MicroUltrasound of the Prostate

Gerald L. Andriole, MD

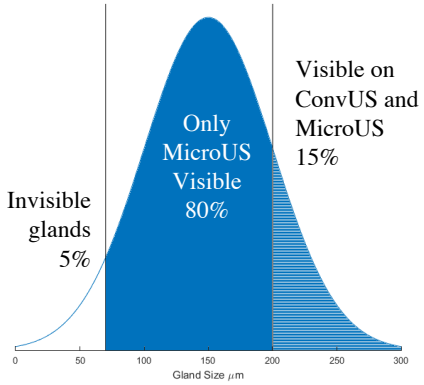
Chief Medical Officer

Prostatype Genomics

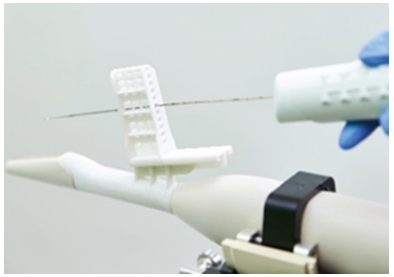
February 6, 2024

What is Micro-Ultrasound?

- Novel micro-ultrasound system **operating at 29 MHz**
  - Much higher than conventional 6-9MHz systems
- 70 micron imaging allows most prostate ducts to be visualized and tissue patterns appreciated
- **PRI-MUS** risk identification protocol for systematically characterizing tissue
- Commercially available (CE, FDA, Health Canada approved)

