NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endoscopic mastectomy and endoscopic wide local excision for breast cancer

Treatment for early breast cancer usually involves surgery to remove all or part of the breast. In this keyhole procedure, part or all of the breast tissue is removed using special instruments inserted through small skin incisions. The skin envelope of the breast and nipple are left intact, ready for an implant that can be inserted during the same operation.

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 September 2008.

Procedure name

- Endoscopic mastectomy and endoscopic wide excision for breast cancer

Specialty societies

- British Association of Surgical Oncology (BASO)
- British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS).

Description

Indications and current treatment

Breast cancer is the most common cancer in women in the UK. The most common presentation is a lump or mass in the breast. However, patients within certain age groups may be diagnosed with breast cancer at an asymptomatic stage through the breast screening programme.

There are several types of breast cancer. Ductal carcinoma in situ (DCIS) is a very early form of non-invasive breast cancer. The cancer cells are contained inside the milk ducts of the breast and have not spread into the surrounding breast tissue. If it is not treated, it may develop into an invasive cancer.

Breast cancer is usually categorised into four stages and three grades. Stage 1 describes a tumour of less than 2 cm in diameter that has not spread to the axillary lymph nodes or any other organs. At stage 4, the tumour has spread to other parts of the body such as the lungs, liver or bones and is known as 'advanced'. Grade 1 or low-grade cancer is slow growing and the tumour cells resemble normal cells. In grade 2 or intermediate grade cancer, the cells are moderately differentiated and grow at a faster rate. Grade 3 or high-grade cancer is fast growing and the cells are poorly differentiated.

Treatment depends on the type, stage and grade of the breast cancer. Surgery is often the first option for early breast cancer (stages 1–3) management and may involve removing the whole breast (mastectomy) or part of the breast ('conservative' or 'breast-conserving surgery'). It can take the form of lumpectomy, wide local excision or segmentectomy. Skin-sparing mastectomies which involve the use of a muscle flap have also been used. Breast tissue excision can be accompanied by sentinel node sampling or axillary lymph node clearance, if appropriate. Breast reconstruction may be appropriate for some patients, using autologous flaps and/or implant insertion, and may take place as part of the same operation that removes the tumour, or as a subsequent operation. Radiotherapy, chemotherapy or hormone therapy may be administered as an adjuvant to surgery to lower the risk of local tumour recurrence.

What the procedure involves

These procedures are performed with the patient under general anaesthesia. The patient is placed in a supine position with their arm abducted to 90°. The location of the tumour is confirmed by palpation, mammography, ultrasonography, MRI, or a combination of these.

These procedures are usually performed through an axillary incision, which ranges from 2.5 to 7 cm (more recent studies use a 2.5 cm incision). Depending on the location of the tumour and size of the breast, they also can be performed through a periareolar incision or with the use of both an axillary and a periareolar incision.

Initially, an endoscopic sentinel node biopsy may be performed through one of these incisions. If the results of the biopsy are positive, endoscopic axillary lymph node dissection may be performed.

Under the guidance of an endoscope, carbon dioxide insufflation is used to create a working space, and the breast tissue dissected (often by using electrocautery or a harmonic scalpel), which is held open with external skin retractors in order to perform the excision.

For an endoscopic mastectomy, the mammary gland is separated from the muscle and removed.

For an endoscopic wide excision, the tumour and the breast tissue are separated from the muscle. Tumour margins of the dissected tissue may be checked for malignancy by frozen section and, and if excision margins are found to be positive, more breast tissue may be removed.

Reconstruction of the breast with an implant or autologous tissue is often done at the same time as these procedures through the same incisions used to remove breast tissue. Drains are inserted and the incisions closed.

As with other types of breast cancer surgery, adjuvant radiotherapy, chemotherapy or hormonal therapy may be considered if clinically appropriate.

List of studies included in the overview

This overview is based on approximately 809 patients, from one non-randomised trial[1] and eight case series[2,3,4,5,6,7,8,9,10].

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

Efficacy

Survival and local control

A non-randomised controlled trial comparing 21 patients treated by endoscopic mastectomy to 25 patients treated by subcutaneous mastectomy without an endoscope reported that all patients were alive at a median 19.2-month follow-up (range 5.8–35.2 months)[1].

A case series of 551 patients treated by endoscopic mastectomy reported distant-metastasis-free survival rate of 100% in patients who presented with ductal carcinoma in situ (n = 47), 96% in patients with T1 tumours (n = 190), and 91% in patients with T2 tumours (n = 314) at 66-month follow-up. Overall survival was reported to be 100%, 97%, and 96% in these groups, respectively (according to Kaplan-Meier survival analysis) [9].

The same case series reported local recurrence in 4% (23/551) of patients after a mean follow-up of 38.4 months. A case series of 82 patients with malignant tumours treated by endoscopic mastectomy (video-assisted breast surgery) reported no locoregional recurrence at a mean follow-up of 25 months (recurrence was not reported for the comparator, conventional breast therapy)[3]. A case series which included the above 82 patients plus an additional 49 patients reported no locoregional recurrence at a mean follow-up of 28 months (maximum of 56 months)[2].

A case series of 33 patients treated by endoscopic mastectomy reported a 100% overall survival and no locoregional recurrence or distant metastases at a mean follow-up of 51.2 months[10].

A case series of 20 patients also reported that 1 woman required total salvage endoscopic mastectomy because of microcalcification in her remnant breast (shown on 6-month mammography).

No other studies reported on cancer recurrence or survival outcomes.

Adequacy of tumour resection

In the non-randomised controlled trial of 46 patients comparing endoscopic mastectomy with subcutaneous mastectomy without an endoscope, histological examination revealed positive resection margins in 5% (1/21) and 8% (2/25) of patients, respectively[1]. Each of these patients required radiation therapy 4 weeks after surgery.

The case series including 82 and 131 patients (which included the first 82 patients) with malignant tumours reported clear permanent histological margins in all patients (within 5 mm from the stump)[2,3]. However, the earlier study of 82 patients also reported safety events in 4 patients who required an additional resection because of positive intra-operative fast-frozen surgical margins.

