Review

Determinants of optimal mastectomy skin flap thickness

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Background: **There is a limited evidence base to guide surgeons on the ideal thickness of skin flaps during mastectomy. Here the literature relevant to optimizing mastectomy skin flap thickness is reviewed, including anatomical studies, oncological considerations, factors affecting viability, and the impact of surgical technique and adjuvant therapies.**

Methods: **A MEDLINE search was performed using the search terms 'mastectomy' and 'skin flap' or 'flap thickness'. Titles and abstracts from peer-reviewed publications were screened for relevance.**

Results: **A subcutaneous layer of variable thickness that contains minimal breast epithelium lies between the dermis and breast tissue. The thickness of this layer may vary within and between breasts, and does not appear to be associated with obesity or age. The existence of a distinct layer of superficial fascia in the breast remains controversial and may be present in only up to 56 per cent of patients. When present, it may not be visible macroscopically, and can contain islands of breast tissue. As skin flap necrosis occurs in approximately 5 per cent of patients, a balance must be sought between removing all breast tissue at mastectomy and leaving reliably viable skin flaps.**

Conclusion: **The variable and unpredictable thickness of the breast subcutaneous layer means that a single specific universal thickness for mastectomy skin flaps cannot be recommended. It may be that the plane between the subdermal fat and breast parenchyma is a reasonable guide for mastectomy flap thickness, but this may not always correspond to a subcutaneous fascial layer.**

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Introduction

Breast surgical practice has evolved considerably, with a trend towards more conservative approaches. Despite advances in neoadjuvant therapies and partial breast reconstruction, including tissue displacement and replacement techniques, mastectomy remains a common breast surgical procedure. Mastectomy is used to treat extensive invasive, *in situ* or multicentric disease not amenable to breast conservation, and is offered as a risk reduction strategy to women at high risk of developing breast cancer. In the UK, 53 per cent of women with symptomatic breast cancer and 27 per cent of those with screen-detected breast cancer are treated surgically with mastectomy[1]. Therefore, approximately 21 500 women undergo mastectomy in the UK each year. Furthermore, a dramatic increase in mastectomy rate has been reported in the USA[2]. There are several reasons for this development, such as availability of *BRCA* mutation testing, increased magnetic resonance imaging detection of additional tumour foci at time of diagnosis, and an increase in patient request for mastectomy[3].

Mastectomy may be combined with breast reconstruction, either immediately (at the time of the mastectomy) or as a delayed procedure. Conservative mastectomy techniques have evolved, including both skin-sparing and nipple-sparing approaches, with descriptions of the surgical technique for simple mastectomy[4,5] and skin-sparing mastectomy (SSM)[6]. Traditional surgical teaching is that, during a simple mastectomy, an ellipse is drawn on the breast, incorporating the nipple–areola complex. The skin and subcutaneous adipose tissue are incised along this ellipse. These are then lifted, while countertraction is applied to the underlying breast to reveal a surgical plane of dissection; by following this plane, the superior and inferior skin flaps are formed, and extended to the fascia of the pectoralis major muscle. The breast is then dissected off the pectoralis major[7]. However, the ideal thickness for the skin flaps during mastectomy is not clearly described. The skin flap thickness is important, however, as too thick a flap leaves residual breast tissue, and potentially disease within the skin flap, whereas too thin a flap risks flap necrosis. In addition to the physical and psychological impact, the complication of skin flap necrosis can potentially lead to delays in adjuvant therapies. The optimal plane between subcutaneous fat and breast parenchyma is also important in breast conservation using oncoplastic methods, where the skin is raised over a tumour via a remote (for example periareolar) incision.

SSM involves preservation of the native skin envelope and may achieve a superior cosmetic result in immediate breast reconstruction[8]. The surgical technique was first described by Freeman[9] in 1962, and later modified by Toth and Lappert[10] in 1991. A surgical plane is developed between the breast and subcutaneous fat, preserving the natural breast skin (*Fig. 1*). Concerns were raised that preservation of the skin may increase the probability of a positive superficial margin. Several non-randomized series[11–13] of SSMs suggest that recurrence rates are similar to those of simple mastectomy. However, the skin flaps after SSM are longer (more skin preserved) but no thicker than those in simple mastectomy, and this is associated with an increase in skin flap necrosis rates[14]. The skin flap thickness sufficient to preserve flap viability is particularly important with SSM for several reasons. First, because this is combined with immediate breast reconstruction, aesthetic outcome is important to the patient and may be diminished by scarring and distortion resulting from necrosis. Second, if the reconstruction uses a tissue expander or fixed-volume implant, the risk of infection resulting from skin flap necrosis is a major concern because of the potential for implant loss. However, the management of skin flap necrosis may also be complicated in the patient who has not undergone reconstruction, as there may be an underlying seroma cavity and serous exudate.

A search of the literature revealed a number of anatomical, physiological and clinical studies that addressed the subject of mastectomy flap thickness. This review summarizes the available information on mastectomy flap thickness with reference to oncological safety and avoidance of mastectomy skin flap necrosis. As adjuvant treatments reduce local recurrence after mastectomy, the impact of local treatment and systemic adjuvant treatment is also discussed briefly.

