7

Breast-conserving surgery: the balance between good cosmesis and local control

J. Michael Dixon
E. Jane Macaskill

Introduction

The aim of local treatment of breast cancer is to achieve long-term local disease control with the minimum of local morbidity. The majority of women presenting symptomatically to breast clinics and those who are diagnosed through screening programmes have small breast cancers, which are suitable for breast-conserving therapy (BCT), defined as breast-conserving surgery (BCS) and whole-breast radiotherapy.

✔✔ The major advantages of breast-conserving treatment are:

- equivalence in terms of disease outcome compared with mastectomy as demonstrated in two systematic reviews;[1,2]
- an acceptable cosmetic appearance for the majority of women with breast cancer;[3]
- fewer complications and more cost-effective than mastectomy;
- lower levels of psychological morbidity compared with mastectomy, with less anxiety and depression and improved body image, sexuality and self-esteem.[4,5]

The Early Breast Cancer Trialists Collaborative Group (search date 1995) analysed data from six randomised controlled trials that compared BCT with mastectomy.[1] A meta-analysis of data from five of these six trials involving 3006 women found no significant difference in the risk of death at 10 years (odds ratio 0.91, 95% CI 0.78–1.05). The sixth randomised trial used different protocols. A second systematic review included nine randomised controlled trials involving 4981 women randomised to mastectomy or BCT.[6] A meta-analysis of these nine trials found no significant difference in the risk of death over 10 years: the relative risk reduction for BCT compared with mastectomy was 0.02 (95% CI −0.05 to +0.09).[6] There was also no difference in the rates of local recurrence in the six randomised controlled trials involving 3006 women where data were available: the relative risk reduction for mastectomy versus BCT was 0.04 (95% CI −0.04 to +0.12).[1] Longer-term follow-up of these trials did show an excess of local recurrences with BCT in four of the trials (OR 1.561, 95% CI 1.289–1.890, P <0.001), but the pooled analysis for mortality showed no effect (OR 1.070, 95% CI 0.935–1.224, P = 0.33).[2] Many of the later local events in treated patients are second breast cancers rather than true local recurrences and this may explain why even with the increase in local events there was no survival benefit for mastectomy. The current use of long-term adjuvant hormone therapy now prevents many of these new events.

These randomised trials comparing BCT with mastectomy were performed many years ago. Over the time period since these trials enrolled patients, recurrence rates have fallen dramatically.[7] One reason for the continued high and increasing mastectomy rate in some countries is that patients and doctors continue to make decisions based on results from these older studies. Other potential reasons include the increasing use of

MRI[7,8] and in the United States, which has one of the highest mastectomy rates,[9] reasons include improvements in reconstructive techniques, and a reported reduction in anxiety and the wish to avoid regular mammography. [9] There is, however, new evidence from a number of cohort studies that BCT produces survival and local recurrence rates at least equivalent and that BCT is associated with better outcomes than mastectomy in specific tumour types. The studies from different countries that have reported better outcomes with BCT are outlined in Table 7.1.[10–15]

A Dutch population-based review of BCT compared with mastectomy alone in 37 207 patients reported a 39% lower loco-regional recurrence rate with BCT (HR = 0.61, 95% CI 0.41–0.90) and 43% improved overall survival for BCT (HR = 0.57, 95% CI 0.31–1.02, $P = 0.012$).[12] An increasing number of studies have suggested that women treated with BCT may have a better breast cancer-specific survival than women treated with mastectomy, independent of tumour characteristics.[16] These reports importantly include all cancer phenotypes. They are in the main observational studies and some of the difference in outcomes is likely to be due to selection bias. The rate of surgical complications and economic burden particularly with brachytherapy is better for BCT.[17] Mastectomy has twice the rate of complications compared with BCT, and is a much less cost-effective option than BCT, particularly when mastectomy is combined with breast reconstruction.

It seems unlikely that having mastectomy in itself is detrimental; however, patients undergoing BCT receive radiotherapy to the breast area whereas only a minority of those having mastectomy do. It is therefore possible that the radiotherapy contributes to the apparent benefit of BCT. BCT may also offer the possibility of omitting further axillary treatment for those with limited nodal involvement at sentinel node biopsy under criteria for the ACOSOG Z011 trial.[18]

✔ Originally it was thought that local therapy had little influence on overall survival but it is clear that a proportion of local failures are responsible, at least in part, for some patients developing metastatic disease.[19,20]

It is thus important in patients selected for breast-conserving surgery to minimise local recurrence while at the same time achieving a good cosmetic outcome.[21]

Selection of patients for breast conservation

Traditionally, single cancers measuring 4 cm or less, without signs of local advancement, have been selected for BCS. Currently any cancer, single or multiple, that can be excised to clear margins before or after neoadjuvant therapy and leave a satisfactory cosmetic outcome can be treated with BCS (Box 7.1).

Box 7.1 • Indications and contraindications for breast-conserving surgery

Indications

- Single or multiple lesions that can be excised to leave a satisfactory cosmetic outcome
- Most T1, T2 (<4 cm) cancers or T2 > 4 cm*
- T3 cancers in larger breasts*

Relative contraindications†

- T4, N2 or M1
- Patients who prefer mastectomy‡
- Collagen vascular disease§
- Large or central tumours in small breasts¶
- Women with a strong family history of breast cancer or who are proven *BRCA1* and *BRCA2* mutation carriers

*Consider neoadjuvant therapy first.
†None of these are absolute contraindications.
‡Following a fully informed discussion of the pros and cons of breast-conserving surgery versus mastectomy.
§Many patients with collagen vascular disease are suitable for wide excision and whole-breast radiotherapy.
¶Can be suitable for BCS after neoadjuvant treatment.

Table 7.1 • Studies comparing BCT with mastectomy demonstrating better overall survival outcomes with BCT

Author	Country	No. of pts	RR	95% CI
Hwang et al.[9]	USA	112 154	0.81	0.80–0.83
Saadatmand et al.[10]	Netherlands	83 191	0.87	0.81–0.93
Van Maaren et al.[11]	Netherlands	37 207	0.81	0.78–0.85
Hofvind et al.[12]	Norway	9547	0.59	0.42–0.77
Hartmann-Johnsen et al.[13]	Norway	13 015	0.61	0.53–0.70
Agarwal et al.[14]	USA	132 149	0.76	0.72–0.78

✔ Increasing tumour size does not equate with increasing local recurrence rate and so limiting breast-conserving surgery to cancers below a certain size is illogical.

Clinical measurements overestimate tumour size so this is best estimated by imaging, with ultrasound assessment of tumour size being more accurate than mammographic measurements.[22] Magnetic resonance imaging (MRI) appears even better than ultrasound in assessing disease extent, particularly in invasive lobular carcinoma.[23] The problem with MRI is that it has a low specificity and a low positive predictive value and only two-thirds of lesions identified by MRI as suspicious of malignancy are subsequently confirmed as malignant.[24] The role of MRI in assessing patients for breast-conserving surgery has been investigated in a randomised study that showed that routine use of MRI is not worthwhile.[22,25] MRI did not reduce the rate of incomplete excisions and was not associated with a reduction in short-term local recurrence, but did significantly increase the mastectomy rate in patients who were otherwise considered good candidates for breast-conserving surgery.

✔ It is the balance between tumour size as assessed by imaging and breast volume that determines whether a patient is suitable for breast-conserving surgery.

Options for patients with tumours considered too large, relative to the size of the breast, for breast-conserving treatment include neoadjuvant systemic therapy to shrink the tumour, an oncoplastic procedure (transfer of tissue into the breast or remodelling one or both breasts to obtain symmetry; see Chapter 8).[26,27] In a patient with small breasts, excision of even a small tumour may produce an unacceptable cosmetic result without tissue transfer.

Patients with multiple tumours in the same breast have not previously been considered good candidates for breast-conserving treatment because they were reported to have a high reported incidence of in-breast recurrence[28,29] and so have usually been treated by mastectomy. Recent evidence has, however, demonstrated similar rates of local recurrence for patients with unifocal and multifocal and even multicentric disease providing all disease is excised to clear margins.[30–35] If it is feasible to excise the separate cancers in different parts of the breast and produce an acceptable cosmetic outcome then such patients should no longer be treated routinely by mastectomy. Patients with bilateral cancers can also be treated by bilateral BCS.

The rates of breast-conserving surgery vary significantly between countries and within countries. These rates are clearly influenced as much by the views of the surgeon as other issues such as the availability of radiotherapy locally. Failure to offer BCS to suitable and appropriate patients has become a medicolegal issue. If a patient who fulfils the criteria for BCS is treated by mastectomy then the reasons for the decision to proceed to mastectomy should be recorded clearly in the patient's notes. Some patients choose mastectomy in preference to BCS but may do so because they do not appreciate that outcomes for BCT are at least as good as mastectomy in both survival and recurrence rates. In one series of patients choosing mastectomy rather than breast-conserving surgery, over half of patients did not know that mastectomy and BCT produce identical rates of survival.[36]

A range of clinical and pathological factors have influenced surgeons when selecting patients for BCS because of their perceived impact on local recurrence. These include young age (under 35–39 years), the presence of an extensive in situ component associated with an invasive tumour, grade 3 histology and widespread lymphatic/vascular invasion. These are considered in detail below.

