MRI-TRUS Prostate Biopsy: How We Use it in Practice

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NATIONAL® CANCER INSTITUTE

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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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- Research lab @ National Institutes of Health and Philips have a CRADA (Cooperative Research and Development Agreement) which resulted in the development of UroNav (MRI - TRUS prostate fusion biopsy system)

NIH Research Team

- Molecular Imaging
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  - Baris Turkbey, M.D.
  - Marcelino Bernado, PhD
  - Vijay Shah, PhD
  - Tom Pohida, PhD
  - Dagane Daar
- Interventional Radiology
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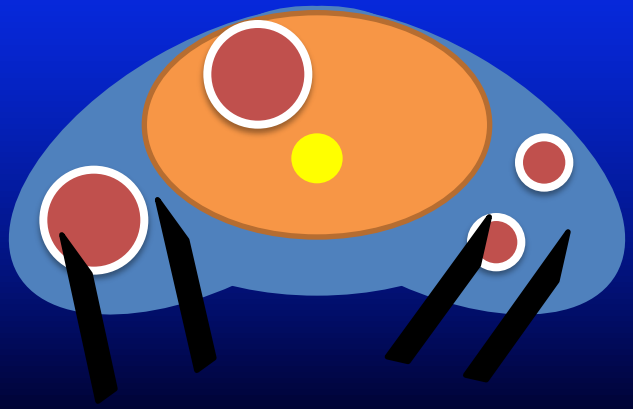
- Biometric Research Branch
  - Richard Simon, D.Sc.
- Pathology
  - Maria Merino, M.D.

“Physicians are frequently presented with the dilemma of a patient who has had one or more negative TRUS prostate biopsies yet continues to have an elevated PSA value or abnormal digital rectal examination of concern for prostate cancer.”

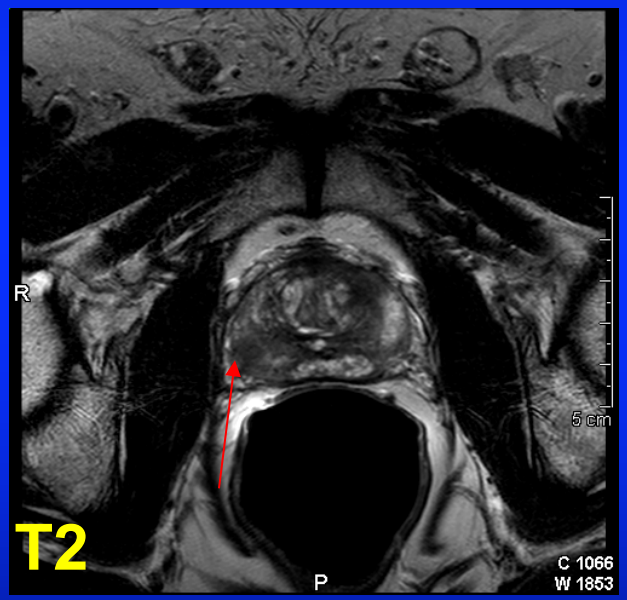
Campbell-Walsh Urology 9th ed. 2007

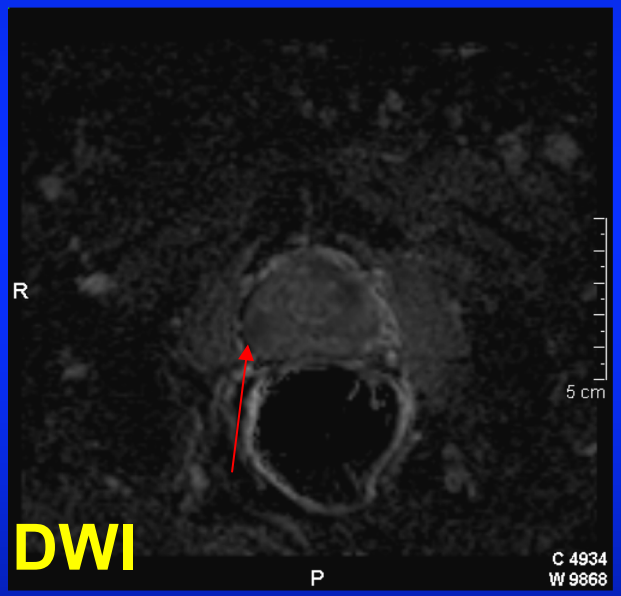
Traditional Method to Detect Prostate Cancer

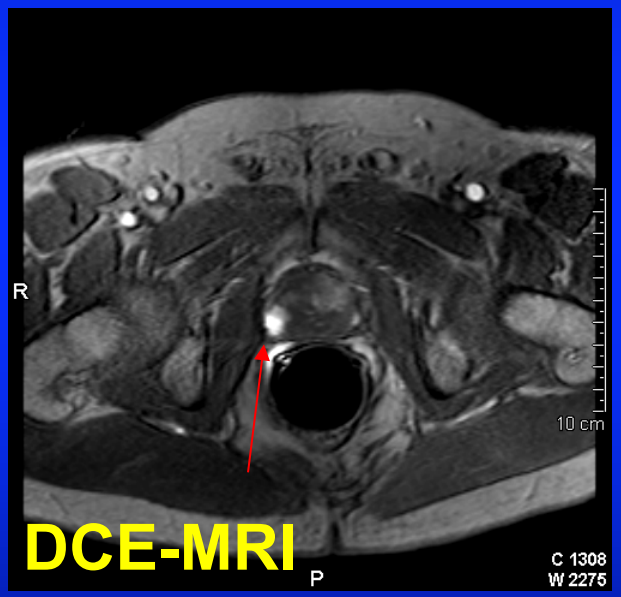
- PSA leads to a systematic 12 core prostate biopsy blind to the tumor(s) location
  - Prostate cancer is the only solid-organ tumor diagnosed without image guidance in the hopes of accidentally “hitting” the tumor
  - Often miss the lethal tumors and detect clinically insignificant cancer



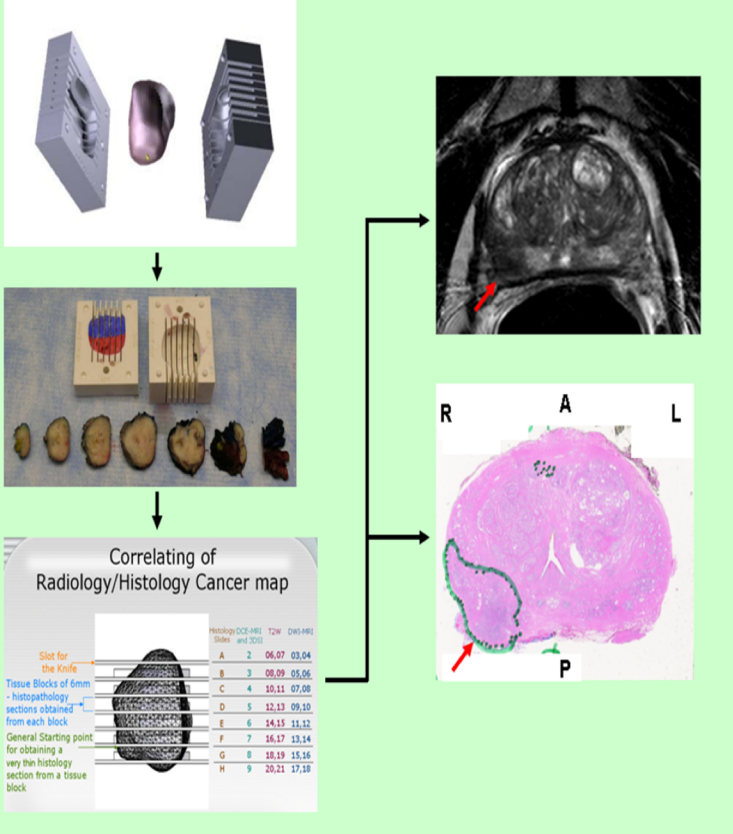
Multi-parametric 3Tesla endorectal MR Imaging of the prostate







Prostate MRI: Correlation with Whole-Mount Histopathological Specimens



- Rev Sci Instrum. 2009 Oct; 80(10):104301
- Radiology. 2010 Apr;255(1):89-99
- J Urol 2011 Nov;186(5): 1818-24
- J Urol.2012 Oct;188(4):1157-63
- BJU Int. 2012 Dec;110 (11 Pt B):E694-700
- Urology. 2012 Jan;79(1):233-9
- J Urol 2011;Oct:185:815-20

MRI - TRUS fusion guided prostate biopsy systems

- *Uronav (In Vivo, Philips)*
- Eigen Artemis
- Koelis
- Esaote
- MedCom Biopsee
- Geo Scan Biojet
- Ultrasonics
- Fusion Healthcare
- Many more being developed

NCI Clinical Experience: Select Papers

- JNCI. 2016; April 108(9)
- JAMA. 2015 Jan 27;313(4):390-7
- J Urol. 2013 Dec;190(6):2020-5
- Eur Urol. 2013 Nov;64(5):713-9
- J Urol. 2012;188(6):2152-7.
- J Urol. 2011;186:1281-5.
- J Urol. 2011;185:815-20.

How to Best Use this for Your Patients

- Screening with MRI and targeted bx
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Original Investigation

Comparison of MR/Ultrasound Fusion–Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer

M. Minhaj Siddiqui, MD; Soroush Rais-Bahrami, MD; Baris Turkbey, MD; Arvin K. George, MD; Jason Rothwax, Nabeel Shakir, BS; Chinonyerem Okoro, BS; Dima Raskolnikov, BS; Howard L. Parnes, MD; W. Marston Linehan, MD; Maria J. Merino, MD; Richard M. Simon, DSc; Peter L. Choyke, MD; Bradford J. Wood, MD; Peter A. Pinto, MD

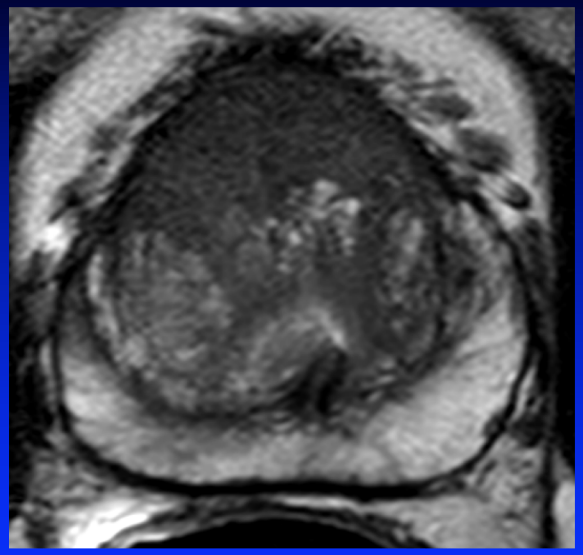
JAMA®
The Journal of the American Medical Association

- Prospective cohort study of 1,003 men undergoing both mpMRI tumor targeted and standard biopsy at the NCI
- Primary Endpoint: Compare each for the detection of high grade PCa (gleason $\geq$ 4+3)
- Secondary Endpoints: Detection of low risk PCa and ability for bx to predict whole gland pathology

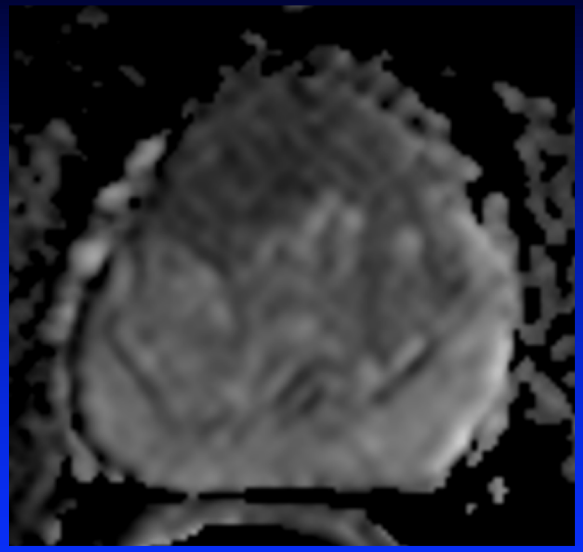
JAMA. 2015 Jan 27;313(4):390-7

	All patients biopsied	No prior biopsy cohort	Prostatectomy cohort
Number of Men	1003	196	170
Age (years, mean)	62.1 ± 7.5	61.2 ± 8.1	60.2 ± 7.3
PSA (ng/ml, median)	6.7 [4.4]	5.3 [3.3]	6.8 [4.4]
Prior negative biopsy	432 (43%)	0	45 (26%)
Cancer Suspicion Score			
Low	176 (18%)	37 (19%)	28 (16%)
Moderate	718 (72%)	129 (66%)	114 (67%)
High	109 (11%)	30 (15%)	28 (16%)
Patients with anterior lesions	446 (44%)	67 (34%)	87 (51%)