Two case series of 20 and 6 patients reported positive histological margins in 1 patient each[7,5]. The first required total salvage endoscopic mastectomy 10 days after the first operation; the second was treated with ‘additional adjuvant radiotherapy’.

A case series of 9 patients reported clear histological margins in all patients[8]. However, the first study reported that 2 patients required a modified radical mastectomy because of diffuse ductal spread and direct skin invasion (time of re-operation not stated).

Cosmesis

The non-randomised controlled trial of 46 patients reported that 86% (18/25) and 60% (15/25) of patients treated by endoscopic mastectomy and subcutaneous mastectomy without an endoscope were considered to have an ‘excellent’ cosmetic score (that is, both the patient and surgeon were satisfied with the symmetry of the breast)[1]. The difference was not considered statistically significant.

The case series of 551 patients reported overall patient satisfaction results from a postal questionnaire 6 months following surgery: 76% (366/481) reported 'good' results, 14% (66/481) reported 'fair' results and 10% (49/481) reported 'poor' results (not further defined; only 481 patients responded)[9].

In the case series including 82 patients treated by endoscopic mastectomy, cosmetic results were reported by patients to be 'good'[3]. According to a scoring system, ABNSW (asymmetry, breast shape, nipple shape, skin condition and woundcare), the mean score was 13.5 (on a scale of 0 [poor] to 15 [excellent]).

The case series of 20 patients reported that 89% (17/19) of patient-assessed cosmesis was excellent or good (using the patient's own criteria) at 3-month follow-up[7]. Reconstruction was not performed at the same time as mastectomy in these patients.

The case series of 9 patients reported a mean patient-satisfaction score to be 8/10 (using the Patient Self-Assessment Satisfaction Index ranging from 0 [very dissatisfied] to 10 [very satisfied])[8].

The case series of 7 patients reported 'satisfaction' in the shape and size of the breasts at 1- to 22-month follow-up (not specified if patient or clinician reported)[4].

A case series of 6 patients reported that they were 'satisfied' with the condition of the breast after surgery[6].

Operative time

The non-randomised controlled trial of 46 patients reported mean operative times of 237 and 176 minutes in the endoscopic mastectomy and subcutaneous mastectomy groups, respectively[1].

The case series including 82 patients with malignant tumours reported that the mean operating time for all patients treated by endoscopic mastectomy (for benign and malignant tumours) was 173 minutes compared with 149 minutes in 34 patients treated by conventional breast conserving therapy[3] (conventional therapy not described).

In the case series of 20 patients (whose surgery did not include reconstruction), the mean operative time of the surgery was 163 minutes (excluding 3 patients who also had axillary node resection)[7].

In case series of 9, 7, 6, and 6 patients, the mean operative time ranged from 165 to 445 minutes[8,4,5,6]. The first case series of 6 patients reported that the mean score for endoscopic glandectomy without lymph node resection was 84 minutes[5].

Safety

Seven studies reported no major complications associated with the procedure[1,2,7,9,8,4,5].

The case series including 82 patients with malignant tumours reported subcutaneous haemorrhage in 7 patients (9%) and haematoma in 2 patients which was resolved without the need for reoperation[3].

Postoperative complications

The case series of 551 patients reported skin necrosis in 4% (22/551) of patients and fat and/or muscle flap necrosis in 3% (17/551) of patients (time of occurrence not stated) [9].

The case series including 82 patients with malignant tumours reported second degree burns in 4 patients (1 on the skin flap and 3 during additional resection for positive surgical margins found on fast-frozen sections)[3].

The case series of 33 patients reported nipple necrosis in 9% (3/33), primary nipple excision following positive margin in 24% (8/33) and 'second-look' nipple excision following positive margin in 9% (3/33) of patients (exact time of occurrence not stated)[10]. The case series of 7 patients reported burning of the skin caused by the electrocautery in 2 patients[4]. In the first, this was a result of contact with the electrical scalpel and was treated conservatively; in the second, the burn was a wide and deep dermal burn requiring skin debridement.

The case series of 9 patients reported skin bruises from excessive retraction in the first 2 patients treated[8].

The case series of 6 patients reported bloody nipple discharge in the contralateral breast in 1 woman; this required duct lobular segmentectomy[5].

Blood loss

The non-randomised controlled trial of 46 patients reported a mean blood loss of 356 ml in patients treated by endoscopic mastectomy and 189 millilitres (ml) in patients treated by subcutaneous mastectomy without the use of an endoscope ($p = 0.0266$)[1].

With the exception of the case series of 7 patients which reported a mean blood loss of 486.4 ml[4], reported blood loss in the other studies ranged from 53.1–292 ml[3,4,8,6,5].

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endoscopic mastectomy or wide excision for breast cancer. Searches were conducted of the following databases, covering the period from their commencement to 10 September 2008: 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).

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 with breast cancer.
Intervention/test	Endoscopic mastectomy.
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.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

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

- Brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision. NICE interventional procedures guidance IPG268 (July 2008). Available from www.nice.org.uk/IPG268
- Laparoscopic mobilisation of the greater omentum for breast reconstruction. NICE interventional procedures guidance IPG253 (Oct 2007). Available from www.nice.org.uk/IPG253
- Endoscopic axillary lymph node retrieval for breast cancer. NICE interventional procedures guidance IPG147 (Dec 2005). Available from www.nice.org.uk/IPG147
- Interstitial laser therapy for breast cancer. NICE interventional procedures guidance 89 (Sept 2004). Available from www.nice.org.uk/IPG089

Technology appraisals

- Docetaxel, hormonal therapies, paclitaxel, and trastuzumab for the adjuvant treatment of early breast cancer]. NICE technology appraisal 109, 112, 108, 107 (2006). Available from http://www.nice.org.uk/Guidance/TA109, http://www.nice.org.uk/Guidance/TA112, http://www.nice.org.uk/Guidance/TA108, and http://www.nice.org.uk/Guidance/TA107.

Cancer service guidance

- Improving outcomes in breast cancer – manual update. Cancer service guidance (2002). Available from www.nice.org.uk/csgbc

Clinical guidelines

- Clinical guidelines on early and locally advanced breast cancer, and advanced breast cancer are in development. These guidelines are due to be published in February 2009.

