

High resolution micro-ultrasound of the prostate, PRI-MUS™ protocol guidance along with clinical variables: Combined approach for reducing unnecessary biopsies

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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
- The PRI-MUS™ (prostate risk identification using micro-ultrasound) protocol has been developed to aid in the analysis of the new, more detailed images generated by this system (Fig 1)
- Combining patient screening data with micro-imaging data (by applying PRI-MUS™ to real-time micro-ultrasound imaging) may allow forgoing biopsy of certain low-risk areas of the prostate without substantially increasing false negative rates

Material & Methods

Cine loops of transrectal micro-ultrasound-guided (TRUS) biopsies were examined from an large multicenter clinical trial¹ 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. 300 loops were read according to the PRI-MUS protocol² by 2 investigators. These loops were divided into a training set (200) and test set (100). Clinical screening data and PRI-MUS scores were analyzed in the training set to determine criteria for potentially avoiding biopsy. These criteria were then applied to the test set to determine the outcome of simulated biopsies where samples below the threshold were omitted.

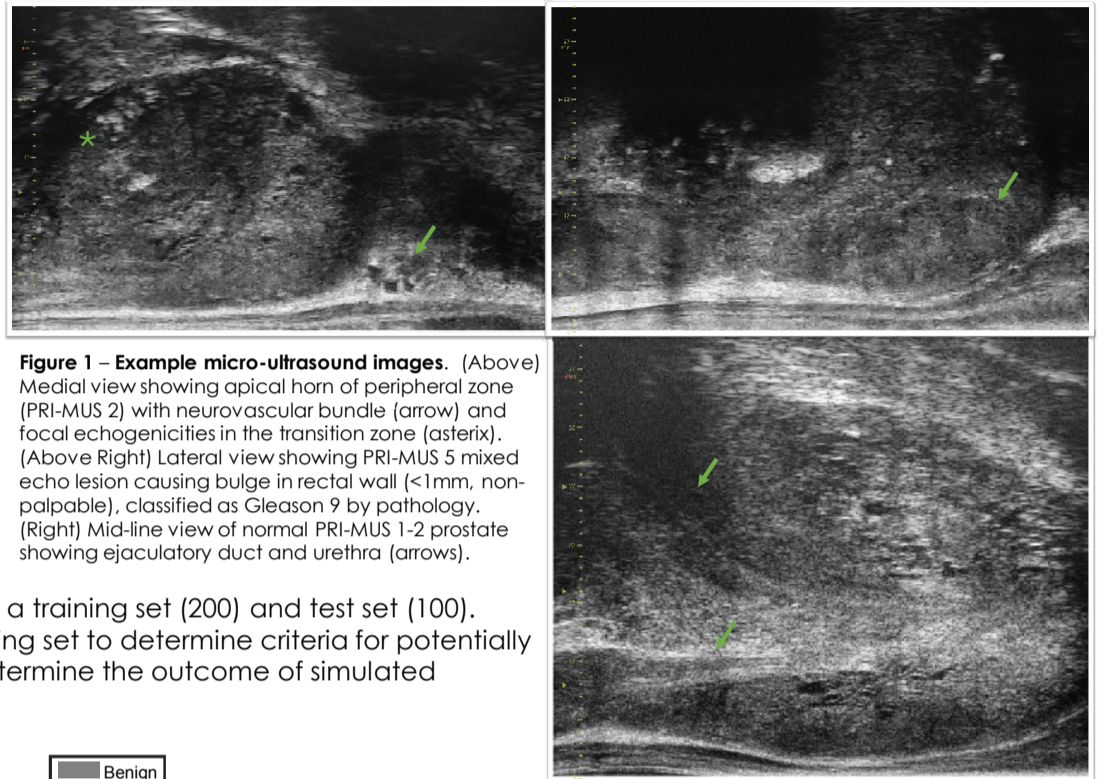


Figure 1 – Example micro-ultrasound images. (Above) Medial view showing apical horn of peripheral zone (PRI-MUS 2) with neurovascular bundle (arrow) and focal echogenicities in the transition zone (asterisk). (Above Right) Lateral view showing PRI-MUS 5 mixed echo lesion causing bulge in rectal wall (<1mm, non-palpable), classified as Gleason 9 by pathology. (Right) Mid-line view of normal PRI-MUS 1-2 prostate showing ejaculatory duct and urethra (arrows).

