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Submission to Breast Cancer Research and Treatment

Endoscopic Breast Surgery:

Where are we now and what might the future hold for video-assisted breast surgery?

Daniel Richard Leff (MB BS, MRCS Eng, PhD)^{1,3}, Rajiv Vashisht (MBBS, FRCS MPhil, FICS)³, Gabriella Yongue², Mohammed Keshtgar (BSc, MB BS, FRCSI, FRCS (Gen), PhD)⁴, Guang-Zhong Yang (PhD)¹ and

Ara Darzi (MD MRCS FACS FMedSci KBE)¹

Corresponding Author

Mr Daniel Richard Leff MBBS MRCS Eng PhD

Academic Clinical Lecturer in General Surgery,

Department of Biosurgery and Surgical Technology,

The 10th Floor, QEQM Wing,

St Mary's Hospital,

Paddington, London. W2 1NY

Tel: +44(0)7515 257 731

Email: d.leff@imperial.ac.uk

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¹ Department of Biosurgery and Surgical Technology, and Royal Wolfson Medical Image Computing Laboratory, Imperial College London;

² Imperial College School of Science, Technology and Medicine, Imperial College London;

³ Departments of Breast and General Surgery, West Middlesex University Hospital NHS Trust;

⁴ The Breast Unit, Academic Department of Surgery, Royal Free Hospital, London.

Abstract

Endoscopic surgery has been extensively used for many surgical conditions and has gained acceptance as an alternative and less invasive approach to open surgery. However, minimal access endoscopic techniques have yet to be translated into mainstream clinical practice in breast surgery. More recently, technical innovations have made it feasible to conduct endoscopic breast cancer resection, with or without breast reconstruction, through wounds inconspicuously hidden in the axilla and periareolar region. Several clinical trials have now been conducted to demonstrate technical feasibility, assess safety and provide follow up data regarding oncological success of endoscopic breast surgery. This primary aim was to critically evaluate the literature in order to determine the oncological and cosmetic efficacy of endoscopic breast surgery. A systematic review was conducted using Medline, Ovid and Embase to identify original data from studies of endoscopic breast surgery. Initial results have demonstrated that endoscopic breast surgery is safe and technically feasible. Early data suggests that it is possible to achieve disease control with high rates of overall survival and low rates of local relapse recurrence and/or distant metastases. However, the absence of level I randomised clinical evidence currently precludes a recommendation that endoscopic breast cancer surgery is capable of achieving equivalent oncological outcomes to open surgery.

Abbreviations: skin sparing subcutaneous mastectomy (SSM); endoscopic subcutaneous mastectomy (ESM); video-assisted breast surgery (VABS); breast conserving surgery (BCS); sentinel lymph node biopsy (SLNB); axillary lymph node dissection (ALND); ductal carcinoma *in situ* (DCIS); lobular carcinoma in situ (LCIS); invasive ductal carcinoma (IDC).

Introduction

Minimal access endoscopic techniques have transformed many fields of surgery through the provision of improved body cavity access, enhanced visualisation via magnification, and minimisation of tissue trauma. Breast cancer surgery, however, represents a major field of surgical oncology in which endoscopy has yet to be adopted in mainstream clinical practice. This may be due to the fact that breast surgery is inherently low morbidity, results in low levels of pain, and that breast tumours can commonly be accessed through small incisions [1]. However, in cases where mastectomy is deemed necessary, a more extensive incision is required which is detrimental to cosmesis and body image. Theoretically, if endoscopic mastectomy combined with immediate breast reconstruction (IBR) could be proven to be oncologically safe, there may be tremendous gains in terms of reducing surgical morbidity and improved aesthetics.

Mastectomy techniques have undergone a significant improvements since William Halstead first proposed the radical mastectomy in 1891 [2]. By 1948, a less radical approach to mastectomy, preserving the pectoralis muscle and overlying skin without compromising oncological quality had been proposed by Patey and Dyson [3]. More recently, Toth and Lappert developed the technique of *skin sparing subcutaneous mastectomy* (SSM) in order to preserve skin and facilitate breast reconstruction without adversely affecting oncological safety [4]. Therefore, endoscopic mastectomy represents a minimally invasive approach in a field of surgical oncology with the aim of complete cancer clearance and preservation or restoration of the patient's body image. Endoscopic subcutaneous mastectomy (ESM) may particularly benefit women with small breasts in whom breast conserving surgery (BCS) may result in obvious breast asymmetry, inadequate resection margins and poor cosmesis [5] and therefore the main protagonists of ESM have been in Asian countries such as Japan, Korea and China. Despite the appeal of ESM, concerns surrounding endoscopic breast cancer resections relate to the

oncological safety, the additional cost in terms of operative time, equipment and training, as well as the wider applicability for patients with larger breast volumes [1, 5, 6]. Some surgeons have even suggested that ESM may not be justified if it is merely to reduce the size of the scar on the breast [1].

The aim of the current systematic review is to evaluate the evidence for full and partial ESM. We will also evaluate different operative techniques and assess oncological safety in terms of adequacy of tumour margins, rates of local recurrence and distant metastases, as well as overall survival (OS) and disease free survival (DFS). Moreover, surgical morbidity, cosmetic outcomes and economic cost implications associated with ESM with IBR are evaluated and compared to simple mastectomy and open SSM. Although reviews and editorial comment pertaining to ESM do exist in the literature [1, 5, 6], they are either not sufficiently systematic in nature [1, 5], or have been outdated by virtue of the pace of technological developments which have enabled simplification of endoscopic techniques [6].

Description of the Operative Techniques for Endoscopic Breast Conserving Surgery and Endoscopic Subcutaneous Mastectomy

Table 1 outlines a number of different techniques described for endoscopic partial or total subcutaneous mastectomy. Regardless of the differences between techniques in terms of the devices used for endoscopic visualisation, dissection and specimen retrieval, there is uniformity in many aspects of the procedure. Patients are typically placed in the supine position on the operating table, with the surgery-side arm placed at 90° to extend the axilla. Tumour localisation is usually achieved via a combination of palpation and radiological guidance, with the proposed resection margins being marked preoperatively

on the patient's skin surface. For partial mastectomy and endoscopic BCS, identification of the proposed resection margins may be further enhanced by the appearance of dye injected at several points at the tumour periphery. Skin incisions are placed in either a periareolar location or in the axilla, working planes are achieved by subcutaneous and sub-mammary elevation, balloon dissection and/or retractors. Endoscopic dissection is performed between the posterior breast and pectoralis fascia, between the breast and subcutaneous tissue and along the lateral and medial resection margins, haemostasis being achieved through ligation and electrical coagulation. Finally, the specimen is retrieved via one of the port sites for histological assessment. Each stage of endoscopic subcutaneous breast resection is discussed in the following section with the aim of highlighting the different technical approaches attempted to date.

