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# **A Systematic Review of Autologous Fat Transfer for Breast Augmentation**

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# *A Systematic Review of Autologous Fat Transfer for Breast Augmentation*

*AE Chapman  
W Cockburn  
W Morrison  
GJ Maddern*

*C Moore  
D Watters  
M Henderson*

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*PO Box 688, North Adelaide, South Australia 5006*

*AUSTRALIA*

*Fax: 61-8-82391244*

*E-mail: [College.asernip@surgeons.org](mailto:College.asernip@surgeons.org)*

*<http://www.surgeons.org/asernip-s>*

The Safety and Efficacy Classification for the Systematic Review of Autologous Fat Transfer for Breast Augmentation was ratified by:

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## EXECUTIVE SUMMARY

**Background:** Fat transfer for cosmetic defects has been experimented with since the beginning of the 20<sup>th</sup> century, often with mixed results. However, with the recent controversy surrounding silicone breast implants, advocates of fat injection to the breast have argued that this procedure provides a safe method for achieving modest breast augmentation. Doubts remain though as to not only whether the procedure is at all effective, but whether it presents the risk of calcified fat droplets masking the presence possible breast cancer, with life-threatening implications.

**Method:** Electronic databases were systematically searched for references relating to breast augmentation by 1) fat injection, 2) multicentre studies of the saline implant, and/or 3) cohesive silicone gel implants.

**Results:** No studies comparing fat injection with other techniques for breast augmentation were recovered. Of the 10 fat injection studies retrieved, only 3 were case series, the others being case studies. Only 5 studies were retrieved that reported data on the saline implant, although one of these was a comprehensive review of published data. The very small amount of data available for the fat injection technique suggested that somewhere between 20% - 100% of the injected fat was reabsorbed. There was little data available to assess the procedure's safety and a comparison with saline implants, for which there was considerably larger amounts of data, was not possible.

**Conclusions:** The ASERNIP-S Review Group determined that the evidence base for Autologous Fat Transfer for Breast Augmentation was poor and consequently safety and efficacy could not be determined. The review group further recommended that owing to the lack of evidence regarding patient gain from the procedure of Autologous Fat Transfer for Breast Augmentation, coupled with the theoretical dangers of obscuring carcinoma of the female breast, the ASERNIP-S review group could not endorse the collection of data within Australia for this procedure.

## **Safety and Efficacy Classification**

**The Review Group allocated the following classification for Autologous Fat Transfer for Breast Augmentation:**

**For Evidence:**

Poor.

**For Safety:**

Safety cannot be determined.

**For Efficacy:**

Efficacy cannot be determined.

**Recommendations regarding the need for further research:**

Owing to the lack of evidence regarding patient gain from the procedure of Autologous Fat Transfer for Breast Augmentation, coupled with the theoretical dangers of obscuring carcinoma of the female breast, the ASERNIP-S review group could not endorse the collection of data within Australia for this procedure.

## **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**

*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.

*Unsafe 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**

*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.

*Not 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).

*We aim for continuous improvement and therefore welcome comments on our classification scheme.*

## **Review Group Membership**

### **ASERNIP-S Director**

Professor Guy Maddern  
ASERNIP-S  
Royal Australasian College of Surgeons  
North Adelaide SA 5006

### **Protocol Surgeon**

Mr Colin Moore  
Neutral Bay NSW 2089

### **Advisory Surgeon**

Professor Wayne Morrison  
Department of Surgery  
St Vincent's Hospital  
FITZROY VIC 3065

### **Nominated Surgeon**

Mr William Cockburn  
AUCHENFLOWER QLD 4066

### **Other Specialty Surgeon**

Professor David Watters  
Department of Surgery  
Geelong Hospital  
Geelong VIC 3220

### **Invited Surgeon**

Mr Michael Henderson  
Department of Surgery  
Vincent's Hospital  
FITZROY VIC 3065

### **ASERNIP-S Researcher**

Andrew Chapman  
ASERNIP-S  
Royal Australasian College of Surgeons  
North Adelaide SA 5006

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## **Review Protocol**

# **Autologous Fat Transfer for Breast Augmentation**

**September 2001**

## 1. OBJECTIVES

To assess the literature regarding the procedure of Autologous Fat Transfer for Breast Augmentation and make recommendations on the safety and efficacy of this technique compared to the gold standards of saline and cohesive silicone gel implants.

## 2. BACKGROUND

Female breast augmentation is a commonly requested cosmetic procedure which, until recently, was typically effected using silicone gel prostheses.<sup>1</sup> However, these prostheses have become controversial owing to the increasingly frequent concern that silicone, either in the form of leaking gel from implants or from the envelope of the implant itself irrespective of content, is associated with the occurrence of low-grade chronic inflammation and, as a direct result of this, elevated concentration of various growth factors.<sup>2</sup> Most concern appears to have been directed at the silicone gel filled prostheses, since the most commonly used prostheses now appear to be saline filled silicone.

Saline filled prostheses would appear to overcome the difficulties associated with leaking silicone from ruptured silicone-gel prostheses, and may be implanted either via a submammary approach or a submuscular approach, where the implant is placed behind the pectoral muscles.<sup>3</sup> It has been claimed that subpectoral placement results in a superior aesthetic result.<sup>1</sup>

However, saline filled prostheses are not without their problems. Handel *et al.*<sup>4</sup> monitored complications in 1655 breast implants over 15 years, both silicone and saline filled, and reported capsular contracture, skin wrinkling, and a low rate of infection and rupture. Connective tissue disease was noted in only one case. Other surgeons have also reported capsular contracture,<sup>5</sup> calcification rates of between 11.2 to 25 percent (typically taking around 11 years to manifest itself clinically),<sup>6</sup> spontaneous autoinflation,<sup>7</sup> postoperative toxic shock,<sup>8</sup> and rich internal contamination of prostheses with the fungus *paecilomyces variotii*.<sup>9</sup> Indeed, the Institute of Medicine in its recently completed review of silicone breast implant safety has identified that local complications with silicone (including saline filled) breast implants are the primary safety issue with breast implants (see Table 1).<sup>10</sup>

Table 1: Reported Local and Perioperative Complications of Silicone & Saline Implants

Implant fibrous capsular contracture	Skin rashes
Gel implant rupture (intra- and extracapsular)	Skin blistering, cysts, and necrosis
Gel migration	Swelling of the breast
Silicone granuloma	Nipple or flap necrosis
Axillary adenopathy	Implant extrusion
Silicone exudation through skin or nipple	Implant misplacement
Saline implant deflation	Implant shifting or displacement
Implant filler port or valve leakage	Acute and chronic breast and chest wall pain
Operative wound infection	Loss or change in sensation of the breast or nipple
Peri-implant infection	Chest wall skeletal changes
Intra-implant infection	Pneumothorax
Infection with toxic shock syndrome	Peri-implant calcification
Hemorrhage at the operative site	Lactation and galactocele
Peri-implant hematoma or seroma	

Of course techniques have evolved over the years which may have significantly reduced the operative risks. Yet, many of these complications will still remain relevant for saline or other prostheses that are implanted for breast enhancement. As the IOM report stated:

First, reoperations and local and perioperative complications are frequent enough to be a cause for concern and to justify the conclusion that they are the primary safety issue with silicone breast implants. Complications may have risks themselves, such as pain, disfigurement, and serious infection and they may lead to medical and surgical interventions, such as reoperations, that have risks. Second, risks accumulate over the lifetime of the implant, but quantitative data on this point are lacking for modern implants and deficient historically. Third, information concerning the nature and the relative high frequency of local complications and reoperations is an essential element of adequate informed consent for women undergoing breast implantation.