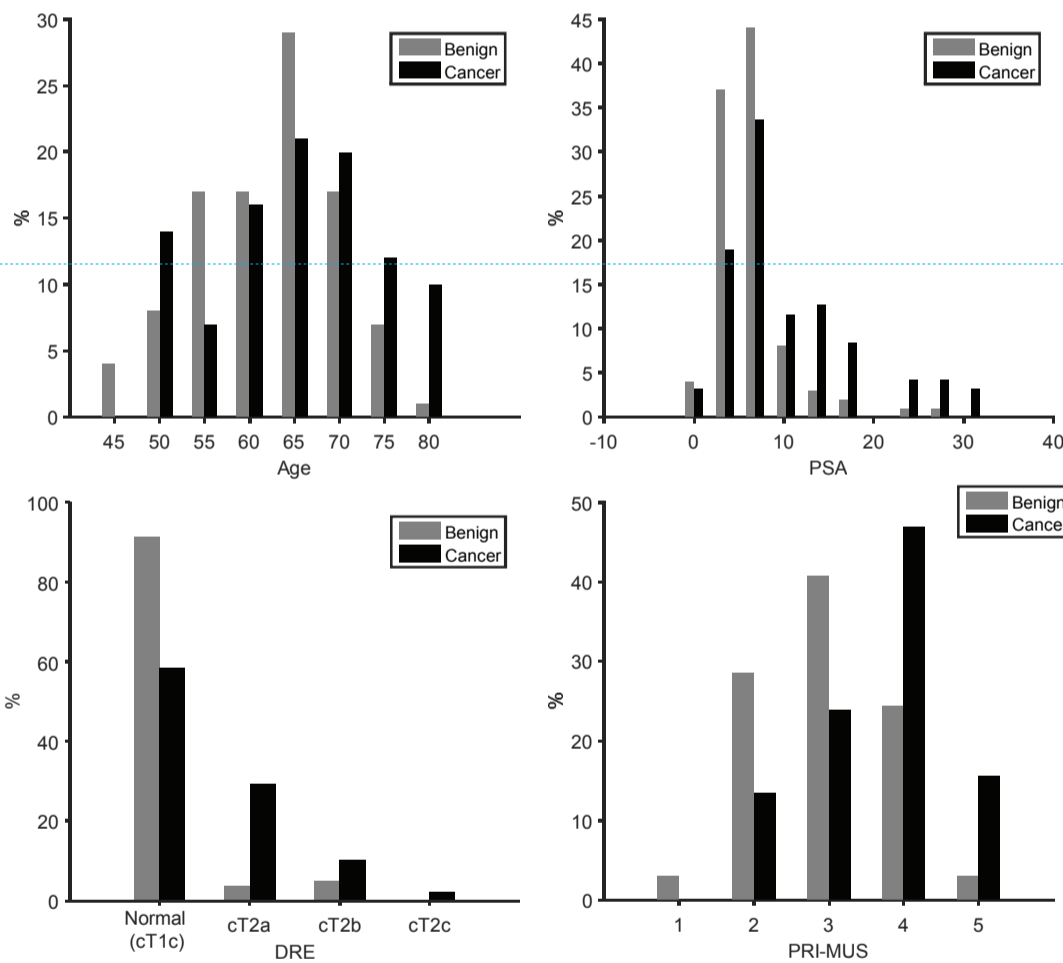


Figure 2 (above) – Histograms of training set data for various clinical screening data and PRI-MUS. All histograms show percentage of counts within each range for training data only. Benign and cancerous samples are plotted separately as grey and black bars respectively. (A) Age, showing moderately lower risk in the area around 55-65 years old. (B) PSA, showing a clear shift in the distribution towards lower values with a cross-over point around 10ng/ml. (C) DRE, showing any abnormality in DRE resulting in a substantially higher risk of cancer. (D) PRI-MUS Score, showing lower risk profile for samples in the 1-3 range.

