The approach to an isolated close anterior margin in breast conserving surgery

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ABSTRACT

INTRODUCTION Although close radial margins after breast-conserving surgery routinely undergo re-excision, appropriate management of patients with close anterior margins remains a topic of controversy. An increasing body of literature suggests that re-excision of close anterior margins yields low rates of residual malignancy and may only be necessary in selected patients. The aim of this study was to examine the management of close anterior margins after breast conserving surgery in a single institution and to analyse the rate of residual disease in re-excised anterior margins.

METHODS All patients having breast conserving surgery at St Vincent's University Hospital from January 2008 to December 2012 were reviewed retrospectively. Data collected included patient demographics, tumour characteristics, margin positivity, re-excision rates and definitive histology of the re-excision specimens. A close margin was defined as less than 2 mm.

RESULTS A total of 930 patients were included with an average age of 65 years (range 29–94 years). Of these, 121 (13%) had a close anterior margin. Further re-excision of the anterior margin was carried out in 37 patients (30.6%) and a further 16 (13.2%) proceeded to mastectomy. Residual disease was found in 18.5% (7/36) of those who underwent re-excision and 7/16 (43.75%) of those who underwent mastectomy. Overall, 11.57% (14/121) of patients with close anterior margins were subsequently found to have residual disease.

CONCLUSION The low yield of residual disease in re-excised anterior margins specimens supports the concept that routine re-excision of close anterior margins is not necessary. Further research is required to definitively assess its influence on the risk of local recurrence.

KEYWORDS

Anterior margins – Breast-conserving surgery – Residual disease – Breast carcinoma – Margin involvement

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Introduction

Recent decades have seen a paradigm shift in the surgical management of breast cancer. Breast-conserving surgery is widely accepted as an alternative to a mastectomy and, in combination with adjuvant radiotherapy, has been shown to have equivalent outcomes in terms of survival.^{1–3}

Margin status remains an important predictive factor in determining the risk of local recurrence.^{4–5} The management of the surgical margin is crucial in patients who have undergone breast-conserving surgery to deliver an appropriate balance between optimising cosmetic outcomes and minimising the risk of local recurrence. Re-excision, while necessary in selected patients to achieve adequate margin clearance, is associated with poorer cosmetic outcomes, an

increase in the interval time to adjuvant radiotherapy and increased patient distress.^{6,7}

Previously published work has suggested that involvement of the anterior or posterior margin is of less significance than involvement of the radial margins with regard to local recurrence,⁸ and therefore re-excision of these margins may be unnecessary.^{4,6,9} There is little published information documenting the specific impact of a close anterior margin on local recurrence rates. Management of the close anterior margin therefore varies widely. Marked regional differences also exist, with previous literature reporting that only 29% of British surgeons would re-excite a close anterior margin compared with 53% of American surgeons.^{4,10}

The aim of this study was to examine the management of close anterior margins after breast conserving surgery

in a single institution and to analyse the rate of residual disease in re-excised anterior margins.

Methods

A retrospective review of a prospectively maintained database was performed and all patients undergoing breast-conserving surgery for either an invasive breast carcinoma or ductal carcinoma in situ at a tertiary referral centre between January 2008 and December 2012 were identified. Patients with both symptomatic and screening detected lesions were included.

Patient demographics, tumour characteristics and hormone receptor status were recorded. Surgical margin status including radial margin status was documented. Also recorded was whether or not re-excision was undertaken in the presence of close margins and the presence or absence of residual disease in the re-excision specimen. A close surgical margin was defined as tumour cells identified less than 2 mm from the cut edge of the specimen.

All patients received adjuvant radiotherapy postoperatively with a conventional dosing schedule of a total of 45–50 Gy delivered over four to five weeks. Patients received a radiotherapy boost subsequent to this schedule, depending on clinical and pathological variables, including patient performance status and margin involvement.

Statistical analysis was carried out using IBM SPSS Statistics version 21.

Results

Full cohort characteristics

A total of 930 patients undergoing breast conserving surgery were identified. The average age was 65 years (range 29–94 years). Just under one-third of patients ($n = 306$, 32.9%) were 70 years of age or above while 94 patients (10%) were less than 50 years of age. Ductal carcinoma in situ, with no invasive component was diagnosed in 90 patients (10%). Invasive ductal carcinoma was identified in 723 patients (78%) and invasive lobular carcinoma in 71 (8%). Among the 836 patients with a diagnosis of invasive carcinoma, the majority ($n = 395$, 47%) were grade 2, with 326 (39%) and 117 (14%) being grade 3 and grade 1, respectively.

