every occasion, given the variability of their pedicle. This necessitates the use of other abdominal flaps to complete reconstruction, and these conversions usually occur during the operation when the surgeon discovers that the intended flap type is inappropriate. When SIEA flap reconstruction is intended but not suitable, DIEP or TRAM flap reconstruction is used. When DIEP flap reconstruction is intended but not suitable, TRAM flap reconstruction is used. This was the case in the studies by Wolfram et al (2006), Holm et al (2008) and Hofer et al (2007). Unfortunately, this conversion can confound results, as it is not always clear which flap was responsible for a given outcome.

Gluteal flaps

Most of the complications encountered as a result of gluteal flap breast reconstruction (using the superior gluteal artery perforator or the inferior gluteal artery perforator) were considered serious in nature. Bleeding complications were particularly common following the use of these flaps. Flap loss did occur, although it was not a common event, occurring in 2-14% of patients.

The need for reoperation following gluteal flap breast reconstruction ranged from 5-17%.

Latissimus dorsi flaps

There were a large number of studies available for breast reconstruction using latissimus dorsi flaps, including comparative evidence; however, no studies were found that compared latissimus dorsi flaps with autologous fat transfer. Most of the complications reported following latissimus dorsi flap reconstruction were considered major complications.

Only one of the latissimus dorsi flap studies reported patient and surgeon satisfaction. In this study patients and surgeons reported high satisfaction with the procedure. Like autologous fat transfer, latissimus dorsi flap breast reconstruction is associated with a smaller volume increase compared with more conventional reconstructive procedures, which is why implants are often used in conjunction with these flaps in order to add volume to the newly constructed breast. The need for reoperation was also reported in one of the included studies, in 4% of patients.

Tissue expanders and breast implants

The evidence base for tissue expanders and breast implants for breast reconstruction was large, although there were an inadequate number of level II studies to permit their inclusion in the review; and all of the studies included for this procedure were level IV studies.

Complications that occurred following tissue expander procedures were generally considered major. Similar to the use of prostheses for cosmetic mammaplasty, reoperation occurred in order to exchange implant types, or to correct a complication (such as implant deflation or capsular contracture). One study reported a 95% patient satisfaction rate.

Summary

Studies using prostheses for cosmetic breast augmentation generally reported complication rates higher than those using autologous fat transfer. It was difficult to compare the efficacy of autologous fat transfer with that of the various prostheses used, given the variability of the outcomes reported. The rate of reoperation in order to treat a complication following surgery was generally higher following cohesive silicone implants compared with autologous fat transfer; however, reoperation rates following saline implants were generally comparable to autologous fat transfer. It is also important to note the increased invasiveness of reoperation for breast implants compared with autologous fat transfer when comparing reoperation rates.

Most of the prostheses studies evaluated the efficacy of augmentation with implants using breast consistency outcomes, such as BAC grade and tonometric impression. However, these outcomes are not used in autologous fat transfer studies; therefore, no further comparison could be made, although the breast consistency achieved using different prosthesis types was able to be assessed.

In general, overall complication rates following breast reconstruction using the comparator procedures were higher than those for autologous fat transfer. Fat or flap necrosis generally occurred at a similar frequency following abdominal and gluteal flaps compared with autologous fat transfer, suggesting that fat necrosis can occur as a result of any type of surgical trauma to the breast tissue, not only autologous fat transfer.

In terms of efficacy, autologous fat transfer may not be as effective as breast reconstruction using autologous tissue transfer due to insufficient volume filling; therefore, in reconstructive cases, particularly following complete mastectomy where the entire breast volume must be replaced, autologous fat transfer may be used in conjunction with breast reconstruction using flaps, to assist in achieving contour and symmetry. Reoperation rates following DIEP, gluteal, latissimus dorsi flaps, and tissue expanders were similar to those following autologous fat transfer; whereas the

need for reoperation following SIEA flap breast reconstruction was higher compared with autologous fat transfer. This may be due to the difficulty associated with the reduced length and size of the SIEA pedicle.

Patient satisfaction was reported in autologous fat transfer studies and IGAP flap and latissimus dorsi flap studies. Patients receiving fat transfer reported favourable results, whereas patients receiving IGAP flap reconstruction reported being very satisfied with their procedure. Patient satisfaction also appeared higher following latissimus dorsi flap reconstruction compared to autologous fat transfer.

The durability of the fat injection procedure cannot be compared with flap loss in autologous tissue reconstructions, as flap loss is uncommon and fat reabsorption occurred in most cases during the early postoperative period following autologous fat transfer.

In general, women with smaller, minimally ptotic breasts were considered the best candidates for unilateral breast reconstruction using prostheses. Similarly, these patients would be ideal candidates for autologous fat transfer reconstruction, as it is not necessary to achieve a large volume increase to match the contralateral breast. Autologous fat transfer may also be a feasible alternative for patients undergoing reconstruction who are likely to require irradiation. Due to the increased risk of capsular contracture when radiotherapy is employed, fat transfer would remove the need for a prosthesis and thus eliminate this risk, although the survival of fat following irradiation is also variable.

Conclusions and Recommendations

In conclusion, the literature available for inclusion in this review was of poor quality. The greatest weakness was the absence of comparative evidence for autologous fat transfer which necessitated indirect comparisons of safety and efficacy to be made. It was also difficult to make comparisons between autologous fat transfer and its cosmetic and reconstructive comparator procedures given the differences in breast volume achievable using prostheses and autologous tissue transfers compared with fat injections alone.

Although fat necrosis/calcification/cysts were the most commonly reported complications associated with autologous fat transfer, they appear to occur in a small proportion of patients. There was also no data linking the presence of these complications with long-term mammagraphic and cancer-related outcomes. These complications occurred at a similar frequency in patients undergoing breast reconstruction with gluteal and abdominal flaps. There were a variety of serious complications that were related to some of the comparator procedures, including hernia in reconstructive procedures utilising abdominal flaps, and capsular contracture in cosmetic procedures utilising prostheses.

The efficacy of autologous fat transfer cannot be easily compared with that of prostheses augmentation procedures or breast reconstruction using autologous tissue, due to the variability of outcomes reported in these studies. Patient satisfaction following autologous fat transfer was high, as was patient satisfaction following reconstruction using tissue expanders with breast implants and abdominal flaps. Patient satisfaction with breast reconstruction using gluteal flaps and latissimus dorsi flaps was generally higher than that of autologous fat transfer. For autologous fat transfer the limited breast volume increase was the main complaint associated with the procedure. Latissimus dorsi flap breast reconstruction was also associated with small breast volume increase. However, implants are commonly used in conjunction with flaps in order to achieve a desired volume; similarly, implants could be employed with autologous fat transfer augmentation procedures.

When patients desire a moderate to large increase in breast volume, the use of autologous fat transfer as an adjunct to prostheses or autologous tissue transfer is feasible. Results suggest that autologous fat transfer can be safely and effectively used in conjunction with other augmentative procedures (including implants, TRAM flaps and latissimus dorsi flaps).

Fat reabsorption occurred following autologous fat transfer to varying degrees, usually in the short-term (12- month) follow-up period; however, there were no cases of complete fat reabsorption reported in this review. As a result, multiple autologous fat transfer procedures are often needed to achieve a level of breast augmentation

that may be achievable in one to two procedures when autologous tissue transfer or prostheses are utilised. Flap loss occurred following autologous tissue reconstruction in some cases, but it was uncommon.

Although autologous fat transfer is a less complex method of breast augmentation compared with its comparator procedures, it is not a simple technique. Major complications are generally observed following autologous fat transfer as a result of technical errors and the harvesting and implantation of fat at incorrect anatomic sites (Illouz and Sterodimas 2009). Consequently, autologous fat transfer should only be performed by well-trained and skilled surgeons.

Classifications and recommendations

On the basis of the evidence presented in this systematic review, the ASERNIP-S Review Group agreed on the following classifications and recommendations concerning autologous fat transfer for cosmetic and reconstructive breast augmentation:

Classifications

Evidence rating

The evidence base in this review is rated as poor, limited by the quality of the available studies. Specific limitations of the evidence include the absence of studies comparing autologous fat transfer to the nominated comparator procedures, as well as a lack of standardised reporting of outcomes.

Safety

Autologous fat transfer for cosmetic and reconstructive breast augmentation is considered to be at least as safe as the nominated comparator procedures. It is important to note that this rating is based on indirect comparisons that have been made using overall complication rates. Important safety data examining the effect of microcalcifications following autologous fat transfer on subsequent breast cancer detection were not reported in the studies included in this review; therefore, safety in regards to this outcome cannot be determined.

Efficacy

The efficacy of autologous fat transfer cannot be determined from the studies included in this review. Efficacy outcomes reported in the included autologous fat transfer studies varied from those reported for the nominated comparator procedures; therefore, it was not possible to compare the efficacy of autologous fat transfer with that of the comparator procedures. However, the inability of autologous fat transfer to achieve a volume increase comparable to that of prostheses

or autologous tissue augmentation suggests that it may be less efficacious than these comparator procedures.

Clinical and research recommendations

There is a need for controlled trials (ideally randomised), assessing the effects of microcalcifications following autologous fat transfer on immediate and long-term breast cancer detection, to be conducted. Studies to determine the maximal breast volume increase reliably achieved by autologous fat transfer would also be useful in order to define the patient population that would benefit most from the procedure, as well as which breast indications should be treated using autologous fat transfer.

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Zheng DN, Li QF, Lei H, Zheng SW, Xie YZ, Xu QH, Yun X, Pu LL. Autologous fat grafting to the breast for cosmetic enhancement: experience in 66 patients with long-term follow up. *Journal of Plastic and Reconstructive Aesthetic Surgery* 2008; **61**(7): 792-798.

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Appendix A: Scoring/Grading Systems

Breast augmentation grading, scoring and classification systems

Due to the subjectivity of assessing breast augmentation outcomes various grading, scoring and classification systems have been developed in order to standardise the way in which this is done. Several of the predominant systems used to measure augmentation outcomes are listed and described briefly below.

Baker Classification and Breast Augmentation Classification

These classification systems are used to measure the occurrence and severity of capsular contracture in breasts augmented with implants. Grading ranges from I to IV in both systems, where I and II are considered acceptable grades and III and IV are considered capsular contracture.

Table A1: Baker Classification and Breast Augmentation Classification for assessment of capsular contracture

Grade	Baker classification	Breast Augmentation Classification
I	Cannot tell breast has been augmented.	Soft, no deformation.
II	Can tell breast has been augmented, patient has no complaint.	Slight thickened consistency, none to slight deformation.
III	Patient feels some firmness.	Firm to hard, none to slight deformation.
IV	Implant obvious from observation.	Hard, severe deformation.

Source: Hakelius and Ohlsen 1992; Spear and Baker 1995

Applanation tonometry and relative breast compressibility

Applanation tonometry measures the firmness of the breast, or the breasts relative compressibility. Tonometric area is measured with the patient in the supine position. Gel is placed on the breast and a Plexiglas disk weighing 270g is positioned on top, imprint of the gel on the disk is transferred to filter paper and the area is measured (Fagrell et al 2001). The greater the tonometric area, the greater the relative breast compressibility, and the softer the breast is.

Breast imaging grading systems

There are also scoring systems that measure imaging outcomes. The main system used in regards to breast imaging outcomes is the Breast Imaging Reporting and Data System (BI-RADS).

Table A2: Breast Imaging Reporting and Data System

Grade	Breast Imaging Reporting and Data System
O	Incomplete. Additional imaging or comparison with outside films required.
I	Negative. Routine screening needed.
II	Benign finding. Only routine screening required.
III	Probably benign findings. Short-interval mammographic follow-up suggested to observe stability.
IV	Suspicious finding. Biopsy recommended.
V	Highly suggestive of malignancy. Biopsy required.

Source: American College of Radiology 2009

Point scales and other scoring systems

Point scales, such as the Visual Analogue Scale for pain measurement (VAS), are used across surgical fields to standardise a measurement of something that is subjective. Similarly for breast augmentation, point scales, such as a 5- or 10-point scale, are used to gauge the degree of a particular outcome, for example patient satisfaction with an aesthetic result. Generally, the lower the grade the lower the severity of the outcome in question, or in the case of the example the less pleased the patient is with the aesthetic outcome. These and other less common scoring systems are described ad hoc throughout the review and extraction tables.

Appendix B: Search Strategy

Table B1: Search terms

Database	Cosmetic breast augmentation search	Reconstructive breast augmentation search
Current contents	*Text words*	
	breast implan*, breast augmen*, breast enhanc*, mammaplasty, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, saline, silicone	breast augmen*, breast reconstruct*, mammaplasty, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, perforator flap*, deep inferior epigastric perforator flap*, superficial inferior epigastric artery, superior gluteal artery perforator flap*, inferior gluteal artery perforator flap*, latissimus dorsi flap, transverse rectus abdominis myocutaneous flap*, tissue expand*, breast implan*, saline, silicone
	MeSH terms	
	NA	NA
York CRD and The Cochrane Library	*Text words*	
	breast implan*, breast augmen*, breast enhanc*, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, saline, silicone	breast augmen*, breast reconstruct*, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, perforator flap*, deep inferior epigastric perforator flap*, superficial inferior epigastric artery, superior gluteal artery perforator flap*, inferior gluteal artery perforator flap*, latissimus dorsi flap, transverse rectus abdominis myocutaneous flap*, tissue expand*, breast implan*, saline, silicone
	MeSH terms	
	Breast Implantation, Breast Implants, Mammaplasty, Sodium Chloride	Mammaplasty, Breast Implants, Sodium Chloride
PubMed	*Text words*	
	breast implan*, breast augmen*, breast enhanc*, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, saline, silicone	breast augmen*, breast reconstruct*, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, perforator flap*, deep inferior epigastric perforator flap*, superficial inferior epigastric artery, superior gluteal artery perforator flap*, inferior gluteal artery perforator flap*, latissimus dorsi flap, transverse rectus abdominis myocutaneous flap*, tissue expand*, breast implan*, saline, silicone
	MeSH terms	
	Breast Implantation, Breast Implants, Mammaplasty, Autologous Transplantation, Sodium Chloride, Silicones	Mammaplasty, Autologous Transplantation, Breast Implantation, Breast Implants, Sodium Chloride, Silicones
EMBASE	*Text words*	
	breast implan*, breast augmen*, breast enhanc*, mammaplasty, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, saline, silicone	breast augmen*, breast reconstruct*, mammaplasty, autologous fat trans*, autologous fat, fat trans*, fat injection, lipoinjection, lipoaugmentation, perforator flap*, deep inferior epigastric perforator flap*, superficial inferior epigastric artery, superior gluteal artery

		perforator flap*, inferior gluteal artery perforator flap*, latissimus dorsi flap, transverse rectus abdominis myocutaneous flap*, tissue expand*, breast implan*, saline, silicone
	MeSH terms	
	Breast Augmentation, Breast Endoprosthesis, Autotransplantation, Sodium Chloride, Silicone, Silicone Prosthesis	Breast Augmentation, Breast Reconstruction, Autotransplantation, Breast Endoprosthesis, Sodium Chloride, Silicone, Silicone Prosthesis

Note: * is a truncation character that retrieves all possible suffix variations of the root word; for example, surg* retrieves surgery, surgical, surgeon, etc.

Appendix C: Included Studies

Autologous fat transfer

Case series

Carvajal J and Patino JH. Mammographic findings after breast augmentation with autologous fat injection. *Aesthetic Surgery Journal* 2008; **28**(2): 153-162.

Coleman SR and Saboeiro AP. Fat grafting to the breast revisited: safety and efficacy. *Plastic and Reconstructive Surgery* 2007; **119**(3): 775-785.

Fulton JE. Breast contouring with "gelled" autologous fat: A 10-year update. *International Journal of Cosmetic Surgery and Aesthetic Dermatology* 2003; **5**(2): 155-163.

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Zocchi ML and Zuliani F. Bicompartmental breast lipostructuring. *Aesthetic Plastic Surgery* 2008; **32**(2): 313-328.

Saline implants

Randomised controlled trials

Fagrell D, Berggren A, Tarpila E. Capsular contracture around saline-filled fine textured and smooth mammary implants: a prospective 7.5-year follow-up. *Plastic and Reconstructive Surgery* 2001; **108**(7): 2108-2112.

Tarpila E, Ghassemifar R, Fagrell D, Berggren A. Capsular contracture with textured versus smooth saline-filled implants for breast augmentation: a prospective clinical trial. *Plastic and Reconstructive Surgery* 1997; **99**(7): 1934-1939.

Cohesive silicone implants

Randomised controlled trials

Coleman DJ, Foo ITH, Sharpe DT. Textured or smooth implants for breast augmentation? A prospective controlled trial. *British Journal of Plastic Surgery* 1991; **44**(6):444-448.

Hakelius L and Ohlsen L. A clinical comparison of the tendency to capsular contracture between smooth and textured gel-filled silicone mammary implants. *Plastic and Reconstructive Surgery* 1992; **90**(2): 247-254.

Hakelius L and Ohlsen L. Tendency to capsular contracture around smooth and textured gel-filled silicone mammary implants: a 5-year follow-up. *Plastic and Reconstructive Surgery* 1997; **100**(6): 1566-1569.

Malata CM, Feldberg L, Coleman DJ, Foo ITH, Sharpe DT. Textured or smooth implants for breast augmentation? Three year follow-up of a prospective randomised controlled trial. *British Journal of Plastic Surgery* 1997; **50**(2):99-105.

Niechajev I, Jurell G, Lohjelm L. Prospective study comparing two brands of cohesive gel breast implants with anatomic shape: 5-year follow-up evaluation. *Aesthetic Plastic Surgery* 2007; **31**(6): 697-710.

TRAM flaps

Randomised controlled trials

Temple CL, Tse R, Bettger-Hahn M, MacDermid J, Gan BS, Ross DC. Sensibility following innervated free TRAM flap for breast reconstruction. *Plastic and Reconstructive Surgery* 2006; **117**(7): 2119-2127.

DIEP flaps

Case series

Gill PS, Hunt JP, Guerra AB, DellaCroce FJ, Sullivan SK, Boraski J, Metzinger SE, Dupin CL, Allen RJ. A 10-year retrospective review of 758 DIEP flaps for breast reconstruction. *Plastic and Reconstructive Surgery* 2004; **113**(4): 1153-1160.