Factors affecting local recurrence after breast-conserving surgery

Over 80% of all local recurrences were initially reported to be located adjacent to the site of initial excision. This is no longer true and an increasing percentage of 'recurrences' in treated breasts are second primary cancers.[37] Megavoltage radiation therapy delivered to the whole breast in a dose of 4000–5000 cGy given over 3–5 weeks continues to be used in most patients after breast-conserving surgery because radiotherapy both reduces the rate of local recurrence and improves overall survival.[38] Studies continue to evaluate whether localised radiotherapy delivered either during or within a few days of surgery is as effective as whole-breast radiotherapy.[39,40] One study enrolled 1356 patients from 1992 to 2013 treated by BCS and accelerated partial breast irradiation (APBI) using interstitial multicatheter brachytherapy. The 10-year actuarial risk of an ipsilateral breast recurrence was 7.6% (95% CI 5.6–10.1).[41] Physician-reported cosmesis was rated excellent or good in 84%. Results from a more recent randomised study comparing 551 BCS patients who underwent whole-breast irradiation with tumour-bed boost with 633 patients who had BCS and APBI using interstitial multicatheter brachytherapy reported a 5-year cumulative incidence of local recurrence of 1.44% (95% CI 0.51–2.38) with APBI and 0.92% (0.12–1.73) with

whole-breast irradiation (difference 0.52%, 95% CI −0.72 to 1.75; $P = 0.42$).[42] This remains a topic of ongoing debate, and is discussed in detail in Chapter 17.

In low-risk cancers partial breast irradiation is now considered standard treatment in some countries. It has not been possible to identify groups of patients who do not require radiotherapy. However, there is a group of older patients with low-risk cancers (completely excised, node-negative and hormone receptor-rich on adjuvant hormone therapy) and women of any age whose cancers have an extremely good prognosis (small grade 1 or special-type cancers that are completely excised, node-negative and hormone receptor-positive on adjuvant hormone therapy) whose rates of local recurrence without radiotherapy are acceptable.[43,44]

Following whole-breast radiotherapy, it is possible to increase the local dose of radiotherapy by boosting the tumour bed. This reduces local recurrence rates, particularly in younger women and women with DCIS outwith the invasive cancer, although there are cosmetic penalties associated with the use of boost.[45] Further discussion on these issues can be found in Chapter 17.

The rates of in-breast tumour recurrences (IBTR) following BCT have reduced dramatically over the past two decades[46,47] (**Fig. 7.1**). Whereas a 1% annual rate of in-breast cancer events was formerly considered acceptable, rates are often now less than 0.25% per annum. In-breast tumour recurrence rates for women with BCT do, however, remain at this rate for at least 20 years after treatment. This needs to be borne in mind when considering surveillance programmes for such patients. Even patients treated by mastectomy are at risk of local recurrence over this 20-year period.

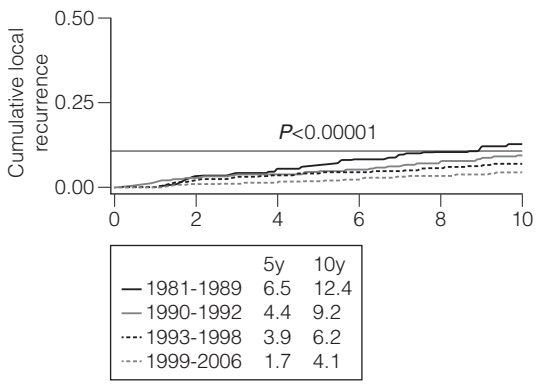


Figure 7.1 • Local recurrence rates in Edinburgh over four separate time periods showing a significant and continued fall in local recurrence rates over time. (Data unpublished, courtesy of Gill Kerr, Edinburgh Cancer Centre.)

Patient-related factors

✔✔ Local recurrence following breast-conserving therapy is significantly more common in younger patients.[48–51]

Multiple studies have demonstrated that local recurrence is more common in younger women.[48–51] While most of the randomised studies had only small numbers of younger women, cohort studies of younger women confirm these findings but have found that with modern treatment regimens, outcomes can be improved.[52] The most recent analysis of the EORTC boost trial by age has confirmed IBTR of up to 34% at 20 years in women under 40, compared to 14% for women aged 41–50 and 11% in women aged over 50 ($P < 0.001$),[45] although addition of radiotherapy boost reduced risk in women under 50, as discussed in Chapter 17. However, these rates of recurrence are not what is reported in more recent series and local recurrence rates with BCT have fallen significantly over time.[47] Risk appears to be higher in younger women, in particular where there is evidence of an extensive intraductal component of disease, and close margins.[53] However, a recent meta-analysis of studies of women under age 40 undergoing BCT or mastectomy for breast cancer demonstrated no difference in overall survival (HR 0.90, 95% CI 0.81–1.00) with actually a trend in favour of BCT.[54] A further review demonstrated that the recurrence-free survival for mastectomy and BCT was identical.[55] These observations do not support avoidance of BCT in younger patients in whom clear margins can be achieved, and while patients should be counselled regarding the potential for local recurrence, there is no evidence mastectomy improves their outcome.

Local recurrence is less common after BCS in older patients (>65 years). Recurrence is also less frequent in women with large breasts but whether this relates to the larger excisions that can be performed in these patients or to alterations in steroid metabolism (fat is known to be an important site of conversion of androgens to oestrogens) is uncertain.[56] A strong family history of breast cancer, and specifically carriage of a pathogenic mutation in one of the breast cancer genes, increases the risk of developing a second primary cancer in both the treated and contralateral breasts unless the woman undergoes a prophylactic oophorectomy, when the local recurrence rate falls in at least certain populations of women to levels similar to those of the general population.[57–59]

Tumour-related factors

Tumour location, tumour size, the presence of skin or nipple retraction, and the presence or absence

of axillary node involvement have not been shown consistently to predict for local recurrence after breast-conserving surgery.[60–63] The hormone receptor status of a breast cancer does not seem to exert any influence on local control rates.[48–51,60–64]

Tumour phenotype

In-breast tumour recurrence following BCS is more common in triple-negative and human epidermal growth factor receptor (HER2)-positive cancers. This has been confirmed by multiple studies, a systematic review and a meta-analysis.[65–70] Regional recurrence and recurrence after mastectomy are also higher in patients with HER2-positive cancers and triple-negative breast cancers, but type of surgery does not appear to influence outcomes[66,69–71] (**Fig. 7.2**). Given that a recent meta-analysis of 15 312 patient with triple-negative breast cancer showed fewer local recurrences (RR 0.75, 95% CI 0.65–0.87, P <0.0001) and fewer distant metastases (RR 0.68, 95% CI 0.60–0.76, P <0.00001) for BCT compared with mastectomy[71] then tumour phenotype is not a reason to choose mastectomy over BCS, rather it is a reason to choose BCS rather than mastectomy.

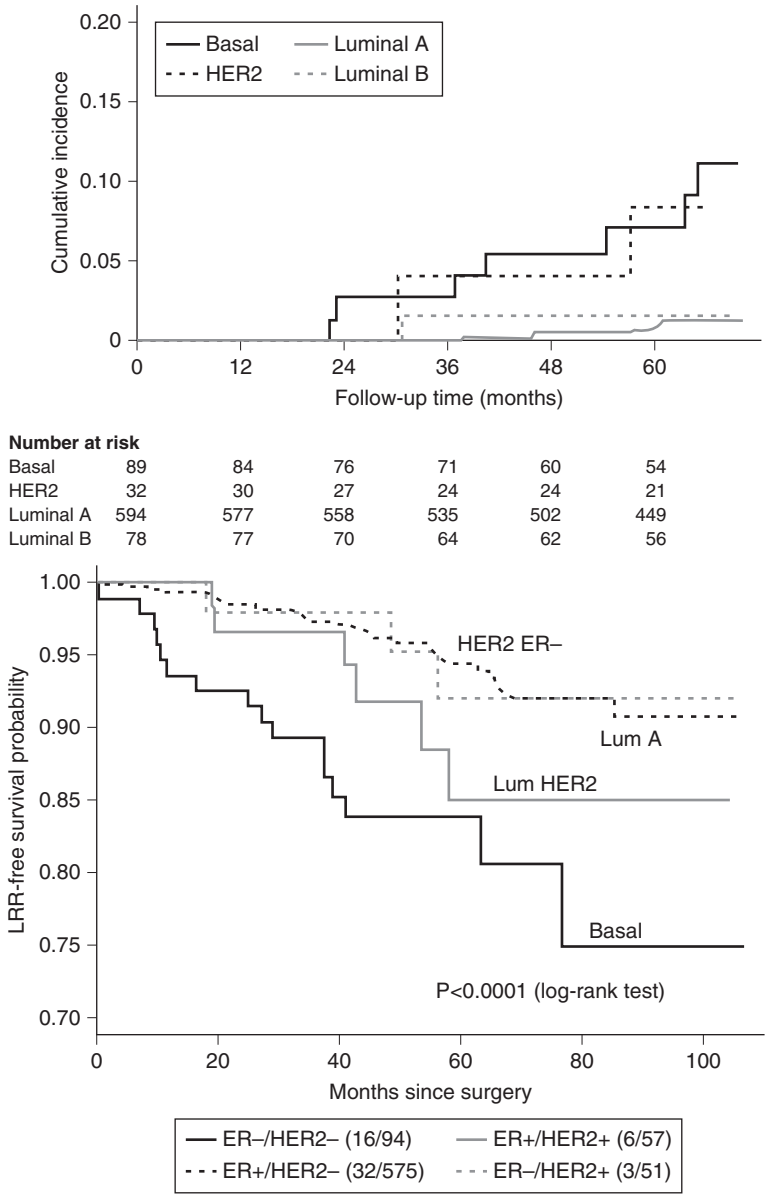


Figure 7.2 • **(a)** and **(b)** showing local recurrence rates after BCT by tumour phenotype.[62,63]

Table 7.2 • Size of tumour related to local recurrence

Size (cm)	Local recurrence (%)
0–1	21
1.1–2	8
2.1–3	13
3.1–4	17
4.1–5	4

Data from Eberlein TG, Connolly JN, Schnitt JS, et al. Predictors of local recurrence following conservative breast surgery and radiation therapy: the influence of tumour size. Arch Surg 1990;125:771–9.