Methods

A MEDLINE search was performed in March 2013, using the search terms 'mastectomy' and 'skin flap' or 'flap thickness'. All directly relevant primary studies were included and referenced. Articles not relevant to the aims of the review were excluded, as were abstracts and reports from meetings not included in peer-reviewed publications. Additional potentially important references known to the authors, or cited within relevant papers, were also investigated. Only articles published in English were included.

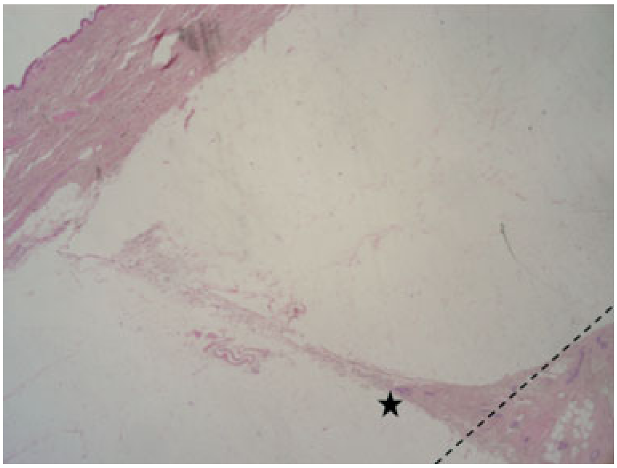

Fig. 1 Breast dermis, subcutaneous adipose tissue and breast glandular tissue. A layer of subcutaneous adipose tissue exists between the dermis and glandular tissue of the breast. The dermis-to-breast thickness varies from 7 to 17 mm in this single section. Elevation of the ('oncoplastic') plane between the subcutaneous adipose tissue removes most, but not all, breast tissue. An approximation to the oncoplastic plane is illustrated by the dotted line. Breast tissue is seen superficial to this plane (adjacent to the star) (haematoxylin and eosin stain, magnification ×15). Figure kindly supplied by A. Nerurkar (Royal Marsden Hospital, Sutton, UK)

Results

The search identified 179 papers (*Fig. 2*). A total of 85 articles were included in the review: three meta-analyses, eight randomized clinical trials, two national reports/national audits, eight review articles, six anatomical studies, eight comparative studies (6 comparative series, 2 case–control studies), three cohort studies, 42 case series, three book chapters and two case report/surgical technique papers. These papers can broadly be divided into: anatomical studies aiming to provide a histological basis for the surgical plane; clinical series investigating the effect of residual breast tissue on the underside of mastectomy skin flaps (flaps too thick); clinical series examining risk factors for skin flap necrosis (flaps too

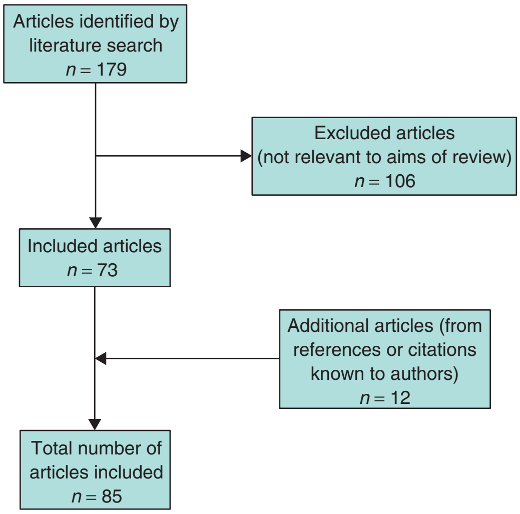

Fig. 2 Flow diagram showing selection of articles for review

thin); and physiological studies investigating techniques for assessing skin flap viability in the operative setting.

Oncological considerations

Mastectomy and breast-conserving therapy (wide local excision, lumpectomy, partial mastectomy) when combined with radiotherapy have demonstrated equivalent survival in randomized trials[15]. The goal of mastectomy is to remove the breast. Thick mastectomy skin flaps may, however, result in residual breast tissue on the underside of the skin flap, and this residual breast tissue may be of significance after therapeutic mastectomy, particularly in the absence of radiotherapy. Residual breast tissue and the risk of subsequent development of cancer are of particular importance in the setting of prophylactic mastectomy in patients with a high genetic risk.

Anatomical studies of the breast superficial fascial layer

The superficial fascial system of the body is a connective tissue network extending from the subdermal plane to the underlying muscle fascia[16]. These horizontal membranous sheets are separated by fat and interconnecting fibrous septae[17]. The superficial fascial system of the thorax is known to communicate with that in the abdomen and limbs. However, there has been controversy surrounding the precise architecture of the superficial fascia in the breast. Histological studies summarized in *Tables 1* and *2* indicate that the superficial fascia divides into a superficial layer (Camper's fascia) and deeper layer (Scarpa's fascia), with the mammary gland in between[18,19]. Van Straalen and colleagues[19] focused on the inframammary ligament, observing this structure as a dense fibrous strand in the same anatomical plane as the superficial fascia. However, Muntan and co-workers[18] reported that Camper's fascia was composed mainly of adipose tissue. Beer *et al.*[20] performed a histological examination of 62 breast specimens from women undergoing breast reduction and reported

