NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of breast reconstruction using lipomodelling after breast cancer treatment

Restoring breast volume after breast cancer surgery using injections of the patient's own fat

Surgical treatment for breast cancer involves either removal of the breast (a mastectomy) or removal of the tumour and some adjacent breast tissue (breast-conserving surgery or lumpectomy). Following mastectomy, many women choose some type of breast reconstruction. However, after breast-conserving surgery, which can produce a significant deformity, very few options are normally offered. This procedure involves taking fat from the abdomen or thighs and injecting it into the breast in the area of the deformity caused by surgery.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2010 and updated in May 2011.

Procedure name

- Breast reconstruction using lipomodelling after breast cancer treatment

Specialty societies

- British Association of Surgical Oncology
- British Association of Plastic, Reconstructive and Aesthetic Surgeons
- Royal College of Radiologists Breast Group.

Description

Indications and current treatment

Surgery for breast cancer may involve removing the whole of the breast (mastectomy) or part of the breast (breast-conserving surgery). After such surgery, breast reconstruction is often performed in order to create a new breast that is similar in size, shape and texture to the original one. This can be done at the same operation or at a later date.

Several techniques are in use for breast reconstruction. These involve either using prosthetic material (implant) alone, or autologous tissue (tissue from elsewhere in the body, usually the abdomen, buttocks or back), or a combination of the two. When prosthetic material is used alone, an implant is placed under the skin or muscle. Autologous tissue implants may either be a free flap or a 'pedicled' (or 'mobilised') flap with its 'native' blood supply preserved.

Lipomodelling involves the transfer of fat from the abdomen or thighs into the breast. It is used to replace volume after breast reconstruction or to fill defects in the breast following breast-conserving surgery. It can be used on its own or as an adjunct to other reconstruction techniques.

This procedure may also be used for congenital breast deformity or soft-tissue deformity elsewhere on the body.

What the procedure involves

With the patient under general or local anaesthesia, fat cells are harvested from a donor site using needle aspiration with a syringe and cannula. Common donor sites used are the abdomen, outer thigh and flank. The fat is usually washed and decanted with saline, and may be purified via centrifugation to remove dead cells and debris. The aspirate may also be treated with a device that aims to maximise the number of adipose-derived regenerative cells (ADRCs) – which are often called 'stem cells' – that are within it. It is thought that these cells may improve angiogenesis (the growth of new blood vessels from existing ones) and help to regenerate damaged tissue. The fat is then injected into the breast, usually in small parcels and thin strips, at different levels in the subcutis. A degree of fat resorption is common, mostly within the first 6 months following fat transfer. Patients usually have 2 to 4 sessions of lipomodelling depending on their condition.

One of the possible benefits of the procedure is that it can restore volume to the breast without the morbidity associated with other reconstruction techniques. However, there is a concern that it may make it difficult to interpret future mammographic images. There is also a theoretical concern that introducing stem cells into the breast might promote cancer re-growth.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to breast reconstruction using lipomodelling after breast cancer treatment. Searches were conducted of the following databases, covering the period from their commencement to 24 March 2011: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients who have had breast cancer treatment.
Intervention/test	Breast reconstruction using lipomodelling after breast cancer treatment.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 2162 patients from 6 case series and 1 non-randomised comparative study[1–7].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on breast reconstruction using lipomodelling after breast cancer treatment

