# Image Guided Biopsy of Prostate Cancer: Implications for Diagnosis and Therapy

**Peter A. Pinto**

Urologic Oncology Branch
Center for Cancer Research
National Cancer Institute
National Institutes of Health

National Cancer Advisory Board
December 7, 2010

# Clinical Questions for Research

- Why is prostate cancer the only solid tumor that is diagnosed by randomly sampling the organ in the hopes of hitting the tumor ?
- If organ sparing treatment has been developed for other cancers (breast, kidney, bladder, etc.) why not prostate ?

# Clinical Questions for Research

- Both of these questions were linked to the lack of reliable imaging for localizing tumors within the prostate and beyond it

- Can MRI, PET, and other imaging modalities change this ?

# Diagnosis

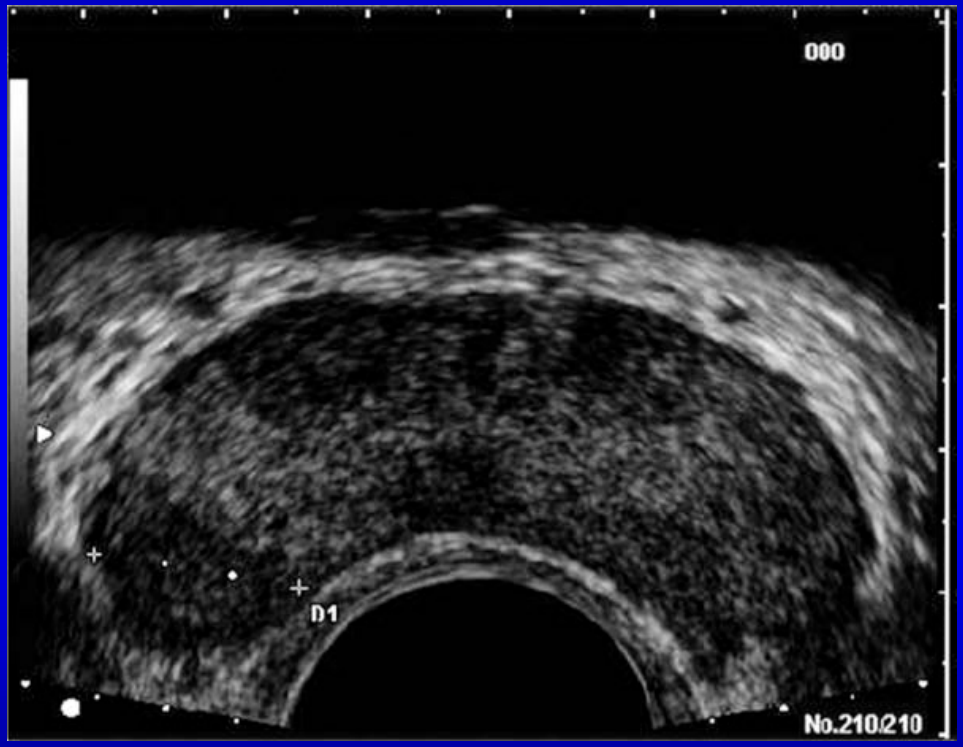
- Digital Rectal Exam (DRE)
- Blood Test – Prostate Specific Antigen (PSA)
- 12 core Prostate Biopsy

# Prostate biopsy

- 1st described by Fergusson (1930): transperineally
- Astraldi (1937) described transrectal
- Use of TRUS first in 1955 (Wild & Reid), popularized by Watanabe et. Al. in 1970s
- Hodge proposed “sextant” biopsy model in 1989
- Estimated over a million biopsies annually in U.S.
- Despite technical advances, biopsies are still NOT based on imaging

# Trans Rectal Ultrasound (TRUS)

- How is it clinically used today?
- Most urologists use TRUS to ensure the needle samples the prostate, few use TRUS to look for areas suspicious for cancer




Wein et. al. Campbell-Walsh Urology. 9th ed. 2007:Philadephia, PA

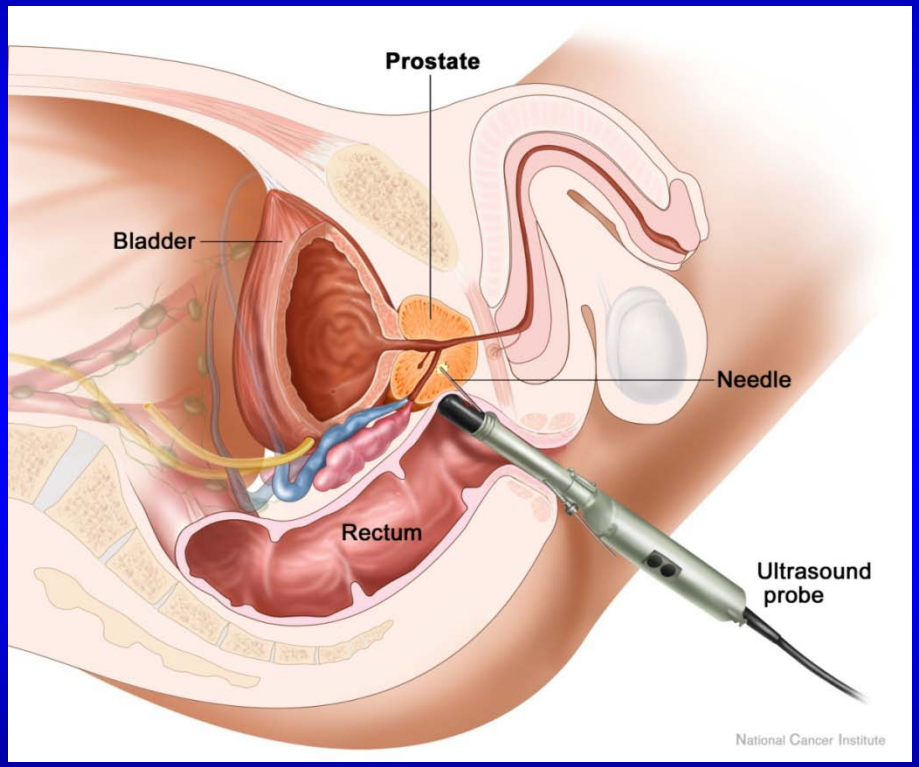
# Prostate Cancer

- Current detection suffers from low sensitivity and poor localization.
- 60% of ultrasound-morphologically suspicious lesions are biopsy negative[1]
- Prostate cancer is the only solid-organ tumor currently diagnosed without routine imaging.

1-Loch, T. et al., Transrectal ultrasound-guided biopsy of the prostate: random sextant versus biopsies of sono-morphologically suspicious lesions, World J. Urol, **22**: 357-360, 2004

# Cancer Detection Rate

- 6 core biopsy
  - 20 to 30%
- 12 core biopsy
  - 27 to 40%




Wein et. al. Campbell-Walsh Urology. 9th ed. Philadelphia, PA. 2007.

# When the biopsy is negative ?

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

Wein et. al. Campbell-Walsh Urology. 9th ed. 2007:Philadephia, PA

# Cancer detection on repeat biopsies

| | Sextant | Saturation biopsy |
|---|---|---|
| 1 prior negative biopsy | 10-17% | 36% |
| 2 prior negative biopsies | 5-14% | 31% |
| 3+ prior negative biopsies | 4-12% | 14-36% |

Wein et. al. Campbell-Walsh Urology. 9th ed. 2007:Philadephia, PA

# Biopsy is not just for diagnosis

- Crucial to the management of patients on active surveillance (AS)
- Role of AS is increasing
- Without good imaging, yearly biopsy currently required for men on AS

# Role of biopsy in active surveillance patients

- Active surveillance: distinguish clinically insignificant cancers from life-threatening cancers while still localized to delay definitive therapy

- Monitoring: interval PSA testing, repeated biopsies every 12 months

# Role of biopsy in AS

- Carter et al, (2002): PSA not likely to reveal disease progression accurately, need annual surveillance biopsies

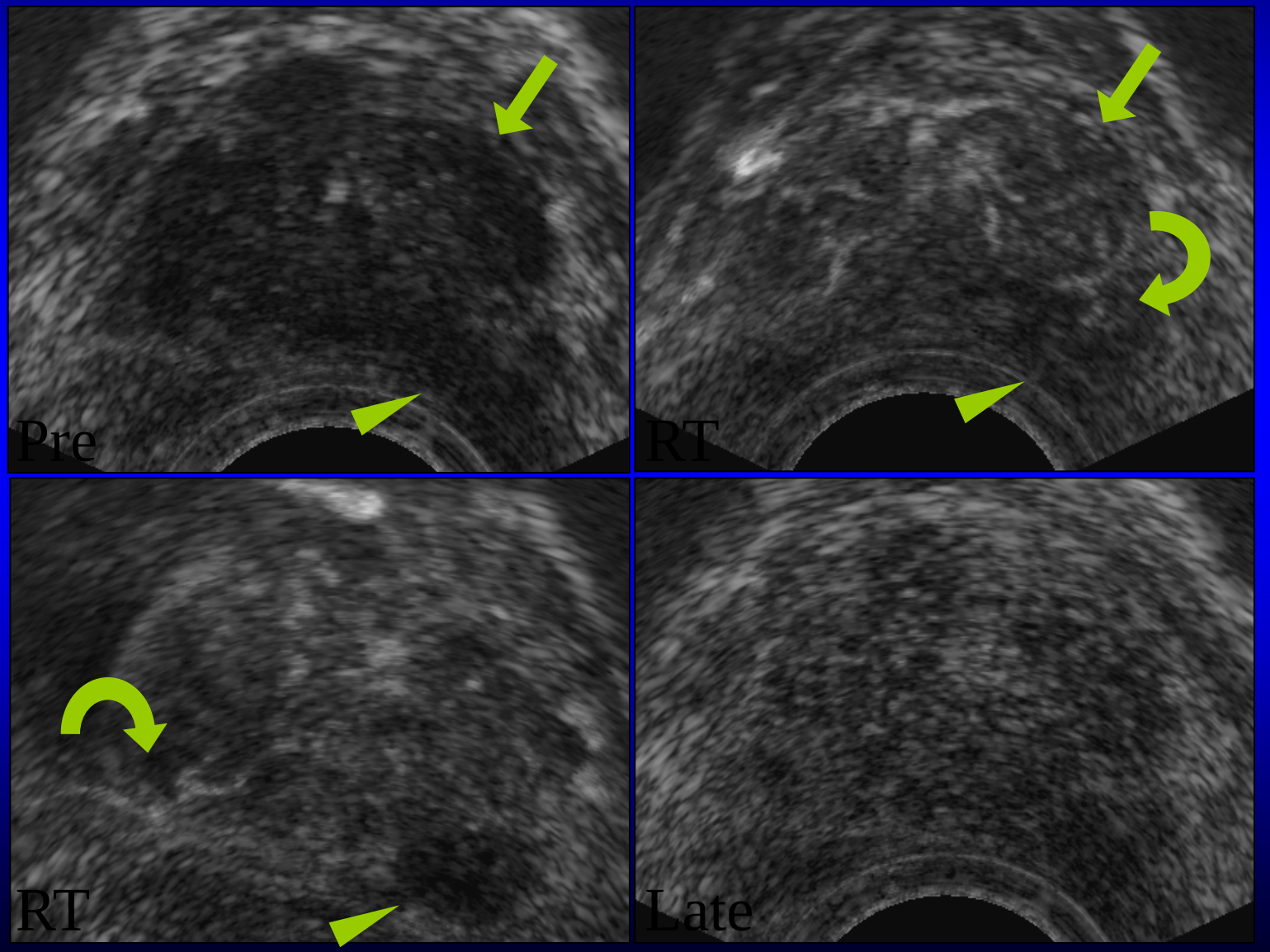
- Abnormal biopsy found to be most significant prognostic factor for progression (Patel et al,  2004)