Table 2 Summary of key efficacy and safety findings on Endoscopic mastectomy or wide excision for breast cancer

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Kitamura (2002)[1] **Non-randomised controlled trial** Country: Japan Study period: Aug 1998 – Mar 2001 n = **46 (21 E-SMR, 25 SMR)** Study population: patients with early breast cancer (stage I or II using TNM system [T value <2, diameter ≤5.1 cm, N value <1, ipsilateral axillary node swelling with mobility; M10, no distant metastasis]). Mean age: 43.4 years (E-SMR); 44.3 years (SMR) Sex: not stated Inclusion criteria: free of any signs of skin invasion or of any major pectoral muscle fixation; microcalcification or intraductal spread was extended; multiple cancers in the ipsilateral breast; breast volume too small for acceptable symmetry after BCT; choice of prophylactic irradiation, BCT, or a combination of both were rejected by the patient. Technique: 6 cm mid-axillary incision (average E-SMR incision 5.7 cm and SMR incision 10 cm), lap retractor was put on the incision and a composition-type retractor was used to retract the skin upwards to obtain a field of operative vision (CO_2 gas was used in the first 2 patients), endoscopic dissection followed by axillary lymph node dissection and reconstruction with a saline prosthesis. (For SMR, the same procedure is completed under direct vision). Follow-up: **19.2 months median (range: 5.8 - 35.2)** Conflict of interest: not stated	***Survival*** All patients were reported to be alive at 19.2 month follow-up (range: 5.8–35.2 months). ***Surgical margin*** A positive surgical margin requiring radiation therapy 4 weeks after treatment was detected in 5% (1/21) of patients in the E-SMR group and 8% (2/25) of patients in the SMR group. ***Cosmetic results*** Reported cosmesis was based on a postoperative questionnaire given to both the patient and the surgeon 6 months after the operation or later. **Cosmesis score** / **E-SMR (n = 21)** / **SMR (n = 25)** Excellent: 18 (86%) / 15 (60%) Good: 1 (5%) / 4 (16%) Fair: 1 (5%) / 3 (12%) Poor: 1 (5%) / 3 (12%) Where 'excellent' - patient and surgeon both satisfied with symmetry of breast, 'good' - patient satisfied but surgeon worried about slight asymmetry, 'fair' - patient and surgeon both worried about asymmetry, and 'poor' - severe asymmetry existed. The difference was not considered statistically significant (p = 0.1531). ***Operative time*** (including reconstruction) E-SMR: 237 min SMR: 176 min (p = 0.0001)	***Complications*** No critical complications were reported. 4 patients had prosthesis-related morbidity: 3 patients in SMR group had severe capsular contracture requiring surgical repair. 1 patient in E-SMR group had nonbacterial phlegmonosis in the operated breast after irradiation. Fluid accumulation with no bacterial infection around the prosthesis was frequent, but always improved after several punctures. ***Average estimated blood loss*** E-SMR: 356 ml SMR: 189 ml (p = 0.0266)	The study stated that clinicopathologic data between groups was similar. Method of allocation to treatment groups not described. Safety outcomes were related to the reconstruction element of the procedure/ prosthesis. Cosmetic results are likely to be the result of both the mastectomy and reconstruction.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Nakajima (2009)[9] **Case series** Country: Japan Study period: November 1999 – July 2007 n = **551** Study population: 47 with DCIS, 190 with T1, 314 with T2 Age: not stated Sex: not stated Inclusion criteria: tumour diameter of ≤ 4cm (in ≤ 5 cm in some who insisted on procedure), no invasion of skin Technique: video-assisted breast conserving surgery; mid-axillary incision for lateral tumour or peri-areolar incision when tumour located near the nipple, skin separated from gland (using a bladeless trocar), retracted using a subcutaneous tunneling method or with a retractor using a lifting method, and removed (all under video guidance); followed by reconstruction with existing tissue if the loss was small or using autologous tissue such as the latissimus dorsi muscle flap; axillary staging was performed by sentinel lymph node biopsy; all patients had stage-specific adjuvant therapy according to published 2007 guidelines by NCCN in the US. All received breast irradiation and those with positive margins received addition irradiation at tumour bed. Mean follow-up: **38.7 months (range: 5 – 96)** Conflict of interest: none stated	***Survival*** Distant-metastasis-free survival rate (using Kaplan-Meier survival rates) at 66 months was: 100% for DCIS (n = 47) 96% for T1 (n = 190) 91% for T2 (n = 314) (overall survival was 100%, 97%, and 96%, respectively). ***Morbidity*** DCIS / T1 / T2 / Total Local recurrence: 0 / 7 (3.7) / 16 (5.1) / 23 (4.2) Distant metastasis: 0 / 7 (3.7) / 18 (5.7) / 23 (4.2) Death (%): 0 / 3 (1.6) / 4 (1.3) / 7 (1.3) Mean follow-up in months (range): 25 (5-73) / 38 (5-96) / 36 (5-95) / 35 (5-96) ***Surgical margin*** DCIS / T1 / T2 / Total Node positive (%): 2 (4.3) / 24 (12.6) / 97 (30.9) / 123 (22.3) Margin positive (%): 16 (34) / 35 (18.4) / 62 (19.5) / 113 (20.5) (differences between groups not significant; high incidence of margin-positive DCIS patients was because of intraductal spread; no margin positive patients had additional resections because there was no major tumour infiltration) ***Patient satisfaction/cosmesis*** A patient questionnaire was sent to patients 6 months after surgery. The response rate was 87% (481/551). Overall patient satisfaction was: 'good' in 76% (366/481) , 'fair' in 14% (66/481) and 'poor' in 10% (49/481)	***Complications*** Skin necrosis in 4% (22) of patients. Fat and/or muscle flap necrosis in 3% (17) of patients. The study reported that there were no other serious complications.	Some patients had previous neoadjuvant chemotherapy (exact number not stated). All patients received adjuvant radiation therapy and those with positive margins received additional irradiation at the tumour bed. The authors also stated that all patients underwent stage-specific adjuvant therapy according to the NCCN Clinical Practice Guidelines in Oncology Breast Cancer (2007) and consistent with the international expert consensus on primary therapy of early breast cancer (publication by Goldhirsch et al, 2005). Cosmetic results are likely to be the result of both the mastectomy and reconstruction.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Yamashita (2008)[2] **Case series** Country: Japan Study period: Dec 2001 – Aug 2006 n = **131 (plus 19 patients with benign tumours)** Study population: early breast cancer or benign breast disease; mean tumour size 2.1 cm; 7-TO, 68-T1, 32-T2, 2-T3, 6-T4. Age: mean 55.1 years Sex: not stated Exclusion criteria: severe complications; tumour extension to nipple or direct invasion to skin; severe comorbid conditions (such as heart disease, renal failure, liver dysfunction, poor performance status). (Unlike the study published earlier by the same authors, some patients with advanced cancer with axillary lymph node metastasis were included after pre-operative systemic therapy because of its tumour-shrinking effect). Technique: 2.5 cm axillary incision and/or periareolar, skin flap formation (using tunnel method), pectoral muscle fascia dissection, vertical section of the mammary gland, SLN biopsy with dye-staining method guided by pre-operative 3D-CT lymphography marking and axillary lymph node dissection. Reconstruction using an absorbent synthetic fiber filling was then performed. Ultrasonography was used every 3 months and magnetic resonance every 6 months to detect local recurrence. All patients with malignant disease received radiotherapy, hormone therapy and/or chemotherapy. **Follow-up: not stated;** Conflict of interest: not stated	***Recurrence*** No locoregional recurrence was detected at follow-up of 56 months (mean 28 months). ***Surgical margin*** Surgical margin was negative within 5 mm from the stump (observed from permanent histological sections). ***Conversion to radical mastectomy*** Two patients required modified radical mastectomy because of diffuse ductal spread and direct skin invasion (time of re-operation not stated).	