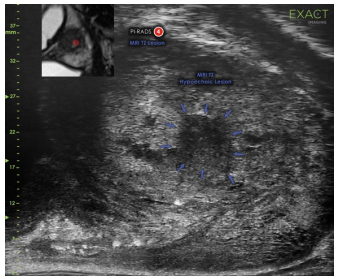


Transperineal



Transrectal

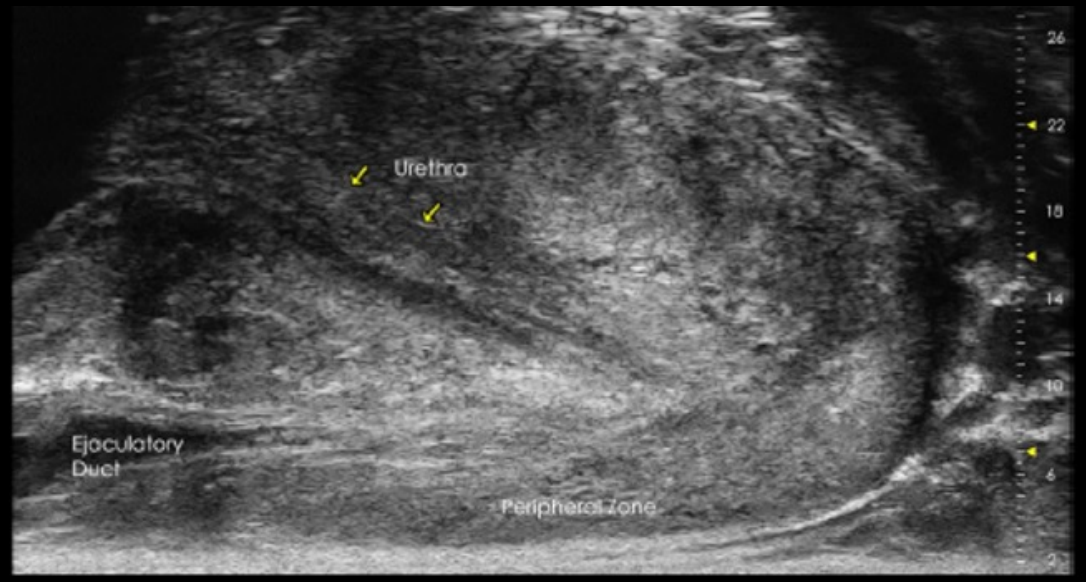
MRI Fusion



Imaging Detail

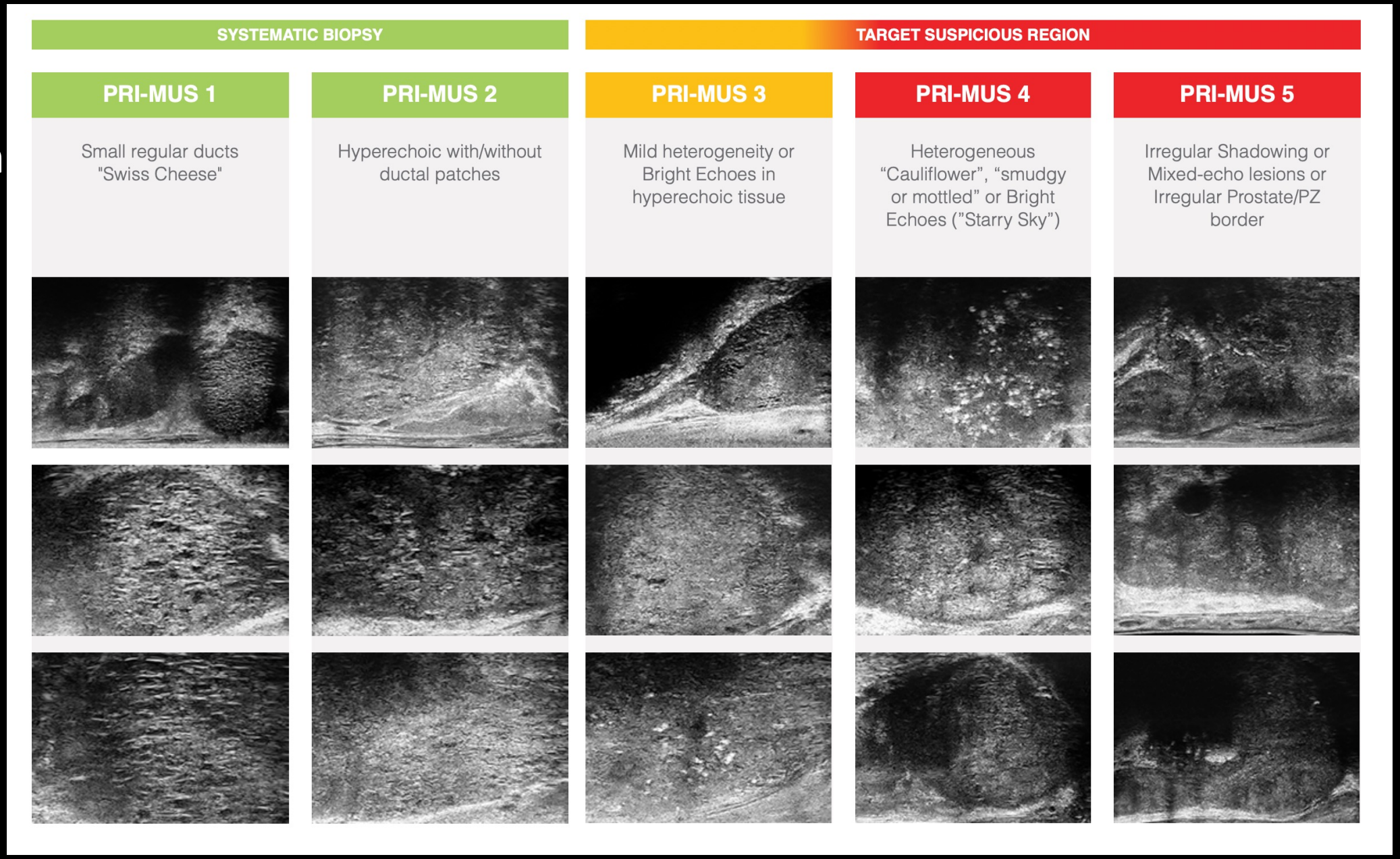
Able to resolve anatomical details down to 70 microns

- Individual glands are often seen
- Margins of zones
- Small calcified lesions
- Subtle deviations in prostate margin
- Neurovascular bundles
- Prior biopsy needle tracks
- Textural changes within tissue