# Imaging

- Is improving ultrasound sufficient?
  - 3D ultrasound
  - Contrast enhanced ultrasound (black box)
  - 3D models: Imaging based on vascularity
  - Transurethral ultrasound: reduced anatomic coverage than TRUS but higher resolution

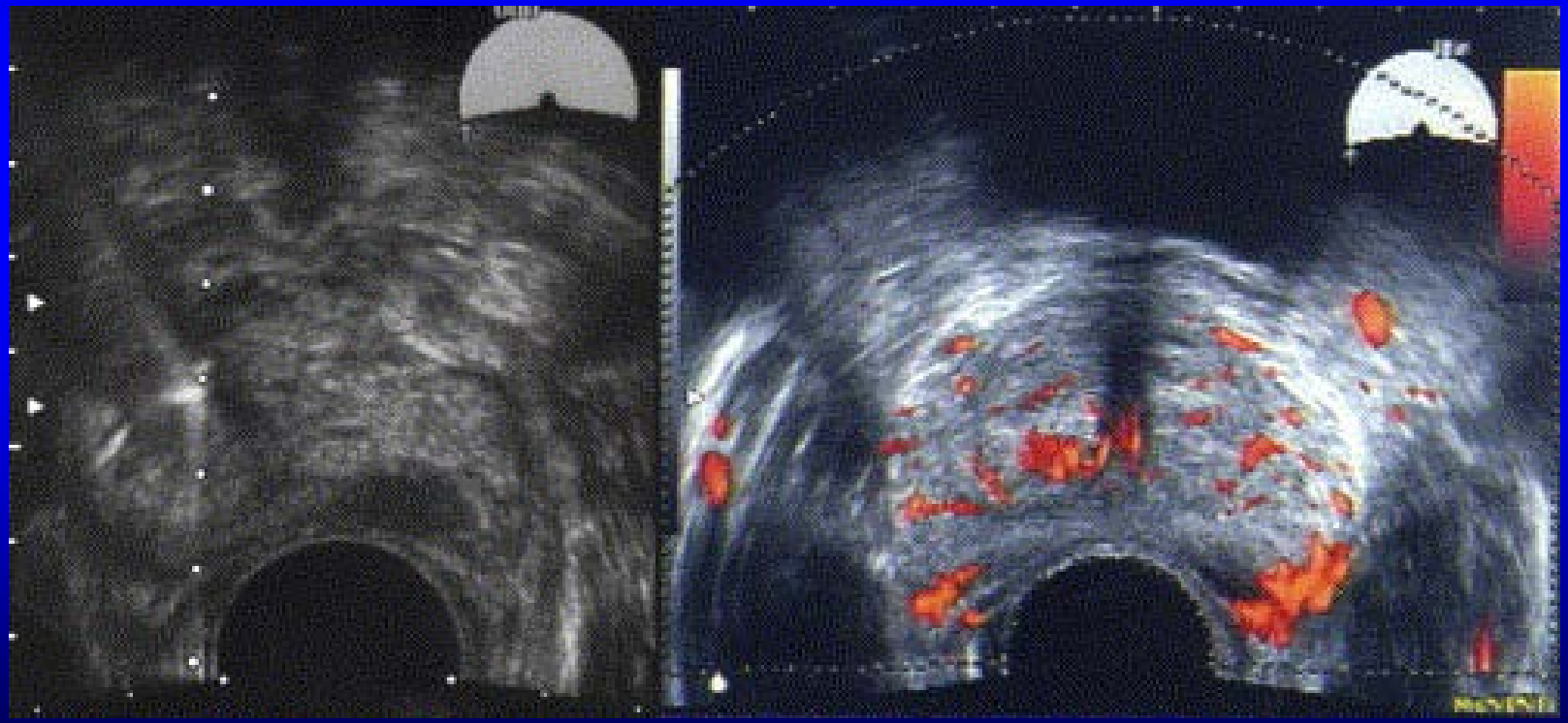
# Improving ultrasound ?

## Ultrasound Contrast (black box warning)



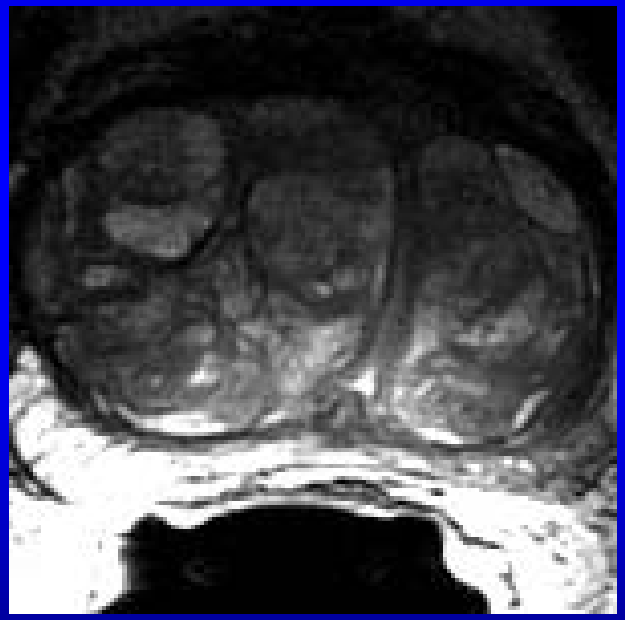
# Improving ultrasound ?

- Hypervascularity is not an independent factor in distinguishing between various pathologic entities, and therefore cannot serve as a tool to decrease the number of prostate biopsies (Arger et. al. 2004)

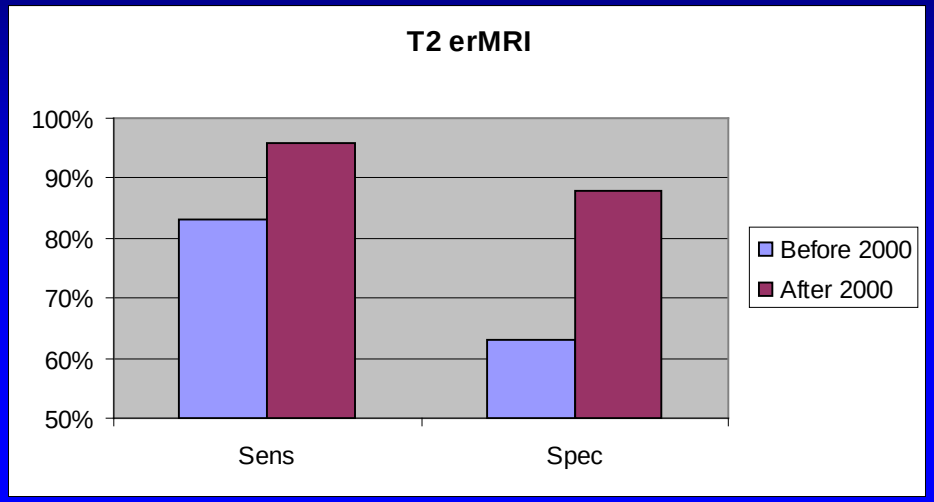


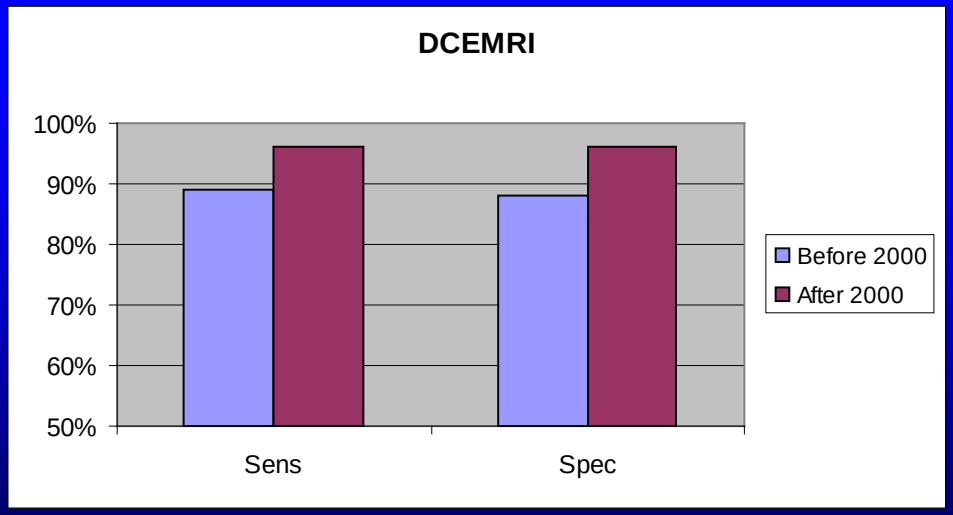
Amiel et. al. Newer modalities of ultrasound imaging and treatment of prostate cancer. Urol Clin N Amer 33 (2006) 329-337.