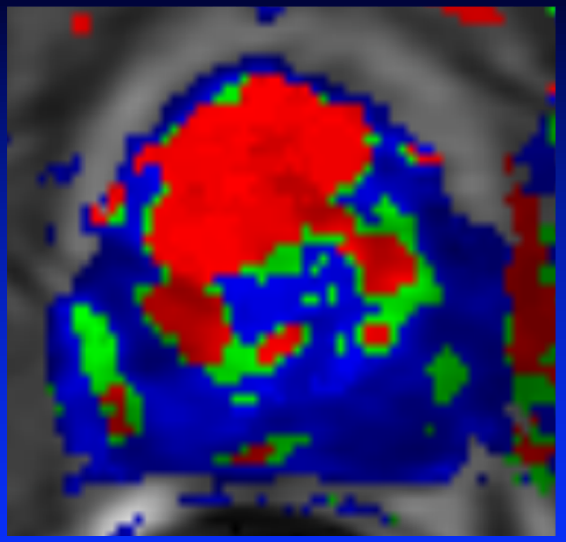
JAMA 313: 2015



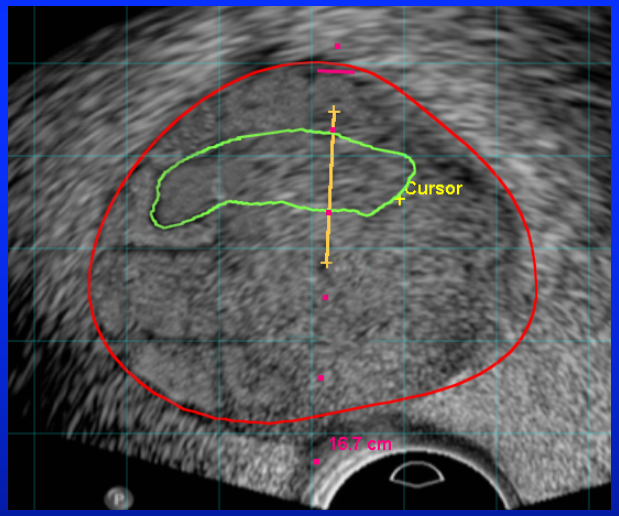
Axial T2W MRI



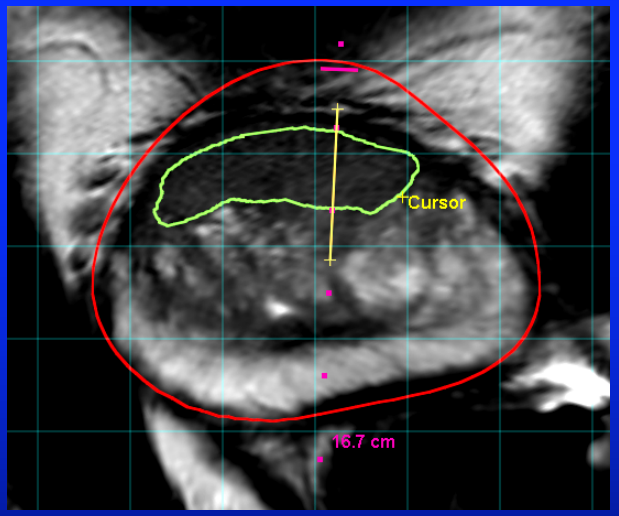
ADC map of DW MRI



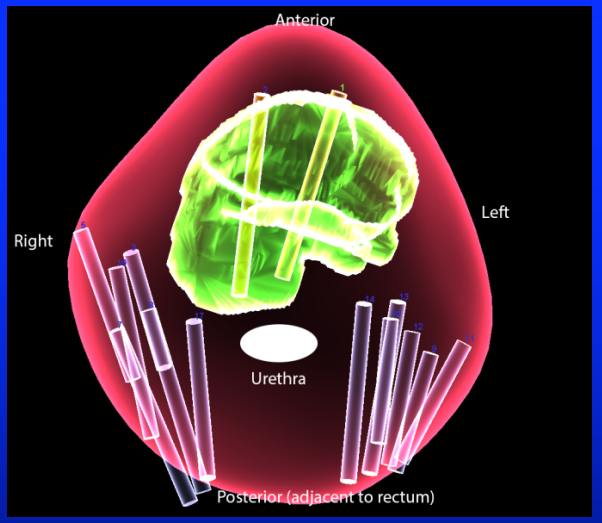
Quantitative DCE MRI map



Real time axial TRUS



Correlated T2W MRI



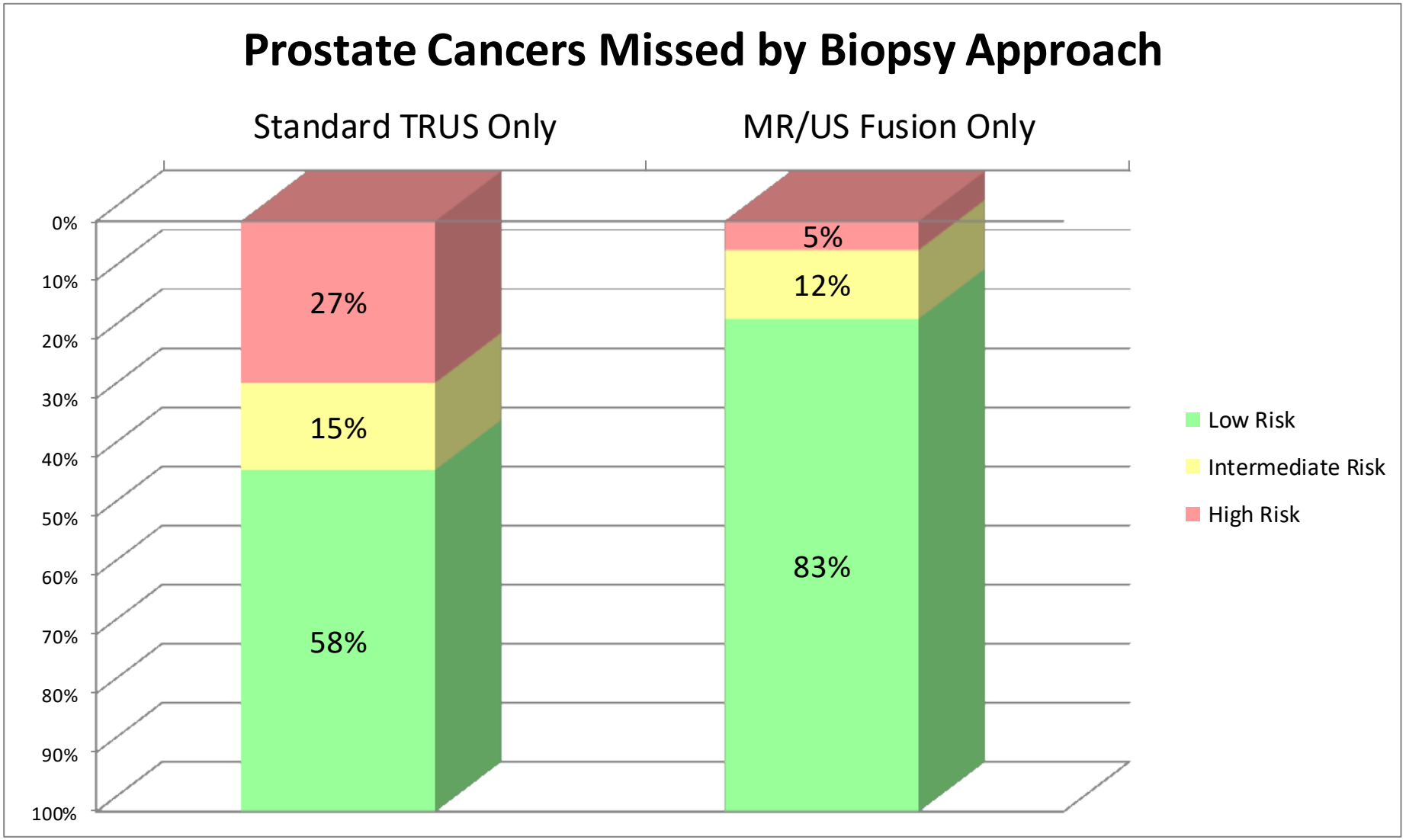
3D reconstruction of prostate with core mapping

JAMA 313: 2015

Pathologic Outcomes: MR-TRUS Fusion vs. Standard Biopsy

			Standard extended-sextant TRUS biopsy				
				Low	Intermediate	High	
			No Cancer	Gleason 6	Gleason 3+4 Low volume	Gleason 3+4 High volume	≥ Gleason 4+3	Totals
Targeted MRI/TRUS Fusion biopsy		No Cancer	439	74	12	12	5	542
	Low	Gleason 6	38	84	12	10	3	147
	Low	Gleason 3+4 Low volume	17	14	9	19	7	66
	Intermediate	Gleason 3+4 High volume	14	21	7	29	4	75
	High	≥ Gleason 4+3	26	13	12	19	103	173
		Totals	534	206	52	89	122	1003

JAMA 313: 2015



JAMA 313: 2015

Conclusion

- MRI - TRUS targeted biopsy diagnosed 30% more high risk cancer (GI score $\geq$ 4+3) than standard TRUS biopsy and 17% fewer low risk cancer
- MRI - TRUS targeted biopsy better predicted whole-gland pathology after prostatectomy than standard TRUS biopsy

JAMA 313: 2015

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0022-5347/12/1886-2152/0
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http://dx.doi.org/10.1016/j.juro.2012.08.025
Vol. 188, 2152-2157, December 2012
Printed in U.S.A.

Multiparametric Magnetic Resonance Imaging and Ultrasound Fusion Biopsy Detect Prostate Cancer in Patients with Prior Negative Transrectal Ultrasound Biopsies

Srinivas Vourganti,*,† Ardeshir Rastinehad,†,‡ Nitin K. Yerram,* Jeffrey Nix,* Dmitry Volkin,* An Hoang,* Baris Turkbey,* Gopal N. Gupta,* Jochen Kruecker,‡ W. Marston Linehan,* Peter L. Choyke,* Bradford J. Wood§ and Peter A. Pinto*,‖

From the Urologic Oncology Branch (SV, AR, NKY, JN, DV, AH, GNG, WML, PAP) and Molecular Imaging Program (BT, PLC), National Cancer Institute, and Center for Interventional Oncology, Department of Radiology and Imaging Sciences (BJW, PAP), National Institutes of Health, Bethesda, Maryland, and Philips Research North America, Briarcliff Manor, New York (JK)

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Table 2. Biopsy results stratified by standard TRUS vs targeted MRI/US fusion platform

	All cancers	Low Grade (GS 6)	Intermediate Grade (GS 7)	High Grade (GS 8+)
Either modality detected	73	28	24	21
MRI targeting detected	56 (76.7%)	16 (57.1%)	19 (79.2%)	21 (100%)
US guided detected	45 (61.6%)	23 (82.1%)	12 (50%)	10 (47.6%)
Both modalities detected	28	11	7	10
MRI targeting upgraded risk	28 (38.4%)	5 (17.9%)	12 (50%)	11 (52.3%)