Guerra AB, Metzinger SE, Bidros RS, Rizzuto RP, Gill PS, Nguyen AH, Dupin CL, Allen RJ. Bilateral breast reconstruction with the deep inferior epigastric perforator (DIEP) flap: an experience with 280 flaps. *Annals of Plastic Surgery* 2004c; **52**(3): 246-252.

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Keller A. The deep inferior epigastric perforator free flap for breast reconstruction. *Annals of Plastic Surgery* 2001; **46**(5): 474-479.

SIEA flaps

Case series

Arnez ZM, Khan U, Pogorelec D, Planinsek F. Breast reconstruction using the free superficial inferior epigastric artery (SIEA) flap. *British Journal of Plastic Surgery* 1999; **52**(4): 276-279.

Holm C, Mayr M, Hofter E, Raab N, Ninkovic M. Interindividual variability of the SIEA Angiosome: effects on operative strategies in breast reconstruction. *Plastic and Reconstructive Surgery* 2008; **122**(6): 1612-1620.

Wolfram D, Schoeller T, Hussl H, Wechselberger G. The superficial inferior epigastric artery (SIEA) flap: indications for breast reconstruction. *Annals of Plastic Surgery* 2006; **57**(6): 593-596.

SGAP flaps

Case series

Blondeel PN. The sensate free superior gluteal artery perforator (S-GAP) flap: A valuable alternative in autologous breast reconstruction. *British Journal of Plastic Surgery* 1999; **52**(3): 185-193.

DellaCroce FJ and Sullivan SK. Application and refinement of the superior gluteal artery perforator free flap for bilateral simultaneous breast reconstruction. *Plastic and Reconstructive Surgery* 2005; **116**(1): 97-103.

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IGAP flaps

Case series

Allen RJ, Levine JL, Granzow JW. The in-the-crease inferior gluteal artery perforator flap for breast reconstruction. *Plastic and Reconstructive Surgery* 2006; **118**(2): 333-339.

Beshlian KM and Paige KT. Inferior gluteal artery perforator flap breast reconstruction. *American Journal of Surgery* 2008; **195**(5): 651-653.

Latissimus dorsi flaps

Randomised controlled trials

Daltrey I, Thomson H, Hussien M, Krishna K, Rayter Z, Winters ZE. Randomized clinical trial of the effect of quilting latissimus dorsi flap donor site on seroma formation. *British Journal of Surgery* 2006; **93**(7): 825-830.

Tissue expanders and breast implants

Case series

Cordeiro PG. A single surgeon's 12-year experience with tissue expander/implant breast reconstruction: Part II. An analysis of long-term complications, aesthetic outcomes, and patient satisfaction. *Plastic and Reconstructive Surgery* 2006; **118**(4):832-839.

Wright JL, Cordeiro PG, Ben Porat L, Van Zee KJ, Hudis C, Beal K, McCormick B. Mastectomy with immediate expander-implant reconstruction, adjuvant chemotherapy, and radiation for stage II-III breast cancer: treatment intervals and clinical outcomes. *International Journal of Radiation Oncology, Biology, Physics* 2008; **70**(1): 43-50.

Appendix D: Excluded Studies

Autologous fat transfer

Non-English study that did not provide additional data to included studies

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Saline implants

Randomised controlled trials

Greater than 10% patients lost to follow-up

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Cohesive silicone implants

Randomised controlled trials

Greater than 10% patients lost to follow-up

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TRAM flaps

Randomised controlled trials

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Same patient population as previous excluded study

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Non-blinded

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DIEP flaps

Less than 100 patients

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Case report

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Not breast related

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Randomised controlled trials

Less than 5 RCTs

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SIEA flaps

Letter

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Did not report outcomes of interest

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Case report

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IGAP flaps

Same patient population as previously included study

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Case report

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Latissimus dorsi flaps

Randomised controlled trials

Did not report outcomes of interest

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Non-blinded

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Discussion

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Less than 100 patients

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Yiacoumettis AM. Two staged breast reconstruction following prophylactic bilateral subcutaneous mastectomy. *British Journal of Plastic Surgery* 2006; **58**(3): 1066-1067.

Less than 2 years follow-up

Calderoli H. Immediate placement of tissue expander during mastectomy: Analysis of 162 patients. *Breast* 1997; **6**(2): 61-64.

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Non-cohesive silicone implants used

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Randomised controlled trials

Less than 5 RCTs

May-Jr JW, Bucky LP, Sohoni S, Ehrlich HP. Smooth versus textured expander implants: A double-blind study of capsule quality and discomfort in simultaneous bilateral breast reconstruction patients. *Annals of Plastic Surgery* 1994; **32**: 225-233.

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[Same patients as above]

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Cosmetic augmentation

Did not report patient outcomes

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Review

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News article

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Reconstruction augmentation

Did not report patient outcomes

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Baildam AD. Breast reconstruction - state of the art. *Breast* 2006; **15**(SUPPL. 2): S27-S30.

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Review

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Granzow JW. Breast reconstruction with perforator flaps. *Plastic and Reconstructive Surgery* 2007; **120**(1): 1-12.

Question and answer

Robb GL. Breast reconstruction after therapy for early breast cancer. *Clinical Advances in Hematology and Oncology* 2008; **6**(5): 341-344.

Letter

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Multiple procedures used

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Appendix E: Extraction tables

Table E1: Extraction table for included autologous fat transfer studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Fulton 2003 Location Private Practice, Tustin, California Single centre/ multicentre NR Study period Examined over 10 year period (dates not reported) Data collection Prospective Patient selection NR Level of evidence Level IV – case series Objective To examine results of breast augmentation using 'gelled' autologous adipose tissue enmeshed in a fibrin clot of platelet-rich plasma over a 10 year period	n (patients) 65 n (implants/flaps/breasts) NR Bilateral/unilateral NR Inclusion criteria Healthy women with no personal history of malignancy, sufficient areas of disharmonious obesity, and no severe breast ptosis. Women who were realistic and would be content with one cup size increase in volume were chosen. Patients with violin-type deformity were preferred Exclusion criteria NR Indication Cosmetic **Procedural details** Whole blood (400-500cc) was collected from the patient. The blood was processed using 2 separate centrifugation steps to obtain the purified platelet rich plasma Purified platelet rich plasma then aspirated into 60cc syringe and held at room temperature until fat ready for supplementation. Fat was obtained predominantly from the outer thigh	Infection NR Lumps NR Fat necrosis NR Inflammation Minimal bruising during immediate follow up period Haemorrhage/bleeding complications (haematoma) 0 patients Death NR Implant related complications NR Pain Minimal during immediate follow-up period Fat emboli 0 patients Striae	Operative time NR Reoperation NR Readmission NR Mammographic issues Fatty infiltration of pectoralis muscle and prepectoral space (number not reported) Masking or compression of breast tissue: 0 patients Benign 'eggshell' calcifications: 9% patients (usually bilateral). Small spiculed calculi: 0 patients Psychosocial issues NR Patient satisfaction Subjective patient remarks from 3 patients included. All 3 reported favourable results Fat reabsorption NR Scarring	Duration of follow-up Occurred at 3 months, 6 months, and annually thereafter Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	and flank (approximately 500-600cc adipose tissue per side, for total of 100-1200cc) using the syringe method. Aspirate washed 2-3 times to remove broken fat and red blood cells prior to addition of platelet rich plasma and 15 minute incubation. Following incubation, approximately 50% of supernatant fat remained for lipoinjection (free water and oil discarded). Platelet rich plasma-adipose tissue transferred to injection guns and 200-300cc platelet rich plasma-adipose tissue injected into each breast below the inframammary fold. Small tissue filaments were injected (0.3cc) into sites through each port as needle withdrawn. Approximately 100cc platelet rich plasma-adipose tissue distributed as filaments into subpectoral plain, 100 cc into plane of pectoralis muscle, and 100cc into retroglandular space below parenchyma breast tissue. Between syringes, breast tissue gently massaged to disperse any globules Operative details NR Volume of injected fat 200-300cc of platelet rich plasma-adipose tissue injected into each breast Patient demographics Age: mean 38 years (range, 18–72 years) Body mass index: NR Smoker: NR	2 patients *improved with daily application of tretinoin *ecchymosis reported in abstract (incidence not reported)	NR **Durability of enhancement** Mean residual augmented breast volume (repeated volumetric measurements): 73% Breast volume reduction during first 60-90 days 20-30% Breast volume reduction after 90 days Constant (except for changes with weight and menstrual cycle) *Breast augmentation equivalent to 200-250cc implant Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year Spear et al 2005 Location Division of Plastic Surgery,	n (patients) 37 *total of 47 treatment events n (implants/flaps/breasts)	Infection 1 patient *with cellulitis of left breast, detected 2 weeks postoperatively, resolved with antibiotics without	Operative time NR Reoperation 2nd fat grafting procedure: 3	Duration of follow-up 15 months (range, 3 weeks to 7 years) Losses to follow-up None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Georgetown University Hospital, Washington, DC, USA Single centre /multicentre Single centre Study period 1993 to 2003 Data collection Retrospective review Patient selection NR Level of evidence IV – case series Objective To describe the experience of one senior surgeon using fat injection to correct contour deformities associated with breast reconstruction	43 breasts Bilateral/unilateral 6 patients/31 patients Inclusion criteria Patients who underwent autologous fat transfer for contour deformities following reconstruction, whose medical records could be located Exclusion criteria NR Indication Reconstructive – correction of contour deformities following reconstruction with implants or autologous tissue **Procedural details** Fat harvested using the Tulip low-pressure syringe lipoaspiration system and treated with repetitive saline washing to remove blood. Fractional injection into depression, primarily around the periphery of the breast, was performed with multiple passes through separate tunnels. Operative details Single surgeon Type of reconstruction Implants: 25 breasts (58%) TRAM flaps: 17 breasts (40%) TRAM and implant: 1 breasts (2%) Volume of injected fat Mean 116 cc (range, 30-260 cc)	need for implant removal. Lumps 3 patients *small, superficial lumps in the area of injection Fat necrosis Removal of 2/3 lumps (above) revealed 1-2cm liponecrotic cysts Inflammation NR Haemorrhage/bleeding complications NR Death NR Implant related complications No implant ruptures as a result of AFT Overall complication rate 4/47 procedures (8.5%) Other NR	patients 3rd fat grafting procedure: 1 patient Readmission NR Mammographic issues 2/3 patients undergoing mammogram or ultrasound had palpable masses with the radiographic appearance of fat necrosis *biopsy confirmed these observations Psychosocial issues NR Patient satisfaction NR Fat reabsorption NR Scarring NR Aesthetic outcome (panel-judged contour improvement) Substantial improvement: 10 breasts (23 %) Moderate improvement: 30 breasts (70 %) No improvement: 7 breasts (16%)	Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Patient demographics Age: NR Body mass index: NR Smoker: NR		Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year Coleman and Saboeiro 2007 Location New York University School of Medicine, New York, N.Y., USA Single centre/multicentre NR Study period November 1995 to June 2000 Data collection Retrospective study Patient selection NR Level of evidence Level IV – case series	n (patients) 17 n (implants/flaps/breasts) 37 breasts Bilateral/unilateral 14 patients/3 patients Inclusion criteria Signed consent Exclusion criteria NR Indication Cosmetic and reconstructive *for indications including micromastia (10 patients) (cosmetic) and postaugmentation deformity after breast implant removal (1 patient), postaugmentation deformity with breast implants (2 patients), tuberous breast deformity (1 patient), Poland's syndrome (1 patient) or postmastectomy reconstruction deformity (2 patients)	Infection 1 patient *local infection near silicone implant Lumps (nodules) 3 patients Fat necrosis 2 patients Inflammation Immediately following the procedure, all patients experienced significant oedema of the donor and recipient sites Haemorrhage/bleeding complications NR Death NR	Operative time NR Reoperation 2nd fat grafting performed: 3 patients Readmission NR Mammographic issues (15/17 patients underwent mammography) Normal postoperative mammogram: 8/15 patients Breast cancer detected on mammography: 2/15 patients *1 in location of fat graft Benign-appearing calcifications: 4/15 patients Nodules: 3/15 patients Psychosocial issues NR	Duration of follow-up (office) Mean 62.2 months *13 patients Duration of follow-up (telephone) Mean 50.8 months *4 patients Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Objective To re-examine the safety and efficacy of fat grafting to breasts in light of opinions provided in 1987 American Society of Plastic and Reconstructive Surgeons position paper	**Procedural details** The Coleman method of structural fat grafting. Fat harvested using 10 ml syringe attached to two-hole Coleman harvesting cannula, followed by centrifugation and refinement. Fat transferred to 3 ml syringes. Blunt infiltration cannulas then used to place fat through 2 mm incisions. No sharp needles were used for injection into the breast. Incisions positioned to allow placement from at least 2 directions in each area grafted. Approximately 0.2ml placed with each cannula withdrawal. Shaping of breasts achieved by layering fat into different levels until desired contour was achieved. Operative details Single surgeon (senior author) Volume of injected fat Mean 278.6 cc per operation per breast Patient demographics Age: mean 38.2 years (range, 25 -55 years) Body mass index: NR Smoker: NR	Implant related complications NR Other NR	Patient satisfaction *At follow-up, all patients reported enlargement of breasts and improvement in surface contours. *All patients pleased with postoperative results (13 patients, followed up in office) or had favourable results (4 patients, followed up by telephone) Fat reabsorption Despite initial oedema in all cases immediately postoperative, by 4 to 6 months, breast volume stabilised and little apparent reduction in size over ensuing years reported Scarring NR Durability of enhancement At follow-up, all patients reported enlargement of breasts and improvement in surface contours Length of hospitalisation NR Healing time/time to normal activity or work NR Other	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			NR	
Author, year Missana et al 2007 Location Department of Surgical Oncology and Breast Reconstructive Surgery, Gustave Roussy Institute, Comprehensive Cancer Centre, Villejuif, France Single centre/ multicentre NR Study period September 2001 to September 2005 Data collection Prospective Patient selection NR Level of evidence Level IV – case series Objective To report findings on the application of autologous fat transfer or lipoinjection, in reconstructive breast surgery to improve cosmetic results and correct certain sequelae of	n (patients) 69 patients n (implants/flaps/breasts) 74 breasts Bilateral/unilateral 5 patients/ 64 patients Inclusion criteria Patients who underwent autologous fat transfer whether bilaterally or unilaterally during the study period Exclusion criteria NR Indication Reconstructive Reconstructive type Conservative treatment: 9 breasts Implants: 25 breasts Latissimus dorsi flap and implant: 29 breasts Latissimus dorsi flap alone: 5 breasts TRAM flap alone: 6 breasts **Procedural details** The fat was usually harvested from the abdominal subcutaneous tissues (in some cases taken from hips, inside of thighs, gluteus maximus, or the back) using a foam cannula, and centrifuged (3500 rpm, 4 minutes). Three layers formed, of which the middle layer composed of the adipose tissue for use. The breast was incised with several 1mm incisions	Infection 0 patients Lumps/microcalcifications 0 patients Fat necrosis (cytosteatonecrosis) 5 patients Inflammation NR Haemorrhage/bleeding complications NR Death NR MRI findings (signs of necrotic changes) 5 patients	Operative time Mean 115 minutes (range, 60-165 minutes) Reoperation (reinjection to obtain satisfactory result) 11 patients (14.86%) *1 additional injection in 9 patients and 2 additional injections in 2 patients Number of sessions by type of surgery Implant: mean 1.04 sessions Latissimus dorsi and implant: mean 1.17 sessions (range, 1-2 sessions) Autologous latissimus dorsi: mean 1.2 sessions (range, 1-2 sessions) TRAM: mean 1.67 sessions (range, 1-2 sessions) Conservative treatment: mean 1.56 sessions (range, 1-3 sessions) Readmission NR Mammographic issues No cases of microcalcifications suggestive of malignancy Psychosocial issues NR	Duration of follow-up Mean 11.7 months (range, 1 month to 32 years) Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

<table>
<tr><th>Study profile</th><th></th><th>Safety outcomes</th><th>Effectiveness outcomes</th><th>Methodological quality</th></tr>
<tr>
<td>conservative breast treatment</td>
<td>distant to the injection site to create crossed and superimposed planes creating a 3-dimensional lattice.