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
Delay E (2009)[1] **Case series** France Recruitment period: 1998–2008 Study population: patients who have had conservative treatment for breast cancer or breast reconstruction; patients with congenital deformities; patients requesting aesthetic breast surgery. n = **880 procedures (734 for breast reconstruction, 106 for correction of congenital deformities, 30 for aesthetic breast surgery, 10 for the correction of previous surgery defects).** Age: not reported Patient selection criteria: not reported Technique: the procedure was performed with the patient under general anaesthesia in the majority of cases; fat was usually harvested from the abdomen and was prepared by centrifugation. Follow-up: **up to 10 years** Conflict of interest/source of funding: none	Number of patients analysed: **880 procedures** The results were considered 'very good' or 'good' in the majority of cases. Very few results were considered 'moderately good' and no results were considered 'poor'. **Note** - results were evaluated by clinical examination, the patient's opinion and comparison of photographs taken at each postoperative consultation with earlier photographs. Results after correction of sequelae of conservative treatment (absolute figures not stated): • Very good: 50% • Good: 40% Moderately good: 10% 30–40% of the volume gained by fat transfer was gradually lost (confirmed by 3-dimensional imaging [interferometry]). Volume was stable after 3–4 months and remained so if the patient maintained a constant weight.	Imaging in the majority of reconstructed breasts was normal, with some images of oily cysts and fat necrosis. Oily cysts occurred in 15% of cases (absolute numbers not stated). The authors noted that the most complex situation concerned lipomodelling for the sequelae of conservative treatment because fat necrosis developed in about 20% of patients (absolute numbers not stated) from this population; lipomodelling doubles this rate by generating mainly oily cysts, but occasionally more complex lesions of fat necrosis. One case of unevenness in the suprailiac region (harvesting site) required secondary correction of a hollow area by lipomodelling. • Local infection in harvesting site = 0.1% (1/880) (treated by antibiotics, with no long-term consequences). • Infections in the breast = 0.7% (6/880) (resolved with topical treatment and antibiotics with no impact on the final result). • Intraoperative pneumothorax = 0.1% (1/880) (probably caused by the transfer cannula piercing the pleura, resolved with insertion of pleural drain). • Focal clinical fat necrosis = 3% (absolute numbers not stated). • No reported cases of fat embolism. 10 years of oncological follow-up did not reveal any increased risk of local recurrence after mastectomy or after conservative treatment.	**Follow-up issues**: • All patients were clinically followed-up after 15 days, 3 months and 1 year. Patients who previously had breast cancer were then followed by their oncologist, who referred them back to the study centre if there was any change. For the other patients, long-term follow-up was done by shared computerised medical records. • No increased risk of local cancer recurrence reported but numbers and statistical analysis not provided • Details of how patient opinions gathered, not provided **Other issues**: • The authors noted that the incidence of fat necrosis was higher during the early experience (15% in the first 50 cases of the series).

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Illouz YG (2009)[2]

Case series

France

Recruitment period: 1983–2007

Study population: patients with breast asymmetry after mastectomy and breast reconstruction (n = 381); patients with congenital breast asymmetry (n = 54); patients requesting bilateral breast augmentation (n = 385).

n = 820 patients

Mean age: 46 years (range 19–78)

Patient selection criteria: patients with the American College of Radiology Breast Imaging Reporting and Data System category 1 or 2 (negative or benign preoperative mammography and ultrasound examination). Mastectomy patients were disease-free for at least 1 year after breast reconstruction.

Technique: Fat was aspirated using a syringe from abdominal, flank, thigh and knee fat areas. The aspirated fat was decanted before grafting into the subcutaneous and intraglandular spaces of the breast (25–180 ml of fat was grafted into each breast in each session).

Mean follow-up (years): 11.3 (range 2–25)

Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 820

Mean number of sessions needed to achieve the desired result = 3 (range 1–5)

Long-term breast asymmetry = 4.1% (34/820) (‘long-term’ not otherwise defined)

The report states: ‘The majority of the women had a significant improvement in their breast size and/or shape postoperatively.’</td>
<td>Complications
• Ecchymosis = 9.3% (76/820).
• Striae = 4.4% (36/820).
• Haematoma = 1.5% (12/820) (resolved without any intervention).
• Infection = 0.6% (5/820) (treated with antibiotics).

The authors noted that the majority of complications resulting from the procedure were seen during the first 6 months after each session. They believe that breast lesions, including calcifications, cysts and cancer, that are not apparent in the first year after the procedure, may not be directly associated with the lipomodelling. They state that this was confirmed by the long-term follow-up of 230 patients who were followed up yearly with mammographic examination for a mean of 11 years.

Classification of the patients who underwent mammographic examination 6 months and 1 year after their primary breast autologous fat transplantation (n = 670)
<table>
<tr><th rowspan="2">ACR BI-RADS category</th><th colspan="2">Percentage of patients (%)</th></tr>
<tr><th>6 months</th><th>1 year</th></tr>
<tr><td>0 (incomplete)</td><td>10</td><td>4.5</td></tr>
<tr><td>1 (negative)</td><td>41</td><td>47</td></tr>
<tr><td>2 (benign finding)</td><td>23.5</td><td>31</td></tr>
<tr><td>3 (probably benign finding)</td><td>25.5</td><td>17.5</td></tr>
<tr><td>4 (suspicious abnormality)</td><td>0</td><td>0</td></tr>
<tr><td>5 (highly suggestive of malignancy)</td><td>0</td><td>0</td></tr>
</table>
</td>
<td>Follow-up issues:
• 82% (670/820) of patients underwent mammography and ultrasonography 6 months and 1 year after the primary lipomodelling.
• 28% (230/820) of patients had long-term follow-up (mean 11 years) with annual mammograms. The results of these were not presented.