Table 1 Studies investigating the presence of a fascial layer in the breast

Reference	Year	Study type	Tissue used	Numbers	Findings
Lockwood[16]	1991	Anatomical study	Cadavers, cross-sectional cadaver segments, body-contour patients	12 cadavers, 20 body-contour patients	Superficial fascial system of thorax communicates with that in abdomen and limbs
Muntan *et al.*[18]	2000	Anatomical study	Cadavers (chest wall)	12 cadavers (10 female and 2 male)	Superficial fascia divides into superficial (Camper's fascia) and deep (Scarpa's fascia) layer with mammary gland in between. Camper's layer composed mainly of adipose tissue
van Straalen *et al.*[19]	1995	Case series	Inframammary ligaments from female-to-male transsexuals undergoing subcutaneous mastectomy	10 breast specimens	Postulated existence of a true inframammary ligament, which is part of the superficial fascia rather than an extension of the deeper prepectoral fascia
Beer *et al.*[20]	2002	Case series	Breast tissue from women undergoing breast reduction	62 breast specimens	No superficial fascial layer in up to 44% of breasts. In those containing this layer, it was irregular and contained islands of breast tissue in 42% of specimens. Minimal distance between breast parenchyma and dermis was 0·4 mm
Abu-Hijleh *et al.*[17]	2006	Anatomical and ultrasound radiological study	Cadavers Volunteers	3 male and 3 female 2 men and 2 women	Superficial fascia consisted of 'thin, horizontal membranous sheets separated by varying amounts of fat' with a deep layer adjacent to the muscle fascia

Table 2 Studies evaluating volume of breast tissue superficial to fascial layer

Reference	Year	Study type	Tissue used	Numbers	Findings
Larsen *et al.*[21]	2011	Case series	Reduction mammoplasty specimens	76 breasts (38 women)	Consistent non-breast-bearing subcutaneous layer between dermis and breast parenchyma. Subcutaneous thickness variable (few millimetres to < 3 cm) and difficult to predict (no correlation with body mass index, age, breast weight or thickness in contralateral breast)
Beer *et al.*[20]	2002	Case series	Breast tissue from women undergoing breast reduction	62 breast specimens	No breast tissue detected superficial to superficial fascial layer. Minimum distance between superficial layer and dermis varied from 0·2 to 0·4 mm

that as many as 44 per cent did not contain a superficial fascial layer. In breasts that did contain this layer, in 42 per cent of instances it was irregular and contained islands of breast tissue within the layer. However, no breast tissue was detected superficial to this layer. From this anatomical study it was concluded that the superficial layer of fascia is not present in all breasts, and therefore cannot be used as a reliable plane of dissection. When present microscopically, it may be too thin and delicate to detect macroscopically. Furthermore, the superficial layer was considered too superficial to be used as a landmark for adequate skin flap thickness as the minimum distance between this superficial layer and dermis varied from 0·2 to 0·4 mm, and the resulting skin flaps would be too thin. Thus this layer is not the same as the plane noted by surgeons.

In contrast, Larson and colleagues[21] tried to identify the non-breast-bearing subcutaneous layer of tissue between the dermis of the breast skin and the underlying parenchyma. A breast pathologist prospectively examined 76 breast specimens from 38 women undergoing reduction mammoplasty, without knowledge of the clinical details. Subcutaneous tissue thickness was measured from the deepest skin dermis to the most superficial breast tissue. A consistent and distinct layer of non-breast-bearing subcutaneous tissue between the dermis and the breast parenchyma was identified. The median thickness was 10 (range 0–29) mm. Half of the women (the interquartile range) had a subcutaneous tissue thickness between 6 and 17 mm. No correlation was found between the thickness of this subcutaneous tissue and body mass index, patient age, breast specimen weight, or dermis-to-breast thickness of the contralateral breast. The absence of correlation with the contralateral breast raises questions about the validity of such measurements. It is possible that the wide ranges in measurement in this study are explained by the lobular nature of the underlying breast, with the overlying skin forming a smooth contour, such that the measurement obtained will depend on the location within the superficial lobules from which the section is taken (*Fig. 1*). Alternatively, technical or fixation issues may influence the results. Although the authors concluded that an oncologically safe and viable skin flap can be achieved if the subcutaneous layer present in most breasts is used as a guide for elevating the skin flaps, this study is prone to selection bias as all samples were taken from a population undergoing reduction mammoplasty and there was a lack of information regarding which breast quadrant the specimens were taken from. These limitations, combined with lack of a description about the superficial fascial layer, and the variation in measured dermis-to-breast parenchyma distance, are such that the 10 mm reported median should be interpreted with caution in surgical oncological clinical practice.

According to anecdotal surgical experience, there can be quite wide variations in the thickness of the subcutaneous layer between patients, and even between quadrants in a single patient. In some patients the plane can be found easily and in others is more difficult to locate. It is therefore not surprising that there is discrepancy among histological studies about the presence or absence of a distinct fascial layer and its depth beneath the dermis. Furthermore, differing fixation protocols may contribute to discrepancies between histological studies. Formalin fixation can cause alterations in different tissue thicknesses within a specimen. For example, in a recent porcine limb study[22], 10 per cent formalin fixation caused muscle expansion but fatty tissue shrinkage. Beer and colleagues[20] fixed their tissue in 4 per cent buffered formalin and sectioned at 2 μm thickness, whereas Larson and co-workers[21] fixed in 10 per cent buffered formalin and sectioned at a thickness of 3–4 μm, which perhaps may contribute to the differing observations between these studies.