Operative details
NR

Volume of injected fat

<table>
<tr><th>Reconstructive procedure</th><th>Mean volume injected (ml)</th><th>Volume of 1st injection (ml)</th><th>Volume of 2nd injection (ml)</th></tr>
<tr><td>Implant</td><td>107</td><td>105.24 (range, 18-220)</td><td>150</td></tr>
<tr><td>Latissimus dorsi and implant</td><td>147.24</td><td>142.46 (range, 66-360)</td><td>174 (range, 70-300)</td></tr>
<tr><td>Latissimus dorsi flap</td><td>142.5</td><td>135 (range, 65-180)</td><td>180</td></tr>
<tr><td>Transverse rectus abdominis myocutaneous flap</td><td>142.14</td><td>115.83 (range, 60-160)</td><td>300</td></tr>
<tr><td>Conservative treatment</td><td>75</td><td>77 (range, 40-180)</td><td>67 (range, 50-80)</td></tr>
</table>

Adjunct chemotherapy or radiotherapy
Pre-reconstructive radiotherapy: 30/60 patients

Patient demographics
Age: 51 years (range, 21-73 years)</td>
<td></td>
<td>Patient satisfaction
NR

Fat reabsorption
NR

Scarring
NR

Aesthetic outcome (surgeon’s observation)
Good to very good: 64 breasts (86.5%)
Moderate: 10 breasts (13.5%)
*primarily due to insufficient quantity of adipose material that could be removed

Durability of enhancement (implant volume changes)
Implant: 36% cases
Latissimus dorsi with implant: 62% cases

Length of hospitalisation
NR

Healing time/time to normal activity or work
NR

Other
NR</td>
<td></td>
</tr>
</table>

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Body mass index: NR Smoker: NR			
Author, year Pinesolle et al 2007 Location Service de Chirurgie Plasttique, CHU Bordeaux/Universite Bordeaux 2, Hospital Pellegrin Tondu, France Single centre/multicentre Single centre Study period 1 January 2003 to 31 December 2005 Data collection Retrospective review Patient selection NR Level of evidence IV – case series Objective To report preliminary results of grafting autologous fat cells according to Coleman's method to treat Poland's syndrome	n (patients) 6 n (implants/flaps/breasts) NR Bilateral/unilateral NR Inclusion criteria Patients requiring breast/chest wall reconstruction for Poland's syndrome. Exclusion criteria NR Indication Reconstructive – for disfigurement caused by Poland's syndrome. Poland's syndrome grade Grade I: 3 patients Grade II: 2 patients Grade III: 1 patient **Procedural details** Fat grafting was performed by Coleman method. Autologous fat harvested by syringe from abdominal or trochanteric region. The injection was performed with a 1.5mm diameter cannula. Additional associated reconstructive procedures are shown below. This sample was centrifuged and reinjected by separate microtunnels in site to be filled.	Infection 0 Lumps 0 Fat necrosis 1 patient *progressed favourably after surgical drainage and general anaesthesia Inflammation 0 Haemorrhage/bleeding complications 0 Death 0 Implant related complications NR Other NR	Operative time NR Reoperation 1 patient *drainage of fat necrosis under general anaesthesia Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Fat reabsorption NR Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation NR	Duration of follow-up NR Losses to follow-up NA Sub-group analysis None Conflicts of interest None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
NOTE: original study reported outcomes for 8 patients; however, for the purposes of this review 2 were excluded because they were either under the age criteria for inclusion or were male	Operative details NR Patient treatment characteristics Patient 1: received 30 cc autologous fat in 1 session. Associated treatments included latissimus dorsi flap, customised silicone implant), skin expansion, and breast implant (320cc) Patient 3: received 250cc autologous fat in 2 sessions. Associated treatments included skin expansion and breast implant (255cc) Patient 5: received 200cc autologous fat in 2 sessions. Associated treatments included breast implant (205cc) Patient 6: received 150cc autologous fat in 2 sessions. Associated treatments included breast implant (275cc) Patient 7: received 300cc autologous fat in 3 sessions. Associated treatments included breast implant (375cc) Patient 8: received 110cc autologous fat in 1 session. No associated treatments Volume of injected fat (total per patient) Mean 173 cc (range, 30-300 cc) Number of injection sessions Mean 1.8 sessions (range, 1-3 sessions) Patient demographics Age: mean 24.7 years (range, 17-40 years) Body mass index: NR Smoker: NR		Healing time/time to normal activity or work NR Other NR	
Author, year Rigotti et al 2007	n (patients) 20	Infection NR	Operative time NR	Duration of follow-up Mean 30 months (range, 18-33 months)

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Location Milan and Verona, Italy Single centre/multicentre NR Study period Commenced 2002 *included data from an initial pilot study Data collection Prospective Patient selection Consecutive Level of evidence Level IV – case series Objective To assess the presence of adipose-derived adult stem cells left in their natural scaffold in the purified lipoaspirate and to assess the clinical effectiveness of lipoaspirate transplantation in the treatment of radiation side effects NB: LENT SOMA: Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic scale	n (implants/flaps/breasts) NR Bilateral/unilateral NR Inclusion criteria Patients with LENT-SOMA grade 3 (severe symptoms) or grade 4 (irreversible functional damage) Exclusion criteria Medical history of connective, metabolic, or skin disease Indication (cosmetic) Progressive lesions after radiation therapy and screened according to LENT-SOMA scale **Procedural details** Tissue donor sites included medial area of the knee, the abdominal region, and trochanteric region. Tissue was removed with cannula and 2 cc syringe followed by lipoaspirate purification (centrifugation at 2700 rpm for 15 minutes, oil and liquid layers discarded) to remove large part of triclyceride stored in tissue and caused lesion in the thin cytoplasmic sheets of mature adipocytes for their rapid clearance after injection. Stem cells not isolated and remained in natural 3D scaffold. Patients underwent between one and six injections of purified lipoaspirate. Lipoaspirate extractions analysed using in vitro characterisation of adipose-derived stem cells including – isolation and culturing of stromal vascular fraction, mesenchymal stem cell expansion, clonogenic assays for counting fibroblastic colonies, characterisation of	Lumps NR Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications NR Death NR Implant related complications NR Other NR	Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Fat reabsorption NR Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR **LENT-SOMA grade improvement** Improvement in grade 4 patients	Losses to follow-up NR Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	immunophenotypes and cell differentiation assays. A computerised model for injection was used to implant the adipose tissue. Ultrastructural studies were also performed by electron microscopy with examination after lipoaspirate purification and at 1, 2, 4, to 6 and 12 months after last procedure. Operative details NR Adjunct chemotherapy or radiotherapy Radiotherapy: all patients *with prescribed total dose 45-55 Gy administered in 20-25 irradiations (2-2.25 Gy per session) Duration of radiation injuries 4.5 ± 8 (quartile) years (range, 1-30 years) Volume of injected fat Range, 60-80 cc per fraction Patient demographics Age: mean 50.9 years (range, 37-71 years) Body mass index: NR Smoker: NR		(11 patients initially graded 4) Grade 4 to 0: 4 patients Grade 4 to 1: 5 patients Grade 4 to 2: 1 patient No improvement: 1 patients Improvement in grade 3 patients (9 patients initially graded 3) Grade 3 to 0: 4 patients Grade 3 to 1: 4 patients Other results reported (but not extracted) *Purified lipoaspirate ultrastructural characterisation results *Purified lipoaspirate cytologic characterisation results *Ultrastructural analyses	
Author, year Carvajal and Patino 2008 Location Medellin, Colombia Single centre/multicentre NR Study period February 1999 to June	n (patients) 20 n (implants/flaps/breasts) 40 breasts Bilateral/unilateral 20 bilateral Inclusion criteria Patients who had undergone mammography after	Infection NR Lumps See mammography results Fat necrosis 4/20 patients (20%) *presented with typical oil cysts at mammogram (considered pathognomonic of breast fat	Operative time NR Reoperation NR Readmission NR Mammographic issues All patients were reported as	Duration of follow-up Mean 34.5 months (range, 6 months to 7 years) Losses to follow-up NR Sub-group analysis NR Conflicts of interest

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
2006 Data collection Retrospective review Patient selection NR Level of evidence Level IV – case series Objective To evaluate mammographic findings of fat necrosis in patients who had undergone breast lipoinjection and determine whether any specific features help to distinguish fat necrosis by fat injection from more from worrisome findings	standard microlipoinjection technique Exclusion criteria NR Indication NR **Procedural details** This study used the standard microlipoinjection technique. Fat for transfer was usually obtained from several donor sites (e.g. abdomen, back, thighs, and arms) through the conventional method of lipoplasty. Small skin incisions were then made around the breast, and fat generally injected in small quantities (fat injected into and under the breast parenchyma and pectoral muscle) Operative details 'several different surgeons, all of whom stated that they had used a standard microlipoinjection technique' Volume of injected fat per breast Mean 235 cc (range, 150-300 cc) Patient demographics Age: mean 36.9 years (range, 31-46 years) Body mass index: NR Smoker: NR	necrosis) Inflammation NR Haemorrhage/bleeding complications NR Death NR Implant related complications NR Microcalcifications (wide variety of appearances) 9 (45%) Patients with different types of microcalcifications Round: 5 patients Spherical: 4 patients Punctuate: 2 patients Dystrophic: 2 patients Cluster: 3 patients Coarse: 0 patients Typical oil cysts 4 (20%) Lipid cysts 4 (20%)	symptom free at time of mammography Axillary lymph nodes 16 (80%) *in one of these, an intramammary lymph node was also noted Coarse calcifications 0 (0%) Focal masses 0 (0%) Spiculated areas of increased opacity 0 (0%) No abnormality 0 (0%) Heterogeneity of pectoral muscle density 16 (80%) Post-operative mammogram classification, Breast Imaging Reporting and Data System Grade II (85%) Grade III (15%) *3 Breast Imaging Reporting and Data System III patients re-classified as Breast Imaging Reporting and Data System II upon mammographic follow-up	NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Psychosocial issues NR Patient satisfaction NR Fat reabsorption NR Scarring NR Aesthetic outcome NA Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year Yoshimura et al 2008 Location Department of Plastic Surgery, University of Tokyo School of Medicine	n (patients) 40 n (implants/flaps/breasts) NR Bilateral/unilateral NR	Infection NR Lumps 1 patient (group B) *fibrous breast tissue and fibrosis on sternum observed by computer tomography scan at 6 months.	Operative time 257.1 ± 39.1 (standard deviation) minutes *time of injection process ranged from 35 to 60 minutes for both breasts Reoperation	Duration of follow-up >6 months (19/40 patients) *maximum 42 months follow-up Losses to follow-up NR Sub-group analysis

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Single centre/multicentre NR Study period 2003 to 2007 Data collection NR Patient selection NR Level of evidence Level IV – case series Objective To report on novel technique, cell-assisted lipotransfer, used in conjunction with lipoinjection	Inclusion criteria Patients undergoing cell-assisted lipotransfer for purely cosmetic breast augmentation with healthy thoraxes and breasts Exclusion criteria Patients who underwent breast reconstruction for inborn anomaly or after mastectomy Indication Cosmetic **Procedural details** Adipose tissue suctioned using 2.5 mm inner diameter cannula and conventional liposuction machine. Approximately half of aspirate used for isolation of stromal vascular fraction. Other half of lipoaspirate harvested as graft material. Operative details NR Patients were placed into 1 of 3 groups Group A (6 patients): adipose portion of liposuction aspirates washed and placed in upright position to separate fluids and oil, then put in metal jar, which was placed in water with crushed ice. Stromal vascular fraction isolated from, both the adipose and fluid portions added to graft material. After gentle mixing and 10 to 15 minute wait (for cell adherence to aspirated fat), cell supplemented fat placed in injection syringe. Group B (2 patients): As per group A, except stromal vascular fraction resuspended in 60ml saline then diffusely injected into whole breast mounds separately (30ml/breast) immediately after	Breasts in this patient were found to be harder than in other cases Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (subcutaneous bleeding) Occasionally observed in some parts of the breast (resolved in 1 – 2 weeks) Death NR Implant related complications NR Cyst formation (<12mm) 2 patients	NR Readmission NR Mammographic issues (microcalcification) 2 patients *detected by mammography at 24 months Psychosocial issues NR Patient satisfaction Reported all patients satisfied with texture, softness, contour, and absence of foreign materials despite the limited size increase Fat reabsorption *Transplanted adipose tissue was gradually absorbed during the first 2 post-operative months (especially during 1st month) *Breast volume showed minimal change thereafter *Skin tension also sometimes lessened after 2 months Scarring NR Aesthetic outcome *Difference in breast circumference had increased in all cases by 4–8 cm or 2–3	NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	conventional lipoinjection Group C (32 patients): As per group A, except centrifugation at 700g for 3 minutes used to separate fluids and oil Donor site Thighs; 25 patients Thighs and abdomen: 13 patients Thighs and lower legs: 2 patients Volume of injected fat Left breast: mean 268.1 ± 47.6 (standard deviation) ml Right breast: mean 277.3 ± 39.1(standard deviation) ml Patient demographics Age: mean 35.8 ± 1.9 (standard deviation) years (range, 20-62 years) Race: Japanese Body mass index: 19.7 ± 1.9 (standard deviation) kg/m^2 Smoker: NR		brassiere cup sizes at 6 months *Circumference increase appeared to correspond with a 100-200ml volume increase in breast mound – partially confirmed by preliminary 3-dimensional quantitative measurement system Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year Zheng et al 2008 Location Department of Plastic & Reconstructive Surgery, Shanghai Ninth People's Hospital, Shanghai, China Single centre/multicentre Single centre Study period	n (patients) 66 n (implants/flaps/breasts) 132 breasts Bilateral/unilateral NR Inclusion criteria Patients who underwent autologous fat grafting for correction of contour deformities after removal of silicone implants, micromastia, or ptotic breasts. Fat	Infection NR Lumps Clinically palpable mass: 11 patients (see mammographic findings) *these were detected at mean 3.4 months (range, 2-4 months) postoperatively. Mean lump size was 7.1mm (range, 5-25 mm) Fat necrosis by sonography	Operative time NR Reoperation (fat extirpation of fat necrosis lump) 2 patients *one reoperation at 24 months and the other at 52 months. Diameter of cysts ranged from 5-21 mm Readmission NR	Duration of follow-up Mean 37 months (range, 13-61 months) Losses to follow-up NR Sub-group analysis Yes, for aesthetic outcome and patient satisfaction between the three indications for autologous fat transfer Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
August 2000 to March 2005 Data collection Retrospective Patient selection NR Level of evidence Level IV – case series Objective To evaluate the efficacy and long term complications of autologous fat transfer to the breast and study the features of fat necrosis caused by fat transplantation	grafting was conducted 1–3 times. Exclusion criteria NR Indication Cosmetic and reconstructive *indications including correction of contour deformities after removal of silicon implants (19 patients) (reconstructive) and micromastia (24 patients) or ptotic breasts (23 patients) (cosmetic) **Procedural details** Fat grafts harvested from lower abdomen, trochanter areas, and inner thigh. Aspirates purified after washing with normal saline and centrifuged (600 rpm, 2 minutes). Middle layer then put into several 5 ml syringes. Fat transfer performed with one-holed blunt cannula connected to 5ml syringe. Two small incisions were made in each breast. Through inframammary incision, fat grafts infiltrated into subglandular and subcutaneous tissue of lateral half of breast. Breasts were supported with a surgical bra for 7 days post-operative. All patients had at least one sonogram, 11 patients who presented with palpable mass had mammography, and 9 patients (based on willingness and cost) had a magnetic resonance imaging scan. Operative details NR Volume of injected fat (into subcutaneous tissue) Mean 101ml (range, 60 -120 ml) Volume of injected fat (into subglandular tissue) Mean 73ml (range, 60-90 ml)	11 patients Inflammation NR Haemorrhage/bleeding complications NR Death NR Implant related complications NR Cysts Mean 8.9 cysts per breast (range, 2-36 cysts per breast)	Mammographic issues Clinically palpable masses: 11 patients *diagnosed with liponecrotic cysts with benign calcifications Calcifications: 7 patients *mammogram took place at mean 23 months follow-up (range, 12-52 months) *9/11 patients with palpable masses underwent magnetic resonance imaging at 25.4 months (range, 12-53 months) to confirm diagnosis Psychosocial issues NR Patient satisfaction Very satisfied: 27 patients (40.9%) Satisfied: 26 patients (39.4%) Unsatisfied: 13 patients (19.7%) Fat reabsorption NR Scarring NR Aesthetic outcome (breast contour evaluation at 12 months) Significantly improved: 28 patients (42.4%) Improved: 24 patients (36.4%) Not Improved: 14 patients	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Patient demographics Age: range, 19-39 years Race: Chinese Body mass index: NR Smoker: NR		(21.2%) Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year Zocchi and Zuliani 2008 Location Institute for Aesthetic Plastic Surgery, Torino, Italy Single centre/multicentre NR Study period 1998 to 2007 Data collection NR Patient selection NR Level of evidence Level IV – case series	n (patients) 181 n (implants/flaps/breasts) 326 breasts Bilateral/unilateral 145 patients/36 patients Inclusion criteria NR Exclusion criteria NR Indication Cosmetic and reconstructive *indications including augmentation and volume asymmetry (60% patients – 12% of these had reductive mastoplasty on the contralateral breast) or symmetry volume augmentation bilaterally (36% patients) (cosmetic) and correction of sequelae from	Infection NR Lumps NR Fat necrosis 2 patients (1.2%) Inflammation (oedema) 181 patients (100%) Haemorrhage/bleeding complications NR Death NR Implant related complications Bruising 143 patients (78%)	Operative time NR Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction (aesthetic result) Insufficient: 5 patients (3%) Fair: 10 patients (6%) Good: 128 patients (72%) Excellent: 38 patients (23%)	Duration of follow-up Sonography: 6 months and 1 year Mammography: 1 year MRI: on demand *follow up was scheduled according to imaging method Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Objective To study a new method of fat transfer developed by the authors	previous breast surgery (11% patients) as well as augmentation (6%), reduction (2%) or mastopexy (3%) (reconstructive) Adjunct procedures Major or mild body contouring in all patients **Procedural details** The procedure consists of eight major steps: 1. external breast skin expansion (to stimulate vasculogenesis and lymphatic activity 2. surgical planning of the breast and donor areas 3. body contouring setup 4. fat harvesting 5. fat preparation (involving: gentle washing in saline, stratification by vibration, stratification by decantation and conservation in cold saline before transplantation) 6. breast setup 7. fat transplantation into retroglandular and prefascial space and into superficial subcutaneous plane of upper pole of breast 8. manual reshaping Operative details NR Volume of injected fat Mean 375ml (range, 160-745 ml) Patient demographics Age: mean 33 years Body mass index: NR Smoker: NR	Dysesthesia 14 patients (5.8%) Microcyst 3 patients (1.8%) *spontaneously resolved over 6 month period Microcalcifications 7 patients (3.9%) *one bilateral in upper pole and others unilateral in prefascial retroglandular plane Other NR	Surgeon satisfaction (aesthetic result) Insufficient: 10 patients (6%) Fair: 25 patients (12%) Good: 123 patients (69%) Excellent: 23 patients (13%) Fat reabsorption NR Scarring NR Aesthetic outcome See patient and surgeon satisfaction above Durability of enhancement (volume persistence at 1 year) Mean 55% (maximum 70%) Length of hospitalisation NR Healing time/time to normal activity or work NR Other NR	
Author, year	n (patients)	Infection	Operative time	Duration of follow-up

