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Metastases Detection in Dissected Human Lymph Nodes Using Three-dimensional High-frequency Ultrasound

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1. Introduction

High-frequency ultrasound (HFU) operating at frequencies > 15 MHz is of great interest in many biomedical-imaging applications because its short wavelengths (e.g., 60 µm at 25 MHz) and small focal-zone beam diameters produce exquisite images. Therefore, HFU has great value for imaging shallow or low-attenuation tissues. For example, HFU already has been successful in small-animal [1], ocular [2], intravascular [3], and dermatological imaging [4].

Most normal human lymph nodes are smaller than 1 cm in their long-axis dimension. Therefore, fine-resolution images of human lymph nodes can be formed using HFU.

Tissue-characterization methods using backscattered ultrasound radio-frequency (RF) signals have been investigated by several research groups, and many tissue properties have been estimated from signal parameters and related to tissue types. In this study, three-dimensional (3D) HFU tissue-characterization methods were developed to estimate slope and intercept from the spectrum of the RF echo signals obtained from lymph nodes excised from cancer patients. These methods are derived from the theoretical framework of weak ultrasound scattering in biological tissues formulated by Lizzi et al. [5]. Frequency-dependent information derived from RF backscattered signals can be quantitatively related to tissue micro-structural properties. Our hypothesis is that slope and intercept estimates may help to detect metastases in freshly dissected human lymph nodes.

2. Methods

Lymph nodes were dissected from recruited patients with histologically proven colorectal or gastric cancers at the Kuakini Medical Center (KMC) in Honolulu, HI. De-identified patient information was coded and sent to Riverside Research Institute (RRI) in New York, NY. Pathologists at KMC also provided RRI with a tracing of the boundary of each cancerous region in every histological section for each node.

The pathologist grossly prepared the freshly dissected lymph nodes for histology. Then individual, manually defatted, nodes were placed in a water bath containing isotonic saline (0.9% sodium chloride) at room temperature and scanned individually. Ultrasonic, RF, echo-signal data were acquired with a focused, single-element, transducer (PI30, Olympus NDT, Waltham, MA) having an aperture of 6.1 mm and a focal length of 12.2 mm. The transducer had a center frequency of 25.6 MHz and a -6-dB bandwidth that extended from 16.4 to 33.6 MHz. The transducer was excited by a broadband impulse generated by a Panametrics (Olympus NDT) 5900 pulser. The RF echo signals were digitized at 400 MHz, and a 3D scan of each lymph node was obtained by scanning adjacent planes and lines every 25 µm.

After 3D ultrasound scanning was completed, a semi-automatic 3D segmentation algorithm was used to detect the boundaries of the residual fat layer and of the actual lymph-node tissue. Following segmentation, slope and intercept estimates were computed using 3D cylindrical regions of interest (ROIs) of 1-mm diameter and 1-mm length. (Estimation was performed only when the ROI was entirely in the tissue region found by the 3D segmentation algorithm.) Each individual RF-segment spectrum within the ROI was compensated for attenuation and the spectra of each RF segment within one ROI were averaged and log compressed. A calibration spectrum obtained from a planar reflector was subtracted from the log-compressed ROI spectrum to obtain a normalized spectrum that was independent of the instrumentation. The normalized spectrum was fit to a linear scattering model [5] yielding spectral slope (in dB/MHz) and spectral intercept (in dB) estimates. The fitting bandwidth was varied for each ROI based on a local SNR estimator. The fitting bandwidth for ROIs having satisfactory SNR was chosen broader than that used for ROIs having less satisfactory SNR. Using the largest fitting bandwidth possible is advantageous because theory predicts that the standard deviation of the slope estimates is inversely proportional to the bandwidth squared.

Adjacent cylindrical ROIs overlapped by 0.9 mm in each direction and parametric images were generated by color-coding estimates and overlaying them on conventional B-mode images. The 3D slope (or intercept) parametric volumes had a voxel size of 0.1 x 0.1 x 0.1 mm because of the 0.9-mm overlap.

3. Results

The estimation methods were performed on a set of 59 lymph nodes from 35 patients. 48 lymph nodes did not contain metastatic tissue and 11 were almost entirely filled with metastatic tissue.

Figure 1 displays representative cross-section slope images at the focal depth of the transducer for a non-cancerous (**Fig. 1a**) and a cancerous (**Fig. 1b**) lymph node (the same color scale was used for both images). Visually, important contrast is visible between the two nodes. The non-cancerous and the cancerous nodes had mean estimates of 0.48 ± 0.06 and -0.02 ± 0.12 dB/MHz, respectively.