Residual breast tissue following mastectomy

In 1937, Hicken studied over 385 mammograms with ductal contrast injection and observed that the breast ducts

Table 3 Studies evaluating residual breast tissue within mastectomy flaps

Reference	Year	Study type	Tissue used	Numbers	Findings
Hicken[23]	1940	Case series	Dye extravasation study on mastectomy specimens	17 mastectomy specimens	Residual breast tissue left in 94% of mastectomy skin flaps
Barton *et al.*[24]	1991	Case series	Multiple mastectomy site biopsies at time of reconstruction following TGM or MRM	27 patients having TGM (159 biopsy specimens) 28 patients having MRM (161 biopsy specimens)	Residual breast tissue in > 20% patients in both groups. Average residual breast tissue in each patient < 1 g
Carlson *et al.*[25]	1996	Case series	Tissue specimens taken from inframammary fold following mastectomy for breast cancer	24 specimens from 22 patients	Residual breast tissue present in 13 of 24 specimens
Torresan *et al.*[26]	2005	Case series	Tissue from SSM skin flaps	42 patients with breast cancer	Terminal ductal lobular units in 60% of residual skin flaps and residual disease in 10% of patients. Both were associated with skin flap thickness > 5 mm
Cao *et al.*[27]	2008	Case series	Analysis of superficial specimen margin involvement. Additional intraoperative biopsy from overlying dermis of skin flap	168 SSMs	64 patients (38·1%) had positive superficial specimen margin,13 (20%) of whom had residual breast carcinoma in additional skin flap biopsy
Tewari *et al.*[28]	2004	Case series	Four quadrant biopsies from under skin flap following Patey mastectomy	37 patients	Residual breast tissue in 8 patients, which contained tumour in 3

TGM, total glandular mastectomy; MRM modified radical mastectomy; SSM, skin-sparing mastectomy.

extended much further across the anterolateral chest wall than previously appreciated. The ducts extended up into the axilla in 95 per cent of cases, sometimes following the brachial plexus and blood vessels into the very apex of the axillary fossa. In 15 per cent the ducts extended downwards and medially into the epigastric space and in 2 per cent they extended laterally beyond the anterior border of latissimus dorsi. These findings should be interpreted with some caution because, even though the axillary tail of the breast is recognized widely, it seems unlikely that ducts commonly extend high into the axilla. Although intraductal injection of methylene blue via cannulation of each duct at the nipple surface was intended with this technique, inadvertent injection into the lymphatics may have occurred, and is an alternative explanation for the findings. Hicken was also surprised by the frequency with which the injected ducts came in close contact with the skin. He therefore hypothesized that a very extensive chest wall resection would be necessary to remove all mammary tissue, and suspected that only a proportion of the breast was actually being removed at mastectomy. He went on to perform dye injection studies on 17 mastectomy specimens[23]. Methylene blue was injected into the specimen ducts at the nipple surface. If no dye escaped, the ductal system was assumed to be intact. Areas from which dye escaped indicated where the lactiferous ducts had been severed or left *in situ*, implying incomplete removal. Evidence of residual breast tissue in mastectomy skin flaps was found in 94 per cent of specimens in this study. The most common region of dye extravasation was the axillary segment (in 88 per cent), but the sternal border accounted for 23 per cent and epigastric border in 11 per cent. Hicken went on to use intraoperative methylene blue in an attempt to achieve complete glandular excision, but, interestingly, commented that on two occasions the blue ducts were seen to penetrate the pectoral fascia and enter the underlying muscle.

More recent studies have also provided evidence of residual breast tissue following mastectomy (*Table 3*). Barton and colleagues[24] carried out biopsies of the mastectomy site at the time of breast reconstruction, following total glandular mastectomy or modified radical mastectomy. Residual breast tissue was identified in just over 20 per cent of patients in both groups. Carlson *et al.*[25] analysed 24 tissue specimens taken from the inframammary fold following mastectomy for breast cancer in 22 patients. They found breast tissue in 13 of the 24 specimens. However, the actual amount of breast tissue in these 13 specimens was minimal (mean 0·04 per cent). Tewari and co-workers[28] studied whether breast tissue was left under the skin flaps of 37 consecutive patients undergoing modified radical mastectomy. From each patient, four quadrant biopsies were taken from under the skin flaps, 3 cm from the skin edge. Residual breast tissue was present in eight of 37 patients, and in three of these it contained tumour tissue. Although this series represents the experience of only a single surgeon, it highlights the potential for leaving residual breast tissue behind with the consequent risk of disease recurrence.

Even when very thin skin flaps are fashioned, residual breast tissue may be found. This was observed in biopsies following subcutaneous mastectomy in cadavers[29]. In this experiment, very thin skin flaps were fashioned, resembling full-thickness skin grafts. Residual breast tissue was still found in the majority of cases and in a variety of locations, including the skin flaps. These studies highlight the difficulty of achieving complete removal of all breast tissue at mastectomy and suggest that this is an unattainable goal.