Study design issues:
• Consecutive patients.
• The rate of fat resorption was not objectively measured.

Study population issues:
• Only a proportion of patients had the procedure after breast cancer treatment.</td>
</tr>
</table>

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
Rigotti G (2010)[3] **Case series** Italy Recruitment period: 2000–5 Study population: patients who have had a modified radical mastectomy for breast cancer. n = **137** Median age (years): 46.5 (range 20–68) Patient selection criteria: patients who had modified radical mastectomies and at least a 3-year follow-up by March 2009. Technique: patients usually had 2–4 sessions of fat grafting at intervals of 2 to 3 months. The volume administered varied according to the amount of radiation injury, whether a prosthesis was present, and the level of capsular contraction when a prosthesis was present. Fat was harvested from the knee, abdomen or trochanteric region and prepared by centrifugation. Placement of the lipoaspirate was performed under local anaesthesia with deep sedation. **Median follow-up (years): 7.6 (range 3–19)** Conflict of interest/source of funding: not reported	Number of patients analysed: **137**	**Recurrence incidence** 9 local and 9 distant recurrences were observed in 16 patients (11.7%). 4 local recurrences occurred before fat grafting and 5 afterwards. In period I (from surgery to first graft), annual local recurrence rate = 9.1 per 1000 patient-years. In period II (from first fat graft to end of follow-up), annual recurrence rate = 7.2 per 1000 person-years. During the follow-up period, 2 patients died with no signs of local or distant recurrences. At 5-year follow-up, 95.6% of patients were free from local relapse. At 8-year follow-up, the relapse-free probability was 91.5%. At 5-year follow-up, 97.7% of patients were free from distant metastasis. At 8-year follow-up, the relapse-free probability was 92.4%. Overall probability of developing any recurrence after 5-year of follow-up = 5.9%. Crude cumulative incidence of ipsilateral locoregional relapses = 6.5% (median follow-up = 7.6 years). The authors concluded that the use of lipoaspirate in breast reconstruction does not increase the incidence of local recurrence of breast cancer after modified radical mastectomy.	**Study design issues**: • A within-group comparison was done for each patient, comparing the period immediately after surgery and before the first fat graft with the period starting immediately after the first fat graft to the end of follow-up. **Study population issues**: • 16% (22/137) of patients had radiotherapy treatment prior to lipomodelling.

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
Missana MC (2007)[4] **Case series** France Recruitment period: 2001–5 Study population: patients who have had breast reconstruction or conservative breast treatment. n = **69 patients; 74 breasts** Mean age (years): 51 (range 21–73) Patient selection criteria: no details listed. 60 patients underwent autologous fat transfer to improve the result of reconstructive breast surgery, 30 of whom had undergone parietal radiotherapy prior to breast reconstruction. In 9 patients the aim was to correct deficits caused by conservative treatment. Technique: the procedure was performed under general anaesthesia; fat was usually taken from the abdominal subcutaneous tissues and was centrifuged. Excess correction was not performed; a second or third procedure was done at a later date if necessary. The volume of fat injected ranged from 40 ml to 360 ml. **Mean follow-up: 11.7 months (range 1 month–3.2 years)** Conflict of interest/source of funding: not reported.	Number of patients analysed: **69 (74 breasts)** **Reinjection required to achieve a satisfactory result = 14.9% (11/74)** **Improvement (as assessed by an independent panel of 2 surgeons examining preoperative and postoperative photographs):** • **Good to very good = 86.5% (64/74)** • **Moderate = 13.5% (10/74)** (primarily due to the insufficient quantity of adipose material that could be removed from these patients)	No immediate complications such as haematoma, infection, cellulitis or thromboembolism were observed. Liponecrotic cysts (identified on MRI scans at 3-month follow-up) = 6.8% (5/74). No cases of microcalcifications suggestive of malignancy were observed on radiology (assessed using ACR BI-RADS grading system).	**Follow-up issues**: • MRI scans with contrast medium were done preoperatively and at 3 months after the fat transfer. **Study population issues**: • Different techniques were used for the initial reconstruction (implant alone, latissimus dorsi flap plus implant or autologous flap). The authors reported improved cosmetic results irrespective of the technique used. **Other issues**: • The authors note that the main limitation to the procedure is the quantity of fat available for grafting. • The time period between the original surgery and lipomodelling was not stated in the paper.