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Illouz and Sterodimas 2009 Location Department of Plastic Surgery, Saint Louis Hospital, Paris, France Single centre/multicentre NR Study period 1983 to 2007 Data collection NR Patient selection Consecutive Level of evidence Level IV – case series, with selected detailed case reports Objective To present the authors technique for autologous fat transfer and report his 25 years of experience using the procedure	Total: 820 Group 1: 381 Group 2: 54 Group 3: 385 n (implants/flaps/breasts) NR Bilateral/unilateral Both, number not clearly reported Inclusion criteria Candidate for breast augmentation or breast reconstruction following tumour resection, preoperative mammography and ultrasonography, American College of Radiology Breast Imaging Reporting and Data System Category of 1 or 2, disease free for ≥ 1 year (group 1) and signed consent Exclusion criteria NR Indication Cosmetic and reconstructive Patients were grouped by their indication for autologous fat transfer so that group 1 included patients with asymmetry as a result of mastectomy and reconstruction, group 2 contained patients with congenital asymmetry and group 3 contained patients requesting bilateral breast augmentation *Group 1: previous failed unilateral silicone implant (n=253 patients), adjunct reconstruction with unilateral myocutaneous flaps (n=98 patients) and unilateral lumpectomy (n=30 patients)	5 patients (0.6%) *antibiotics given Lumps NR Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (haematoma) 12 patients (1.5%) *resolved without intervention Death NR Implant related complications NR Ecchymosis 76 patients (9%) Striae 36 patients (4.5%)	NR Reoperation NR Readmission NR Mammographic issues (American College of Radiology Breast Imaging Reporting and Data System category at 6 months) Category 0: 10% patients Category 1: 41% patients Category 2: 23.5% patients Category 3: 25.5% patients Category 4: 0% patients Category 5: 0% patients Mammographic issues (American College of Radiology Breast Imaging Reporting and Data System category at 12 months) Category 0: 4.5% patients Category 1: 47% patients Category 2: 31% patients Category 3: 17.5% patients Category 4: 0% patients Category 5: 0% patients Psychosocial issues NR Patient satisfaction NR	Maximum 12 months *230 patients had long-term follow-up: mean 11.3 years (range, 2-25 years). These patients had annual mammograms and ultrasounds. These results were not provided, author states these patients confirm that any breast lesions (including calcifications, cysts, recurrent or primary cancer) not apparent < 12 months following fat injection are not associated with it Losses to follow-up 150 patients (no reason given) *670 had mammogram at 6 and 12 months follow-up Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	*Group 2: congenital deformation (n=43 patients), Poland's Syndrome (n=11 patients) *Group 3: adjunct implants for increased volume (n=36) **Procedural details** 1. Marking of breast and donor site with patient in standing position 2. Preoperative sedation at surgical sites 3. Injection of wetting solution at donor site and insertion of syringe (attached to blunt cannula) into area to be lipoaspirated 4. Fat aspirated from donor site using syringe method 5. Syringe containing aspirated fat held vertically with open end down to allow fat to decant. After 10-15 minutes fat is yellow (blood separated) and 10ml syringes are prepared for injection into breast tissue 6. Fat is woven into subcutaneous and intraglandular spaces of breast using a 2.5mm cannula attached to the 10ml syringe (containing fat) with multiple passes, injecting only a small amount of fat with each pass as the cannula is withdrawn to obtain the most reliable clinical outcome 7. Light dressing applied <u>Operative details</u> NR <u>Volume of injected fat</u> (per session) Mean 145ml (range, 25-180ml) <u>Volume of injected fat</u> (total per breast) Mean 540ml (range, 25-900ml) <u>Number of sessions to obtain desired result</u> Mean 3 sessions (range, 1-5 sessions)		<u>Fat reabsorption</u> 'fat graft reabsorption was observed in our series' (not quantified) <u>Scarring</u> NR <u>Aesthetic outcome</u> (long-term asymmetry) 34 patients *13/34 only had 1 session of autologous fat transfer *'majority of the women had a significant improvement in their breast size and/or shape postoperatively' (not quantified) <u>Durability of enhancement</u> NR <u>Length of hospitalisation</u> NR <u>Healing time/time to normal activity or work</u> NR <u>Other</u> NR	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Patient demographics Age: mean 45.6 years (range, 19-78 years) Body mass index: NR Smoker: NR			

NR: not reported; AFT: autologous fat transfer; MRI: magnetic resonance imaging; TRAM: transverse rectus abdominis myocutaneous; NA: not applicable; LENT-SOMA: Late Effects Normal Tissue Task Force Subjective, Objective, Management, Analytic scale.

Cosmetic mammaplasty

Table E2: Extraction table for included saline implant studies

Study profile		**Safety outcomes**	**Effectiveness outcomes**	**Methodological quality**
Author, year Tarpila et al 1997 Location Linkoping University Hospital, Linkoping, Sweden Single centre/multicentre Single centre Study period January 1994 to September 1994 Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To see if the risk of capsular fibrosis was less with textured-surfaced than with conventional smooth-surfaced saline-filled breast implants Study arm Smooth saline	n (patients) 21 n (implants/flaps/breasts) 21 Inclusion criteria Healthy women Exclusion criteria NR **Procedural details** Implant name Biocell®, style 68 (Allergen Inc., US) Fill Saline Surface type Smooth Incision type Inframammary Implant position Subglandular Implant volume 125, 150 or 180ml *overfilled 10ml Indication Cosmetic	Capsular contracture (at 6 months) 6 patients (32%) Baker classification (at 6 months) Baker 1: 4 patients Baker 2: 9 patients Baker 3: 6 patients Capsular contracture (at 12 months) 8 patients (38%) *2/3 external decompressions performed were successful in treating capsular contracture Baker classification (at 12 months) Baker 1: 3 patients Baker 2: 10 patients Baker 3: 8 patients Implant rupture NR Infection 0 Fat necrosis NR Implant leakage NR Inflammation NR	Operative time NR Reoperation 0 patients Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction See patients' questionnaire results below Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR	Method of randomisation Insertion sites were coded and varied equally between both implants. The code was broken preoperatively by the surgeons and stored enclosed in an envelope with the patient's records Power calculation None Blinding/method of allocation concealment Patients were blinded to implant allocation Duration of follow-up Maximum 2 years Losses to follow-up 2 patients Use of intention to treat NR Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Primary/secondary augmentation NR Operative details Single surgeon Patient demographics Age: mean 33 years (range, 22-48 years) Body mass index: NR Smoker: NR	Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (haematoma) 0 Death NR Implant rotation NR Other NR	Failure NR Mean tonometric areas of imprint from the breast (taken visually from graph) At 6 months: ~26 cm^2 At 12 months: ~27 cm^2 Patients' opinion questionnaire (at 12 months) Smooth breast felt harder: 4 patients Can feel smooth prosthesis: 12 patients (equal with contralateral breast) Preferred smooth breast: 6 patients Wanted to operatively change smooth breast: 3 patients Pain in smooth breast: 0 patients	
Author, year Tarpila et al 1997 Location Linkoping University Hospital, Linkoping, Sweden Single centre/multicentre Single centre Study period January 1994 to September 1994 Data collection NR	n (patients) 21 n (implants/flaps/breasts) 21 Inclusion criteria Healthy women Exclusion criteria NR **Procedural details** Implant name Biocell®, style 168 (Allergen Inc., US)	Capsular contracture (at 6 months) 5 patients (26%) Baker classification (at 6 months) Baker 1: 3 patients Baker 2: 11patients Baker 3: 5 patients Capsular contracture (at 12 months) 6 patients (29%) Baker classification (at 12 months) Baker 1: 0 patients Baker 2: 15 patients Baker 3: 6 patients	Operative time NR Reoperation 0 patients Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction	Method of randomisation Insertion sites were coded and varied equally between both implants. The code was broken preoperatively by the surgeons and stored enclosed in an envelope with the patient's record Power calculation None Blinding/method of allocation concealment Patients were blinded to implant allocation Duration of follow-up

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Patient selection NR Level of evidence II – randomised controlled trial Objective To see if the risk of capsular fibrosis was less with textured-surfaced than with conventional smooth-surfaced saline-filled breast implants Study arm Textured saline	Fill Saline Surface type Textured Incision type Inframammary Implant position Subglandular Implant volume 125, 150 or 180ml *overfilled by 10ml Indication Cosmetic Primary/secondary augmentation NR Operative details Single surgeon Patient demographics Age: mean 33 years (range, 22-48 years) Body mass index: NR Smoker: NR	Implant rupture NR Infection 0 Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (haematoma) 0 Death NR Implant rotation NR Other NR	See patients' questionnaire results below Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Mean tonometric areas of imprint from the breast (taken visually from graph) At 6 months: ~26 cm^2 At 12 months: ~25 cm^2 Patients' opinion questionnaire (at 12 months) Textured breast felt harder: 7 patients Can feel textured prosthesis: 12 patients (equal with contralateral breast) Preferred textured breast: 6 patients Wanted to operatively change	Maximum 2 years Losses to follow-up 2 patients Use of intention to treat NR Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			textured breast: 1 patients Pain in textured breast: 2 patients	
Author, year Fagrell et al 2001 Location Linkoping, Sweden Single centre/multicentre Single centre Study period NR Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To compare capsular contracture around saline-filled smooth and textured prosthesis. To evaluate the long-term progress of breast hardness and patient satisfaction Study arm Smooth saline	n (patients) 20 n (implants/flaps/breasts) 20 Inclusion criteria NR Exclusion criteria NR **Procedural details** Implant name Siltex®, style 1800 (Mentor® Corp., US) Fill Saline Surface type Smooth Incision type Submammary Implant position Subglandular Implant volume 125 and 175 cc *overfilled with 5-15ml of volume recommended by manufacturer Indication	Capsular contracture (at 1 year) 4 patients Capsular contracture (at 7.5 years) 6 patients Hardness (Baker grade III or IV) At 0.5 years: 1 patient At 1 year: 4 patients At 7.5 years: 6 patients Implant perforation 1 patients *reoperation for exchange at 5 years follow-up Infection 0 Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling NR Implant deflation NR	Operative time NR Reoperation 2 patients *one for postoperative bleeding, unknown if origin of bleeding was textured or smooth breast and the other for implant exchange at 5 years due to perforation of smooth prosthesis (this patient had Baker class II on both breasts) Readmission 1 patient *for implant exchange at 5 years due to perforation of smooth prosthesis (same patient reported above) Mammographic issues NR Psychosocial issues NR Patient satisfaction See patients' opinion questionnaire findings below Scarring NR Aesthetic outcomes NR	Method of randomisation Implantation 'site was randomised and varied equally', method NR Power calculation None Blinding/method of allocation concealment Patients unaware of breast allocation until 1 year follow-up Duration of follow-up Mean 7.5 years (range, 5 years and 11 months to 8 years and 4 months) Losses to follow-up 2 patients lost by 6 and 12 months follow-up (remaining 18 patients continued with follow-up) *all 20 patients filled in questionnaire Use of intention to treat No Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Cosmetic Primary/secondary augmentation All primary Operative details Two surgeons Patient demographics Age: mean 30 years (range, 16-43 years) Body mass index: NR Smoker: NR	Haemorrhage/bleeding complications (postoperative bleeding) 1 patient *unknown if due to textured or smooth breast implant Death NR Implant rotation NR	Durability of enhancement NR Length of hospitalisation NR Mean tonometric area of imprint from the breast (taken visually from graph) At 0.5 years: ~25 mm^2 At 1 year: ~28 mm^2 At 7.5 years: ~24 mm^2 Healing time/time to normal activity or work NR Failure NR Patients' opinion questionnaire (at 7.5 years) Smooth breast felt harder: 8/20 patients (40%) Preferred smooth breast: 8/20 patients (40%) Wanted to operatively change smooth breast: 3/20 patients (15%) Pain in smooth breast: 0/20 patients (0%)	
Author, year Fagrell et al 2001 Location Linkoping, Sweden	n (patients) 20 n (implants/flaps/breasts) 20 breasts	Capsular contracture (at 1 year) 1patient Capsular contracture (at 7.5 years) 4 patients	Operative time NR Reoperation 1 patient *for postoperative bleeding, unknown	Method of randomisation Implantation 'site was randomised and varied equally', method NR Power calculation None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Single centre/multicentre Single centre Study period NR Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To compare capsular contracture around saline-filled smooth and textured prosthesis. To evaluate the long-term progress of breast hardness and patient satisfaction Study arm Textured saline	Inclusion criteria NR Exclusion criteria NR **Procedural details** Implant name Siltex®, style 2800 (Mentor® Corp., US) Fill Saline Surface type Textured Incision type Submammary fold Implant position Subglandular Implant volume 125 and 175 cc *overfilled 5-15ml of volume recommended by manufacturer Indication Cosmetic Primary/secondary augmentation All primary Operative details Two surgeons Patient demographics	Hardness (Baker grade III or IV) At 0.5 years: 0 patients At 1 year: 1 patient At 7.5 years: 4 patients Implant rupture NR Infection 0 patients Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (postoperative bleeding) 1 patient *unknown if due to textured or smooth implant Death NR Implant rotation NR	if origin of bleeding was textured or smooth breast Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction See patients' opinion questionnaire findings below Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Mean tonometric area of imprint from the breast (taken visually from graph)	Blinding/method of allocation concealment Patients unaware of breast allocation until 1 year follow-up Duration of follow-up Mean 7.5 years (range, 5 years and 11 months to 8 years and 4 months) Losses to follow-up 2 patients lost by 6 and 12 month follow-up (remaining 18 patients continued with final follow-up) *all 20 patients filled in questionnaire Use of intention to treat No Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Age: mean 30 years (range, 16-43 years) Body mass index: NR Smoker: NR		At 0.5 years: ~26mm^2 At 1 year: ~27mm^2 At 7.5 years: ~24mm^2 Patients' opinion questionnaire (at 7.5 years) Textured breast felt harder: 6/20 patients (30%) Preferred textured breast: 5/20 patients (25%) Wanted to operatively change textured breast: 2/20 patients (10%) Pain in textured breast: 3/20 patients (15%)	

NR: not reported.

Table E3: Extraction table for included cohesive silicone implants studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Coleman et al 1991 Location Department of Plastic Surgery, St Luke's Hospital, Bradford, West Yorkshire Single centre/multicentre Single centre Study period Augmentation procedures took place over a 3 month period Data collection NR Patient selection Consecutive Level of evidence II – randomised controlled trial Objective To answer the question, 'does a textured surface implant decrease the incidence of adverse capsular contracture in breast augmentation?' Study arm Smooth silicone implant	n (patients) 26 n (implants/flaps/breasts) 52 Inclusion criteria Informed and signed consent Exclusion criteria NR **Procedural details** Implant name NR (Mentor® Corp., US) Fill Silicone Surface type Smooth Incision type Inframammary Implant position Submammary Implant volume Chosen per patient, volume not reported Indication Cosmetic Primary/secondary augmentation All primary	Capsular contracture, Baker classification (12 months) Grade 1: 11 breasts Grade 2: 9 breasts Grade 3: 16 breasts Grade 4: 12 breasts *62.5% incidence of capsular contracture in breast Implant rupture NR Infection 0 patients Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (haematoma – MAJOR complication) 1 breast *immediately postoperative, requiring reoperation	Operative time NR Reoperation 1 patient *immediately postoperative to treat haematoma with evacuation and implant replacement Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR	Method of randomisation Patients were randomised to receive either two textured or smooth silicone breast implants. This allocation was placed in an envelope, which was opened during surgery after the incision was made and the submammary pocket prepared for insertion Power calculation Yes *it was calculated that about 100 breasts, or 50 patients, would be needed in order to be able to produce a study with a power of 0.8 and a significance level 0.05 and thus withstand statistical scrutiny Blinding/Method of allocation concealment The type of implant allocated was not recorded on the patient records; it remained in the envelope (labelled with the patient's details) under lock and key by the surgeon's secretary. Assessing surgeons (three, who did not discuss the results with one another) and patients were unaware of the implant allocation during follow-up. Patients were made aware of their allocation at the end of follow-up, assessors were not *patients were made aware of allocation at 12 months

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Operative details NR Patient demographics Age: average 30 ± (standard deviation) 5 years (range, 21-44 years) *results not separated between implant types Body mass index: NR Smoker: NR	Death NR Implant rotation NR Other NR	Failure NR Other NR	Duration of follow-up 12 months Losses to follow-up n=2 Compliance at follow-up 24 patients, 48 breasts Use of intention to treat Yes *where outcome of lost patient known Sub-group analysis None Conflict of interest None
Author, year Coleman et al 1991; Malata et al 1997 *short- and mid-term follow-up for same patient population reported per paper, respectively Location Department of Plastic Surgery, St Luke's Hospital, Bradford, West Yorkshire Single centre/multicentre Single centre Study period Augmentation procedures	n (patients) 27 n (implants/flaps/breasts) 54 Inclusion criteria Informed and signed consent Exclusion criteria NR **Procedural details** Implant name Siltex® (Mentor® Corp., US) Fill Silicone	Capsular contracture, Baker classification (12 months) Grade 1: 29 breasts Grade 2: 19 breasts Grade 3: 4 breasts Grade 4: 0 breasts *7.7% incidence of capsular contracture in breasts Capsular contracture, Baker classification (3 years) Grade 1 and 2: 24 patients Grade 3 and 4: 3 patients Implant rupture NR Infection (12 months)	Operative time NR Reoperation (3 years) 2 patients *bilateral anterior disc capsulectomy and implant exchange due to severe capsular contracture Readmission NR Mammographic issues NR Psychosocial issues NR	Method of randomisation Patients were randomised to receive either two textured or smooth silicone breast implants. This allocation was placed in an envelope, which was opened during surgery after the incision was made and the submammary pocket prepared for insertion Power calculation Yes *it was calculated that about 100 breasts, or 50 patients, would be needed in order to be able to produce a study with a power of 0.8 and a significance level 0.05 and thus withstand statistical scrutiny