Bircoll has argued that because of the recent concerns regarding the possibly serious complications associated with silicone, the search for alternative transplant materials intensified, and that autologous fat provides a suitable material for breast augmentation.<sup>11</sup> He claims that the first clinical fat transplantation was performed in 1893 by Neuber, who filled out depressed scars with small pieces of autogenous fat. Fat transplantation increased in popularity until the advent of silicone, which became the preferred material because of the lack of absorption or reaction. However, fat transplants could only consist of small pieces of tissue, since problems with vascularisation would lead to necrosis of the fat.

Bircoll's<sup>11,12</sup> own breast enhancement technique involves collecting fat using standard liposuction techniques, with the exception that the material is collected in sterile conditions. The fat is mixed with insulin and injected using a 16 gauge needle and a small syringe. Fat is injected into multiple submammary areas in very small quantities to prevent absorption or necrosis of the fat.

A variation on the technique has been reported by Lee *et al.*<sup>13</sup> whereby autologous fat is harvested by liposuction before being utilised as the fillant in saline implants rather than using saline. The fat is left to undergo liquefaction and necrosis, without interfering with mammography. Despite claiming good outcomes in 6 cases, one implant leaked part of its necrotised contents, while both implants in the last patient became internally infected with bacteria and warranted removal.

Breast augmentation by fat injection has been condemned by the American Society of Plastic and Reconstructive Surgeons<sup>14</sup> and others<sup>15</sup> as irresponsible for reason of potentially obscuring carcinoma of the breast, necessitating many biopsies to assess the numerous false positives that may arise. Although mammographic evaluation of augmented breasts is difficult, alternative methods such as MRI potentially overcome these problems in women who have received prostheses.<sup>16</sup> It is uncertain whether the potential of this technique can be extended to overcoming the difficulties associated with fat injection in the breast. Certainly some have argued that conventional breast augmentation via prosthesis presents as serious a challenge to mammography as fat injection,<sup>17</sup> a view that has not gone unchallenged.<sup>18</sup>

Critics have also maintained that much of the injected fat will not survive.<sup>14</sup> However, donor sites from which fat is removed appear to have differing lipogenic potentials, with gluteal/femoral adipocytes possessing both larger size and greater lipogenic activity than cells taken from the abdomen, breast or face.<sup>19</sup> Proponents of fat transfer for breast augmentation claim up to 80% fat survival for cells injected into the breast, although also

noting that different sites in the body have differing fat reabsorption rates.<sup>20</sup> However, others have reported complete reabsorption of fat cells injected into the breast over a 12 month period, even using fat liposuctioned from the thighs.<sup>21</sup>

Various complications have also been associated with fat transfer to the breast. Castello *et al.*<sup>22</sup> report 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<sup>23</sup> reports a case in which fat directly injected into the breast resulted in painful calcified capsules which required removal through an inframammary approach as in a subcutaneous mastectomy. He states "This case clearly warns against augmentation using fat taken from liposuction."

Breast augmentation by autologous fat transfer appears to be a controversial procedure. It is the purpose of this review to establish the procedure's safety and efficacy.

### **3. INCLUSION CRITERIA**

Papers were selected for inclusion in this review of fat transfer for breast augmentation on the basis of the following criteria:

#### **➤ Participants :**

Human and animal studies were included in this review. Specifically, human studies were on individuals undergoing breast augmentation for aesthetic purposes rather than for breast reconstruction.

#### **➤ New Intervention :**

If the paper included concerned the new intervention, it related to autologous fat transfer for breast augmentation.

#### **➤ Comparative Intervention :**

If the paper included concerned a comparative intervention, it related to saline or cohesive silicone gel implants.

#### **➤ Exclusion of Intervention :**

Papers were excluded if in the opinion of the reviewers they represented multiple publications of the same series, were isolated case reports (unless a report of a complication), or were published in a language other than English. Specific types of breast enhancement implants were also excluded from consideration, and included hydrogel implants, tissue expanders, inflatable implants, and silicone gel implants.

#### **➤ Outcomes :**

A specific outcome that was not considered was the effect of silicone on human tissues, nor were papers included that dealt with any putative association between systemic disease

and breast enhancement implants. Papers included must have contained information on at least one of the following outcomes of the new or comparative interventions:

1. Mortality rates.
2. Morbidity rates.
3. Mammographic issues
4. Psychosocial effects, including measures of patient satisfaction.
5. Effectiveness of enhancement, including:
  - measures of fat reabsorption
  - scarring
  - durability of enhancement
6. Cost effectiveness.
7. Failure of operation.

➤ **Types of studies:**

Papers included in the study were in one of the following forms:

- Randomised controlled trials and controlled clinical trials. In the case of the new intervention, case series and case reports were also included. In the case of the comparator procedure, due to the volume of literature, case series were only included if from multicentre trials.
- Additional relevant published material in the form of letters, conference material, commentary and discussions were included as background information.
- Studies other than those mentioned above can be included as long as reasons are given in the protocol. Reasons must also be given for excluding references. ASERNIP-S Researchers will exclude references that clearly do not meet the inclusion criteria.

➤ **Language :**

Papers in all languages were considered in the literature search. However after the initial search, papers were restricted to English if other language papers were not considered superior.

#### **4. SEARCHES**

➤ Databases and dates searched :

<u>Current Contents</u>	:	1993 – 2001 Week 20
<u>Medline</u>	:	1980 – 2001 May Week 2
<u>EMBASE</u>	:	1980 – 2001 Week 17
<u>HealthStar</u>	:	1975 – 2000 December
<u>Cochrane Library</u>	:	2001 Issue 2

➤ Search Terms used :

A search strategy was devised by the ASERNIP-S Researcher and Protocol Surgeon for the Medline, Current Contents and Embase databases as follows:

(fat or saline or cohesive silicone) and (breast enhanc\* or breast augmen\* or breast implan\*)

Note that (\*) is a truncation symbol that retrieves variations of the indicated text, eg. Endoscop\* will retrieve the words Endoscopy, Endoscope, Endoscopic etc.

The ASERNIP-S Researcher used a different strategy for The Cochrane Collection database because the restricted searches turned up very few references. The search terms used were:

- 1: saline and breast and implant\*
- 2: 'cohesive silicone' and breast and implant\*
- 3: fat and breast and augmen\*

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## **Systematic Literature Review**

# **Autologous Fat Transfer for Breast Augmentation**

November 2001

**Andrew Chapman**

*ASERNIP-S Researcher*

*Royal Australasian College of Surgeons*

*North Adelaide, South Australia*

## 1 Method

The method used to select the literature base is outlined in the review protocol. However, some additional criteria used in interpreting studies are outlined below.

After extraction of all relevant data, each paper was evaluated for methodological strength using the NH&MRC criteria as outlined in Table 2, as well as more detailed examination of experimental methods, including study exclusion criteria, quality of reporting and possible confounding variables. All of these results are detailed in Appendices A.1 – A.3. Aggregated results are summarised in the results section below.

In the sections that follow, papers were only included in the analysis if they specifically reported upon the item of interest and no assumptions were made from the absence of data. For example, with complication rates, papers that did not report a complication rate were not assumed to have reported a zero rate of complications, but were treated as if the data were missing and were thus not included in analyses of morbidity data.

Table 2: Hierarchy of Evidence<sup>1</sup>

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 with concurrent controls and allocation not randomised (cohort studies), case-control studies or interrupted time-series with 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.