Three histological studies[26,27,30] have searched for residual breast disease in the skin flaps of patients undergoing SSM. Torresan and colleagues[26] found terminal ductal lobular units (TDLUs) in 60 per cent of residual skin flaps following SSM, and residual disease in 10 per cent of patients. A high prevalence of either residual TDLUs, or residual disease and TDLUs, was associated with skin flap thickness greater than 5 mm in this series. Ho and co-workers[30] investigated the potential incidence of residual cancer after SSM by examining the location of disease in relation to the skin in simple mastectomy specimens. Of 30 specimens, six had skin involvement outside the nipple–areola complex. This finding was significantly related to skin tethering, tumour size and perineural infiltration. In most instances the skin was involved by dermal lymphatic invasion. Cao *et al.*[27] analysed the involvement of the superficial specimen margin in 168 SSMs. During surgery an additional biopsy was taken from the dermis of the skin flap overlying the tumour. Sixty-four patients (38·1 per cent) had a positive superficial specimen margin, 13 (20 per cent) of whom had residual breast carcinoma in the additional skin flap biopsy. The factors associated with positive additional skin flap biopsies were the presence of extensive ductal carcinoma *in situ* (DCIS) ($P = 0{\cdot}002$) and a thicker additional superficial skin flap biopsy (12 mm compared with 9 mm; $P = 0{\cdot}019$). This supports the hypothesis that the risk of superficial mastectomy margin positivity is increased with thicker skin flaps. Only one of 104 patients with a negative superficial mastectomy margin had residual breast carcinoma in the skin flap biopsy; this was in the form of lymphovascular invasion, not amenable to surgical excision. Furthermore, 89 additional skin flap biopsies (53·0 per cent) contained benign breast tissue. The authors acknowledged the concern that not all the breast tissue, and hence potentially not all breast carcinoma, is removed at the superficial specimen margin.

The issue of residual breast tissue arises in the case of nipple-sparing mastectomy. Some advocate removal of all macroscopic breast tissue[31], but others advise retaining a pad of breast parenchyma deep to the areola to preserve vascularization. This potentially increases the risk of local recurrence or development of a *de novo* cancer in that tissue. A recent paper from the Milan group[32] reported a moderate risk of local recurrence if the frozen section of subareolar tissue gave a false-negative result or if the margin was close.

Influence of positive mastectomy margins

The histological studies outlined previously have demonstrated that it is extremely difficult to remove all the breast tissue under the flaps at mastectomy, and that disease may remain after mastectomy. Given the larger surface area of SSM skin flaps, more breast tissue might be expected to be left behind than in simple mastectomy. Comparison of SSM margin involvement and local recurrence rates with those of simple mastectomy may give an indication of the clinical importance of residual breast tissue and residual disease following mastectomy.

Patients undergoing mastectomy have a lower risk of local recurrence than those undergoing breast-conserving surgery, as the whole breast is removed. However, the indication for mastectomy is often more extensive disease and so a small risk of positive margins and consequently local recurrence remains. Case series[33–35] of SSM have reported high rates of close or positive margins ranging from 28·8 to 68·6 per cent. The large variation between studies is probably explained by differences in patient selection.

Sheikh and colleagues[36] analysed mastectomies performed in their institution between 2003 and 2009; 177 SSMs and 249 simple mastectomies were identified. The rate of inadequate margins (either positive margin or close margin less than 2 mm) in the initial specimen was 29 per cent for SSM and 12 per cent for simple mastectomy. Some of those with inadequate margins underwent re-excision to achieve clear margins (7 per cent of patients in the SSM group and 2 per cent in the simple mastectomy group). No data regarding flap thickness were reported for this series, and so no conclusions can be drawn about the relationship between flap thickness and risks of positive margins or local recurrence. However, this paper does document the frequency of positive resection margins, even with formal mastectomy, and revealed a significantly higher risk of inadequate margins with SSM.

Rowell[37] performed a systematic review of mastectomy resection margins and subsequent relapse, examining pooled data from 22 studies involving 18 863 women. Resection margins were characterized as ‘involved’ where tumour was identified at the deep resection margin and 'close' where tumour was identified within a defined distance from the resection margin; the author acknowledged that there is often a lack of consensus on the precise classification of a 'close' margin. An involved postmastectomy margin was identified in 2·5 per cent, a close margin in 8·0 per cent, and muscle or fascia invasion in 7·2 per cent of patients. Meta-analysis of five studies of non-inflammatory breast cancer without radiotherapy found that local recurrence was increased by an involved or close margin (relative risk 2·6; $P < 0·001$). In a separate meta-analysis[38], risk of relapse was related to margin status in women with inflammatory breast cancer (relative risk 3·1; $P < 0·001$). Assessment of risk of relapse in patients undergoing SSM was entirely based on one study[33] and was also found to be related to margin status, although this did not reach statistical significance (relative risk 2·1; $P = 0·16$). Overall, failure to achieve clear resection margins following mastectomy does appear to affect the risk of relapse. It would therefore seem prudent to consider planning excision of close overlying skin during mastectomy for tumours assessed clinically, or that are found to be superficial on preoperative imaging, especially if SSM is being considered.