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
Spear SL (2005)[5] **Case series** USA Recruitment period: 1993–2003 Study population: patients with contour deformities in reconstructed breasts. n = **37 patients; 43 breasts** Age: not reported Patient selection criteria: patients who underwent fat injection to address contour deformities in their reconstructed breasts and whose medical records could be located. Technique: fat was harvested using a low-pressure syringe lipoaspiration system and then treated with repetitive saline washing until all gross blood products were removed. The amount of fat injected per breast during each procedure ranged from 30 ml to 260 ml. Mean follow-up: **15 months (range 3 weeks–7 years)** Conflict of interest/source of funding: not reported	Number of patients analysed: **37 (43 breasts, 47 treatment sessions)** Repeat procedure(s) = 8.1% (3/37) Degree of improvement after each treatment (assessed by an independent, blinded panel of physician observers judging preoperative and postoperative photographs): • **Substantial improvement = 21.3% (10/47)** • **Minimal to moderate improvement = 63.8% (30/47)** • **No improvement = 14.9% (7/47)**	**Complications = 8.5% (4/47 treatments)** • Cellulitis = 2.3% (1/43) (presented 2 weeks postoperatively, resolved with antibiotics without implant removal). • Small, superficial lumps = 7.0% (3/43) (2 were removed and diagnosed as liponecrotic cysts). No implant ruptures occurred as a result of fat injection.	**Study design issues**: • Retrospective review. • Routine post-operative mammography not undertaken. **Study population issues**: • Of the 43 treated breasts, 25 were reconstructed with implants, 17 were reconstructed with TRAM flaps and 1 was reconstructed with a TRAM flap and implant. **Other issues**: • The time period between the original surgery and lipomodelling was not stated in the paper.

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Panettiere P (2009)[6]

Non-randomised comparative study

Italy

Recruitment period: 2006–8

Study population: patients with irradiated breasts reconstructed with prostheses after mastectomy for cancer.

n = 61 patients; 62 breasts (20 serial free fat grafts vs 42 standard treatment only)

Mean age: 49 years

Patient selection criteria: patients with irradiated breasts reconstructed with prostheses after mastectomy for cancer. All patients presented with mild to severe superficial irregularities and different degrees of skin thinning.

Technique: Fat was harvested from the abdomen, hips, or the trochanteric area and then washed and decanted with saline. Minimal overcorrection (10–15%) was used. The volume of fat injected in each session ranged from 8 to 50 ml (mean 24.5 ml). Fat implantation was repeated after a minimum of 20 days until the result was stable or the patient was satisfied.

Mean follow-up: not reported

Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 61 (62 breasts; 20 vs 42)

Mean number of sessions = 3.4 ± 1.9 (range 1–7)

Mean aesthetic result in lipomodelling group (evaluated using a 5-point scale: 5 = very good, 4 = good, 3 = acceptable, 2 = poor, 1 = very poor):
• Baseline = 2.7 ± 0.8
• 3 months after last fat transfer = 4.3 ± 0.6
p ≤ 0.0005

The average aesthetic result was significantly worse in the standard treatment group (3.1 ± 1.6) than in the lipomodelling group (4.3 ± 0.6, p ≤ 0.032) at 3-month follow-up.
Outcome of serial lipomodelling on the effects of radiotherapy (based on the LENT-SOMA scoring system, lower scores denote better outcome)
<table>
<tr><th></th><th>Baseline (n = 20)</th><th>3 months after last fat transfer (n = 20)</th><th>p value</th></tr>
<tr><td>Pain</td><td>1.1 ± 1.1</td><td>0.1 ± 0.3</td><td>≤ 0.002</td></tr>
<tr><td>Teleang-iecta</td><td>0.9 ± 1.1</td><td>0.1 ± 0.2</td><td>≤ 0 006</td></tr>
<tr><td>Atr phy</td><td>1.7 ± 1.1</td><td>0.4 ± 0.5</td><td>≤ 0.000</td></tr>
<tr><td>Br st oedema</td><td>0.8 ± 1.0</td><td>0.1 ± 02</td><td>≤ 0.02</td></tr>
<tr><td>Fibrosis</td><td>1.7 ± 0.9</td><td>0.5 ± 0.6</td><td>≤ 0.0001</td></tr>
</table>
Superficial irregularities completely resolved in 55% (11/20) and significantly improved in 45% (9/20) of cases.</td>
<td>The report states: ‘There were no significant complications.’</td>
<td>Study design issues:
• All 61 patients were offered the procedure and 20 received it. The remaining patients who did not receive it were used as controls. The ‘standard treatment’ was not described.
• The LENT-SOMA scores of the control patients were only reported at baseline and were not statistically significantly different to the baseline results of the treatment group.