Incision placement

Axillary incisions are the most common point of access to facilitate endoscopic subcutaneous full or partial mastectomy as well as axillary node biopsy, which can be performed either endoscopically or under direct vision. The length and number of axillary incisions varies, with some surgeons being able to proceed through a small single axillary point of entry[7-9], whilst others require lengthier incisions (~8cm) [10] or multiple axillary incisions seemingly to mirror the triangulation set-up of traditional abdominal laparoscopy [11-13]. Additional periareolar incisions are adopted for cases in which tumours are located in the inner breast quadrant [14-16] to facilitate subcutaneous dissection [17] or if the patient's breasts are especially large [18]. Finally, depending on tumour location, it may be necessary to place incisions in the infra-mammary crease [10].

Wound protection

The use of a wound protector was infrequently reported and when a device was employed, justification for its use was often not explicit [7-9, 19]. The device most commonly used was 'Lap Protector' (Hakko Co), which consists of two flexible rings made of super elasticity alloys covered with polyurethane polyamide, and a thin silicone rubber membrane that is attached to the outer rim of the two rings. If the two rings are pulled apart the device assumes a cylindrical shape. The device is more commonly used in laparoscopic colorectal cancer surgery to prevent wound contamination with bacteria and cancer cells leading to infection and port site metastases respectively.

Endoscopic visualisation

The majority of authors describe introducing the endoscope through the channel of a bladeless trocar such as ENDOPATH (Johnson & Johnson Medical Arlington, TX) or VISIPORT PLUS (United States Surgical, Norwalk, CT, USA) which enables placement of the visualisation system within tissues under direct vision [8, 10, 15, 16, 20, 21]. The majority of surgeons employed a 10mm, 0° endoscope (Olympus, Co) as the visualisation system of choice. However, 5mm and 30° endoscopes have been used without any obvious increase in adverse events or ergonomic challenges [7, 17, 18, 21].

Methods of creating and maintaining an endoscopic work space

Broadly, there are three methods for creating and maintaining a suitable endoscopic work space to facilitate resection, including inflation of the subcutaneous tissue using carbon dioxide (CO₂) to maintain a pressure of ~8mmHg [11-13, 19], the use of dissecting balloons (*e.g.* PDB) [10-12, 19] as illustrated in **Figure 1**, and tissue elevation either in the form of anchoring sutures [7, 8] or using specific fit for purpose retractors [22, 23] such as the HIROTECHretractor [15, 16] or Clearglide dissector, as depicted in **Figure 2**.

Methods for endoscopic subcutaneous dissection

The most commonly employed technique is known as the 'subcutaneous tunnelling method' [7, 8, 10, 15, 16, 21, 24]. This method involves creating a number of subcutaneous tunnels using the endoscopic or bladeless trocar. The septa between the tunnels are then dissected under endoscopic guidance using either electric or harmonic scalpels and/or powerstar bipolar scissors.

Techniques for endoscopic posterior breast dissection

The use of a retraction device (*e.g.* Ultra Retractor, HIROTECH retractor, Endoscopic Breast Retractor, *etc*) appears to significantly improve visualisation and aids dissection of the posterior aspect of the breast from the pectoralis fascia (see **Figure 2**) [7-9, 15-18, 22, 23, 25]. However, the successful use of balloon dissection has also been reported [10, 24]. Tissue dissection and vessel coagulation is achieved using a harmonic scalpel, ultra retractor vein harvest, and/or powerstar bipolar scissors.

Specimen retrieval

The resected breast specimen is retrieved directly through the axillary or periareolar port sites, with the wound occasionally needing extension to facilitate retrieval. A few authors described the use of a sterile bag device (*e.g. 'Endocatch'*) to aid specimen retrieval and to prevent unnecessary contact between malignant breast cancer cells and the skin [7, 8, 12].

Materials and Methods

Literature Search Criteria

The literature search was performed using Medline, Ovid, Embase, and Cochrane databases. The following MeSH headings were used: "Endoscopy", "Mastectomy", "Video-assisted surgery", "Breast", "Breast Surgery", "Carcinoma" and "Cancer". The related articles function was utilised to broaden the search, and all abstracts, studies, and citations were scanned and reviewed. The bibliography of the acquired articles was also searched manually. Studies were limited to those in the English language. The latest date for this search was 1st March 2010.

Data Extraction

Two reviewers (D.R.L and G.Y), independently extracted the following data from each study: first author, year of publication, study population characteristics, study design, number of subjects, and outcome measures. Two reviewers (D.R.L. and G.Y.) extracted or calculated the rates of loco-regional disease recurrence, metastatic disease recurrence, and overall survival. Three authors (D.R.L., R.V. and R.K.) critically reviewed the design limitations of each study.

Inclusion and Exclusion Criteria

In order to enter our review, studies had to be clinically orientated (defined as involving human patients) and utilise endoscopic techniques or video assistance to guide resection of a specific volume of breast tissue or the entire breast as the primary surgical treatment of neoplastic breast lesions (benign and malignant). Non-human studies and those involving endoscopic methods to treat non-cancer related breast disease (*e.g.* gynaecomastia) or involving reconstruction in the absence of neoplastic resection were all excluded.

Results

Study Identification

The systematic search strategy is summarised in **Figure 3.** 185 publications were identified in the initial search. 171 articles were excluded following title and abstract review. This included 9 relevant articles written in foreign languages, 25 articles pertaining to endoscopic primary breast augmentation or gynaecomastia surgery, 14 papers related to other breast surgical techniques (*e.g.* mammaplasty), 16 articles related to ductoscopy, 1 article involving non-human data, 1 editorial commentary, 14 review papers and 91 papers unrelated to breast surgery. This resulted in 14 studies that were investigated in detail. Examination of the references revealed a further 5 studies that fulfilled the inclusion criteria. In total, this left 19 studies for inclusion and data extraction. Study synopses of the included articles are summarised in **Table 2.** In total, 1, 389 patients have undergone ESM or endoscopic BCS for neoplastic breast lesions.

What are the patient and tumour-specific factors that define eligibility for endoscopic mastectomy / endoscopic breast conserving surgery?

The primary indication for endoscopic mastectomy is extensive ductal carcinoma *in situ* and early invasive breast cancer (T1/T2), particularly in women with smaller breasts in whom breast conserving surgery (BCS) may result in obvious deformity[5]. Tumour size appears to be the single most important eligibility criteria defining entry into endoscopic mastectomy trials. Several researchers have limited their trials of endoscopic breast cancer surgery to T1 and small T2 tumours (<3cm in size) [14, 18, 21-23], whilst others have included patients with larger T2/T3 tumours (>3 but <6cm) and/ or multifocal disease [11, 15-17, 24]. Patients with a distribution of invasive disease that would otherwise be suitable for standard BCS, but in whom post-operative radiotherapy was not deemed acceptable were also candidates for endoscopic mastectomy in certain trials [18].

Common exclusion criteria include the presence of nipple deviation or retraction or suspicion of nipple-areolar complex involvement detected clinically or radiologically [9, 13, 16-20], Paget's disease [17], obvious skin involvement [9, 15-17, 19-21], confirmation of distant metastasis [9, 13, 14], associated co-morbidity or poor performance status [9, 20], and in certain cases the presence of obvious axillary lymph node involvement [9, 13, 21, 23]. In circumstances where endoscopic techniques were employed to achieve BCS, disease multifocality was also an exclusion criterion [21].

