2077

Intraoperative tissue 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 a strong predictor for local failure. A primary goal of breast surgeons is to obtain adequate negative margins of excision. While postoperatively, permanent histology is a gold standard for margin status data, intraoperatively, margin assessment remains an elusive goal.
A novel electromagnetic tissue characterization modality holds promise of evolving into a surgical tool for intraoperative margin assessment at the hands of the breast surgeon. This study assesses the technology's potential in providing the surgeon with real-time data on tissue status at the surgical margins as well as collects data essential to the product.

Methods

Tissue samples were obtained from freshly excised lumpectomy and mastectomy specimens. Segments were sampled based on their gross appearance: malignant or normal. Each tissue sample was cylindrically shaped, with a volume of 0.1 ml. Tissue segments were analyzed using the probe, by transmitting electromagnetic pulse waves through the tissue, while collecting and analyzing the reflected waveforms (Figure 1). The same tissue segments to which the probe was applied subsequently undergo routine fixation and histological evaluation, resulting in an identified normal/malignant composition proportion for every segment.

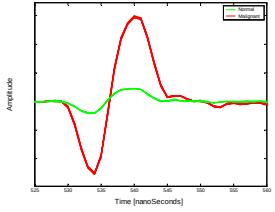

Figure 1 : Typical waveforms reflected by normal and malignant tissue types.

Data Analysis

Based on the histological evaluation, tissue samples were categorized into well-defined groups of homogenous composition, "malignant" and "normal". The homogeneous tissue samples were then randomly divided into a "learning group" and "classification group". Classification was performed on the relevant group. Figure 2 describes the stages of data analysis.
The classification procedure (Figure 2, Step 4) is based on parametric representation of the collected waveforms. A sub-set of parameters (frequency, amplitude, etc.) derived from each reflected waveform and characterizing the tissue response was chosen, so as to yield optimal classification performance. Figure 3 graphically illustrates initial classification of the tissue types based on two out of the various parameters.

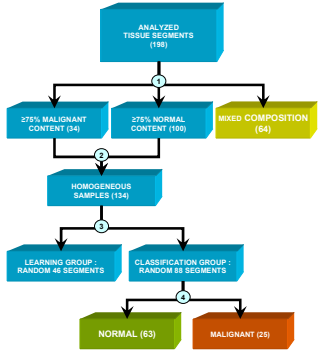

Figure 2 : 1) Out of all tissue segments which qualify for analysis, those samples with a content of ≥75% of malignant or of normal tissue are identified. 2) These are defined as being of homogenous content of that type. 3) As part of the classification process, tissue samples are randomly divided into two sub-groups. 35% are used for the learning group and the rest, 65%, are the classification group. This random selection is repeated 100 times, and the results are averaged for all cases. 4) Classification as "normal" or "malignant" is performed on the classification group, and compare to histological results for assessment of performance.

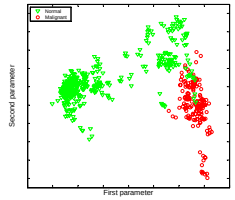

Figure 3 : A parametric representation of normal and malignant tissue samples.

Results

From 57 patients, a total of 231 tissue samples were obtained. From these, 198 (86%) tissue samples qualified for analysis, while the rest were disqualified due to poor signal integrity or excluded tissue types. In all, 134 (67%) tissue samples contained ≥75% of a specific tissue type. The breakdown of these tissue samples according to their grouping is described in figure 2. The probe sensitivity = 0.95 (95% CI: 0.77-0.99) and specificity = 0.94 (95% CI: 0.85-0.98) (Figure 4). Qualitative assessment of measured parameters from tissue samples with 50%-75% malignant tissue content showed that they are located in the range of values between the normal and malignant groups (Figure 5). Thus, classification ability of mixed content tissue samples exists. However, in this probe configuration, it somewhat decreases as composition of the tissue becomes less homogeneous.

BP probe

Pathology	Malignant	Normal	
Malignant	21	1	22
Normal	4	62	66
	25	63	88

Figure 4 : The classification table of the capsule probe compared to pathology

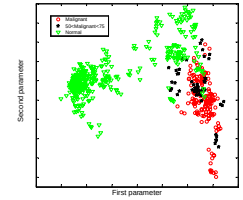

Figure 5 : Representation in the parameter space of tissue samples including those with malignant content of 50%-75%.

Conclusions and Discussion

Normal and malignant breast tissue distinctly differ in their electromagnetic signatures. These differences, when measured for small interaction volumes, can be utilized to develop a surgical tool for intraoperative margin status assessment. The first step toward development of this device is accomplished in this study by demonstrating that 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 probe and complimentary software and hardware design features should be further optimized for enhanced surface detection and small malignant cell cluster detection, which are necessary for real-time intraoperative use. A new hand-held probe, with enhanced features for the operating room environment is currently being studied for its performance in margin assessment. Figure 6 demonstrates intraoperative application of this newer version probe to freshly excised breast tissue.

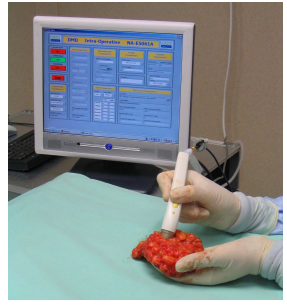

Figure 6 : A newly designed probe applied to freshly excised breast tissue as part of an ongoing study.