# MRI of the Prostate ?



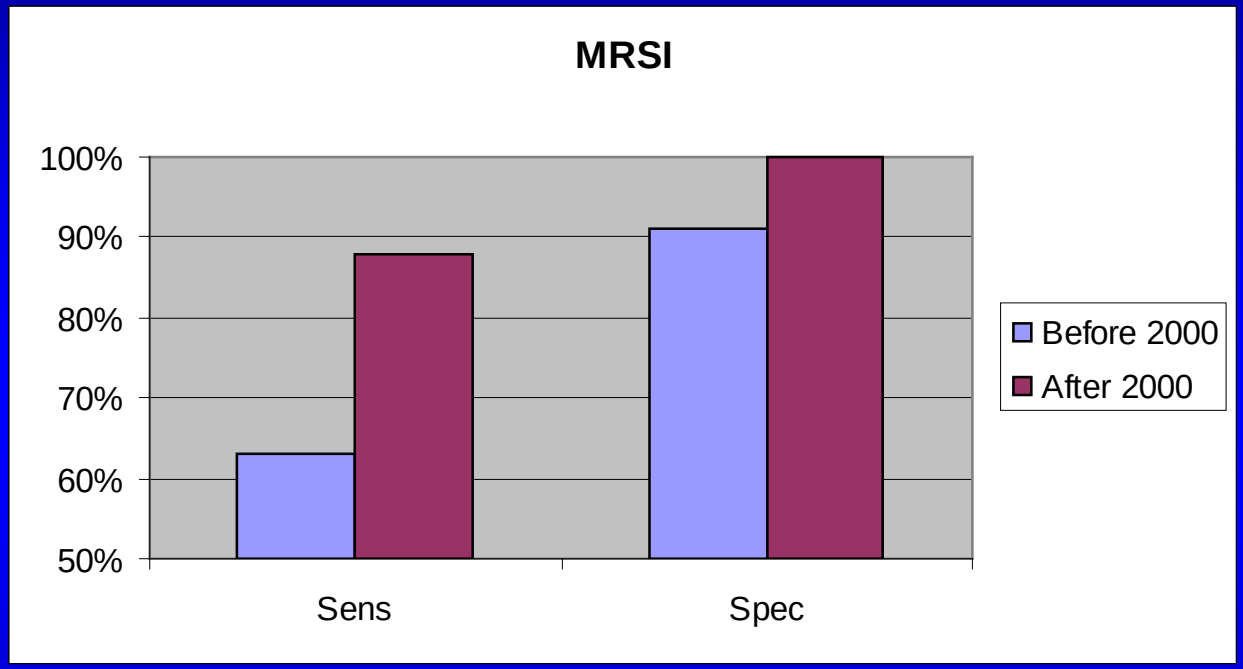
# Prostate MRI



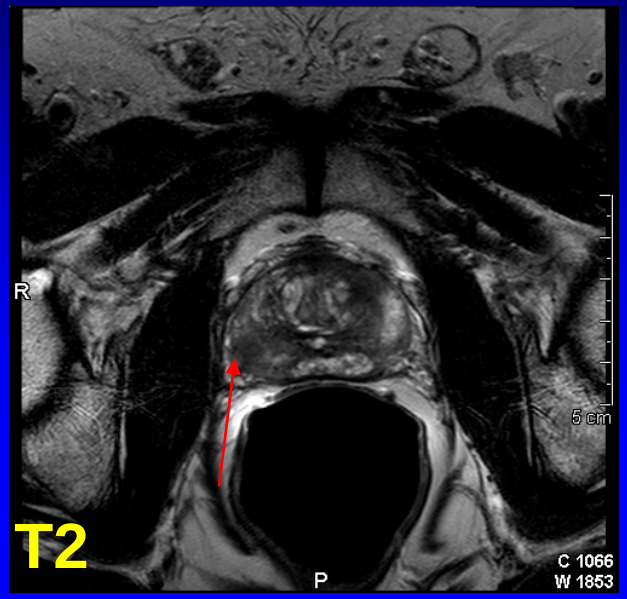

Kirkham et. al. How Good is MRI at Detecting and Characterizing Cancer within the Prostate? European Urol 50 (6). 2006: 1163-1175.

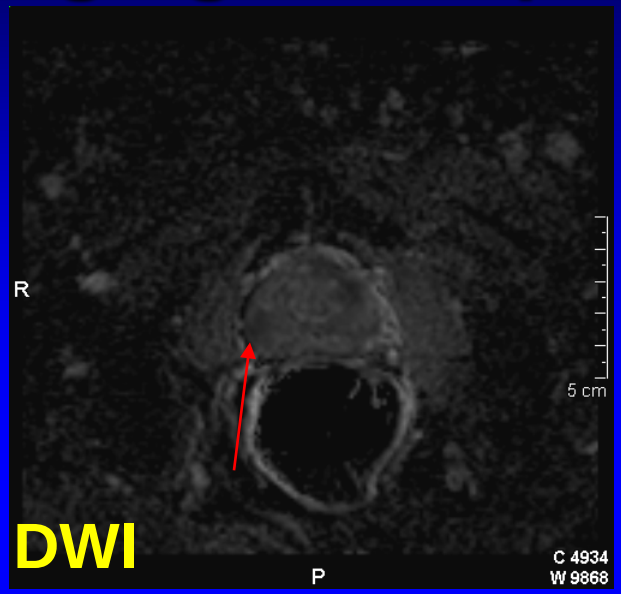
# Prostate MRI

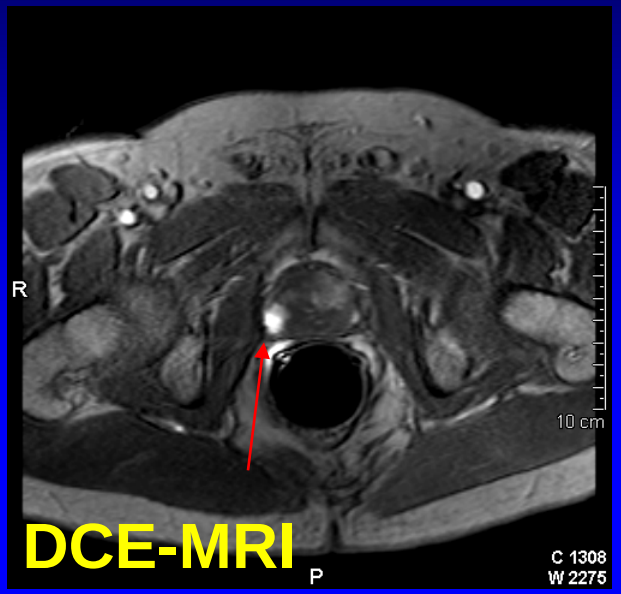



Kirkham et. al. How Good is MRI at Detecting and Characterizing Cancer within the Prostate? European Urol 50 (6). 2006: 1163-1175.

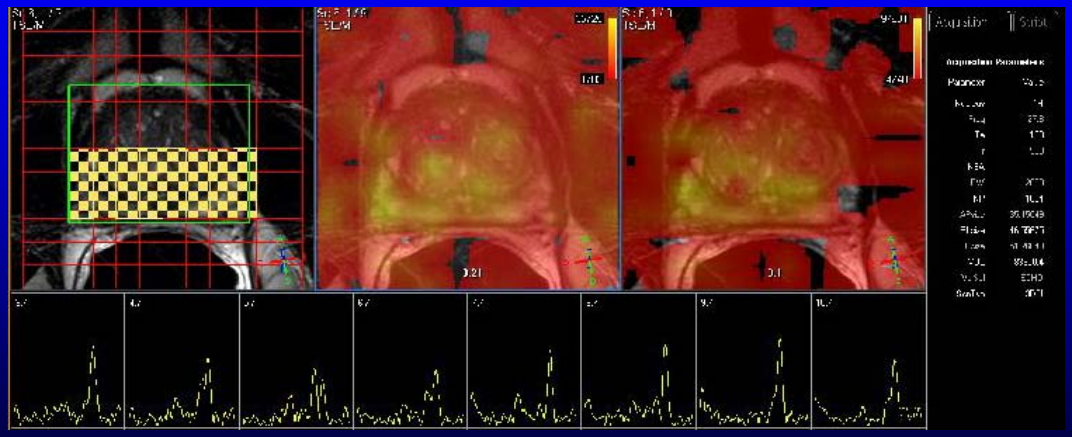
# Multi-parametric 3Tesla endorectal MR Imaging of the prostate




Spectroscopy



# Clinical Questions

**Can MRI detect and characterize cancer within the gland:**

- **Location?**
- **Size?**
- **Grade?**

# Clinical Questions

- Can MRI allow better sampling of the prostate when biopsied?

# Clinical Questions

- **Can MRI increase our confidence in excluding cancer in patients with negative biopsies?**

# Clinical Questions

- **Can MRI be used for men undergoing active surveillance?**

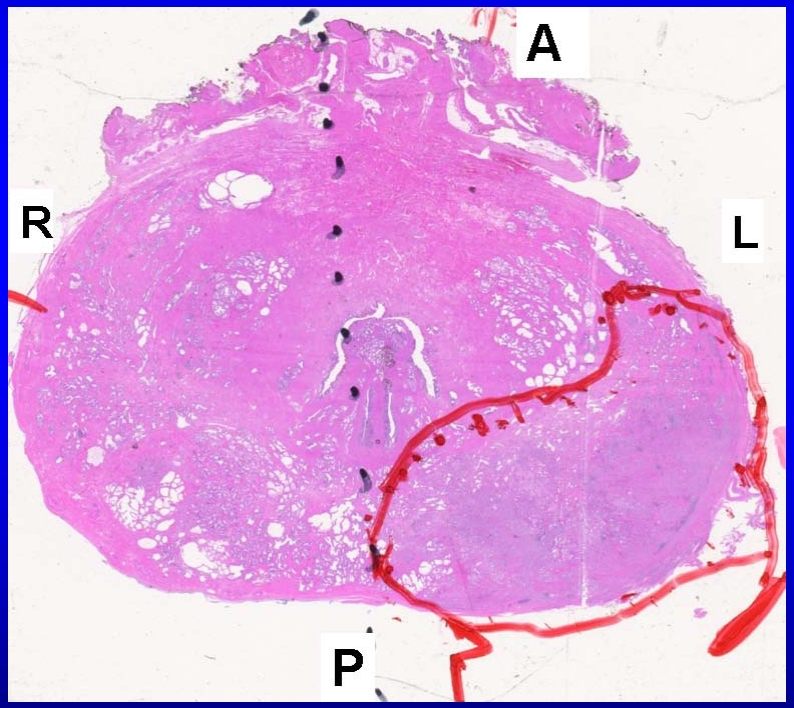
# Clinical Questions

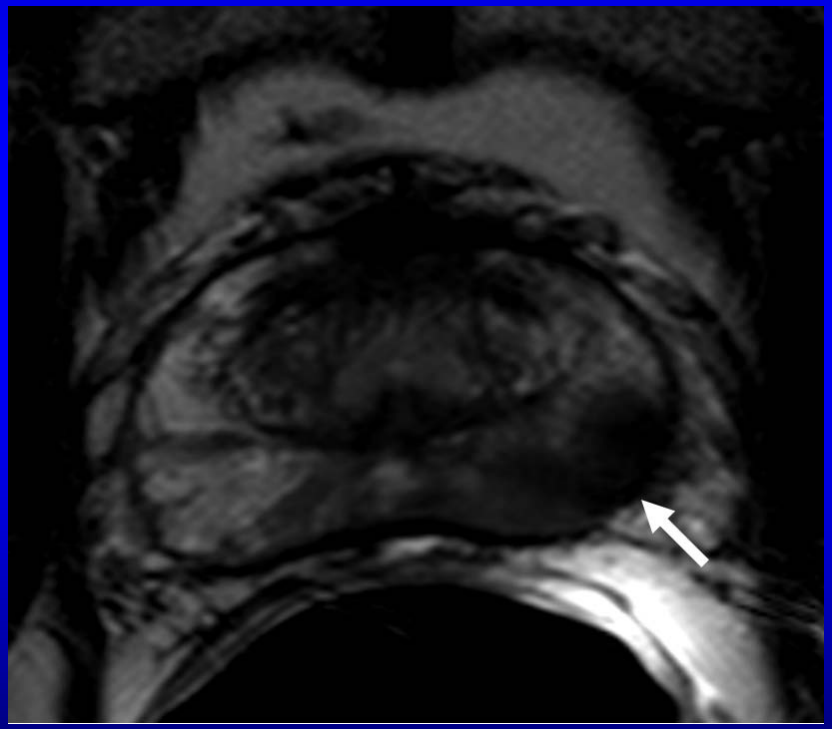
- **Can MRI be used to change how we treat prostate cancer?**
  - **Image guided focal therapy**

# Two Research Endeavors

- **Develop a research platform to ensure the prostate MR Images correlates with pathology**
- **Develop a prostate biopsy platform that uses image guidance (MRI)**