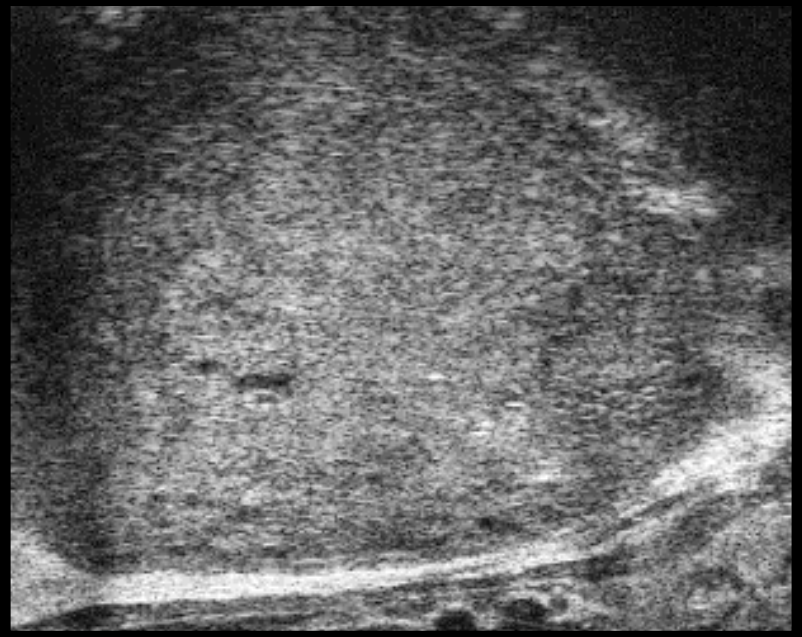


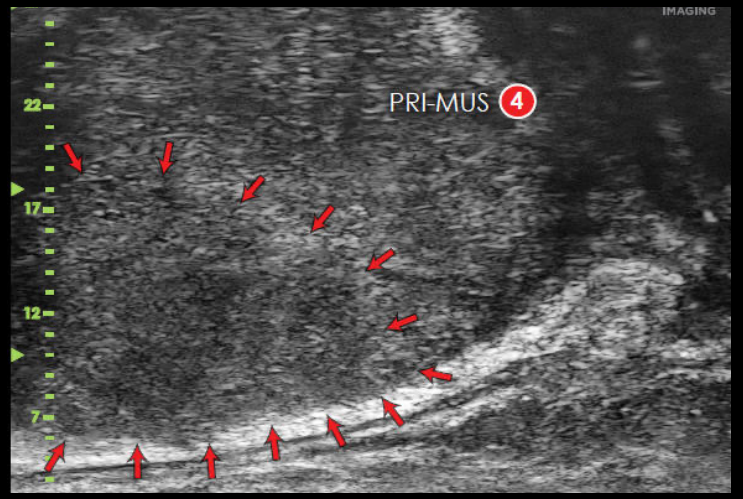
Prior Biopsy Tracks

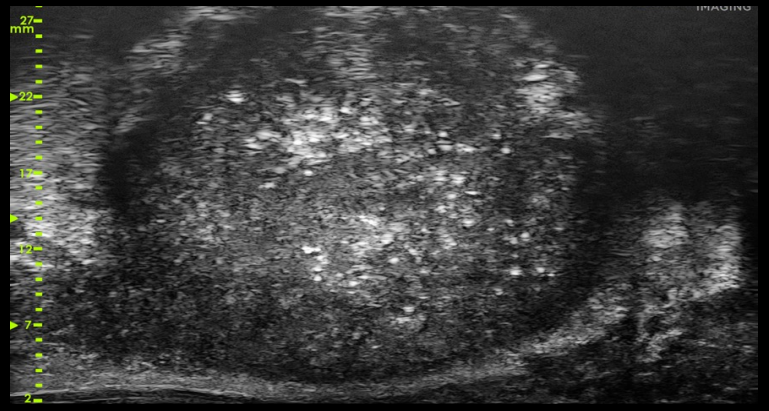
Prostate Risk Identification using Micro-Ultra-Sound

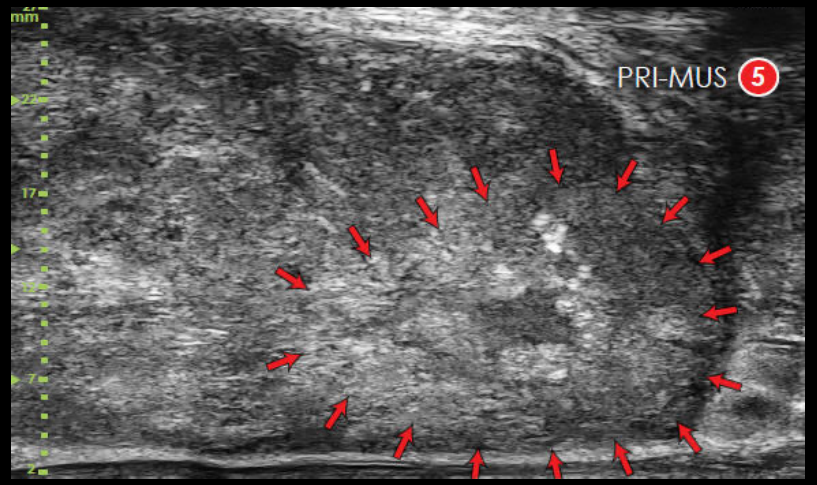


Ghai, S. et al, (2016) "**Assessing *Cancer Risk in Novel 29 MHz Micro-Ultrasound Images of the Prostate: Creation of the PRI-MUS (prostate risk identification using micro-ultrasound) protocol***", *Journal of Urology vol. 196 no. 2*




IMAGING
PRI-MUS 4
22
17
12
7


mm
27
22
17
12
7
2


mm
PRI-MUS 5
22
17
12
7
2

On-Line PRIMUS Training

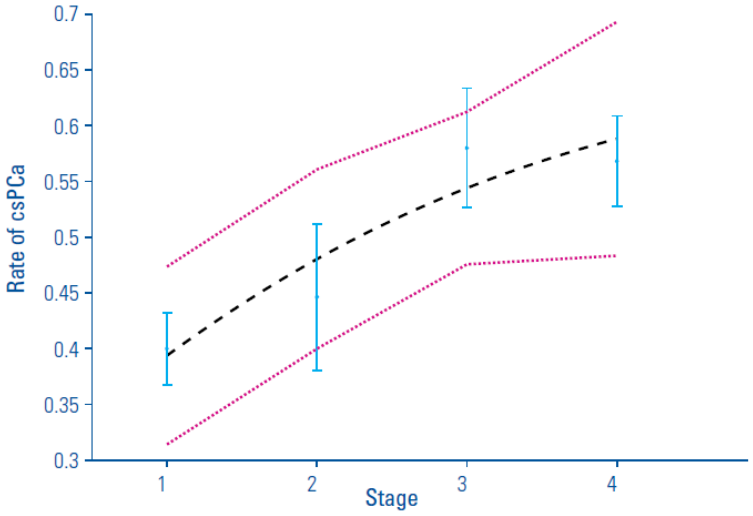
1. **Pre-training** – e-Learning modules and online assessments are provided to all urologists prior to system installation

2. **On-Site training** – instructor-lead on-site training as well as “shadowing” the urologists in using the ExactVu system clinically to ensure:
   - optimal use of the system,
   - optimal technique, and
   - comfort with the PRI-MUS risk protocol to identify and target suspicious regions

3. **On-going training and support** – access significant inventory of online videos, e-learning modules, online manuals, and mini-online case studies

Prostate Cancer Detection by Novice Micro-Ultrasound Users Enrolled in a Training Program

Hannes Cash,[✉1,2] Sebastian L. Hofbauer,[3] Neal Shore,[4] Christian P. Pavlovich,[5] Stephan Bulang,[6] Martin Schostak,[1] Erik Planken,[7] Joris J. Jaspars,[7] Ferdinand Luger,[8] Laurence Klotz,[9] Georg Salomon[10]



Blue error bars represent the standard error of the mean. Black dashed line is the Gompertz function fit with 95% CI shown in magenta. The fit indicates the most likely learning curve with clear improvement by stage outside of the 95% CI. The lack of a plateau suggests further improvement may be possible.