Do the results of current trials confirm the oncological safety of endoscopic mastectomy in terms of positive histological margins?

As with any new technique, concerns have been expressed regarding the ability of ESM to achieve local disease control. This is outcome measure is extremely important as positive margins not only herald local recurrence but also increase the likelihood of post-operative radiotherapy threatening the cosmetic outcome and negating the benefits of a minimal access approach. Taking this into account, surprisingly 47.3% of the reviewed papers failed to provide data on the ability of ESM / endoscopic BCS to achieve complete histological excision (Table 3 and 4) [8, 11-14, 20, 22, 25]. Only one non-randomised study [19] has compared the rates of local margin involvement between endoscopic and open subcutaneous mastectomy for breast cancer. Kitamura *et al* [19] were unable to demonstrate a statistically significant difference in the rate of local margin involvement following open and endoscopic subcutaneous mastectomy (open versus endoscopic = 8.0% versus 4.8%, p=0.1851).

Of even greater concern is the wide range of positive histological margins (3-24%) observed amongst studies that do report data for this endpoint [9, 15, 16, 19, 21, 23, 24]. The reasons for failure to obtain adequate tumour margins at the time of endoscopic

breast resection are likely to be multifactorial, although learning curve, tumour multicentricity and sub-radiological disease foci may be contributory. Nakajima *et al* [15] subcategorised margin involvement by tumour size demonstrating an increasing probability of margin involvement for *in situ* disease (Tis=34% versus T2=19.2%), and by tumour stage demonstrating a similar likelihood of margin involvement between stage I and II disease (stage I=12.8 versus stage II=15.3, p=NS) [16]. However, since all the studies reporting margin involvement limited ESM recruitment to patients with T2 disease, tumour size may not rationally explain the variation in positive margin involvement between studies. It appears that margin involvement is in part explained by the type of technology, operator experience and patient volume, with lower rates of margin involvement in studies involving larger cohorts (**Table 3 and 4**).

Table 5 highlights the rates of positive margin involvement following subcutaneous mastectomy and nipple sparing mastectomy. It is evident that rates of margin positivity are an under-reported endpoint per se. Nevertheless, margin positivity rates where reported, have been observed to be as low as 0.3% in recent large series of SSM [26] and ESM has yet to replicate this accuracy in terms of oncological clearance. Moreover, there have been no randomised controlled trials comparing ESM to open SSM and / or NSM therefore there is an absence of level I evidence available to definitively demonstrate the oncological safety of ESM.

Is endoscopic mastectomy associated with an increased risk of local and/or distant disease recurrence and poorer overall survival?

a) Local recurrence

The local recurrence rate (LR) following endoscopic breast cancer surgery is infrequently reported in papers describing novel endoscopic methodologies as these studies were not designed to collect prospective follow-up data [8, 11, 14, 18, 20-22, 25]. In eight studies, following an average follow-up duration of 24.1 months there was no reported LR [7, 9, 11, 13, 17, 19, 23, 24]. However, notwithstanding some exceptions [17, 24], the average duration of follow-up has been less than two years and investigators have observed LR following endoscopic resection when follow-up is extended beyond three years [15]. Only two non-randomised studies have compared the rates of LR between patients undergoing endoscopic subcutaneous mastectomy versus open breast conserving surgery [13] and versus open subcutaneous mastectomy [19]. Fan et al [13] failed to observe any significant difference in the rate of LR between patients undergoing endoscopic breast resection and those undergoing breast conservation following an average follow-up duration of 16.9 months (LR = BCS versus ESM = 1.9% versus 0%, p=0.247). Similarly, following an average of 19.2 months follow-up Kitamura et al [19] failed to demonstrate clinical recurrence in patients undergoing subcutaneous mastectomy and reconstruction regardless of whether operative mode was open or endoscopic. One risk factor for the development of subsequent LR following endoscopic resection may be tumour size. Nakajima et al [15] recently demonstrated that LR was more likely following endoscopic resection of larger breast cancers (Tis = 0, T1 = 3.7% and T2 = 5.1%). The theoretical increased risk of LR following skin-side / muscle side positivity does not appear to be proven, and indeed Nakajima et al [15] were unable to demonstrate a statistically significant difference in the rates of LR between margin positive versus margin negative patients (LR rates= 4/113 for margin +ve versus 19/438 for margin -ve, p=NS). Finally,

there have been no reports of local recurrence in the vicinity of axillary or peri-areolar incisions that would mirror port-site recurrence observed following laparoscopic cancer surgeries [27].

b) Distant metastatic disease

Five studies report rates for detection of distant metastatic disease over the duration of follow-up [13, 15-17, 19]. The rates of distant metastases detected over a mean duration of follow up of 38.3 months range from 4.5% to 10% [13, 15-17, 19]. The study with the highest incidence of distant metastases detection was observed to have a significant proportion of node positive patients at the outset (~41% axillary node positive), possibly contributing to the burden of distant disease recurrence[17]. Similarly, in the cohort study by Nakajima et al [15] the chances of subsequent distant disease detection were related to tumour size, which itself was observed to correlate with the risk of node positivity (metastases%: Tis=0, T1=3.7, and T2=5.7; node +ve%= Tis=4.3, T1=12.6, and T2=30.9). However, in a cohort study of 244 patients undergoing endoscopic skin sparing partial mastectomy, the same authors were unable to demonstrate a statistically significant difference in the detection rate of distant metastases between stage I and stage II disease (metastases%: stage I=6.4 versus stage II=10, p=NS) [16]. Two non-randomised studies involving a combined total of 143 patients have failed to demonstrate a statistically significant difference between endoscopic and open breast cancer resection in terms of the likelihood of developing subsequent metastatic disease [13, 19]. However, the duration of follow-up reported in these non-randomised trials is relatively short (average follow-up = 16.9 - 19.2 months).

c) Overall survival (OS)

Results from two non-randomised studies suggest that the overall survival (OS) following endoscopic and open breast cancer resection for early stage disease is comparable over a maximum average follow-up duration of 19.2 months [13, 19]. Other cohort studies with follow-up durations ranging from 12 months to approximately 4 years suggest excellent OS following endoscopic breast cancer resection (100%) [7, 24]. Nakajima *et al* [16] were unable to demonstrate a significant difference in OS between patients with stage I and stage II disease, but variation in OS was influenced by tumour size (OS% = Tis=100, T1=97.3, T2=95.7).

