Handheld Intraoperative Margin Assessment Device for Partial Mastectomy Specimens

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ABSTRACT

Objective: The positive margin rate for partial mastectomy remains significant and contributes to decreased patient satisfaction, increased health care costs, and poorer cosmetic results. Attempts to decrease this rate with currently available technology (frozen section, gross examination, intraoperative ultrasound, or touch prep) can be inaccurate, costly, and time consuming. A device that can rapidly differentiate malignant from benign breast tissue was evaluated.

Methods: A probe (Dune Medical Devices, Caesarea, Israel) was designed to detect differences in electrical waveforms reflected from tissue based on its electromagnetic properties. Preliminary work[1] established the ability to differentiate malignant from normal tissue. An IRB approved, currently ongoing, multicenter trial was initiated. Patients with diagnosed breast cancer and treated with partial mastectomy were candidates. Probe measurements were taken intraoperatively on 1) slices from 41 fresh bread-loafed lumpectomy specimens (39 patients) or 2) the surface of 46 fresh intact lumpectomy specimens (45 patients). All measured points were than separately evaluated by pathology for the presence of DCIS and/or invasive disease. Surgeons and pathologists were blinded to the probe results and the results were not used to guide excision.

Results: Eighty-four patients have enrolled in the study. A total of 748 points on 85 specimens were analyzed pathologically and compared to probe output data. Overall sensitivity is 78%, specificity 92%, and accuracy is 91%; the negative predictive value is 98% and the positive predictive value was 43%. The 7 mm footprint handheld probe was easy to use, having gentle suction that allowed accurate, reproducible data points. Each measurement took 1-2 seconds for acquisition.

Conclusion: This device holds promise for the detection and assessment of margins intraoperatively. Results of the ongoing trial may help to determine its ability to decrease the number of patients that must return to the operating room. Further evaluation and comparison to other intraoperative methods may also be warranted.

INTRODUCTION

Obtaining clear margins with a single surgical procedure remains a significant challenge in breast conserving surgery (BCS). Re-excision rates are reported as high as 60% and contribute to decreased patient satisfaction, increased health care costs and poorer cosmetic results. Currently available methods for intraoperative margin assessment (frozen section, gross examination, intraoperative ultrasound, touch prep) have met with variable success and often present technical and practical limitations. In this study, we evaluated a novel probe that can easily and rapidly differentiate malignant and benign breast tissue intraoperatively (Figure 1) by using a fringe field sensor to collect electromagnetic reflection from a 7mm wide coin-shape tissue volume on the surface of a lumpectomy specimen. Preliminary work[1] in the pathology lab established the modality's ability to reliably differentiate benign and malignant breast tissue based on the electromagnetic properties with sensitivity and specificity as high as 95% and 94% respectively. In the current study, the probe is tested intraoperatively, with the main goal of assessing the device performance compared to pathological specimen evaluation for the prediction of margin status and its potential beneficial impact on clinical outcomes.

Figure 1 ***Tissue characterization probe (Dune Medical Devices, Caesarea, Israel)***

Inclusion Criteria	Exclusion Criteria
Diagnosis of breast carcinoma (infiltrating or in situ)	Neoadjuvant chemotherapy
Undergoing breast conserving surgery	Prior surgical procedure of the breast
Over 18 years of age	Implants in the operated breast
Signed informed consent	Participating in any other investigation which may interfere with the protocol or device reading

Table 1

METHODS

An ongoing, international, multicenter, IRB approved, prospective study included 84 patients (87 specimens) undergoing BCS for invasive and non-invasive breast cancer. A probe (Dune Medical Devices, Caesarea, Israel) that detects differences in electrical waveforms reflected from malignant and benign breast tissue (Figure 2) was used to evaluate bread-loafed lumpectomy specimens (39 patients, 41 specimens) and the margins of fresh, intact lumpectomy specimens (45 patients, 46 specimens). Inclusion and exclusion criteria are listed in Table 1. Nine patients were excluded due to the presence of implants, a benign tumor and other deviations from the protocol. All patients signed informed consent and underwent standard partial mastectomy procedures with suture orientation of the specimens by six surgeons. The probe was placed in contact with multiple 7mm wide tissue points (sites) and measurements were taken for which malignant/non malignant device outputs were rendered (Figure 3). Numbered pins were placed in the specimen marking the sites at which the probe measurements were taken and then specimens were processed in a standard fashion by three pathologists (Figure 4). For each pinned site a corresponding 7mm wide coin-shape tissue specimen was evaluated by pathologists and recorded as positive or negative for malignancy. Probe output and pathology data were then analyzed. For the intact specimen group a margin was considered positive if one or more of its sites were positive. In order to evaluate the potential impact on patient outcome, it was assumed that if the device data been available intraoperatively, a detected positive margin would have been excised intraoperatively. The analysis targeted three parameters, the potential re-excision reduction and the probe performance at the site and margin levels, i.e. specificity and sensitivity. Both pathologists and surgeons were blinded to the probe results.