Local recurrence after skin-sparing mastectomy and simple mastectomy

Overall rates of local recurrence appear unchanged over the past 50 years, despite changes in the indication for mastectomy and in mastectomy technique. In a retrospective review of over 3600 patients undergoing radical mastectomy and modified radical mastectomy over 30 years (from 1948 to 1978), Gilliland and colleagues[39] found a local recurrence rate of 4·6 per cent, although the duration of follow-up was not stated. Only one-third of these had local recurrence as the primary and only site (60) and, of these, over one-half were in the scar (39) rather than the skin flaps themselves. More recently, Carlson *et al.*[40] reviewed 565 SSMs for breast cancer and found a local recurrence rate of 5·5 per cent after a mean follow-up of 65 months. These very similar recurrence rates over half a century, despite evolution in indication and technique, suggest that other factors may be playing a role in influencing relapse rates, and that the impact of differing small amounts of breast tissue left behind with different techniques is overshadowed by other factors.

There is a growing body of evidence to show that, within the limitations of patient selection, SSM has equivalent oncological outcomes to simple mastectomy[8,41,42]. Case series of SSM have reported local recurrence rates ranging from 0·6 to 10 per cent[43–45], but only the comparative studies can truly inform practice regarding selection of surgical technique. Sheikh *et al.*[36] analysed mastectomies in their institution between 2003 and 2009. The mean follow-up was only 28 months, but with a 0·9 per cent recurrence rate and no significant difference between SSM and simple mastectomy over this interval. In another study[46] of 1810 patients undergoing either SSM or simple mastectomy, 6·6 per cent of patients developed locoregional or systemic recurrence after a median follow-up of 53 months. This did not differ significantly between the SSM and simple mastectomy groups (5·3 *versus* 7·6 per cent). Even after adjusting for clinical tumour node metastasis (TNM) stage and age, local recurrence rates did not differ significantly between the two groups, although the numbers were small in the subgroups with more advanced tumour stage. These outcomes lend weight to the argument for SSM as an acceptable treatment option for selected patients suitable for immediate breast reconstruction in centres experienced in this technique.

A meta-analysis[11] of observational studies comparing SSM and simple mastectomy for breast cancer suggested that rates of local recurrence do not differ significantly between the two techniques. The local recurrence rate in comparative studies included in the meta-analysis varied from 3·8 to 10·4 per cent after SSM and from 1·7 to 11·5 per cent after simple mastectomy. This was not significantly different (odds ratio 1·22, 95 per cent confidence interval (c.i.) 0·85 to 1·74), and there was no significant difference in disease stage or axillary node status between the two groups. Insufficient information was provided by the contributory studies to be certain that grade was matched, and a slight increase in distant recurrence in the simple mastectomy group (12·0 per cent *versus* 10·0 per cent for SSM; odds ratio 0·67, 95 per cent c.i. 0·48 to 0·94) suggests there may have been a difference in grade or tumour size. Furthermore, there was no significant difference in the incidence of severe postoperative adverse events between SSM and simple mastectomy (18·7 *versus* 22 per cent; odds ratio 0·81, 95 per cent c.i. 0·57 to 1·16). This included skin flap necrosis, implant loss, severe infection or any complication requiring surgical intervention. The studies included in this meta-analysis have the disadvantages of being non-randomized and with only limited follow-up. However, the suggestion is that, in appropriately selected patients, the small amount of residual breast tissue left under the additional longer skin flaps in SSM does not necessarily lead to a clinically significant increase in local recurrence rates.

Prophylactic mastectomy

Many women with *BRCA1* and *BRCA2* gene mutations choose bilateral mastectomy, often combined with immediate breast reconstruction, as a risk-reducing measure for their high lifetime risk of breast cancer[47]. Although effective removal of at-risk breast tissue is the primary aim, the long-term aesthetic outcome is also very important in this group of often young women. Nipple-sparing mastectomy and SSM may achieve particularly pleasing cosmetic outcomes and this in turn may increase uptake over what would occur if simple mastectomy were the only surgical option[48]. The landmark study[49] in this area showed that prophylactic mastectomy could reduce breast cancer risk by 90 per cent. Only seven cancers occurred among 639 high- and moderate-risk women (risk determined by the Gail model) at a median follow up of 14 years; 90 per cent of the surgical group underwent 'subcutaneous' mastectomy at which an estimated 90 per cent of breast tissue was removed. Although not statistically significant ($P = 0{\cdot}38$), all seven cancers occurred in the subcutaneous mastectomy group. This may indicate that residual breast tissue on thick skin flaps subsequently developed disease.

In more recent studies in which an SSM was performed, with presumed increased awareness and attention to skin flap thickness, the results of risk-reducing mastectomy were even more encouraging. In a study[50] of 358 women with a high genetic risk of breast cancer (236 of whom were *BRCA1* or *BRCA2* mutation carriers), who underwent prophylactic mastectomy using a SSM technique, there were no primary cancers at a median follow-up of 4·5 years. However, in one patient an axillary breast cancer metastasis was detected at 3·5 years' follow-up, despite no breast cancer being detected at the time of surgery. Explanations for this include some residual breast tissue or an undetected occult primary cancer at the time of surgery. Despite this, the study clearly demonstrated that prophylactic mastectomy does reduce the risk of breast cancer development, and other studies[51–55] support this finding.

