Assessing cancer risk in 29 MHz micro-ultrasound images of the prostate: Creation of the PRI-MUS™ (**p**rostate **r**isk **i**dentification using **m**icro-**u**ltra**s**ound) protocol

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Introduction & Objectives

- A novel 29 MHz high resolution micro-ultrasound system (ExactVu™*) has been developed enabling ~ 300% higher resolution than conventional TRUS systems for prostate imaging
- First clinical use of this platform is the detection of PCa during TRUS to guide prostate biopsies in real-time
- This study uses data from the first half of a randomized clinical trial[1] to establish a newly developed protocol (PRI-MUS) for analyzing prostate micro-ultrasound images to better detect and grade cancer
- This PRI-MUS protocol will be applied in the second half of the clinical study to determine its effectiveness

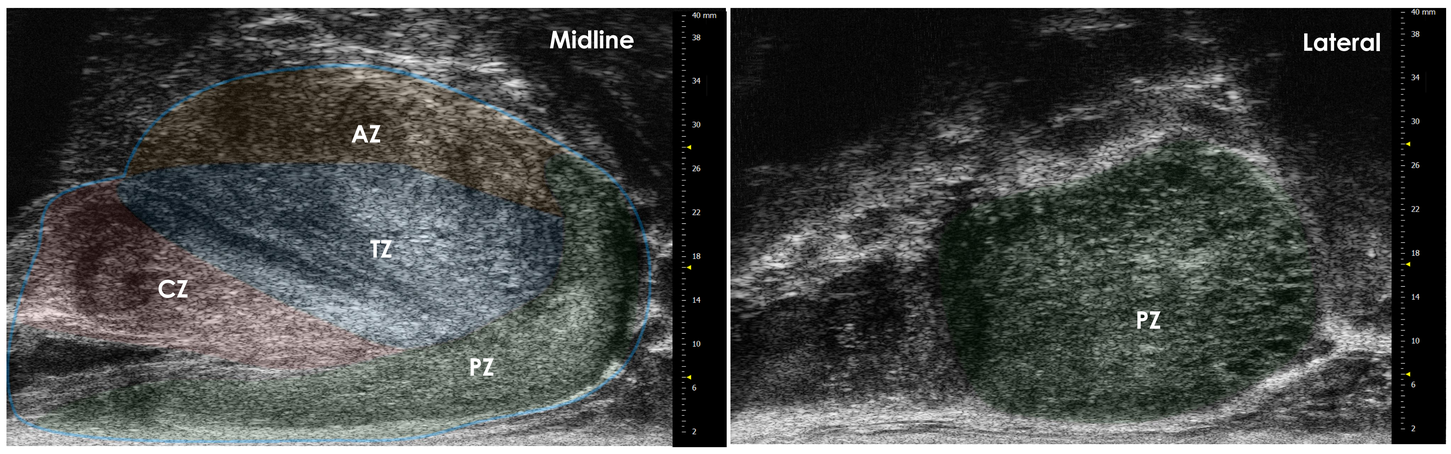
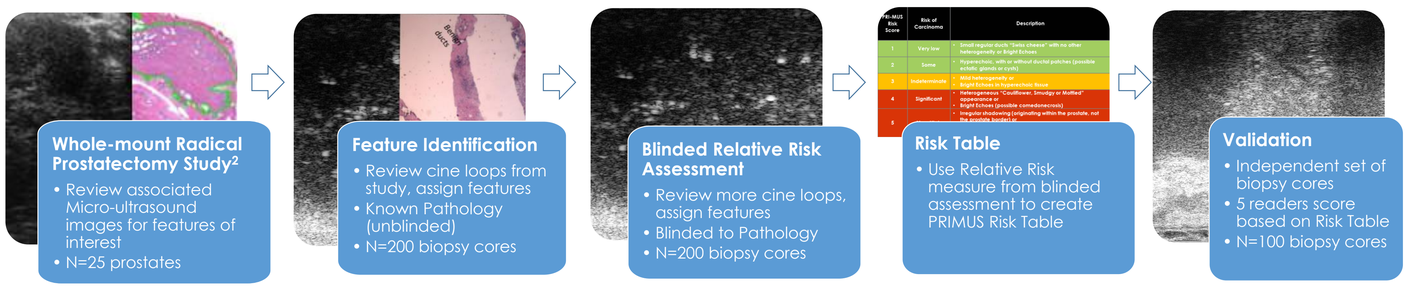


Figure 1 (above) - Sagittal Midline (left) and para-sagittal Lateral (right) views of the prostate using micro-ultrasound. The prostate margin has been labeled in blue with the zones highlighted. Ejaculatory duct and urethra are both visible, as well as all zone margins. Scale is in milometers (mm).