Peri-operative and post-operative morbidity

a) Intra-operative blood loss

The mean volume and weight of intra-operative blood loss following endoscopic breast cancer resection across all trials is 189ml and 84.4g respectively. In the non-randomised trial by Kitamura and colleagues, the volume of intra-operative blood loss was significantly (p<0.05) greater following endoscopic subcutaneous mastectomy and reconstruction versus the open equivalent [19]. Conversely, the volume of intra-operative blood loss and post-operative drainage were not found to be significantly different between the patients undergoing endoscopic subcutaneous mastectomy versus open BCS in another prospective non-randomised trial [13]. The results of the latter study by Fan *et al* [13] are especially relevant as the BCS group would have undergone a more conservative dissection, and therefore one would have anticipated greater intra-operative blood loss in the group undergoing mastectomy.

b) Skin, muscle and nipple necrosis, and prostheses-related complications

The two non-randomised clinical studies observed a similar overall complication rate following endoscopic and open breast cancer surgeries, but the nature of the complications varied depending upon operative mode [13, 19]. Complications observed by Kitamura et al [19] were predominantly prosthesis related, and these were significantly more common in patients treated with conventional subcutaneous mastectomy (endoscopic = 4.8% versus open = 12%, p=0.4). Similarly, three patients treated with conventional breast surgery experienced capsular contractures whereas no patients treated with endoscopic mastectomy and reconstruction experienced this complication [19]. All the complications in the open surgical group treated by Fan et al [13] were related to hydrops all of which required repeat needle puncture and aspiration (n=6/54). Hydrops was not observed in the group treated endoscopically, however patients in this group were observed to experience skin blistering and necrosis of the nipple areolar complex (overall complication rate = 5/43)[13]. Complications associated with ESM that were not infrequently observed in cohort studies and case series include skin and muscle flap necrosis, superficial and deep skin burns associated with the use of electrocautery [9, 13, 15-17], skin bruising and subcutaneous emphysema [11, 12]. Infection and haematoma were complications rarely observed following endoscopic breast cancer surgery. Interestingly, there have been no studies comparing levels of pain and analgesic requirements between patients treated with conventional versus minimal access endoscopic breast surgery.

Does endoscopic mastectomy offer superior cosmesis compared to conventional mastectomy?

Endoscopic mastectomy, especially if combined with IMBR results in minimal scarring and restoration of breast volume. Similarly, endoscopic BCS with reconstruction may result in excellent cosmesis, as illustrated in Figure 4. However, as highlighted in Table 3, there was a considerable range of methods used for reporting satisfaction with the cosmetic result following endoscopic breast surgery. Some investigators merely reported whether or not patients were 'satisfied' with the final outcome [12, 14, 22, 23], others employ more objective methods including self satisfaction indices and rating scales anchored with specific descriptors (0-3 = poor-excellent) [13, 15, 16, 19, 21] or used a sub classification system such as the asymmetry, breast shape, nipple shape, skin condition and wound scar (ABNSW system) [7-9]. From the reviewed data, the majority of patients who have undergone endoscopic breast resection are satisfied with the cosmetic outcomes. In only two studies was the cosmetic outcome following endoscopic surgery compared to that achieved following conventional open resection [13, 19]. The authors failed to observe a statistical difference in patient's self-reporting of cosmetic outcomes at six months or more following open and endoscopic breast surgery [13, 19]. However, in the study by Kitamura and colleagues [19] there was a trend towards superior cosmetic outcomes following endoscopic subcutaneous mastectomy and reconstruction with 85.6% reporting excellent outcomes following endoscopic resection compared to 60.0% after open breast surgery. Interestingly, Fan et al [13] did not observe a high rate of patient satisfaction with only 20.9% reporting 'excellent' results following endoscopic subcutaneous mastectomy and immediate implant reconstruction. Notwithstanding this, the overall cosmetic satisfaction rate was comparable to patients treated in the open BCS study arm [13].

Is endoscopic breast surgery cost effective?

There have been no randomised or non-randomised studies specifically comparing the cost-effectiveness of open versus endoscopic breast cancer surgery. As Table 2 highlights, average operating times required for endoscopic breast cancer surgery are longer than those for open surgery. Only three studies [9, 13, 19] incorporated comparative data on the average operative durations for endoscopic and open breast resection (average operating time, mean $\pm SD = ESM$: 192.6 ± 38.5 versus Open: 154.6±19.1 minutes). Therefore, our calculations suggest that an endoscopic approach adds on average approximately 38 minutes to the operating time (192.6-154.6=38.0). This is likely to have significant repercussions on theatre productivity and capacity to meet national targets for cancer treatments. Not only is operating time expensive, but the instrumentation would add considerably to the costs [1]. Although the current review has failed to find objective data comparing equipment costs, Kitamura et al [19] estimated that endoscopic lumpectomy would cost approximately \$1,150 for one hospital stay versus \$500 for the conventional open surgical procedure [19]. In our opinion, this represents a gross underestimate of the additional costs required to support an ESM breast service. Training in performing endoscopic breast surgery is paramount to oncological and cosmetic success and inevitably involves significant investments in terms of time and finances to train and certify surgeons and theatre nurses. Finally, the cost involved in failure of endoscopic mastectomy, conversion to open mastectomy and salvage open mastectomy for margin involvement needs to be configured into any future formal cost analysis.

Discussion and Conclusions

As endoscopic breast resection is still in its infancy, it is unsurprising that data supporting the efficacy of the endoscopic and video assisted breast cancer surgery is relatively sparse. In fact, there is a lack of high quality randomised clinical trials providing level I evidence in support of ESM and endoscopic BCS. The data that are available are from case series, cohort studies and non-randomised trials, and these provide level II-IV evidence in support of ESM techniques. This is compounded by the fact that comparative data is between ESM and open BCS [13], when perhaps a more suitable comparison would be open SSM with retro pectoral implant reconstruction. The current paper has reviewed the evidence for ESM and endoscopic BCS in order to evaluate case selection, morbidity and mortality, oncological success, cosmetic acceptability and cost efficiency of endoscopic breast cancer surgery.

As with many new technologies, case selection for ESM appears to be critical, hinging on identifying patients with either early T1/2 tumours or high grade DCIS in whom conventional open BCS is either inappropriate or likely to lead to significant volume loss and unsatisfactory cosmetic results, or in patients who wish to avoid post-operative radiotherapy. ESM may be preferable for multifocal tumours where breast conservation is not suitable. However, disease multicentricity has typically been an exclusion criterion in most ESM trials and there is no current evidence to support the use of ESM in patients with multifocal disease. Similarly, some protagonists state that tumour size and position should not pose restriction on suitability for ESM providing the skin and primary duct are cancer free [13]. However, patients with large tumours are typically excluded from endoscopic breast surgery trials. Therefore, future studies will need to objectively assess the suitability of ESM in patients with large tumours, disease multifocality and larger

breasts in whom conventional open BCS may not necessarily result in significant deformity.