TABLE 3.

Multivariate logistic regression model results accounting for patient risk levels

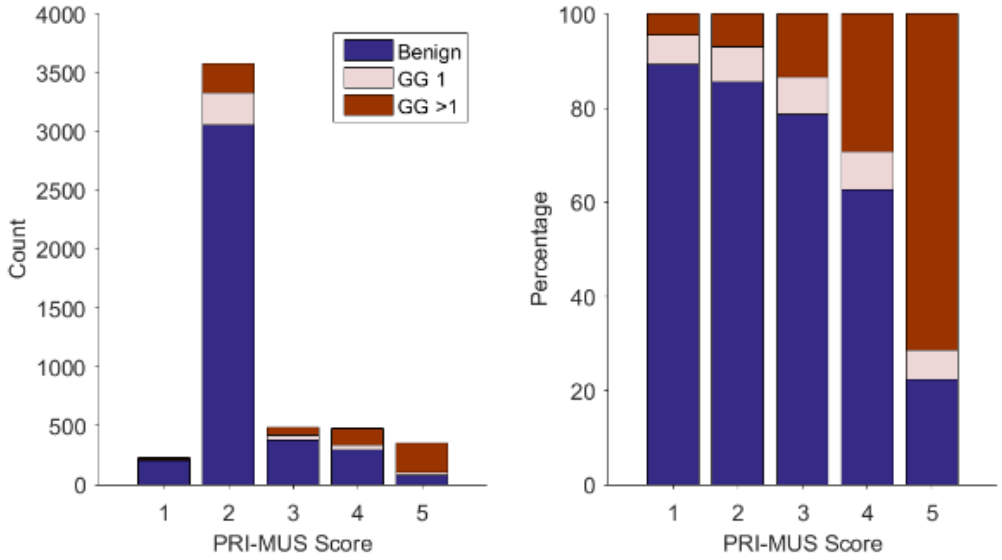
Variable	OR	*P*-value
Stage 1	Reference	N/A
Stage 2	0.835	0.551
Stage 3	1.714	0.057
Stage 4	1.953	0.029
PBCG Risk Score	23.987	<0.001

Stages 3 and 4 were associated with increased odds of detecting clinically significant cancer, with stage 4 achieving statistical significance at P = 0.03.

Cancer Detection Rates in Targeted Biopsy Plateau after 30-40 cases

Validation of PRI-MUS classification for Micro-Ultrasound

- PRI-MUS accuracy assessed prospectively in 5833 biopsy samples from 399 biopsy sessions
- AUC of 0.76 to predict GG > 1 cancer
- Positive rates for GG>1 ranged from 4.4% (PRI-MUS 1) to 71.4% (PRI-MUS 5)

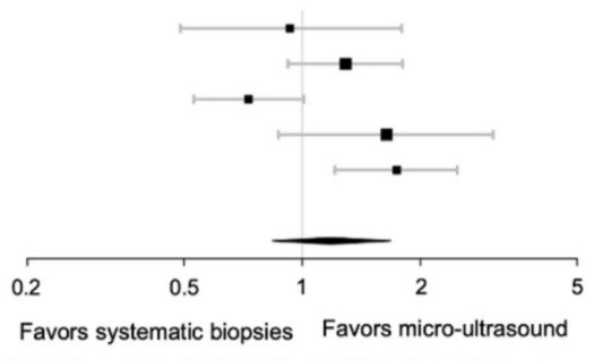


Luger, et al. Annals of Urology & Nephrology 2019

Micro-ultrasound-guided biopsies versus systematic biopsies in the detection of prostate cancer: a systematic review and meta-analysis

Study	Patients with both tests	MicroUS	SB	DR	95%CI
Abouassaly 2020	67	14	15	0.93	[0.49-1.79]
Hofbauer 2021	203	58	45	1.29	[0.92-1.80]
Rodriguez-Socarras 2021	194	47	64	0.73	[0.53-1.01]
Rojas-Claros 2020	47	18	11	1.64	[0.87-3.06]
Wiemer 2020	159	59	34	1.74	[1.21-2.48]
Random effect model	**670**	**196**	**169**	**1.18**	**[0.84-1.68]**

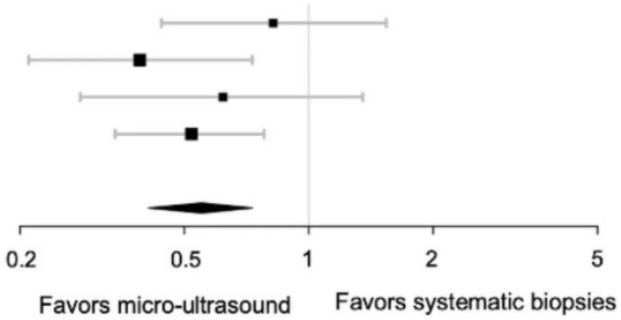
Heterogeneity I^2=69.9%, p=0.0056



Detection ratio of clinically significant prostate cancer (Gleason Grade Group ≥2)