No major complications reported.	The starting point for recruitment for all Yamashita studies is the same (others published in 2006 – one in table 2 and the other in appendix A). It appears that all three studies include the same base of patients, each increasing in size as new patients were recruited. This is the most recent study and includes the most patients and the most recent information on recurrence and surgical margin. While this study has reported negative tumour surgical margins, the Yamashita 2006 study (see below) which includes the same patients had inconsistencies in reported surgical margin. Cosmetic results are likely to be the result of both the mastectomy and reconstruction. Other outcomes reported in this study were on the ability to detect SLN metastases, not specifically related to the mastectomy procedure. The length of follow-up was reported for recurrence, however, it was not stated whether and for how long these patients were followed up for other safety outcomes.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Yamashita (2006)[3] **Case series** Country: Japan Study period: Dec 2001 – Apr 2005 n = **82 (plus 18 patients with benign tumours)** Study population: early localised breast cancer, tumour sizes ranging from 1.9 to 6.5 cm; disease classified as earlier than stage IIb (equivalent to T3); axillary node metastases was observed in 19 patients Mean age (years): 53.7 for both malignant and benign Sex: not stated Exclusion criteria: severe complications; tumour extension to nipple or direct invasion to skin; advanced cancer with axillary lymph node metastasis; severe comorbid conditions (such as heart disease, renal failure, liver dysfunction, poor performance status). Technique: axillary incision (2.5 cm) under endoscopic monitoring (periareolar incision for SLN biopsy and axillary node dissection), lap protector inserted into incision, tunnelling method, blue-dye to check margins, lap retractor, gland resection preserving various nerves and veins, breast reconstruction (using an absorbent synthetic fiber filling), wound closure. Ultrasonography every 3 months and magnetic resonance every 6 months to detect local recurrence. All patients with malignant disease received radiotherapy, hormone therapy and chemotherapy. Follow-up: **not stated** Conflict of interest: not stated	***Recurrence*** No locoregional recurrence was detected at follow-up of 50 months (mean 25 months). ***Surgical margin*** Surgical margin was reportedly negative within 5 mm from the stump (observed from permanent histological sections). (However, the authors reported 2nd degree burns in 3 patients who had positive surgical margins observed on intra-operative fast frozen sections. This means that although final surgical resection was with clear margins, this was not always achieved the 'first time'.) ***Cosmesis*** Cosmetic results in all patients treated by VABS were reported to be 'good'. They also created a scoring system, ABNSW (asymmetry, breast shape, nipple shape, skin condition and woundcare) with a scale of 0–15 ranging from 'poor' to 'excellent'. The mean score for VABS patients was 13.5 (90% of evaluated cases had good or excellent scores - over 11). ***Patient satisfaction*** Almost all patients were satisfied with the VABS surgery (this was evaluated with a quality of life questionnaire, the QOL-ACD-B; no more details provided). ***Operative time*** (including reconstruction). VABS: 173 ± 45 min Conventional BCT: 149 ± 32 min (p = 0.131)	***Early post-operative complications (VABS)*** 7 subcutaneous haemorrhage 2 haematoma (resolved without operation with a puncture; not further described) 4 patients had 2nd degree burns less than 1 cm (1 during skin flap and 3 during additional resection for positive surgical margins). It was stated that these were less severe than for conventional surgery. ***Blood loss*** VABS: 174 ± 118 g Conventional BCT: 147 ± 118 (p = 0.909)	The starting point for recruitment for all Yamashita studies is the same (other 2 in table [published 2008] and appendix A [also published 2006]). It appears that all three studies include the same base of patients, each increasing in size as new patients were recruited. There were 34 patients who met the eligibility criteria for VABS, but chose to have conventional BCT (details of BCT not described). Postoperative complications and surgical outcomes were compared between these patients and all patients treated by VABS. Two of the 82 patients with malignant tumours that underwent VABS went on to have skin-sparing mastectomy; the other 80 had BCT. The authors stated that the length of the incision started as 4 cm, but gradually decreased to 2.5 cm. There are inconsistencies in the reporting of tumour surgical margins – see comment in the 'Key efficacy findings' column. Conversion to modified radical mastectomy was required in 2 patients because of diffuse ductal spread and direct skin invasion. Cosmetic results are likely to be the result of both the mastectomy and reconstruction. The length of follow-up was reported for recurrence, however, it was not stated whether and for how long these patients were followed up for other safety outcomes.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Ito (2008)[10] **Case series** Country: Japan Study period: April 2000 – November 2006 n = **33** Study population: patients with primary breast cancer (29 DCIS, 3 T1, 1 T2); these patients were not indicated for standard breast conservation either because of intraductal cancer or multicentric tumours Age: 46.5 (range: 35-66) Sex: not stated Inclusion criteria: not stated Technique: endoscopic assisted skin-sparing mastectomy; 5-cm axillary incision, sentinel lymph node biopsy in some (followed by axillary lymph node dissection if positive), electric coagulator created skin flap around skin incision under direct vision, subcutaneous tunnelling and dissection with the use of an endoscope, use of a dissecting balloon and harmonic scalpel, removal of tissue through incision; followed by reconstruction in all but 3 patients. Mean follow-up: **51.2 months** Conflict of interest: not stated	***Survival*** Overall survival at time of publication was 100% ***Recurrence*** No locoregional recurrence or distant metastases was detected at follow-up. Post-operative diagnosis: 64% (21) DCIS or LCIS 33% (11) IDC (8 of these had widespread intraductal component) 3% (1) invasive lobular carcinoma Three patients (9%) tested positive for lymph node metastasis.	***Complications*** Necrosis of nipple in 9% (3). Primary excision of nipple because of a positive margin in 24% (8) Excision of nipple because of positive margin (on 'second-look') in 3 (9%; not otherwise described). Infection in prosthesis requiring removal in 9% (3) The time of occurrence for the above events was not stated.	Immediate reconstruction was performed in 30 of the 33 patients. Cosmetic results are likely to be the result of both the mastectomy and reconstruction. Two patients received preoperative chemotherapy (one was the patient with a T2 tumour). Postoperative adjuvant chemotherapy in 2 (6%), endocrine therapy in 30 (91%) and radiation therapy in 1 (3%).