Tumour size

Size is not significantly associated with local recurrence. Only 3 of 28 series that have examined the relationship of tumour size and recurrence have shown any significant association.[72,73] A large study from Boston[73] demonstrated that cancers over 4 cm in size that were treated by BCS had a rate of recurrence similar to that of smaller cancers (Table 7.2).

Tumour grade

A number of reports have analysed the relationship between tumour grade and local recurrence.

✔ The lowest rates of local recurrence are reported in grade 1 tumours.

Although some series report a higher recurrence rate in grade 3 compared with grade 2 cancers, this is by no means universal.[48–51,60–64] The relative risk of local recurrence between grade 1 and grade 2/3 cancer is approximately 1.5. The British Association of Surgical Oncology undertook a trial that randomised patients with node-negative grade 1 or special-type cancers to no further treatment, tamoxifen alone, radiotherapy alone or both radiotherapy and tamoxifen. An update of this study reported an exceedingly low rate of recurrence in patients randomised to radiotherapy and tamoxifen, and acceptably low rates of annual recurrence in patients treated with either tamoxifen alone or radiotherapy alone. Higher rates of recurrence were seen in patients who received neither radiotherapy nor tamoxifen. In these low-risk cancers treatment by radiotherapy alone or tamoxifen alone can produce an acceptable rate of long-term control.[44]

Histological type

There are few data relating histological tumour type to recurrence. Invasive lobular cancer was reported to be associated with a higher recurrence rate than so-called invasive 'ductal' carcinoma.[74–77] One study did suggest that patients with invasive lobular carcinoma who developed local recurrence were more likely to develop multifocal recurrence[63] but this has not been confirmed by others. Patients with invasive lobular cancer appear more likely than patients with no special-type tumours to have an incomplete excision. This is explained in part by the underestimation of tumour extent by mammography and ultrasound and the inability of surgeons to feel the extent of the cancer at operation. Patients with invasive lobular cancer on core biopsy should be warned of an increased likelihood of positive margins. Where the extent of disease is not easy to assess on mammography and/or ultrasound, MRI appears more accurate in estimating extent of ILC than other imaging modalities but both under- and overestimates extent, so if the MRI shows more extensive disease this needs to be confirmed histologically before the patient is considered inappropriate for BCS.[23]

Lymphatic/vascular invasion

Increased local failure rates have been reported in most, but not all, series in patients with histological evidence of lymphatic/vascular invasion (LVI).[48–51,60–64,74–77] Of concern, the percentage of tumours reported to have LVI varies widely between different series by up to a factor of 4.

✔ Carcinomas with LVI have approximately double the rate of local breast recurrence compared with tumours with no evidence of this feature.

LVI is more common in and around the cancer of younger women (<35 years) compared with cancers in older women (>50 years).

Extensive in situ component

A tumour is defined as having an extensive in situ component (EIC) if 25% or more of the tumour mass is non-invasive and non-invasive carcinoma is also present in the breast tissue surrounding the invasive cancer.[77] This was initially thought to be associated with an increased rate of local recurrence and a predictor of residual disease within the breast following an incomplete wide excision. Views on EIC have changed and, providing clear margins are obtained, EIC does not appear to increase the rate of local recurrence following BCT[78–80] (Table 7.3). DCIS outwith the invasive cancer increases incomplete excision rates and is currently used to select patients for boost radiotherapy. The problem with the boost data is that they are old and do not take into account the beneficial effects of prolonged endocrine therapy in reducing local in-breast recurrence.[45]

Multiple tumours

Patients with macroscopically multiple cancers were formerly considered to have an increased risk of local recurrence compared with a patient with a unifocal

Table 7.3 • Local recurrence rates (%) at 5 years in patients from Boston[69] and Stanford[71] subdivided by margin status and the presence (EIC+) or absence (EIC–) of an extensive in situ component

	Boston		Stanford	
Margins	**EIC+**	**EIC–**	**EIC+**	**EIC–**
Positive/ non-negative	37	7	21	11
Close	0	5		
Negative	0	2	0	1

cancer but patient numbers in such early series on which this evidence is based were small and often had incomplete excisions.[28,29] Studies have now shown that multifocality or multicentricity, however identified, can be treated by BCS with acceptable local recurrence rates provided that all margins of excision are clear of disease.[30–35] It is thus time to stop performing mastectomy for such patients as a matter of course and it is no longer acceptable to deny patients BCS based solely on identification of multifocal or multicentric disease.

Treatment-related factors

The most important surgical-related factor for local recurrence is completeness of excision. Current practice is to aim for at least microscopically disease-free margins. Ideally, there should be a clear rim of normal tissue (≥1 mm) around the carcinoma at all radial margins.[46,47]

It is only recently that a consensus view on what constitutes an adequate margin for BCS for invasive cancer has been agreed.[81] This consensus statement was based on two meta-analyses and the views of an expert panel.[47,82] The second meta-analysis included 28 162 patients with 1506 local recurrences. Positive margins were defined as the presence of invasive or in situ cancer at the transected or inked margin. Negative margins were defined as the absence of tumour within a specified distance (mm) of the resection margin, with a close margin indicating the presence of tumour within that distance but not at the resection margin. Compared to a negative margin, close margins were associated with an odds ratio for an increased rate of in-breast tumour recurrence (IBTR) of 1.74 (95% CI 1.42–2.15). Positive margins were associated with a 2.44 odds of IBTR (95% CI 1.93–3.03). The 2898 patients who had margins greater than no tumour at ink had an odds ratio of IBTR of 1.47 (95%CI 0.67–3.20). The odds ratio of IBTR was significantly higher for no tumour on ink than margins of 5 mm or more ($P = 0.021$).

Both meta-analyses concluded that when looking at different thresholds for different margins, 1 mm was as good as wider margins. The US Consensus Conference, aware of the decreasing rates of IBTR and the issue of measuring margin distance accurately, concluded that no tumour on ink was an adequate margin for BCS in invasive cancer.[81] The majority of units in the UK use 1 mm based on the findings of the two meta-analyses.

A recent systematic review investigated the association between margins and IBTR following BCS for DCIS to determine the optimal negative margin width.[83] A problem with this review was that there was heterogeneity of margin definitions across studies, and only a small number of studies included margin widths of 1 mm and 2 mm. The authors thus had to combine >0 mm and >1 mm into one group. Patients with margins of ≥2 mm in this review had a significantly lower rate of local recurrence than margins <2 mm. The conclusion of the review was that negative margins in DCIS reduce the odds of IBTR but that margin distances above 2 mm are not significantly associated with a further reduction of odds of local recurrence compared to 2 mm.[83] A recent study from Edinburgh measured distance to the nearest margin in patients having BCS for DCIS and found no evidence that margin widths >2 mm resulted in a lower rate of IBTR than margin widths of 1–2 mm.[84] The disease that is most often closest to the margin in patients undergoing BCS for invasive disease is DCIS.[85] Having different margins for BCS for invasive cancer and for DCIS also makes little biological sense. It also seems illogical that a patient with DCIS with microinvasion requires a ≥2 mm margin, whereas a patient with a 2.2 cm invasive cancer with widespread DCIS requires no tumour on ink. It makes biological and clinical sense to have a single margin width definition for BCS irrespective of whether the disease is invasive or in situ. Based on the currently available data the margin width to define complete excision after BCS either for invasive or in situ cancer should be 1 mm. However, pathological assessment of margins varies between units and countries and audit of unit local recurrence rates is required to ensure satisfactory practice.

Two meta-analyses concluded that wider margins do not reduce rates of local recurrence. Incomplete excision, i.e. tumour at a margin, does, however, result in an unacceptable rate of local control.[46,47] A 1-mm margin is sufficient for BCS for both invasive and in situ cancer.