Study	Patients with both tests	MicroUS	SB	DR	95%CI
Abouassaly 2020	67	14	17	0.82	[0.44-1.54]
Rodriguez-Socarras 2021	194	13	33	0.39	[0.21-0.73]
Rojas-Claros 2020	47	8	13	0.62	[0.28-1.35]
Wiemer 2020	159	27	52	0.52	[0.34-0.78]
Random effect model	**467**	**62**	**115**	**0.55**	**[0.41-0.73]**

Heterogeneity I^2=0%, p=0.403

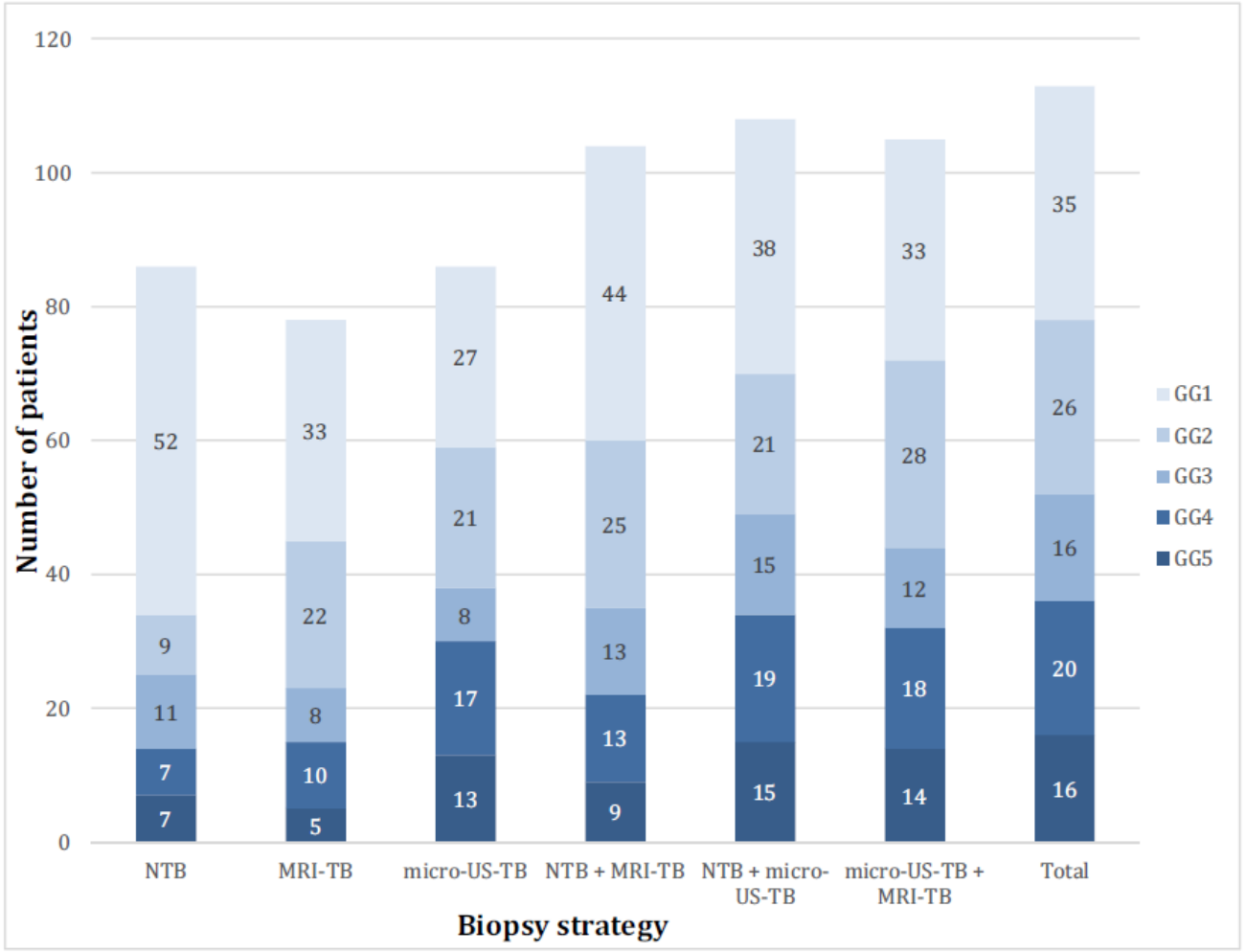


Detection ratio of non-clinically significant prostate cancer (Gleason Grade Group =1)

World Journal of Urology
https://doi.org/10.1007/s00345-022-04087-z

Value of MicroUS targets during MRI-targeted biopsy

Wiemer et al, EU Focus *2020*



NTB= non targeted biopsy, MRI-TB= Magnetic Resonance Imaging-targeted biopsy micro-US-TB= micro-ultrasound targeted biopsy, GG= ISUP grade group

Fig. 4 – Distribution of grade groups depending on different biopsy strategies. GG = ISUP grade group; ISUP = International Society of Urological Pathology; micro-US-TB = microultrasound-targeted biopsy; MRI-TB = magnetic resonance imaging–targeted biopsy; NTB = nontargeted biopsy.