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<sup>1</sup> National Health and Medical Research Council. A Designation of levels of evidence. In 'Guide to the development, implementation and evaluation of clinical practice guidelines'. Commonwealth of Australia. 1999 Appendix B, 52.

## 2 Results

The literature search resulted in 10 autologous fat transfer and 6 implant studies being retrieved.<sup>8,24-28</sup> All of the papers were of low evidence quality, and are fully detailed in Appendix A.1. The literature search found no studies that compared autologous fat transfer with breast enhancement via either saline or cohesive gel implants. A single study compared saline with silicone gel implants, but since the silicone gel data was excluded by this review's protocol, the saline data was treated as case series data. Thus all of the studies found were either case series or case studies (level IV evidence). Of the autologous fat transfer studies, 7 represented case studies,<sup>11,12,22,23,29-31</sup> 2 were small case series of no more than 20 patients,<sup>21,32</sup> and 1 was a case series with an unknown number of patients.<sup>20</sup> Hence the evidence base for autologous fat transfer is extremely sparse. The 4 saline implant studies were all retrospective multicentre case series or single institution case studies reporting complications; both cohesive silicone gel studies were case series. The implant studies retrieved presented a problem in that they were largely uninformative in terms of the broader range of outcomes measures considered to be of interest. After perusing their bibliographies, one additional paper was identified as relevant, an extensive review of silicone and saline breast implant literature by the American Institute of Medicine (IOM).<sup>10</sup> This paper was used extensively to supply safety data in particular for saline breast implants.

### 2.1 Safety

In this section such data as mortality, overall morbidity and specific morbidity rates were considered.

#### 2.1.1 Mortality

Mortality rates were generally not discussed in any of the studies. Bondurant *et al.*<sup>10</sup> discussed it as a possible risk associated with an operation such as breast enhancement using saline implants, but otherwise did not attempt to derive any actual statistic of this risk. Since case studies are uninformative in deriving estimates of mortality rates they have been excluded from this section (see Table 3). No deaths were reported. However, from the limited data it is not possible to give a meaningful estimate of risk of mortality for any of the procedures considered here.

Table 3: Mortality Rates

Study	n	Mortality rate
Fat transfer		
Fulton <sup>32</sup>	20	0
Illouz <sup>21</sup>	19	0
Bircoll <sup>20</sup>	??	0
Cohesive gel implant		
Bogetti <i>et al.</i> <sup>27</sup>	14	0
Heitmann <i>et al.</i> <sup>28</sup>	98	0
Saline implant*		
Bondurant <i>et al.</i> <sup>10</sup>	??	#??

\*Refs from IOM report; #Mortality rates were not discussed, but risk identified as real.

### 2.1.2 Morbidity

As there were no comparative studies it was not possible to undertake a statistical comparison of the overall morbidity rates associated with fat transfer and breast implants (see Table 4). There were only 2 fat transfer studies that reported overall morbidity rates, which ranged from 0% to 11%, whereas those associated with saline implants ranged from 19% to 62% per patient (as opposed to per breast) and morbidity rates for two cohesive silicone gel studies ranged from 0% to 22%. Although superficially it may appear that breast implants are associated with a higher overall rate of morbidity than fat transfer, the two fat transfer studies had very small numbers of patients and reported on only a very restricted range of morbidity outcomes (ie hematoma, infection and rejection).

Table 4: Overall Morbidity Rates

Study	n	Morbidity rate
Fat transfer		
Fulton <sup>32</sup>	20	†0 (a few minor bruises)
Illouz <sup>21</sup>	19	‡11%
Cohesive gel implant		
Bogetti <i>et al.</i> <sup>27</sup>	14	†0
Heitmann <i>et al.</i> <sup>28</sup>	98	~22%
Saline implant		
Cunningham <i>et al.</i> <sup>24</sup>	450	*27.6%/20.2%
Fryzek <i>et al.</i> <sup>25</sup>	288	Not calculated
Strom <i>et al.</i> <sup>26</sup>	292	Not calculated
Bondurant <i>et al.</i> <sup>10</sup> –		
- McGhan large simple trial	2855	#*18.9%/- @ 1 year
- Cocks (1994)	75	52% @ 1.5 – 13 years
- McKinney (1983)	58	^62%

† Hematoma and infection, ‡ Infection and rejection only, \* By patient/implant, # infection, deflation, explant, severe capsular contracture, ^ deflation, infection, capsules, hematomas, ~ hematoma, infection, implant rotation/mobility, implant descent, upper pole fullness, Baker IV contracture (includes initial and reaugmentation).

#### *Morbidities reported in case studies:*

Three case studies reported the occurrence of large necrotic cysts subsequent to fat injection, all of which required excision and treatment with prostheses to rectify the subsequent breast deformities.<sup>22,23,31</sup> Calcifications were also reported in three fat transfer case studies.<sup>22,23,29</sup> The single case study of a patient who received saline implants related a case of toxic shock subsequent to infection with *S. Aureus*.<sup>8</sup>

#### *All other specific morbidity reports:*

A narrow range of morbidities was reported in fat transfer patients. These are summarised in Table 5, and consisted of infections and calcifications of fat droplets, with no hematomas recorded. However, only three case series reported any complications, and one of these gave no details of the patients.<sup>20</sup> Calcification was the most commonly reported complication, with 3 out of 20 patients developing this condition in one case series,<sup>32</sup> although Bircoll stated that in his series of 70 patients, only 1 developed a calcified lipid droplet.<sup>20</sup>

Table 5: All reported complications for fat transfer except for case studies.

Complication	n/N	Percent
Infection		
Fulton <sup>32</sup>	0/20	0%
Illouz <sup>21</sup>	2/19	10.5%
Calcifications		
Bircoll <sup>20</sup>	1/70	1.4%
Fulton <sup>32</sup>	3/20	15%
Hematoma		
Fulton <sup>32</sup>	0/20	0%

N=number of women; n=number of complications. Percentages are number of women affected unless otherwise specified.

Unlike autologous fat transfer, there were abundant data available for complications relating to saline breast implants. Although it is difficult to compare complication rates across case series, the most commonly reported complication would generally appear to be capsule formation (see Table 6). Large numbers of women who receive breast implants appear to develop hard capsules around the implants, and these capsules create a breast that is firm with visible distortion (Baker class III) or a breast that is hard, painful and looks abnormal (Baker class IV). The rates, however, varied widely across series, from as low as 1.1% of all breasts up to a rate as high as 40.5% per patient. There was also some indication that smooth implants are more likely to develop hardened capsules than textured implants.

Table 6: Capsule formation in saline breast implants.

Study	n/N	Percent
Cunningham <i>et al.</i> <sup>24</sup> (Baker III/IV)	38/450	8.4%
Bondurant <i>et al.</i> <sup>10</sup>		
- Worseg (1995) (Severe contracture)	29/77	37.6%
- Capozzi (1986) (Contracture)	?/100	3.4% *
- Cocke (1994) (Constricture requiring surgery)	23/75	30.7%
- McKinney (1983) (Capsules)	14/58	24%
- Mladick (1993) (Constrictures)	?/1327	1.1% *
- Lavine (1993) (Baker III/IV)	?/2018#	1.3%
- Apslund (1984) (Baker III/IV)	?/?	20% *
- Gylbert (1990) (Baker III/IV) same group as Apslund + 5 years.	?/?	16% *
- Hetter (1979) (Baker III/IV)	?/?	40% *
- Cairns (1980) (Baker III/IV)	?/?	8.3% *
- Reiffel (1983) (Firmness)	71/307	23%
- Edworthy (1998) (Baker III/IV)	143/352	40.5%
- Rheingold (1994) (Baker III/IV)	?/?	9.5%
- McGhan LST (Baker III/IV)	157/2855	5.5%
- Burkhardt (1994) (Baker III/IV)	?/?	Smooth: 40% Textured: 2%
- Tarpila (1997) (Baker III/IV)	?/21	Smooth: 38% Textured: 29%

\*Per breast rather than per patient. #Implants rather than women. N=number of women; n=number of complications. Percentages are number of women affected unless otherwise specified.