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0022-5347/12/1886-2152/0
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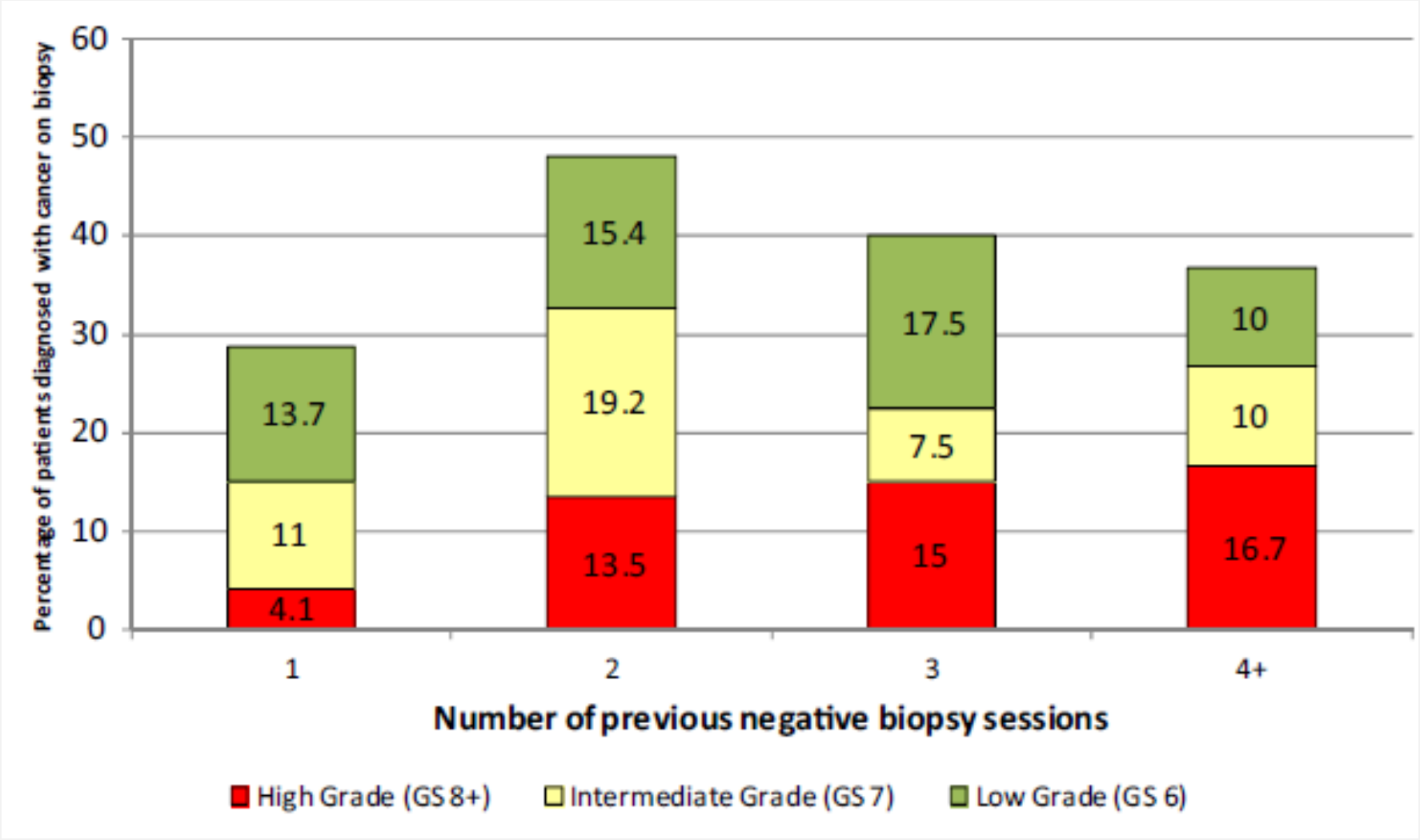
Diagnostic Yield



AUA / SAR Consensus Paper: MRI and Targeted Bx in Patients with Prior Neg Bx

- **When high quality prostate MRI and interpretation is available, it should be strongly considered followed by targeted biopsy for men with prior negative TRUS biopsy and continued suspicion of cancer**

J Urol 196; 1613-18: Dec 2016

AUA / SAR Consensus Paper: MRI and Targeted Bx in Patients with Prior Neg Bx

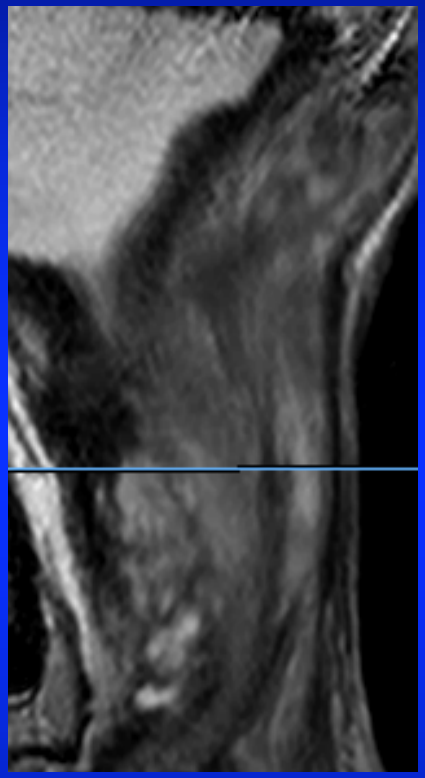
- **Case specific decision should be made whether to also perform a 12 core systemic biospy or just targeted**

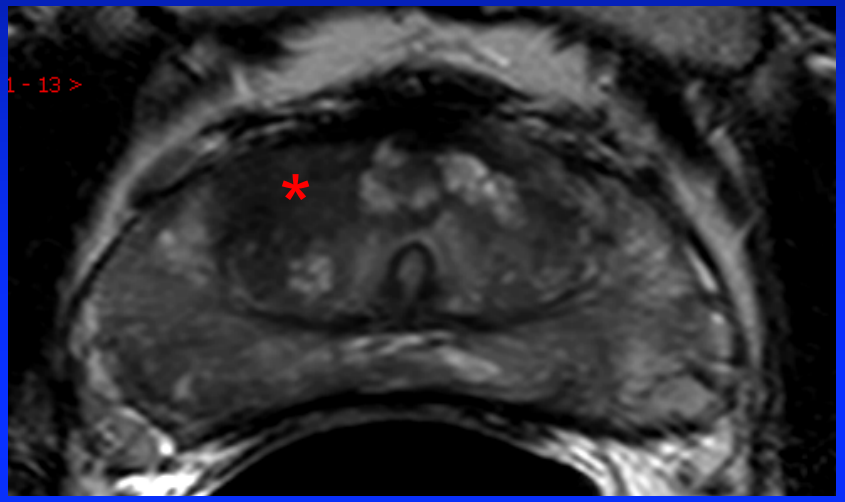
J Urol 196; 1613-18: Dec 2016

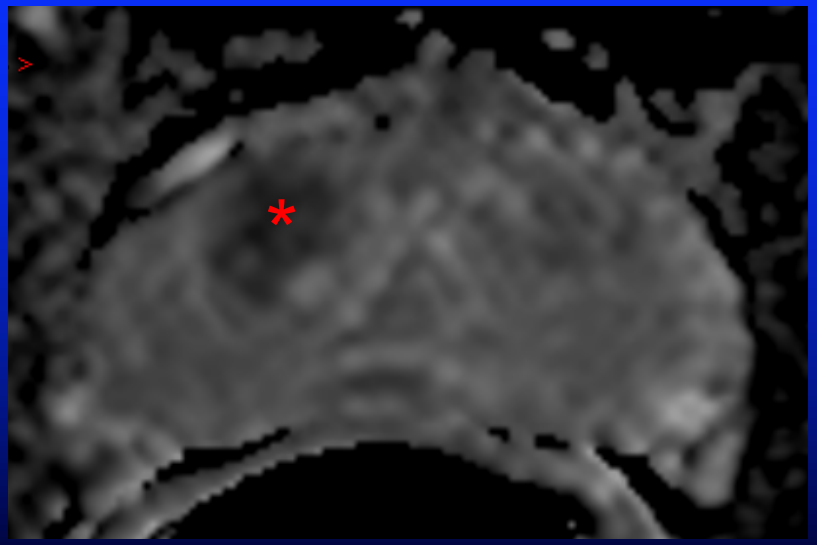
68 year old with elevated PSA

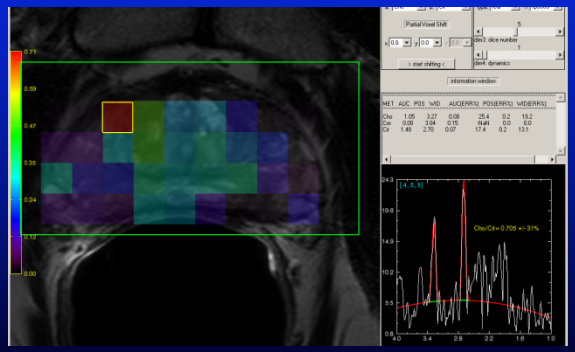
- Extended sextant 12 core TRUS biopsy is negative for cancer
- PSA continues to rise
- Each year for the next 5 years TRUS biopsies are negative
- 7^{th} year a saturation prostate biopsy under anesthesia is negative