Micro Ultrasound in Men with Negative MRI

- 125 pts
- Targeted and Systematic MicroUS TR Biopsy
- 47 had cancer; 34 (27%) were clinically significant
- MicroUS identified 33 of 34 clinically significant cancers

EUROPEAN UROLOGY OPEN SCIENCE 47 (2023) 73–79

Prospective Comparison Study of MRI and Microultrasound

Lughezzani et al. Eur Uro Foc 2020

Blinded Prospective study of 320 Patients:

Table 3 – Comparison of mpMRI and microUS-targeted biopsy results.

		ISUP Gleason grade on mpMRI-targeted biopsies						
		0	1	2	3	4	5	Total
ISUP Gleason grade on microUS-targeted biopsy	0	194	10	16	3	0	0	223
	1	4	8	1	0	0	0	13
	2	5	0	25	0	0	0	30
	3	1	0	0	27	0	0	28
	4	2	0	0	0	9	0	11
	5	4	1	0	0	0	10	15
	Total	210	19	42	30	9	10	320

13 csPCa missed by MRI, found by MicroUS

ISUP = International Society of Urological Pathology; microUS = microultrasound; mpMRI = multiparametric magnetic resonance imaging.

A non-inferiority comparative analysis of micro-ultrasonography and MRI-targeted biopsy in men at risk of prostate cancer

Table 2 Detected clinically significant prostate cancer (PCa) and PCa according to different Prostate Risk Identification for Micro-Ultrasonography and Prostate Imaging Reporting and Data System scores.

csPCa/PCa (ratio %)	PI-RADS 1 + 2 *n/N* (%)	PI-RADS 3	PI-RADS 4	PI-RADS 5	Total
PRI-MUS 1 + 2	0/0 (-)	0/4 (0.0)	2/9 (22.2)	0/3 (0.0)	2/16 (12.5)
PRI-MUS 3	2/6 (33.3)	3/17 (17.6)	10/28 (35.7)	2/5 (40.0)	17/56 (30.4)
PRI-MUS 4	2/7 (28.6)	3/16 (18.8)	29/60 (48.3)	7/12 (58.3)	41/95 (43.2)
PRI-MUS 5	1/2 (50.0)	0/0 (-)	3/12 (25.0)	14/21 (66.7)	18/35 (51.4)
Total	5/15 (33.3)	6/37 (16.2)	44/109 (40.4)	23/41 (56.1)	78/202 (38.6)

csPCa, clinically significant prostate cancer; PCa, prostate cancer; PI-RADS, Prostate Imaging Reporting and Data System; PRI-MUS, Prostate Risk Identification for Micro-Ultrasonography.

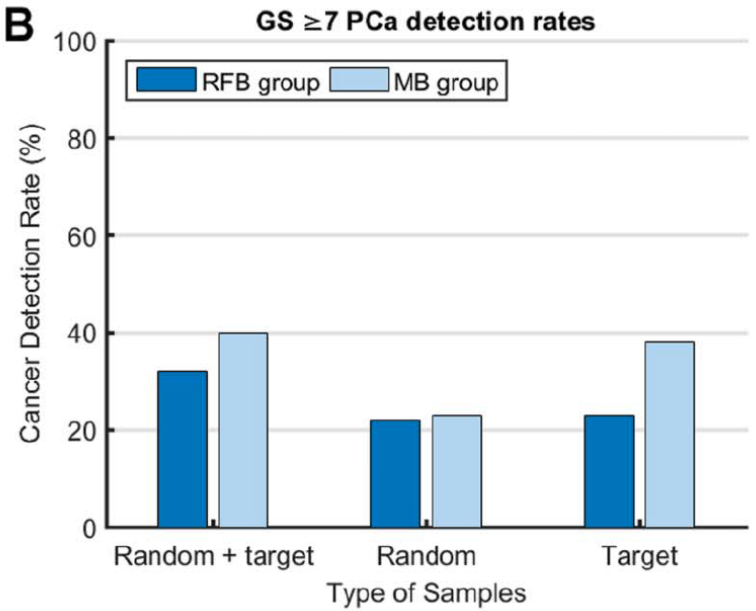
BJU Int 2022; **129:** 648–654 doi:10.1111/bju.15635

Comparison of Initial Experience with Transrectal Magnetic Resonance Imaging Cognitive Guided Micro-Ultrasound Biopsies versus Established Transperineal Robotic Ultrasound Magnetic Resonance Imaging Fusion Biopsies for Prostate Cancer

Oliver Rojas Claros,* Rafael Rocha Tourinho-Barbosa,* Aude Fregeville, Anna Colomer Gallardo,

RFB: Robotic Fusion Biopsy (Artemis)

