A Multi-Institutional Randomized Controlled Trial Comparing Novel First-Generation High-Resolution Micro-Ultrasound with Conventional Frequency Ultrasound for Transrectal Prostate Biopsy

Pavlovich CP[1], Hyndman ME[2], Eure G[3], Ghai S[4], Fradet V[5]

[1]Johns Hopkins - The James Buchanan Brady Urological Institute, Baltimore, USA, [2]Prostate Cancer Centre, Calgary, Canada, [3]Urology of Virginia, Virginia Beach, USA, [4]Joint Department of Medical Imaging, University Health Network, University of Toronto, Toronto, Canada, [5]Université Laval, Quebec City, Canada

BACKGROUND:

To compare first-generation high-frequency **29 MHz** transrectal **micro-ultrasound** ("micro-US") with conventional low-frequency 7–12 MHz transrectal ultrasound ("conv-US") for the detection of clinically-significant prostate cancer (csPCa).

METHODS:

- **1,676** men indicated for prostate biopsy and without known prostate cancer were randomized 1:1 to micro-US or conv-US guided biopsy at 5 sites (Johns Hopkins, Urology of Virginia, Prostate Cancer Centre Calgary, UHN/Princess Margaret, Université Laval).
- Exactly 12-cores were taken transrectally from each subject, with each core taken either systematically or from a target near the systematic position.
- The trial was paused after 1,113 subjects to train investigators on the new **PRI-MUS**™,[1] (**P**rostate **R**isk **I**dentification using **M**icro-**U**ltrasound) protocol for micro-ultrasound targeting, developed using pathology data from the first portion of the trial.
- csPCa was defined as any **Grade Group > 1** and/or any core with **> 50%** cancer.

Figure 1: First-generation **ExactVu**™ micro-ultrasound system used in this study

	Overall	Micro-Ultrasound	Conventional Ultrasound
Total Enrolled	1,676	837	839
Age (median+IQR)	63	63 [57-68]	63 [56-68]
PSA (median+IQR)	6.0	6.0 [4.1-8.4]	6.0 [4.3-8.1]
Family History of PCa	22.9%	21.5%	24.2%
Positive DRE	21.2%	21.0%	21.4%
PCPT Risk Score	44% [38-52]	44% [38-52]	44% [37-52]

Table 1: Study Demographics

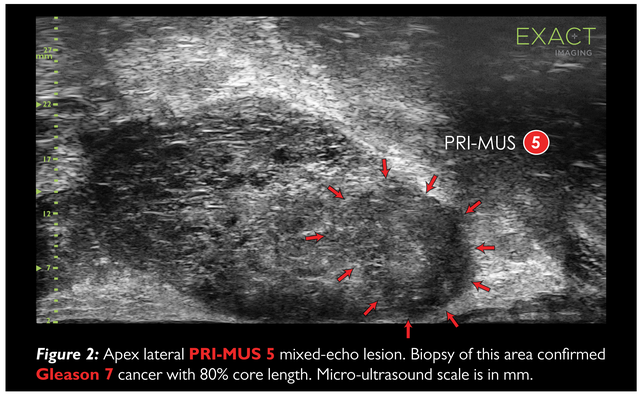

Figure 2: Apex lateral **PRI-MUS 5** mixed-echo lesion. Biopsy of this area confirmed **Gleason 7** cancer with 80% core length. Micro-ultrasound scale is in mm.

Inclusion Criteria	Exclusion Criteria
Men aged 40-79	History of prostate cancer
Indication for prostate biopsy (e.g. abnormal PSA, abnormal DRE)	Undergoing TRUS-guided prostate biopsy in the OR under anesthesia
PSA level <50ng/mL	Known prostate volume (from prior imaging) of > 60cc
Clinical stage < T3	Anorectal abnormalities preventing TRUS-guided prostate biopsy
	Unable to provide their own informed consent

RESULTS:

- No effect seen in ITT analysis (34.6% vs. 36.6%), due to errors in sampling of apical horn using prototype transducer
- Significantly greater csPCa detection in per-protocol group (PP) with micro-US (43.7% vs. 36.6% conv-US, p=0.02) after PRI-MUS training. PRI-MUS training provided guidance on relevant imaging characteristics not previously seen with conventional ultrasound.
- After PRI-MUS training, sensitivity improved to 63.4% from 24.7% for micro-US (p<0.01), at cost of lower specificity (63.2%)

	ITT				PP			
	Overall	Micro-US (%)	Conv-US (%)		Overall	Micro-US (%)	Conv-US (%)	
N	1,676	837	839		1109	286	823	
Any PCa	864	415 (49.6%)	449 (53.5%)	p=0.05	693	173 (60.5%)	442 (53.7%)	p=0.02
csPCa	597	290 (34.6%)	307 (36.6%)	p=0.21	426	125 (43.7%)	301 (36.6%)	p=0.02

Table 2: **Patient-level outcome**. While no improvement was seen with micro-US in the ITT population, the Per Protocol group showed a significant improvement in detection rate for csPCa on micro-US, without an increase in percentage of insignificant cancers diagnosed.

	N	PPV	NPV	Specificity	Sensitivity
Conv-US Pre-Training	6636	31.0%	91.1%	90.8%	31.9%
Micro-US Pre-Training	**6600**	**16.9%**	**89.6%**	**84.2%**	**24.6%**
Micro-US Post-Training	**3384**	**18.5%**	**92.2%**	**63.2%**	**60.8%**
Conv-US Post-Training	3372	32.5%	91.6%	89.5%	38.0%

p<0.001

p<0.001

Table 3: **Per biopsy core statistics and effect of mid-trial training**. Significant improvements in Sensitivity were seen post training in the micro-US arm of the study. There was also a significant improvement in sensitivity noted between the post-training micro-US and post-training conv-US arms.

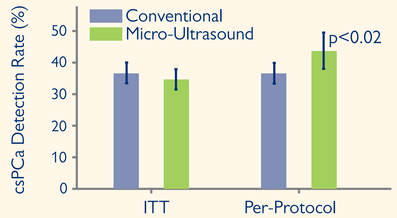

Figure 3: **Subject-level detection rate per modality and arm of study**. Intent-To-Treat (ITT) analysis includes all randomized subjects, regardless of protocol deviations, while Per-Protocol (PP) analysis includes only subjects where the correct protocol was followed including adequate systematic sampling of all sextant areas both medially and laterally. While the ITT analysis did not demonstrate any benefit, the **PP analysis** demonstrated a **19.4% improvement in detection of clinically significant cancer (p<0.02)**.

CONCLUSIONS:

- First-generation micro-US with PRI-MUS achieved greater sensitivity to detect significant prostate cancers than conventional TRUS
- Instruction on micro-US interpretation using PRI-MUS and proper systematic biopsy technique further improved cancer detection rates of clinically significant cancer with the same number of biopsy samples.

REFERENCES

1. Ghai S, Eure G, Fradet V, et al: ***Assessing Cancer Risk on Novel 29 MHz Micro-Ultrasound Images of the Prostate: Creation of the Micro-Ultrasound Protocol for Prostate Risk Identification***. J. Urol. 2016; 196: 562–569.