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
took place over a 3 month period Data collection NR Patient selection Consecutive Level of evidence II – randomised controlled trial Objective To answer the question, 'does a textured surface implant decrease the incidence of adverse capsular contracture in breast augmentation?' Study arm Textured silicone implant	Surface type Textured Incision type Inframammary Implant position Submammary Implant volume Chosen per patient, volumes not reported Indication Cosmetic Primary/secondary augmentation All primary Operative details NR – possibly single surgeons 'the the patients were independently assessed in a specially organised review clinic by three investigators, one of whom was the surgeon who carried out the surgery' Patient demographics Age: average 30 ± (standard deviation) 5 years (range, 21-44 years) *results not separated between implant types Body mass index: NR Smoker: NR	0 patients Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications NR Death NR Implant rotation NR Other NR	Patient satisfaction NR Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Other NR	Blinding/method of allocation concealment Implant allocated was not recorded on the patient records; it remained in the envelope (labelled with the patient's details) under lock and key by the surgeon's secretary. Assessing surgeons (three, who did not discuss the results with one another) and patients were unaware of the implant allocation during follow-up *patients made aware of allocation after 12 months Duration of follow-up 12 months (short-term), 3 years (mid-term) Losses to follow-up 12 months: 1 patient 3 years: 0 patients Compliance at follow-up 12 months: 26 patients, 52 breasts 3 years 27 patients, 54 breasts Use of intention to treat Yes *where outcome of lost patient known Sub-group analysis None Conflict of interest None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997* *this study reports the extended follow-up (5 years) of Hakelius and Ohlsen 1992 (12 month follow-up) Location Department of Plastic and Hand Surgery, University Hospital, Uppsala, Sweden Single centre/multicentre Single centre Study period March to June 1989 Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To find out if there is a difference in capsular contracture rate between silicone implants with smooth and textured surface as the only difference Study arm	n (patients) 25 n (implants/flaps/breasts) 25 Inclusion criteria Bilateral mammary hypoplasia Exclusion criteria NR **Procedural details** Implant name McGhan style 40 Intrashiel (Allergen Corp., US) Fill Silicone gel Surface type Smooth Incision type Inframammary fold Implant position Subglandular Implant volume 160, 180, 200 or 220 cc Indication Cosmetic (hypoplasia) Primary/secondary augmentation All primary	Capsular contracture (12 months) 1 patient Implant rupture NR Infection (12 months) 0 patients Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling (palpable ripples, 5 years) 6 patients *these patients were 6 out of the 17 patients who replaced their smooth implants with new textured implants Implant deflation NR Haemorrhage/bleeding complications (haematoma, 12 months) 1 patient Death NR Implant rotation NR	Operative time Average 40 minutes (range, 30-50 minutes) Reoperation (12 months) 12 patients *requested reoperation at the end of 12 months follow-up because of a hard smooth breast implant Reoperation (5 years) 17 patients (68%) *exchanged smooth implants for textured Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction See patient's opinion of softer breast below Scarring NR Aesthetic outcomes NR Durability of enhancement NR	Method of randomisation The side in which the prosthesis would be implanted was chosen by lottery before the operation Blinding/method of allocation concealment Patients were blinded to the allocation of the smooth prosthesis until the end of follow-up. Investigators were also unaware of the allocation until the end of follow-up, as it was not documented in the patients record Power calculation NR Duration of follow-up 12 months; 5 years Losses to follow-up 12 months: Yes 5 years: none Compliance at follow-up 2 weeks: 25 patients (100%) 6 weeks: 23 patients (92%) 12 weeks: 24 patients (96%) 24 weeks: 25 patients (100%) 36 weeks: 23 patients (92%) 52 weeks: 25 patients (100%) 5 years: 25 patients (100%) Use of intention to treat None Sub-group analysis

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Smooth silicone implants	Operative details Two surgeons (authors) Patient demographics Age: average 31 years (range, 20-45 years) Body mass index: NR Smoker: NR	Hardness (5 years) 17 patients (68%) *subsequent exchange to textured implant	Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Breast consistency, patient's opinion 2 weeks Smooth softer: 2 patients (8%) Smooth harder: 3 patients (12%) Equally soft: 20 patients (80%) 6 weeks Smooth softer: 5 patients (22%) Smooth harder: 2 patients (9%) Equally soft: 16 patients (70%) 12 weeks Smooth softer: 1 patient (4%) Smooth harder: 16 patients (67%) Equally soft: 7 patients (29%) *values are visual estimates from graph 24 weeks Smooth softer: 2 patients (8%) Smooth harder: 13 patients (52%) Equally soft: 10 patients (40%) *values are visual estimates from graph 36 weeks Smooth softer: 3 patients (13%)	None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Smooth harder: 15 patients (65%) Equally soft: 5 patients (22%) *values are visual estimates from graph <u>12 months</u> Smooth softer: 2 patients (8%) Smooth harder: 16 patients (64%) Equally soft: 7 patients (28%) Breast Augmentation Classification <u>2 weeks</u> Grade 1: 20 patients (80%) Grade 2: 5 patients (20%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>6 weeks</u> Grade 1: 19 patients (83%) Grade 2: 4 patients (17%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>12 weeks</u> Grade 1: 17 patients (71%) Grade 2: 6 patients (25%) Grade 3: 1 patients (4%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>24 weeks</u> Grade 1: 13 patients (52%)	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Grade 2: 9 patients (36%) Grade 3: 3 patients (12%) Grade 4: 0 patients (0%) *values are visual estimates from graph 36 weeks Grade 1: 9 patients (39%) Grade 2: 5 patients (22%) Grade 3: 9 patients (39%) Grade 4: 0 patients (0%) *values are visual estimates from graph 12 months Grade 1: 10 patients (40%) Grade 2: 4 patients (16%) Grade 3: 11 patients (44%) Grade 4: 0 patients (0%) 5 years Grade 1: 4/8 implants (50%) Grade 2: 3/8 implants (37.5%) Grade 3: 1/8 implants (12.5%) Tonometry area (12 months) Mean 34.46 cm^2 (range, 21.7-56.4 cm^2)	
Author, year Hakelius and Ohlsen 1992; Hakelius and Ohlsen 1997* *this study reports the extended follow-up (5 years) of Hakelius and Ohlsen 1992 (12 month follow-up)	n (patients) 25 n (implants/flaps/breasts) 25 Inclusion criteria Bilateral mammary hypoplasia	Capsular contracture (12 months) 0 patients Implant rupture NR Infection (12 months) 0 patients	Operative time Average 40 minutes (range, 30-50 minutes) Reoperation (12 months) 1 patient *requested reoperation at the end of follow-up due to a hard textured	Method of randomisation The side in which the prosthesis would be implanted was chosen by lottery before the operation Blinding/method of allocation concealment Patients were blinded to the allocation

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Location Department of Plastic and Hand Surgery, University Hospital, Uppsala, Sweden Single centre/multicentre Single centre Study period March to June 1989 Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To find out if there is a difference in capsular contracture rate between silicone implants with smooth and textured surface as the only difference Study arm Textured silicone implants	Exclusion criteria NR **Procedural details** Implant name McGhan style 40 Biocell® (Allergen Corp., US) Fill Silicone gel Surface type Textured Incision type Inframammary fold Implant position Subglandular Implant volume 160, 180, 200 or 220 cc Indication Cosmetic (hypoplasia) Primary/secondary augmentation All primary Operative details Two surgeons (authors) Patient demographics Age: average 31 years (range, 20-45 years) Body mass index: NR Smoker: NR	Fat necrosis NR Implant leakage NR Inflammation NR Skin wrinkling (palpable ripples, 5 years) 1 patient (4%) Implant deflation NR Haemorrhage/bleeding complications (haematoma, 12 months) 2 patients Death NR Implant rotation NR Hardness (5 years) 1 patient (4%) *subsequent exchange to smooth implant	breast implant Reoperation (5 years) 1 patient (4%) *exchanged textured implant to smooth Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction See patient's opinion of softer breast below Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure	of the smooth prosthesis until the end of follow-up. Investigators were also unaware of the allocation until the end of follow-up, as it was not documented in the patients record Power calculation NR Duration of follow-up 12 months; 5 years Losses to follow-up 12 months: yes 5 years: none Compliance at follow-up 2 weeks: 25 patients (100%) 6 weeks: 23 patients (92%) 12 weeks: 24 patients (96%) 24 weeks: 25 patients (100%) 36 weeks: 23 patients (92%) 52 weeks: 25 patients (100%) 5 years: 25 patients (100%) Use of intention to treat None Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			NR Breast consistency, patient's opinion <u>2 weeks</u> Textured softer: 3 patients (12%) Textured harder: 2 patients (8%) Equally soft: 20 patients (80%) <u>6 weeks</u> Textured softer: 2 patients (9%) Textured harder: 5 patients (22%) Equally soft: 16 patients (70%) <u>12 weeks</u> Textured softer: 16 patient (67%) Textured harder: 1 patients (4%) Equally soft: 7 patients (29%) *values are visual estimates from graph <u>24 weeks</u> Textured softer: 13 patients (52%) Textured harder: 2 patients (8%) Equally soft: 10 patients (40%) *values are visual estimates from graph <u>36 weeks</u> Textured softer: 15 patients (65%) Textured harder: 3 patients (13%) Equally soft: 5 patients (22%) *values are visual estimates from graph <u>12 months</u> Textured softer: 16 patients (34%) Textured harder: 2 patients (8%)	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Equally soft: 7 patients (28%) Breast Augmentation Classification <u>2 weeks</u> Grade 1: 21 patients (84%) Grade 2: 4 patients (16%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>6 weeks</u> Grade 1: 17 patients (74%) Grade 2: 6 patients (26%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>12 weeks</u> Grade 1: 24 patients (100%) Grade 2: 0 patients (0%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>24 weeks</u> Grade 1: 23 patients (92%) Grade 2: 2 patients (8%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph <u>36 weeks</u> Grade 1: 21 patients (91%)	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Grade 2: 2 patients (9%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) *values are visual estimates from graph 12 months Grade 1: 23 patients (88%) Grade 2: 2 patients (8%) Grade 3: 0 patients (0%) Grade 4: 0 patients (0%) 5 years Grade 1: 21/24 implants (88%) Grade 2: 3/24 implants (13%) Tonometry area Mean 41.43 cm^2 (range, 33.1-54.9 cm^2)	
Author, year Niechajev et al 2007 Location Lidingo Clinic, Stockholm, Sweden Single centre/multicentre Single centre Study period May 1997 to May 1999 Data collection NR Patient selection	n (patients) 40 *32 examined by surgeon, 37 answered questionnaire n (implants/flaps/breasts) 80 implants *64 examined by surgeon, 74 answered questionnaire Inclusion criteria Healthy women, with no history of any systemic disease according to the American Society of Anaesthesiology Status (ASA class I) Exclusion criteria	Capsular contracture 14/64 breasts (22%) Implant rupture NR Infection 1 patient *with 340ml implant, in the subglandular position Fat necrosis NR Implant leakage NR	Operative time NR Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction Not reported individually	Method of randomisation 'assigned randomly', method not reported Power calculation None Blinding/method of allocation concealment Only operating surgeon knew implant type (assessing surgeon was different to operating surgeon) Duration of follow-up Median 5 years (range, 4-6 years) *results not separated between implant types

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Consecutive Level of evidence II – randomised controlled trial Objective To compare mid- and long-term results with the use of cohesive gel-filled silicone implants from two manufacturers, in a prospective, randomised, controlled and blinded study Study arm McGhan Style 410 gel-filled implants	NR **Procedural details** Implant name McGhan Style 410 (Allergen Corp., US) Fill Cohesive silicone gel Surface type Textured Incision type Inframammary fold: 69 patients (86%) Periareolar: 10 patients (12.5%) Transaxillary: 1patient (1.5%) *results not separated between implant types Implant position Submuscular placement in slimmer, petite patients with very small breasts or in secondary augmentations or athletes (22 patients, 28%) Subglandular placement for correction/ camouflage of mild breast ptosis (58 patients, 22%) *results not separated between implant types Implant volume Median 300ml, average 310 ml (range, 240-500 ml) *results not separated between implant types Indication Cosmetic and reconstructive *for indications including postpartual atrophy and micromastia (cosmetic) and pectus	Inflammation NR Seroma (aseptic) 1patient *with 270ml implant, in the subglandular position Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (postoperative bleeding) 0 patients Death NR Implant rotation 3 patients *1 with 300ml implant, in the subglandular position, the second with 400ml implant, placed in the submuscular position and the third with 270ml implant, placed in the subglandular position	Scarring NR Aesthetic outcomes (asymmetry) Not reported individually Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Breast consistency, patients' opinion (4-6 years) Left breast Soft: 28/37 patients (76%) Firmer than desired: 7/37 patients (19%) Too soft: 2/37 patients (5%) Right breast Soft: 29/37 patients (78%) Firmer than desired: 7/37 patients (19%) Too soft: 1/37 patients (3%) Both breasts Soft: 77% patients Firmer than desired: 19% patients	Losses to follow-up 8 lost to follow-up by surgeon 3 lost to follow-up by questionnaire Use of intention to treat None Sub-group analysis Yes Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	exacatum, tubular breast deformity, deficiency of the lower medial quadrant and breast base constriction (reconstructive) <u>Primary/secondary augmentation</u> NR <u>Operative details</u> Single surgeon <u>Patient demographics</u> Age: median 28 years (range, 17-51 years) *results not separated between implant types Body mass index: NR Smoker: NR		Too soft: 4% patients Breast consistency, Breast Augmentation Classification (4-6 years) <u>Left breast</u> Grade 1: 7/32 patients (22%) Grade 2: 19/32 patients (59%) Grade 3: 7/32 patients (22%) Grade 4: 0/32 patients (0%) <u>Right breast</u> Grade 1: 6/32 patients (19%) Grade 2: 18/32 patients (56%) Grade 3: 7/32 patients (22%) Grade 4: 0/32 patients (0%) <u>Both breasts</u> Grade 1: 20% patients Grade 2: 58% patients Grade 3: 22% patients Grade 4: 0% patients Breast skin sensitivity (4-6 years) <u>Left breast</u> Normal: 28/37 patients (76%) Increase: 1/37 patients (3%) Slight loss: 8/37 patients (22%) Severe loss: 0/37 patients (0%) No sensitivity: 0/37 patients (0%) <u>Right breast</u> Normal: 27/37 patients (73%) Increase: 1/37 patients (3%) Slight loss: 9/37 patients (24%) Severe loss: 0/37 patients (0%) No sensitivity: 0/37 patients (0%)	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Both breasts Normal: 74% patients Increase: 3% patients Slight loss: 23% patients Severe loss: 0% patients No sensitivity: 0% patients Nipple sensitivity (4-6 years) Left breast Normal: 32/37 patients (86%) Increase: 2/37 patients (5%) Slight loss: 2/37 patients (5%) Severe loss: 0/37 patients (0%) No sensitivity: 1/37 patients (3%) Right breast Normal: 31/37 patients (84%) Increase: 3/37 patients (8%) Slight loss: 3/37 patients (8%) Severe loss: 0/37 patients (0%) No sensitivity: 0/37 patients (0%) Both breasts Normal: 85% patients Increase: 7% patients Slight loss: 7% patients Severe loss: 0% patients No sensitivity: 1% patients	
Author, year Niechajev et al 2007 Location Lidingo Clinic, Stockholm, Sweden	n (patients) 40 *32 examined by surgeon, 37 answered questionnaire n (implants/flaps/breasts) 80 implants	Capsular contracture 15/64 breasts (23%) Implant rupture NR Infection	Operative time NR Reoperation NR Readmission	Method of randomisation 'assigned randomly,' method not reported Power calculation None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Single centre/multicentre Single centre Study period May 1997 to May 1999 Data collection NR Patient selection Consecutive Level of evidence II – randomised controlled trial Objective To compare mid- and long-term results with the use of cohesive gel-filled silicone implants from two manufacturers, in a prospective, randomised, controlled and blinded study Study arm Eurosilicone Vertex gel-filled implants	*64 examined by surgeon, 74 answered questionnaire Inclusion criteria Healthy women, with no known history of any systemic disease according to American Society of Anaesthesiology Status (ASA class I) Exclusion criteria NR **Procedural details** Implant name Vertex (Eurosilicone, France) Fill Cohesive silicone gel Surface type Textured Incision type Inframammary fold: 69 patients (28%) Periareolar: 10 patients (12.5%) Transaxillary: 1patient (1.5%) *results not separated between implant types Implant position Submuscular placement in slimmer, petite patients with very small breasts, or in secondary augmentations or in athletes (22 patients, 28%) Subglandular placement for correction/camouflage of mild breast ptosis (58 patients, 22%) *results not separated between implant types	0 patients Fat necrosis NR Implant leakage NR Inflammation NR Seroma (aseptic) 1 patient *with 500ml implant, placed in subglandular position Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications (postoperative bleeding) 1 patient *with 300ml implant, placed in submuscular position Death NR Implant rotation 1 patient *with 275ml implant, placed in subglandular position	NR Mammographic issues NR Psychosocial issues NR Patient satisfaction Not reported individually Scarring NR Aesthetic outcomes (asymmetry) Not reported individually Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure NR Breast consistency, patients' opinion(4-6 years) Left breast Soft: 26/37 patients (70%) Firmer than desired: 9/37 patients (24%) Too soft: 2/37 patients (5%)	Blinding/method of allocation concealment Only operating surgeon knew implant type (assessing surgeon was different to operating surgeon) Duration of follow-up Median 5 years (range, 4-6 years) *results not separated between implant types Losses to follow-up 8 lost to follow-up by surgeon 3 lost to follow-up by questionnaire Use of intention to treat None Sub-group analysis Yes Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Implant volume Median 300ml, average 310 ml (range, 240-500 ml) *results not separated between implant types Indication Cosmetic and reconstructive *for indications including postpartual atrophy and micromastia (cosmetic) and pectus exacatum, tubular breast deformity, deficiency of the lower medial quadrant and breast base constriction (reconstructive) Primary/secondary augmentation NR Operative details Single surgeon Patient demographics Age: median 28 years (range, 17-51 years) *results not separated between implant type Body mass index: NR Smoker: NR		Right breast Soft: 26/37 patients (70%) Firmer than desired: 10/37 patients (27%) Too soft: 1/37 patients (3%) Both breasts Soft: 70% patients Firmer than desired: 26% patients Too soft: 4% patients Breast consistency, Breast Augmentation Classification (4-6 years) Left breast Grade 1: 9/32 patients (28%) Grade 2: 15/32 patients (47%) Grade 3: 0/32 patients (0%) Grade 4: 0/32 patients (0%) Right breast Grade 1: 9/32 patients (28%) Grade 2: 16/32 patients (50%) Grade 3: 7/32 patients (22%) Grade 4: 0/32 patients (0%) Both breasts Grade 1: 28% patients Grade 2: 48% patients Grade 3: 23% patients Grade 4: 0% patients Breast skin sensitivity (4-6 years) Left breast Normal: 26/37 patients (70%) Increase: 1/37 patients (3%)	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Slight loss: 9/37 patients (24%) Severe loss: 1/37 patients (3%) No sensitivity: 0/37 patients (0%) <u>Right breast</u> Normal: 25/37 patients (68%) Increase: 1/37 patients (3%) Slight loss: 10/37 patients (27%) Severe loss: 1/37 patients (3%) No sensitivity: 0/37 patients (0%) <u>Both breasts</u> Normal: 69% patients Increase: 3% patients Slight loss: 26% patients Severe loss: 3% patients No sensitivity: 0% patients Nipple sensitivity (4-6 years) <u>Left breast</u> Normal: 29/37 patients (78%) Increase: 5/37 patients (13%) Slight loss: 2/37 patients (5%) Severe loss: 1/37 patients (3%) No sensitivity: 0/37 patients (0%) <u>Right breast</u> Normal: 27/37 patients (73%) Increase: 5/37 patients (13%) Slight loss: 2/37 patients (5%) Severe loss: 2/37 patients (5%) No sensitivity: 1/37 patients (3%) <u>Both breasts</u> Normal: 76% patients Increase: 13% patients Slight loss: 5% patients	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			Severe loss: 4% patients No sensitivity: 1% patients	

NR: not reported.