Study population issues:
• There were no statistically significant differences in LENT-SOMA scores between the two groups.</td>
</tr>
</table>

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
	Implant exposure requiring prosthesis removal (in patients with severely thinned flaps) after mean follow-up of 17.6 months: • Lipomodelling group = 0 out of 4 • Control group = 2 out of 2 One patient in the treatment group had a capsular contracture, which was downgraded after one fat-transfer session. No contracture relapse was observed after 20 months.		

Abbreviations used: ACR BI-RADS, American College of Radiology Breast Imaging Reporting and Data System; LENT-SOMA, Late Effects Normal Tissue Task Force – Subjective, Objective, Management, Analytic; MRI, magnetic resonance imaging; TRAM, transverse rectus abdominis muscle

Study details	Key efficacy findings	Key safety findings	Comments
Rietjens M (2011)[7] **Case series** Italy Recruitment period: 2005–8 Study population: patients with unaesthetic breast defect after previous breast surgery. **n = 158 patients (155 oncological patients), 194 breast fat grafting procedures** Mean age: 48 years (range 22–70) Patient selection criteria: patients with previous breast surgical procedure either for oncological or functional reasons, which led to an unaesthetic breast defect. Only patients who were free of local breast disease were considered eligible. Technique: the procedure was performed with the patient under local or general anaesthesia. The harvested fat was centrifuged before injecting into the defect area. **Follow-up: 6 months** Conflict of interest/source of funding: none	Number of patients analysed: 158 Mean estimated volume of main defect = 19.7 ml Mean volume of fatty tissue injected = 48 ml (range 6–183).	There were no complications in any of the donor sites. Immediate complications (194 procedures): • liponecrosis = 2.6% (5/194) • cellulitis = 0.5% (1/194) • abscess = 0.5% (1/194). (All were conservatively managed; liponecrosis was drained in the outpatient department and the other 2 patients were treated with oral antibiotics.) Among the 7 immediate complications, 6 were in patients who previously received locoregional radiotherapy. Abnormal mammogram after fat grafting = 5.2% (4/77) (All were classified as benign not requiring further investigation.) 1 local recurrence was observed at follow-up, diagnosed about 2 weeks after breast fat grafting. The authors note that this was probably misdiagnosed at the fat grafting procedure and was unlikely to be have been caused by it.	**Follow-up issues:** • 6% (9/158) of patients were lost to follow-up. **Study population issues:** • 98% of patients had a history of breast cancer, treated by mastectomy and reconstruction (n = 93) or conservative surgery (n = 62). **Other issues:** • The average interval between oncological interventions to fat grafting procedure was 35 months. In case undergoing radiation treatment, at least 6 months was left after completion of radiotherapy. • Only 17% (26/158) of patients underwent more than 1 fat grafting procedure.

Efficacy

Aesthetic assessment

In a case series of 880 procedures, including 734 for breast reconstruction, the results after correction of sequelae of conservative treatment were judged to be 'very good' in 50% of procedures, 'good' in 40% and 'moderately good' in 10% (absolute numbers not stated; results were evaluated by clinical examination, the patient's opinion and comparison of photographs were taken at each postoperative consultation with earlier photographs)[1].

A case series of 820 patients, including 381 with asymmetry after mastectomy and breast reconstruction, reported that the majority of patients had a 'significant improvement in their breast size and/or shape postoperatively'[2]. Long-term breast asymmetry was reported in 4% (34/820) of patients.

A case series of 69 patients (74 breasts) reported a 'good to very good' improvement in 86.5% (64/74) of breasts and a moderate improvement in 13.5% (10/74) (as assessed by an independent panel of 2 surgeons examining preoperative and postoperative photographs)[4].

A case series of 37 patients (43 breasts) reported a substantial improvement after 21% (10/47) of treatment sessions and a minimal to moderate improvement after 64% (30/47) of treatment sessions (assessed by an independent, blinded panel of physician observers judging preoperative and postoperative photographs)[5].