Characteristics of patients with close anterior margins

Of the total, 121 patients (13%) had a close anterior margin. An isolated close anterior margin was identified in 57 patients (47%), while 64 patients (53%) had a positive anterior margin in conjunction with one or more close radial margins (Fig 1). The average age was 64 years, with a range of 29–87 years. Ductal carcinoma in situ alone was diagnosed in four patients (3%). Invasive lobular carcinoma was diagnosed in 11 patients (9%). The majority of patients ($n = 89$, 74%) had a primary tumour measuring less than 3 cm. Lymphovascular invasion was identified in almost 50% of the patients ($n = 56$, 46%). Metastatic disease in the axillary lymph nodes was identified in 49 patients (40%) with a close anterior margin. The majority

of tumours with close anterior margins were found to be estrogen receptor positive ($n = 95$, 79%).

Re-excision of margins

Of the 121 patients with a close anterior margin, 75 underwent re-excision. The overall rate of residual disease in these re-excision specimens was 32%. Patients with larger tumours (greater than 5 cm) were more likely to undergo further excision ($P = 0.041$). There was no statistically significant difference in hormonal status, nodal status, histological subtype or grade between those who underwent further surgery ($P = 0.204$, $P = 0.31$, $P = 0.129$, $P = 0.374$, respectively) and those who did not (Table 1).

Re-excision was pursued more aggressively in the 64 patients who had concomitant close radial margins, with 86% of these proceeding to further surgery. In this group, 39 patients underwent re-excision of margins while 16 underwent completion mastectomy. Residual disease was identified in 38% of re-excision specimens. However, the burden of residual disease was predominantly found in the re-excised radial margins, and the rate of residual disease in the re-excised anterior margins was low, at 10.9%.

A further 57 patients then had an isolated close anterior margin. Of these, 22 underwent re-excision. Although there was no statistically significant correlation between re-excision rates and tumour characteristics, there was a trend towards an increasing likelihood of re-excision for tumours demonstrating adverse features, such as larger tumour size and higher grade (Table 2). The rate of residual disease in this group was 13.6% on final pathological analysis. Of the three patients with residual disease, all had had tumour at ink on initial histopathologic analysis.

In 50 of these 57 patients, where the tumour was felt to be particularly superficial at initial surgery, a skin ellipse had been taken. Of the seven who had not had resection of skin in the initial surgery, only two underwent re-excision and neither had residual disease.

Discussion

Breast-conserving surgery aims to achieve an adequate oncological resection while optimising long-term cosmetic outcomes. This mandates achieving a clear surgical margin. The definition of what constitutes an acceptable margin has been widely debated since the introduction of breast-conserving surgery and remains somewhat controversial.^{11–15} There is little evidence that a wider surgical margin is associated with decreased rates of local recurrence. A recent meta-analysis failed to find a significant association between wider margins and reduced rates of local recurrence,⁵ and hence, recommended that as no significant benefit was achieved, that a narrower margin can be routinely used.^{14,15} The most recent Society of Surgical Oncology guidelines have defined a negative margin as 'no tumor at the inked margin',¹⁶ while Association of Breast Surgery guidelines from 2015 describe an acceptable margin of 1 mm for both invasive and in situ disease.¹⁷ However, practice varies widely at an individual, institutional and international level.^{18–20}

More than 50% of all re-excision specimens are found to have no residual disease.^{14,21} There are no reliable predictors of residual disease; however, a study by Gurdal *et al*¹⁴ concluded that patients with close margins and unfavourable risk factors (positive margins, multifocal disease, node positive) should undergo re-excision, but in patients with favourable risk factors, such as unifocal disease, and uninvolved lymph-nodes, re-excision may be omitted.

It has been suggested that involvement of the anterior margin carries less significance than the radial margin in terms of risk of local recurrence.⁸ A retrospective review by Mullen *et al*²² found that only 4% (2/49) of re-excised anterior margins contained residual disease compared with over one-third of re-excised non-anterior margins. Given this low yield of residual disease found in re-excision specimens of close anterior margins in recent trials, it has been queried whether re-excision of close anterior margins is routinely required.^{4,6,9}

This is echoed by a systematic review of the literature on positive anterior margins carried out by Ang *et al*.²³ This concluded that there remained no consensus at that time among surgeons regarding their approach to a positive anterior margin. However, they noted that while there is no specific literature assessing the impact of positive

anterior margins on local recurrence, the low rate of residual disease described in the studies above supports the concept that re-excision is likely to be of limited benefit.²³

Those studies are, however, limited by the small number of patients included with isolated close anterior margin. In this study, only 22 patients underwent re-excision of an isolated anterior margin. Although not statistically significant, there was a trend towards re-excision for those tumours demonstrating adverse features such as larger size and higher grade, reflecting the decision-making process of the surgeon and multidisciplinary team. Only three patients (13.6%) had residual disease in the re-excised specimen. In comparison, the rate of residual disease was 38% in patients who had close anterior with or without radial margins, although only 10.9% of patients who underwent re-excision of margins for close anterior with or without radial margins had residual disease in the re-excised anterior margin. These data support the theory that close anterior margins are less clinically significant than close radial margins.