Material & Methods

Cine loops of transrectal micro-ultrasound-guided (TRUS) biopsies were examined from an ongoing multicenter clinical trial[1] of high-resolution TRUS vs standard TRUS for detection of clinically significant prostate cancer using the 29 MHz Exact Imaging system. Subjects underwent TRUS biopsy for suspicion of cancer due to PSA elevation and/or abnormal DRE. Features were identified and used to create the risk table (shown below). 3 of the 5 investigators who performed the blinded validation were familiar with the Exact Imaging system but naïve to the PRI-MUS protocol and received only 1 hour of PRI-MUS training.



Results

Ten sonographic features, confirmed by pathology to be malignant or benign tissue were identified during initial review. 6 features were significant when tested on the blinded data set. These features were incorporated into a 5-level PRI-MUS risk scale ranging from "Very Low" (mean relative risk 0.28) to "Very High" (1.99) risk for clinically significant prostate cancer.

Sonographic Feature (based on micro-ultrasound imaging)	N (Total)	N (Cancer)	RR [90% CI]	Assigned PRI-MUS Risk Score
Small regular ducts "Swiss cheese"	7	1	0.28 [0.05 - 1.72]	1
Hyperechoic, with or without ductal patches	50	14	0.49 [0.31 - 0.78]	2
Mild heterogeneity	42	24	1.19 [0.87 - 1.62]	3
Bright Echoes in hyperechoic tissue	10	4	0.79 [0.37 - 1.71]	3
Heterogeneous "Cauliflower/Smudgy/Mottled" appearance	32	22	1.48 [1.11 - 1.97]	4
Bright Echoes	30	18	1.24 [0.89 - 1.73]	4
Irregular Prostate (PZ)	1	1	2.01 [1.75 - 2.31]	5
Irregular PZ border	1	1	2.01 [1.75 - 2.31]	5
Mixed-echo lesions	2	2	2.02 [1.76 - 2.33]	5
Irregular Shadowing	12	11	1.94 [1.54 - 2.43]	5

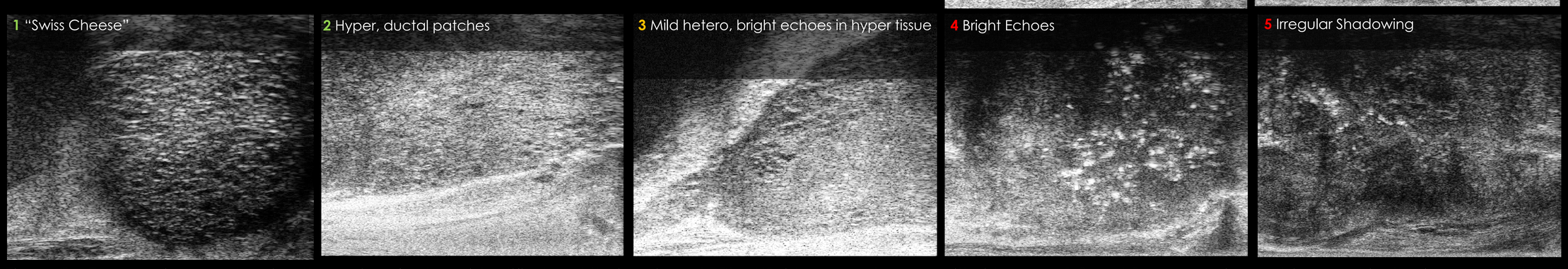
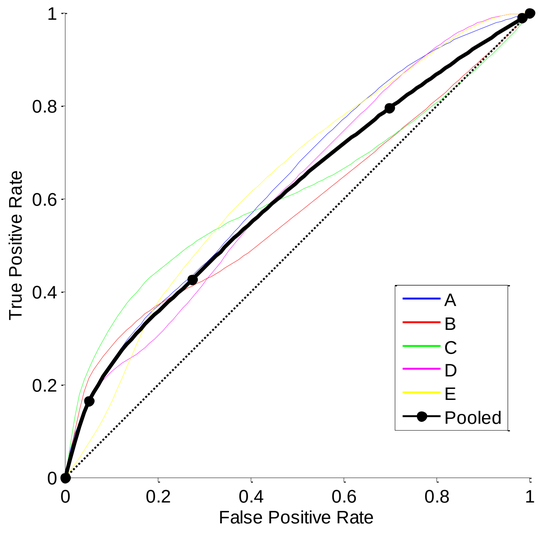