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Lee (2006)[7] **Case series** Country: Korea Study period: Oct 2002 – Oct - 2004 n = **20** Study population: patients with clinically-proven breast cancer; mean tumour size 2.2 cm (range 0.2-4.0 cm); 13 premenopausal and 7 postmenopausal; 4 stage 0, 8 stage I, 8 stage IIa Age: mean 45 (range 25-64) Sex: not stated Inclusion criteria: tumours < 3 cm, axillary lymph node negative without invasion into skin or pectoralis major muscle (confirmed by preoperative study using mammography, ultrasonography and/or MRI) Technique: confirmation of location by palpation and ultrasonography, 2.5 cm axillary incision to perform SLN biopsy (and axillary dissection, if necessary), retromammary space dissected under endoscope guidance, semicircular periareolar incision on side of tumour, subcutaneous tunnelling via this incision and tissue extracted through incision under endoscopic monitoring. All patients received radiotherapy 3 months after treatment; 5/8 stage IIa patients received chemotherapy (because of the presence of any of the high risk factors), and all patients with oestrogen or progesterone receptor-positive breast cancer received hormone therapy. Follow-up: **not stated** Conflict of interest: not stated	***Surgical margin*** One patient had a positive resection margin (intraductal carcinoma) requiring total salvage endoscopic mastectomy 10 days after the operation. Mean surgical margin of other patients was 3.3 cm (range 1.2 - 4.5). All primary tumours were >2 cm away from the nipple-areolar complex and not fixed to muscle or skin. ***Reoperation*** In addition to the above patient who required total salvage endoscopic mastectomy, another patient who had microcalcification in her remnant breast (showed on 6-month mammography) required salvage-modified radical mastectomy. ***Patient satisfaction/Cosmesis*** Patients scored their own cosmetic evaluation (using their own criteria) at 3 month follow-up. **Assessment** / **Patients (n = 19)** Excellent: 7/19 (37%) Good: 10/19 (53%) Fair: 2/19 (10%) Poor: 0 (0%) (this excluded the patient who required immediate reoperation due to positive surgical margin). ***Mean operative time*** 163 min (range 115 – 205) (excluding 3 cases who also had axillary node dissection) 178 min in 9 early cases 130 min in 8 later cases	No major complications reported. Haemoglobin levels decreased 14% postoperatively (no more details given). Haematocrit levels decreased 17% postoperatively (exact values not given).	Patient selection: 35% (7/20) of patients were detected during screening exam, 11 attended hospital for breast mass and 2 for breast pain. Reconstruction was not performed at the time of mastectomy.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Ho (2002)[8] **Case series** Country: China Study period: Dec 1998 – May 1999 n = **9** Study population: patients with primary invasive breast cancer < 3 cm or with extensive DCIS who did not want lumpectomy and postoperative radiotherapy or mastectomy (5 had DCIS, 2 had TI tumours, 2 had T2 tumours). Age: mean 38.8 years Sex: not stated Exclusion criteria: tumour >3 cm, tumour fixed to skin or muscle, retroareolar tumours. Technique: 5 cm axillary incision, wound deepened to border of pectoralis major muscle, breast dissector and harmonic scalpel used to create subpectoral pocket, breast retractor used to create working space (circumareolar incision made in larger breasts to facilitated dissection), breast tissue excised; this procedure was followed by axillary dissection and reconstruction with expandable mammary implants. Postoperative radiotherapy and chemotherapy were then given. Follow-up: **not stated** Conflict of interest: not stated	***Surgical margin*** Clear margins were shown on histological exam. ***Patient satisfaction/Cosmesis*** Patient satisfaction was given a mean score of 8 out of 10 (from the Patient Self-Assessment Satisfaction Index, ranging from very dissatisfied [0] to very satisfied [10]). ***Operative time*** (including reconstruction) Mean 234 min (range: 195 - 275) (last two patients were 210 min) ***Hospital stay*** Mean of 6.78 days (range: 4 – 12)	No major complications reported. Skin bruises from excessive retraction were reported in the first 2 patients. Mean blood loss: 135 ml.	Cosmetic results are likely to be the result of both the mastectomy and reconstruction.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Tamaki (1998)[4] **Case series** Country: Japan Study period: Dec 1995 – Sept 1997 n = **7** Study population: tumour locations were limited to the upper-outer quadrant in 4 patients, the lower-outer quadrant in 1 patient, both the upper- and lower-outer quadrant in 1 patient, and both lower–outer and inner quadrants in 1 patient; tumour size from 1.1 to 2.5 cm. Age: mean 41 years Sex: not stated Inclusion criteria: admitted to Osaka University Hospital Technique: injection of pyoktanin for identification of surgical margin, 5 cm axillary incision, skin flap created by electrocautery, retractor and 10-mm laparoscope (combined retractor and laparoscope used for last 3 patients), injection of saline, mammary gland incised and tumour with subcutaneous fat and fascia of pectoralis major was excised (if specimens showed cancer at margins, additional resection was completed), axillary node dissection, if necessary, followed by reconstruction (achieved by filling the area with remaining mammary gland and subcutaneous fat flap). All patients had adjuvant irradiation (50 Gy). Follow-up: **not stated** Conflict of interest: not stated	***Satisfaction*** Shape and size balance between breasts was considered to be satisfactory at 1- to 22-month follow-up (not specified if patient or clinician reported). ***Operative time*** (including reconstruction) Mean 387 min (range: 340 to 423 min)	Burning of skin caused by electrocautery occurred in 2 patients: In the first the burning occurred at the incision because of contact with the electrical scalpel; this was treated conservatively (not otherwise described) and a scar was not noticeable after irradiation. In the second, a wide and deep dermal burn occurred so skin debridement was required. No other significant complications observed. Mean blood loss was 486.4 ml (range: 338.3–597.5 ml).	Cosmetic results are likely to be the result of both the mastectomy and reconstruction. Patient satisfaction was reported at 1- to 22-month follow-up, however it is not clear how long individuals were followed up for other outcomes (ie safety).