Figure 2 displays a scatter plot of the estimates of the 59 nodes. This figure reveals that the method allows perfect differentiation of the two types of lymph nodes; the metastatic lymph nodes have smaller slope estimates.

4. Conclusions

The results obtained using the described methods are encouraging, and the methods will be investigated further using lymph nodes associated with additional types of cancers. The present results suggest great potential for the specific localization of micrometastases often missed during conventional histology.

Acknowledgments
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References

1. D. H. Turnbull: Methods Mol. Biol. **135** (2000) 235.
2. R. H. Silverman, J. A. Ketterling, J. Mamou and D. J. Coleman: Arch Ophthalmol. **126** (2008) 94
3. Y. Saijo, A. Tanaka, N. Owada, Y. Akino, and S. Nitta: Ultrasonics. **42** (2004) 753
4. M. Vogt M and H. Ermert: IEEE Trans. Ultrason. Ferroelectr. Freq. Control. **54** (2007) 1551
5. F. L. Lizzi, M. Greenebaum, E. J. Feleppa, M. Elbaum and D. J. Coleman: J. Acoust. Soc. Am. **73** (1983) 1366
6. P. Chaturvedi and M. F. Insana: J. Acoust. Soc. Am. **100** (1996) 1366

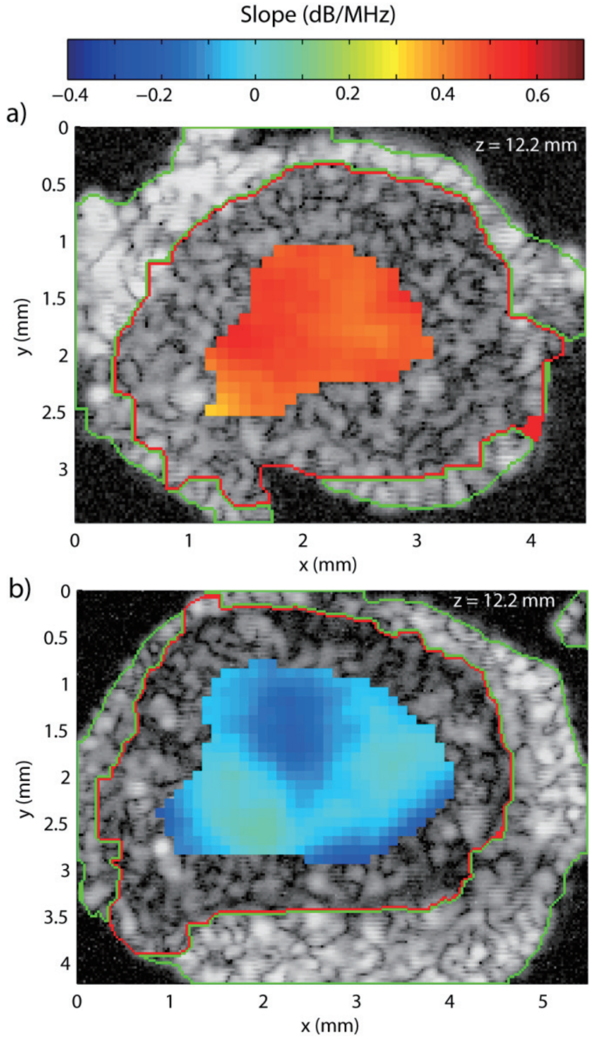

Fig. 1 Typical cross-section slope images of a non-metastatic (a) and entirely metastatic (b) lymph node from two colon-cancer patients. (Segmentation results are shown by the green and red highlights.)

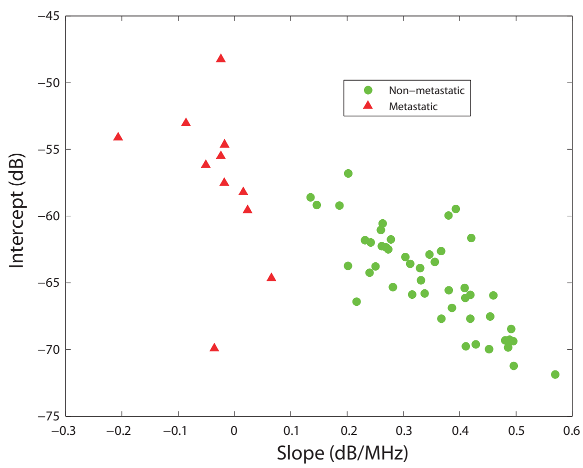

Fig. 2 Scatter plots of estimates of 59 lymph nodes.