Neither lobular carcinoma in situ[86] nor atypical ductal hyperplasia[87] at the margins significantly increases IBTR, so there is no need for re-excision in such patients. Adjuvant systemic therapy with

aromatase inhibitors, tamoxifen and chemotherapy, in the presence of radiotherapy, reduce IBTR after BCS.[88,89] In the absence of radiotherapy, aromatase inhibitors, tamoxifen or chemotherapy alone do not produce satisfactory rates of local control apart from in low-grade, node-negative cancers.[90] The interval between surgery and radiotherapy may be important and IBTR rates appear to increase if radiotherapy is delayed.[91]

Breast-conserving surgery

Two surgical procedures have been described: quadrantectomy and wide local excision. Quadrantectomy was based on the belief that the breast is organised into segments, with each segment draining into its own major duct, and that invasive cancer spreads down the duct system towards the nipple.[92] Both of these premises are incorrect.

✔ A single major subareolar duct does not drain a localised segment of tissue but can drain widespread areas of the breast.

Quadrantectomy or segmental excisions are no longer appropriate breast-conserving options because they do not produce better rates of local recurrence compared with wide excision but do produce significantly poorer cosmetic outcomes compared with wide excision.[93]

✔ Patients having breast-conserving surgery are adequately treated by wide local excision and do not require either a segmental or quadrantic excision.[94,95]

Special technical details: wide local excision

The aim of wide local excision is to remove all invasive and any ductal carcinoma in situ with a margin of normal surrounding breast tissue. Controversy has surrounded which incisions give the best cosmetic results. The predominant orientation of collagen fibres in the skin was described by Langer[96] and these skin crease lines around the breast are essentially circular (**Fig. 7.3**). Subsequent work by Kraissl[97] demonstrated that the lines of maximum resting skin tension run in a more transverse orientation across the breast (**Fig. 7.3**). In general, scars that are parallel to the lines of maximum resting skin tension produce the best cosmetic outcomes, with the lowest rates of scar hypertrophy and keloid formation.

✔ Incisions that follow the lines of maximum resting skin tension produce the most cosmetically acceptable scars.

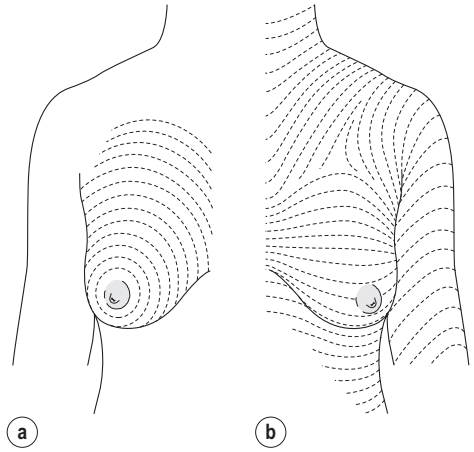


Figure 7.3 • The direction of Langer's lines[88] **(a)** and lines of maximum resting skin tension in the breast **(b)** (so-called dynamic lines of Kraissl[89]).

It has been tradition to place an incision to excise a cancer directly over the lesion, but this can result in an unsightly scar, particularly if the cancer is high and medial. In such instances placing the scar some distance below in the skin crease lines and tunnelling up to the lesion produces a better cosmetic result. Cancers close to the nipple and even those some distance away in the upper half of the breast can be excised through a circumareolar incision. The use of periareolar incisions avoids scars in the visible part of the breast, particularly in the upper inner quadrant (**Fig. 7.4**). There is no doubt that the operation is easier if the incision is placed over the cancer but incisions in the upper breast do have an adverse impact on cosmetic outcomes.[98] Re-excision through these incisions is also feasible. A cancer low in the breast close to the inframammary fold can similarly be excised through an incision placed in the fold. A cancer in the upper outer quadrant

Figure 7.4 • Result from wide local excision right of a cancer in the upper inner quadrant via a circumareolar incision with immediate lipofilling and postoperative radiotherapy.

can be excised easily through an axillary incision. Given the importance of achieving good cosmetic outcomes, increasing numbers of surgeons are using these remote incisions because they produce better cosmetic outcomes. There is no evidence that such incisions compromise local control. Excising skin directly overlying a cancer is only necessary if the skin is involved. It is not necessary to remove dimpled or tethered skin. The aim should be to minimise skin excision and to remove only sufficient skin to get microscopically clear margins.

✔ Routine excision of skin when performing a wide excision cannot be justified.[84,99]

Limiting the length of incision is also important, as longer incisions produce significantly poorer cosmetic outcomes. Knowledge of the depth of the cancer within the breast provided by preoperative or intraoperative breast ultrasound can be valuable when planning the extent of excision. For instance, if a cancer is 2 cm deep within the breast, then at least 1 cm of fat and subcutaneous tissue can be left on the skin flaps; leaving this tissue improves the cosmetic outcome. Whatever incision is used, it is important to have discussed the position of any scar with the patient prior to surgery.

Having made the skin incision, the skin and subcutaneous fat are dissected off the breast tissue. Care should be taken when elevating skin not to remove subcutaneous fat unnecessarily as thin skin flaps give a poor postoperative cosmetic result. Where the cancer is close to the skin, hydrodissection infiltrating 1 in 500 000 adrenaline in saline can help to separate the skin and subcutaneous fat from the breast tissue and breast fat, and facilitates skin elevation over the cancer. Skin flaps beyond the edge of the cancer for at least 1–2 cm are raised. This allows the fingers of the non-dominant hand to be placed over the palpable cancer. The breast tissue is then divided beyond the fingertips. The line of incision through the breast should be approximately 1 cm beyond the limit of the palpable mass. Having incised through the breast tissue, dissection continues under the cancer. In the majority of patients the whole thickness of breast tissue down to the pectoral fascia is removed to ensure that there is an adequate margin deep to the cancer. If the lesion is superficial, and there is a significant amount of breast tissue deep to the cancer, full thickness of breast tissue does not need to be removed. Likewise, if the lesion is deep, more tissue can be left superficially on the skin flaps. Having reached the deep margin, which is usually the pectoral fascia, the breast tissue and cancer are lifted from this fascia. It is not necessary to excise pectoral fascia unless it is tethered to the tumour or the tumour is involving it. If a carcinoma is infiltrating one of the chest wall muscles, then the affected portion of the muscle should be excised beneath the tumour, the aim being to remove sufficient muscle to get beyond the limits of the cancer. Having dissected under the cancer, it is then possible to grasp the cancer and surrounding tissue and to complete excision of the cancer at the other margins. The specimen should be orientated immediately following excision with Liga-clips, sutures or metal markers, prior to specimen radiography and submission to the pathologist.[100] Metal markers or Liga-clips are preferred because they can be seen on specimen radiography. Routine X-ray of orientated specimens is recommended because it has been shown to help the surgeon confirm the target lesion has been excised and allows assessment of completeness of excision at the radial margins.[100] If the specimen radiograph shows the cancer or any associated microcalcification is close to a particular margin, then further tissue can and should be removed from the margin of concern, before being orientated and sent to pathology.

Between 11% and 46% of patients having a wide excision for invasive cancer and 31–46% with DCIS have involved margins.[82,83] Residual disease in re-excisions varies from 21% to 77%.[101–103] While it is tempting to assume that current pathology margin assessment has a high false-positive rate, further tissue will often have been vapourised by diathermy and unless cancer is transected at the margin then one would not necessarily expect further disease to be found. Routine cavity margin shavings have been taken in an attempt to reduce the positive margin rate. A randomised study performed in Yale showed that taking routine cavity shavings did almost halve the incomplete excision rate from 34% to 19%. It did, however, increase the total volume of tissue removed from 74 cm^3 to 115 cm^3.[104] Although the Yale study did not demonstrate an impact on cosmetic outcome, a study by Hennigs et al. showed that specimen weights over 75 g produce a cosmetic result that gradually worsens over time.[98]

There have been a variety of methods used to assess margins intraoperatively.[105–114] The Marginprobe is FDA approved, uses radiofrequency spectroscopy and takes about 1.5 seconds per measurement, with multiple measurements usually required from each margin.[115,116] It has the potential to reduce re-excisions by 60%. The Clear Edge device uses bioelectrical impedance spectroscopy that is sensitive to extracellular and intracellular tissue dielectric properties.[117] A baseline reading is taken on the patient's normal breast tissue and produces an image of pixels within a few seconds, which are either green (normal), fatty tissue or fibrous tissue (yellow) or red (abnormal, either cancer or cellular tissue). It is currently in trials and has the potential

to reduce margin re-excision rate by at least 50%. A new portable MRI system using magnetic resonance diffuse-weighted imaging and no contrast agents is currently in trials. Using light emitted from fluorodeoxyglucose, it has been shown possible to identify disease at margins of BCS specimens with a mini PET scan. Other techniques undergoing evaluation are rapid evaporation mass spectrometry, which analyses an aspirated aerosol of the tissue cut through and so assesses material close to the margin, and optical adherence tomography, which can image structures below the margin.

Having excised the cancer from the breast, suturing the defect in the breast without mobilisation of breast tissue usually results in distortion of the breast contour. Defects in the breast are best closed by mobilising surrounding breast tissue from the overlying skin and subcutaneous tissue: in some patients mobilisation from the underlying chest wall is also required. Large defects (>10% breast volume) that are left open fill with seroma; these frequently absorb, following which scar tissue develops and this then contracts to produce breast distortion. Following wide local excision it is usually possible to close defects in the breast tissue by a series of interrupted absorbable sutures. Drains are not necessary after wide local excision and should not be used routinely. They do not protect against haematoma formation and increase infection rates. Breast skin wounds should be closed in layers with absorbable sutures, finishing with a subcuticular suture.