Multiparametric Prostate MRI









Right mid anterior central gland lesion

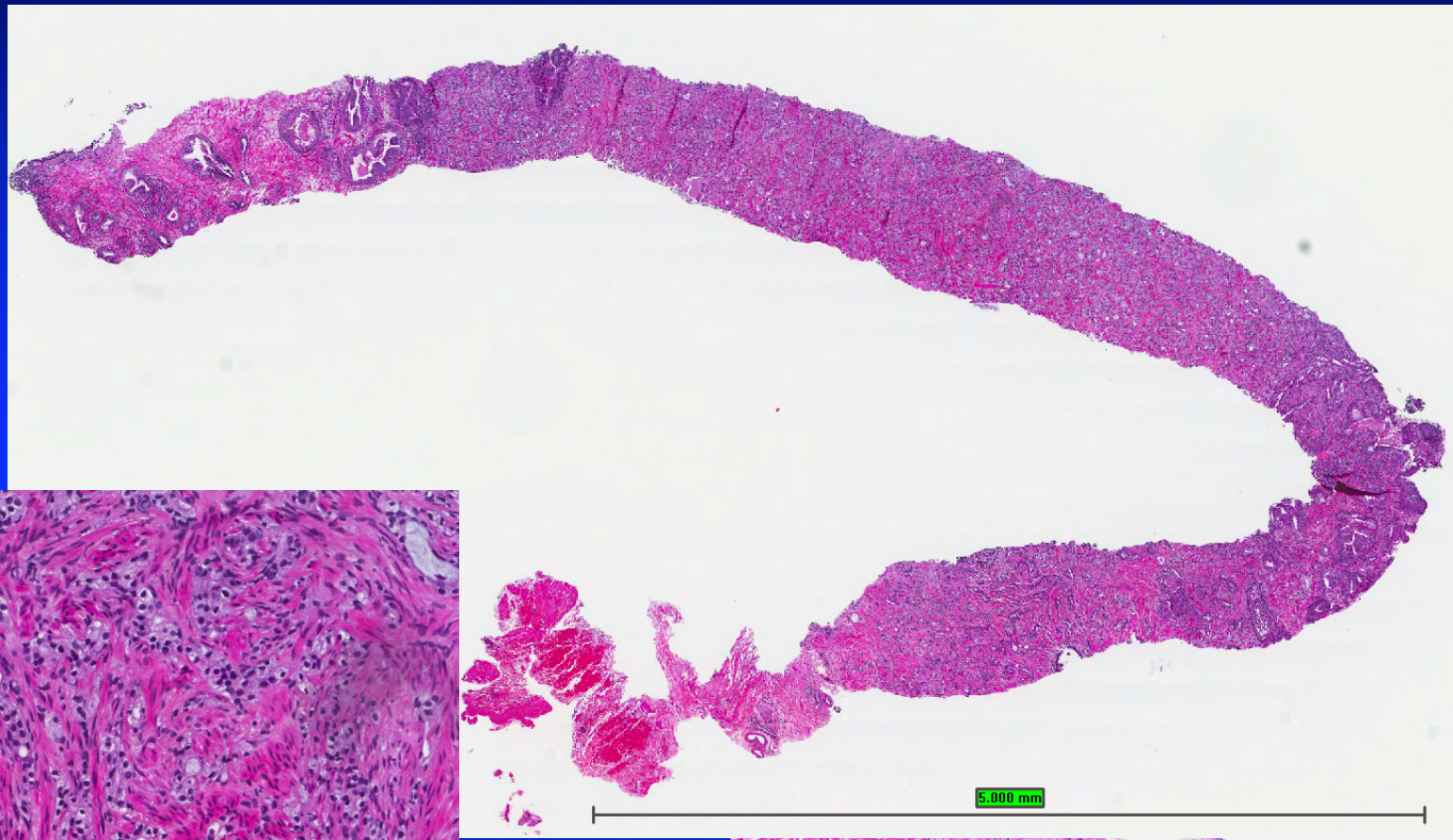
T2 +

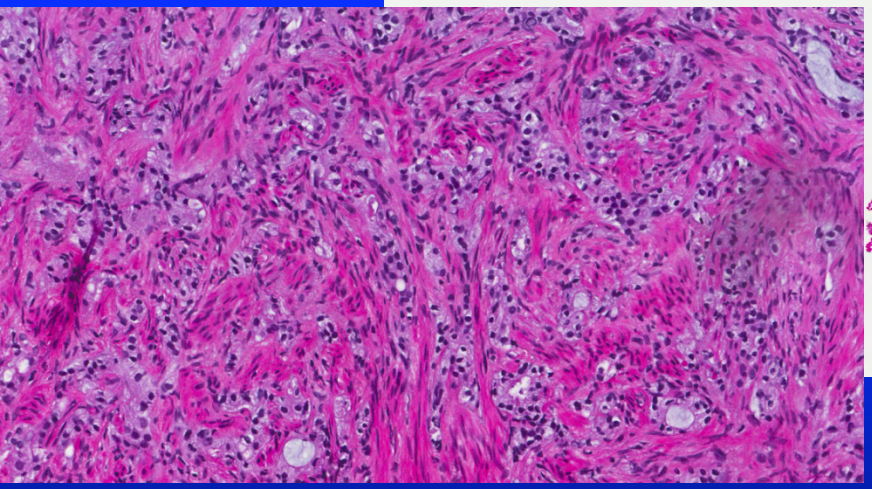
DWI +

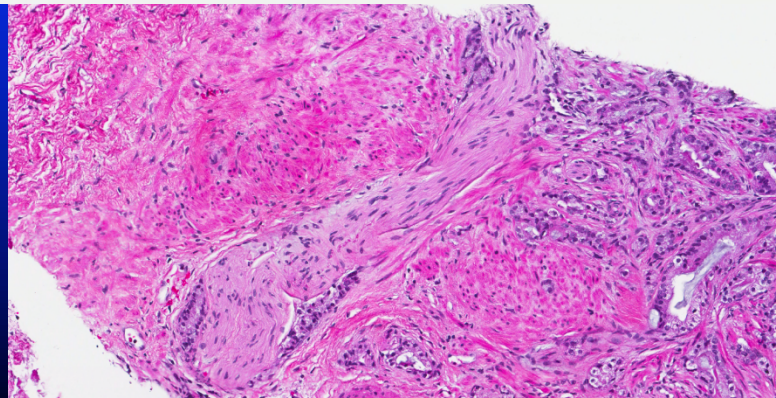
DCE +

MRS +

MRI - TRUS Guided Biopsy







Gleason 4+5=9

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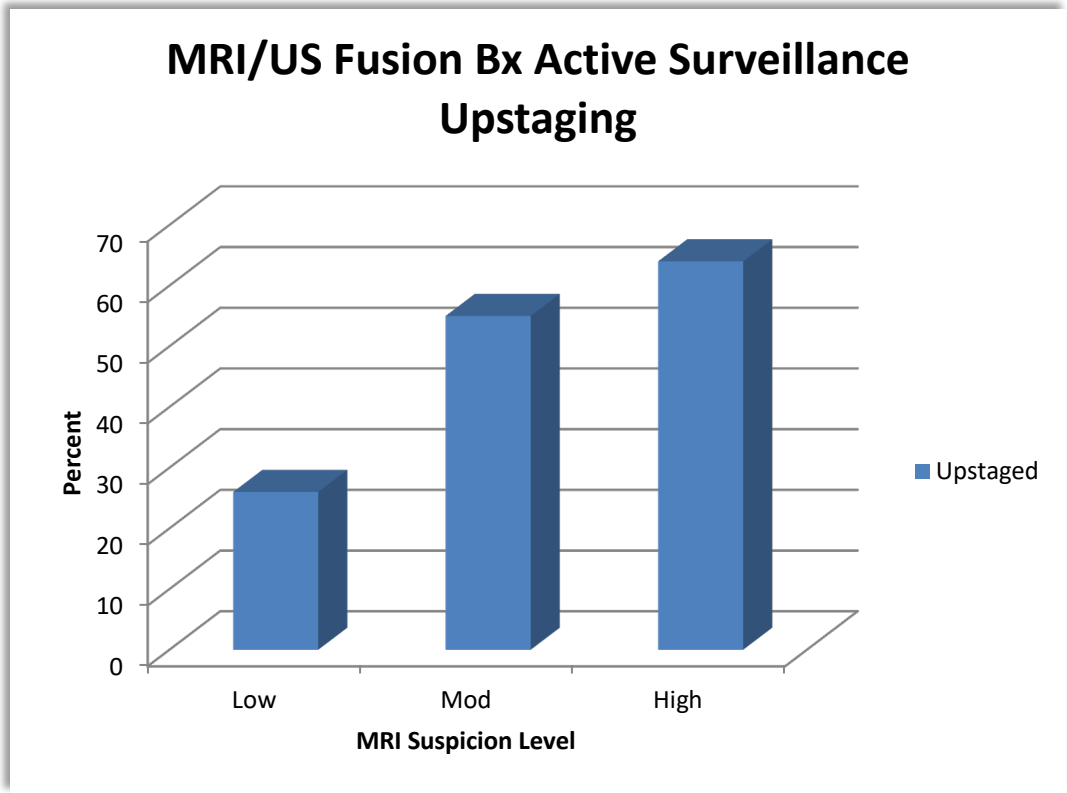
Active Surveillance

- Established treatment option for low grade low volume prostate cancer
- Can MRI help ?
  - Detect higher grade or volume tumors who would be theoretically disadvantaged if put on AS
  - Allow ***patients*** to feel more comfortable with AS
  - Allow ***urologists*** to feel more comfortable with AS

NCI Results

- MRI/US fusion bx was median 8 mo from initial OSH Bx
- 41% of patients re-staged & no longer AS candidates based on grade/volume
- Risk of staging out of AS increases based on MRI suspicion level



BJUI
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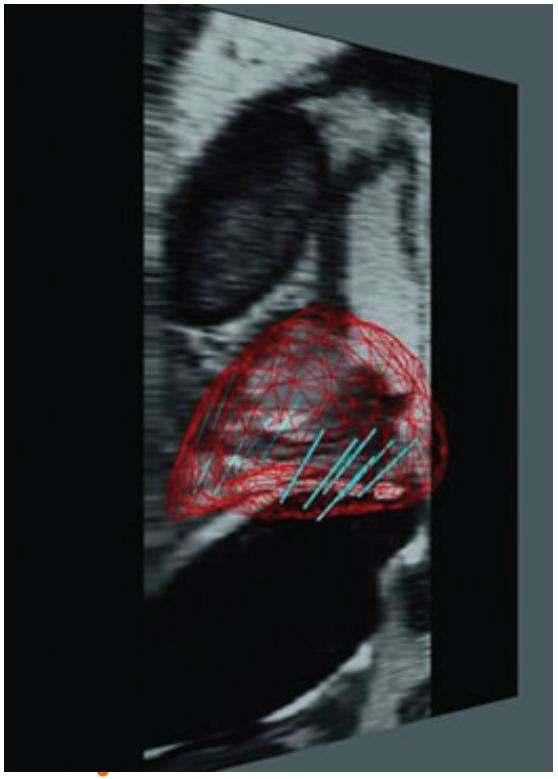
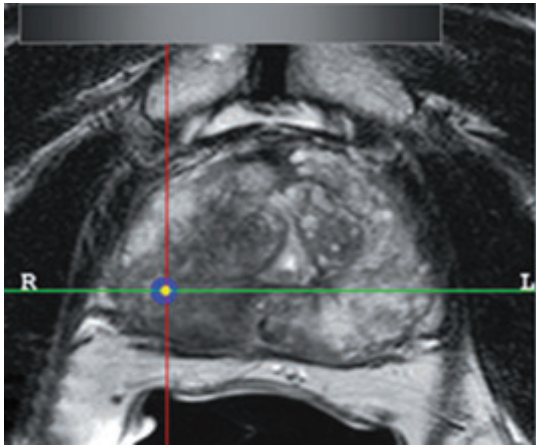
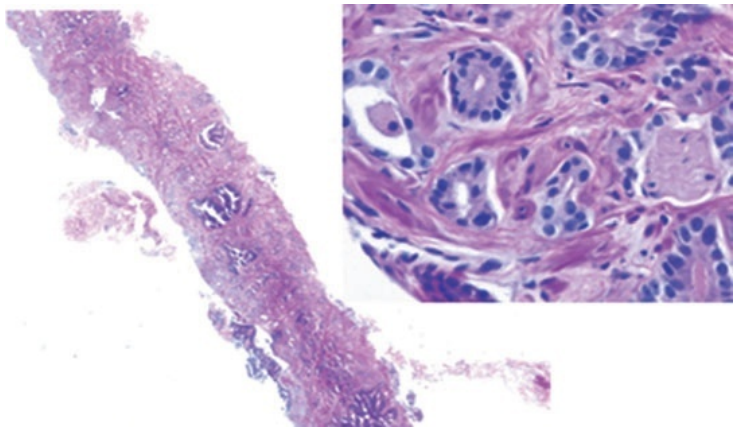
Documenting the location of prostate biopsies with image fusion

Baris Turkbey*, Sheng Xu†, Jochen Kruecker†, Julia Locklin‡, Yuxi Pang§, Marcelino Bernardo*,¶, Maria J. Merino††, Bradford J. Wood‡, Peter L. Choyke* and Peter A. Pinto‡‡

**Molecular Imaging Program, ††Laboratory of Pathology, and ‡‡Urologic Oncology Branch, NCI, NIH, ‡Center for Interventional Oncology, NCI and Radiology and Imaging Sciences, Clinical Center, NIH, Bethesda, MD, †Philips Research North America, Briarcliff Manor, NY, §Philips Healthcare, Cleveland, OH, and ¶SAIC-Frederick, NCI-Frederick, Frederick, MD, USA*







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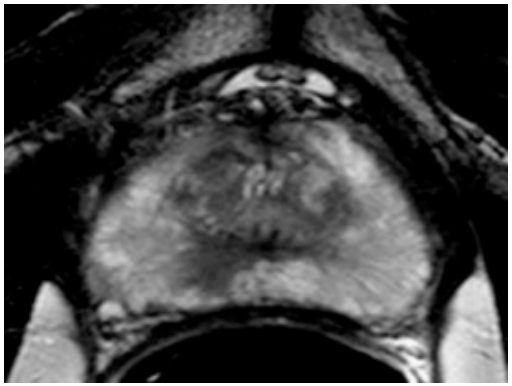
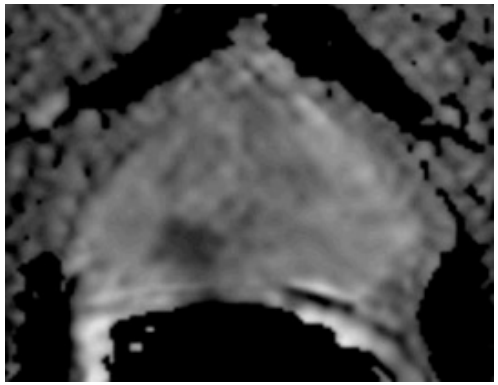
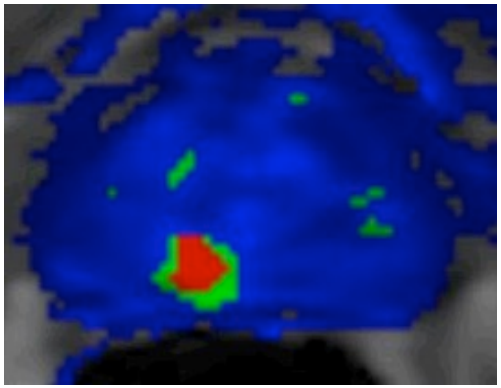
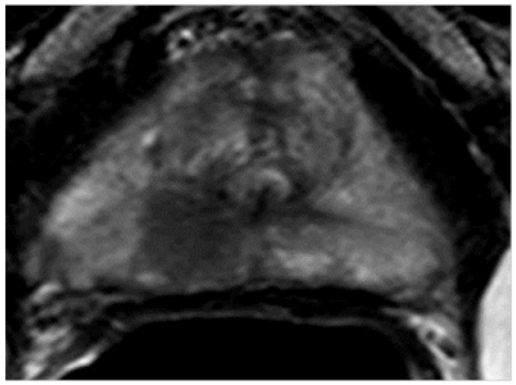
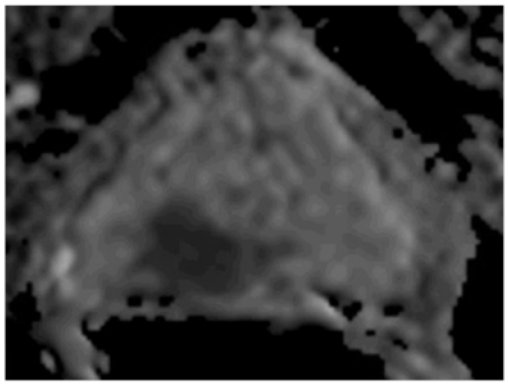
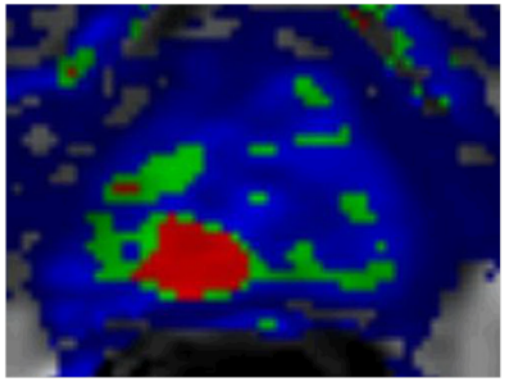
71 y.o. PSA 3.04 Gleason 3+4=7 from 2 MRI-TRUS fusion cores, all systematic biopsies were negative. Enrolled on NIH AS trial.

