



Challenges in Decreasing Incidence of Positive Margins in Breast-Conserving Surgery for Breast Cancer

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Abstract

Breast cancer remains the most common cancer worldwide. 1 in 9 women is diagnosed in their lifetime with an increasing trend. Surgery has been the mainstay of treatment for breast cancer, accompanied by chemotherapy, radiotherapy, hormone therapy, and biological therapies. Evolution away from a radical approach toward breast-conserving procedures brought in major advantages for the patient's benefit providing overall equivalence in outcomes. One of the most important conditions for such outcomes while preserving the breast in early breast cancer is represented by surgery with negative margins. In 2014 The Society of Surgical Oncology (SSO) and the American Society for Therapeutic Radiology and Oncology (ASTRO) established guidelines for breast-conserving surgery margins for early breast cancer, followed by 2016 guidelines for margins on carcinoma in situ. These guidelines were internationally adopted and have a strong impact on clinical practice. We present our experience and challenges in decreasing the incidence of positive margins in lumpectomies for invasive and in situ carcinomas.

This is an observational study with a comparison to new data consensus while recognizing the challenges in decreasing the incidence of positive margins in our breast-conserving surgeries.

Keywords: Breast-Conserving Surgery, Margins, Shavings, Guidelines.

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Material and methods:

100 consecutive lumpectomies done in our Breast Unit from Jan 2018 to Feb 2023 for diagnosed breast carcinomas invasive and in situ, were analyzed retrospectively; data included age, triple assessment, type of cancer, grade, and receptor status, lymph node status, treatment approach

whether upfront or post neoadjuvant chemotherapy, type of axillary surgery, use of radiological guidance for a lumpectomy- guide wire, or ultrasound-guided, use of shavings, re-excision of margins data, complications if any and recurrence status were evaluated. Exclusion criteria -no definite surgery, prior radiotherapy, male cancer.

The summary of clinical characteristics of the cases is shown in Table 1.

	Total number of cases	Positive margins invasive cancer	Positive margins DCIS
Age median and range	53.7 (31 to 80 years old)	54.5 (35 to 79 years old)	57.2 (38 to 71 years old)
Histology			
Ductal, lobular, mucinous, papillary	83	20	-
The presence of DCIS adds to the invasive component	40	17	-
DCIS	16	-	5
LCIS	1	-	-
Pathological stage invasive cancers			
T1	36	7	-
T2	42	12	-
T3	5	1	-
Node positive disease	40	8	-
Grade of invasive tumors			
Grade 1	7	1	1
Grade 2	45	14	2
Grade 3	31	5	2
Receptor status			
ER/PR positive	66	15	4
Triple negative disease	10	3	-
HER2 positive	12	2	-
Neoadjuvant treatment	27	4	-
Use of imaging localization	35	7	4
Shavings taken	30	9	2
Presence of residual disease on 25 re-surgery	-	5	1
Follow up range	10-71 months		
Local Recurrence status	0*		

*Total 4 recurrences, 1 of them axillary, 3 distant metastases- died of cancer - very young patients, very aggressive tumours.

Cases were evaluated in a multidisciplinary meeting for the plan of management including the technical aspect of surgery to take place, the use of preoperative localization when needed, and the most suitable type for individual cases. A definitive

diagnosis of carcinoma was confirmed by biopsy with clip markings in the tumour. Patients who underwent excisional biopsy elsewhere were included, provided that microscopic diagnosis was confirmed by our histopathology department, and margins status was affirmed. Lumpectomies were performed as an upfront surgery or after neoadjuvant chemotherapy when eligible.

Preoperative images were done with the use of localization techniques by the guide wire, single or bracketed, or ultrasound marking for all non-palpable tumours. Specimens were checked intraoperatively by the appropriate imaging, with radiological confirmation of adequate, macroscopic margins. Additional shaving margins were taken when the tumour was believed to be close to the edge of the specimen. Frozen sections of margins or shavings were not performed.

The surgical lumpectomy technique implied the standard cylinder of breast tissue containing the tumour from under the skin down to the pectoralis fascia, with clipping of the tumour bed for further radiotherapy guidance.