For patients having a large volume of their breast excised, options include volume replacement with a local flap such as a lateral intercostal perforator flap (LICAP) or a latissimus dorsi muscle flap that can be a thoracodorsal artery perforator flap (TDAP) or the whole of the muscle alone with or without overlying skin. Although there are proponents of these local flaps, they do produce extra scarring and flaps that involve the latissimus dorsi muscle do not always allow an LD flap to be available for later whole-breast reconstruction should the patient develop recurrence (see Chapter 13). Another and potentially simpler option is volume replacement with fat transfer or lipofilling. Wide excision and immediate lipofilling has been evaluated in three studies. Two of these studies reported good outcomes but neither evaluated patient outcomes in detail or compared immediate wide excision and lipofilling with standard breast conserving surgery.[118,119] The third study from Edinburgh compared 32 patients having breast conserving surgery with immediate lipofilling with 39 women who had standard breast conserving surgery.[120] In the Edinburgh study a standard wide excision was performed and fat of approximately double the volume excised was injected into the subcutaneous fat, underlying muscle and breast tissue surrounding the wide local excision and at the end of the operation the defect was closed. In this study the cancers in the lipofilling group were significantly larger (median 21 mm vs 16 mm) and the patients were slightly younger (median age 49 vs 54, $P = 0.06$) than the comparison group. At a median follow-up of 36 months significantly better cosmetic outcomes were seen in the lipofilling group and these women complained of less postoperative pain ($P = 0.0045$). At 3 years there were no local recurrences and only one of 32 lipofilled patients had developed any calcification at the wide local excision site. BCS and immediate lipofilling thus provides superior cosmetic outcomes to standard breast-conserving surgery and is a potential option for some patients (**Fig. 7.5**).

✔ Staples and interrupted sutures do not produce satisfactory results and are not an acceptable method of wound closure in the breast.

Complications of wide excision include haematoma, infection, incomplete excision, seroma and poor cosmetic results. Haematoma requiring evacuation is uncommon but occurs in approximately 2% of patients. Infection requiring treatment affects 5–10% and is more common when combined with an axillary dissection. Incomplete excision rates are usually in the range 10–25%. The presence of in situ cancer outwith the invasive cancer is the major reason why breast cancers are so commonly incompletely excised. Almost two-thirds of incomplete excisions can be explained by the pathology features of the cancer so incomplete excision rates should not be used to compare surgeons.[85] Although large volume excisions increase complete excision rates they adversely affect cosmetic outcome. This is important as the most common long-term problem following BCS is a poor cosmetic result. Factors influencing cosmetic outcome and methods of avoiding this are considered in detail below.

Excising impalpable cancers

Impalpable lesions can be localised prior to surgery using one of a number of different techniques, including skin marking, injection of blue dye, carbon or radioisotope injection or seed, insertion of a hooked wire, savi scout® or intraoperative ultrasound. Although excising an impalpable cancer is easier if the skin incision is made directly over the cancer, remote incisions produce the best cosmetic results. Most impalpable cancers can be approached through a cosmetically placed incision (**Fig. 7.6**). The location of the lesion can be determined in a number

Figure 7.5 • Results from patients undergoing BCT and immediate lipofilling after completion of treatment.

of ways: (i) the surgeon can calculate the position of the breast lesion from the mammogram taken after wire insertion; (ii) the radiologist or the surgeon can mark the skin overlying the lesion using ultrasound; or (iii) if an isotope has been used to localise the cancer, the surgeon can use a gamma probe to localise the area of maximum radioactivity. After making an appropriately sized and cosmetically placed skin incision, this is deepened. If a wire is in place, then dissection continues towards the wire in the plane between the breast and subcutaneous fat so that the wire can be located some distance before it enters the lesion. For instance, if a mammographic abnormality has been localised in the craniocaudal position, then it helps to identify the wire superiorally before it enters the cancer. Wires that are marked with beads or that change in diameter, or have a guide that can be placed over the wire, help the surgeon to determine exactly how far along the wire the lesion is situated. Ideally the hook of the wire should be 1 cm through the lesion rather than within its centre. The direction of the wire on the preoperative mammogram is not always a reliable guide to the course of the wire through the breast. Once the wire is in place, standard mammographic views are not always possible and thus a lesion that is apparently lateral to the entry point of the wire may not be lateral on the check craniocaudal film once the compression from the breast has been released. The aim is to remove the mammographic lesion with a 1-cm clear radiological margin and in most women to excise tissue up to subcutaneous fat and down to pectoral fascia.

As for palpable lesions, all specimens should be orientated with Liga-clips or markers, or secured to an orientated grid so that orientated specimen radiographs can be performed. Radiography is best performed in an X-ray machine designed specifically to X-ray specimens, such as a Faxitron® machine. There have been conflicting reports about whether compressing the specimen affects the incidence of subsequent positive margins as reported by the pathologist. Orientated specimen radiography improves the rate of complete excision of impalpable cancers.[100] Cooperation between surgeon and pathologist is required so that the area of concern can be identified and assessed by the pathologist to ensure adequacy of excision.

The majority of wide excisions of palpable and impalpable cancers are performed under general anaesthesia, but it is possible to perform these procedures under local anaesthesia.

Factors influencing cosmetic outcome after breast-conserving surgery

There is a great variation in different series in the number of patients with good to excellent cosmetic results after breast-conserving surgery (**Fig. 7.7**).

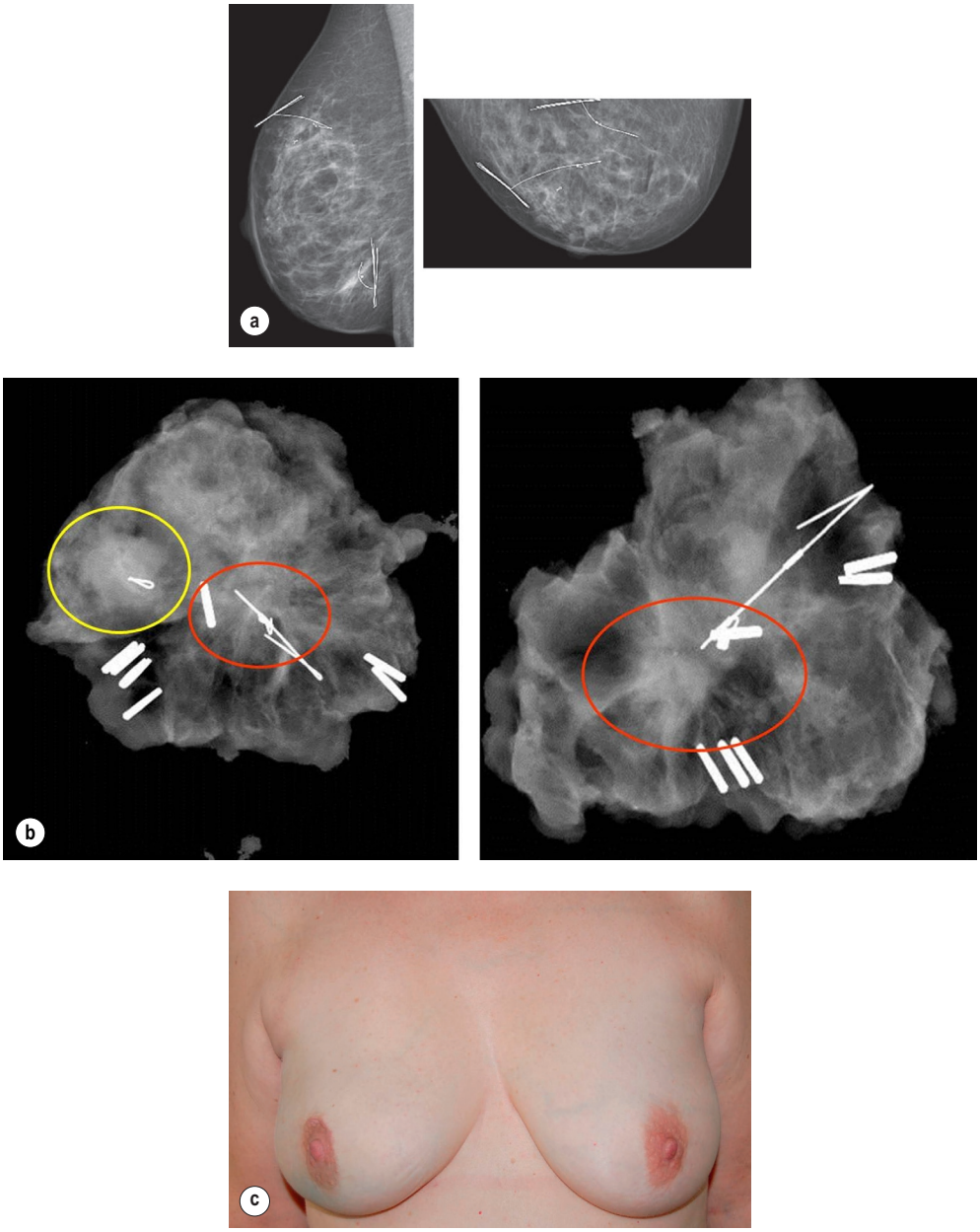


Figure 7.6 • Patient undergoing BCT for impalpable multisite disease with wire-guided excision.