# Prostate Cancer Localization with 3T erMRI: Correlation with Whole-Mount Histopathological Specimens



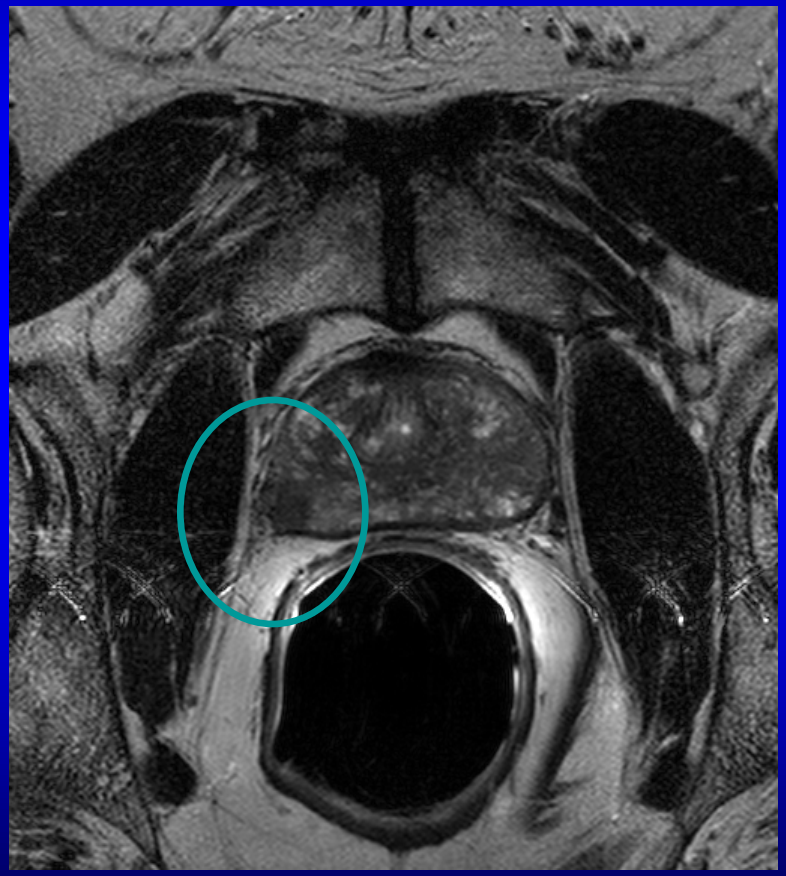
# MRI and Histology Correlation for prostate cancer

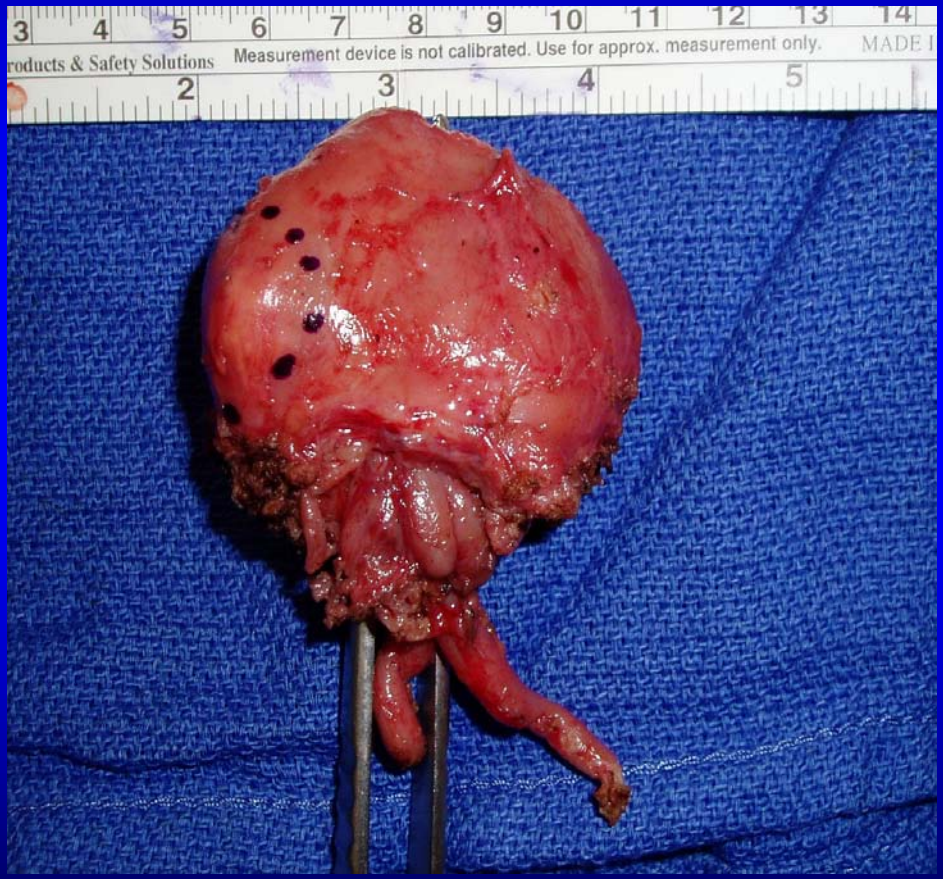
Protocol 04-CC-0109: Comprehensive Prostate MRI for the Evaluation of Prostate Cancer at 3.0T

Men undergo multi-parametric 3T endorectal coil MRI prior to radical prostatectomy.

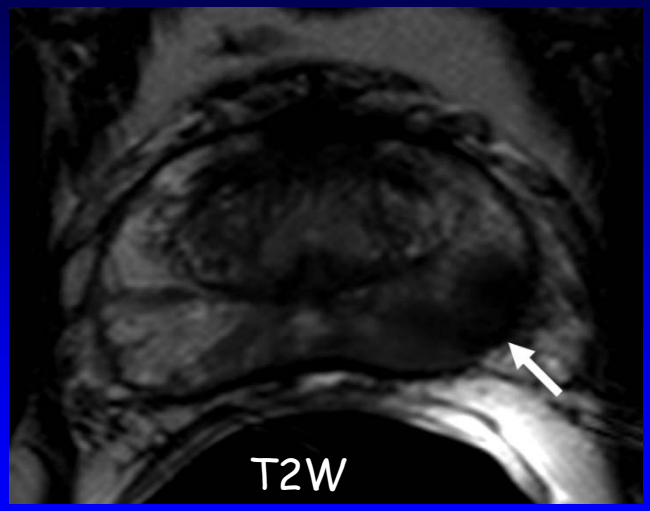
Prostate is whole mount sectioned and compared to MR's axial images