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Tamaki (2001)[5] **Case series** Country: Japan Study period: 1999 - 2000 n = **6** Study population: patients with breast cancer - one tumour in upper inner quadrant. Age: mean 42.8 years Sex: not stated Inclusion criteria: admitted to Osaka University Hospital, tumour size < 2 cm and located in inner quadrant, axillary node status N0. Exclusion criteria: suspected invasion to skin. Technique: transareolar endoscopic partial mastectomy (TAREPM): location confirmation by palpation and echogram, pyoktanin injection to indicate surgical margin, semicircular incision around areola, skin flap created with scissors, additional skin flap created endoscopically, mammary gland incised vertically, retractor inserted, mammary gland excised (if the edges of the excised tissue were positive for cancer, additional excision was performed); axillary lymph node or SLN biopsy was performed (by decision of patient). Postoperative radiation therapy was performed in all patients except 1. Follow-up: **not stated** Conflict of interest: not stated	***Surgical margin*** Permanent histological specimens were negative in 4 and positive in 1. The latter patient received additional adjuvant radiation therapy. No lymph metastases were observed. ***Operative time*** Mean 84 min (range: 69 to 113 min) (this was only for the endoscopic glandectomy; mean procedure time for the whole procedure was 256 min, range: 190 to 315). One of the 7 patients switched to total glandectomy after the procedure because the intraoperative pathologic study showed positive margins with wide-spreading invasive lobular carcinoma.	No significant complications except minor fluid accumulation in the wound area. Mean blood loss was 193 ml (range: 60 to 290)	The same authors performed this procedure by transaxillary approach, but developed a transareolar approach for patients with tumours in the inner quadrants of the breast. They state it can be used for all small tumours in any quadrant. Reconstruction was not performed at the time of mastectomy. All patients, except the patient treated by total glandectomy, received adjuvant radiation therapy.

Abbreviations used: SMR, subcutaneous mastectomy and reconstruction; E-SMR, endoscopically-assisted subcutaneous mastectomy and reconstruction; VABS, video-assisted breast surgery; BCT, breast conserving therapy; SLN, sentinel lymph node; SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; ICS, invasive ductal carcinoma)

Study details	Key efficacy findings	Key safety findings	Comments
Owaki (2005)[6] **Case series** Country: Japan Study period: not stated n = **6** Study population: early breast cancer in situ or tumours less than 1.5 cm in diameter without clinical metastases Age: mean 53.8 years Sex: not stated Exclusion criteria: tumours > 1.5 cm Technique: identification with 5 cm axillary skin incision, SN biopsy with gamma-detection probe (and axillary lymph node dissection, if necessary), workspace created with double retractors, areolar incision for assistance with endoscope if tumour in upper-inner or lower-inner quadrant, 1/6 – 1/4 of breast removed, reconstruction with remaining mammary gland tissue (not further described). Follow-up: **not stated** Conflict of interest: not stated	***Patient satisfaction*** All patients reported they were satisfied with the condition of the breast after surgery. ***Operative time*** (including reconstruction) Mean operative time was 165 ± 73.4 cm.	***Mean blood loss*** Mean blood loss was 150 ± 96.9 ml.	Cosmetic results are likely to be the result of both the mastectomy and reconstruction.

Validity and generalisability of the studies

- Only one comparative study was identified; the rest were case series.
- All studies reporting on this procedure were from Asia, where breast size is generally smaller than in Western countries.
- There was some duplicate reporting of the same patients in three identified studies (Yamashita studies: two in table 2 and one in appendix A). However, it appears that they were periodic reports of continuing recruitment so the more recent studies included more patients. The studies varied in the outcomes reported so the most recent report on recurrence is included in the table, as is the study which included safety data and other outcomes deemed to be important by the Specialist Advisers.
- The intervention varied between the studies, from the location of the incision, the method of skin retraction and the imaging techniques used.
- The size of the incision varied from 2.5 cm to 7 cm in the studies. Smaller incisions tended to be used in the more recent studies; this may reflect improvement in the technique over time.
- Tumour sizes ranged from around 1 cm to 6.5 cm across the studies. Tumour stage also varied across the studies. While many of the studies performed endoscopic mastectomy for tumours ≤ T2[1,2,7,8], three studies included T3 tumours[2,3,9], one included T4 tumours[2] and three did not classify tumour stage[4,5,6].
- Many of the patients received adjuvant radiotherapy, chemotherapy and/or hormone therapy.
- While many of the studies performed reconstruction at the same time as the endoscopic mastectomy, we have not shown the detail about the reconstruction in the evidence presented. Scarring from the mastectomy will surely affect cosmetic outcome/patient satisfaction, but this outcome will be greatly influenced by the success of the reconstruction for the studies which have performed reconstruction at the time of mastectomy.