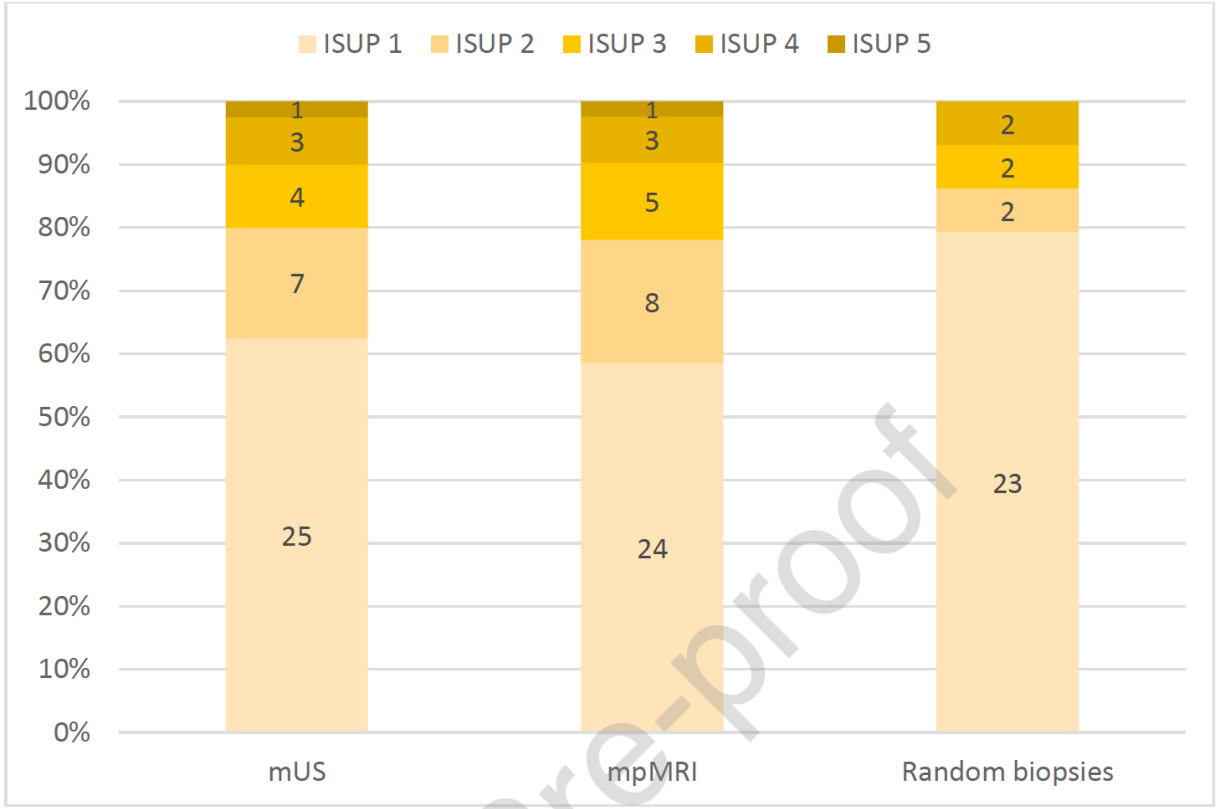
MB: Microultrasound Biopsy



0022-5347/20/2035-0918/0
THE JOURNAL OF UROLOGY®

https://doi.org/10.1097/JU.0000000000000692
Vol. 203, 918-925, May 2020
Printed in U.S.A.

DETECTION RATE OF CLINICALLY SIGNIFICANT PROSTATE CANCER BETWEEN MICROULTRASOUND-GUIDED PROSTATE BIOPSY (EXACTVU™) AND MULTIPARAMETRIC RESONANCE IMAGING-GUIDED PROSTATE BIOPSY (KOELIS SYSTEM™)Running head: Microultrasound-guided prostate biopsy vs multiparametric resonance imaging-guided prostate biopsy , *Urology,* (2023)



doi:https://doi.org/10.1016/j.urology.2023.09.049

Superior Sensitivity and NPV to mpMRI

Klotz et al, *CUAJ 2020*

- **1040 men at 11 institutions** with mpMRI imaging and micro-ultrasound biopsy

Modality	Sensitivity	Specificity	PPV	NPV
mpMRI	**90%** (371/411)	**22%** (136/629)	**43%** (371/864)	**77%** (136/176)
Micro-ultrasound	**94%** (386/411)	**22%** (138/629)	**44%** (386/877)	**85%** (138/163)
p-value (non-inferiority)	< 0.001	< 0.001	< 0.001	< 0.001
p-value (superiority)	0.03	0.45	0.32	0.04

Comparison Between Micro-Ultrasound and Multiparametric MRI Regarding the Correct Identification of Prostate Cancer Lesions

Table 3 Diagnostic Values of the Index Lesion Identification by Micro-Ultrasound and mpMRI With the Reference of Whole Mount Section After Radical Prostatectomy.

	Sensitivity	Specificity	NPV	PPV	Accuracy
Micro-ultrasound	77%	77%	86%	64%	77%
mpMRI	65%	93%	83%	84%	82%
p	0.5	0.2	0.8	0.2	0.7

Clinical Genitourinary Cancer, Vol. 20, No. 4, e339–e345 © 2022

Microultrasound in the detection of the index lesion in prostate cancer

	Sens	Spec	PosPV	NegPV
MicroUS	68.7	96.3	80.8	93.1
MRI	68.6	97.2	86.1	92.5

TABLE 2 Uni- and multivariable logistic regression analysis predicting the probability of missing the IL with the MUS.