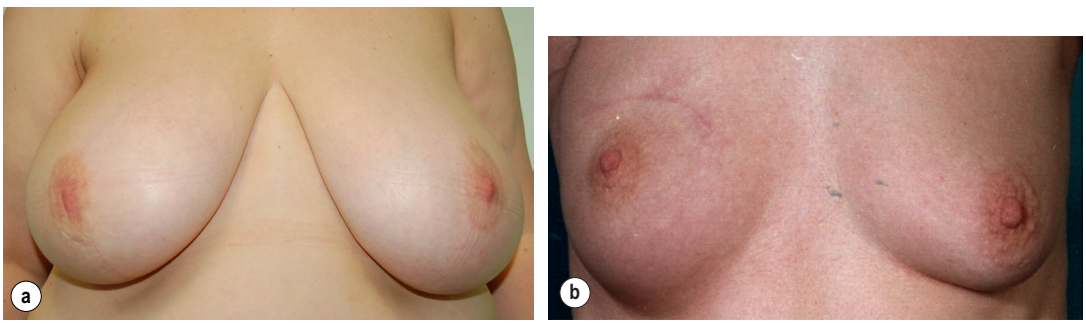


Figure 7.7 • Examples of excellent **(a)** and poor **(b)** cosmetic results from breast-conserving surgery and radiotherapy.

The importance of a good cosmetic outcome is based on studies that have shown a significant correlation between poor cosmetic outcome and increased levels of anxiety, depression, poor body image, problems with sexuality and low self-esteem.[4]

Patient factors

There is conflicting evidence about whether age influences cosmetic outcome, with some studies claiming that older women have worse cosmetic results than younger women.[3] A treated breast that is symmetrical immediately following BCS can become asymmetrical over time.

There is a trend towards increased fibrosis in larger breasts, which leads to poorer cosmetic results than seen in smaller breasts.[121] For this reason large-breasted women may be best treated by BCS combined with breast volume reduction by a therapeutic mammoplasty. Better cosmetic results following BCT are obtained in medium- and moderate-sized breasts; achieving a good cosmetic outcome can sometimes be difficult in smaller breasts.[3]

Tumour factors

Increasing tumour size means that increasingly large amounts of tissue have to be removed. The volume of tissue excised is the most important factor relating to cosmetic outcome and so for simple BCS, the larger the cancer generally the worse the cosmetic result.[122,123]

Location of tumour

Cosmetic outcomes tend to be better if the tumour is located in the upper outer quadrant.[124] Cancer in the upper breast at 12 o'clock or the upper inner breast has a worse outcome than other locations.[98] Downward displacement of the nipple can occur when surgery is performed on tumours located in the inferior half of the breast. This can be corrected at the time of initial surgery by mobilising the nipple and surrounding skin or de-epithelialising a crescentic portion of skin above the nipple, the aim being to re-centre the nipple on the breast mound (see Chapter 8). Central cancers can be challenging to excise and get a good cosmetic outcome.[3] This is why central tumours were at one time considered a relative contraindication to breast-conserving surgery. Excision of central cancers not directly involving the nipple–areola complex can be treated by wide excision and nipple preservation, without significantly increasing the rate of local recurrence compared with more peripherally situated cancers.[125] Good cosmetic outcomes can be obtained providing that surrounding breast tissue is mobilised and the central defect closed (Fig. 7.8). In women with moderate-sized breasts, the nipple and/or areola can be excised in continuity with the cancer if the cancer involves the nipple: the skin can be closed by a purse-string suture (Fig. 7.9). Another option is to advance or rotate a dermoglandular local flap from the lower part of the breast to fill the defect. To advance a flap of skin requires at least 9 cm of skin between the margin of skin excision and the inframammary fold (Figs 7.7, 7.10, 7.11).

Figure 7.8 • Good cosmestic results from excision of a subareolar cancer left breast via a circumareolar incision.

Surgical factors

The extent of surgical excision or the volume of resected breast tissue is the most important factor affecting cosmesis.[3,122]

The poorer cosmetic results obtained with quadrantectomy, even in the most experienced hands, compared with wide excision are well documented and are related to the much larger volumes of tissue removed by quadrantectomy.[126]

Figure 7.9 • Result after a central excision of a cancer and use of a purse-string suture to close the central defect.

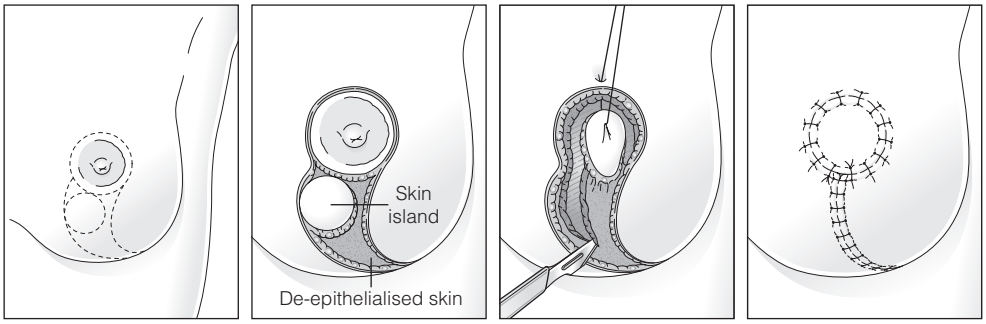
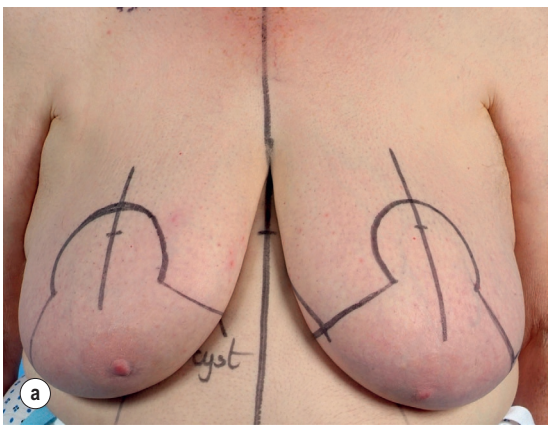


Figure 7.10 • **(a)** How to excise a central cancer under the nipple and produce a satisfactory cosmetic outcome without major breast distortion (Grissotti flap). This procedure has been called central quadrantectomy. The nipple–areola complex is excised and a portion of skin inferior is marked out. An incision around the circular skin island is made and the remaining skin around the island is de-epithelialised. A full-thickness incision is then made in the breast and the skin island is rotated to fill the central defect. Staples are useful to position the flap. When the flap is deemed to be in an optimal position, the staples are removed and the wound closed in two layers with absorbable sutures. **(b)** Final result from a right wide local excision Grissotti flap and nipple reconstruction.



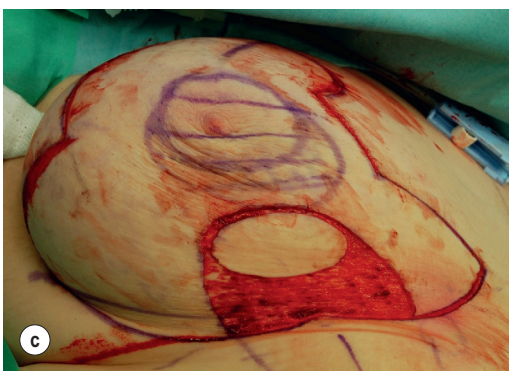


Figure 7.11 • **(a)** Patient prior to operation – cancer under right nipple evident by asymmetry with right nipple flatter and right nipple higher than left. **(b)** Preoperative markings showing the area around the nipple that will be excised. **(c)** Operative view of the island of skin that is mobilised on a de-epithelialised inferior dermoglandular flap. **(d)** Final result after radiotherapy prior to nipple reconstruction.

Even more critical than the volume of tissue resected is the percentage volume of the breast excised (**Fig. 7.12**). Excisions of less than 10% of breast volume are generally associated with a good cosmetic outcome, whereas excisions over 10% often produce a poor cosmetic result (**Fig. 7.13**). If more than 10% of breast volume needs to be excised then consideration should be given to volume replacement with a myocutaneous or local lipocutaneous flap,[26,27] volume replacement using immediate lipofilling following the tumour excision, an oncoplastic reduction procedure (therapeutic mammaplasty), neoadjuvant drug therapy or a mastectomy with or without immediate reconstruction.

Re-excision and number of procedures

Re-excision of the tumour bed has a negative impact on cosmesis.[122] This is mainly as a consequence of the increased total volume of tissue excised from the breast. There is no limit to the number of re-excisions that a patient can have to achieve complete removal of all invasive and in situ disease,[127] but with the greater number of re-excisions more tissue is removed and so the likelihood of a good cosmetic result decreases. For patients who require multiple excisions to get clear margins then consideration should be given to correcting any volume deficit prior to delivery of radiotherapy or considering subsequent contralateral symmetrising surgery.