Another complication to which saline implants appear to be prone is deflation, or the leaking of the saline contents into the tissues of the body (see Table 7). Since the saline is readily absorbed by the body and has no toxicity, this leakage in itself poses no safety risk. However, deflated or partially deflated implants must generally be removed and possibly replaced because of the failure of the aesthetic intent of the operation, and any such re-

operation has its own attendant risks.<sup>10</sup> Reported deflation rates varied widely across case series, from as low as 0.56% up to 37.7%. However, there was some evidence that the older style implants were much more likely to deflate than more recent models. In one case series, for instance, modern implants were found to have a 98.4 – 99.8% chance of survival at 5 years and a 96.9 – 98.9% chance of survival at 10 years.<sup>24</sup>

Table 7: Deflation in saline breast implants.

<b>Study</b>	<b>n/N</b>	<b>Percent</b>
Cunningham <i>et al.</i> <sup>24</sup>	?/450	8.3%*
Bondurant <i>et al.</i> <sup>10</sup>		
- Worsseg (1995)	18/77	23.9%
- Capozzi (1986)	?/100	3.4%*
- McKinney (1983)	9/58	15.5%
- Bell (1983)	10/193	5.1%
- Mladick (1993)	?/1327	Old: 37.7% New: 1.33%
- Lavine (1993)	?/2018#	All: 2.3% New: 0.56%
- Robinson (1992)	?/1600#	0.6%
- Rheingold (1994) 10 years	?/?	32.66%
- Rubin (1983) 5 years	29/478#	6%

\*Per breast rather than per patient. #Implants rather than women. N=number of women; n=number of complications. Percentages are number of women affected unless otherwise specified.

Several other types of complication were related for saline breast implants, including infection, hematoma and pain (see Table 8). Infection rates appeared to be low, ranging from 0% in a large series of 1327 women up to 6.9% in a small and early series of 58 women.<sup>10</sup> It does not seem possible to meaningfully compare these rates with those reported for patients who received fat injections (0 – 10.5% in two small case series). Hematomas were reported in only two saline implant case series, with rates reported to be 3.1% and 15.5%.<sup>10,24</sup> Again these rates cannot be meaningfully compared with the single rate of 0% reported for fat injection.<sup>32</sup> Pain was reported as a complication in only one study, with the interesting result that some 33% of women undergoing breast enhancement with saline implants experienced significant pain thereafter.<sup>10</sup>

Table 8: Other complications after saline breast implants.

<b>Complication</b>	<b>n/N</b>	<b>Percent</b>
<b>Infection</b>		
Cunningham <i>et al.</i> <sup>24</sup>	2/450	0.4%
Bondurant <i>et al.</i> <sup>10</sup>		
- McKinney (1983)	4/58	6.9%
- Mladick (1993)	0/1327	0%
- McGhan LST	?/2855	1.1%*
- Rheingold (1994)	?/?	1.5%
<b>Hematoma</b>		
Cunningham <i>et al.</i> <sup>24</sup>	14/450	3.1%
Bondurant <i>et al.</i> <sup>10</sup>		
-McKinney (1983)	9/58	15.5%
<b>Pain</b>		
Bondurant <i>et al.</i> <sup>10</sup>		
- Wallace (1996)	?/282	33%

\*Per breast rather than per patient. #Implants rather than women. N=number of women; n=number of complications. Percentages are number of women affected unless otherwise specified.

Complications associated with cohesive silicone gel implants were reported in only two case series (see Table 9). Additional types of complications which were not reported for fat injection or saline implants were implant rotation/mobility (4%), implant descent (5%), and upper pole fullness (4%). However, extrusion of saline implants through flaws in the breast capsule are not unknown, even if no exact rate has been reported in the literature.<sup>10</sup> Regardless, no particular type of complication was reported to occur in more than 5% of cases.

Table 9: Complications after cohesive silicone gel implantation.

Complication	n/N	Percent
Infection		
Bogetti <i>et al.</i> <sup>27</sup>	0/14	0%
Heitmann <i>et al.</i> <sup>28</sup>	0/98	0%
Hematoma		
Bogetti <i>et al.</i> <sup>27</sup>	0/14	0%
Heitmann <i>et al.</i> <sup>28</sup>	5/98	5%
Implant rotation/mobility		
Heitmann <i>et al.</i> <sup>28</sup>	4/98	4%
Implant descent		
Heitmann <i>et al.</i> <sup>28</sup>	5/98	5%
Upper pole fullness		
Heitmann <i>et al.</i> <sup>28</sup>	4/98	4%
Capsule formation		
Bogetti <i>et al.</i> <sup>27</sup>	0/14	0%
Heitmann <i>et al.</i> <sup>28</sup>	4/98	4%

### 2.1.3 Reoperation rate

Neither of the two fat transfer case series reported whether any reoperations were necessary to treat complications that resulted from the procedure. Of the case studies, Bircoll<sup>11,12</sup> reported that neither of his patients required reoperation. However, the three case studies that reported the presence of necrotic cysts related a total of 6 reoperations, including lumpectomies, placement of subsequent implants and periareolar dermopexy.<sup>22,23,31</sup> The remaining case study, which reported upon the unusual mammographic appearance of the fat-injected breast, stated that a fine needle biopsy was carried out.<sup>29</sup>

Table 10: Reoperation rates per patient.

Study	n/N	Percent
Saline breast implants		
Cunningham <i>et al.</i> <sup>24</sup> (Capsulotomy)	118/450	26%
(Prosthesis replacement)	55/450	12.2%
Bondurant <i>et al.</i> <sup>10</sup>		
- Worseg (1995) (Secondary operation)	83/77	...
- Cocke (1994) (Secondary surgery)	22/75	29%
- Mladick (1993) (Secondary surgery)	121/1327	9.1%
- Lavine (1993) (Revisions)	?/2018*	4.2% <sup>^</sup>
Cohesive silicone gel implants		
Heitmann <i>et al.</i> <sup>28</sup> (Reoperation)	6/98	6%
(Prosthesis replacement)	2/98	2%

\*Number of implants rather than patients; <sup>^</sup>Patients rather than implants

#### 2.1.4 Radiological Measures

As noted above, calcifications that could potentially be confused with carcinoma occurred at a rate of between 1.4 – 15% in patients who received fat injections to the breast. Cheung *et al.*<sup>29</sup> also relate the case of multiple calcifications observed at mammography in the breasts of a woman who underwent fat injection for breast enhancement, and noted that the breasts presented with a “highly unusual appearance.” Otherwise there were no further data available regarding the mammographic interpretation of calcifications in the fat-injected breast.

