# Handheld Intraoperative Margin Assessment Device for Partial Mastectomy Specimens

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## ABSTRACT

**Objective:** The positive margin rate for partial mastectomy remains significant. Re-excision procedures 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 or touch prep) are inaccurate, costly and time consuming. We evaluated a new device that rapidly differentiates malignant from benign breast tissue intraoperatively and the potential impact on patient outcome.

**Methods:** A probe (Dune Medical Devices, Caesarea, Israel) was designed to detect differences in electrical waveforms reflected from tissue based on the electromagnetic properties of benign and malignant breast tissue. Preliminary work established the probe's ability to differentiate malignant and benign breast tissue. This ongoing, multicenter, IRB approved study includes patients with diagnosed invasive and non-invasive breast cancer treated with partial mastectomy. Multiple probe measurements were taken intraoperatively on the surfaces of fresh, intact lumpectomy specimens and a malignant vs. non-malignant device output was recorded. For each measurement point (site), corresponding 7mm wide tissue points were separately evaluated by two pathologists and recorded as positive or negative for malignancy. Pathologic and device output data were then analyzed. Both surgeons and pathologists were blinded to the probe results, which was not used to guide excision.

**Results:** Thirty-seven lumpectomy specimens of 36 patients were evaluated by the probe and analyzed pathologically, yielding a total of 539 tissue data sites and 222 margins for comparison. A margin was considered positive if one or more sites on it were positive. A positive patient was considered successfully detected by the device only if all of its positive margins were detected. Eleven patients (29.7%) were identified by pathology as having positive margins. The probe correctly identified 9 of 17 positive sites, 10 of 12 positive margins, and 9 of 11 positive patients. Of negative results, the probe correctly identified 475 out of 522 sites and 183 out of the 210 pathology negative margins. The per-margin calculations, and therefore most clinically relevant analysis, demonstrated the sensitivity and specificity of the device were 83.3% and 87%, respectively. The handheld probe was easy to use and allowed accurate, reproducible data points. Each measurement took 1-2 seconds for acquisition. These results translate into an 82% re-excision reduction potential, whereby 9 of 11 patients might have avoided a second operation if the results of the probe had been used intraoperatively.

**Conclusions:** This device holds promise for intraoperative margin assessment. Its rapidity, ease of use and reproducible results make it an attractive alternative to currently available methods of intraoperative margin assessment. Results of the ongoing trial may help to determine its ability to decrease the number of patients that must return to the operating room for re-excision. Further evaluation and comparison to other intraoperative methods of evaluating partial mastectomy specimens 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 41 patients (42 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 the margins of fresh, intact lumpectomy specimens. Inclusion and exclusion criteria are listed in Table 1. Five 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 four surgeons. The probe was placed in contact with multiple 7mm wide tissue points (sites) on each margin of the specimen 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 inked in a standard fashion by two pathologists (Figure 4). For each pinned site a corresponding 7mm wide coin-shape tissue specimen was separately evaluated by two pathologists and recorded as positive or negative for malignancy. Probe output and pathology data were then analyzed. 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.

## RESULTS

The probe's diagnostic performance on 37 lumpectomy specimens (36 patients) was analyzed by evaluating 539 tissue data points and comparing the histology to device output measurements (Table 2) as well as comparing the histology of 222 margins with the per-margin device assessment (Table 3). Table 4 summarizes the potential impact on patient outcome if the per-margin device data had been used to guide intraoperative management. 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. Eleven (29.7%) patients were identified by site pathology as having positive margins. Of 17 sites that were histologically positive in these patients, 9 sites were correctly identified by the probe as being malignant (7 patients, 8 margins). The 8 sites for which the probe gave a false negative reading resided on 7 margins, 5 of which were detected by the probe based on per-margin analysis. Of 12 margins that were histologically positive, 10 were correctly identified by the probe. If the probe data had been both available and used intraoperatively, 16 of 26 (61%) negative margin breasts would have had no intraoperative tissue removal based on probe output. Seven (27%) would have had an extra one or two margins re-excised, and only 3 of 26 (12%) breasts would have had the full cavity re-excised. Without the device, the re-excision rate is 29.7%. With the device, 82% of (9 of 11) patients with positive margins would have been identified and potentially spared a second operation resulting in a potential re-excision rate of 5%. Each probe measurement took only 1-2 seconds to acquire. The handheld probe was simple to use and yielded rapid, easily reproducible results.

## 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 5% re-excision rate. 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.

**Figure 2**

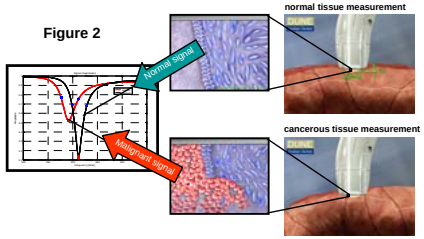
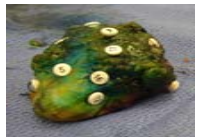



**Figure 3:** ***Probe assessment of margin status***

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



| | | Histology | | |
|---|---|---|---|---|
| | | Malignant | Non malignant | |
| Probe | Malignant | 9 | 47 | 56 |
| | Non malignant | 8 | 475 | 483 |
| | | 17 | 522 | 539 |

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

| | | Histology | | |
|---|---|---|---|---|
| | | Malignant | Non malignant | |
| Probe | Malignant | 10 | 27 | 37 |
| | Non malignant | 2 | 183 | 185 |
| | | 12 | 210 | 222 |

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

| | Positive margin | Clean margin |
|---|---|---|
| Without Probe | 11 | 26 |
| With Probe | 2 | 35 |

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

| Statistical parameter | Value |
|---|---|
| Positive margin rate (without probe) | 29.7% |
| Re-excision reduction potential | 82% |
| Potential positive margin rate (with probe) | 5% |
| Per-margin sensitivity | 83.3% (95% CI: 0.51 - 0.97) |
| Per-margin specificity | 87% (95% CI: 0.82- 0.91) |
| False positive rate | 12% |
| False negative rate | 16% |

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

**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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