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 Mo Keshtgar, Association of Breast Surgery at British Association of Surgical Oncology and Mr Kieran Horgan, British Association of Surgical Oncology.

- One of the two Specialist Advisers has performed these procedures.
- These procedures are performed by less than 10% of specialists in the UK and both Advisers consider them as novel and of uncertain safety and efficacy.
- One Adviser commented that these procedures are considered established practice in most major centres in Japan. The same Adviser performs these procedures at the Royal Free Hospital after training in the procedure in Japan.
- Comparators include open simple mastectomy, skin- or nipple-sparing mastectomy and subcutaneous mastectomy.
- Both Advisers commented that the diffusion of this technique is likely to be slow; one Adviser commented that this may change with published outcomes from randomised controlled trials and that not all patients will be suitable for this procedure.
- This approach could provide minimal scarring to improve cosmetic outcomes. It is currently only offered to patients with small- to moderate-sized breasts because the reconstructive procedure requires an implant the efficacy of which in larger breasts is uncertain.

Efficacy

- Both Advisers considered key efficacy outcomes to include: lack of wound complications/problems, local cancer recurrence, cosmesis, hospital stay, patient satisfaction, postoperative pain control, and time to return to work.
- One Adviser stated that there may be limited experience of these procedures and many breast surgeons may not be familiar with equipment.

Safety

- Theoretical adverse events identified by the Advisers included: pneumothorax, major neurovascular injury, non-viable skin flaps, longer operating time and, with lack of experience, lack of clearance of cancer and resection margins.
- The Adviser who has completed these procedures commented that they take twice as long to perform in the 'learning phase'.
- Safety concerns/uncertainties include the adequacy of tumour clearance, postoperative complications (both early and late), local disease control and long-term survival.

Training and facilities required

- Training in breast surgical oncology is required.
- Both training and experience in endoscopic procedures is also required.
- Familiarity with the instruments and equipment is important since they are not normally used in laparoscopic surgery.
- The Advisers recommended that after training, experts in performing these procedures should oversee or monitor trained clinicians. Results of these procedure should be audited. After satisfactory outcomes have been achieved, clinicians can then perform these procedures.

Issues for consideration by IPAC

- There are a number of non-English publications (particularly Japanese) on these procedures, but we have not looked at them (we do not normally order non-English publications).
- The majority of the evidence is on the use of these procedures to remove the tumour and the area around the tumour, rather than removing the whole breast gland.
- Not all studies stated the sex of the patients involved.
- It has been noted in the literature that these procedures are most appropriate for patients with smaller breasts.
- Recurrence outcomes have not been reported on in a significant number of the studies. It is possible that this is because of a general lack of longer term

follow-up in these studies. Also, the focus of many of the studies was on the cosmetic impact of using this procedure with or without immediate reconstruction rather than on the outcome of cancer recurrence.

- The literature was searched for the use of these procedures on patients with breast cancer. There has been a substantial volume of evidence on the use of these procedures for benign tumours; however, these were excluded from our search. The studies could theoretically provide information on outcomes other than for cancer margin/recurrence which would also apply to the use of this procedure in breast cancer patients, particularly safety outcomes.
- Only the non-randomised trial and the case series of 17 patients explicitly stated patient follow-up (median 19.2 months and mean 14 months, respectively). The two publications from the same centre and author reported recurrence rates for up to 50 months (mean 25 months). Many of the authors acknowledge that further study with more patients and longer-term follow-up is needed.

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9. Nakajima H, Sakaguchi K, Mizuta N et al. (2009) Video-assisted skin-sparing breast-conserving surgery for breast cancer and immediate reconstruction with autologous tissue. Annals of Surgery 249:91-96.

10. Ito K, Kanai T, Gomi K et al. (2008) Endoscopic-assisted skin-sparing mastectomy combined with sentinel node biopsy. ANZ Journal of Surgery 78:894-898.

Appendix A: Additional papers on endoscopic mastectomy and endoscopic wide excision for breast cancer

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
Nakajima H, Sakaguchi K, Mizuta N et al. (2002) Section 5. Breast: Video-assisted total glandectomy and immediate reconstruction for breast cancer. Biomedicine and Pharmacotherapy 56:205s-208s	Case series n = 17 Mean follow-up = 14 months	All patients were satisfied with the cosmetic result Mean operative time (including reconstruction) was 265 min more than the reported normal mastectomy operative time (which the authors stated to be 180 min).	Patients are likely to be included in the Nakajima 2009 study in table 2 (from the same centre and recruited within the same time period).
Tamaki Y, Tsukamoto F, Miyoshi Y et al. (2002) Section 5. Breast: Overview: video-assisted breast surgery. Biomedicine and Pharmacotherapy 56 (Suppl 1): 187s – 191s.	Review (for benign and malignant tumours) Patient numbers not specified.	Operation time across the studies ranged from 87 min to 158 min to 387 – 241 min. Blood loss in one of the studies was 25 – 250 g in a study published in 1997.	This was a review of various studies, however, it is more on the historical development of the technique.
Yamaguchi S, Asao T, Uchida N et al. (2008) Endoscopy-assisted subcutaneous mastectomy and immediate breast reconstruction for breast cancer: advantage of the posterior approach. International Surgery 93:99-102.	Case series n = 21 Follow-up not stated	Posterior approach: Mean surgical duration 216 min, mean blood loss 238 ml Skin flap approach: Mean surgical duration 251 min, mean blood loss 238 ml	Does not report on outcomes deemed important by the Committee.
Yamashita K and Shimuzu K. (2006) Video-assisted breast surgery: reconstruction after resection of more than 33% of the breast. Journal of Nippon Medical School 73: 320 – 327.	Case series n = 112 with malignant tumours (there were 18 patients with benign tumours)	Patient-reported cosmetic results reported good aesthestic results. No locoregional recurrence at mean 19 months (up to 36 months); surgical margin (permanent histological sections) was reported as negative within 5 mm from the stump. However, this is inconsistent with the study reporting avoidance of mastectomies because of cancer cells in the surgical margin on intraoperative histological examination of fast-frozen sections.	Outcomes were mostly related to reconstruction of the breast. Since the recruitment start date and recruitment centre appear to be the same, it is likely that the patients reported here are also reported in the other two publications by Yamashita in table 2.