Specific original data on the effectiveness of mammography for women who had received saline implants was not retrieved. However, the IOM report on the safety of silicone breast implants noted that several authors had observed that the nonvisibility of breast tissue in the presence of silicone was about 25% in one series and 41% in another.<sup>10</sup> Large amounts of tissue remain obscured even with implant-displaced views, although sub-pectoral placement would appear to increase the amount of breast tissue that can be visualised compared with subglandular placement. Quoting Destouet *et al.* the IOM report noted that subpectoral placement of the implants resulted in universally excellent ratings for imaging as opposed to only 7% for sub-glandular placement. However, the same report, quoting Lindbichler *et al.*, found that examinations of 29% of sub-pectoral and 22% of sub-glandular silicone gel implanted breasts were of limited quality.

## 2.2 **Efficacy**

The efficacy of a procedure, though naturally related to safety issues, is principally concerned with how effectively the surgical intervention achieves the technical goals that are not directly related to issues of safety. In this particular section the question is dealt with in terms of breast enhancement measures and patient satisfaction measures.

### 2.2.1 Breast Enhancement Measures

The reported volumes of liposuctioned fat that has been injected into female breasts ranged from as little as 30ml<sup>31</sup> up to 400cc.<sup>32</sup> Hin<sup>30</sup> transferred fat in two or three stages, each of 30ml. Illouz<sup>21</sup> used a similar approach, with months between sessions, whereas others<sup>11,12,32</sup> appear to have injected the desired amount of fat in single sessions.

There was wide variation in the limited data relating to how well this injected fat survived the process. Bircoll,<sup>20</sup> in a case series which did not specify the number of patients, reported that less than 20% of fat was reabsorbed after 1 year, with additional bulk maintained by 10-20% of fibrous material. Similarly, Fulton<sup>32</sup> found that 29% of fat was reabsorbed in 75% of his patients over a mean 19 months. However, Illouz<sup>21</sup> reported that even in cases where fat was reinjected up to twice after the initial treatment, all of the fat was reabsorbed after 12 months in all 19 of his patients.

There were no data available on the volume of saline prostheses implanted, but these devices are available in a range of volumes or may be filled to a specified volume without fear of absorption in the same manner as fat (except in the case of deflation, an issue which has been addressed in the safety section). It should be noted, though, that along with its important implications for safety, capsular contracture could also be considered an efficacy issue.

Bondurant *et al.*<sup>10</sup> note that skin wrinkling over a wrinkled implant can be pronounced. They observe that several studies have reported a rate of skin wrinkling of 3.3-5% in subglandular, smooth saline implants for augmentation. Another two studies quoted in the same paper report that skin wrinkling occurred in 14% of smooth saline implants and 7.3% of textured saline implants. This is an aesthetic problem that would appear not to be relevant to fat injection.

### 2.2.2 Patient Satisfaction Measures

No case series related measures of patient satisfaction with fat transfer to the breast. In two case studies, Bircoll<sup>11,12</sup> claimed that patients were “very pleased”.

Cunningham *et al.*<sup>24</sup> reported that 92.9% of 450 patients surveyed were either satisfied or very satisfied with their saline implants and that 95.9% would choose to have saline prostheses implanted again. Of those with hard or firm breasts (ie capsular contracture), only 16.3% described the complication as very bothersome, with 36.9% describing it as somewhat bothersome, 20% not very bothersome, and 26.9% not bothersome. Strom *et al.*{1997} utilised a different approach and found that on 5-point Likert scales, 64.4% of 292 patients strongly agreed with the statement “I am satisfied with the results of my breast augmentation”, whereas only 2.8% strongly disagreed. Similarly, large proportions strongly agreed with such statements as “I would recommend the procedure to others” (57.9%), “Breast implant surgery has improved the quality of my life” (45.7%), and “The implants have improved my sexual attractiveness” (51.5%). However, neither of these studies employed any controls, which suggests caution in interpreting these enthusiastic endorsements.

## 3 Discussion

There are clearly insufficient data available to come to any firm conclusions regarding the safety and efficacy of autologous fat transfer to the breast for the purposes of breast augmentation. While some alarming complications have been reported in case studies, the few case series would appear to be based on too few patients to produce reliable estimates of the risks of morbidity from the procedure. And while the morbidity rates appear to be low, there is contradictory and, again, too little evidence as to the effectiveness of the procedure, with one case series reporting 20% fat re-absorption, another 30% and yet another 100%. The issue of greatest concern is of course the production of calcifications, particularly multiple calcifications, which may potentially obscure or be mistaken for carcinoma of the breast. Here again there is too little evidence, with only two small series reporting on the matter. However, it is clear that calcifications do occur, and have been reported even by the most enthusiastic proponents of this technique. It is not possible to calculate the exact risk these calcifications pose, since the data are too few.

There is much better data for the safety of saline implants, which are not without their own risks. While effective at enhancing the female breast, the prostheses are associated with capsule formation and contracture, as well as deflation, with the attendant risks of reoperation. There are also small risks associated with other complications such as infection, hematoma, and – more uncertainly – breast pain. Both fat injection and saline prosthesis implantation are associated with mammographic problems. Whatever the deficiencies in the amount of breast tissue potentially obscured to mammography by breast prostheses, this would appear to be a somewhat different issue from the potential dangers posed by fat injection, whereby calcified fat droplets may have the appearance of carcinoma. But again the data and the necessary controlled trials are simply not available

to provide adequate information on the matter. Despite the clearer evidence with regard to saline implants, there remains the problem that too little is known about the safety of fat injections to the breast and the ultimate fate of that fat for the two techniques to be adequately compared.

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## 4 Glossary

Baker Capsular Contracture scale:

Grade I: the breast is normally soft and looks natural.

Grade II: the breast is a little firm but looks normal.

Grade III: the breast is firm and looks abnormal.

Grade IV: the breast is hard, painful, and looks abnormal.

Na: not applicable.

N/c: not calculable.

### **Treatment of figures:**

Values with standard deviations ( $\pm$ ) are means. Unless stated otherwise, values with ranges alone (x-y) are medians.

