



## Review

## Positive anterior margins in breast conserving surgery: Does it matter? A systematic review of the literature



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## ABSTRACT

Positive margins are associated with an increased risk of ipsilateral breast tumor recurrence (IBTR); therefore re-excision of positive margins is recommended. Involvement of anatomically non-breast margins, such as anterior margins, has been associated to a lower risk of IBTR than radial margins. Although many surgeons do not re-excite positive anterior margins (PAM); there is no consensus regarding this approach. The objective of this study is to find evidence that assesses this practice.

A systemic literature review was performed through six databases from January 1995 to July 2014. Studies that discussed anatomical location of involved margins in BCS were included.

Six studies were identified evaluating PAM. One study reported a 2.5% rate of IBTR in patients with non-negative margins treated with radiotherapy (of which 23% had a PAM). Another study showed 4% of residual disease after re-excision of PAM, but did not report IBTR rates. A later observational study reported that 87.5% of positive anterior and posterior margins were re-excised. One survey from America and one from the UK showed that 47% and 71% of surgeons would not re-excite PAM, respectively. A later survey in the UK reported that 43.8% of surgeons would not re-excite PAM in DCIS, whilst 29.2% would not for invasive carcinoma.

Common surgical practices to not re-excite PAM contradict current guidelines that recommend obtaining negative margins to reduce the risk of IBTR. However, there is little evidence detailing the relationship between PAM and IBTR rates. Low residual disease after re-excision of PAM supports the limited benefit of re-excite this margin; however further studies are required to evaluate this topic.

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## Introduction

Breast conserving therapy (BCT), which involves breast conserving surgery (BCS) and post operative radiotherapy, constitutes the standard treatment for early breast cancer. Six prospective RCT have demonstrated that the recurrence rate and survival outcomes are equivalent between mastectomy and BCT, with the latter having cosmetic advantages for breast cancer patients [6]. However, the lack of consensus on what constituted an adequate negative margin in BCS result in re-excisions to achieve wider negative margins, often at the cost of cosmesis.

A multidisciplinary consensus panel recently developed guidelines for the management of margins in patients with invasive breast cancer treated with BCT, based on the results of a meta-analysis of 33 studies including 28,162 patients [11]. Positive margins, defined as “ink on tumour”, were associated with more than two-fold increase in the risk of ipsilateral breast tumour recurrence (IBTR) [6]. Therefore re-excision for positive margins is recommended. In contrast, wider margins than “no ink on tumour” do not significantly lower the risk of IBTR [11].

There is ongoing debate regarding the management of positive anatomically non-breast margins (anterior and deep margins). To date, there is no consensus regarding this practice. The motivation to identify reasons for re-excision is to reduce secondary operations and ultimately improve patient safety and care. Thus, the primary aim of this study was to investigate IBTR in patients who had re-excisions for PAM following BCS for stage I and II breast cancer. The secondary aim was to identify the re-excision rates among breast surgeons in this patient population.

## Methods

### Literature search strategy

A systematic literature review was performed through Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club and Database of Abstracts of Review of Effectiveness (DARE) from January 1995 to July 2014. Relevant studies included those that discussed anatomical location of involved margins in breast conserving surgery. To achieve maximum sensitivity we combined the terms ‘breast conserve\*’, ‘surgery’, ‘wide local excision’, ‘margin’ and ‘recurrence’ as key words or MeSH terms. Studies were limited to human studies in English. Articles that did not describe margins according to anatomical location were excluded. Abstracts, case reports, conference presentations, and editorials were also excluded. Two independent investigators (E.D. and B.K.) screened abstracts identified in the literature search ( $n = 677$ ) and full-text of potentially relevant studies ( $n = 143$ ). All data were extracted from article texts, tables and figures. Two investigators (S.C.A. and G.T.) independently reviewed each retrieved article. Discrepancies between the two reviewers were resolved by discussion and consensus. The final results were reviewed by senior investigators S.W. and H.C.

## Results

### Quantity and quality of studies

A total of 701 references were identified through the six electronic databases. After exclusion of duplicate or irrelevant references, 143 potentially relevant articles were retrieved for more detailed evaluation. After applying the selection criteria, six studies remained for assessment, three articles reported quantitative data and three articles contained qualitative results from cross-sectional

surveys on this topic. The study selection process is presented in Fig. 1 according to the PRISMA statement.