In recent years, there has been a trend toward oncoplastic surgery for breast cancer. Several studies have shown that oncoplastic breast surgery leads to enhanced postoperative quality of life and self-esteem and improved cosmetic

Table 1 Comparison of the characteristics of patients with close anterior margins with or without close radial margin, comparing those who underwent further excision and those who did not.

Characteristic	Further excision				P-value
	No		Yes		
	(n)	(%)	(n)	(%)	
Tumour size:					0.041
< 30 mm	54	60.7	35	39.3	
31–50 mm	11	12.3	15	57.7	
> 50 mm	1	16.7	5	83.3	
Hormone receptor status:					0.204
Triple negative	9	75	3	25	
Estrogen-receptor positive	48	50.5	47	49.5	
HER2 positive	9	64.3	5	35.7	
Nodal status:					0.31
Negative	42	58.3	30	41.7	
Positive	24	49	25	51	
Grade:					0.374
n/a	4	80	1	20	
1	11	68.8	5	31.3	
2	28	50.9	27	49.1	
3	23	51.1	22	48.9	
Histology:					0.129
Ductal carcinoma in situ	3	75	1	25	
Invasive ductal carcinoma	57	58.2	41	41.8	
Invasive lobular carcinoma	2	18.2	9	81.8	
Mixed	1	50	1	50	
Other	3	50	3	50	
HER2, human epidermal growth factor receptor 2.					

Table 2 Comparison of the characteristics of patients with isolated close anterior margins, comparing those who underwent further excision and those who did not.

Characteristic	Further excision				P-value
	No		Yes		
	(n)	(%)	(n)	(%)	
Tumour size:					0.518
< 30 mm	31	62	19	38	
31–50 mm	3	75	1	25	
> 50 mm	1	33.3	25	66.7	
Hormone receptor status:					0.369
ER +ve, HER2 –ve	25	58.1	18	41.9	
ER +ve, HER2 +ve	4	40	3	60	
ER –ve, HER2 +ve	2	100	0	0	
Triple negative	6	85.7	1	14.3	
Nodal status:					0.866
Negative	28	60.9	18	39.1	
Positive	7	63.6	4	36.4	
Grade:					0.285
n/a	1	100	0	0	
1	6	75	2	25	
2	16	69.6	7	30.4	
3	12	48	13	52	
Histology:					0.829
Ductal carcinoma in situ	1	100	0	0	
Invasive ductal carcinoma	30	61.2	19	38.8	
Invasive lobular carcinoma	2	66.7	1	33.3	
Other	2	50	2	50	
ER estrogen-receptor; HER2, human epidermal growth factor receptor 2; +ve, positive; –ve, negative.					

outcomes,^{24,25} while maintaining oncological outcomes comparable with routine breast conserving surgery.²⁶ The advent of oncoplastic breast surgery has reduced rates of re-excision for smaller tumours and rendered some larger tumours suitable for breast-conserving surgery that would previously have warranted mastectomy.^{27,28} Many of the techniques employed do not involve the excision of an ellipse of skin. In some cases, the incision is remote to the site of the tumour. Excision of an anterior margin would have severe cosmetic consequences in these cases. With low residual disease rates, the rationale behind proceeding with re-excision in this setting is questionable.

A close anterior margin may be due to disease in the skin or in anterior breast tissue. In this study, we did not differentiate between these two definitions. The clinical significance has not been reported.

The primary limitation of this study is the definition of a positive margin. This is as a result of the changing definition of a positive margin: where 5 mm was previously the required margin, recent guidelines now accept 'no tumour at the ink' as a negative margin.²⁹ However, as alluded to above, this is not universally accepted and also varies with respect to invasive disease versus ductal carcinoma in situ.³⁰

Our study demonstrated a re-excision rate of 38.6% for isolated close anterior margins. This is consistent with previously published re-excision rates of between 22% and 72% for breast-conserving surgery. The rate of residual disease (13.6%) in the re-excised specimens, although low, was markedly higher than the rate of residual disease found in the study by Mullen *et al.*²⁴ However, this may be accounted for by the more aggressive approach to

re-excision which was adopted by Mullen *et al*, with over 94% of patients with an involved anterior margin proceeding to re-excision. In contrast, this study demonstrated a more conservative approach to re-excision, with lower-risk patients foregoing surgery and only 39% of those with an isolated anterior margin proceeding to re-excision.

As the present study was a retrospective study spanning several years, if the current guidelines were applied, the rate of isolated close anterior margins may have been even lower. Similar to other studies, it is also limited by the small number of patients who actually underwent re-excision in the setting of an isolated anterior margin, which unquestionably alters the conclusions which can be safely drawn.

Conclusion

The necessity of involved anterior margin re-excision warrants further investigation, particularly on a prospective basis. In addition, follow-up to determine long-term outcomes will be required to definitively assess its influence on the risk of local recurrence.

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