Influence of postmastectomy adjuvant therapy

Chest wall radiotherapy

In the presence of nodal involvement, postmastectomy radiotherapy can produce a substantial absolute reduction in the risk of local recurrence, and a definite but moderate reduction in long-term breast cancer mortality[56–62]. Collaborative meta-analyses from the Oxford Overview[15] included 8500 women with mastectomy, axillary clearance and node-positive disease in trials of radiotherapy generally to the chest wall and regional lymph nodes. Radiotherapy resulted in a 17 per cent reduction in local recurrence (6 *versus* 23 per cent) and a 5·4 per cent reduction (54·7 *versus* 60·1 per cent) in 15-year breast cancer mortality risk. Consistent with this, the Oxford Overview demonstrated that, for every four local recurrences avoided, one breast cancer death is prevented. Three-quarters of the eventual local recurrence risk occurred during the first 5 years. In local treatment comparisons, if the 5-year local recurrence risk was less than 10 per cent, there was little difference in 15-year breast cancer mortality if adjuvant radiotherapy was given. However, if the 5-year local recurrence risk exceeded 10 per cent, significant reductions in 15-year breast cancer mortality were found. This is presumably through ablation of microscopic residual disease, which is consistent with the findings described above that breast tissue remains following mastectomy. However, the reductions in local recurrence were at the price of significant side-effects from the radiotherapy, including a significantly increased incidence of contralateral breast cancer (with older radiotherapy regimens), angiosarcoma and non-breast cancer mortality in irradiated women (largely from heart disease and lung cancer)[63]. Given a 5 per cent risk nationally of mastectomy flap necrosis[14], the use of adjuvant radiotherapy in high-risk cases may produce better outcomes than attempts to create ever thinner mastectomy skin flaps.

Chest wall relapse following mastectomy for DCIS is uncommon. Kim and colleagues[64] reported on ten such instances and discovered that the presence of residual normal breast tissue was a common feature. Chadha *et al.*[65] carried out a retrospective review of 207 patients treated by mastectomy for DCIS between 1997 and 2007. Only two (1·0 per cent) developed a local recurrence and both patients had a final mastectomy margin of less than 1 mm. Other studies[35,65–68] examining outcomes following mastectomy for DCIS have similarly reported low overall local recurrence rates. However, the small number of patients and retrospective nature of the data make it difficult reliably to identify risk factors for relapse in patients treated with mastectomy for DCIS, and hence patients with DCIS who may benefit from postmastectomy radiotherapy.

Adjuvant systemic therapy

Local recurrence rates following mastectomy are reduced by adjuvant systemic therapies, similar to local recurrence rates following breast conservation. In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 trial[69], 2818 patients with oestrogen receptor-positive breast cancer were randomized to receive either tamoxifen or placebo. Equal proportions in both groups (62 per cent) were treated with mastectomy. In those randomized to mastectomy the local relapse rate (within the chest wall and scar) was reduced from 6·7 to 2·3 per cent at 10 years by the addition of tamoxifen. Similarly, in both NSABP B-13 and B-19 studies[70], in which a similar proportion was treated with mastectomy, local relapse rates were reduced in those randomized to chemotherapy (8·4 to 5 per cent, and 6 to 2·8 per cent respectively).

Mastectomy skin flap viability

The National Mastectomy and Breast Reconstruction Audit Third Annual Report[14] described outcomes in over 18 000 women undergoing mastectomy with or without reconstruction between 1 January 2008 and 31 March 2009. In response to questionnaires collected 3 months after surgery, 4 per cent of women in the mastectomy alone group reported that the 'breast skin turned dark and died', whereas 6·1 per cent reported this complication in the immediate reconstruction group and 5·5 per cent in the delayed reconstruction group. These data indicate that skin flap necrosis occurs in approximately one in 20 patients undergoing mastectomy. No data have been reported on skin flap thickness, but an approximately 5 per cent rate of skin flap necrosis highlights the importance of achieving a sufficient skin flap thickness to preserve the vascular supply to the skin. This must be balanced against the risk of leaving residual disease if the flap is too thick.

Factors affecting skin flap viability

Surgical technique and patient risk factors may both influence skin flap viability. The influence of surgical technique is discussed in more detail below. Patient risk factors for poor healing include the effects of smoking, previous scars, previous radiotherapy, diabetes, obesity and severe co-morbidities[71–74]. Many of these risk factors are not modifiable in the timescale between diagnosis and surgery. Smoking is known to impair wound healing and significantly increases the risk of mastectomy skin flap necrosis following reconstruction[72]. A recent study[75] also suggested that patients undergoing mastectomy following previous breast-conserving surgery (lumpectomy and radiotherapy) may have an increased incidence of mastectomy skin flap loss, presumably mediated in part by the effects of previous chest wall radiotherapy.

The blood supply to a skin flap is an important determinant of flap viability. The blood supply to the breast is provided by perforating branches from the axillary artery (namely the superior thoracic, thoracoacromial, lateral thoracic and subscapular arteries), the internal thoracic artery, and the second to fourth anterior intercostal arteries[76,77]. Perforating cutaneous branches supply the overlying breast skin. These arterial and arteriolar vessels are linked to form a continuous plexus, which is best developed in the subdermal plexus and on the undersurface of the subcutaneous fat[77]. An earlier observation by Maliniac[78] was that the depth of the subcutaneous vessels depends on the amount of fatty tissue present, being found at a deeper level in breasts with a thicker layer of subcutaneous fat.