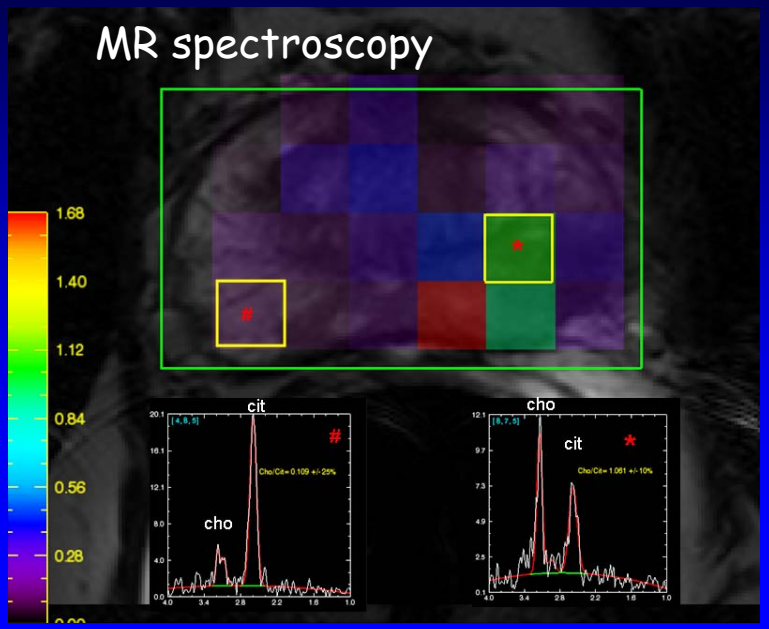
# MRI / Path Correlation

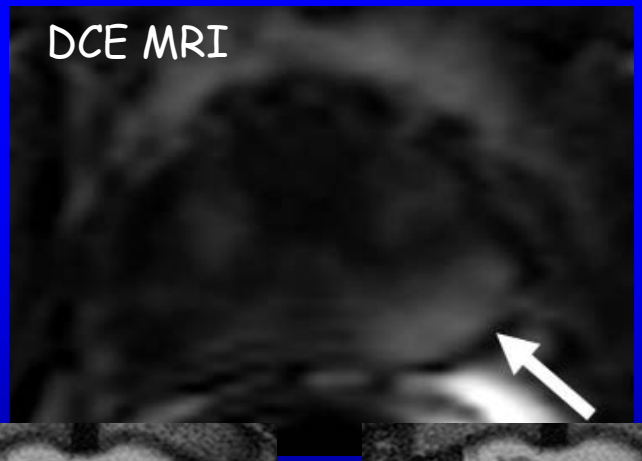


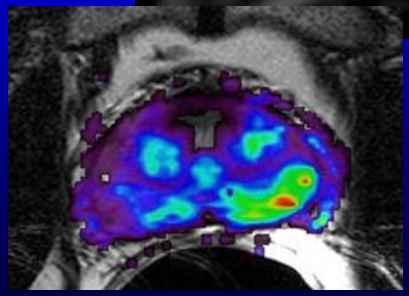


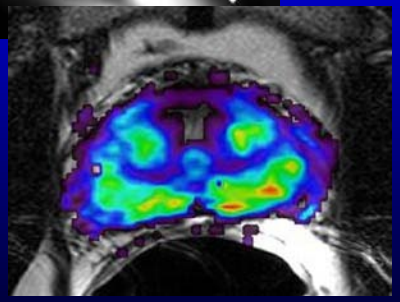
# 58-year-old male, PSA=7 ng/mL

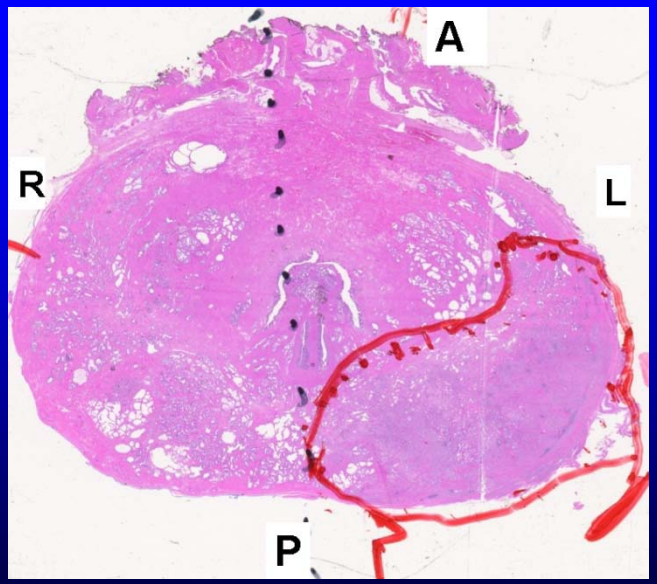


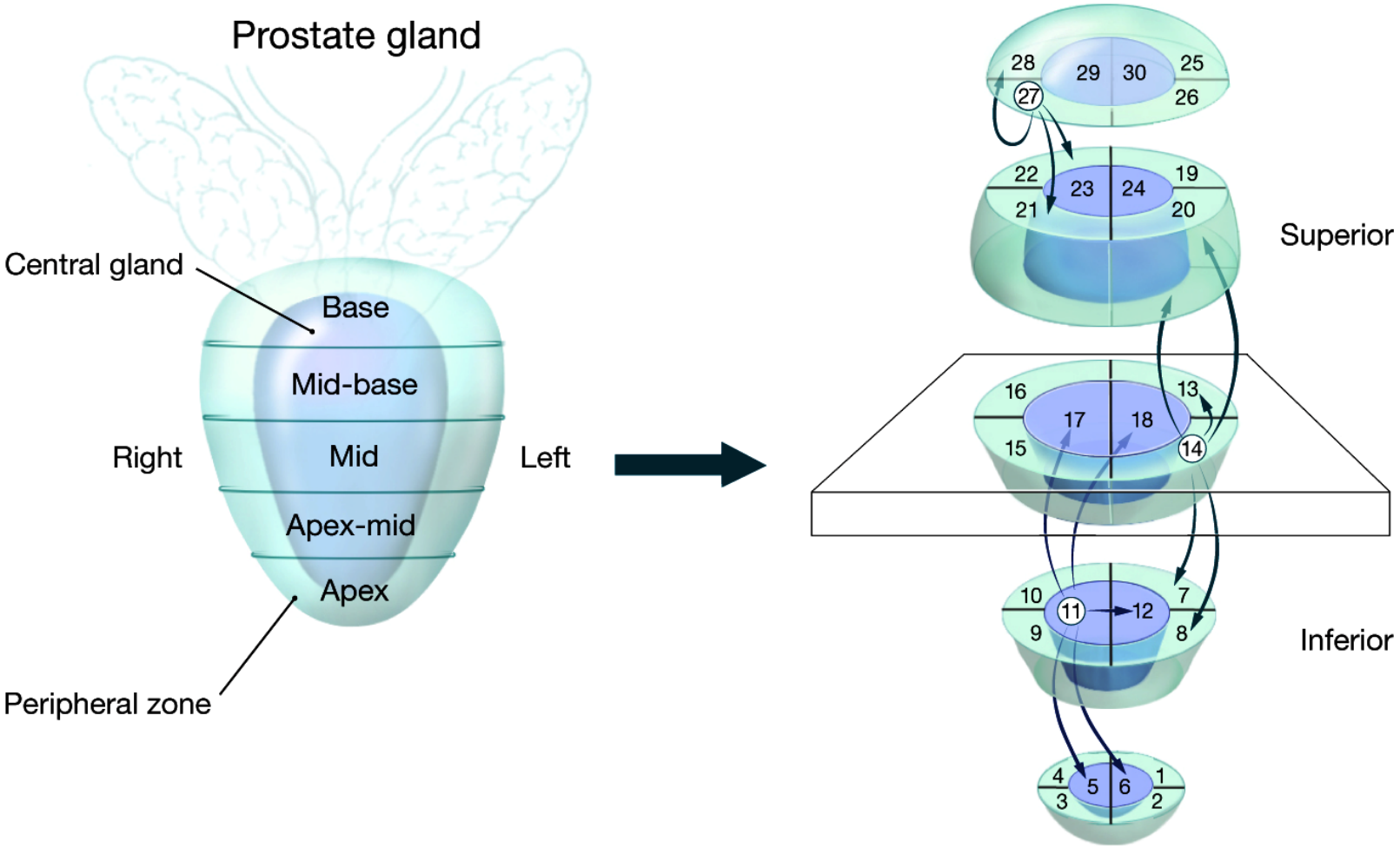





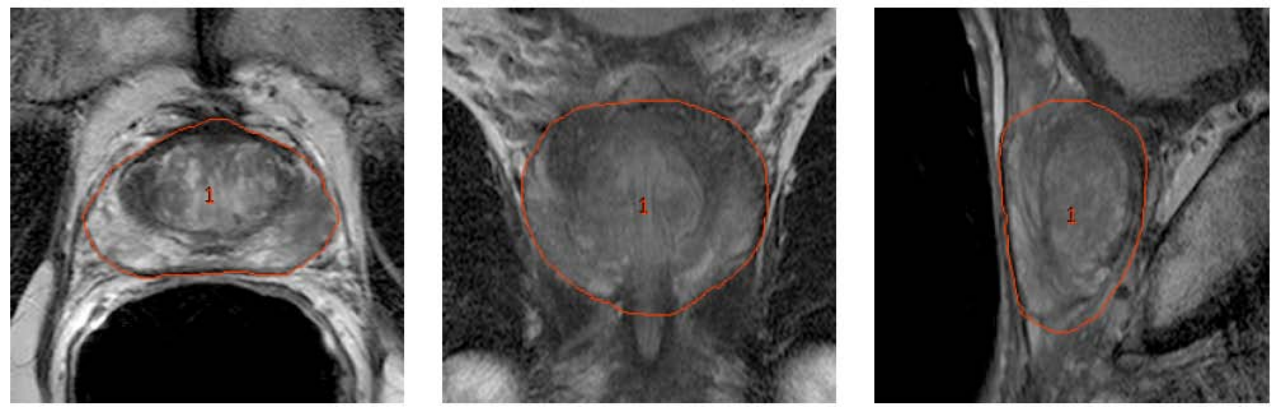