Figure 2 – Example images showing the various features identified and their assigned PRI-MUS risk scores. Images with risk scores 1,2 and 3 were benign on biopsy, while the images marked 4 and 5 were all proven cancerous on biopsy with Gleason Scores of 8, 8, 9, and 7 (from left to right).

Validation results showed an AUC of 0.60 ± 0.02 over 5 independent reviewers. Each reviewer's ability to detect clinically significant cancer using PRIMUS was significant at the $p<0.1$ level, and overall with $p=0.0001$.



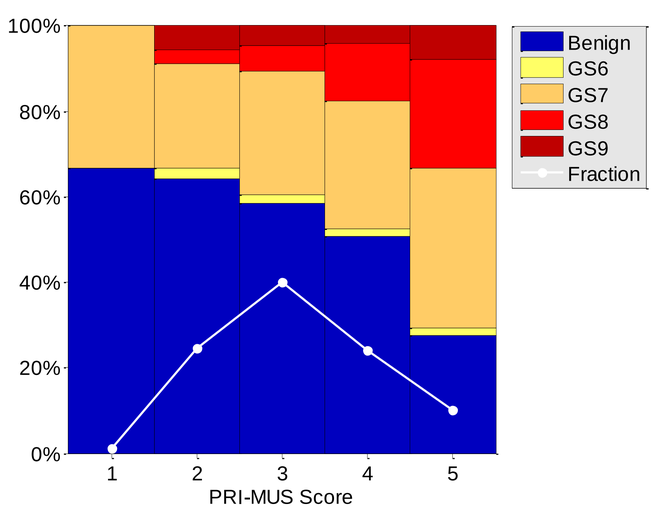


Figure 3 (left) – **Receiver-Operator Characteristic for each investigator** (A-E) on the Validation data set. Investigators B-D received only 1 hour of training on the protocol. No significant differences in performance were found between any of the investigators. Area under the curve overall is 0.60 ± 0.02 [range 0.57-0.63].

Figure 4 (right) – Distribution of Gleason Scores for each Risk Score. Distribution of Risk Scores overall is shown overlaid in white. Note that the higher risk scores tend to include not only more cancer, but more of the higher Gleason Scores as well. The high percentage of GS7 for the Risk Score of 1 is likely an artifact of the very low number of times it was marked

Conclusions

- The resolution of micro-ultrasound, paired with the PRI-MUS protocol, shows significant promise in aiding real-time visualization of prostate cancer
- More significant disease (higher Gleason Scores) associated with higher PRI-MUS Risk Scores
- This first implementation of PRI-MUS will undergo ongoing refinement, including expansion to a multi-parametric micro-ultrasound approach incorporating functional scans for optimal diagnostic accuracy and a more direct comparison with MRI-based PI-RADS

References

1. 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
2. Pavlovich CP, Cornish TC, Mullins JK, et al. High-resolution transrectal ultrasound: Pilot study of a novel technique for imaging clinically localized prostate cancer. Urol Oncol. 2013; 32(1): 34.e27-32 doi:10.1016/j.urolonc.2013.01.006.

** Please note that ExactVu micro-ultrasound system has not yet received FDA or CE approval, and so is not yet available for commercial release.*