	Univariable analysis			Multivariable analysis		
Covariate	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Location of IL						
Posterior	Reference			Reference		
Anterior	4.27	2.34–7.79	**<0.001**	4.87	2.53–9.36	**<0.001**
Anteroposterior	0.40	0.21–0.74	**0.004**	0.53	0.27–1.02	0.06

Prostate. 2023;1-8. doi:10.1002/pros.24628

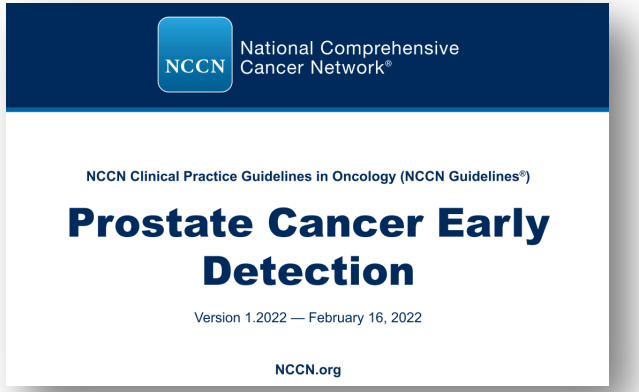
MicroUS and MRI at Wash U

- 161 men with elevated PSA and initial MRI
  - 92 (57%) had PIRADS 3-5 lesion on MRI
- All 161 underwent MicroUS and TP targeted and systematic biopsies
  - 111(69%) had PRIMUS 3-5 lesion
  - 36/69 (52%) with neg MRI had PRIMUS 3-5
  - 75/92 (82%) with PIRADS 3-5 MRI had PRIMUS 3-5
- Clinically Sig. Cancer Detection: 73 (45%)
  - 18/69 (26.0%) with a negative MRI of which 14 had PRIMUS 3-5
  - 7/21 (33.3%) with PRI-MUS 3, 27/63 (42.8%) with PRI-MUS 4, and 24/27 (88.9%) with PRI-MUS 5 lesions

NCCN v1.2022 Guidelines

"It is recommended that MRI should precede biopsy and image-guided biopsy techniques be employed routinely."

*"Recently, the use of **high-resolution micro-ultrasound** has been compared to mpMRI and **found to perform similarly** for the detection of prostate cancer."*

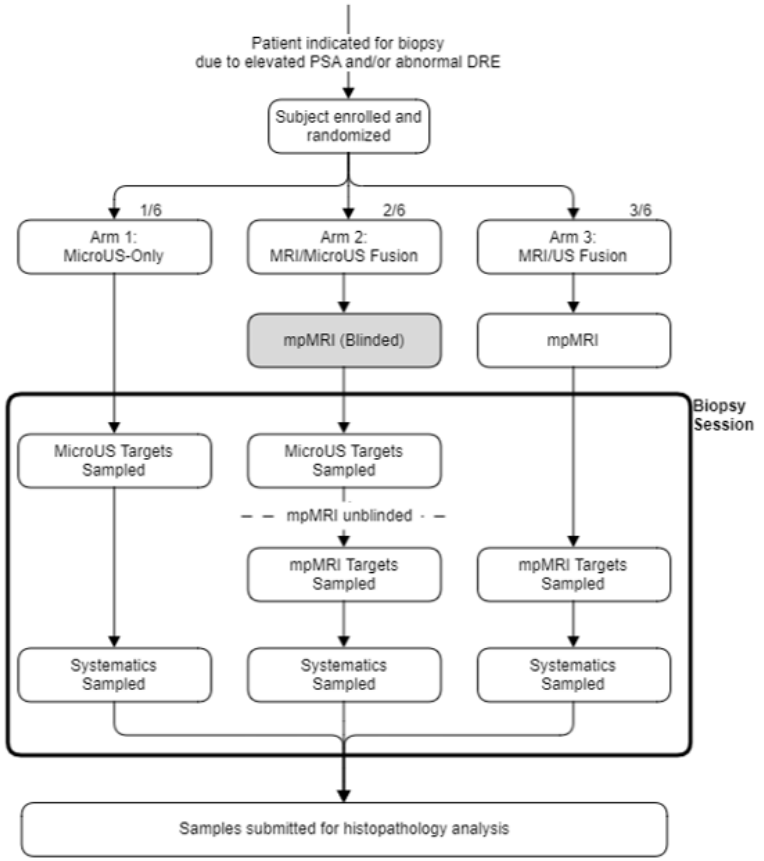


EXACT IMAGING

Optimization of Prostate Biopsy – Micro-Ultrasound vs. MRI (OPTIMUM) Trial

- 3-arm international RCT planned to provide level-1 evidence supporting use of microUS in Prostate Biopsy

- 1200 biopsy naïve subjects randomized to:
  - MicroUS-only biopsy
  - MRI/MicroUS "FusionVu" biopsy
  - MRI/US biopsy with conventional fusion system



Please cite this article as: L. Klotz, G. Andriole, H. Cash, et al., Optimization of prostate biopsy - Micro-Ultrasound versus MRI (OPTIMUM): A 3-arm randomized controlled trial evaluating the role of 29 MHz micro-ultrasound in guiding prostate biopsy in men with clinical suspicion of prostate cancer, *Contemporary Clinical Trials* (2021), https://doi.org/10.1016/j.cct.2021.106618

- Microultrasound may significantly improve prostate biopsy

- Allows real-time targeted biopsy (Both MicroUS and MRI)
  - May improve accuracy of MRI-targeted biopsy
- In comparison to MRI
  - Similar diagnostic accuracy
  - Lower overall cost
  - Reverts the diagnostic pathway entirely back to the urologist
  - Avoids the need for an extra procedure/test
- Early data are highly encouraging
- Await results of Optimum Study