Endoscopic breast surgery appears to be well tolerated and a relatively safe technique. Complications commonly observed following open breast surgery; in particular seroma (hydrops) formations, haematoma, infection and prosthesis-related complications are less frequently encountered following ESM. However, certain complications are more frequently observed following ESM and include: skin bruising and blistering from electrocautery, skin and muscle flap necrosis, and necrosis of the nipple areolar complex. Furthermore, there is some evidence to suggest that ESM may be associated with greater intra-operative blood loss than open breast surgery [19]. It is possible that these complications are related to the learning curve and/or limitations of current endoscopic instruments, influenced by training and technological advances respectively. For example, Fan et al [13] observed a reduction in the incidence of nipple areolar complex necrosis by reversing the tip of the suction nozzle away from the skin and subcutis. Interestingly, we were unable to identify studies comparing post-operative pain levels and analgesic requirements between open breast surgery and ESM. Theoretically, by significantly reducing the size of the operative incision, the pain and analgesic requirements following ESM should be substantially lower, but this clearly needs to be evaluated systematically and objectively.

For endoscopic breast cancer surgery to gain acceptance in clinical practice, it must demonstrate itself to be at least as efficacious as open surgery in terms of oncological success. From the reviewed data it is evident that endoscopic breast resection either as ESM or BCS is capable of achieving local disease control in the majority of patients. However, rates of positive margin involvement are at best highly variable (3-24%) and at

worst not yet comparable to those achievable with open SSM and NSM (Table 5). Therefore, one must conclude that at the current time, the rates of positive margin with ESM are not reproducibly low enough, even if margin positivity is not the only factor contributing to local failure [16]. This is extremely important as margin positivity resulted in patients necessitating additional therapies including revision surgery such as primary or secondary NAC excision [24], salvage mastectomy [21] as well as unplanned radiotherapy [19].

Data from non-randomised studies provide limited evidence to suggest an equivalent risk of developing LR and distant metastatic disease following endoscopic breast resection and open breast cancer surgery [13, 19]. The risk of developing LR and distant disease appears to relate more to clinical / pathological tumour characteristics (*e.g.* size, grading, *etc*) [15] rather than the mode of operative intervention. However, follow-up for detection of LR and disease recurrence has rarely extended beyond two years, which in our view is too short to demonstrate comparable oncological outcomes with open surgery. The same argument could be levelled at the data pertaining to OS, which although encouraging (> 95% following an average follow-up of 19.2 months) is not supported by long-term results.

Those who champion endoscopic breast cancer surgery argue that one of the primary advantages of ESM with immediate breast reconstruction (IMBR) is restoring the patient's body image and improving cosmesis over open BCS. The majority of revised studies include some reference to the patients' overall satisfaction with the outcome, but it is not always transparent how this assessment was obtained, whether or not these assessments were subjective and how if at all bias was minimised. Perhaps rather disappointingly, comparative data relating to cosmetic satisfaction following ESM versus

open breast cancer surgery has failed to demonstrate the superiority of endoscopic surgery. In fact, in one comparative study, the rates of cosmetic satisfaction were actually worse for ESM (88.4%) versus open BCS (92.6%) [13]. The reasons for this may include prosthesis deviation, asymmetry due large ptotic contralateral breast, and/or unrealistic expectations regarding outcomes following ESM with IMBR.

In summary, significant recent progress in the arena of minimal access breast surgery has demonstrated endoscopic breast cancer surgery to be technically feasible and relatively safe. Initial results are encouraging and suggest that obtaining equivalent oncological results to open surgery should be achievable. However, there is a lack of level I evidence in support of endoscopic breast cancer surgery and there is now an urgent need for high quality, randomised clinical studies to confirm oncological success and demonstrate superior cosmesis, patient satisfaction and quality of life. Even if ESM does not become routine practice, research in this arena is likely to yield improve instrumentation, with greater flexibility and new platforms for the delivery of chemotherapeutics, radiotherapy [28], and high intensity focused ultrasound (HIFU) therapy [29].

Table 1 Comparison between different endoscopic mastectomy techniques and instrumentation (1/2)

Author	T	Wound	M-41-16	Port /	Subcutaneous dissection techniques /	Posterior dissection	Specimen
Author	Incision(s) placement	protector	Method for creating work space	Endoscope	instruments	techniques / instruments	retrieval
Fan[13]	3 incisions each 0.5cm = AAL, axillary transverse striation, and MAL	no data	insufflation of CO ₂ , at 8mmHg	no data	lipolysis solution, liposuction and electric hook	lipolysis solution, liposuction and electric hook	no data
Ho[18]	5cm along lowest axillary crease, in large breast add a periareolar	no data	no data	10mm, 30°	direct vision, harmonic	endoscopic breast retractor, harmonic scalpel	axilla
Ito[24]	axillary	no data	no data	10mm	tunnelling method, harmonic scalpel	PDB dissecting balloon	axilla
Kitamura[11]	infra mammary or axillary, 12mm centre and x 2 5mm either side	no data	dissection balloon, CO ₂ at 5-6mm	5mm or 3mm	5-10mm harmonic scalpel	5-10mm harmonic scalpel	via 12mm incision
Kitamura[12]	infra mammary or axillary, 12mm centre and x 2 5mm either side	no data	dissection balloon, CO_2 at 5-6mm	10mm	5-10mm harmonic scalpel	5-10mm harmonic scalpel	via 12mm endocatch
Kitamura[19]	6cm MAL	yes, lap protector	2 patients = insufflation of CO ₂ , 19 patients = retractor technique	no data	no data	no data	no data
Lee[21]	2.5cm along lowest axillary crease, semicircular periareolar	no data	no data	visiport / 5mm 0°	tunnelling method, powerstar scissor	vein harvest, powerstar	axillary or periareolar
Nakajima[25]	5-7cm MAL	no data	lifting fan	10mm	bipolar scissors under video guidance	vein harvest	no data
Nakajima[16]	lateral tumour - axilla, medial tumour - circumareolar	no data	Hirotech retractor	ENDOPATH /	tunnelling method, trabecula separated using electric scalpel (MERA)	Hirotech retractor,	no data
Nakajima[15]	lateral tumour - axilla, medial tumour - circumareolar	no data	Hirotech retractor	ENDOPATH /	tunnelling method, trabecula separated using electric scalpel (MERA)	Hirotech retractor,	no data
Owaki[14]	5cm axilla, for inner quadrant tumouradd a periareolar	no data	double retractor method	no data	no data	no data	no data
Sakomoto[17]	3cm extending to 5cm in axilla, periareolar to facilitate subcut dissection	no data	ultra retractor, lift method	5mm, 30°	tunnelling method, powerstar scissors	direct vision, ultra retractor, power star scissors	periareolar or axilla

Table 1 continued (2/2)

Author	Incision(s) placement	Wound protector	Method for creating work space	Port / Endoscope	Subcutaneous dissection techniques / instruments	Posterior dissection techniques / instruments	Specimen retrieval
Tamaki[22]	5cm axilla	no data	retractor	10mm	no data	no data	no data
Tamaki[23]	circumareolar incision	no data	retractor for face lifting	4mm	powerstar scissors	retractor and powerstar scissors	circumareolar incision
Yamaguchi[10]	8cm incision IM crease or axilla depending on tumour location	no data	PDB balloon	opitiview, 12mm	using endoscope but no specific details	with or without PDB balloon	via axilla or IM crease incision
Yamashita[7]	2.5cm axilla	yes, lap protector	sutures to elevate the breast tissue	5mm	tunnelling method using endodissector	ultraretractor vein harvest	endocatch, via axilla
Yamas hita[20]	axilla		no data	visiport, 10 mm	no data	no data	no data
Yamashita[8]	2.5cm axilla	yes, lap protector	sutures to elevate the breast tissue	bladeless trocar, 5mm	tunnelling method using endodissector, septa divided with harmonic	ultraretractor vein harvest	endocatch, via axilla
Yamashita[9]	2.5cm axilla	yes, lap protector	skin pulled up with muscle clasps	10mm	tunnelling method using endodissector, septa divided with harmonic	ultraretractor vein harvest	no data

Table 1 legend.