### Quantitative studies

In 2007, McIntosh et al. examined the risk of local recurrence in patients who had undergone BCS for stage I and II breast cancer with close margins (less than 2 mm) or positive margins [9]. All patients in this study received adjuvant radiotherapy and did not undergo re-excision. Of the 200 patients that participated in this study, 71% of patients had close margins and 29% had positive margins, of which 23% had PAM. It was reported that the five and ten year risk of IBTR was 3% and 5% respectively, which is comparable to local recurrence rates in most series with adequate negative margins [9]. In addition, of the five local recurrences over a 71-month follow up period, none of the patients had PAM following their initial operation.

More recently, Mullen et al. investigated the clinical benefit of re-excising a PAM following BCS by examining re-excised tissue for residual disease. This study examined 172 positive margins in 114 patients with one or more positive margins who subsequently underwent re-excision. Of the 49 patients with PAM who had a second operation, two (4%) were found to have residual disease. In contrast, 18 of 23 patients (82%) with positive radial margins were found to have residual disease and they underwent a mastectomy [12].

A large observational study by McCahill et al., in 2012 reported that 87.5% (42/48) of patients across four institutions with positive anterior or posterior margins underwent a re-excision. IBTR rates and residual disease in re-excised tissue were not reported [8].

### Qualitative studies

Young et al. conducted a survey among 127 British breast surgeons on current practices in BCS in 2007. Responders chose between four options: do not re-excite/rarely/usually and definitely re-excite. The study reported that 71% of surgeons would not re-excite a negative anterior margin of 1 mm. Of note, the survey also found that while 61% will not re-excite a PAM of less than 1 mm, 20% of surgeons would definitely re-excite a similar margin width [14].

A separate survey conducted in the United Kingdom in 2013 reported that 29.2% of the 281 breast surgeons who participated in the survey would never re-excite a close anterior margin in invasive breast cancer. It also reported that 61% of breast surgeons would routinely excise the overlying skin if the anterior margins were close to skin, compared to 28% of surgeons in 2007 [5].

In the United States, Blair et al. published a survey to investigate common practices in attaining a negative surgical margin in BCS. Breast surgeons could choose between never, sometimes, half the time, the majority of the time and always re-excite. The study reported that 53% of 351 surgeons would re-excite a PAM the majority of the time [1]. All three qualitative studies did not publish data to allow a direct comparison.

## Discussion

Our findings indicate a paucity of studies exploring the anatomical location of positive margins and so far, there are no specific guidelines to approach the management of anatomically non-breast margins involved.

Surveys among British and American surgeons highlight the practice inconsistencies amongst surgeons regarding the decision to re-excite specific margins according to anatomical location, particularly in relation to a anterior and posterior margins. Comparison of the results of the survey among American breast

