Promising initial results of semi-automated quantitative-ultrasound-based (QUS) algorithm for assessment of prostate cancer using a novel 29 MHz micro-ultrasound

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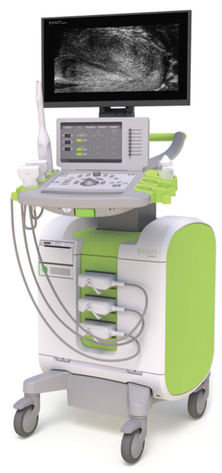
Introduction & Objectives

Currently, no technology is available that reliably detects cancerous regions in the prostate for guiding biopsies, which contributes to false-negative diagnoses and unnecessary biopsies. Previous studies by our group[1] demonstrated that quantitative ultrasound (QUS)-based algorithms have a strong potential for detecting cancerous prostate tissue in conventional 6-9-MHz TRUS systems. Micro-ultrasound is a novel modality operating at far higher frequencies (29 MHz) that enables ultrafine resolution of the prostate. We performed a preliminary study to investigate potential of incorporating our quantitative-ultrasound-based (QUS) approaches in the ultrasound micro-scanner for identifying cancerous regions in the prostate.



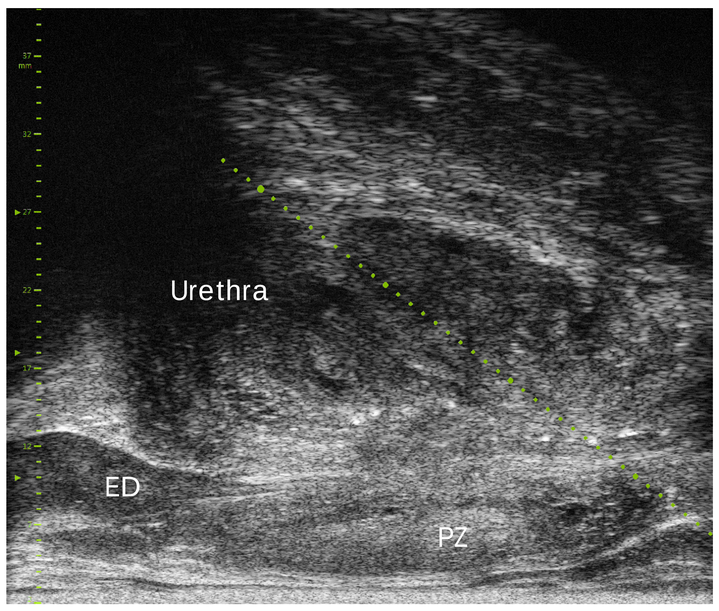
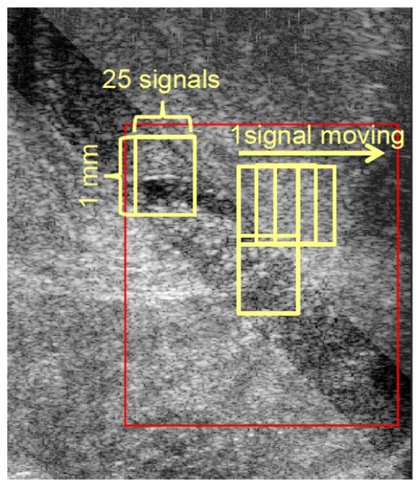
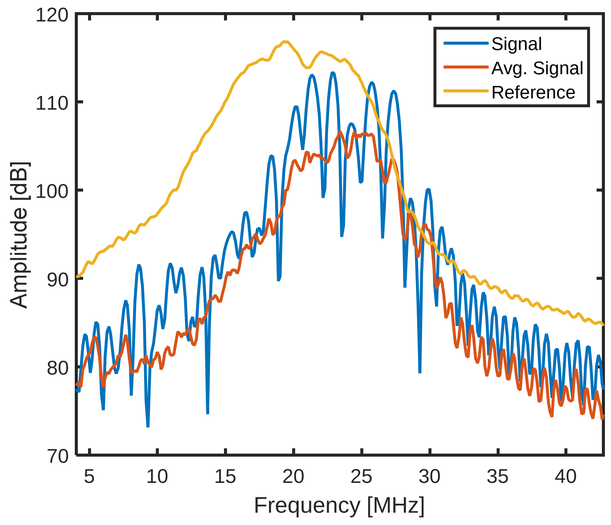


Figure 1 (Right) – **Example micro-ultrasound image and ExactVu™ 29 MHz Micro-Ultrasound system.** This image shows a midline sagittal view of the prostate. The urethra and ejaculatory duct (ED) are clearly visualized along with the peripheral zone (PZ) of the prostate which can be seen in exquisite detail. Imaging scale is in mm.





