Intra-OperativeTissue Characterization Probe as a Potential Tool for Surgical Margin Assessment.

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Background

The surgical margin status after breast-conserving surgery is considered the strongest predictor for local failure. Therefore, a primary goal of breast surgeons is to obtain adequate negative margins of excision. This study was designed as a study of a novel electromagnetic tissue characterization modality developed by Dune Medical Devices. The study assesses the technology's potential in providing the surgeon with real-time data on tissue status at the surgical margins. The measurements were performed on freshly excised breast tissue.

Methods

The study was performed in two medical centers. Inclusion criteria specified patients diagnosed with palpable tumors of breast carcinoma, undergoing lumpectomy or mastectomy procedures.
Following inking, the specimen was sliced by the pathologist in a "bread-loaf" fashion. Pieces of tissue grossly assessed by the pathologist to contain primarily tumor, or primarily normal tissue were cut from the specimen by the pathologist and individually placed into the probe's cavity. Each tissue sample was cylindrically shaped, with a volume of 0.1 ml. The measurement system is comprised of a probe and a console. A measurement sequence involves transmitting electrical pulses through the tissue sample and receiving the reflected waveforms. Typical waveforms reflected by normal and malignant tissue types are shown in figure 1.
Following completion of the measurements the tissue was placed into cassettes for a routine fixation process and slide preparation. Every slide was microscopically examined by a pathologist to yield the tissue composition in percentage terms of tumor and normal tissue.

Data analysis

Based on the histological evaluation, tissue samples were categorized into well-defined groups of homogenous composition: malignant and normal. Composition was considered homogenous if it contained 75% or more of one tissue type.
Parameters were derived from the collected waveforms, so that they optimally depict the waveforms representing malignant vs. normal tissue.
A parametric representation of the tissue samples is shown in figure 2.
As part of the classification process, tissue samples were randomly divided into two sub-groups. 46 (35%) were used for the learning group, providing the basic data base for tissue recognition by the device, and the rest, 88 (65%), were the classification group. For the latter, malignant tissue detection by the device was compared to the histological assessment.

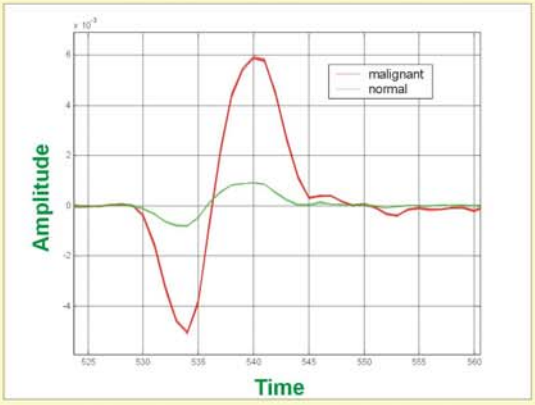

Figure 1 - Typical waveforms reflected by normal and malignant tissue types

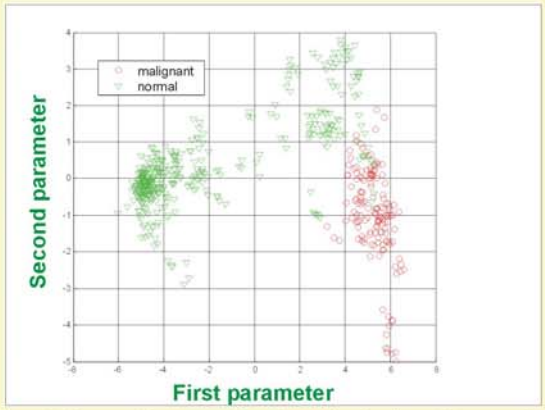

Figure 2 - A parametric representation of normal and malignant tissue samples

Results

From 57 patients, a total of 231 tissue samples were obtained. From these, 198 (86%) tissue samples qualified for analysis. In all, 134 (67%) tissue samples contained 75% of a specific tissue type. The breakdown of these tissue samples according to their grouping was as follows: Malignant breast tissue 34 (25%), Normal breast tissue 100 (75%).
Classification performance of the probe was: sensitivity = 0.95 (95% CI: 0.77-0.99) and specificity = 0.94 (95% CI: 0.85-0.98). Classification ability of mixed content tissue samples exists, however it somewhat decreased as composition of the tissue becomes less homogeneous. Figure 3 shows the classification table of the device compared to pathology.
Qualitative assessment of tissue samples with 50%-75% malignant tissue content shows that they are located in the parameter space as expected, on the range of values between the normal and malignant groups, as shown in figure 4.

		Dune Probe: Positive	Dune Probe: Negative	Total
Pathological analysis	Positive	21	1	22
	Negative	4	62	66
		25	63	88

Figure 3 - The classification table of the probe compared to pathology

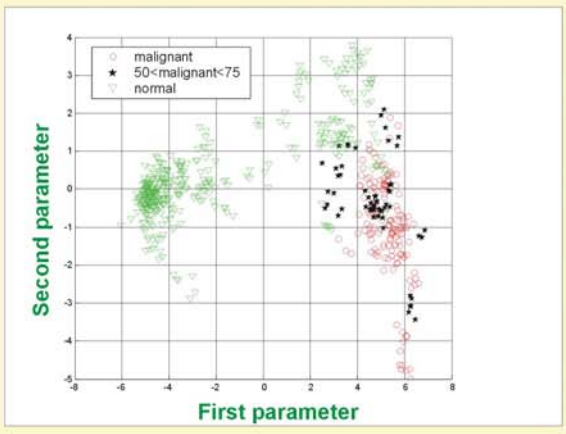

Figure 4 - Representation in the parameter space, of tissue samples with malignant content of 50%-75%.

Conclusions

Cancer tissue can be detected by the probe with excellent sensitivity and specificity. The new modality has the potential of providing the necessary accuracy for a real-time margin assessment tool. The interaction volume in this configuration is a crucial element of design and should be further optimized for enhanced surface detection and small malignant cell cluster detection, which are necessary for real-time intra-operative use.