Assessment of mastectomy skin flap viability

Although skin colour, capillary refill and dermal bleeding have been used traditionally to assess viability before completing immediate reconstruction, fluorescein dye test techniques have been used to evaluate skin flaps in plastic surgery for many years. These may have a role in evaluating equivocal mastectomy flaps, particularly in SSM, and allow excision of areas likely to undergo necrosis. Losken and co-workers[73] studied flap viability following SSM with autologous breast reconstruction using an intravenous fluorescein dye to assess flap perfusion. Fifty consecutive periareolar mastectomy skin flaps were studied; 31 had transverse rectus abdominis myocutaneous flap reconstructions and 19 latissimus dorsi with expander. Seven of 50 flaps developed necrosis. Two of these were in fully fluorescent flaps, giving a positive predictive value of 96 per cent, and five in the non-fluorescent group. Although flap thickness was not measured directly or compared in this series, flaps with areas of non-fluorescence smaller than 4 cm^2 typically survived, except in the irradiated breast. Flaps with areas of non-fluorescence larger than 4 cm^2 tended not to survive, unless very proximal on the flap. The authors went on to recommend that any area of non-fluorescence in the irradiated flap be excised, and that this test may be a helpful adjunct in the evaluation of such flaps during surgery.

Intraoperative oxygen tension was studied in the mastectomy flaps of ten patients undergoing either simple mastectomy or SSM, to identify factors predicting flap necrosis[79]. Only one patient in this pilot study experienced flap necrosis, but the authors identified reductions in medial and inferior skin flap tissue oxygen saturation measurements and flap length as predictors of this.

Influence of surgical technique

The perceived advantages of immediate breast reconstruction by the development of SSM techniques has emphasized the importance of understanding how thick skin flaps should be to maintain their viability. Some authors[80] have reported rates of flap necrosis close to 17 per cent with flaps 4–5 mm thick, whereas others[81,82] have achieved less than 5 per cent flap necrosis with thicker 10-mm flaps. These reports suggest that leaving thicker flaps might reduce rates of flap necrosis. Unfortunately, the method of measurement of skin flap thickness is not standardized and may be difficult to reproduce.

Some have suggested that a tumescent technique, whereby saline with local anaesthetic and adrenaline is injected into the subcutaneous plane, may make the fascial plane thicker and easier to adhere to, while also minimizing blood loss and the use of diathermy. However, a retrospective review[83] of 380 consecutive mastectomies with immediate reconstruction, with 100 procedures performed using tumescence, found that this was a significant risk factor for developing postoperative major skin flap necrosis (odds ratio 3·93; $P < 0.001$). Other risk factors were previous irradiation, age and body mass index.

Another suggestion is that the use of diathermy rather than scalpel may increase the risk of skin flap necrosis. In a retrospective study[84] of 151 SSMs there was no significant difference between diathermy and scalpel. Despite this, dissection devices with a low risk of low thermal injury are being proposed in an attempt to minimize skin flap necrosis[85].

Discussion

Recommendations have been made for surgeons raising mastectomy flaps[21]. The main findings of the present review are that a subcutaneous layer lies between the dermis and breast tissue, which contains minimal breast epithelium. The thickness of this subcutaneous layer is variable and is difficult to predict before surgery. Evidence from women undergoing breast reduction suggests that it can measure from less than a millimetre to 29 mm. The thickness may vary between breasts, and between different parts of the same breast, and there is no good evidence that it is associated with obesity or age. Thus the existence of a distinct layer of superficial fascia in the breast remains controversial; it may be present in only up to 56 per cent of patients. It is not possible to remove all breast tissue at mastectomy and leave reliably viable skin flaps. Taken together, owing to the paucity of evidence or investigation into mastectomy skin flap thickness, and the variable as well as unpredictable thickness of the breast subcutaneous layer, a single specific universal thickness for mastectomy skin flaps cannot be recommended currently.

The existing evidence suggests that the ideal skin flap thickness is variable, and therefore the surgeon must use skill and judgement to identify the oncoplastic plane when macroscopically visible, and to gauge the level of the plane where it is not so obvious. It may be that the plane between the subdermal fat and the breast parenchyma is a reasonable guide[20], but this may not always correspond to a subcutaneous fascial layer. It is logical that thicker flaps risk leaving breast tissue, and that this may have negative oncological consequences, as do positive surgical margins, and this seems to be supported by the literature.

Achieving complete removal of all breast tissue at mastectomy appears an unattainable goal. Despite evolution in mastectomy techniques, local recurrence rates over the past 50 years remain at around 5 per cent. This may be because, when performed carefully, the differences between the techniques (simple mastectomy and SSM) do not greatly affect outcome, or because other factors such as adjuvant systemic therapies, chest wall radiotherapy and patient selection are also at play. Whatever the explanation, achieving clear resection margins remains an important surgical goal to reduce the risk of local relapse. Avoiding local relapse is extremely important, as survival will be compromised for one in four patients with local recurrence. On the other hand, in the UK, approximately 5 per cent of patients undergoing mastectomy experience flap necrosis. Although patient risk factors influence this, surgical technique also plays a role both in optimizing oncological outcomes and in reducing the risk of local complications.

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