Appendix A.1: Study Profiles.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Bircoll M	1987	Beverly Hills, California, USA.	<b>Autologous Fat Transfer:</b> Fat extracted from donor sites via liposuction and treated with insulin. Fat loaded into multiple 3cm syringes with 16 gauge needles. Fat injected in small quantities into multiple areas in breast to ensure vascularisation. Visual evaluation of symmetry and contour. Sterile pads placed in elastic bra. Patient resumes normal activity by 3 <sup>rd</sup> postop day. Max fat transfer appears to be around 130 cm <sup>3</sup> .	<u>Level of evidence:</u> IV <u>Follow up:</u> 2.5 years. <u>Duration of study:</u> not stated, presumably 2.5 years. <u>Critique:</u> Case report	<u>Sample size:</u> n=1 <u>Age:</u> 20	Breast hypoplasia.
Bircoll M, Novack BH.	1987	Division of Plastic Surgery, Beverly Hills Medical Center, & Cedars-Sinai Medical Center, Los Angeles, California, USA.	<b>Autologous Fat Transfer:</b> Fat extracted from donor sites via liposuction and treated with insulin. Fat loaded into small syringe with 16 gauge needle. Fat injected in small quantities into multiple areas in breast to ensure vascularisation.	<u>Level of evidence:</u> IV <u>Follow up:</u> nearly 3 years. <u>Duration of study:</u> nearly 3 years. <u>Critique:</u> Case report	<u>Sample size:</u> n=1 <u>Age:</u> 45	Breast asymmetry following reconstruction to one breast.
Bircoll M	1988	Beverly Hills Medical Center, Beverly Hills, California, USA.	<b>Autologous Fat Transfer:</b> No method given, although implication that surgical technique follows that of Bircoll (1987) and Bircoll & Novack (1987). Other experimental procedures reported to have occurred such as mammographic evaluation of post-augmented breast and biopsy of surviving fat in breast, but no method reported.	<u>Level of evidence:</u> IV <u>Follow up:</u> not stated. <u>Duration of study:</u> up to 5 years. <u>Critique:</u> No method given. Results quoted with no reference to experimental technique or patient characteristics.	<u>Sample size:</u> n=not stated <u>Median age:</u> not stated. <u>Other factors:</u>	Not stated.
Castello JR, Barros J, & Vazquez R.	1999	Department of Plastic Surgery, Hospital Ramon y Cajal, Madrid, Spain.	<b>Autologous Fat Transfer:</b> Bilateral augmentation by injection of unknown amount of autologous fat after trochanteric and abdominal liposuction.	<u>Level of evidence:</u> IV <u>Follow up:</u> 10 months. <u>Duration of study:</u> not stated. <u>Critique:</u> Case report	<u>Sample size:</u> n=1 <u>Age:</u> 24 <u>Other factors:</u> Non plastic surgeon.	Not stated.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Cheung M, Houssami N, Lim E.	2000	Sydney Square Breast Clinic, Medical Benefits Fund of Australia, Sydney, Australia.	<b>Autologous Fat Transfer:</b> Bilateral breast augmentation undergone outside Australia. Fat retrieved from thighs via liposuction and injected into breasts on three occasions. Presented to breast clinic following patient becoming aware of a lump in each breast.	<u>Level of evidence:</u> IV <u>Follow up:</u> 12 months. <u>Duration of study:</u> not stated. <u>Critique:</u> Case report	<u>Sample size:</u> n=1 <u>Age:</u> 30 <u>Other factors:</u>	Not stated.
Hin LC	1988	Supreme House, Singapore, Republic of Singapore.	<b>Autologous Fat Transfer:</b> Liposuction performed with lidocaine 0.5%, 1:200,000 epinephrine. Fat harvested with 3cc syringes & 14 gauge needles. Transplanted using 16 gauge needle. No more than 30cc fat injected per session into subcutaneous tissues between skin and glandular tissue and retromammary space: no more than 0.5cc per site. Use fat devoid of blood. Repeat procedure at 2 weekly intervals until patient satisfied or runs out of donor sites.	<u>Level of evidence:</u> IV <u>Follow up:</u> up to 2 weeks. <u>Duration of study:</u> not stated <u>Critique:</u> Case reports. Mainly technical paper. Very few details of outcomes or patients given. Unvalidated claims of 70%-80% fat survival at 12 months.	<u>Sample size:</u> n=3 <u>Median age:</u> not stated <u>Other factors:</u>	Mammary hypoplasia, mammary asymmetry, breast augmentation/ firming.
Fulton JE	1992	Not stated	<b>Autologous Fat Transfer:</b> Wet technique of liposuction used to recover fat. Fat washed 3 times in Lactated Ringer's solution to remove broken cells, blood & serum. Fat packed in 50cc syringe injection guns. Individual 1-3cc aliquots injected in pre-pectoral fascial plane: 200-300cc per breast.	<u>Level of evidence:</u> IV <u>Follow up:</u> mean 19 months (9 – 58) <u>Duration of study:</u> not stated <u>Critique:</u> Case series	<u>Sample size:</u> n=20 <u>Mean age:</u> 38 (22 – 57) <u>Other factors:</u>	Good health with 'disharmonious' obesity. 'Violin' type of fat deformity preferred. Candidates had to be satisfied with prospect of a modest increase in breast size.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Illouz Y-G	1990	Not stated, but chapter published in Boston.	<b>Autologous Fat Transfer:</b> Fat injected in to breast in retromammary plane in 5ml drops in different sites in a radial manner. Use fat devoid of blood.	<u>Level of evidence:</u> IV  <u>Follow up:</u> up to 12 months  <u>Duration of study:</u> June 1983 – June 1987  <u>Critique:</u> Case series.	<u>Sample size:</u> n=19  <u>Median age:</u> not stated  <u>Other factors:</u>	Breast augmentation.
Maillard GF	1994	Lausanne, Switzerland.	<b>Autologous Fat Transfer:</b> Bilateral augmentation by injection of unknown amount of autologous fat after trochanteric and abdominal liposuction.	<u>Level of evidence:</u> IV  <u>Follow up:</u> Uncertain ~ 5 years?  <u>Duration of study:</u> not stated.  <u>Critique:</u> Case report	<u>Sample size:</u> n=1  <u>Age:</u> 20  <u>Other factors:</u> Non genuine aesthetic surgeon.	Not stated.
Vizcaino JM, Montilla PB, Ruiz JB	1990	Gran Via Fernando el Catolico, Valencia, Spain.	<b>Autologous Fat Transfer:</b> Fat extracted from thighs and buttocks. 30ml injected in left breast; 120ml in right. Fat injected through one puncture wound in each breast in a radial manner and then massaged into homogeneous distribution.	<u>Level of evidence:</u> IV  <u>Follow up:</u>  <u>Duration of study:</u>  <u>Critique:</u> Case report in a letter.	<u>Sample size:</u> n=1  <u>Age:</u> 32  <u>Other factors:</u>	Ptotic and asymmetrical breasts.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Cunningham B, Lokeh A, Gutowski K	2000	Division of Plastic & Reconstructive Surgery, University of Minnesota Medical School, Minnesota, USA.	<b>Saline-filled implant:</b> Each centre was paid \$1500 to identify and contribute data on 50 patients (range 11-96). Surgeons instructed to enrol consecutive patients. Data collected via telephone, and medical chart review.	<b>Level of evidence:</b> IV  <b>Follow up:</b> 13 years (9.8 – 20.0)  <b>Duration of study:</b> 1/1/80 – 30/6/86 (27 patients from 1/1/77 – 31/12/80)  <b>Critique:</b> Retrospective Industry-funded Multicentre (11 centres, 9 contributing, 2 withdrew) Only 51.3% participation rate from patients. Stats: Kaplan-Meier actuarial survival stats; odds ratios; stepwise logistic regression.	<b>Sample size:</b> n=450  <b>Other factors:</b> 882 implants. Purpose: Augmentation: 93.9% Reconstruction: 16.1% Placement: Submammary: 74% Subpectoral: 25.6% Subcutaneous: 0.2% Brand: Heyer-Schulte: 59.7% Mentor: 29.2% Surgitek: 8.4% Mean volume: 250cc Within 25cc of recommended: 90.9% Overfilled > 25cc: 7.2% Underfilled < 25cc: 1.9%	Single lumen saline filled breast implants of any manufacturer, in any anatomic location, for any condition. Only the first set of breast implants was included.
Fryzek JP, Signorello LB, Hakelius L, Feltelius N, Ringberg A, Blot WJ, McLaughlin JK, Nyren O.	2001	International Epidemiology Institute, Maryland, USA; The Departments of Medical Epidemiology & Rheumatology, Karolinska Institute; Department of Plastic Surgery, Uppsala University Hospital; Department of Plastic Surgery, Malmo University Hospital, Sweden.	<b>Saline and Silicone Breast Implant:</b> Random sample of eligible women drawn.  <b>Breast Reduction:</b> Random sample frequency matched to the implant patients for age and calendar year at the time of surgery.  <b>Both:</b> Trained nurse abstractors used standardised form to obtain case record info on patient height, weight, type of implant, volume, and weight/volume of tissue removed. All patients also mailed questionnaire regarding 28 specific symptoms; nonresponders contacted by phone.	<b>Level of evidence:</b> III-3  <b>Follow up:</b>  <b>Duration of study:</b> 1965 – 1993.  <b>Critique:</b> Retrospective. Multicentre (registry covering entirety of Sweden) cohort study. Stats: Multivariate logistic regression models used to obtain risk ratio estimates. Nonresponders not significantly different from responders with regard to age and date of op.	<b>Sample size:</b> n=2376 implants (1369 responders); 3470 breast reduction (2211 responders).  <b>Mean age:</b> implant – 44.3(±10.0) reduction – 42.2(±10.8)  <b>Mean BMI:</b> implant – 21.0(±2.7), reduction – 24.5(±3.9), p<0.001  <b>Ever smoked:</b> implant – 74.2%, reduction – 65.2%, p<0.001.  <b>Ever pregnant:</b> implant – 90.7%, reduction – 86.5%, p<0.001.  <b>Treated at University Hospital:</b> Implant – 63.0%, reduction – 58.2%  <b>Other factors:</b> Reason for nonparticipation: Active refusal: 27% Silent telephone #: 14% Other administrative cause: 4% Unknown: 54.8% Death/mental/illness: 0.2%	Group 1): Women recorded in Inpatient Registry with a procedure code for breast implant operation with foreign material (non-malignant indication). Group 2): Women who had undergone breast reduction surgery. Both groups: excluded women with previous mastectomy or past or concomitant breast cancer diagnosis.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Strom S, Baldwin B, Sigurdson A, Schusterman M.	1997	Departments of Epidemiology and Plastic Surgery, The University of Texas M D Anderson Cancer Center, Houston, Texas, USA.	<b>Saline-filled implant:</b> Standardised telephone questionnaire used to extract data from saline-implant recipients. Chart review used to extract complications.	<u>Level of evidence:</u> IV  <u>Follow up:</u> mean 7 years (1.9 – 19)  <u>Duration of study:</u> 1976 – 1993  <u>Critique:</u> Retrospective Multicentre (2 large private practises) 292 of original 497 patients were followed up. Telephone interview. Chart review used to establish representativeness of responding sample.	<u>Sample size:</u> n=292  <u>Mean age:</u> At implant: 33.1 (16-68) At interview 40.3 (21-79)  <u>Race (White/other):</u> 98.8%/1.2%  <u>Marital Status:</u> Married: 66.6% Divorced: 15.8% Widow ed: 1.3% Single: 15.5%  <u>Education:</u> < high school: 4.1% High school: 51.9% College: 32.3% Advanced degree: 11.7%  <u>Other factors:</u> 497 patients in original cohort 375 were contactable 292 agreed to interview 31 refused 2 moved out of country 1 died 49 did not return contact card	Saline breast implant surgery at one of 2 centres in Texas and Louisiana.
Poblete JVP, Rodgers JA, Wolfort FG.	1995	Division of Plastic and Reconstructive Surgery, New England Deaconess Hospital and Cambridge Hospitals, Boston, Mass., USA.	<b>Saline-filled implant:</b> 150cc injectable implants placed in sub- glandular position six days prior to admission to hospital for toxic shock. Inflation of left implant done by "an alternative method." 1 gram of intravenous cefazolin administered at implantation as antibiotic.	<u>Level of evidence:</u> IV  <u>Follow up:</u> not stated.  <u>Duration of study:</u> not stated.  <u>Critique:</u> Case report	<u>Sample size:</u> n=1  <u>Age:</u> 21 years  <u>Other factors:</u>	Not stated.