18 month later PSA 3.28 but the MRI showed progression. Targeted biopsy revealed Gleason 4+4=8. RARP demonstrated Gleason 4+4=8 organ confined with negative margins.

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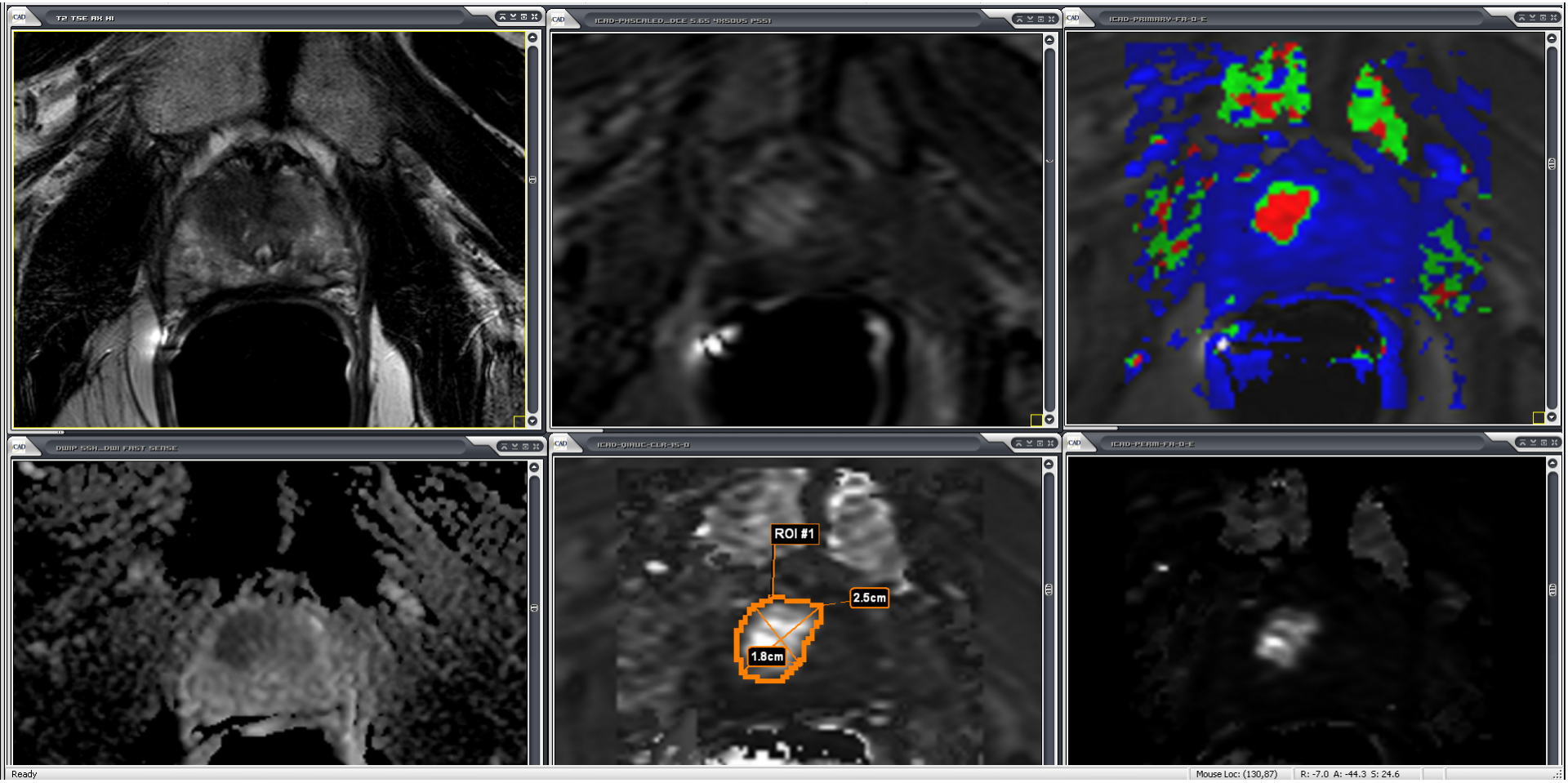
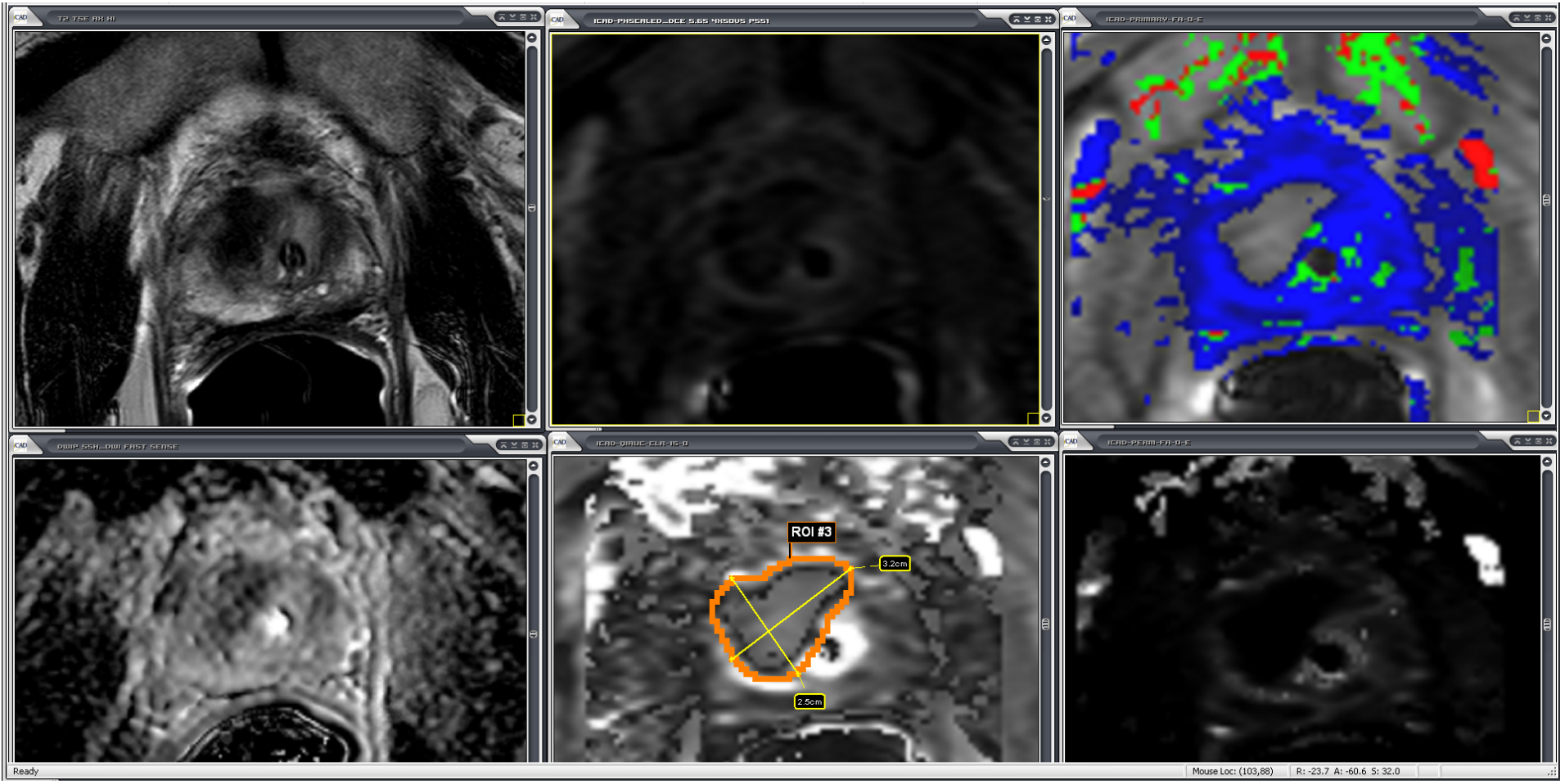
Pre-Treatment



Post-Treatment (Focal Laser Ablation)



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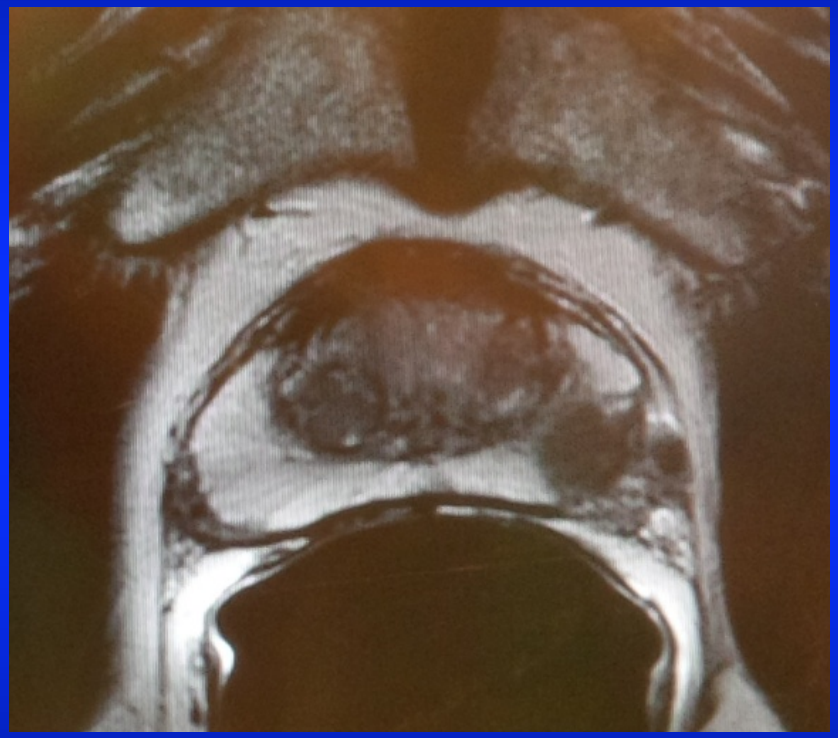
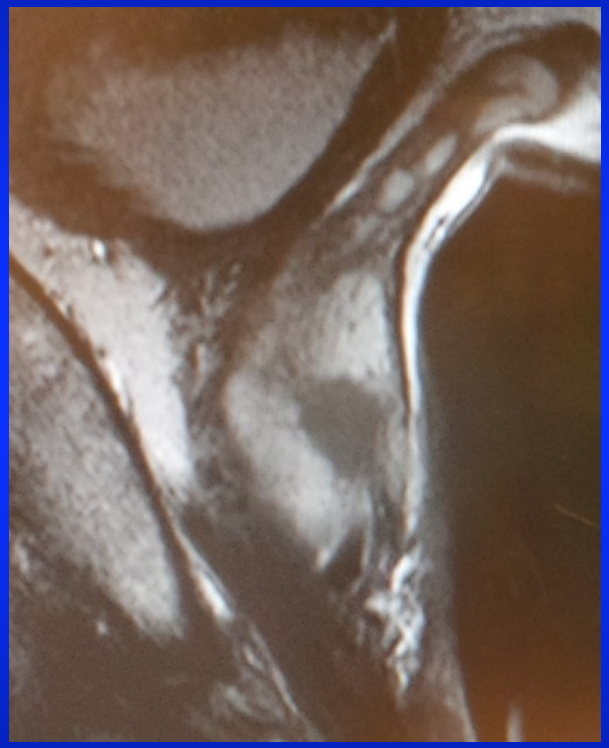
57 year old healthy male

- 57 year old healthy male T1c prostate cancer Gleason 3+3=6 in 5% of 1 out of 12 standard biopsy cores
- Patient considering
  - Active Surveillance
  - Bilateral nerve sparing radical prostatectomy
  - Radioactive seed implantation