The lumpectomy specimen was oriented on three orthogonal faces according to our unit protocol-superior, lateral, and deep margin. Additional shavings were also oriented to designate the true new margin and the location in relation to the tumour.

Postoperatively lumpectomy specimens were evaluated grossly and histologically with inking and by serial slicing perpendicular to margins. Distance from the nearest margin to the microscopic tumour and to the shaving margin was recorded for invasive and in situ tumours.

A negative margin was defined as no tumour on ink for invasive cancers and more than 2mm for in situ tumours, each margin being recorded separately.

The formal histopathological report was discussed in the multidisciplinary meeting, and, when the margin was positive, a decision was taken for re-excision, or mastectomy, accordingly. No further re-excision was proposed for a positive anterior or posterior margin, as technically, no further tissue could be obtained, and other modalities of treatment were employed.

The positive margins cases were stratified into further re-excision of margins or mastectomy considering the patient's age/ life expectancy, comorbidities, presence of residual microcalcifications, and expected impact of re-excision on cosmesis. The cases were analyzed for

further pathological positive margins versus no more cancer present.

Results:

A total of consecutive 100 surgeries for lumpectomies were taken from April 2018 to March 2023.

The median age of the individual patients was 54.5 years ranging from 31 to 80 years old. The positive margins cases median age- 55.2 years for invasive and 53 years for in situ disease.

Based on pathological diagnosis 83 patients had invasive cancer, 3 of them with bilateral cancer, 5 patients had invasive lobular cancers, and 16 cases had ductal carcinoma in situ.

Positive margins on invasive cancer were found in 20 cases (24%), and ductal carcinoma in situ were found in 5 cases (31.2%)

In cases with invasive cancer clinical T stage found T1 in 36 cases (43.3%), T2 tumours in 42 cases (50.6%), T3 tumours only in 5 cases (6%). The T staging distribution when margins were positive is as follows: T1 in 7 cases (35%) , T2 in 12 (60%) cases, T3 in 1 case (5%).

The grading of invasive tumours was found as grade 1 in 7 cases (8.4%), grade 2 in 45 cases (54%) grade 3 in 31 cases (37%), whereas the grading of invasive tumors when margins were found positive is as follows: grade 1 in 1 case (5%), grade 2 in 14 cases (70%), Grade 3 in 5 cases (25%).

There was a total number of 66 cases ER/PR positive invasive cancers (79.5%), 10 cases triple negative cancers (12%), and 12 cases Her2 positive cancers (14.4). Upon positive margins cases 15 had positive ER/PR (75%), 3 had triple negative disease (15%), and 2 had Her2 positive disease (10%).

The majority of ductal carcinoma in situ cases were ER/PR positive -15 cases (93.7%), 4 out of 5 positive margins also being ER/PR positive.

Total number of neoadjuvant cases undergoing lumpectomy was 27 (32 %), only 4 cases having

had positive margins (14.8% of total number of cases). Complete PCR achieved in 8 cases (29%).

There was a total number of 35 cases (35%) with the use of imaging localization either guide wire or ultrasound localization, 25 cases of the invasive cancers and 10 cases of ductal carcinoma in situ. In the positive margins cases imaging localization technique was done in 7 of the invasive cancers (35%) and 4 of the ductal carcinomas in situ (25%) had imaging localization.

The shavings for the lumpectomy specimen were taken in 30 cases (30%). 9 cases with positive margins invasive cancers and 2 of DCIS were encountered.

Case with positive margins that underwent re-surgery were 25 in total, with findings of residual disease in 11 cases (44%). Only 2 cases out of those needed- a third surgery, as mastectomy.

The follow-up range at the time of this analysis was 10 to 71 months.

We had a total of 4 deaths- where recurrences were marked as 1 axillary recurrence and 3 distant metastases; no breast recurrence was encountered.

Discussion:

We conducted a retrospective observational study to evaluate our rate of positive margins compared to a set international benchmark of quality. We looked at our data and considered the challenges related to improvement and the possible ways leading to it.

Preservation of the breast offers several advantages over mastectomy- shorter operative times, less postop pain, fewer clinically significant complications such as hematoma or seroma [1] shorter recovery period with early return to work, reduction of the economic impact of the cancer treatment, and better cosmetic outcome [2], [3].