Authors	Year	Location	Intervention	Study Design	Study Population	Inclusion Criteria
Bogetti P, Boltri M, Balocco P, Spagnoli G.	2000	Turin, Italy.	<b>Cohesive Silicone Gel:</b> Device: Polytech Silimed code 20675. Volumes ranged from 165cc – 245cc. Positioned in sub-glandular area using sub-mammary approach: 4.5cm cut 1 cm above sub-mammary fold. Drains inserted prior to placement of prosthesis & removed 48 hours later.	<u>Level of evidence:</u> IV  <u>Follow up:</u> 2 years  <u>Duration of study:</u>  <u>Critique:</u> Case series.	<u>Sample size:</u> n=14  <u>Age:</u> 23-30  <u>Other factors:</u>	All patients with thin chest and poor subcutaneous tissue.
Heitmann C, Schreckenberger C, Olbrisch RR.	1998	Department of Plastic Surgery, Diakoniekrankenhaus Kaiserwerth, Dusseldorf, Germany.	<b>Cohesive Silicone Gel:</b> Device: McGhan Style 410. Inserted via 5cm inframammary crease incision. No steroids or antibiotics used. Subglandular placement for aesthetic augmentation; retropectoral in cases of reconstructive surgery; both subglandular (24) and retropectoral (33) in reaugmentation cases.	<u>Level of evidence:</u> IV  <u>Follow up:</u> 2 weeks, 3, 6 & 12 months, and annually thereafter; min 6 months – max 3 years. Mean 1.5 years.  <u>Duration of study:</u> Jan 1993 – Jan 1996  <u>Critique:</u> Case series. Figures in text & one table (1) do not match.	<u>Sample size:</u> n=132 (98 valid)  <u>Mean age:</u> 32 years.  <u>Other factors:</u> Mean implant size: 300 grams. Min – 210g Max – 610g	Indications for surgery: 1) aplasia/hypoplasia (n=40) 2) problems with previous prosthesis (n=58) 3) postmastectomy deformity (n=34); these last were invalid for this systematic review.

## Appendix A.2: Safety Tables

	Bircoll (1987) n=1	Bircoll & Novack (1987) n=1	Bircoll (1988) n=unknown	Castello <i>et al.</i> (1999) n=1	Cheung <i>et al.</i> (2000) n=1	Fulton (1992) n=20	Illouz (1990) n=19	Maillard (1994) n=1	Vizcaino <i>et al.</i> (1990) n=1
Mortality									
Overall mortality rate				0				0	0
Morbidity									
Liponecrotic pseudocyst(s)				1				1	1
Infection						0	*2		
Hematoma						0			
Implant rotation/mobility									
Implant descent									
Upper pole fullness									
Capsule formation (n of patients)									
Implant deflation rate (per implant)									
Prosthesis displacement									
Other									
Revision Rates									
Correction of asymmetry									
Repair of wound complications									
Reoperation (n of instances)	0	0		*2	*1			*3	1
Replacement with(of) prosthesis (n of patients)				1				1	1
Radiological outcomes									
Calcifications present (n of patients)			*1/70 cases followed for 1 year and evaluated by mammography (1.4%)	1	1	3 (1.5%)		1	0
Other					Described as "highly unusual appearance".				
Other									
Other health conditions									
Other complications									
Overall postoperative morbidity rate									
Overall morbidity rate									
Notes			*Microcalcification, claimed to be qualitatively different from carcinoma.	*Lumpectomy and later implant	*Fine needle biopsy.		*Infection or rejection	*Resection of cysts and later implants and later periareolar dermopexy.	

