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The Value of Intraoperative Frozen Section in Wide Local Excision for Breast Cancer

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Abstract: Wide Local Excision (WLE) is a better alternative to mastectomy as it preserves the desired cosmetic outcome without compromising the patient survival rate. Margin involvement is the main pitfall for WLE. It leads to reoperation which technically can be more challenging and potentially causes emotional stress to the patient. This study evaluates intraoperative Frozen Section (FS) in determining the margin status during WLE. All breast cancer patients who underwent wide local excision were included in the study. In our institution, intraoperative frozen section for WLE was started in 2015. This cohort of patients was compared with earlier patients whom WLE were performed without frozen section. Patients demographic, tumour characteristics, margin status and number of reoperations were analysed. A total of 20 patients aged 43-71 years (mean 56 years) were included in this study. Frozen sections were performed on the last eight of the patients. Six patients (30%) had at least one positive margin involvement. Three patients who had no frozen section were scheduled for reoperation after 2 weeks. Another three patients had frozen section and cavity shaving in the same operation. Total margins evaluated for frozen section were 39. Out of these, 6 (15.4%) were positive for malignancy. One (2.6%) was falsely reported as positive for malignancy. Overall sensitivity and specificity of frozen section in this study were 100 and 96.9%, respectively. FS could help surgeon to minimize the extent of excision during WLE to attain the optimal cosmetic outcome. Positive margin at FS should be taken cautiously, especially when it involves decision to convert the surgery to mastectomy. In that case, it could be wise to wait for confirmation of the margin status by paraffin section.

INTRODUCTION

Wide Local Excision (WLE) is a better alternative to mastectomy as it preserves the desired cosmetic outcome without compromising the patient survival rate. Margin involvement is the main pitfall for WLE. It leads to reoperation which technically can be more challenging and potentially causes emotional stress to the

Table 1: Margins of WLE evaluated by frozen section

	Margin						
Margins evaluated	Superior	Inferior	Lateral	Medial	Superficial	Deep	Total
Frozen section (n = 8)							
Margins evaluated by FS	10	9	9	10	1	0	39
Positive on FS	2	1	1	2	1	0	7
Positive on PS	2	1	1	2	0	0	6
No Frozen section (n = 12)							
Margins evaluated by FS	0	0	0	0	0	0	0
Positive on FS	0	0	0	0	0	0	0
Positive on PS	0	0	1	0	1	2	4

FS = Frozen Section; PS = Paraffin Section

patient. This study evaluates intraoperative Frozen Section (FS) in determining the margin status during WLE (Table 1).

MATERIALS AND METHODS

All breast cancer patients who underwent wide local excision were included in the study. In our institution, intraoperative frozen section for WLE was started in 2015. This cohort of patients was compared with earlier patients whom WLE were performed without frozen section. Patients demographic, tumour characteristics, margin status and number of reoperations were analysed. All tumours were excised together with a rim of 1-2 cm thickness of normal tissue. The extent of excision was guided by digital palpation. Upon completion of WLE, a 2×2 mm cube of tissue were taken from radial (inferior, superior, medial and lateral) margins of the resulting cavity for the frozen section analysis. Presence of malignant cells in the specimen would necessitate cavity shaving of the respective margin. Re-excision of the margin would be done until frozen section was negative. All patients were explained possibility of mastectomy should multiple cavity shavings lead to disproportionate residual breast tissue causing distorted and unacceptable reconstruction.

RESULTS

A total of 20 patients aged 43-71 years (mean 56 years) were included in this study. Frozen sections were performed on the last eight of the patients. Six patients (30%) had at least one positive margin involvement. Three patients who had no frozen section were scheduled for reoperation after 2 weeks. Another three patients had frozen section and cavity shaving in the same operation. Three patients had multiple cavity shavings, two were extensive Ductal Carcinoma in Situ (DCIS) and one was invasive ductal carcinoma with DCIS component. Two patients were converted to mastectomy after persistent positive margin despite twice cavity shavings.