The first breast-conserving therapy studies proved that there is residual disease left behind, the disease that can be kept in check by radiotherapy and systemic therapy [4,5,6]. The data of the Z0011 trial on early breast cancer [7] brought in the concept that complete surgical resection of all subclinical disease is not necessary for an

acceptable locoregional control, concentrating on the ipsilateral axilla. The inference brings into question why, then, the re-excision is necessary at all [8]. The reason relates to the local recurrence rate that is critically determined by the margin status at the time of primary surgery [9]. A positive margin poses a 5-fold increased risk of recurrence, a risk which is persistent at a 2-fold increase even if re-excision takes place, as a marker of tumour biology [10,11].

So, how much of excision is needed in the first place, got settled at lumpectomy with ‘no tumour on ink’, for invasive cancer and more than 2 mm for DCIS [10]. The margin status definition as negative margin with no ink on the tumour was coined initially by the NSABP B-06 trial reporting a breast recurrence rate of 14.3% in patients receiving radiotherapy at 10 years of follow-up[4,5] The ASCO-SSO-ASTRO brought in the guidelines for margins definition for invasive cancer and later for ductal carcinoma in situ, establishing that ‘more’ is not necessarily better. However new studies are challenging the notion of ‘no tumour on ink’ as the definition of the standard, finding out increased risk of recurrence when compared with accepting 1mm margin as a negative [11,12].

The positive margin rate mentioned in the literature ranges from 0-70% [13]. Most of the studies show 25% for invasive cancers and 30% for ductal carcinoma in situ [14,15]. Our study showed a positive margin in 24% of cases for invasive cancers and 31% of DCIS cases, which complies with international standards on average.

Looking upon the invasive cancers, when DCIS component is present, our data show the rate of margin positivity more than double. Studies bring into view the acceptance of DCIS component as a risk factor of local recurrence in the presence of positive margins [16], prompting attention to further accuracy in the perioperative assessment with consideration of other imaging modalities and devices [17,18,19].

Our data had 5 invasive lobular cancers treated with breast-conserving surgery, 3 of them having had

positive margins. The attention is brought for seemingly unifocal disease or same quadrant localization pertaining to lumpectomy. Most of these cases were led by patient factors and dealt with, in the era of COVID-19 when appropriate imaging such as preoperative MRI, although part of the assessment, was not performed.

We found an average size of tumours at 22.5mm, which in the case of positive margins increased to 26 mm, re-instating the notion of increased size of tumour, increased positive margins risk.

The Grading of tumours was also significant by a higher number of Grade 2 and 3 in the positive margins cases. It is worth noting the odds of G2 tumours in the majority of cases including the ones with positive margins.

The majority of our cases were hormone-positive and we found no association of receptor status to the positivity of margins.

The image localization was used for nonpalpable cancers. We did not find an increased risk of margin positivity when not indicated. However, caution is advised for invasive cancers with the presence of DCIS component while the tumour is palpable rendering better perioperative onlook assessment.

The previous trials [20] followed by the trial of shavings in 2015 [21] showed a halving rate of positive margins when shavings were used. Our study also showed a decrease in margin positivity by at least 10% in the small sample of our study, imposing further implementation as a standard for the use of shavings, when appropriate.

Our study showed the presence of residual disease in 44 % of our cases on re-surgery, mostly represented by DCIS.

Our data have a breast recurrence rate of 0%, the cases being followed up on an average of 38 months. The 4% of deaths presented, appeared in the first 18 months, all of them attributed to heavy initial involvement of the axilla disease or distant recurrences for very young patients, as a marker of tumour biology rather than local recurrence. All our cases are to be followed up and revised on the local recurrence rate after 5 and 10 years respectively.

Conclusion:

The need for negative margins in breast-conserving surgery for locoregional disease control even in the era of multimodality treatment settings with better adjuvant treatments cannot be overemphasized. The standard triple assessment with multidisciplinary team decision and patient involvement leads to appropriate management. To decrease the positive margins, we are to look for invasive cancers with DCIS component, for the use of imaging localization perioperative even in palpable tumours, and for the use of shavings as a routine for all our cases.

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