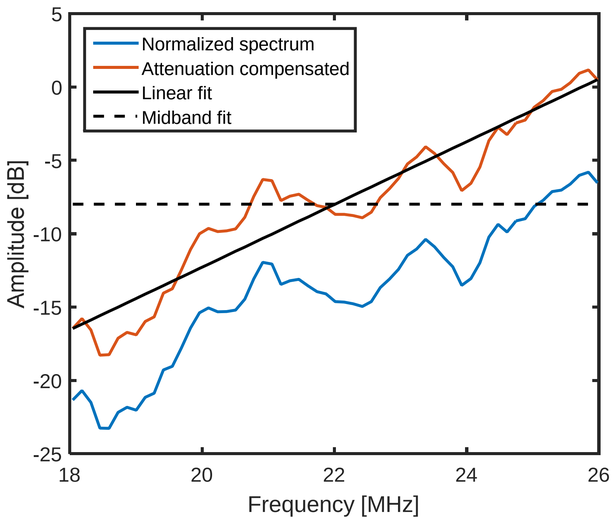


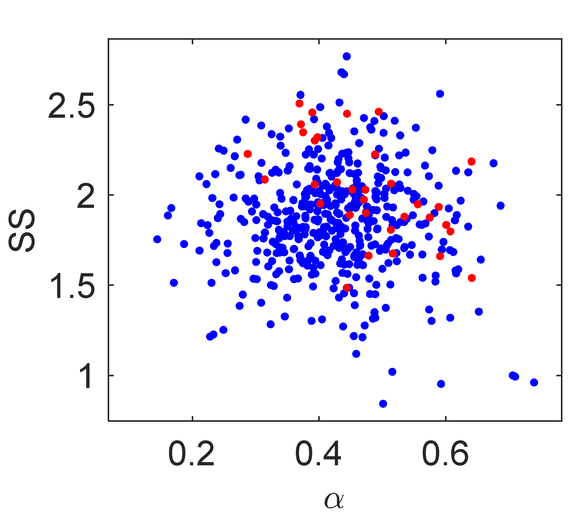
Figure 2 – **Analysis and Normalization Procedure**. (Left) The portion of the image through which the biopsy needle travelled was highlighted and sampled with a sliding window. This window was used to extract an estimate of the local power spectrum of the signal, which was then normalized based on the reference as shown in (Center). On the (Right) we see the normalized spectrum within the bandwidth of the system corrected for attenuation. A linear fit is applied to this corrected data to obtain the QUS features.

Data Collection

RF data from 67 patients (532 biopsy cores) were acquired using a 29-MHz, transrectal, micro-ultrasound system and transducer (ExactVu™ micro-ultrasound, Exact Imaging, Markham, Canada) as part of a multi-site clinical trial[2]. 75 of these biopsy samples had pathology-determined Gleason Sums (GS) of 7 and above (positive class), and 457 had benign biopsy results (negative class). Directly before each biopsy, a frame of RF data was acquired allowing imaging data to be directly compared to the pathology sample.

Data Analysis

For each RF data set, power spectra were computed along the biopsy needle trace located inside the prostate using a sliding region of interest (ROI) of approximately 1 mm^2 in size (Fig. 2). Spectra from the set of ROIs, were averaged and normalized by a reference spectrum. The reference spectrum was computed from RF data acquired from a calibration phantom consisting of 18-µm polystyrene beads. A linear model was fit to the normalized spectra, and QUS estimates of midband fit (MF), intercept (I_0) and spectral slope (SS) were calculated. The QUS estimates were used to train a linear discriminant classifier (LDC). Classifier performance was assessed using area under the curve (AUC) values obtained from receiver operating characteristic (ROC) analyses with leave-one-out cross validation. The Nakagami alpha envelope fit and subject PSA value were also included in the classifier.



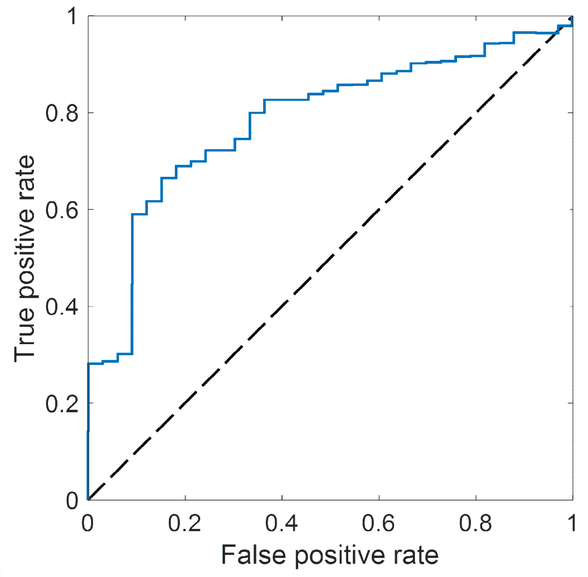


Figure 3 – **Predictive Value of QUS Features.** (Left) Scatter plot showing distribution of benign (blue) and cancerous (red) samples for various values of Spectral Slope (SS) and Nakagami alpha (α). (Right) Receiver operating characteristic plot showing the performance of the LDA classifier trained using all 5 parameters, where the dashed line represents chance-level classification. Total area under the curve (AUC) was 0.74.