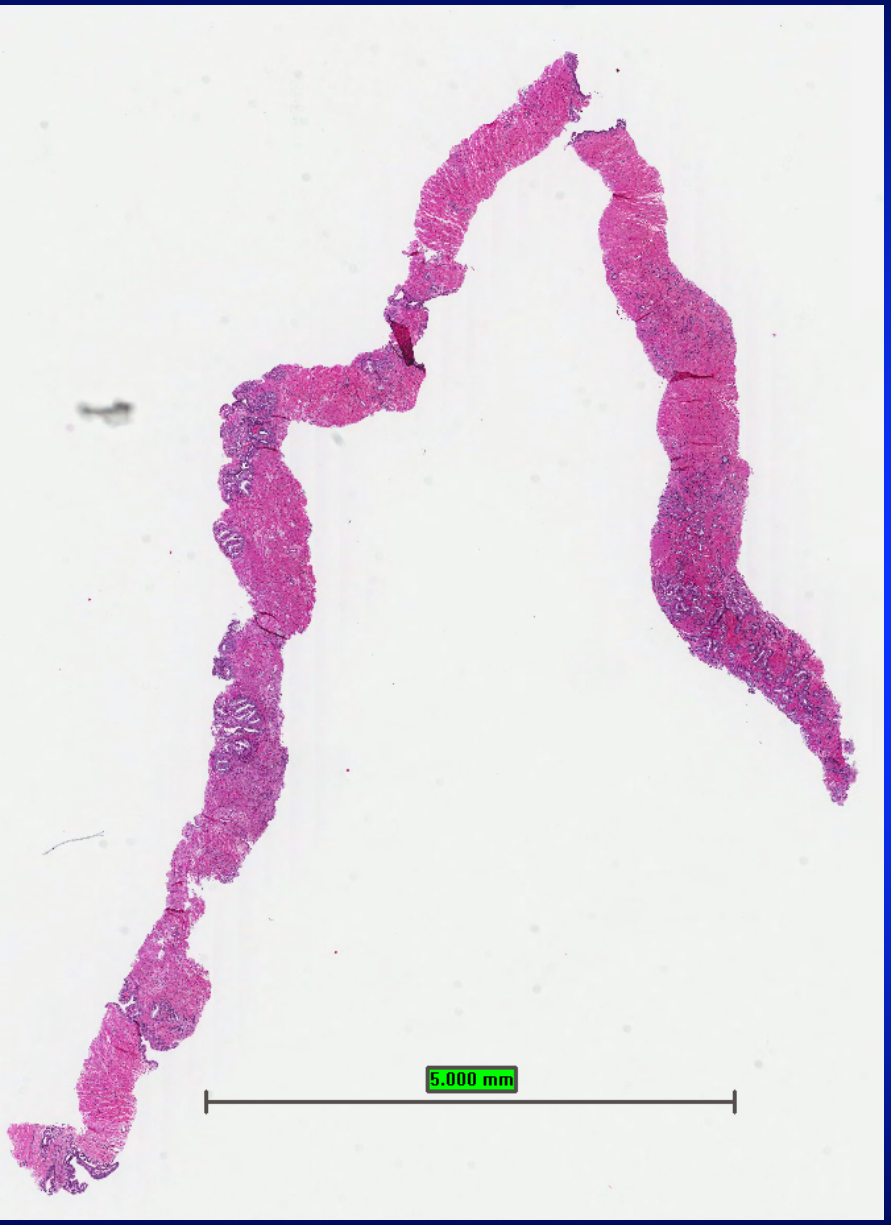
Multiparametric MRI

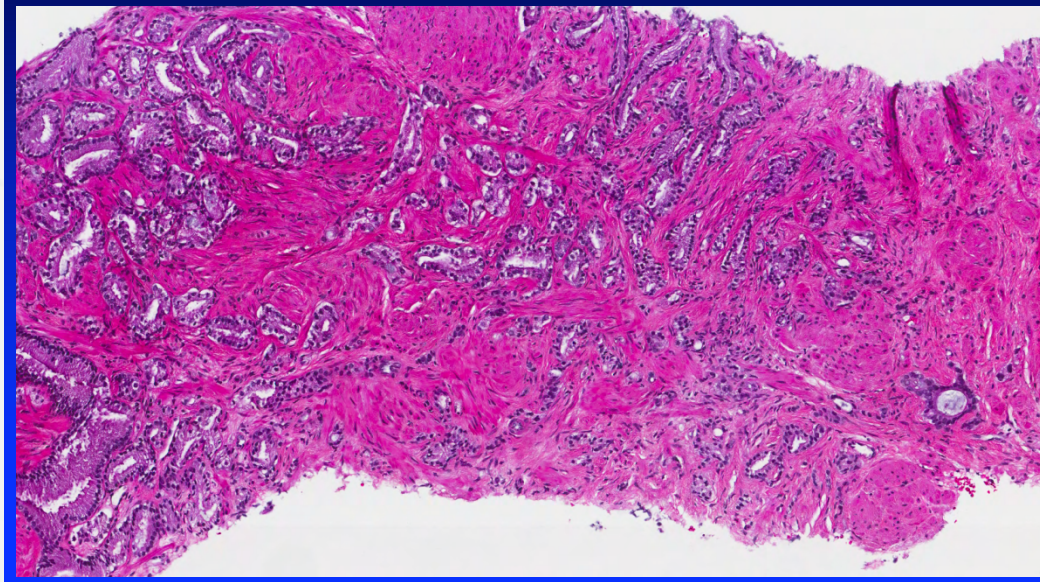


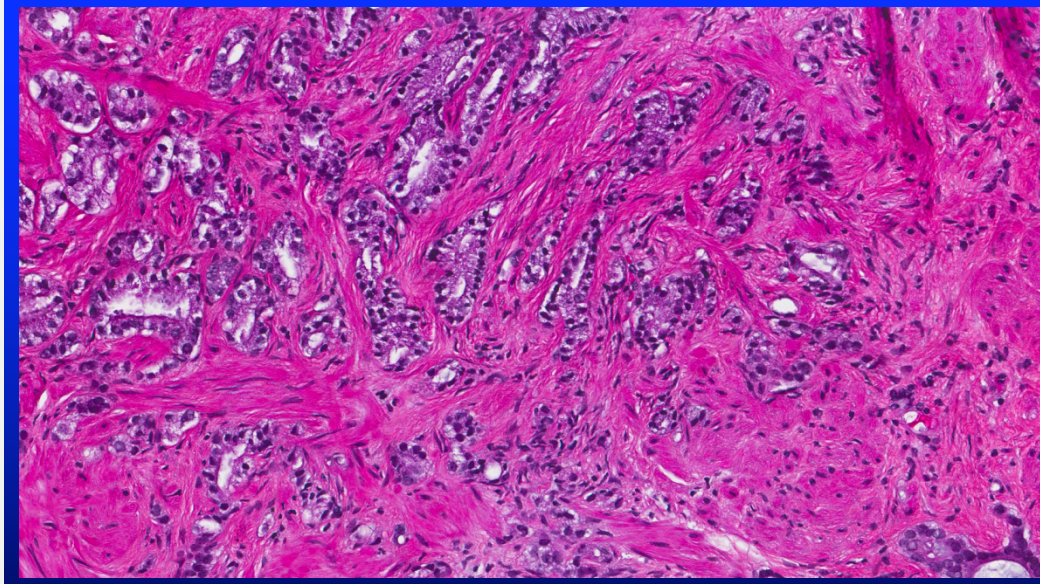


Large left mid lesion suspicious for high grade cancer and extracapsular extension into the left neurovascular bundle