AAL = anterior axillary line, MAL = mid axillary line, IM = inframammary, CO₂=carbon dioxide

Table 2 Summary table detailing study synopsis and demographic data for studies of endoscopic minimally invasive mastectomy (1/2)

Author	Study type	Tumour size limit (cm) for	Full or partial ESM		ber of ents	Av. tumour s		Tumour staging		Chemothera Radiothera Endocrine	ру /	Average ope duratio in minutes (ra SD)	n	Reconstruction	ALND
		ESM		ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open		
Tamaki[22]	series	≤ 2.5	partial	7	-	(0.7-2.5)	-	-	-	DXT (50 Gy) = all patients	-	387 (309-465)	-	mammary gland and fat flap	†
Kitamura[11]	series	≤5.5	lumpectomy	6	-	≤5.5	-	benign	-	-	-	200 (150-360)	-	-	-
Kitamura[12]	cohort	-	lumpectomy	36	-	3.6 (2.5-11)	-	benign	-	-	-	147	-	-	-
Tamaki[23]	series	< 2	partial	6	-	1.6 (1.3-2.2)	-		-	DXT = all BCS pts, boost DXT = 1pt margin +	-	241 (190-315)	-	-	† or SLNB
Kitamura[19]	non-rd control trial	-	full	21	25	2.1 (±1.2)	2.1 (± 1.0)	I=14 II=7	I=16 II=9	DXT for margin+ =1(4.8%)	DXT for margin + = 2 (8.0%)	237±60	176±32	saline filled prosthesis	†
Nakajima[25]	Cohort	-	full	17	-	-	-	-	-	no data	-	~445	-	latissimus dorsi	‡
Owaki[14]	Series	1.5	quadrant	6	-	0.6, ni-2.7	-	-	-	-	-	165 (45-260)	-	mammary gland	† if SLNB+
Lee[21]	Cohort	<3	quadrant	20	-	2.2 (0.2-4.0)	-	0=4, I=8,II=8	-	DXT = 95% (1 required salvage surgery), endothx= if ER+/PR+ adjv=5pts stage Iia	-	163 (115-205)	-	-	† if SLNB+
Yamashita[9]	non-rd	-	partial (2/3 max)	100	34	1.8 (0.1-6.5)	1.7 (1.5- 4.0)	0=5, I=46,IIA=21,IIB=10	0=1, I=15,IIA=13,IIB =5	no data	no data	173 ± 45	149 ± 32	a. remnant gland, b. lateral thoracic fat, c. mesh	‡
Yamashita[20]	Cohort	-	full	150	-	2.1 (0.1-9.0)	-	-	-	DXT=all pts, endocrine and adjv=guided by St Gallen's rec	-	no data	-	-	† n=41, ‡ n=74
Ito[24]	Cohort	<t2< td=""><td>full</td><td>33</td><td>-</td><td></td><td>-</td><td>-</td><td>-</td><td>adjv=6.1%, endothx=90.9% , DXT=3.0%</td><td>-</td><td>~240 (with implant reconstruction)</td><td>-</td><td>mammary prosthesis (n=30)</td><td>†</td></t2<>	full	33	-		-	-	-	adjv=6.1%, endothx=90.9% , DXT=3.0%	-	~240 (with implant reconstruction)	-	mammary prosthesis (n=30)	†
Yamashita[7]	Cohort	-	partial (lump or quadrant)	20	-	2.2 (0.8-4.5)	-	I=13, IIA=4, IIB=3	-	-	-	45min longer versus conventional	-	a.mammary gland, b.lateral thoracic fat, c.mesh or cotton	-
Ho[18]	Series	<3	full	9	-	no data	-	no data	-	adjv and DXT = 'given in usual manner'	-	234 (195-275)	-	prosthesis	24 †

Table 2 continued (2/2)

Author	Study type	Tumour size limit (cm) for ESM	Full or partial ESM		ber of ients	Av. tumour :		Tumoui	· staging	Chemotherapy / Radiotherapy / Endocrine thx ESM Open		Chemotherapy / Radiotherapy / duration Endocrine thx in minutes (range or some state of stat			Reconstruction	ALND
				ESM	Open	ESM	Open	ESM	Open			ESM	Open			
Nakajima[15]	cohort	≤5	partial (BCS)	551	-	Tis=2.5±1.9, T1=1.5±0.5, T2=3.6±0.7	-	-,	-,	DXT (50Gy)=all boost (10Gy)=if margin+	-	Tis=238±47, T1=223±39, T2=239±52	-	breast gland (n=258), LTF (n=107) LDMF (n=186)	SLNB - †	
Nakajima[16]	cohort	≤5	partial (BCS)	244	-	stageI= 1.6 stageII=3.1	-	stage I=94 stage II=150	-	DXT (50Gy)=all, boost (10Gy)= 14.3% for rmargin+ adjv=stage specific	-	stage I=177, stage II=236				
Sakamoto[17]	retrosp	-	full	87	-	2.1 (0.1-5.6)	-	0/1=37 II=50 IIIA=2	-	adjv=64%, DXT=30%	-	No data	-	prosthesis	SLNB †	
Yamashita[8]	cohort	-	partial	12	-	2.0±0.9	-	<iia< td=""><td>-</td><td>DXT=all pts with cancer, endocrine and adjv=guided by St Gallen's rec</td><td>-</td><td>208±44</td><td>-</td><td>a.mammary gland, b.lateral thoracic fat, c.mesh or cotton</td><td>†</td></iia<>	-	DXT=all pts with cancer, endocrine and adjv=guided by St Gallen's rec	-	208±44	-	a.mammary gland, b.lateral thoracic fat, c.mesh or cotton	†	
Yamaguchi[10]	series	-	full	21	-	no data	-	no data	-	no data	-	adv skin flap= 251±55 posterior approach =216±55	-	prosthesis	†	
Fan[13]	pros non-rd control trial	<3	full	43	54	2.7±0.9	2.6±0.9	I=,15 II=22, IIIA=6	I=,22 II=27, IIIA=5	cycles of neoadjv=2.1±1.1, adjv=all DXT=not routine, Endthx=if ER/PR+	cycles of neoadjv=1.1±1.1, adjuv=all DXT – routine, Endthx=if ER/PR+	168±32	139±37	prosthesis	†	

<u>Legend for Table 2</u>.