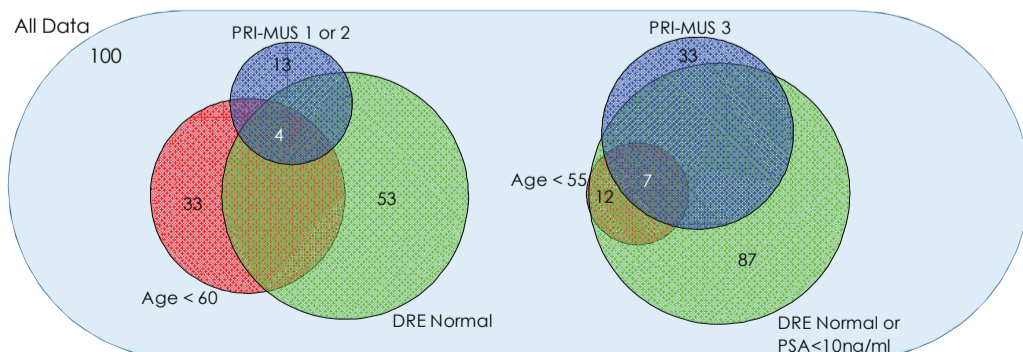


Figure 3 (above) – Criteria for avoiding biopsy and number of subjects in each group. (Left) Criteria for low risk tissue with PRI-MUS 1 or 2 scores. This criteria selected 4 samples for exclusion. (Right) Criteria for indeterminate risk tissue with PRI-MUS 3 score. This criteria selected 7 samples for exclusion. The Venn diagrams displayed are approximate. PRI-MUS scores are for reader 1, values for reader 2 were similar.

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. Ghai, S., Eure, G., Fradet, V., Hyndman, M. E., McGrath, T., Wodlinger, B., & Pavlovich, C. P. (2016). Assessing Cancer Risk on Novel 29 MHz Micro-Ultrasound Images of the Prostate: Creation of the Micro-Ultrasound Protocol for Prostate Risk Identification. *Journal of Urology*, 196(2), 562–569.

Results

Based on analyzing the histograms in the training set (Fig 2), PRI-MUS score, Age, DRE result, and PSA were identified as important criteria for selecting low-risk samples for removal. The criteria selected (Fig 3) were: PRI-MUS 1 or 2, DRE normal, Age < 60 years Or PRI-MUS 3, (PSA < 10ng/ml or DRE normal), Age < 55 years

The test set contained 45 biopsy samples which pathology identified as clinically significant cancer, and 55 biopsy samples which were identified as benign. If biopsy samples meeting either criteria above had been skipped, the result would have been 11/100 samples avoided for each investigator (22/200 overall). 3 of these 22 samples were positive for cancer on histopathologic analysis resulting in a 96% per-sample sensitivity. 1 of the missed samples was a low-risk Gleason 6 lesion, another was a Gleason 9 lesions which was identified by surrounding high-PRI-MUS score samples leading to the same overall diagnosis for the patient. The third missed sample was a small Gleason 7 sample with 35% core length which would have been missed.

In total, diagnosis of cancer and grade of the index lesion would have been changed in 1 of the 100 subjects for investigator 1, and for none of the 100 subjects for investigator 2. This suggests an overall per-subject sensitivity of 98.7% (specificity 19.4%) and NPV of 95.5% (PPV 47.0%).

	Sensitivity	Specificity	NPV	PPV
Per-Subject	98.7%	19.4%	95.5%	47.0%
Per-Core	95.6%	16.4%	81.8%	48.3%

Figure 4 (above) – Table of resulting sensitivities and specificities. Without excluding any cores, the Sensitivity would be 100% and the Specificity 0%. The goal is to increase specificity as high as possible, while maintaining an acceptable sensitivity to avoid missing clinically significant cancer in any subject.

Conclusions

- Clinical variables and micro-ultrasound imaging (with PRI-MUS™) provide synergistic information about cancer risk
- Avoiding certain systematic samples in low-risk individuals with low-risk micro-ultrasound imaging may be feasible (per-subject sensitivity 98.7%) and yield improved patient care
- Application of this technique (and PRI-MUS in general) is easily performed live and in real-time during the biopsy procedure with no additional equipment or personnel other than the micro-ultrasound system