Reconstructive mammaplasty

Table E4: Extraction table for included TRAM flap studies

Study profile		**Safety outcomes**	**Effectiveness outcomes**	**Methodological quality**
Author, year Temple et al 2006 Location St Joseph's Health Centre, London, Ontario, Canada Single centre/multicentre Single centre Study period 2000 to 2001 Data collection NR Patient selection NR Level of evidence II – randomised controlled trial Objective To determine whether neurotisation of the free transverse rectus abdominis myocutaneous flap improves sensation of the reconstructed breast Study arm Non-innervated flap patients	n (patients) 12 n (implants/flaps/breasts) 18 breasts Inclusion criteria Informed consent Exclusion criteria NR **Procedural details** Flap type Free Pedicle type NR Recipient vessel Internal mammary vessel or subcapsular system Immediate/delayed reconstruction 72% flaps/28% flaps Adjunct chemotherapy or radiotherapy Radiation: 17% flaps Chemotherapy: 44% flaps Adjunct procedure NR	Infection NR Lumps NR Skin necrosis NR Inflammation NR Haemorrhage/bleeding complications NR Death NR Other NR	Operative time NR Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Fat reabsorption NR Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation NR	Method of randomisation NR Blinding/method of allocation concealment Examiners blinded Power calculation None Duration of follow-up Mean 16 months Losses to follow-up NR Use of intention to treat NR Sub-group analysis None Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Indication Reconstructive – following simple mastectomy (72% flaps) or modified radical mastectomy (28% flaps) for benign (50% flaps) or malignant (50% flaps) tumours Operative details Two surgeons Patient demographics Age: mean 52 ± (standard deviation) 9.45 years Body mass index: NR Smoker: 8% flaps		Healing time/time to normal activity or work NR Failure NR Pressure threshold *unable to obtain data for mean pressure threshold in nipple area, areola area and peripheral skin area of reconstructed breast because these values were only presented in a graph, with an exponential scale, therefore estimates cannot be obtained visually Temperature discrimination Nipple area (preoperative) 0.625 Nipple area (postoperative) 0 Areola area (preoperative) 0.625 Areola area (postoperative) 0.125 Peripheral skin area (preoperative) 0.5 Peripheral skin area (postoperative) 0.0625 *temperature discrimination reports the proportion of patients where hot and cold	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
			stimuli could be distinguished between, these value were analysed by chi-square or fisher's exact test. The smaller the value the less sensation measured Two-point discrimination Nipple area (preoperative) 1cm Nipple area (postoperative) 0.75 cm Areola area (preoperative) 1.2 cm Areola area (postoperative) 1 cm Peripheral skin area (preoperative) 1 cm Peripheral skin area (postoperative) 0.75 cm *two-point discrimination measures sensation by determining how close together two 'points' of contact can be on a specific area of the breast before the patient cannot be distinguished as two separate 'points'. The smaller this value the greater the sensation *all values reported for temperature discrimination and two-point discrimination were taken visually from graphs, therefore are estimates	

Table E5: Extraction table for included DIEP flap studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Keller 2001 Location North Shore Long Island Jewish Health Care System Manhasset, NY and New York University, New York, NY, USA Single centre/multicentre Single centre Study period April 1994 to February 2000 Data collection NR Patient selection Consecutive Level of evidence IV – case series Objective Summarise data collected for 148 consecutive deep inferior epigastric perforator flaps	n (patients) 108 n (implants/flaps/breasts) 148 flaps Bilateral/unilateral 23 patients/85 patients *17 patients required two flaps to make a single larger breast Inclusion criteria Well-controlled diabetics, patients with collagen vascular disease, obese patients (less than 30% to 40% over the ideal body weight), and patients with advanced breast cancer but in whom a mastectomy was indicated (even after preoperative chemotherapy and/or radiation) Exclusion criteria Abdominal scars that would interfere directly with the blood supply of the flap, severe medical problems, morbid obesity, minimal excess abdominal tissue Indication Reconstructive – following mastectomy **Procedural details** Flap type Free Pedicle type Unipedicle	Infection 1 patient *postoperative infection of abdomen and chest requiring drainage and readmission for intravenous antibiotics Fat necrosis 10 flaps (6.8%) *fat necrosis defined as 2cm firm area present 3 months after reconstruction Necrosectomy (as 2nd stage of reconstruction) 7/10 patients *no separate procedures because of fat necrosis Inflammation NR Haemorrhage/bleeding complications NR Death NR Abdominal wall hernia 2 patients (1.4% of flaps) Abdominal wall weakness 4 patients (2.7% of flaps) *2/4 pts have had this addressed by reopening the anterior rectus sheath and placing a sheet of polypropylene mesh Pulmonary embolism (non lethal) 1 patient (0.92%)	Operative time 6 to 14 hours Reoperation (emergency) 6 patients (4% of flaps) *indications included venous obstruction (3 patients), haematoma (1 patient), spasm (1 patient) and inflow problem (1 patient) *all flaps salvaged except for patient with inflow problem Readmission 1 patient *for infection Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Durability of enhancement NR Length of hospitalisation Mean 3.5 days (range, 3–7 days) Healing time/time to normal activity or	Duration of follow-up Mean 28.9 months (range, 0.5–59.5 months) Losses to follow-up NR Sub-group analysis NA Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	*in case where single flap not enough volume, two deep inferior epigastric perforator flaps dissected and one pedicle anastomosed end to side to the other pedicle Recipient vessel Internal thoracic vessels *4 earlier cases appear to be internal mammary Immediate/delayed reconstruction 98/7 *combined reconstruction (prior mastectomy in 1 breast, then mastectomy required in other breast) in 3 patients (2.8%) Adjunct chemotherapy or radiotherapy Preoperative chemotherapy or radiotherapy in some cases (number NR) Adjunct procedures NR Operative details Single surgeon Patient demographics Age: mean 48 years (range, 32–68 years) Body mass index: NR Smokers: NR	Pneumothorax from mammary vessel dissection 0 patients (0%)	work NR Failure (flap loss) 1 flap (0.7%) Other NR	
Author, year Gill et al 2004 Location Louisiana State University Health Sciences Center-New Orleans-	n (patients) 609 n (implants/flaps/breasts) 758 flaps	Total complications 229 flaps (30.2%) *Smoking (P=0.0000), postreconstruction radiotherapy (P=0.0000), and hypertension (P=0.0370) increased the incidence of	Operative time (unilateral) Mean 4.6 hours Operative time (bilateral) Mean 7.3 hours	Duration of follow-up Mean 13.2 months (range, 1 week–88.1 months) Losses to follow-up NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
affiliated hospitals, New Orleans, LA, USA Single centre/multicentre Multicentre Study period August 1992 to August 2002 Data collection Retrospective review of hospital and office records Patient selection NR Level of evidence IV – case series Objective Examine patients undergoing deep inferior epigastric perforator flap breast reconstruction, with respect to risk factors and associated complications	Bilateral/unilateral 149 patients/460 patients Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following mastectomy for cancer (622 flaps), prophylactic mastectomy (93 flaps) or mastectomy for failed implants (42 flaps) **Procedural details** Flap type Free Pedicle type NR Recipient vessel Internal mammary vessel; either single (585 flaps, 77.2%) or double (173 flaps, 22.8%) anastomosis performed depending on the availability of recipient vessel Immediate/delayed reconstruction 454 flaps/304 flaps Adjunct chemotherapy or radiotherapy Some patients had postreconstruction radiotherapy (number NR) Adjunct procedures	complications. Multivariate analysis confirmed this (smoking P=0.0001, postreconstruction radiotherapy P=0.000, hypertension P=0.039). Age, chemotherapy, diabetes, obesity, abdominal scar, prereconstruction radiotherapy, and having two venous anastomoses did not significantly affect complication rates Total breast complications 153 breasts (20.2%) *Smoking (P=0.0043), postreconstruction radiotherapy (P=0.0000), and hypertension (P=0.0409) increased the incidence of breast complications Infection 21 flaps (2.8%) Lumps NR Fat necrosis 98 flaps (12.9%) *Smoking (P=0.0226) and postreconstruction radiotherapy (P=0.0000) increased the incidence of fat necrosis. Multivariate analysis confirmed this for postreconstruction radiotherapy (P=0.000) but not for smoking (P=0.100). Hypertension, age, chemotherapy, diabetes, obesity, abdominal scar, prereconstruction radiotherapy, and having two venous anastomoses did not significantly	Reoperation 45 flaps (5.9%) Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Durability of enhancement NR Length of hospitalisation Mean 3.86 days Healing time/time to normal activity or work NR Total flap loss 4 flaps (0.5%) Partial flap loss 19 flaps (2.5%) *Chemotherapy, smoking, diabetes, abdominal scar, postreconstruction radiotherapy, and hypertension did not significantly affect complication	Sub-group analysis Yes Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	NR Operative details NR Patient demographics Age: mean 48.9 years (range, 15–74 years) Body mass index: NR Smokers: NR	affect fat necrosis rates Inflammation NR Haemorrhage/bleeding complications NR Blood loss Mean 304.6mL Death NR Seroma 35 flaps (4.6%) Haematoma 14 flaps (1.8%) Venous occlusion 29 flaps (3.8%) *Age, diabetes, number of perforators used, number of venous anastomoses, smoking, prereconstruction radiotherapy, postreconstruction radiotherapy, or chemotherapy did not affect venous occlusion complication rate Arterial occlusion 4 flaps (0.5%) Abdominal complication 103 flaps (13.6%) Postoperative hernia	rates	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
		5 flaps (0.7%) *Smoking (P=0.0033), and chemotherapy (P=0.0337) increased the incidence of donor-site complications. Age, weight, hypertension, radiotherapy, and diabetes did not affect donor-site complication rate		
Author, year Guerra et al 2004 Location Louisiana State University Health Sciences Center, New Orleans, LA, USA Single centre/multicentre NR Study period January 1994 to January 2003 Data collection Retrospective review of patient records Patient selection Consecutive Level of evidence IV – case series Objective To present experience with simultaneous bilateral breast reconstruction with deep inferior	n (patients) 140 n (implants/flaps/breasts) 280 flaps Bilateral/unilateral 140 patients/0 patients Inclusion criteria Simultaneous bilateral breast reconstruction with the deep inferior epigastric perforator flap Exclusion criteria NR Indication Reconstructive – following prophylactic mastectomy or mastectomy for cancer **Procedural details** Flap type Free Pedicle type NR	Total number of patients experiencing complications 50/140 (35.6%) *Obesity, age, or flap weight did not significantly affect complication rate Total number of complications 81 Infection 1 patient (0.8%) *abdominal infection requiring IV antibiotics Lumps NR Fat necrosis 35 flaps (12.5%) in 30 patients *smoking, obesity, radiation, age, or flap weight did not significantly affect fat necrosis complication rate Inflammation NR Seroma (requiring intervention) 4 patients (2.9%)	Operative time Mean 7.3 ± (units not specified) 1.4 hours (range, 5–12 hours) Reoperation 9 patients (6.4%) *had major perioperative complications requiring reoperation Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Durability of enhancement NR Length of hospitalisation	Duration of follow-up Mean 14.6 months (range, 6–76 months) Losses to follow-up NR Sub-group analysis Yes Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
epigastric perforator flaps in consecutive patients	Recipient vessel Internal mammary vessel (99.6%) Immediate/delayed reconstruction 156 flaps/124 flaps *reconstruction was delayed in both patients with previous failed flaps (70 flaps) and no prior reconstruction (54 flaps) Adjunct chemotherapy or radiotherapy Radiation: 10 patients Adjunct procedures NR Operative details NR Patient demographics Age: mean 49 years (range, 27–72 years) Body mass index: mean 27 ± (units not specified) 5 kg/m^2 Smokers: 26 patients (18.6%) Cancer stage: most T1/T2 level, 5 T3 tumours *2nd primary or recurrent cancer previously treated with lumpectomy and radiation (10 patients), bilateral breast cancer (10 patients)	 Seroma (not requiring intervention) 26 patients (18.6%) *Obesity increased the incidence of seroma (P=0.0394) Haemorrhage/bleeding complications NR Blood loss Mean 434 ± (units not specified) 147mL Timing of abdominal drain removal Mean 7.75 ± 3 (units not specified) days (range, 3–20 days) Death NR Vascular complications Anastomotic venous thrombosis 4 flaps (1.4%) Venous congestion/leech therapy 1 flap (0.4%) Arterial ischemia/hyperbaric O_2 2 flaps (0.8%) Breast flap partial dehiscence 16 flaps (5.7%) *smokers (P=0.0033) and patients with preoperative radiotherapy (P=0.039) had higher incidences of breast flap dehiscence	Mean 3.9 days (range, 2–9 days) Healing time/time to normal activity or work NR Total flap loss 0 flaps (0.0%) Partial flap loss 5 flaps (1.8%) *Smoking, obesity, radiation, age, or flap weight did not sig. affect partial flap loss complication rate	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
		Deep vein thrombosis 1 patient (0.8%) Apron necrosis/dehiscence (>5cm^2) 6 patients (4.2%) *Smoking, obesity, age, or flap weight did not sig. affect abdominal necrosis complication rate Hernia, abdominal bulging 3 patients (2.1%) Cancer recurrence 3 patients (2.1%)		
Author, year Hofer et al 2007 Location Department of Plastic and Reconstructive Surgery, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands Single centre/multicentre Single centre Study period February 2002 to February 2006 Data collection NR Patient selection Consecutive Level of evidence	n (patients) 131 n (implants/flaps) 175 flaps *159 deep inferior epigastric perforator flaps, 13 muscle-sparing transverse rectus abdominis myocutaneous flaps and 3 transverse rectus abdominis myocutaneous flaps Bilateral/unilateral 44 patients (34%)/87 patients (66%) Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following oncological	Patients with ≥ 1 complication throughout follow-up 55 patients (42%) Major (surgical) deep inferior epigastric perforator flap complications Acute (<72 hours): 13 flaps (7.4%) Early (72 hours-6 weeks): 4 flaps (2.2%) Minor (conservative) deep inferior epigastric perforator flap complications Acute (<72 hours): 9 flaps (5.1%) Early (72 hours-6 weeks): 6 flaps (3.4%) Major (surgical) abdominal complications Early (72 hours-6 weeks): 7 patients (5.3%) Late (>6 weeks-1 year): 3 patients (2.3%)	Operative time (unilateral) Mean 7.1 ± 1.9 (standard deviation) hours (range, 4–4 hours) *range reporting incorrectly in study Operative time (bilateral) Mean 10.1 ± 2.0 (standard deviation) hours (range, 6–16 hours) Reoperation 29 patients (22.1%) *≥ 1 reoperation to treat complication Readmission NR Mammographic issues NR Psychosocial issues NR	Duration of follow-up Mean 1.8 years (range, 0.3–4.3 years) Losses to follow-up NR Sub-group analysis Yes *No significant relationships between smoking, diabetes, hypertension, high body mass index, pregnancy, previous radiotherapy, previous abdominal operations, intraoperative venous insufficiency requiring additional venous anastomosis, excessive flap weight, ischemia time, or early flap revision and flap complications *Significant relationship between diabetes (P=0.043), hypertension

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
IV – case series Objective To critically evaluate the perioperative complications for deep inferior epigastric perforator flap breast reconstructions	mastectomy (120 flaps, 69%), prophylactic mastectomy (50 flaps, 29%) or previous failed cosmetic augmentation (5 flaps, 3%) **Procedural details** Flap type Free Pedicle type NR Recipient vessel Internal mammary vessels Immediate/delayed reconstruction 44 flaps/103 flaps * tertiary delayed 28 flaps (Neo) adjuvant therapy None: 45 patients (34%) Radiotherapy: 49 patients (37%) Chemotherapy: 69 patients (53%) Hormonal: 35 patients (27%) Combination: 56 patients (43%) Adjunct procedure NR Operative details Two surgeons Patient demographics Age: mean 48 ± (standard deviation) 9 years (range, 23–73 years) Body mass index: mean 27 ± (standard deviation) 4 kg/m^2 (range, 18–35 kg/m^2)	Minor (conservative) abdominal complications Acute (<72 hours): 1 patient (0.8%) Early (72 hours-6 weeks): 16 patients (12.2%) Late (>6 weeks-1 year): 10 patients (7.6%) Infection NR Fat necrosis 10 patients (7.7%) *palpable lump with a diameter larger than 1cm after 12 months Total flap necrosis 1 flap (0.6%) Partial flap necrosis zone 2 Acute (<72 hours): 9 flaps (5.1%) Early (72 hours-6 weeks): 4 flaps (2.2%) Patrial flap necrosis other zones 2 flaps (1.1%) Inflammation NR Haemorrhage/bleeding complications NR Death NR	Patient satisfaction NR Scarring See abdominal complications Durability of enhancement NR Length of hospitalisation Mean 10.1 ± (standard deviation) 7.3 days (range, 4–54 days) Healing time/time to normal activity or work NR Failure (total partial flap failure) 15 flaps (8.6%) *resolved by debridement, medical advancement, and direct closure (12 flaps, 6.8%) or latissimus dorsi flap transposition (3 flaps, 1.8%) Other NR	(P=0.048) and occurrence of abdominal complications Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Smokers: 17 patients (13%)	Other flap complications Arterial insufficiency 2 flaps (1.1%) Venous insufficiency 4 flaps (2.2%) Combined insufficiency 1 flap (0.6%) Haematoma 6 flaps (3.4%) Seroma 1 flap (0.6%) Wound dehiscence 2 flaps (1.1%) Other abdominal complications Abscess 1 patient (0.8%) Haematoma Acute (<72 hours): 1 patient (0.8%) Early (72 hours-6 weeks): 1 patient (0.8%) Skin necrosis 5 patients (3.8%) Dehiscence 16 patients (12.2%) Bulging 4 patients (3.1%)		

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
		Herniation 3 patients (2.3%) Hypertrophic scarring 6 patients (4.5%) Systemic complications Pulmonary embolism 5 patients (3.8%) Deep vein thrombosis 1 patient		

NR: not reported.

