Reviewer's report

Title: High-frequency ultrasound for intraoperative margin assessments in breast conservation surgery: a feasibility study

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Reviewer: Jeong-Won Jeong

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Discritionary Revisions.

The authors obtained ultrasound measurements (in pulse-echo and through-transmission) from a total of 57 sites on the ex-vivo specimens of 17 patients with breast cancers. They employed relatively new two single-element transducers with 50 MHz center frequency and examined attenuation, sound speed, spectra, and cepstra of the measured signals (echo-pulse and transmitted pulse) as features to differentiate 15 pathological categories. By performing multivariate analysis using peak density, slope of the ceptra, and attenuation coefficients, they achieved high sensitivity and specificity for differentiating pathologies from normal tissues, 100% and 86% for lobular carcinomas, 100% and 74% for ductal carcinoma, 80% and 82% for benign pathologies, and 80% and 100% for fat necrosis and adenomas. Also, they showed specificities and sensitivities of 85% and 86% for lobular carcinomas, 85% and 74% for ductal carcinomas, 100% and 61% for benign pathologies, 84% and 100% for fat necrosis and adenomas, and 98% and 80% for normal tissue.

As the authors reported in discussion, there are several limitations in sample preparation such as the difficulty in measuring accurate thickness of sample and not enough numbers of samples which may drive statistical insignificance for the measured performance indices. However, these limitations are acceptable and clearly mentioned in the manuscript. The manuscript is well written, clear, and may make a contribution to the growing literature on objective determination of cancer margin in breast conservation surgery (BCS). The attempt to assess various characteristic of high frequency ultrasound related to the disrupted tissue microstructure is interesting, and probably useful to evaluate the margin of normal tissue in BCS. I do have minor comments that would strengthen the manuscript for the benefit of the readers of BMC cancer as well as for those who investigate ultrasound systems for the diagnosis of breast cancer.

1. ultrasound data analysis

In page 8-9 the authors described overall scheme to acquire and analyze the ultrasound measurements in two modes, echo-pulse and transmission. Although the authors described in text, it would be better to show representative signals of these two modes which are obtained from normal tissue, FN-FA-TA tissue, and LC tissue For instance, these signals in time domain (or frequency domain) may be helpful for the readers to understand how they are different in pattern
depending on the types of pathology. Also, these examples may improve the reliability of the presented work.

2. result

Figure 6-8 summarize the changes of ultrasound characteristics between normal tissue and other pathologies. Please report the statistical significances between each pair of two groups, Normal vs. FN-FA-TA, Normal vs. Benign, Normal vs. DC, Normal vs. LC. The reported P-values with t-scores may be useful for the authors to see their statistical significances.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.