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## Session 4pBA: High-Frequency Ultrasound (20-80 MHz)

# 4pBA4. High-frequency quantitative ultrasound approaches for cancer detection in freshly-excised lymph nodes

**Jonathan Mamou*, Alain Coron, Emi Saegusa-Beecroft, Masaki Hata, Michael L. Oelze, Eugene Yanagihara, Tadashi Yamaguchi, Pascal Laugier, Junji Machi and Ernest J. Feleppa**

***Corresponding author's address: F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, NY 10038, jmamou@riversideresearch.org**

Histology performed to assess lymph nodes excised during node-dissection surgeries from cancer patients suffers an unsatisfactory rate of false-negative determinations due to labor and time constraints. In this study, more than 300 lymph nodes were scanned in 3D using a 26-MHz high-frequency ultrasound transducer. Following scanning, individual nodes underwent a special histology procedure that involved step-sectioning each node at 50-μm intervals to guarantee that no significant cancer foci were missed. The 3D radio-frequency ultrasound dataset was analyzed using overlapping 3D regions-of-interests that were individually processed to yield thirteen quantitative ultrasound (QUS) estimates associated with tissue microstructure and were hypothesized to show contrast between normal and cancerous regions in lymph nodes. Step-wise linear discriminant analyses were performed to yield an optimal QUS-based classifier. ROC curves and areas under the ROC curves (AUCs) were obtained to assess cancer-detection performance. The AUC for the linear combination of four QUS estimates was 0.83 for a dataset of 110 axillary nodes of breast-cancer patients. Similarly, using five QUS estimates, an AUC of 0.97 was obtained for a dataset of 180 nodes of gastrointestinal-cancer patients. These studies demonstrate that QUS methods may provide an effective tool to guide pathologist towards suspicious regions in lymph nodes.

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## INTRODUCTION

Detection of small metastatic regions in excised human lymph nodes is critical to proper staging, patient management, and treatment planning. However, current state-of-the art histopathology procedures are too labor intensive to allow evaluating all dissected nodes in their entirety. In this study, quantitative ultrasound (QUS) methods using high-frequency ultrasound are investigated to detect and localize metastatic tissue within entire lymph nodes. These QUS methods rely on frameworks developed during the past three decades to obtain QUS estimates that quantify tissue properties [1, 2].

## METHODS

A custom-made, high-frequency, ultrasound scanning system using a 26-MHz single-element transducer was developed and used to acquire 3D RF ultrasound data from individual lymph nodes that were excised for histological evaluation and staging according to standard medical practice. Then, novel 3D methods were used to obtain 13 QUS estimates associated with tissue microstructure and to test the hypothesis that QUS estimates can distinguish between cancerous and cancer-free regions in lymph nodes [3, 4]. To test this hypothesis, linear-discriminant classifiers were developed to maximize cancer-detection performance based on QUS estimates [5]. In comparison to standard histopathology procedures, histology thin sections were acquired for this study every 50 $\mu$m to guarantee that no clinically significant metastatic regions would be missed; histological determinations were the gold standard for developing and evaluating the methods.

## RESULTS

The QUS-based classification methods were tested on sets of uniform lymph nodes (i.e., nodes entirely devoid of cancerous regions or nodes almost entirely filled by cancer). In total, more than 300 nodes from more than 110 patients were processed over their full 3D volume, and nodes were separated by primary-cancer organ (i.e., breast, colorectal, or gastric cancers) because of known differences in histology microarchitecture that could affect QUS estimates. The areas under the ROC curve derived from discriminant-analysis classification were greater than 0.95 for nodes obtained from colorectal- and gastric-cancer patients, and 0.83 for the more-complex axillary nodes obtained from breast-cancer patients.

Furthermore, discriminant scores were used to derive *a posteriori* cancer probability estimates [5]. For easy visual assessment of the lymph nodes, these probability estimates were color-coded and overlaid on conventional B-mode images. Figure 1 displays illustrative cancer probability, QUS images of a non-cancerous (Fig. 1a) and a cancerous (Fig. 1b) lymph node obtained from two different colorectal-cancer patients. The QUS image of the non-cancerous lymph node is dominated by green pixels (indicating a cancer probability of <25%). In comparison, the QUS image of the cancerous lymph node is dominated by red pixels (indicating a cancer probability of >75%). Therefore, both QUS images are consistent with histology results. In addition, these QUS images can be interpreted readily by a pathologist.

## CONCLUSIONS

Our results suggest that the proposed 3D QUS methods can detect and localize metastatic regions within lymph nodes with satisfactory specificity and sensitivity. These methods could serve as the basis for a new pathology device to guide pathologists towards suspicious regions quickly and reliably. This device could significantly reduce the rate of false-negative

determinations allowed by current standard histology procedures, which examine only the central plane of each lymph node.

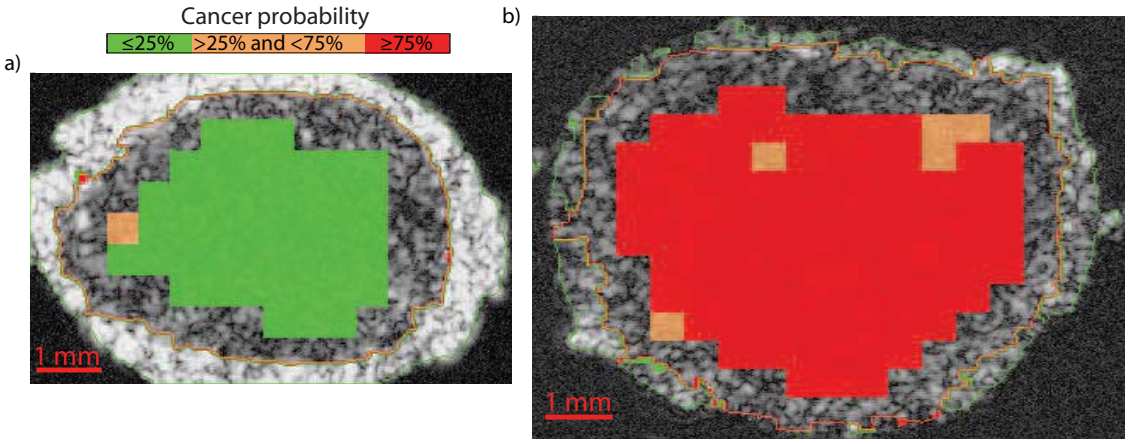


**FIGURE 1:** Illustrative QUS cancer probability images. a) Entirely non-cancerous lymph node obtained from a colorectal-cancer patient. b) Entirely cancerous lymph node obtained from a different colorectal-cancer patient.

## ACKNOWLEDGMENTS

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