Table E6: Extraction table for included SIEA flap studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Arnez et al 1999 Location Department of Plastic Surgery and Burns, University Medical Centre, Ljubljana, Slovenia, and Department of Plastic Surgery, The Queen Victoria Hospital, East Grinstead, UK Single centre/multicentre Single centre Duration of study September 1997 onwards Data collection NR Patient selection NR Level of evidence Level IV – case series Objective To report experience with 5 superficial inferior epigastric artery perforator flap transfers	n (patients) 5 n (implants/flaps/breasts) 5 Bilateral/unilateral NR Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following mastectomy (5 patients) **Procedural details** Flap type NR Pedicle type NR Recipient vessel NR Immediate/delayed reconstruction NR Adjunct chemotherapy or radiotherapy NR	Infection NR Lumps NR Fat necrosis Not quantified but authors reported 'no need for necrosectomy' Inflammation NR Haemorrhage/bleeding complications (haematoma) 1 patient (chest wall) Death NR Other NR	Operative time NR Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction All patients graded their result as excellent (on a scale of excellent, good, fair, poor) Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work	Duration of follow-up Mean 7 months (range, 5–9 months) Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Adjunct procedures NR Operative details NR Patient demographics Age: NR Body mass index: NR Smoker: NR		NR Flap survival 5 flaps (100%)	
Author, year Wolfram et al 2006 Location Department of Plastic and Reconstructive Surgery, Innsbruck Medical University, Innsbruck, Austria Single centre/multicentre Single centre Duration of study April 2002 to July 2005 Data collection NR Patient selection Non consecutive selection Level of evidence IV – case series Objective	n (patients) 11 n (implants/flaps/breasts) 13 flaps Bilateral/unilateral 2 patients/9 patients Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following skin sparing mastectomy (2 patients), standard mastectomy (2 patients), previous reconstruction (5 patients), tumour resection (1 patient), capsular contracture (1 patient) **Procedural details** Flap type Pedicled	Infection NR Lumps NR Total flap necrosis 0 flaps Partial flap necrosis 1 flap *distal tip necrosis, resulting in loss of less than 10% of flap Fat necrosis NR Inflammation NR Seroma 1 patient *requiring reoperation Haemorrhage/bleeding complications	Operative time NR Reoperation 2 patients *due to haematoma or seroma Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Aesthetic outcome NR	Duration of follow-up Mean 23 months (range, 8-47 months) Losses to follow-up NR Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
To highlight the anatomy, operative technique and various indications for SIEA flap in breast reconstruction	<u>Pedicle type</u> Unipedicle: 11 cases Bipedicle: 2 cases <u>Recipient vessel</u> Internal mammary vessel alone: 11 cases Internal mammary vessel and thoracodorsal vessels: 2 cases *as a rule first choice for recipient vessel is internal mammary. Only in case of simultaneous axillary lymph node dissection or bipedicle is additional vascular pedicle anastomosed with already dissected thoracodorsal vessels <u>Immediate/delayed reconstruction</u> 4/7 <u>Adjunct chemotherapy or radiotherapy</u> NR <u>Adjunct procedures</u> Reduction of contralateral breast: 2 patients Flap thinning: 3 patients *if superficial inferior epigastric vessels cannot be identified during the operation or if they are too small, DIEP or TRAM was used <u>Operative details</u> NR <u>Patient demographics</u> Age: mean 52 years (range, 43-60 years) Body mass index: NR Smoker: NR	(haematoma) 1 patient *requiring reoperation <u>Death</u> NR <u>Other</u> NR	<u>Durability of enhancement</u> NR <u>Length of hospitalisation</u> Mean 11 days <u>Healing time/time to normal activity or work</u> NR <u>Other</u> NR	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Holm et al 2008 Location Department of Plastic, Reconstructive, Hand and Burn Surgery, Bogenhausen Hospital, Technical University Munich Single centre/multicentre Single centre Duration of study January 2006 to March 2008 Data collection NR Patient selection NR Level of evidence Level IV – case series Objective To present experience with objective perfusion measurements and present an objectively based intraoperative algorithm for the use of superficial inferior epigastric artery perforator flaps	n (patients) 25 n (implants/flaps/breasts) 25 flaps *16 superficial inferior epigastric artery flaps Bilateral/unilateral (for superficial inferior epigastric artery flap alone) 1 flaps/14 flaps Inclusion criteria All patients undergoing autologous breast reconstruction in one centre who met the anatomical criteria of superficial inferior epigastric artery ≥ 1.5mm (external diameter at level of lower abdominal incision) Exclusion criteria NR Indication Reconstructive – 'breast reconstruction' (20 patients), thoracic wall defect (4 patients), funnel chest correction (1 patient) **Procedural details** It was intended all patients receive pedicled superficial inferior epigastric artery perforator flaps. The actual choice of procedure was made intraoperatively based on the results of perfusion measurements * treatment selection – superficial inferior epigastric perforator artery flap intended first, if not possible → deep inferior epigastric perforator flap used, if perforator anatomy	Infection NR Lumps NR Total flap necrosis NR Partial flap necrosis 1 patient (4%) *bipedicled, adjunct deep inferior epigastric perforator flap Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications NR Death NR No complications 22/25 patients (88%)	Operative time Mean 5.83 hours (range, 4.17–8 hours) Reoperation (reexploration) 3 patients (12%) Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Superficial inferior epigastric artery vascular territory	Duration of follow-up NR Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	unsuitable of perforator flap → transverse rectus abdominis myocutaneous flap used Flap type Pedicled Pedicle type Bipedicled: 5 flaps (20%) Unipedicled: 14 flaps (56%) Recipient vessel NR Immediate/delayed reconstruction NR Adjunct chemotherapy or radiotherapy NR Adjunct procedures Adjunct deep inferior epigastric perforator flap: 4 patients Deep inferior epigastric perforator flap decided intraoperatively: 6 patients *Intraoperative perfusion measurements changed surgical plan in 11 patients (44%) Operative details NR Patient demographics Age: NR Body mass index: NR Smoker: NR		Did not cross midline: 16 flaps (64%) Ranged from 0% (2 flaps) to entire abdominal ellipse (5 flaps) Superficial inferior epigastric artery angiosome Zone I only: 3 flaps Zones I and III: 11 flaps Zones I, II, & III: 4 flaps *entire abdominal ellipse required for reconstruction (8 flaps). *4/8 flaps zones I – IV could be transferred on a single superficial epigastric pedicle *remaining 4 flaps bipedicled technique required for adequate perfusion	

NR: not reported; DIEP: deep inferior epigastric perforator; TRAM: transverse rectus abdominis myocutaneous; SIEA: superficial inferior epigastric artery.

Table E7: Extraction table for included SGAP flap studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Blondeel 1999 Location Department of Plastic and Reconstructive Surgery, University Hospital Gent, Gent, Belgium Single centre/multicentre NR, likely single centre Duration of study April 1996 onwards Data collection Patients prospectively enrolled Patient selection NR Level of evidence IV – case series Objective To describe the first time use of the superior gluteal artery perforator flap as a sensate flap and report experience using this flap for autologous breast reconstruction	n (patients) 16 n (implants/flaps/breasts) 20 flaps Bilateral/unilateral 4 patients/12 patients Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following partial or modified radical mastectomy *indication for mastectomy includes multifocal ductal carcinoma (5 breasts), invasive carcinoma (9 breasts) or fibrocystic disease (4 breasts) Indication for superior gluteal artery perforator flap Excessive abdominal scarring: 5 patients Lack of adipose tissue in lower abdomen: 11 patients **Procedural details** Flap type Free Pedicle type NR	Infection NR Lumps 1 patient *with asymptomatic identification of microcalcifications by mammogram and clinical examination did not reveal nodules Total flap necrosis 1 flap Partial flap necrosis 0 flaps Fat necrosis 1 flap Inflammation NR Gluteal seroma 7 buttocks (35%) Haemorrhage/bleeding complications NR Death NR Pain 0 patients (at donor or recipient site) Wound dehiscence (donor site) 2 buttocks (10%)	Operative time (unilateral) Mean 5 hours and 23 minutes (range, 300-360 minutes) Operative time (bilateral) Mean 11 hours and 6 minutes (range, 540-720 minutes) Reoperation 2 patients *due to venous thrombosis Readmission NR Mammographic issues 1 patient/unilateral flap *at 1 year, routine mammogram picked up two zones of benign microcalcifications (each 0.5cm) Psychosocial issues NR Patient satisfaction NR Scar hypertrophy 1 flap (5%) Aesthetic outcome (gluteal depressions) 4 buttocks (20%) Durability of enhancement NR	Duration of follow-up Mean 11.1 months (range, 3.1-21.6 months) Losses to follow-up None Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Recipient vessel Internal mammary artery Immediate/delayed reconstruction 6 breasts/14 breasts *4 patients (7 breasts) had previous failed reconstruction with implants (3 patients) or free deep inferior epigastric perforator flap (1 patient) Adjunct chemotherapy or radiotherapy Preoperative chemotherapy: 4 patients (25%) Prior radiation: 5 patients (31%) Adjunct procedures None Operative details NR Patient demographics Age: mean 42.2 years (range, 34-56 years) Body mass index: mean 20.2 kg/m^2 (range, 17.4-23.6 kg/m^2) Smoker: 3 patients (19%)	Pneumonia 1 patient	Length of hospitalisation Mean 8.2 days (range, 4-13 days) Healing time/time to normal activity or work Was not quantified, but authors reported 'all patients were able to perform the same physical tasks as before surgery and none of their activities of daily life were affected' Flap failure NR Other NR	
Author, year Guerra et al 2004a Location Department of Surgery, Division of Plastic and Reconstructive Surgery, Louisiana State University Health Sciences Center, New Orleans, LA, USA	n (patients) 142 *6 patients were reconstructed with IGAP flap n (implants/flaps/breasts) 142 flaps Bilateral/unilateral 0 patients/142 patients Inclusion criteria	Overall complication rate 18% *number of perforators associated with pedicle did not effect overall complication rate (P=0.86) Infection NR Lumps NR	Operative time NR Reoperation (take back rate) 8% Readmission NR Mammographic issues NR	Duration of follow-up NR Losses to follow-up NR Sub-group analysis Yes Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Single centre/multicentre Single centre Duration of study February 1993 to April 2002 Data collection NR Patient selection NR Level of evidence IV – case series Objective To analyse the series for operative time, length of stay, flap weight, flap size, blood loss, transfusion requirements, return to the operating suite, fat and/or flap necrosis, and overall flap survival	NR Exclusion criteria NR Indication Reconstructive – following mastectomy (62%), implant failure (25%), breast enlargement (7%), lumpectomy deformity (3%), Poland's syndrome (2%) or pectus excavatum (1%) Indications for gluteal donor site Thin abdomen: 64% Abdominal incisions: 14% Previous abdominoplasty: 8% Patient preference: 7% Nulliparous: 6% Failed abdominal flap: 1% **Procedural details** Flap type Pedicled Pedicle type NR Recipient vessel Internal mammary vessels Immediate/delayed reconstruction NR Adjunct chemotherapy or radiotherapy Preoperative radiation: 27% of patients Adjunct procedures NR	Total flap necrosis NR Partial flap necrosis 6 flaps (4%) *not associated with history of smoking (P=0.11), radiation therapy (P=0.66) or number of perforators associated with pedicle (P=0.14) Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (autologous blood transfusion) 36% of patients Haemorrhage/bleeding complications (banked blood transfusion) 1 patient Death 0 patients Vascular complications 8 flaps (6%) *5/8 survived *not associated with history of smoking (P=0.57), radiation therapy (P=0.9) or number of perforators associated with pedicle (P=0.27) Seroma (donor site)	Psychosocial issues NR Patient satisfaction Not quantified but authors state, 'Satisfaction with the reconstructed breast and donor site has been excellent' Scarring NR Aesthetic outcome (donor site contour deformity) 6 patients (4%) Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Flap survival 98% of flaps Flap loss 3 flaps *causes of flap loss include damaged vascular pedicle and replacement region which did not survive (1 patient), thrombosis at arterial anastomosis (1 patient) and	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Operative details NR Patient demographics Age: (for patients undergoing superior gluteal artery perforator flap procedures): mean 46 years (range, 32–60 years) Body mass index: mean 21 kg/m^2 *unclear if this is mean for patients with a thin abdomen alone (64%) Smoker: 14 patients (10%)	3 patients (2%) Haematoma (breast) 2 breasts (2%) *requiring evacuation operation Haematoma (donor site) 1 patient (1%) *requiring evacuation operation Blood loss Mean 300mL	thrombosis at venous anastomosis (1 patient)	
Author, year Guerra et al 2004b Location Department of Surgery, Division of Plastic and Reconstructive Surgery, Louisiana State University Health Sciences Center, New Orleans, LA, USA Single centre/multicentre Single centre Duration of study February 1993 to November 2003 Data collection NR Patient selection Consecutive	n (patients) 6 n (implants/flaps/breasts) 12 flaps Bilateral/unilateral 6 patients/0 patients Inclusion criteria Subgroup of consecutive patients who underwent simultaneous bilateral breast reconstruction with superior gluteal artery perforator flaps Exclusion criteria NR Indication Reconstructive – following mastectomy (1 patient), mastectomy without immediate reconstruction (2 patients), implant removal and capsulectomies concurrent with reconstruction (2 patients) or prior implant	Overall complication rate 33% Infection NR Lumps NR Total flap necrosis NR Partial flap necrosis NR Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (blood transfusions) 6 patients	Operative time (overall) Mean 9.5 hours Operative time (first 3 cases) Mean 10.3 hours Operative time (last 3 cases) Mean 8.7 hours Reoperation 1 patient *to correct venous thrombosis and hematoma Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction	Duration of follow-up NR Losses to follow-up NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Level of evidence IV – case series Objective To detail the experience with the gluteal region as a reliable source of donor tissue for simultaneous bilateral breast reconstruction	removal and capsulectomies at a different clinic (1 patient) **Procedural details** Flap type Pedicled Pedicle type NR Recipient vessel Internal mammary vessels Immediate/delayed reconstruction 1 patients/5 patients Adjunct chemotherapy or radiotherapy Preoperative radiation: 2 patients Adjunct procedures None Operative details Two teams of surgeons prepare the recipient and donor sites simultaneously with the microvascular anastomosis and flap insetting occurring in the supine position Patient demographics Age: mean 41years Body mass index: NR Smoker: NR	*requiring 1 unit of autologous blood each Death NR Venous thrombosis and hematoma 1 patient Delayed healing 1 patient Breast wound dehiscence 1 patient Blood loss Mean 392mL	NR Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Flap failure 0%	
Author, year DellaCroce and Sullivan 2005 Location	n (patients) 20 n (implants/flaps/breasts)	Infection NR Lumps	Operative time (total) Mean 7 hours and 47 minutes Bilateral flap harvest time	Duration of follow-up NR Losses to follow-up

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Center for Restorative Breast Surgery, LCC, New Orleans, LA, USA Single centre/multicentre NR, likely single centre Duration of study 1 year period Data collection NR Patient selection NR Level of evidence IV – case series Objective To describe the experience and associated technical considerations with an initial 20 patients undergoing superior gluteal artery perforator flap procedure for bilateral simultaneous breast reconstruction	40 flaps Bilateral/unilateral 20 patients/0 patients Inclusion criteria Patients who underwent bilateral simultaneous gluteal artery perforator flap breast reconstruction Exclusion criteria NR Indication Reconstructive – following mastectomy Indications for gluteal donor site Insufficient abdominal fatty tissue volume for inferior epigastric perforator flap to be considered: 16 patients Prior colostomy: 2 patients Prior abdominoplasty: 1 patient History of multiple benign soft-tissue excision from abdominal area: 1 patient **Procedural details** Flap type Free Pedicle type NR Recipient vessel Internal mammary artery and vein Immediate/delayed reconstruction 14 patients/6 patients	NR Total flap necrosis NR Partial flap necrosis (native breast skin) 1 patient Partial flap necrosis (nipple) 1 patient Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (blood transfusions) 0 patients Death NR Seroma (donor-site) 1 patient	Mean 3 hours and 28 minutes Combined bilateral mastectomy and reconstruction operative time Mean 10 hours and 26 minutes Reoperation 1 patient *revisional closure due to partial nipple necrosis Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation Mean 4 days Healing time/time to normal activity or work	NR Sub-group analysis NR Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	*3 patients had previous failed implant reconstruction <u>Adjunct chemotherapy or radiotherapy</u> NR <u>Adjunct procedures</u> None <u>Operative details</u> Team of two microsurgeons working in tandem <u>Patient demographics</u> Age: mean 43 years Body mass index: NR Smoker: 1 patient *quit 2 weeks before procedure		NR <u>Flap failure</u> 0 flaps	

NR: not reported; IGAP: inferior gluteal artery perforator.