SLNB = sentinel lymph node biopsy, ALND = axillary lymph node dissection, NAC = nipple areola complex. †= axillary staging / clearance conducted simultaneously as a open procedure, ‡= axillary staging / clearance conducted simultaneously but performed endoscopically or with endoscopic-assistance, DXT=radiotherapy, Neoadjv=neoadjuvant chemotherapy, Adjx= adjuvant chemotherapy, Endthx=Endocrine therapy.

Table 3 Summary table comparing post-operative complications following endoscopic minimally invasive mastectomy: (1/2)

	Intra-operative	blood loss	Post-opera	tive drainage	Post-op	erative	Skin flap nec	rosis , burns,	Infecti	on rates	Haemor	rhage /	C	ic Outcomes	
Author (year)	(ml / g)		volu	me (ml)	drainag	e (days)	prosthe	esis Cx	(*	%)	Haemato	oma (%)	Cosmetic	Outcomes	
	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open	
Tamaki[22]	486 (310-670)ml	-	no data	-	no data	-	2 burns	-	no data	-	no data	-	7/7 satisfied	-	
Kitamura[11]	<10g	-	no data	-	no data	-	1 burn, 1SCE	-	0	-	0	-	no data	-	
Kitamura[12]	19±7ml	-	no data	-	no data	-	1 burn, 1SCE	-	0	-	0	-	36/36 satisfied	-	
Tamaki[23]	192 (60-290)ml	-	no data	-	no data	-	0	-	0	-	0	-	6/6 satisfied	-	
Kitamura[19]	356 ± 286g	189 ± 72g	no data	no data	no data	no data	3 prosthesis (12%)	1 prosthesis (4.8%)	0	0	0	0	Excellent=85% Good=4.8% Fair=4.8% Poor=4.8%	Excellent=60% Good=16% Fair=12% Poor=12%	
Nakajima[25]	no data	-	no data	-	no data	-	? supf burns	-	0	-	0	-	17/17=good	-	
Owaki[14]	150 ± 96.9ml	-	no data	-	no data	-	no data	-	no data	-	no data	-	6/6 satisfied	-	
Lee[21]	184 ± 130ml	-	no data	-	no data	-	0	-	0	-	0	-	89.5% satisfied Excellent=36.9 Good=52.6 Fair=10.5 Poor=0	-	
Yamashita[9]	174±118g	147±118g	421±263	259±165	4.06±2.0	3.25±1.19	4 burns	no data	0	no data	7 / 2	no data	Av. ABNSW = 13.5, 90% good or excel	no data	
Yamashita[20]	no data	-	no data	-	no data	-	no data	-	no data	-	no data	-	no data	-	
Ito[24]	no data	-	no data	-	no data	-	nacnec 3(9.1)	-	3 (9.1)	-		-	no data	-	
Yamas hita[7]	no data	-	no data	-	no data	-	0	-	0	-	0	-	ABNSW = 14 or 15	-	

Table 3 continued (2/2)

	Intra-operative	blood loss	Post-op	perative	Post-op	perative	Skin flap necro	sis , burn,	Infectio	n rates	Haem	atoma	Cosmetic Outc	omes
Author (year)	(ml / g	()	drainage v	olume (ml)	drainag	ge (days)	prosthesis (Cx (%)	(%	6)	(0	%)		
	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open
Ho[18]	135 ml	-	no data	-	no data	-	2 skin bruises	-	no data	-	no data	-	av. self assessment satisfaction index =8	-
Nakajima[15]	Tis=116±23g T1=107±27g T2=141±34g Total=127±49g		no data	-	no data	-	skin =22 (4.0), muscle= 17 (3.1)	-	no data		no data	-	overall good=76.1% fair=13.7 poor=10%	-
Nakajima[16]	StageI=125g StageII=143g	-	no data	-	no data	-	skin=9(3.7) fat=7(2.9) muscle= 1(0.4)	-	2 (0.8)	-	4 (1.6)	-	overall good=72.3% fair=11.2% poor16.5	-
Sakamoto[17]	No data	-	no data	-	no data	-	skin=3(3.4) nacnec=16(18)	no data	1(1.1)	-	no data	-	no data	-
Yamashita[8]	149±118g	-	no data	-	no data	-	no data	-	no data	-	no data	-	ABNSW= 14or 15	-
Fan[13]	115±44ml	102±48ml	150±63	160±69	6.7±2.1	6.3±2.1	nacnec=2 skin blisters=3 overall=5/43 (11.6)	hydrops (11.6) Overall=6/54 (11.6)	no data	no data	no data	no data	excellent=20.9% good=37.2% fair=30.2% poor=11.6%	overall 92.6% satisfied
Yamaguchi[10]	238±156ml	-	no data	-	no data	-	no data	-	no data	-	no data	-	no data	-

Legend for Table 3

ESM = endoscopic mastectomy, Cx = complications, Nacnec = nipple areolar complex necrosis, supf = superficial, SCE = subcutaneous emphysema

Table 4 Summary table comparing oncological outcomes following endoscopic mastectomy (1/2)

Author (year)	Average follo	w up (months)	Margin Involven	nent	Local Re		Metastatic 1			Survival %)
	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open
Tamaki[22]	22	-	no data	-	no data	-	no data	-	no data	-
Kitamura[11]	no data	-	no data	-	no data	-	no data	-	no data	-
Kitamura[12]	16.7	-	no data	-	0	-	no data	-	no data	-
Tamaki[23]	no data	-	1(16.6)	-	0	-	no data	-	no data	-
Kitamura[19]	19.2± 9.8	19.2± 9.8	1 (4.8)	2 (8.0)	0	0	0	0	20/20 (100)	24/24 (100)
Nakajima[25]	no data	-	no data	-	no data	-	ALN- = 3(17.6) ALN+ =14(82.4)	-	no data	-
Owaki[14]	no data	-	no data	-	no data	-	ALN-=6(100)	-	no data	-
Lee[21]	no data	-	1 (5) margin+ 1 (5) persistent MCC	-	no data	-	ALN-=18(90) ALN+=2(10)	-	no data	-
Yamashita[9]	25	no data	3 (3)	no data	0	no data	excl criteria	excl criteria	no data	no data
Yamashita[20]	no data	-	no data	-	no data	-	SLNB-=88/115 SLNB+= 22/115	-	no data	-
Yamaguchi[10]	no data	-	no data	-	no data	-	no data	-	no data	-

Table 4 continued (2/2)