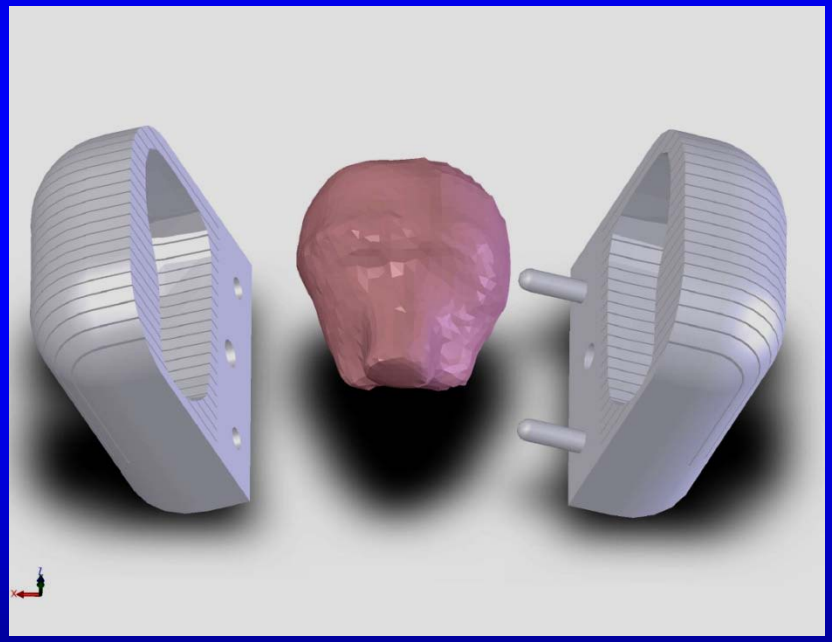
# Neighboring method

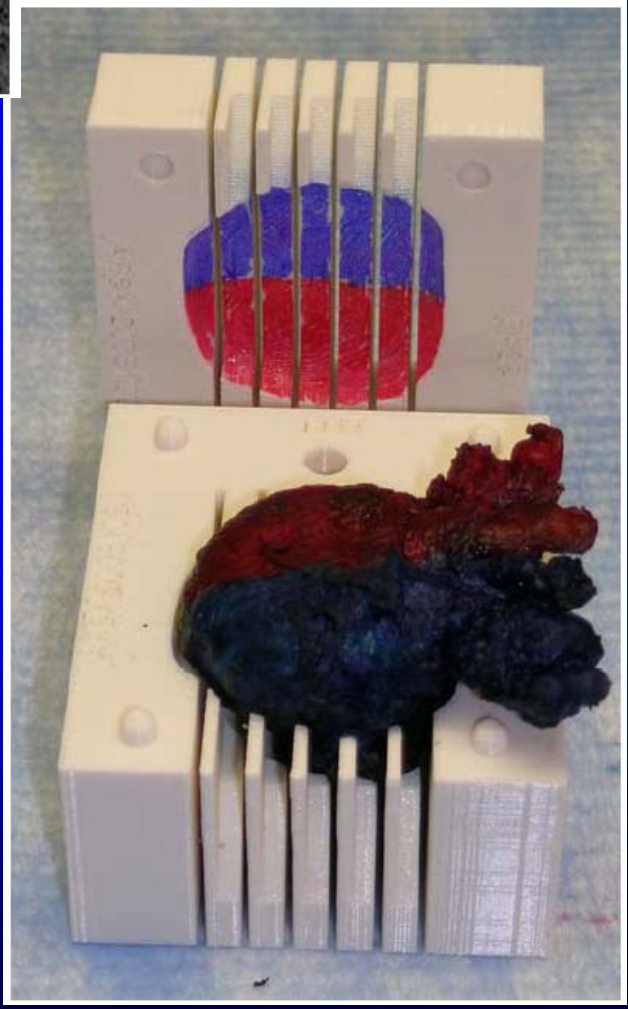


# This work raised another question

- **How can we improve the MRI / Path correlation?**

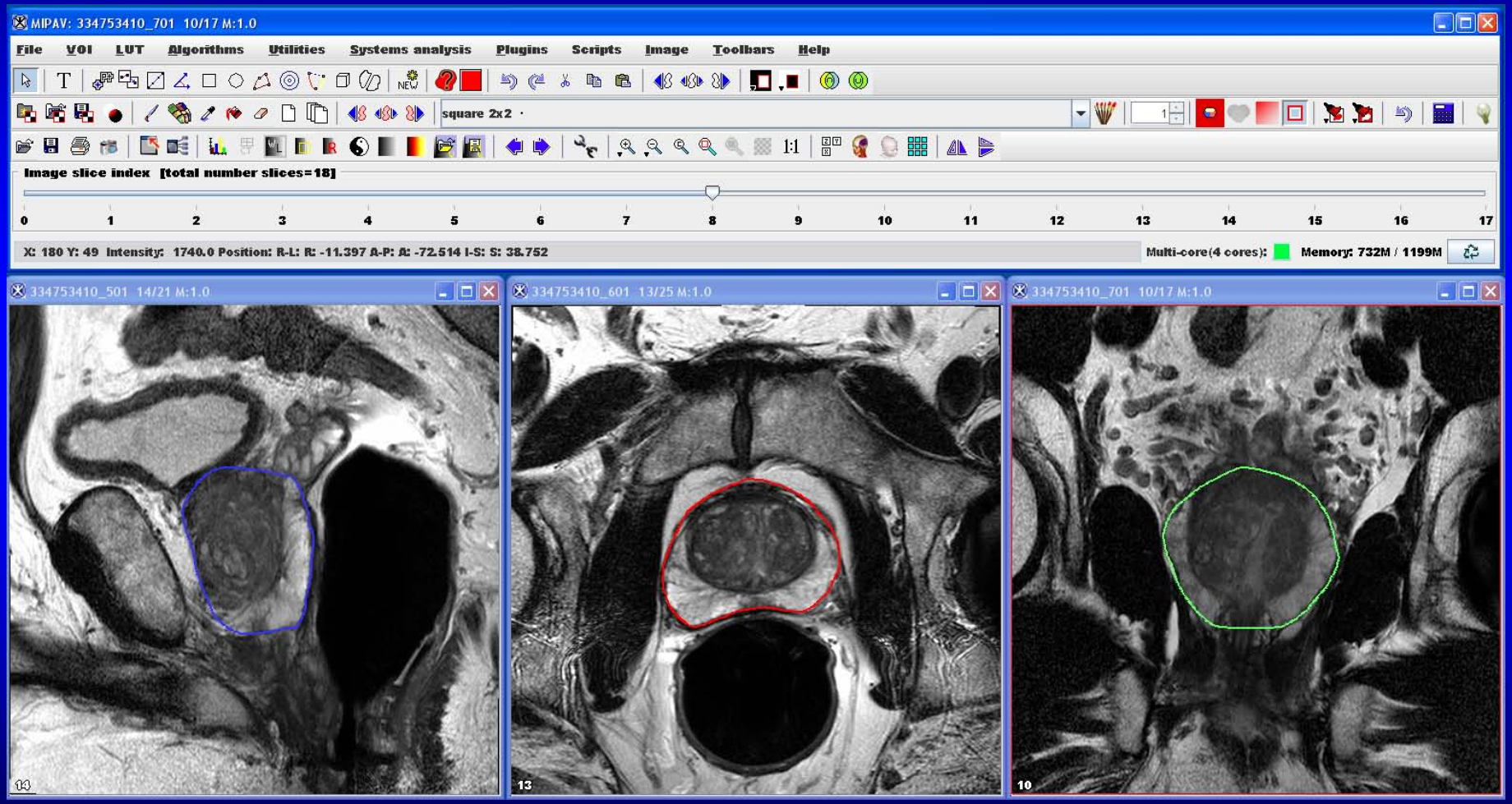


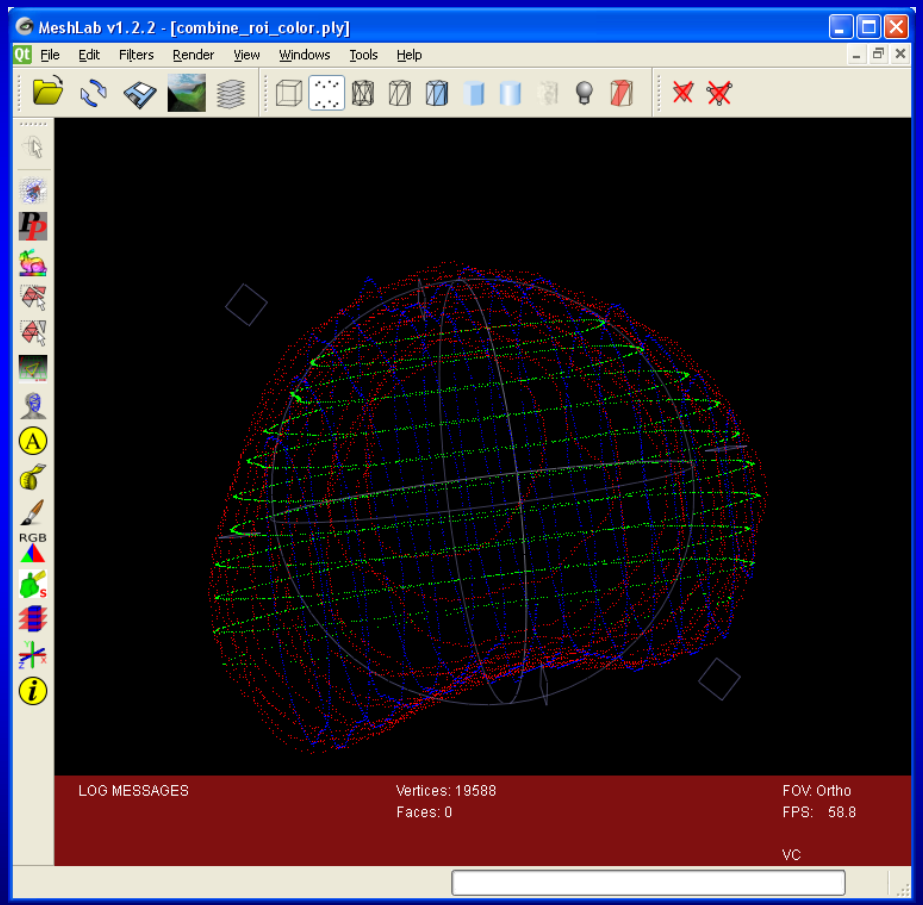


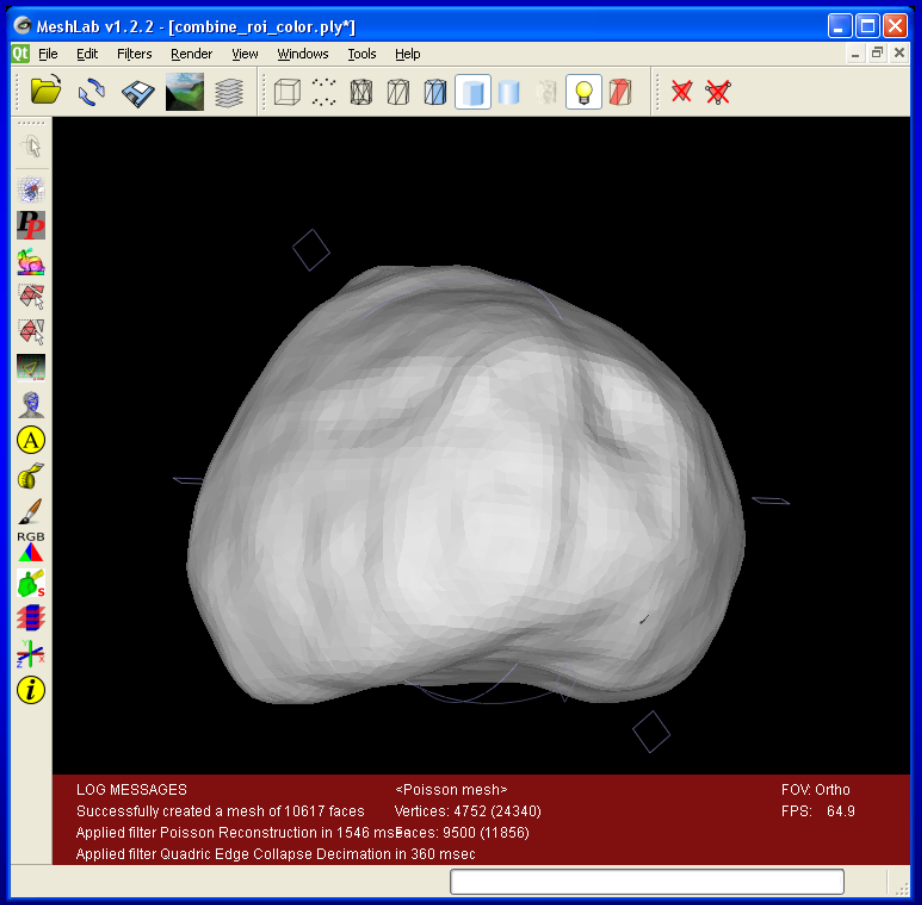
Shah V, et al. Rev Sci Instrum. 2009;80:104301.