MRI - TRUS Guided Biopsy







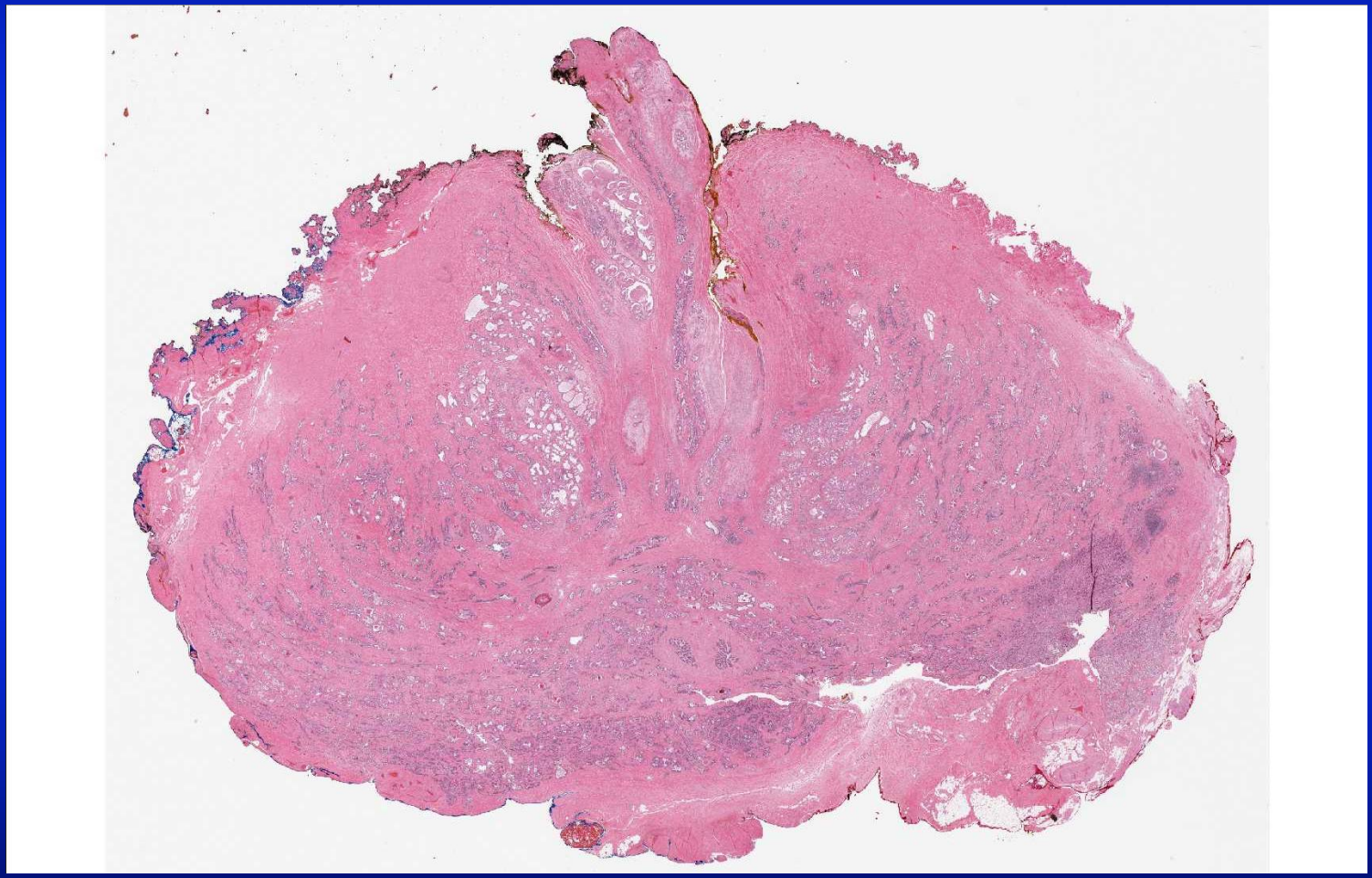
Gleason 4+4=8

57 year old healthy male

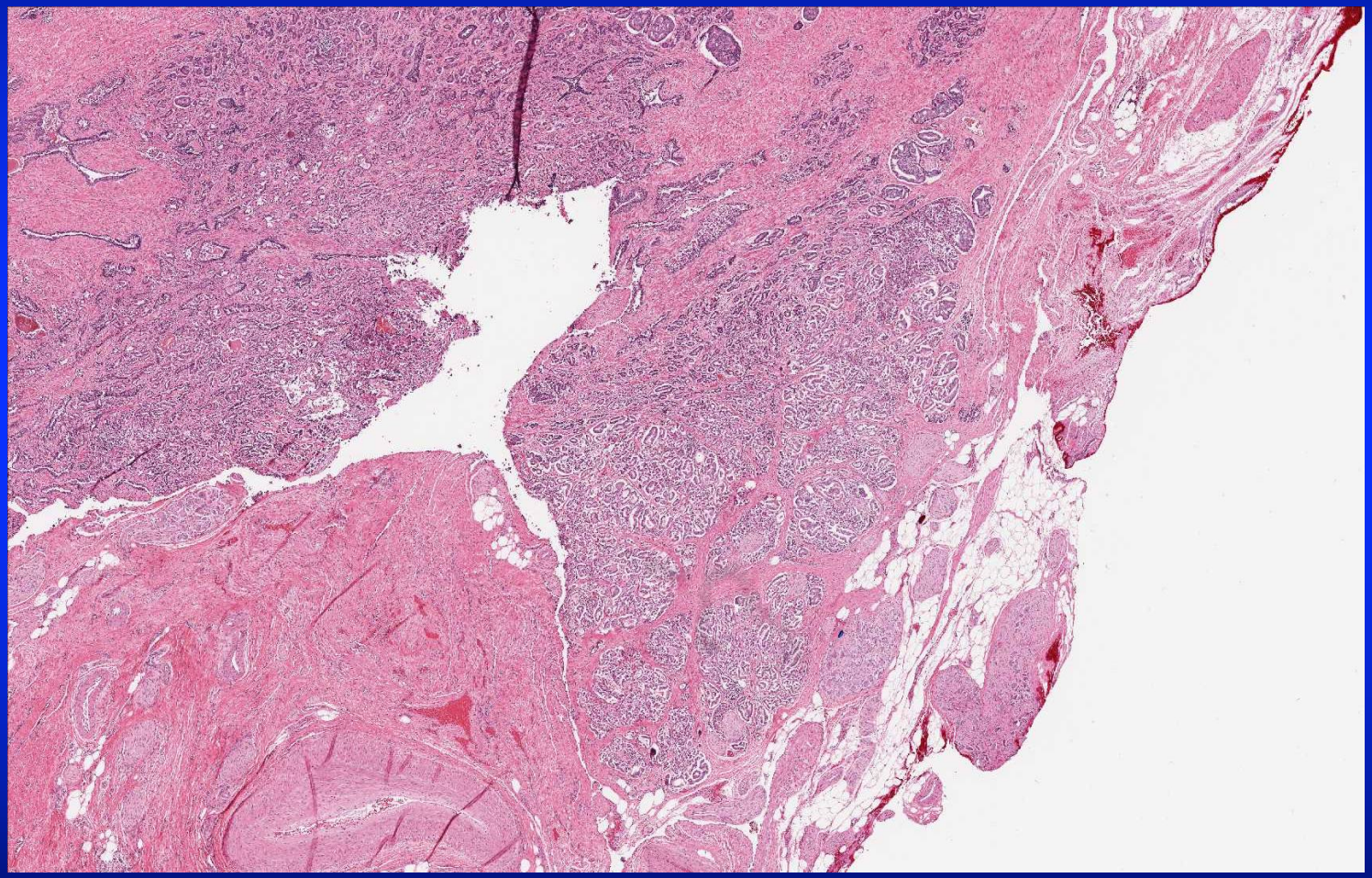
- T1c prostate cancer Gleason 3+3=6 in 5% of 1 out of 12 biopsy cores
- Patient considering
  - Active Surveillance
  - Bilateral nerve sparing radical prostatectomy
  - Radioactive seed implantation

- T3a prostate cancer Gleason 4+4=8 in 60% of the tumor specific biopsy
- Patient considering
  - Unilateral nerve sparing radical prostatectomy with extended LN dissection
  - XRT with 2 to 3 years of medical castration therapy

Focal ECE but Negative Margin



Focal ECE but Negative Margin



Summary

- MRI - TRUS tumor targeted biopsies can increase detection of high risk prostate cancer as compared to standard TRUS biopsy alone and is being quickly incorporated into urologic practice
- The role of mpMRI and targeted biopsy in the diagnosis and treatment of prostate cancer (ie. AS, Focal Tx, …) needs further research and clinical trials

Acknowledgements

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MRI-TRUS Fusion Biopsy Key Concepts in Implementation: Uronav Tips and Tricks

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Director, Fellowship Program

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National Cancer Institute

National Institutes of Health

23rd Annual Mtg
April 12, 2018

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- Research lab @ National Institutes of Health and Philips have a CRADA (Cooperative Research and Development Agreement) which resulted in the development of UroNav (MRI - TRUS prostate fusion biopsy system).

Tips and Tricks

- Build your team (cooperative success)
  - Radiologist
  - Nursing, Tech, Staff
- Prepare ahead of time
  - Review the films in Dynacad to avoid confusion
- Reassure the team, this is a NORMAL biopsy
  - Once established, not different than scheduling standard TRUS

Preparations

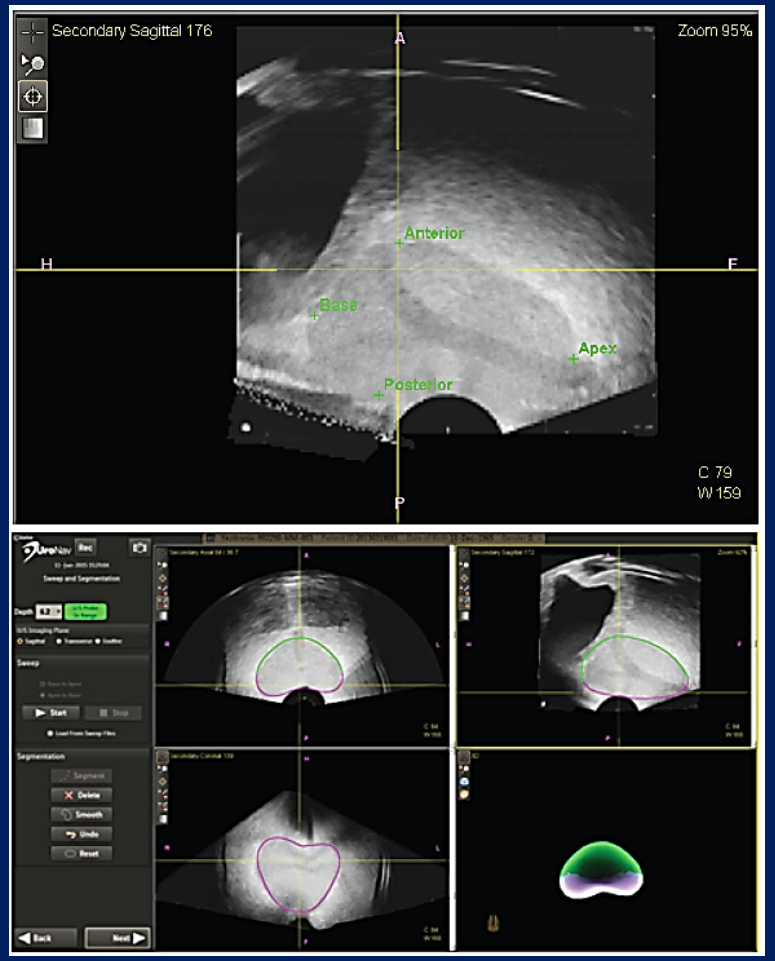
- Nurse/Tech should do a dry run/load targets ahead of time
- Specimen labelling can get complicated !!!!
  - Develop a system (imaging, note, path templates)
  - Include location data on path requisition
    - Ant/post; Base/mid/apex; R/L; CG/PZ
- Awake patients can be easier than MAC
  - can be counselled to be more still, not move

Setup, Sweep, Coregistration

- Anesthetize with local first…
- Sweep requires adjustment of typical pressure
  - Try to minimize difference in shape
  - Generally requires less pressure (esp if no ER coil)
- Make sure it is right, Re-sweep if necessary
- Ensure depth correlates

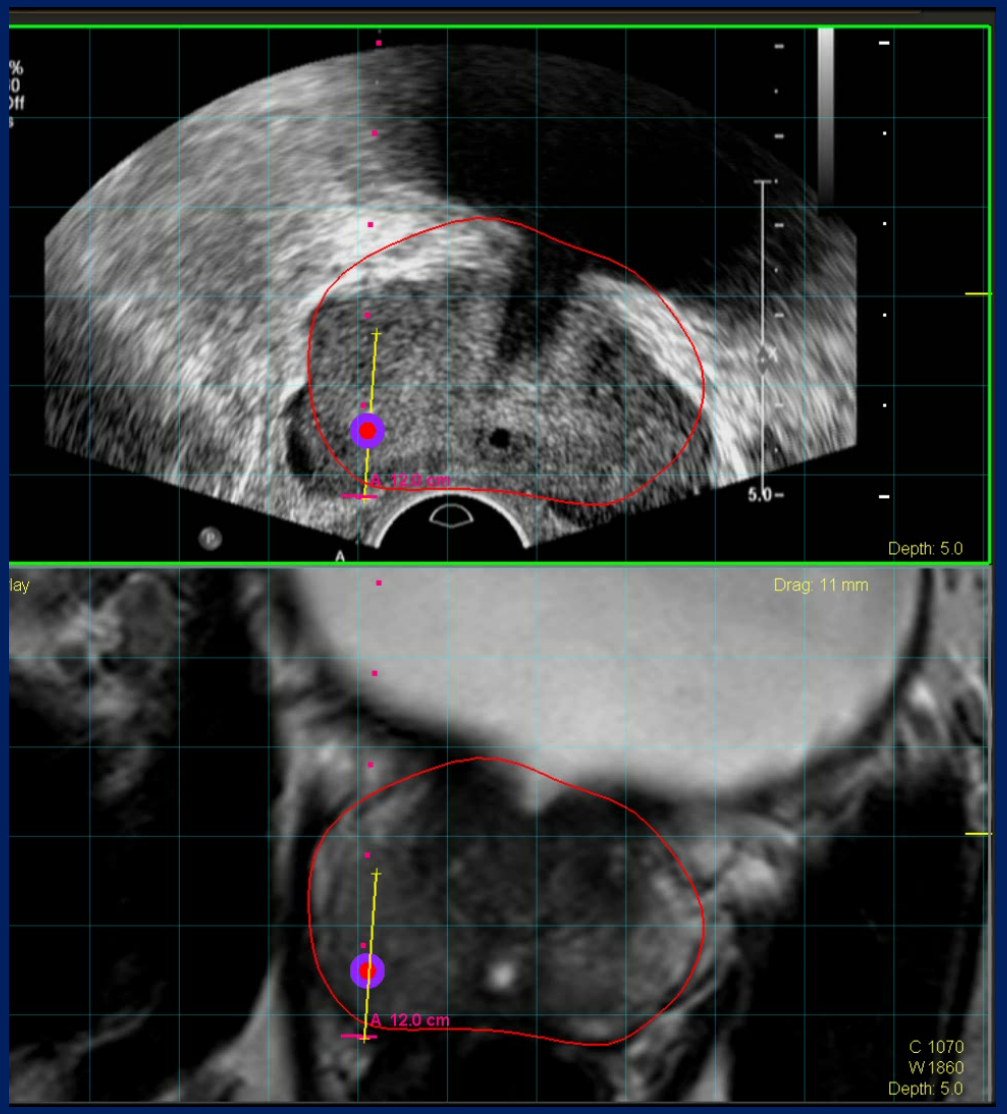
Setup, Sweep, Coregistration

- Calcifications and poor through sono transmission can challenge the auto-segmentation
- Auto segmentation helpful but may need manual adjustments



Setup, Sweep, Coregistration

- Coregistration step is critical
- Use all three planes
- If present, cysts and other features (median lobe, asymmetry) can be helpful
- This is the foundation, needs to be audited throughout the case

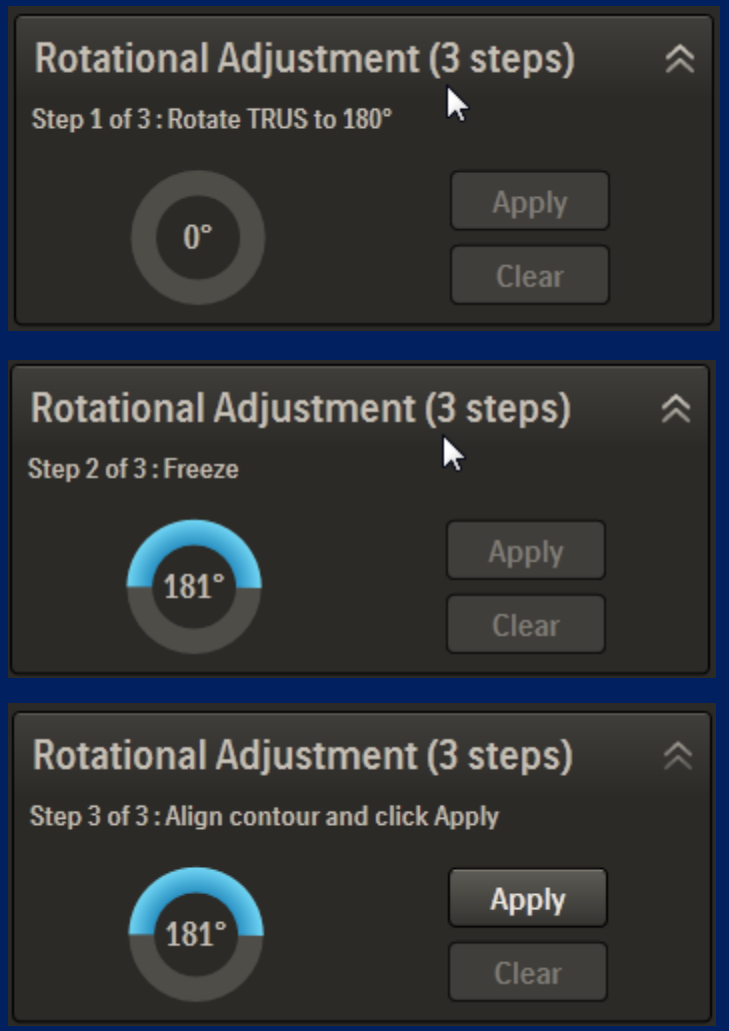


Setup, Sweep, Coregistration

- Rigid vs Elastic Registration, understand the differences
- Accurate initial co-registration is essential
- If utilized, toggle elastics on/off to ensure it is not leading you astray