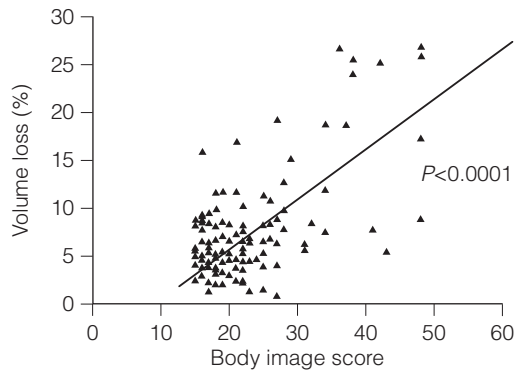


Figure 7.12 • Percentage of breast excised compared with body image score. Percentage of breast excised calculated by measuring total weight of excision and estimating breast volume (from initial diagnostic craniocaudal mammogram). Body image score based on patient-administered questionnaire of 15 questions (score runs from 15, the best possible score, to 60, the worst and highest possible score). Data from a series of 120 patients treated in the Edinburgh Breast Unit.

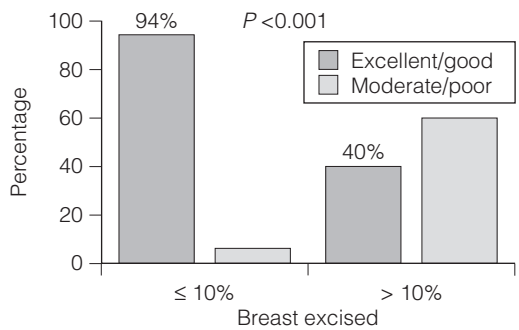


Figure 7.13 • Percentage of good/excellent results in patients subdivided according to whether 10% or less or more than 10% of breast volume was excised by breast-conserving surgery.

Axillary surgery

Axillary clearance is associated with a worse cosmetic outcome compared with sentinel node biopsy, because it can result in an axillary deficit, and it increases the risk of breast oedema.[122,123,128]

Postoperative complications

Development of a haematoma, seroma or post-operative infection can adversely affect cosmetic outcome.[3]

Breast-conserving surgery after neoadjuvant therapy

Many patients with large or locally advanced breast cancer are now treated by neoadjuvant chemotherapy or endocrine therapy and up to a half become candidates for BCS. All patients undergoing neoadjuvant chemotherapy who might be candidates for subsequent BCS should have one or more tumour markers placed centrally in the cancer (and involved node if present) prior to treatment. The patterns of response to neoadjuvant chemotherapy (NAC) and neoadjuvant endocrine therapy (NET) differ, so BCS following NET is more likely to achieve clear margins at one operation than after NAC.[129] The most common form of pathological change following NET is central scar formation, which results in concentric reduction in tumour size and tumour volume, whereas a diffuse pattern of response with little reduction in tumour volume is a feature seen in some patients after NAC.[129] All patients undergoing breast-conserving surgery after NAC should be warned of this rate of incomplete excision and the possible need for a further operation.

✔ MRI following neoadjuvant chemotherapy is the best of the currently available imaging methods to assess extent of disease and is the best predictor of whether a cancer is suitable for breast-conserving surgery.[130–132]

Radiotherapy

Increasing doses of radiotherapy, particularly with the addition of boost, have a detrimental effect on cosmetic

outcomes.[64,122,123] Long-term follow-up is necessary to assess cosmetic outcome; 3 years after treatment, radiotherapy effects tend to stabilise. Fibrosis is a late effect of radiotherapy and produces breast retraction and contour distortion. The treated breast tends not to increase in size to the same extent as the opposite untreated breast, so patients as they age can develop asymmetry even when the initial cosmetic result was excellent. Historically, radiotherapy boost has a negative impact on cosmesis because it produces intense fibrosis and unsightly skin changes, including telangiectasia.[64]

Other treatment effects

Tamoxifen and aromatase inhibitors have little if any effect on cosmetic outcome, whereas some studies have suggested that chemotherapy has a negative impact on the cosmetic outcome of breast-conserving surgery.[3]

Treatment of poor cosmetic results after breast-conserving surgery

Prevention is better than treatment, so closing breast defects and immediate lipofilling (**Fig. 7.5**) are much better options than trying to correct asymmetry once it has developed. One option for improving poor cosmetic outcomes is increasing the volume of one or both breasts if the main problem is essentially loss of volume rather than significant radiation fibrosis. While placement of silicone prosthesis or prostheses has been described, they are successful only for patients with little or no deformity and absence of marked skin changes.[133] The use of implants has been largely superseded by lipofilling. Fat is aspirated from the abdomen and thighs and centrifuged, washed or filtered.[134,135] Having removed the oil and blood it is then injected as micro droplets into the area of distortion and/or asymmetry. Only a fraction of the fat injected survives and multiple episodes of lipofilling combined with scar release or scar excision may be required to correct significant breast deformity and asymmetry (**Fig. 7.14**).[135] If the problem is simply one of asymmetry and the treated breast is a satisfactory shape but smaller than the normal contralateral breast, then the contralateral breast can be reduced. If the treated breast is shrunken, misshapen and scarred, then another option is to excise part or the whole of the treated breast and perform reconstruction. Pedicled myocutaneous latissimus dorsi or transverse rectus abdominis myocutaneous (TRAM) flaps offer an opportunity

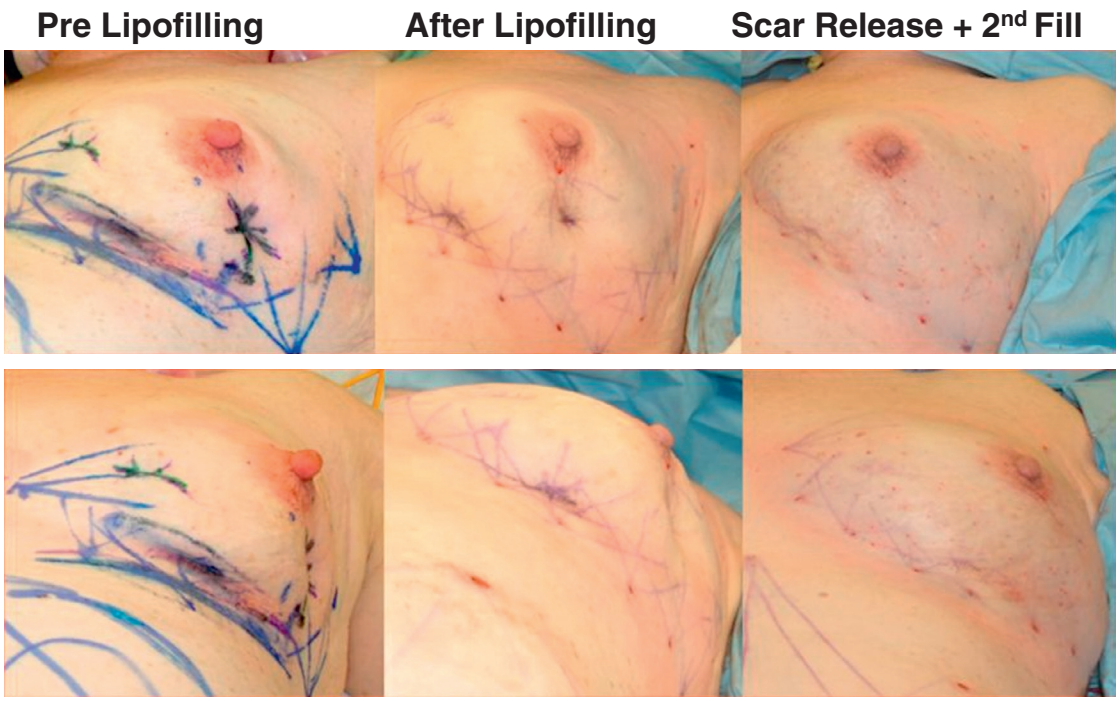


Figure 7.14 • Patient with a defect from a previous wide local excision and radiotherapy before and after lipofilling and then scar release and lipofilling of the left breast.

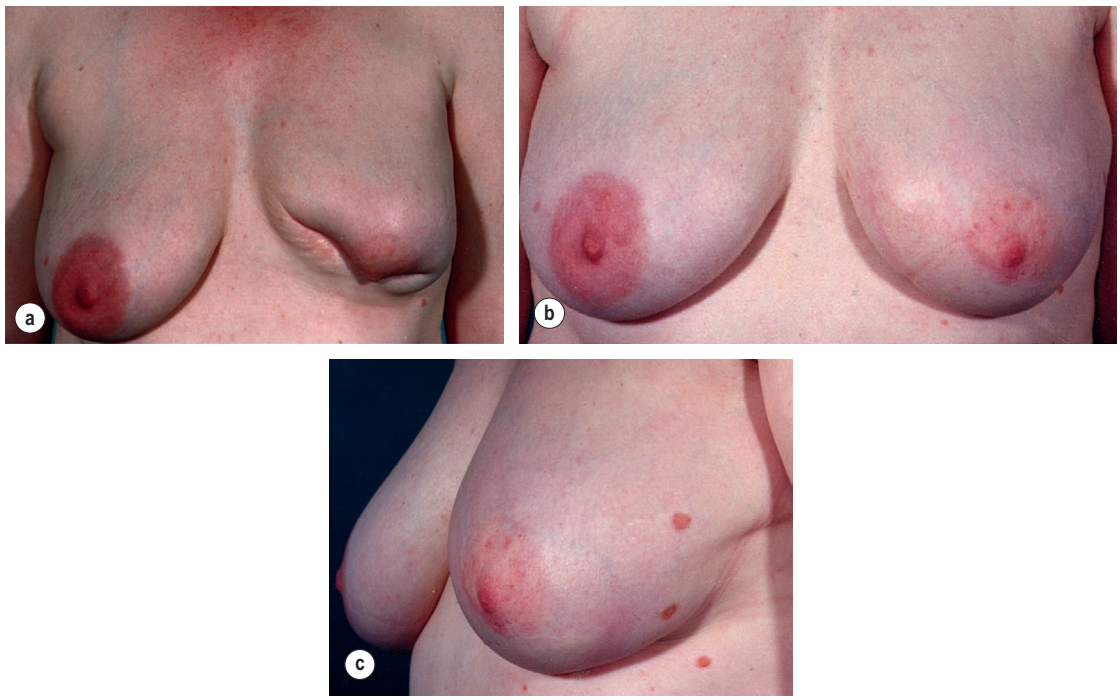


Figure 7.15 • Patient with a poor cosmetic result after breast-conserving surgery before **(a)** and after **(b,c)** partial breast reconstruction with a pedicled latissimus dorsi myocutaneous flap.