Total margins evaluated for frozen section were 39. Out of these, 6 (15.4%) were positive for malignancy. One (2.6%) was falsely reported as positive for malignancy. Overall sensitivity and specificity of frozen section in this study were 100 and 96.9%, respectively.

DISCUSSION

WLE has become a standard procedure for early breast cancer. It is superior over mastectomy because it preserves cosmesis without compromising the survival rate. The main pitfall of WLE is however, its association with high rate of margin involvement that requires second operation. Positive margins after initial surgery have been documented to range from 30-52%. Factors implicated with these include multicentricity, tumour size, histological subtypes and tumour grade (Mendoza-Rojas *et al*., 2015; Hodi *et al*., 2010; O'Flynn *et al*., 2013). Residual diseases were found in 40-43% of re-excision specimens. Tumour close to inked margin, positive lymphovascular invasion and extensive intraductal component were the associated factors (Alrahbi *et al*., 2015).

Current international guidelines on positive margin have recommended shorter distance of surgical margin from tumour. Society of Surgical Oncology (SSO)-American Society for Radiation Oncology (ASTRO)-American Society of Clinical Oncology (ASCO) guideline defines adequate margin for ductal carcinoma in situ (DCIS) as <2 mm (Morrow *et al*., 2016) while SSO-ASTRO guideline on Invasive Ductal Carcinoma (IDC) recommends no ink on tumour as an adequate margin (Moran *et al*., 2014). With these new guidelines, re-excision rate is expected to reduce.

Preoperative assessment of lesion using ultrasound, mammogram or Magnetic Resonance Imaging (MRI) is essential to plan extent of excision. During operation, surgeons rely on digital palpation to determine margins of excision. A tumour tends to be more firm than the normal surrounding tissues, although, lesion with ill-defined margins, especially, those harbouring in situ carcinoma can be impossible to delineate from normal tissue. Intraoperative ultrasound has been used in this context as an adjunct to ensure adequate excision (Thanasitthichai *et al*., 2016).

A reliable intraoperative assessment of surgical margins is important because it determines whether

additional excision is needed until free margin is achieved without having to do second (re-excision) operation. The conventional paraffin section histological analysis is the gold standard but time consuming and impractical for intraoperative use. Other methods that currently being practiced include Intraoperative Specimen Radiography (IOSR) (Layfield *et al*., 2012; Carmichael *et al*., 2004; Ihrai *et al*., 2014), margin assessment of radioactive iodine seed implanted lesion using gamma probe or freehand SPECT device (Pouw *et al*., 2014), imprint or scrap cytology (Muttalib *et al*., 2005) and macroscopic assessment of tumour margin (Fleming *et al*., 2004). Some authors suggested a nomogram for selective assessment whereby an intraoperative margin assessment is only performed when the nomogram score is higher than the predefined cut off (Lee *et al*., 2016).

FS has been used in skin cancers to increase the likelihood of complete excision and to minimize the risk for recurrence (Manstein *et al*., 2003; Kiyan *et al*., 2012). It proved to be efficient, affordable and reproducible technique and particularly an important when resecting cancers at aesthetic areas in which the resection must be as economical as possible.

The question of its accuracy in breast surgery has been addressed in many studies and this article adds data to the discussion. None of the patients in this study had re-excision for falsely negative margins at FS. Three patients (25%) in the cohort of no FS had to undergo re-excision. These results concur with data from larger series that clearly shown the benefit of FS during WLE by reducing re-excision rate from 27-48 to 6-15% (Fukamachi *et al*., 2010; Esbona *et al*., 2012; Jorns *et al*., 2012).

CONCLUSION

In conclusion, FS could help surgeon in curtailing the extent of excision during WLE in order to gain the optimal cosmetic outcome. Positive margin at FS should be taken cautiously, especially when it involves decision to convert the surgery to mastectomy. In that case, it could be wise to wait for confirmation of the margin status by paraffin section.

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