Figure 2

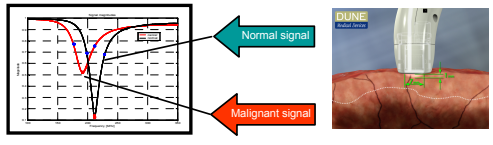
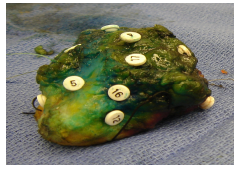


Figure 3: ***Probe assessment of margin status***

Figure 4: ***Tissue data point acquisition***



		Histology		
		Malignant	Non malignant	
Probe	Malignant	43	57	100
	Non malignant	12	636	648
		55	693	748

Table 2: ***Site level performance***

		Histology		
		Malignant	Non malignant	
Probe	Malignant	10	27	37
	Non malignant	3	212	215
		13	239	252

Table 3: ***Margin level performance***

RESULTS

The probe's diagnostic performance on 78 lumpectomy specimens (75 patients) was analyzed by evaluating 748 tissue data points and comparing the histology to device output measurements (Table 2) as well as comparing the histology of 252 margins from the intact specimens (41 patients, 42 specimens) with the per-margin device assessment (Table 3). For the intact specimens, the per-margin diagnostic values are a good measure of the device performance and the re-excision reduction potential measures the effectiveness of the device and procedure for the patient. Twelve (29.3%) patients (13 margins) were identified by standard pathological evaluation as having positive margins. Of the 18 sites that were histologically positive in these patients, 9 sites were correctly identified by the probe as being malignant (7 patients, 8 margins). The 9 sites for which the probe gave a false negative reading resided on 8 margins, 5 of which were detected by the probe on per-margin analysis. Of 13 margins that were histologically positive, 10 were correctly identified by the probe. If the probe data had been both available and used intraoperatively, 19 of 29 (66%) negative margin breasts would have had no intraoperative tissue removal based on probe output. Seven (24%) would have had an extra one or two margins re-excised, and only 3 of 29 (10%) breasts would have had the full cavity re-excised. Without the device, the re-excision rate is 29.3%. With the device, 75% of (9 of 12) patients with positive margins would have been identified and potentially spared a second operation resulting in a potential re-excision rate of 7.3%. Table 4 summarizes the potential impact on patient outcome if the per-margin device data had been used to guide intraoperative management. Each probe measurement took only 1-2 seconds to acquire. The handheld probe was simple to use and yielded rapid, easily reproducible results.

	Positive margin	Clean margin
Without Probe	12	29
With Probe	3	38

Table 4: ***Potential impact on patient outcome***

Statistical parameter	Value
Positive margin rate (without probe)	29.3%
Re-excision reduction potential	75%
Potential positive margin rate (with probe)	7.3%
Per-margin sensitivity	77%
Per-margin specificity	89%
False positive rate	11.3%
False negative rate	23%

Table 5: ***Summary of results based on per-margin data***

CONCLUSIONS

Results from this ongoing trial show that this probe holds promise for a substantial reduction in re-excision rate. According to this data set, it may yield a 7% re-excision rate. The sampling nature inherent to the use of the device leads to enhancement in device performance at the margin level, and at the patient level. The Dune device provides rapidity, ease of use and reproducible results for intraoperative margin assessment, making it an attractive alternative to currently available methods of intraoperative margin assessment. Larger data sets and future device modifications may help to further improve margin re-excision rates. Future studies may include comparison of the probe to other methods of intraoperative margin assessment.

Reference : 1. Karni et al, Intraoperative tissue characterization probe as a potential tool for surgical margin assessment, San Antonio Breast Cancer Symposium, December 2005

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