to excise unsightly areas of skin and/or breast distortion and scarring, and provide one option to regain symmetry (**Fig. 7.15**).

Significance and treatment of local recurrence

Local recurrence rates of 0.25% or less per year after breast-conserving treatment are now achievable.

✔✔ An isolated local breast recurrence does not appear to be a threat to survival, but breast recurrence is a predictor of distant disease,[20,136,137] and the aim of primary treatment is to avoid local recurrence if at all possible.

Isolated recurrences of the breast can be treated by re-excision or mastectomy.[136–138] Re-excision alone is associated with a high rate of subsequent local recurrence if the initial recurrence occurs within the first 5 years of treatment.[136] Until recently, 80% of local recurrences in the conserved breast occurred at the site of the original breast cancer, with 90% of these local recurrences following BCS being invasive. This is no longer true and an increasing percentage of 'recurrences' in treated breasts are now second primary cancers. Local recurrence within the first 5 years is associated with a worse long-term outlook than recurrence thereafter.[20,136,137,139] Giving systemic therapy following mastectomy for an apparently localised breast recurrence improves the long-term outcome.[140] Uncontrollable local recurrence is uncommon after BCS, but when it does occur it is difficult to treat.

✔✔ Extended hormonal treatment of 5–15 years reduces in-breast tumour recurrences by almost two-thirds and also reduces the rate of contralateral breast cancer development.[87,141–144]

Local recurrence is reduced by letrozole compared with tamoxifen given as initial adjuvant therapy to postmenopausal women with ER-positive breast cancer (Table 7.4).

Prolonging adjuvant hormonal therapy beyond 5 years has a significant impact on the rate of subsequent local relapse in postmenopausal patients with hormone receptor-positive breast cancer.[143]

Table 7.4 • Efficacy endpoints in 4922 patients enrolled into the BIG 1-98 trials

	Letrozole (*n* = 2463)		Tamoxifen (*n* = 2459)	
	No. of pts	**%**	**No. of pts**	**%**
Disease-free survival events	352	14.3	418	17.0
Local	19	0.8	38	1.6
Contralateral breast	14	0.6	26	1.1
Regional	13	0.5	11	0.5
Distant	182	7.4	212	8.6
Deaths without cancer	60	2.4	48	2.0
Deaths (overall survival events)	194	7.9	211	8.6
Systemic failures	331	13.4	374	15.2

Modified from Coates AS, Keshaviah A, Thurlimann B, et al. Five years of letrozole compared with tamoxifen as initial adjuvant therapy for postmenopausal women with endocrine-responsive early breast cancer: update of study BIG 1–98. J Clin Oncol 2007; 25(**5**): 486–92. Published by the American Society of Clinical Oncology.

Key points

- For patients with single breast cancers, survival outcomes from breast-conserving treatment are at least equivalent to that of mastectomy.
- Radiotherapy (after breast-conserving surgery) reduces the rate of local recurrence and improves overall survival. No subgroup of patients has yet been identified that can avoid radiotherapy.
- The major surgical factor influencing local recurrence is completeness of excision, and clear margins (≥1 mm) must be obtained when performing breast-conserving surgery either for invasive cancer or DCIS.
- Younger patients have an increased rate of local recurrence versus older patients after both breast-conserving surgery and mastectomy but recurrence rates have fallen over time. Conversely, older patients have a lower rate of local recurrence.
- Tumour phenotype, tumour grade and LVI influence the rate of local recurrence. Patients with these factors should not be denied breast-conserving surgery, providing the cancer can be excised to clear margins.
- There is a direct correlation between cosmetic outcome after breast-conserving surgery and psychological morbidity, with better cosmetic outcomes being associated with less anxiety and depression and better body image and self-esteem.
- The most important factor influencing cosmetic outcome after breast-conserving surgery is the percentage volume of breast excised. Removing more than 10% of the breast volume dramatically increases the number of women having a poor cosmetic outcome.
- Lipofilling or lipomodelling used at the time of breast-conserving surgery or later can significantly improve cosmetic outcomes, reduce pain and improve patients' quality of life
- Patients who develop local recurrence after breast-conserving surgery, particularly in the first 5 years, are at increased risk of having systemic relapse.
  Isolated local recurrences after breast-conserving surgery are usually treated by mastectomy, although re-excision is sometimes possible, particularly if the recurrence develops more than 5 years after treatment or the patient has not received radiotherapy to the breast.
- Prolonging hormonal therapy beyond 5 years in postmenopausal women with hormone receptor-positive breast cancer reduces the rate of subsequent 'in-breast recurrence' and the rate of contralateral breast cancer development.

Full references available at **http://expertconsult.inkling.com**

Key references

1. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer: an overview of the randomised trials. N Engl J Med 1995;333:1444–55.
This review analyses data on 10-year survival from six randomised controlled trails comparing breast conservation with mastectomy. Meta-analysis of data from five of the randomised trials (3006 women) found no difference in the risk of death at 10 years. Level 1 evidence.

6. Morris AD, Morris RD, Wilson JF, et al. Breast conserving therapy versus mastectomy in early stage breast cancer: a meta-analysis of 10 year survival. Cancer J Sci Am 1997;3:6–12. PMID: 9072310.
In this review nine randomised controlled trials involving 4981 women potentially suitable for breast-conserving surgery were analysed. Meta-analysis found no significant difference in the risk of death over 10 years for patients treated by mastectomy or breast-conserving surgery. The authors also found no significant difference in the rates of local recurrence in the six trials where data were available. Level 1 evidence.

9. Gomez SL, Lichtensztajn D, Kurian AW, et al. Increasing mastectomy rates for early-stage breast cancer? Population-based trends from California. J Clin Oncol 2010;28(10):e155–7: author reply e8. PMID: 20159812.
This study demonstrates improved outcomes with breast conservation therapy compared with mastectomy.

24. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of MRI in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008;26(19):3248–58. PMID: 18474876.
This is a review of the accuracy of MRI in breast cancer and shows that MRI has a high sensitivity but poor specificity.

25. Turnbull L, Brown S, Harvey J, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomized controlled trial. Lancet 2010;375(9714):563–71. PMID: 20159292.
This is the only randomised trial of MRI in breast-conserving surgery. This study shows that routine MRI in breast-conserving surgery is not indicated.

38. Early Breast Cancer Trialists' Collaborative Group. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials. Lancet 2011;378(9804):1707–16.
A meta-analysis demonstrating the value of radiotherapy after breast-conserving surgery in both reducing recurrence and improving overall survival.

43. Kunkler IH, Williams LJ, Jack WJL, et al. on behalf of the PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomized controlled trial. Lancet Oncol 2015;16(3):266–73. PMID: 25637340.
These two trials examined the omission of radiotherapy in patients at low risk of local recurrence.

44. Blamey RW, Bates T, Chetty U, et al. on behalf of the BASO II Trialists. Radiotherapy or tamoxifen after breast-conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial. Eur J Cancer 2013;49(10):2294–302. PMID: 23523089.
These two trials examined the omission of radiotherapy in patients at low risk of local recurrence.

46. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg 2002;184:383–93. PMID: 12433599.
Ten-year follow-up of a cohort of patients treated by breast conservation reporting patterns of local, regional and systemic recurrence. Study reports low annual rate of breast tumour recurrence with a ≤1 mm margin.

47. Houssami N, Macaskill P, Marinovich ML, et al. Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. Eur J Cancer 2010;46(18):3219–32. PMID: 20817513.
A meta-analysis of margins that demonstrates that wide margins are unnecessary in breast-conserving surgery. It shows that both involved and close ≤1 mm margins are associated with a significant increase in local recurrence. This meta-analysis concludes that a 1-mm margin is sufficient.

68. Dominici L, Mittendorf EA, Wang X, et al. Implications of constructed biologic subtype and its relationship to locoregional recurrence following mastectomy. Breast Cancer Res 2012;14(3):R82. PMID: 22621306.
These two studies demonstrate breast cancer phenotype as a factor in local relapse.