# Prostate Segmentation

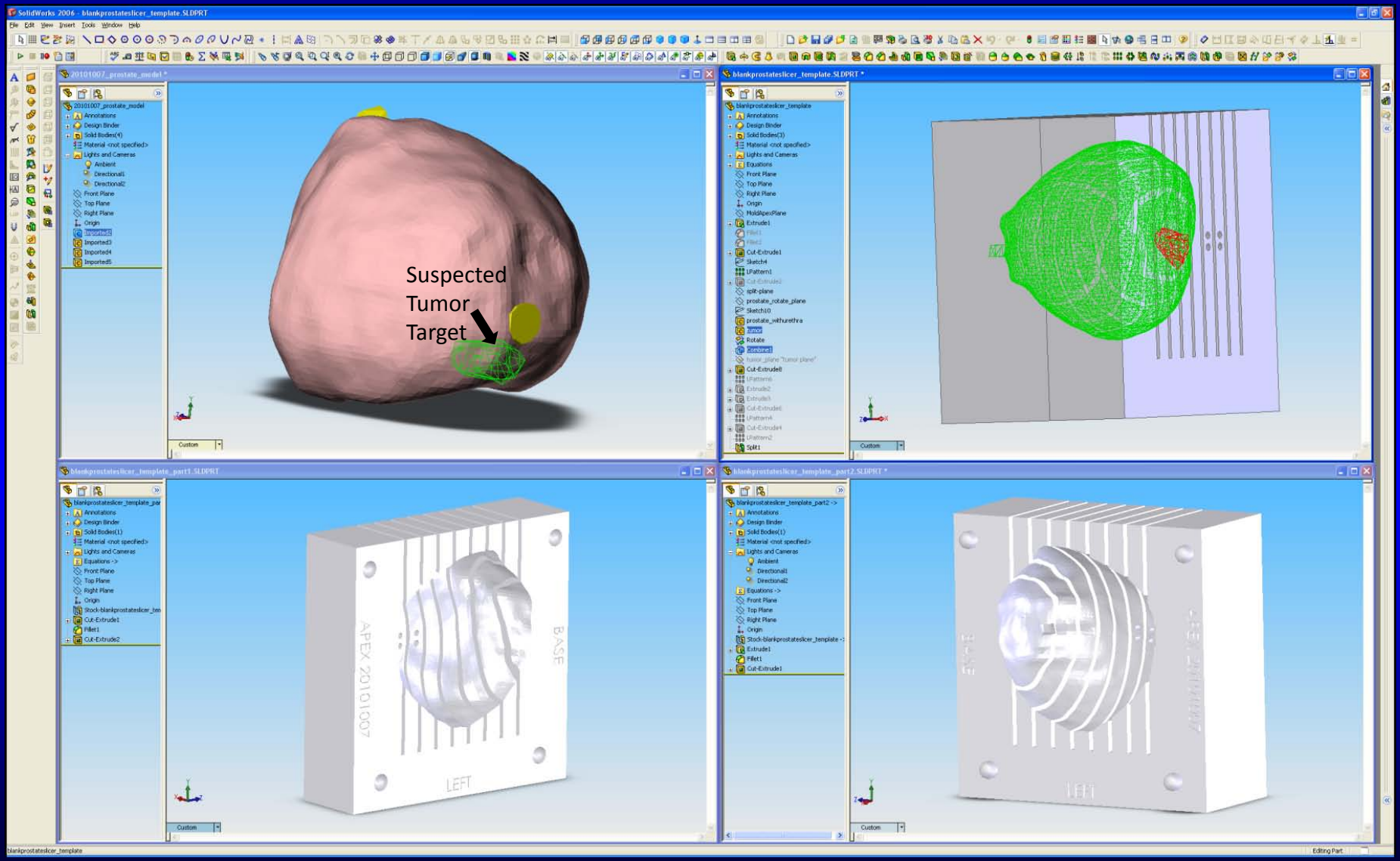


# 3D Modeling

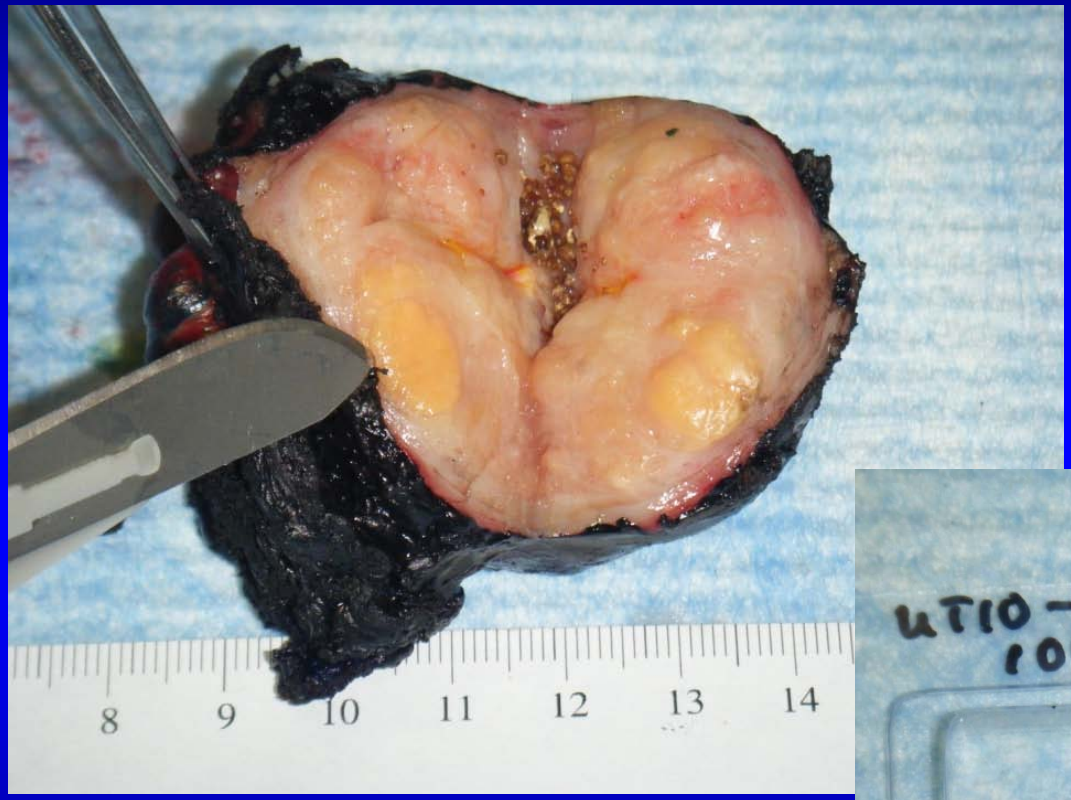

MeshLab v1.2.2 - [combine_roi_color.ply]
File Edit Filters Render View Windows Tools Help
LOG MESSAGES
Vertices: 19588
Faces: 0
FOV: Ortho
FPS: 58.8
VC

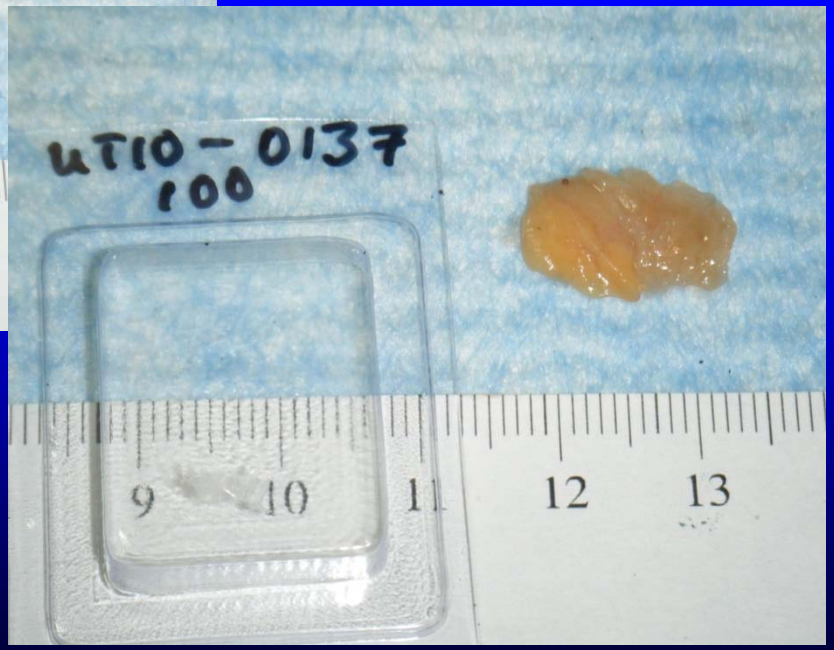

MeshLab v1.2.2 - [combine_roi_color.ply*]
File Edit Filters Render View Windows Tools Help
LOG MESSAGES
Successfully created a mesh of 10617 faces
Applied filter Poisson Reconstruction in 1546 ms
Applied filter Quadric Edge Collapse Decimation in 360 msec
<Poisson mesh>
Vertices: 4752 (24340)
Faces: 9500 (11856)
FOV: Ortho
FPS: 64.9