		1 patient had discharge of fluid through the wound 2 patients had hypersensitivity reactions to the filling content (not stated whether for malignant or benign tumours).	
Yamashita K and Shimizu K. (2008) Transaxillary retromammary route approach of video-assisted breast surgery enables the inner-side breast cancer to be resected for breast conserving surgery. American Journal of Surgery 196:578-581.	Case series n = 20 Follow-up =1 year	No locoregional recurrence or distant metastasis at 1 year. One positive resection requiring further resection. Aesthetic results from ABNSW system were 14 of 15 points in total for all women.	No new outcomes and not significantly new numbers of patients. (2 studies by the same author are in table 2 and 2 studies in appendix A with some duplicate reporting of patients).
Yamashita K and Shimizu K. (20-10-2008) Trans-axillary retro-mammary gland route approach of video-assisted breast surgery can perform breast conserving surgery for cancers even in inner side of the breast. Chinese Medical Journal 121:1960-1964.	Case series n = 12 Follow-up =1 year	Same results reported as above.	Same reason for non-inclusion as above study.

Appendix B: Related NICE guidance for endoscopic mastectomy and endoscopic wide excision for breast cancer

Guidance	Recommendations
Interventional procedures	**Brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision. NICE interventional procedures guidance 268 (July 2008)** 1.1 Current evidence on brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision raises no major safety concerns. Current evidence on its efficacy is limited in quantity and there is little information on long-term outcomes (5 years or more). Therefore, this procedure should be used only in the context of research, which should address control of local disease with a minimum of 5 years of follow-up. The Institute may review the procedure upon publication of further evidence. **Laparoscopic mobilisation of the greater omentum for breast reconstruction. NICE interventional procedures guidance IPG253 (Oct 2007)** 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. **Endoscopic axillary lymph node retrieval for breast cancer. NICE interventional procedures guidance 147**

	(Dec 2005) 1.1 Current evidence on the safety and efficacy of endoscopic axillary lymph node retrieval for breast cancer does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake endoscopic axillary lymph node retrieval should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, use of the Institute's 'Information for the public' is recommended (available from www.nice.org.uk/IGP147publicinfo). • Audit and review clinical outcomes of all patients having endoscopic axillary lymph node retrieval for breast cancer. 1.3 This procedure should only be undertaken by surgeons skilled in endoscopic techniques. **Interstitial laser therapy for breast cancer. NICE interventional procedures guidance 89 (Sept 2004)** 1.1 Current evidence on the safety and efficacy of interstitial laser therapy for breast cancer does not appear adequate to support the routine use of this procedure. It is suitable for use only within good-quality research studies approved by a research ethics committee and with explicit patient consent. 1.2 Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence.

Appendix C: Literature search for endoscopic mastectomy and endoscopic wide excision for breast cancer

Database	Date searched	Version/files	No. retrieved*
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	10/9/08	Issue 3, 2008	0 ***1***
Database of Abstracts of Reviews of Effects – DARE (CRD website)	10/9/08	N/A	0 ***2***
HTA database (CRD website)	10/9/08	N/A	0 ***5***
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	10/9/08	Issue 3, 2008	2 ***5***
MEDLINE (Ovid)	10/9/08	1950 to August Week 4 2008	333 ***195***
MEDLINE In-Process (Ovid)	10/9/08	September 09, 2008	24 ***7***
EMBASE (Ovid)	10/9/08	1980 to 2008 Week 31	307 ***234***
CINAHL (NLH Search 2.0)	10/9/08	1981 to present	8 ***15***
BLIC (Dialog DataStar)	4/8/08	1993 to date	0
National Research Register (NRR) Archive	4/8/08	N/A	0
UK Clinical Research Network (UKCRN) Portfolio Database	4/8/08	N/A	0
Current Controlled Trials *meta*Register of Controlled Trials - *m*RCT	4/8/08	N/A	0
Clinicaltrials.gov	4/8/08	N/A	0

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

1 Endoscopy/ (32235)
2 Surgical Procedures, Minimally Invasive/ (9495)
3 Video-Assisted Surgery/ (943)
4 Endoscop$.tw. (95530)
5 (Minimall$ adj3 Invasive$ adj3 (Surg$ or Procedure$ or Technique$)).tw. (8645)
6 (Video$ adj3 Assist$ adj3 (Surg$ or Procedure$ or Technique$)).tw. (2209)
7 Transareolar$.tw. (19)
8 ((Skin$ or Nipple$ or Areola$) adj3 Sparing).tw. (373)
9 or/1-8 (123020)
10 exp Mastectomy/ (18154)
11 Mastect$.tw. (10945)
12 or/10-11 (21771)
13 exp Breast Neoplasms/ (161058)
14 (Breast$ adj3 (Neoplasm$ or Cancer$ or Carcinoma$ or Adenocarcinom$ or Tumour$ or Tumor$ or Malignan$ or Lump$)).tw. (140990)
15 or/13-14 (186074)
16 9 and 12 and 15 (340)
17 Animals/ (4335755)
18 Humans/ (10668338)
19 17 not (17 and 18) (3257889)
20 16 not 19 (339)
21 Breast/ (22761)
22 Surgery/ (28201)
23 21 and 22 (37)
24 exp Breast/su (4324)
25 exp Breast Neoplasms/su (22731)
26 exp Breast Diseases/su (24125)
27 (Breast$ adj3 (Surg$ or Resection$)).tw. (7424)
28 or/23-27 (30164)
29 Mastectomy, Segmental/ (4002)
30 Lumpectom$.tw. (1454)
31 Segmentect$.tw. (1385)
32 or/29-31 (6011)
33 9 and 28 and 15 (489)
34 9 and 32 and 15 (82)
35 33 or 34 or 16 (536)
36 35 not 19 (534)
37 36 not 20 (195)