Author (year)	Average follow	up (months)	Margin Involvement n (%)		Local Recu		Metastatic D n (%)	isease	Overall Survival (OS) (%)	
	ESM	Open	ESM	Open	ESM	Open	ESM	Open	ESM	Open
Ito[24]	51.2 (16-86)	-	8 (24.3) – required NAC excision	-	0	-	ALN- = 30(90) ALN+ = 3(9.1)	-	33/33 (100)	-
Yamashita[7]	12	-	0	-	0	-	no data	-	20/20 (100)	1
Ho[18]	no data	-	0	-	no data	-	no data	-	no data	-
Nakajima[15]	38.4	-	Tis= 16 (34.0) T1= 35 (18.4) T2= 62 (19.5) Total = 113 (20.5)	-	Tis= 0 T1= 7 (3.7) T2= 16 (5.1) Total = 23 (4.2)	-	ALN + Tis= 2 (4.3) T1= 24 (12.6) T2= 97 (30.9) Total = 123 (22.3) F/U distant Mets Tis= 0 T1= 7 (3.7) T2= 18 (5.7) Total = 25 (4.5)	-	Tis = (100) T1 = (97.3) T2 = (95.7)	-
Nakajima[16]	65.3	-	StageI = 12(12.8) StageII = 23(15.3)	-	StageI = 5 (5.3) StageII = 8 (5.3)	-	ALN+ Stage I = 7 (7.4) Stage II = 41 (27.3) F/U distant Mets Stage I = 6 (6.4) Stage II = 15 (10)	-	Stage I = (95.7) Stage II = (96.9)	-
Yamashita[8]	no data	-	no data	-	no data	-	no data	-	no data	-
Sakamoto[17]	52 (16-80)	=	0	-	0	-	ALN+ <3 nodes=23(26) >4 nodes= 13(15) F/U distant Mets 9(10)	-	no data	-
Fan[13]	16.9±11.2	20.1±11.9	no data	no data	0	1/51=(1.9)	0	2/51=(3.9)	(100)	50/51=(98.0)

Legend for Table 4

ESM = endoscopic mastectomy, NAC = nipple areolar complex, ALN = axillary lymph node, MCC = micro calcification, SLNB = sentinel lymph node biopsy, excl = exclusion, F/U = follow up.

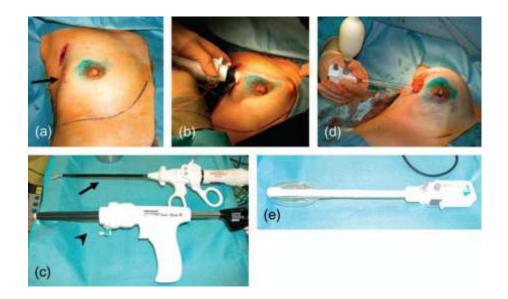
Table 5. Oncological outcomes following open subcutaneous mastectomy and nipple sparing mastectomy in studies with more than 100 patients

Author	Number of Patients	Type of Surgery	Positive Histological	Local Recurrence Rate (%)
		(SSM or NSM)	Margin (%)	
Reefy[30]	137	SSM	0.72	0
Cao [31]	168	SSM	38	-
Medina-Franco[32]	176	SSM	-	4.5
Carlson[33]	539	SSM	-	5.5
*Gerber [34]	48	SSM	-	10.4
Kroll [35]	118	SSM	-	7.0
Vaughan [36]	210	SSM	13% in patients without LR,	5.3
0 1 1 1 1 1 1 1 1	100	CCL	27% in patients with LR	
Spiegel [37]	177	SSM	-	5.6
Greenway [38]	225	SSM	-	1.7
Meretoja [39]	146	SSM	-	2.7
Yi [26]	799	SSM	0.3	0.6
Kim [40]	368	SSM	-	0.8
Cheung [41]	101	SSM	1.9% DCIS in NAC skin	16.0
Petit [42]	679	NSM	In pts with negative NAC cores= 2% invasive, 8.8% DCIS	0.9 / year
*Gerber [34]	60	NSM	-	10.0
Crowe [43]	110	NSM	-	6.7
Kim [40]	152	NSM	-	2.0
Benediktsson [44]	216	NSM	-	24.0

Table 5 legend. SSM = skin sparing mastectomy, NSM = nipple areolar complex sparing mastectomy, DCIS = ductal carcinoma *insitu*, NAC = nipple areolar complex, LR = local recurrence, * included over 100 patients in the SSM / NSM arm with set criteria to determine which procedure was performed.

Figures and Figure Legends

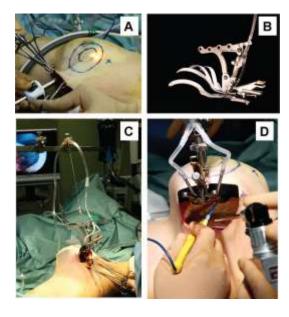
Figure 1



Breast and sentinel lymph node biopsy incision (a), visualisation trocar is inserted through the axillary incision which had been used to conduct SLNB, and a skin flap is created (b), harmonic scalpel (arrow) and visualised trocar (arrowhead) (c), using a dissection balloon the breast tissue is dissected off the pectoralis fascia (d), the dissection balloon (e). Reprinted with kind permission, Wiley and Sons. Original publication: Ito *et al*, ANZ J Surg 2008; 78:894-898 [24].

Figure 2

(i) (ii)





- (i) Subcutaneous tunnelling method and lifting method. (A) Separation between breast gland and skin under video guidance using the subcutaneous tunnelling method, (B) HIROTECH retractor, (C) separation between breast gland and skin under video guidance, (D) separation between breast gland and pectoralis major muscle under video guidance from the mid axillary incision using the lifting method. Reprinted with kind permission from Lippincott, Williams and Wilkins. Original publication: Nakajima *et al* Ann Surg 2009; 249(1):91-96 [15].
- (ii) Endoscopic breast dissection being conducted using the CLEARGLIDE precision bipolar device (Cardiovations, Ethicon).

Figure 3

Systematic literature search strategy.

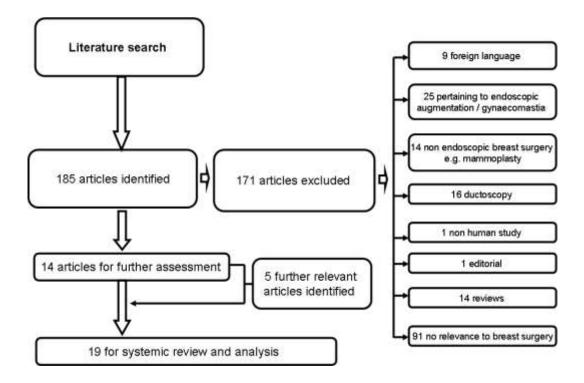


Figure 4



Cosmetic outcomes following endoscopic breast cancer resection and reconstruction. (A) 41-year-old woman with a right sided breast cancer (diameter 2.9 cm) in the upper outer area who underwent video-assisted BCS and reconstruction with latissimus dorsi muscle flap via a midaxillary line incision. Skin incision was invisible from the frontal view as of 3 years after operation. (B) A 48-year-old woman with left breast cancer (diameter 2.2 cm) in the lower-outer area who underwent video-assisted breast-conserving surgery and reconstruction with mobilization of the remnant breast gland and fat tissue via periareolar incision. Skin incision was inconspicuous as of 2 years after operation. Arrows show the skin incisions. Republished with kind permission from Springer. Original publication: Nakajima *et al* Ann Surg Onc 2009 16:1982–1989[16].

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