A non-randomised comparative study of 61 patients (62 breasts) including 20 patients treated by lipomodelling reported that the mean aesthetic result improved from 2.7 at baseline to 4.3 at 3 months after the last fat transfer ($p \leq 0.0005$; evaluated using a 5-point scale: 5 = very good, 4 = good, 3 = acceptable, 2 = poor, 1 = very poor)[6]. This was significantly better than the average aesthetic result in the standard treatment group (3.1 ± 1.6, $p \leq 0.032$) at 3-month follow-up.

Safety

Infection

In a case series of 880 procedures, including 734 for breast reconstruction, infections in the breast were reported in < 1% of procedures (6/880) (all resolved with topical treatment and antibiotics with no impact on the final result)[1]. There was also 1 report of local infection in the harvesting site (successfully treated with antibiotics). A case series of 37 patients reported cellulitis in 2% (1/43) of breasts (presented 2 weeks postoperatively, resolved with antibiotics without implant removal)[5]. A case series of 158 patients reported cellulitis and abscess in 1 patient each[7].

Fat necrosis/liponecrotic cysts

In the case series of 880 procedures, a 3% rate of fat necrosis was reported (absolute numbers not reported)[1]. In the case series of 69 patients, liponecrotic cysts were reported in 7% (5/74) of breasts at 3-month follow-up[4]. In the case series of 37 patients, liponecrotic cysts were reported in 5% (2/43) of breasts[5]. In the case series of 158 patients, liponecrosis was reported after 3% (5/194) of procedures[7].

Intraoperative pneumothorax

In the case series of 880 procedures, there was one report of an intraoperative pneumothorax (probably caused by the transfer cannula piercing the pleura, resolved with insertion of pleural drain)[1].

Recurrence

The case series of 880 procedures reported that 10 years of oncological follow-up did not reveal any increased risk of local recurrence after mastectomy or after conservative treatment[1].

In a case series of 137 patients who had a modified radical mastectomy for breast cancer, 95.6% of patients were free from local relapse at 5 years follow-up[3]. At 8 years follow-up, the relapse-free probability was 91.5%. At 5 years follow-up, 97.7% of patients were free from distant metastasis. At 8 years follow-up, the relapse-free probability was 92.4%.

Validity and generalisability of the studies

- The two largest case series included some patients with indications other than breast cancer treatment[1,2].
- Five of the six studies were from France and Italy.
- Several different breast reconstruction techniques were used prior to lipomodelling, both within and between studies.
- Preparation of the harvested fat varied between studies; the fat was centrifuged prior to transfer in 3 studies[1,3,4], washed with saline in 2[5,6] and just decanted in 1[2].

- One study only included patients who had received radiotherapy treatment and focused on the use of fat transfer to reduce the complications of radiotherapy[6].
- No studies compared cancer recurrence rates between lipomodelling and a control group.

Existing assessments of this procedure

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) published a report on autologous fat transfer for cosmetic and reconstructive breast augmentation in September 2010[8]. The report stated that the available literature was poor with a complete lack of comparative evidence. The report concluded: 'autologous fat transfer 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. The efficacy of autologous fat transfer cannot be determined from the literature included in this review.

'The recommendations state that 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. 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.'

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Laparoscopic mobilisation of the greater omentum for breast reconstruction. NICE interventional procedures guidance 253 (2008). Available from www.nice.org.uk/guidance/IPG253

Clinical guidelines

- Advanced breast cancer: diagnosis and treatment. NICE clinical guideline 81 (2009). Available from www.nice.org.uk/guidance/CG81

- Breast cancer (early and locally advanced): diagnosis and treatment. NICE clinical guideline 80 (2009). Available from www.nice.org.uk/guidance/CG80

Cancer service guidance

- Improving outcomes in breast cancer. NICE guidance on cancer services (2002). Available from www.nice.org.uk/guidance/CSGBC

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr M Lee (Association of Breast Surgery), Mr P Harris (British Association of Plastic Reconstructive and Aesthetic Surgeons), Mr L Martin, Mrs E Weiler-Mithoff (Royal College of Radiologists Breast Group).