	I_0	SS	α	PSA	MF	All
AUC	0.68	0.66	0.64	0.62	0.61	**0.74**

Figure 4 (Left) – **Table of AUC values**. AUC values demonstrating the accuracy of the LDA classifier for each feature individually and for the group as a whole. These values were calculated using a Leave-One-Out validation procedure

Results

When the three QUS parameters (I_0, MF, and SS) were used alone for classification, the AUC values respectively were 0.68, 0.61 and 0.66. No single parameter provided higher accuracy than the QUS **I_0** value. When all parameters were used for classification, then an AUC value of 0.74 was obtained.

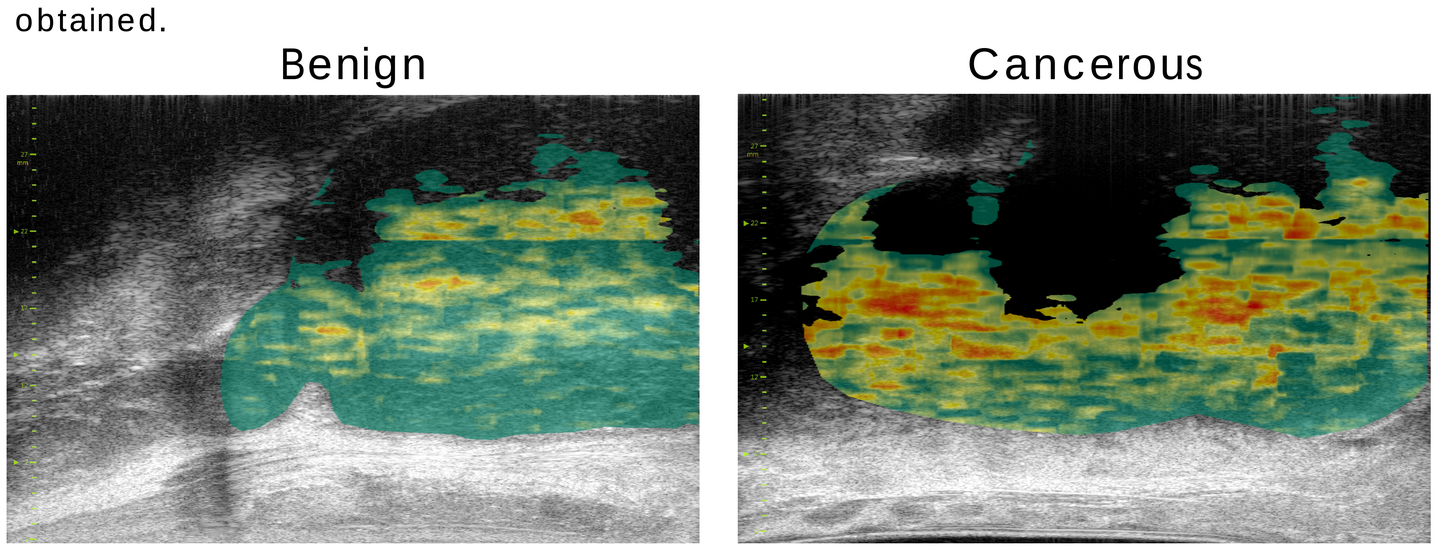


Figure 5 – **Representative micro-ultrasound images with LDA classifier output overlaid**. Color scale represents the probability of cancer according to the QUS data (red = high risk, green = low risk). The corresponding pathology sample from the image on the left was benign, while the sample from the tissue on the right was positive for clinically significant prostate cancer. These diagnoses are consistent with the overlaid data with the left image showing more green low-probability areas while the image on the right shows several patches of high risk tissue. An automated system like this could help clinicians better target suspicious regions for biopsy and reduce the false negative rate of the prostate biopsy procedure.

Conclusions

- Our results showing an AUC value of 0.74 are very encouraging for developing a prostate-cancer risk-assessing tool leveraging these novel high resolution micro-ultrasound images.
- The proposed QUS procedure can be performed automatically, eliminating the need for intensive training and mitigating inter-reader variability.
- An automated system, when used with the micro-ultrasound system like this, could help clinicians better target suspicious regions for biopsy and reduce the false negative rate of the prostate biopsy procedure
- Currently, we are testing approaches involving additional QUS estimates and non-linear classifiers, such as support-vector machines, to further improve the classification performance.

References

1. Feleppa EJ, et al. “Spectrum-Analysis and Neural Networks for Imaging to Detect and Treat Prostate Cancer” Ultrasonic Imaging. 2001; 23(3):135-46
2. Multi-Center Trial of High-resolution Transrectal Ultrasound Versus Standard Low-resolution Transrectal Ultrasound for the Identification of Clinically Significant Prostate Cancer, clinicaltrials.gov ID NCT02079025