	Cunningham <i>et al.</i> (2000) n=450	Fryzek <i>et al.</i> (2001) n=288
Mortality		
Overall mortality rate		
Morbidity		
Liponecrotic pseudocyst(s)		
Infection		
Hematoma		
Implant rotation/mobility		
Implant descent		
Upper pole fullness		
Capsule formation (n of patients)	*20.4%	
Implant deflation rate (per implant)	~8.3% by patient report; 7.6% by physician record	
Prosthesis displacement		
Other	Actuarial survival: 98.4-99.8% @ 5 years; 96.9-98.9 @ 10 years	
Revision Rates		
Correction of asymmetry	0.70%	
Repair of wound complications	2.00%	
Reoperation (n of instances)	25.8% (^69(105 implants), #49(82 implants))	
Replacement with(of) prosthesis (n of patients)	12.2% replacement or removal	
Radiological outcomes		
Calcifications present (n of patients)		
Other		
Other		
Other health conditions		Painful joints > 3 months 0.8 [0.5-1.5], Swelling joints > 1 week 1.1 [0.5-2.2], Muscle pain >3 months 1.3 [0.6-2.5], Persistent muscle weakness 1.5 [0.6-3.6], Regularly burning eyes 0.9 [0.3-2.7], Persistent dry eyes 1.2 [0.4-4.0], Recurrent sensation of sand in eyes 0.9 [0.1-6.6], *Dry mouth > 3 months 5.1 [1.1-24.4], Ulcers in mouth > 3 weeks 2.2 [0.2-24.5], Difficulty swallowing 2.0 [0.5-8.5], Unexplained fever 3.5 [0.7-17.1], Night sweats 1.3 [0.7-2.5], Skin redness on cheeks 1.3 [0.3-6.0], Skin abnormalities worsen in sun 1.2 [0.5-3.2], *Other skin abnormalities 3.9 [1.5-10.2], Hypersensitivity to sunlight 5.0 [0.6-44.1], Impaired toe/finger circulation 1.2 [0.5-3.0], Tingling & numbness 0.7 [0.4-1.3], Persistent headache 0.7 [0.3-1.4], Persistent neck ache 0.9 [0.5-1.5], Persistent shoulder ache 1.1 [0.6-2.0], Persistent backache 1.1 [0.6-2.2], Abnormal fatigue 1.6 [0.8-3.1], Depression 1.8 [0.9-3.3], Memory difficulties 1.1 [0.5-2.6], Wordfinding problems 0.8 [0.3-2.0], Hair loss 0.9 [0.3-2.5], Persist
Other complications		
Overall postoperative morbidity rate		
Overall morbidity rate	27.6% per patient (20.2% per implant)	
Notes	*Baker grade III or IV; Risk factors (Odds ratio): Heyer-Schulte & Mentor 1800 model 0.095 (p<0.01), submammary position 2.05 (p=0.03), implant size 1.01 (p<0.01), intraluminal antibiotics/steroids or pocket antibiotics or filling volume all NS. ^closed capsulotomy, #open capsulotomy. ~Paper broke rates down by implant type; risk factors (odds ratios) Surgitek model - 17.53 (p<0.01), implant size>450cc (p=0.05); Heyer-Schulte & Mentor models 1600 & 1800 only: model 1800 - 3.00 (p=0.01), implant size>450cc - 1.01 (p=0.02)	Note: large saline implant (n=151) compared to small (<=median implant size) saline implant (n=137). Asterisk marks significant result.

	Poblete <i>et al.</i> (1995) n=1	Strom <i>et al.</i> (1997) n=292	Bogetti <i>et al.</i> (2000) n=14	Heitmann <i>et al.</i> (1998) n=98
Mortality				
Overall mortality rate	0			
Morbidity				
Liponecrotic pseudocyst(s)				
Infection			0	*0/0
Hematoma			0	*1/4
Implant rotation/mobility				*1/3
Implant descent				*1/4
Upper pole fullness				*0/4
Capsule formation (n of patients)			0	#*1/3
Implant deflation rate (per implant)				
Prosthesis displacement			0	
Other				
Revision Rates				
Correction of asymmetry				
Repair of wound complications				2 hematomas drained
Reoperation (n of instances)				6
Replacement with(of) prosthesis (n of patients)				2
Radiological outcomes				
Calcifications present (n of patients)				
Other				
Other				
Other health conditions		5 (1.7%) reported conditions at least 1 year post mammoplasty: 1 rheumatoid syndrome, 1 Sjogren syndrome, 1 atypical autoimmune disorder, 2 chronic fatigue syndrome. 1 Colon cancer, 2 cervical cancer in situ post augmentation.		
Other complications	Toxic shock from <i>S. Aureus</i> leading to gangrene of extremities and amputation.			
Overall postoperative morbidity rate				
Overall morbidity rate				
Notes				*Aesthetic augmentation/re-augmentation #Baker class 4

### Appendix A.3: Efficacy Tables

	Bircoll (1987) n=1	Bircoll & Novack (1987) n=1	Bircoll (1988) n=unknown	Fulton (1992) n=20	Hin (1988) n=3	Illouz (1990) n=19	Vizcaino <i>et al.</i> (1990) n=1
Breast enhancement							
Tissue loss/fat reabsorption	none detectable	none detectable	<20% at 1 year; additional bulk maintained by 10-20% fibrous tissue.	29% (-11 - 61); n=15		1st stage @ 3 months: 93%, @ 6 months: 100%; 2nd stage @ 3 months: 81%, @ 9 months: 100%; 3rd stage @ 3 months: 75%, @ 12 months: 100%	
Volume of fat transplanted (cm3)	90	100		289.5cc (125 - 400)	Case 1&2: 30cc x 2 sessions per breast; Case 3: 30cc x 3 sessions per breast.		30ml in left, 120 ml in right
Breast texture:							lumpy & painful
soft & natural							
slightly firm							
moderately firm							
hard							
Altered sensitivity to nipple/areola							
Other							
Psycho-Social							
Patient satisfaction	"very pleased"	"very pleased"					
Breast feeding experience							
Other							
Other							
Notes							

	Cunningham <i>et al.</i> (2000) n=450	Strom <i>et al.</i> (1997) n=292	Bogetti <i>et al.</i> (2000) n=14
Breast enhancement			
Tissue loss/fat reabsorption			
Volume of fat transplanted (cm3)			
Breast texture:			
soft & natural	71%		
slightly firm	16%		
moderately firm	8.50%		
hard	4%		
Altered sensitivity to nipple/areola			0
Other			Aesthetic result for all patients described by authors as "very satisfactory"
Psycho-Social			
Patient satisfaction	Very satisfied or satisfied: 92.9%; would choose again: 95.9%; would choose - same size: 68%, larger: 20%, smaller: 12%; Patients with firm or hard breasts described implants as: not bothersome (26.9%), not very bothersome (20%), somewhat bothersome (36.9%), very bothersome (16.3%).(1)	*Q1: 64.4   16.1   12.1   4.5   2.8; Q2: 57.9   15.4   13.1   5.5   8.0; Q3: 45.7   20.4   15.6   5.9   12.5; Q4: 51.5   17.0   17.4   6.3   6.9	
Breast feeding experience		46 of 272 under 45 (16.9%) had children. 28 breast fed; 11 reported having problems, 8 perceived to be related to implants (7 of these had periareolar incision). Of the 18 who chose not to breast feed, 7 stated fear of problems with the implants as the main reason.	
Other			
Other			
Notes	(1) Risk factors for dissatisfaction: reconstruction for breast cancer - 7.63 (p=0.011); breast firmness- 6.20 (p<0.001); desire for smaller implant - 2.98 (p=0.020); implant position & augmentation - NS	*Percentages: 5 point likert scale from strongly agree to strongly disagree for each of the following questions: Q1=I am satisfied with the results of my augmentation; Q2=I would recommend the procedure to others; Q3=Breast implant surgery has improved my quality of life; Q4=The implants have improved my sexual attractiveness.	