Table E8: Extraction table for included IGAP flap studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Allen et al 2006 Location Section of Plastic Surgery, Louisiana State University Health Sciences Centre, New Orleans, Louisiana Single centre/multicentre NR Study period March to December 2004 Data collection NR Patient selection NR Level of evidence Level IV – case series Objective To assess results for in-the-crease inferior gluteal artery perforator free flaps as a potential improvement on the superior gluteal artery perforator flap method	n (patients) 24 *patient number reported as 31 in text and 24 in Table 1 n (implants/flaps/breasts) 31 breasts Bilateral/unilateral NR Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following mastectomy or prior failed reconstruction Indications for gluteal flap Inadequate abdominal tissue: 14 patients Patient choice: 5 patients Prior reconstruction with deep inferior epigastric perforator flap: 2 patients Prior failed reconstruction with transverse rectus abdominis myocutaneous flap: 2 patients Prior abdominal liposuction: 1 patient **Procedural details** Flap type Free	Infection NR Lumps NR Total flap necrosis NR Partial flap necrosis NR Fat necrosis NR Inflammation NR Haemorrhage/bleeding complications (haematoma) 1 patient *resolved without intervention Death NR Wound dehiscence (recipient site) 2 patients *previous radiation *both wounds eventually healed Wound dehiscence (donor site) 1 patient *wound eventually healed	Operative time Mean 5.3 hours (range, 3.0–9.4 hours) Reoperation 3 patients *treatment to venous insufficiency (2 patients) Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction Not quantified but authors report 'patient satisfaction has been very high' Scarring NR Aesthetic outcome NR Durability of enhancement NR Length of hospitalisation Mean 4.2 days (range, 4–7 days)	Duration of follow-up Maximum 9 months Losses to follow-up NR Sub-group analysis None Conflicts of interest None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Pedicle type NR Recipient vessel Internal mammary vessel: 51 anastomoses (82%) Internal mammary perforator vessel: 5 anastomoses (8%) Thoracodorsal vessel: 6 anastomoses (10%) Immediate/delayed reconstruction 16 (52%)/6 (19%) *9 reconstructions (29%) after failure of previous reconstruction attempt (tertiary reconstruction) Adjunct chemotherapy or radiotherapy Radiation therapy: 6/31 reconstructions (19%) Adjunct procedures Balancing of contralateral breast with mastopexy or augmentation: 5 patients (16 %) *augmentation was with saline implant (1 patient) and autologous lateral thoracic tissue (1 patient) Operative details Two surgical teams Patient demographics Age: 49.4 years (range, 33–61 years) Body mass index: NR Smoker: NR	Intraoperative blood loss Mean 317cc (range, 150–1000cc) Sitting discomfort Initial minor adjustments to sitting position when sitting on hard surface: 1 patient *resolved by 6 weeks *by 3 months follow-up, no patient reported sitting difficulties	Healing time/time to normal activity or work NR Flap failure 1 patient *flap loss secondary to venous thrombosis on 4th postoperative day *successful unilateral deep inferior epigastric perforator flap procedure performed in this patient	
Author, year Beshlian and Paige 2008	n (patients) 14	Infection NR	Operative time Average 9 hours and 7 minutes	Duration of follow-up NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Location Virginia Mason Medical Center, Seattle, WA, USA Single centre/multicentre Single centre Study period July 2001 to March 2007 Data collection Retrospective collection of data from patients who underwent surgery before December 2006 and prospective collection thereafter Patient selection NR Level of evidence IV – case series Objective Summarise experience with inferior gluteal artery perforator flaps in thin patients or patients with previous abdominal surgery precluding them from abdominal flap reconstruction	n (implants/flaps/breasts) 19 breasts Bilateral/unilateral 5 patients/9 patients Inclusion criteria NR Exclusion criteria NR Indication Reconstructive – following mastectomy or prior failed reconstruction Indications for gluteal flap Low body mass index: 9 patients Previous abdominal surgery: 4 patients Patient choice: 1 patient **Procedural details** Flap type Free Pedicle type NR Recipient vessel First 4 flaps: thoracodorsal artery and its associated vena comitantes Subsequent flaps: internal mammary vessels Immediate/delayed reconstruction 6/10 *3 reconstructions after failure of previous reconstruction attempt (tertiary reconstruction)	Lumps NR Total flap necrosis 2 patients (also with flap failure) Partial flap necrosis NR Fat necrosis NR Inflammation NR Seroma (donor site) 3 patients Seroma (breast) 4 patients Haemorrhage/bleeding complications NR Death NR Overall healing complications rate 8/19 breasts (42%) Thrombocytosis 1 patient Donor site dehiscence 1 patient	Reoperation 2 patients *to achieve wound healing Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction Not quantified but authors impression that most patients were very satisfied with reconstruction Scarring NR Aesthetic outcome (type) NR Durability of enhancement NR Length of hospitalisation Average 4 days (≥ 7 days in only 2 patients) Healing time (delayed healing of donor site) 1patient Flap failure 2 patients	Losses to follow-up NR Sub-group analysis None Conflicts of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Adjunct chemotherapy or radiotherapy Radiation: 8 breasts Adjunct procedures None Operative details NR Patient demographics Age: average 49 years Body mass index: range, 18.6-29.3 kg/m^2 Smoker: NR		*both patient with previous irradiation *one prior failed implant reconstruction *in both cases vein grafts were used in attempts to salvage flaps after primary revascularisation failed	

NR: not reported.

Table E9: Extraction table for included latissimus dorsi flap studies

Study profile		**Safety outcomes**	**Effectiveness outcomes**	**Methodological quality**
Author, year Daltrey et al 2006 Location Bristol Breast Unit, Bristol Royal Infirmary, Bristol, UK Single centre/multicentre Single centre Study period February 2002 to January 2005 Data collection NR Patient selection Consecutive Level of evidence II – randomised controlled trial Objective To investigate the effect of quilting after latissimus dorsi breast reconstruction on the incidence of symptomatic dorsal seroma and adverse morbidity involving shoulder movement and back pain Study arm Control group with routine closure of back wound	n (patients) 54 n (implants/flaps/breasts) NR Inclusion criteria Patients with newly diagnosed invasive carcinoma of the breast or ductal carcinoma in situ who required mastectomy with or without level I/II axillary lymph node dissection were eligible for inclusion if they requested immediate breast reconstruction, prophylactic mastectomy or delayed reconstruction. Written, informed consent was also required Exclusion criteria Postoperative exclusions due to missing data on seromas (4 patients), arm abduction (4 patients) and donor site pain (6 patients) **Procedural details** Flap type NR Pedicle type NR Recipient vessel NR Immediate/delayed reconstruction Both, numbers NR Adjunct chemotherapy or radiotherapy NR	Overall complication rate 14 patients Infection (infected seroma) 4 patients *2 became loculated and required reoperation at 3 months Infection (implant) 2 patients Lumps NR Skin necrosis (back) 9 patients Skin necrosis (breast) 1 patient Inflammation NR Haemorrhage/bleeding complications NR Death NR Haematoma (back) 1 patient Pain score (week 1) Mean 2.25 (range, 0-8.3) Pain score (week 2)	Operative time NR Reoperation 2 patients *at 3 months due to infected seroma Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction NR Scarring NR Aesthetic outcomes NR Durability of enhancement NR Length of hospitalisation Median 5.1 days *most women discharged 4-5 days postoperative with 2 drains in situ (back and axilla) Healing time/time to normal activity or work	Method of randomisation Computer generated random numbers and sealed envelopes opened by the theatre nursing staff after harvesting of the latissimus dorsi muscle Blinding/method of allocation concealment Patients blinded to procedure Power calculation Yes Duration of follow-up Maximum 3 months Losses to follow-up 2 patients Use of intention to treat Yes Sub-group analysis Yes Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Adjunct procedure Implants in majority of patients Indication Reconstructive – following mastectomy for invasive malignancy (40 patients), ductal carcinoma in situ (6 patients), benign phyllodes (1 patients) or following prophylactic mastectomy (5 patients) Operative details Two surgeons Patient demographics Age: mean 48.1 ± (standard deviation) 8.9 years Body mass index: mean 24.5 ± (standard deviation) 3.0 kg/m^2 Smoker: NR	Mean 1.86 (range, 0-6.9) *pain scores measured on visual analogue scale Seroma rate 46/48 (96%) Seroma volume Mean 570 ml (range, 0-8185 ml) Frequency of aspiration Mean 4 aspirations (range, 0-14 aspirations) Total volume in back drains Mean 1384 ml (range, 174-4575 ml) Total volume in all drains Mean 1982 ml (range, 807-4685 ml) Overall volume (drains and seroma) Mean 2476 ml (range, 839-11946 ml) Analgesic use Paracetamol (week 1) Mean 8 tablets/day (range, 0.3-16.0 tablets/day) Paracetamol (week 2) Mean 6 tablets/day (range, 0-13.3 tablets/day) Non-steroidal anti-inflammatory drugs (week 1) Mean 2.5 tablets/day (range, 0-3 tablets/day)	NR Failure NR	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
		Non-steroidal anti-inflammatory drugs (week 2) Mean 0.57 tablets/day (range, 0-3 tablets/day) Tramadol (week 1) Mean 0.21 tablets/day (range, 0-6.5 tablets/day) Tramadol (week 2) Mean 0.14 tablets/day (range, 0-4.1 tablets/day)		

NR: not reported.

Table E10: Extraction table for included tissue expander and breast implant studies

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Author, year Cordeiro and McCarthy 2006 Location Plastic and Reconstructive Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA Single centre/multicentre NR Study period July 1992 to June 2004 Data collection Patients selected from larger sample of patients undergoing the same procedure, retrospective Patient selection NR Level of evidence IV – case series Objective To review a single surgeon's 12-year experience with two-stage tissue expander/implant breast reconstruction to evaluate late complications, aesthetic results, and patient satisfaction	n (patients) 315 n (implants/flaps/breasts) 410 breasts Bilateral/unilateral 95 patients/220 patients Inclusion criteria All patients with tissue expander breast reconstructions who returned for routine follow-up at least 1 year after completion of breast mound reconstruction Exclusion criteria NR Indication Reconstructive **Procedural details** Mastectomy type NR Expander Incision type Inframammary fold Position Submuscular Name Inamed style 133FV expander Type	Capsular contracture (Baker classification) Grade 1: 206/410 (50.2%) Grade 2: 130/410 (31.7%) Grade 3: 68/410 (16.6%) Grade 4: 6/410 (1.5%) *10.3% (32/309) of non-irradiated reconstructions developed grade 3 or 4 contracture *20% (6/30) of previously radiated reconstructions developed grade 3 or 4 contracture *50.7% (36/71) of reconstructions radiated after the exchange procedure developed grade 3 or 4 contracture *incidence in patients who had irradiation after placement was significantly higher than in patients who did not receive irradiation (P<0.001) *incidence in patients who had prior irradiation (before placement) was not significantly higher than in patients who where not previously irradiated (P=0.092) Implant rupture NR Infection NR Fat necrosis NR	Operative time NR Reoperation 4% of permanent implants exchanged for second permanent prosthesis *indications for exchange included deflation/leak (10 implants), capsular contracture (7 implants) and volume adjustments (2 implants) Time to implant exchange for deflation/leak Mean 2.6 years (range, 0.75–4.5 years) Time to implant exchange for capsular contracture Mean 3.4 years (range, 1.5–4.5 years) Readmission NR Mammographic issues NR Psychosocial issues NR Patient satisfaction Satisfied 300/315 patients (95%) Would choose the same procedure again	Duration of follow-up Mean 36.7 months (range, 12–103 months) Losses to follow-up NA Sub-group analysis For factors affecting aesthetic outcome and rippling, as well as patient demographics Conflict of interest NR

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Anatomic (contour) Surface Textured Implant Name NR Type Saline (249 patients), silicone gel (66 patients) Surface NR Final volume Mean 451.67 cc (range, 180–800 cc) Duration of expansion NR *expansion began 10–14 days after surgery and exchange of expander to implant was performed ≥6 weeks after completion of expansion Immediate/delayed reconstruction 308 patients/5 patients *combined reconstruction (after metachronous, bilateral mastectomies) in 2 patients Adjunct radiotherapy/chemotherapy Preoperative radiotherapy: 29 patients Post-exchange radiotherapy: 62 patients Chemotherapy: 165 patients Neoadjuvant chemotherapy: 13 patients Adjunct procedures	Implant deflation/leakage 10 implants Inflammation NR Skin wrinkling (rippling) None: 195/410 (47.5%) Minimal: 188/410 (45.9%) Moderate: 25/410 (6.1%) Severe: 2/410 (0.5%) *type of implant (saline versus silicone) did not influence the severity (P=0.814) *there was a weak negative relationship between capsular contracture grade and rippling severity (r=-0.136, P=0.006) *body mass index >30 was associated with significantly lower rippling severity score (P<0.001) Haemorrhage/bleeding complications NR Death NR	288/315 patients (91.4%) Dissatisfied 16 patients *12/16 (75%) of these had graded overall aesthetic result of good to excellent Aesthetic result Graded as good, very good or excellent 279/315 patients (88%) *significantly more bilateral reconstructions had good to excellent result compared with unilateral (P<0.001) *non-irradiated patients had significantly better aesthetic scores than patients with post-exchange radiotherapy (p<0.001) *no significant difference in aesthetic outcome between patents with previous irradiation (before exchange) and those who were never irradiated (P=0.225) *aesthetic outcome not influenced by implant volume (P=0.282), BMI (P=0.472), or preoperative brassiere size (r=0.009, P=0.118). *In multivariate analysis, laterality of reconstruction (bilateral versus unilateral) (P<0.000) and radiation history (P<0.000) remained significant predictors of overall aesthetic result Scarring NR	

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Contralateral reduction: 43 patients Contralateral augmentation: 33 patients Contralateral mastopexies: 45 patients *in order to achieve contralateral breast symmetrisation Operative details Single surgeon Patient demographics Age: mean 48.1 years (range, 26–79 years) Body mass index: 24.5kg/m^2 (range, 18–53 kg/m^2) *34/266 (12.8%) of patients were obese Smoker: NR		Durability of enhancement See reoperation (above) Length of hospitalisation NR Healing time/time to normal activity or work NR Failure (i.e. flap loss, removal of implant) NR *patients with ≥1 year follow -up less likely to live out of state (P=0.010), more likely to have received adjuvant radiotherapy (P<0.001), and more likely to have received adjuvant chemotherapy (P<0.001) *no difference in age (P=0.503) or early complication rate (P=0.4133)	
Author, year Wright et al 2008 Location Memorial Sloan-Kettering Cancer Centre, New York Single centre/multicentre Single centre Study period May 1996 to March 2004	n (patients) 104 n (implants/flaps/breasts) NR Inclusion criteria Patient who initiated treatment at the centre according to the algorithm and were deemed suitable for treatment procedures Exclusion criteria Patients who did not complete the treatment	Capsular contracture NR Implant rupture NR Infection NR Fat necrosis NR Implant leakage	Operative time NR Reoperation NR Readmission NR Mammographic issues NR Psychosocial issues	Duration of follow-up (from surgery) Median 64 months (range, 11-122 months) Duration of follow-up (from completion of radiotherapy) Median 55 months (range, 3-114 months) Losses to follow-up 7 patients lost with >12 months since their last follow-up *follow-up for these patients is

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
Data collection Patients retrospectively reviewed Patient selection NR Level of evidence IV – case series Objective To determine actual time intervals between treatment components of algorithm and evaluate cancer recurrence and survival rates	algorithm in its entirety *'no specific inclusion/exclusion criteria' Indication Reconstructive – following mastectomy **Procedural details** Treatment algorithm Mastectomy, immediate expander placement → adjunct chemotherapy and expansion → completion of chemotherapy→ exchange for permanent implant → start radiation Mastectomy type All patients underwent total mastectomy of affected breast and ipsilateral axillary lymph node dissection Expander Incision type NR Position NR Name NR Type NR Surface NR Implant Name NR	NR Inflammation NR Skin wrinkling NR Implant deflation NR Haemorrhage/bleeding complications NR Death 5 patients *four metastatic breast cancers, one unknown cause Survival rate (5 years) 96% (95% confidence interval 92-100%) Locoregional disease control rate 100% *20 patients (19%) had biopsy for suspected recurrence which proved negative Biopsy proven distant metastasis 15 patients Distant metastasis-free survival rate (5 years) 90% (95% confidence interval 83-96%)	NR Patient satisfaction NR Scarring NR Durability of enhancement NR Length of hospitalisation NR Healing time/time to normal activity or work NR Failure (i.e. flap loss, removal of implant) NR	median 37 months (range, 18-99 months) Sub-group analysis Yes *no significant associations between distant metastasis/death and age, T stage, N stage, extra-nodal extension, tumour histology, presence of vascular involvement, presence of perineural invasion, margin status, chest wall involvement , progesterone receptor status, chemotherapy type, use of hormone therapy or interval between chemotherapy and radiation *negative oestrogen receptor status (P = 0.04) and cancer in right breast versus left (P = 0.007) were significantly associated with poorer distant metastasis-free survival Conflict of interest None

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	Type Saline or silicone, shape NR Surface NR Duration of expansion Approximately 4 weeks, or as long as duration of chemotherapy *expansion began 1-2 wks following placement under care of plastic surgeon Adjunct radiotherapy/chemotherapy Chemotherapy: initiated 4-6 weeks after surgery under the care of medical oncologist Radiation: initiated approximately 4 weeks following exchange to permanent implant Lymph node dissection Median 25 dissections (range, 4-50 dissections) Adjunct procedures None Interval between surgery and chemotherapy Median 5 weeks (range, 1-12 weeks) Duration of chemotherapy/expansion Median 5 months (range, 2-9 months) Interval between completion of chemotherapy to exchange Median 4 weeks (range, 2-13 weeks) Interval between exchange to initiation of	Distant metastasis-free survival rate (5 years, from completion of radiation) 86% (95% confidence interval 78-94%) *2 patients had increase tumour markers but no radiographic evidence of cancer at final follow-up Contralateral breast cancer 7 patients Subsequent non-breast cancer 3 patients		

Study profile		Safety outcomes	Effectiveness outcomes	Methodological quality
	radiotherapy Median 4 weeks (range, 1-11 weeks) Interval between end of chemotherapy to start of radiotherapy Median 8 weeks (range, 4-16 weeks) Interval from mastectomy to initiation of radiation Median 8 months (range, 5-14 months) Operative details NR Patient demographics Age (at time of diagnosis): median 45 years (range, 27-72 years) Body mass index: NR Smoker: NR			

NR: not reported.