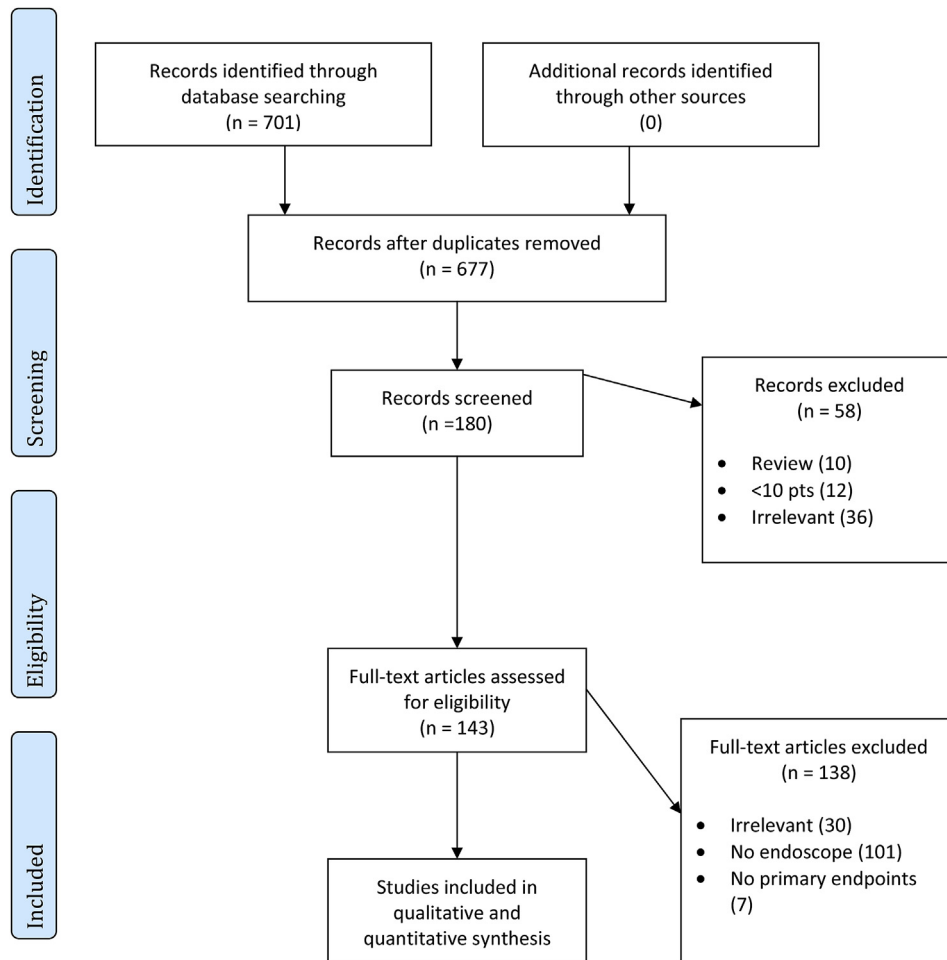


Fig. 1. Search strategy of systematic review.

surgeons with the observational study by McCahill et al. may indicate that surgeon intent and actual clinical practice do not necessarily have full correlation [1,8].

The results of two retrospective studies showing a low IBTR rates in patients with PAM who did not undergo a re-excision and the low residual disease on re-excised tissues of patients with PAM, may support the hypothesis that a PAM does not warrant a re-excision. However this approach contradicts the recent consensus guideline, which encourages re-excision of positive margins [6,11].

Although the addition of adjuvant treatment (radiotherapy, endocrine therapy and chemotherapy) did not eliminate the difference of IBTR between a positive and negative margins [6], quantitative information on the amount of tumor at the margin was not included in these studies. It is likely that lower local recurrence rates are attributed to less residual breast tissue in anterior and posterior margins. This has been the rationale for not re-excising a PAM, along with the fact that avoiding second operations reduces the likelihood of poor cosmetic results and additional stress for patients.

One of the major factors that may contribute to the varying re-excision rates between institutions is the problem of adequately orientating and identifying proper margins. This can be attributed to a number of factors including the method of orientation, size of specimen, tissue fixation time, specimen orientation, cold ischemia time, leaking ink, compression artifact or the 'pancake phenomenon' [2–4,10]. A British survey revealed that nearly 25% of breast

units have no specimen orientation protocol despite the NHS Breast Screening Programme Guidelines [13]. Molina et al. reported an overall 31.1% disagreement rate between orientation marked by the surgeon and that performed by a pathologist. Specific analysis revealed that the deep and superficial (anterior and posterior) margins were associated with higher disorientation rates [10]. Specimen radiography such as intra-operative ultrasound and radioguided localization have demonstrated decreased positive margins in BCS [2].

The available literature to guide the approach to PAM in BCS currently is based on level III evidence. While current guidelines recommend re-excision of positive margins, current studies indicate there is limited benefit in re-excision of PAM in stage I and II breast cancer. Post operative discussions between the surgeon and pathologist should be held on a case-by-case basis within a multidisciplinary setting [7]. Further quantitative studies to investigate local recurrence in relation to anatomic location of margins are required, however this may be challenging given existing low IBTR and the long term follow up required for observational studies. Prospective studies with standardized specimen anatomical markings and reporting will provide more answers to aid better decision-making.

#### Conflict of interest statement

None declared.

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