- Three Specialist Advisers perform the procedure regularly and one has never performed it.
- One Specialist Adviser considered the procedure to be novel and of uncertain safety and efficacy, one described it as established practice and another considered it to be first in a new class of procedure. The third Specialist Adviser stated that fat grafting has been used for many years and there have been new refinements of the technique.
- Adverse events known from reports or experience include infection, altered sensation, fat necrosis, oil cysts, haematoma, calcification, donor and breast site deformity, complete resorption of fat, uncertain findings on clinical surveillance and mammography.
- Theoretical adverse events or safety concerns include fat embolism, damage to breast implants, increased rate of breast cancer recurrence and/or difficulty in detecting recurrent disease.
- Key efficacy outcomes include long-term retention of fat graft volume, aesthetic assessment of breast shape, quality of life and body image assessments.

- There are concerns about the ability to correct large defects adequately, long-term cosmesis, survival of grafted fat and postoperative factors such as smoking and certain medications that may affect revascularisation of the graft.
- Training in breast reconstructive surgery is required.
- In the setting of breast-conserving surgery, close follow-up is necessary.
- One Specialist Adviser thought that the procedure would have a major impact on the NHS, in terms of numbers of patients eligible for treatment and use of resources; two thought the impact would be moderate and the other Specialist Adviser considered the potential impact to be minor.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- There are a number of relevant studies published in French, which have not been included. Table 2 does, however, include 2 large case series from French centres, published in English.
- There are a number of studies describing fat transfer for cosmetic augmentation in patients who have not had breast cancer; these have not been included.

References

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5. Spear SL, Wilson HB, Lockwood MD (2005) Fat injection to correct contour deformities in the reconstructed breast. Plastic and Reconstructive Surgery 116: 1300–5.

6. Panettiere P, Marchetti L, Accorsi D (2009) The serial free fat transfer in irradiated prosthetic breast reconstructions. Aesthetic Plastic Surgery 33: 695–700.

7. Rietjens M, De Lorenzi F, Rossetto F et al. (2011) Safety of fat grafting in secondary breast reconstruction after cancer. Journal of Plastic, Reconstructive and Aesthetic Surgery 64: 477–84.

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

Appendix A: Additional papers on breast reconstruction using lipomodelling after breast cancer treatment

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Coleman SR, Saboeiro AP. (2007) Fat grafting to the breast revisited: safety and efficacy. Plastic and Reconstructive Surgery 119: 775–85.	Case series n = 2	All women had a 'significant improvement in their breast size and/or shape postoperatively'. Free fat-grafting should be considered as an alternative or adjunct to breast augmentation and reconstruction procedures.	Larger studies are included. Paper also includes 15 cases with other indications.
Pulagam SR, Poulton T, Mamounas EP. (2006) Long-term clinical and radiologic results with autologous fat transplantation for breast augmentation: case reports and review of the literature. Breast Journal 12: 63–5.	Case report n = 1	Mammogram revealed a partially calcified mass, compatible with fat necrosis. Ultrasound demonstrated a hypoechoic mass compatible with fat necrosis.	Complication is already described in table 2.
Rigotti G, Marchi A, Galie M et al. (2007) Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: a healing process mediated by adipose-derived adult stem cells. Plastic and Reconstructive Surgery 119: 1409–22.	Case series n = 20 Mean follow-up = 30 months	There was systematic improvement or remission of symptoms in all evaluated patients. Statistically significant decrease in LENT-SOMA scores.	Larger studies are included. The aim of the lipoaspirate transplant was to treat radiation side effects.
Salgarello M, Visconti G, Farallo E. (2010) Autologous fat graft in radiated tissue prior to alloplastic reconstruction of the breast: report of two cases. Aesthetic Plastic Surgery 34: 5–10.	Case reports n = 2 Mean follow-up = 15 months	There were no postoperative complications. There was a good aesthetic outcome and high patient satisfaction.	Larger studies are included.
Serra-Renom JM, Munoz-Olmo JL, Serra-Mestre JM. (2010) Fat grafting in postmastectomy breast reconstruction with expanders and prostheses in patients who have received radiotherapy: formation of new subcutaneous tissue. Plastic and Reconstructive Surgery 125: 12–18.	Case series n = 65 Mean follow-up = 1 year	No complications were recorded with the fat injections. Patients mean satisfaction rating = 4 (scale 1 [low] to 5 [high]) Capsular contracture was never above 1 on the Baker classification. The addition of fat grafting led to better outcomes with the creation of new subcutaneous tissue, accompanied by improved skin quality.	The paper describes fat grafting as part of a bigger procedure, encompassing the whole breast reconstruction.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Sinna R, Delay E, Garson S et al. (2010) Breast fat grafting (lipomodelling) after extended latissimus dorsi flap breast reconstruction: a preliminary report of 200 consecutive cases. Journal of Plastic, Reconstructive and Aesthetic Surgery 63: 1769–77.	Case series n = 200 Follow-up = not reported	Very satisfactory results = 94.5% 80% of patients were very satisfied and 20% were satisfied with the results. Complications = 1.5% (local infection, pneumothorax)	The same patients are likely to be included in Delay et al (2009), which is included in table 2.