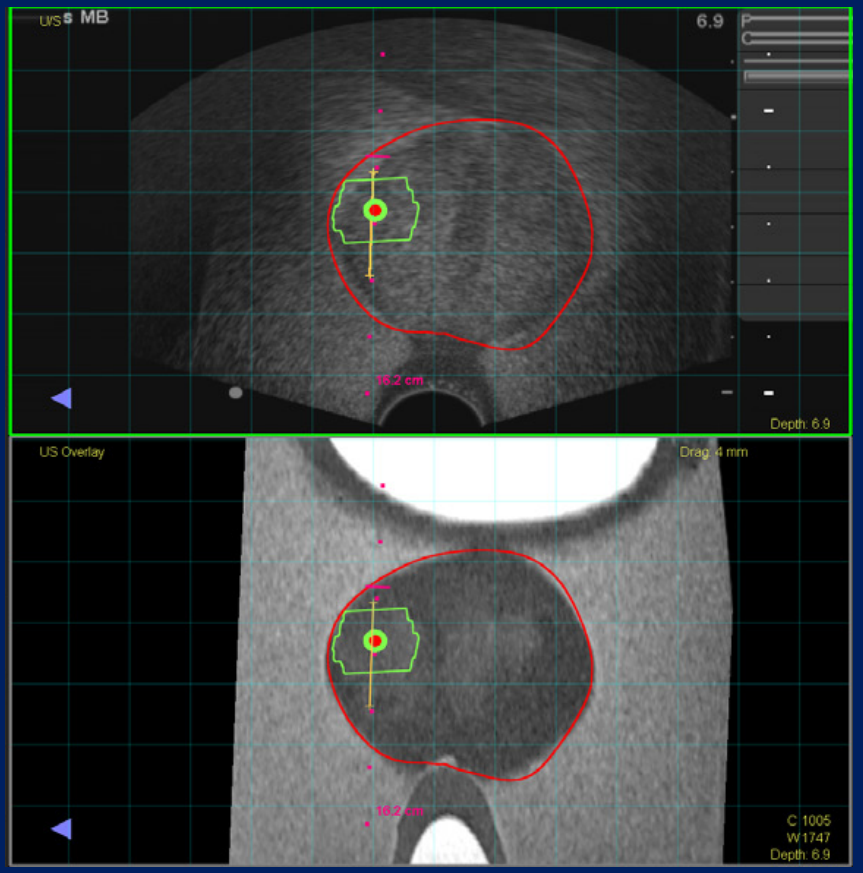
Procedure – Rotational adjustment

- Endfire probes
- R <-> L 180^{o} flip can result in a shift in registration requiring a drag
- Should be small (0-3 mm)
- If large shift, check sensor alignment; get new clips
- Manual sometimes easier
- Do all targets on one side at once, then switch for efficiency

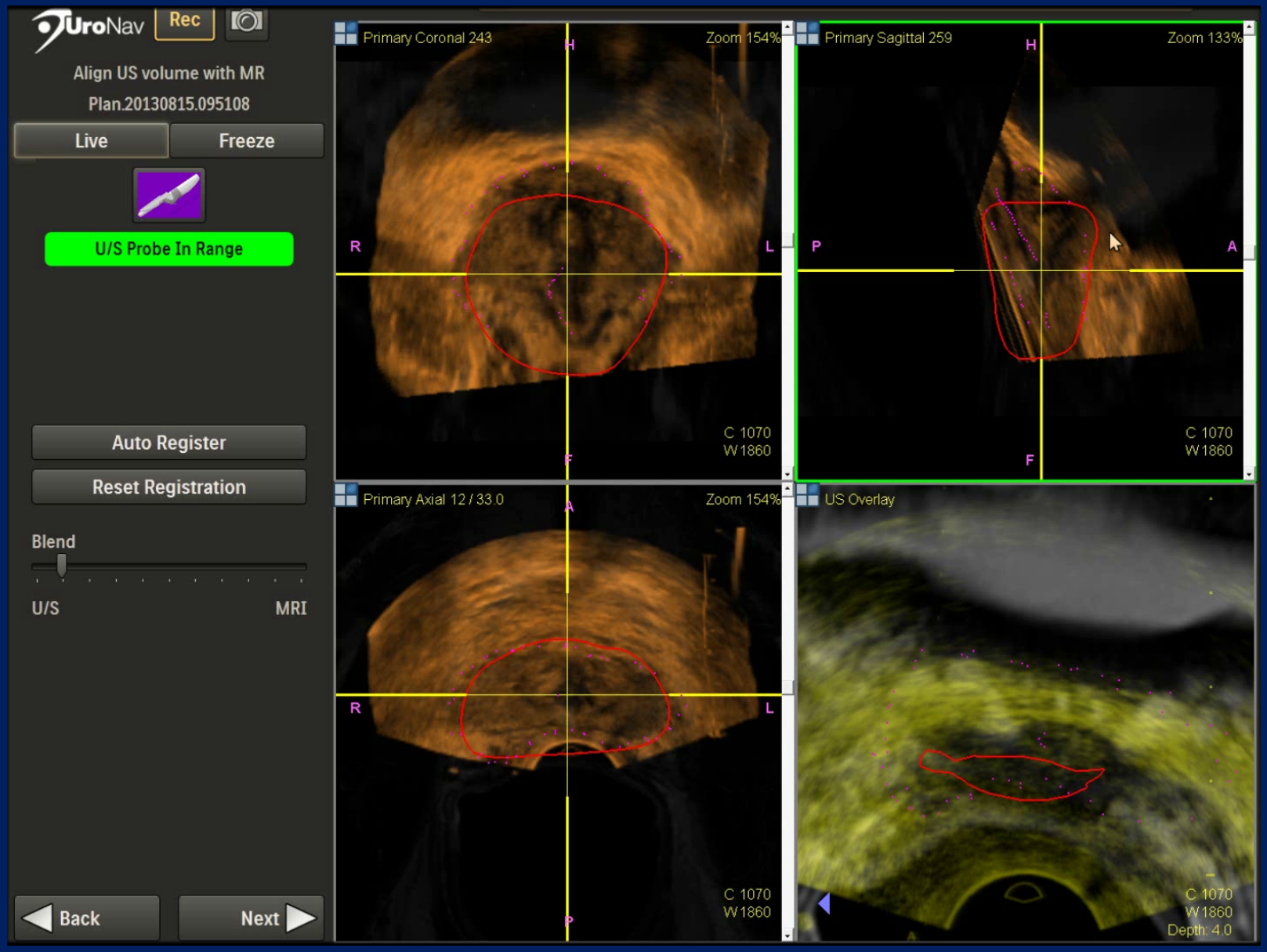


Procedure Tips

- Do not overly rely on the red boundary line
  - E.g. median lobe
- Utilize the entire grid
- Use dynamic imaging
- If it is not right, adjust

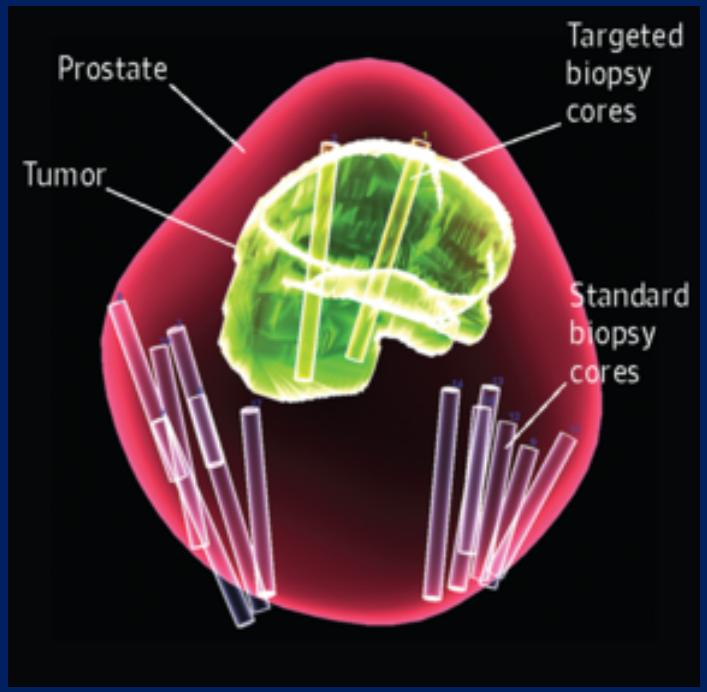


Rigid or Elastic Registration?



Procedure Tips – Anterior lesions

- Floating the needle within the prostate for anterior lesions
- Well tolerated
- May require adjustment of approach to avoid urethra (R vs L, Axial vs Sagittal)



JAMA. 2015 Jan 27;313(4):390-7

Procedure – number of cores/target

- Consider multiple cores (ie axial and sagittal)
- Helps to overcome spatial accuracy, coregistration errors
- Important in small lesions or targets only
- As second core can avoid missed lesions[1]
  - ~8% discordance (missed or upgraded on one)
  - Even with systematics, 1 core would miss ~5%
  - Most important in intermediate risk

1 - Hong, Pinto et al. BJUi 2015

MRI - TRUS Prostate Biopsy Procedure Time

- 3D US acquisition using 2D sweep (10 – 24 secs)
- Reconstruction of reference 3D US (~15 seconds)
- Manual pre-op. MRI/US registration (1 – 2 mins)
- Specimen acquisition (~ 11 minutes)
  - Motion compensation, US/RTUS reg. (~15 seconds)

15 minutes

Efficiency of Prostate Cancer Diagnosis by MR/ Ultrasound Fusion-Guided Biopsy vs Standard Extended-Sextant Biopsy for MR-Visible Lesions

M. Minhaj Siddiqui, Arvin K. George, Rachel Rubin, Soroush Rais-Bahrami, Howard L. Parnes, Maria J. Merino, Richard M. Simon, Baris Turkbey, Peter L. Choyke, Bradford J. Wood, Peter A. Pinto

J Natl Cancer Inst. April 29, 2016

- Study Aim
  - 17,619 prostate bx cores examined to compare efficiency of MRI-TRUS targeted vs standard extended sextant biopsy for the detection of overall and high grade (Gleason > 3+4) PCa

Results

- Mean of 12.3 standard TRUS bx cores and 5.3 MRI-TRUS targeted bx cores taken per patient

Results

- Mean of 12.3 standard TRUS bx cores and 5.3 MRI-TRUS targeted bx cores taken per patient
- % of cores positive to dx Pca irrespective of grade was statistically significantly higher for targeted (27.9%) than standard (13.5%) with 11.5 targeted cores vs 26.2 standard cores

Results

- To detect high grade PCa 30.7 targeted vs 100.8 standard cores were needed

Results

- To detect high grade PCa 30.7 targeted vs 100.8 standard cores were needed
- In all cases MRI-TRUS targeted biopsy was a more efficient biopsy method resulting in fewer negative cores compared with strandard extended sextant 12 core biopsy

Results

- ?? End of systematic TRUS biopsies ??

Data collection/Audit/Quality Improvement

- Be sure to check your work
- There is a learning curve
  - Including Urologist and Radiologist
- Review data with radiology to assist with overcalling
  - Missed lesions and negative lesions
- This will allow improvement of specificity over time

Outside Hospital MRIs

- Fusion biopsy resulting in referral practice
- mpMRI is becoming more disseminated
- Workflow can be challenging
- Ensure that images are diagnostic, quality of the outside read is highly variable
- Getting radiologists on board requires team approach (esp as no billing, for a reasonable amount of work)
- Alternative is segmentation by the urologist

Summary

- At centers with experienced diagnostic radiologists, multiparametric MR prostate imaging is the platform for image guided biopsies
- Image fusion between MRI and TRUS is the BEST of both worlds
  - *Diagnostic Radiologist interpret prostate MRI*
  - *Urologist perform tumor directed prostate biopsy*
- Continued research is necessary to determine how we should incorporate this technology into the care of our patients for diagnosis and treatment (active surveillance, surgery / radiation, focal therapy)

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