Appendix B: Related NICE guidance for breast reconstruction using lipomodelling after breast cancer treatment

Guidance	Recommendations
Interventional procedures	**Laparoscopic mobilisation of the greater omentum for breast reconstruction. NICE interventional procedures guidance 253 (2008).** 1.1 Current evidence on the safety and efficacy of laparoscopic mobilisation of the greater omentum for breast reconstruction is based on limited numbers of patients. However, it is a variation of the open technique, the safety and efficacy of which are known. Therefore, the evidence is considered adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 During consent, patients should be informed that the volume of omentum may be insufficient for full reconstruction, and that further, more complex procedures may be required. 1.3 Patient selection should be carried out in the context of a multidisciplinary team experienced in the management of patients requiring breast reconstruction, and should include a breast cancer specialist and a surgeon experienced in laparoscopic techniques.
Clinical guidelines	**Advanced breast cancer: diagnosis and treatment. NICE clinical guideline 81 (2009)**. None of the key recommendations relate to breast reconstruction. **Breast cancer (early and locally advanced): diagnosis and treatment. NICE clinical guideline 80 (2009).** 1.5.1 Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.
Cancer service guidance	**Improving outcomes in breast cancer. NICE guidance on cancer services (2002).** A range of primary operations should be available. If the cancer is not too large or diffuse, surgical options include mastectomy (removal of the whole breast) or breast conserving surgery (wide local excision or lumpectomy). In such cases, the choice should be made jointly by the surgeon and the patient, who should be

	fully informed of all the options and their potential risks, benefits and implications for further treatment. The proportion of each type of operation done will reflect local differences in case-mix and women's preferences. Surgeons should have the technical skills to support a full range of choices. Suitable patients should be offered breast conserving surgery. Breast reconstruction should be available at the time of, or after, mastectomy, provided either by a plastic surgeon or a breast surgeon trained in the appropriate techniques.

Appendix C: Literature search for breast reconstruction using lipomodelling after breast cancer treatment

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	24 3 2011	Issue 3 of 12, Mar 2011	1
Database of Abstracts of Reviews of Effects – DARE (CRD website)	24 3 2011	March 2011	0
HTA database (CRD website)	24 3 2011	March 2011	0
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	24 3 2011	Issue 1 of 4, Jan 2011	3
MEDLINE (Ovid)	24 3 2011	1948 to March Week 2 2011	19
MEDLINE In-Process (Ovid)	24 3 2011	Mar 22 2011	35
EMBASE (Ovid)	24 3 2011	1980 to 2011 Week 11	20
CINAHL (NLH Search 2.0 or EBSCOhost)	25 3 2011	March 2011	28
Zetoc	25 3 2011	March 2011	7

Trial sources searched on 26/28 October 2010

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched on 26/28 October 2010

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Transplantation, Autologous/
2	Adipose Tissue/
3	(adipose adj3 derive* adj3 cell*).tw.
4	(autologous* adj3 (fat graft* or fat-graft* or graft* or transplant*)).tw.
5	(fat adj3 (transfer* or transplant* or graft*)).tw.
6	(Oncoplastic adj3 surgery).tw.
7	Lipoaspirat*.tw.
8	(lipomodel* or lipo model* or lipo-model*).tw.
9	tissue-regenerat*.tw.
10	(tissue* adj3 (regenerat* or transplant*)).tw.
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	Breast Neoplasms/
13	(breast adj3 (cancer* or carcinoma* or neoplasm* or tumor* or tumour* or adenocarcinom* or malignan* metastas*)).tw.
14	12 or 13
15	Reconstructive Surgical Procedures/
16	Mammaplasty/
17	(mammaplast* or mammoplast*).tw.
18	(breast* adj3 reconstruct*).tw.
19	(reconstruct* adj3 surg*).tw.
20	(breast-conserv* adj3 surg*).tw.
21	(breast adj3 (conserv* or lumpectom*)).tw.
22	(breast adj3 deform*).tw.
23	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	14 and 23
25	11 and 24
26	Animals/ not Humans/

27	25 not 26