# Prostate Mold



# Fresh Tissue Procurement

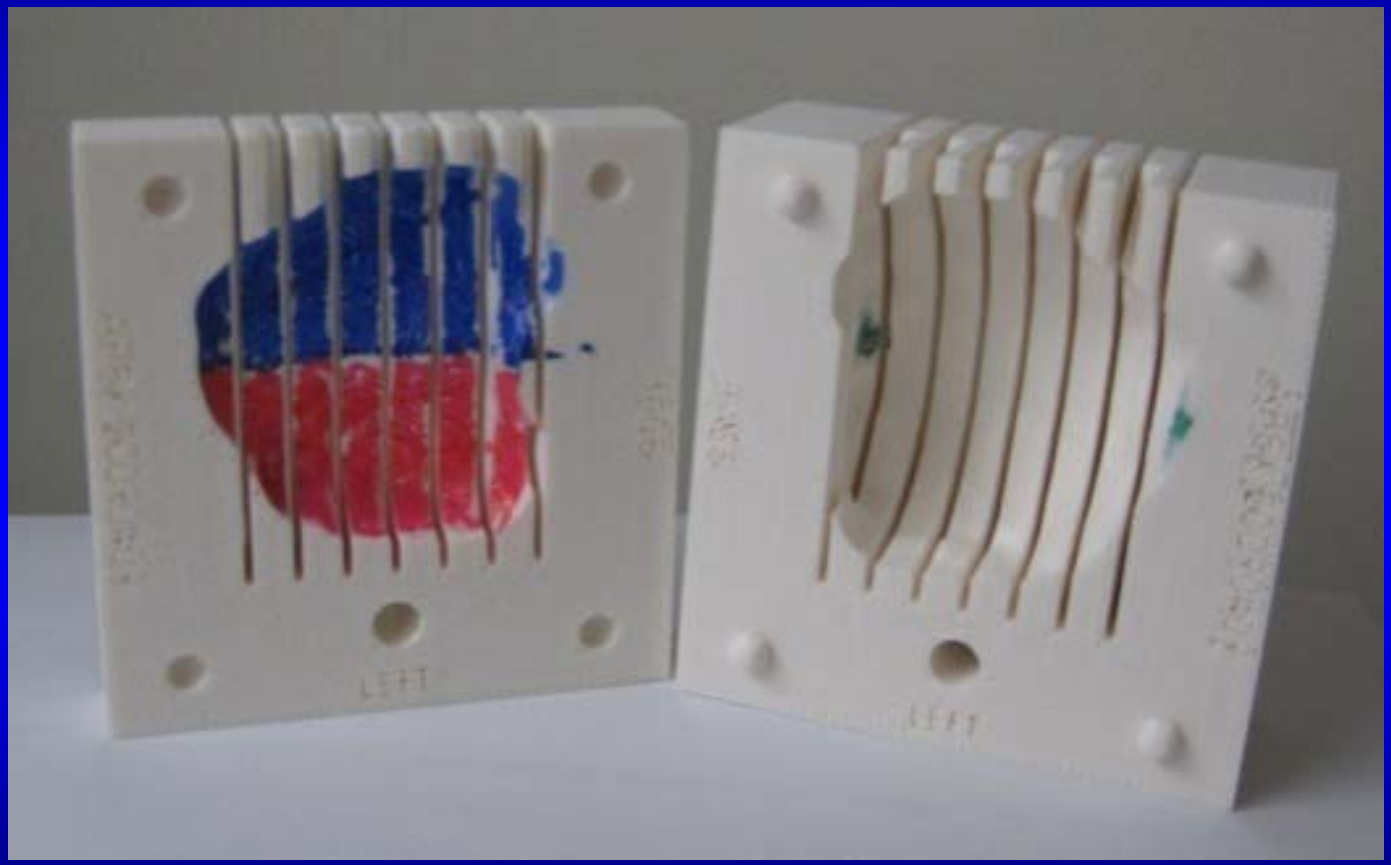


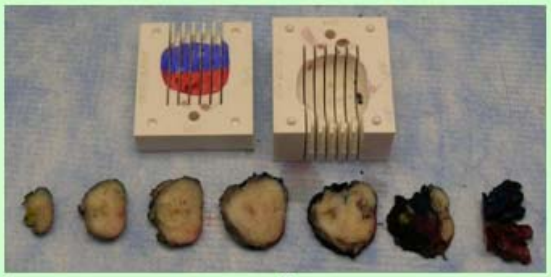
# Printing the Mold

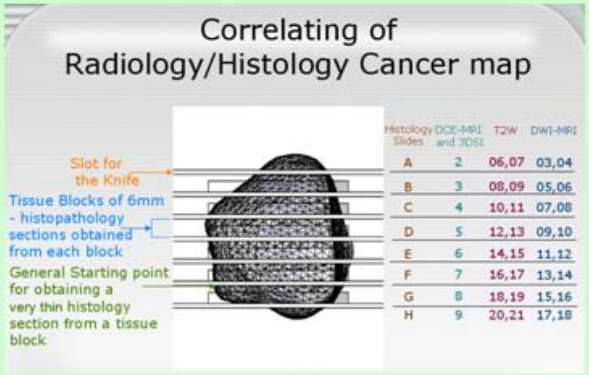
# Printing the Mold

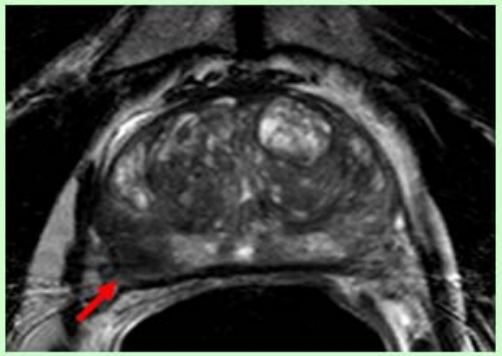
# Printing the Mold

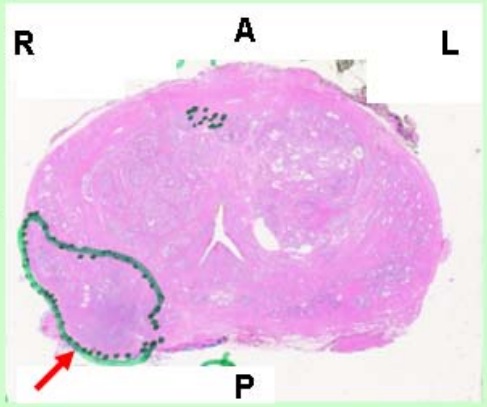


# Prostate Cancer Localization with 3T erMRI: Correlation with Whole-Mount Histopathological Specimens





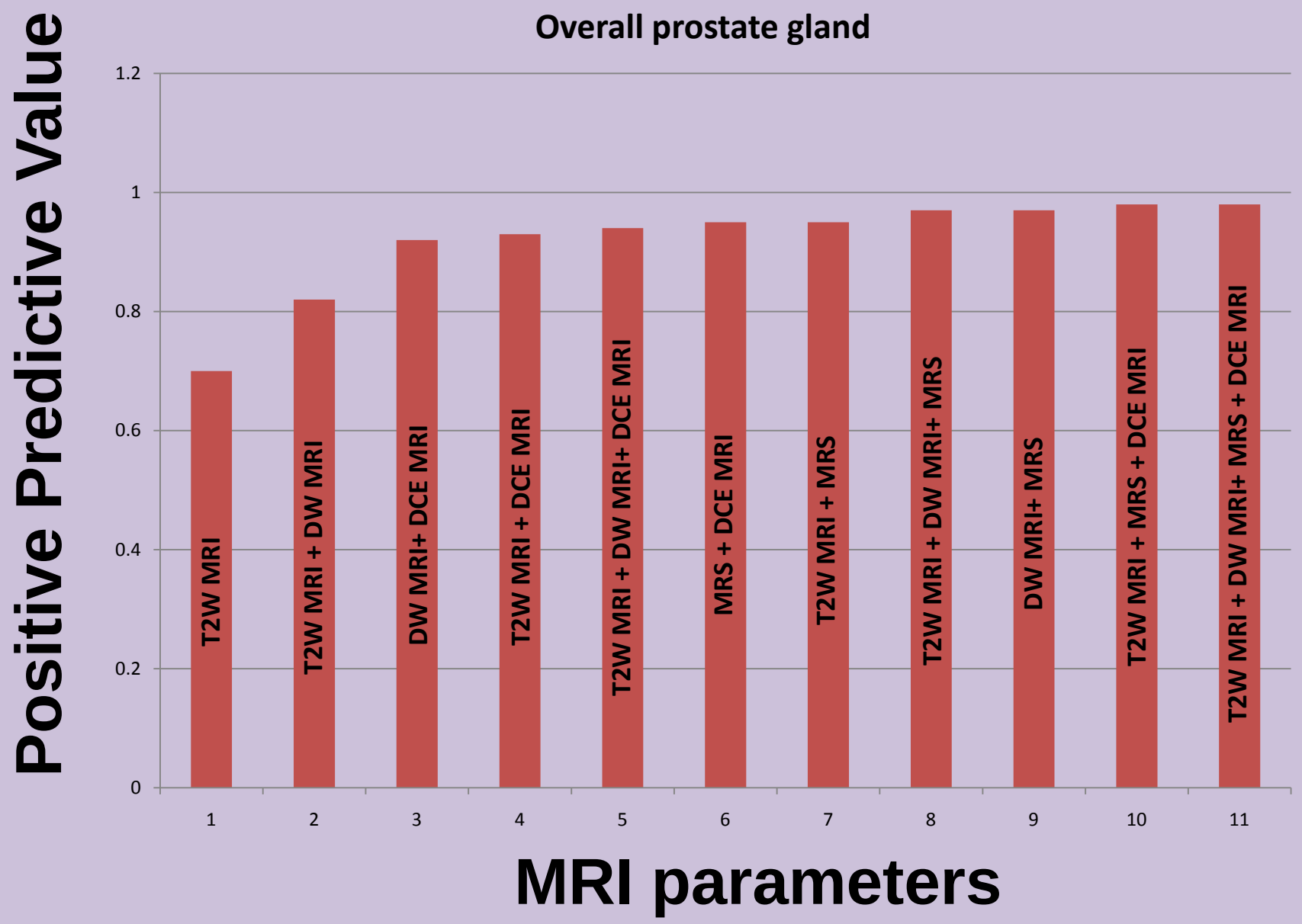





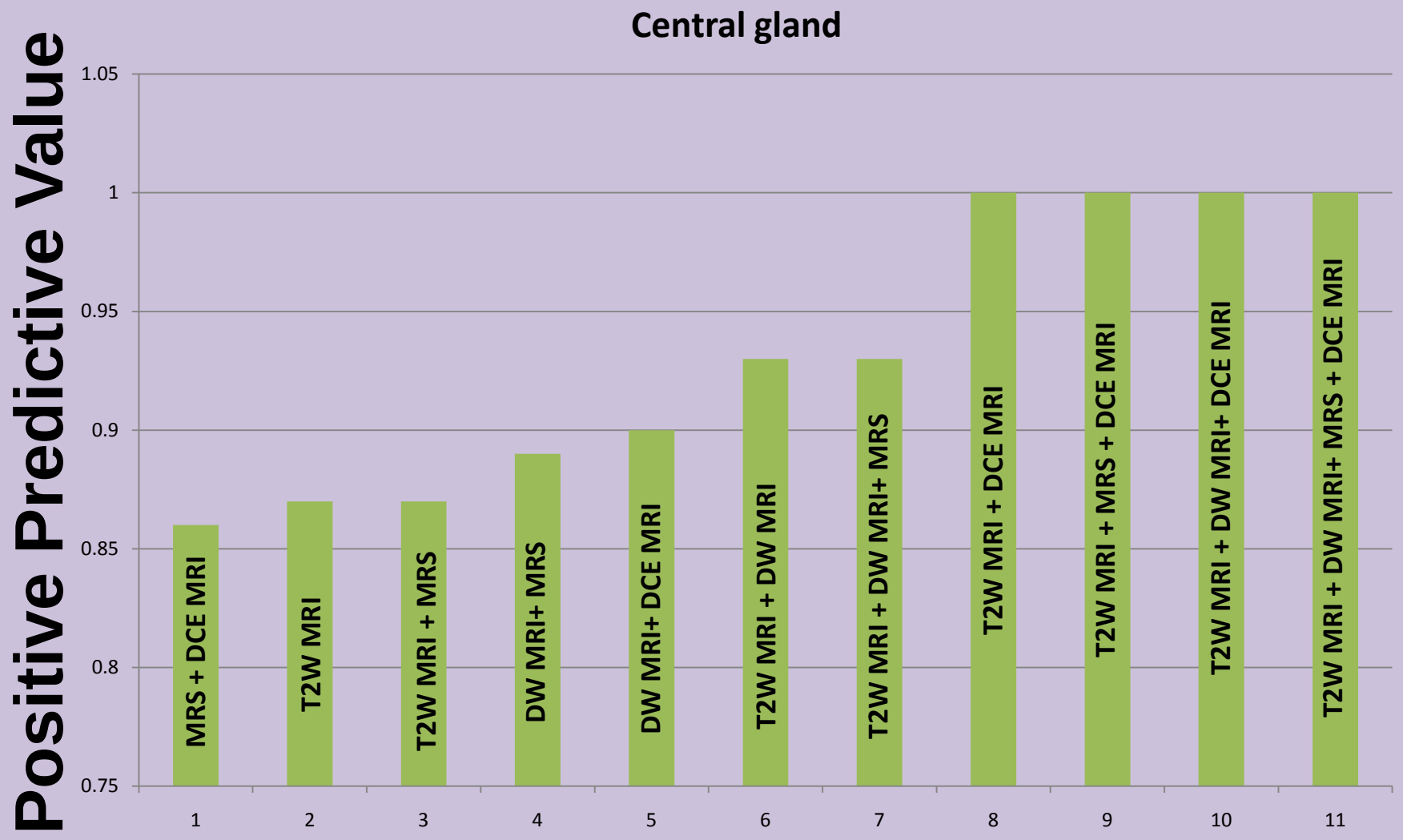
# MRI correlation with radical prostatectomy specimens using the mold slicer for whole mount pathology

- **Analyzed the data from the first 45 patients**

# NCI Results: Tumor Detection



# NCI Results: Tumor Detection



# To Improve current methods of detection / treatment of PCa:

- Diagnostic imaging
  - Improve MR Imaging sequences
  - Other imaging modalities
- Devices
  - If we have imaging that can see the tumor in the prostate can we “hit” it

# Why image (MRI) guided biopsies?

- Lesion-targeted prostate biopsy
  - Increase biopsy yield
  - Reduce number of biopsies
  - Reduce number of failed biopsies
  - Locate cancers outside peripheral zone

- Lesion-targeted localized therapy
  - Eliminate side effects of radical treatment

# In Gantry MRI-Guided Prostate Biopsies?

- Technically challenging
- Uncomfortable, unpleasant for patient
- COSTLY- Becomes hospital based procedure, not office base
- Time in MRI gantry at a premium; diagnostic tests take priority
  - Mean time 1.5-2.5 hours!
- Learning curve
- Patient acceptance low

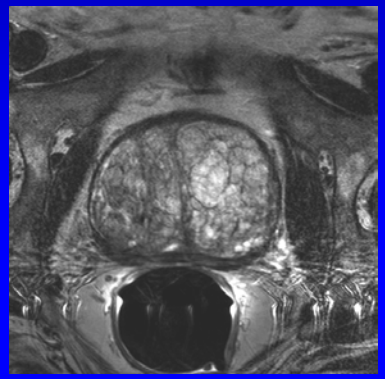
K. Engelhard. Prostate biopsy in the supine position in a standard 1.5-T scanner under real time MR-imaging control using a MR-compatible endorectal biopsy device. Eur Radiol (2006) 16: 1237–1243

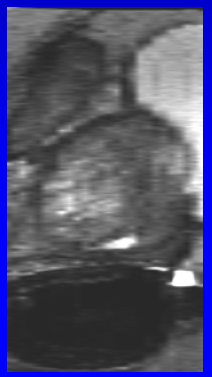
# MRI-TRUS Fusion Prostate Biopsies

- Office-based procedure.
- Minimal additional patient discomfort for significant additional diagnostic yield.
- Utilizes widely available imaging technologies
- Technically feasible with mature technology and proper instruction.

# Why fuse MRI and Ultrasound ?

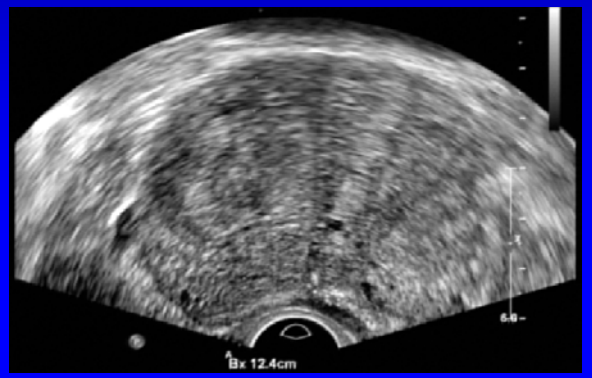
## MRI





- ✗ Temporal resolution
- ✓ **Spatial resolution**
- ✓ **Sensitivity/Specificity**
- ✗ Cost effective

## TRUS




- ✓ **Temporal resolution**
- ✗ Spatial resolution
- ✗ Sensitivity/Specificity
- ✓ **Cost effective**

# Why fuse MRI and Ultrasound ?

- Fusing prior-acquired MRI w/ real-time TRUS brings diagnostic information to the urologist possibly improving office prostate biopsies
- May lead to office based image guided focal therapy

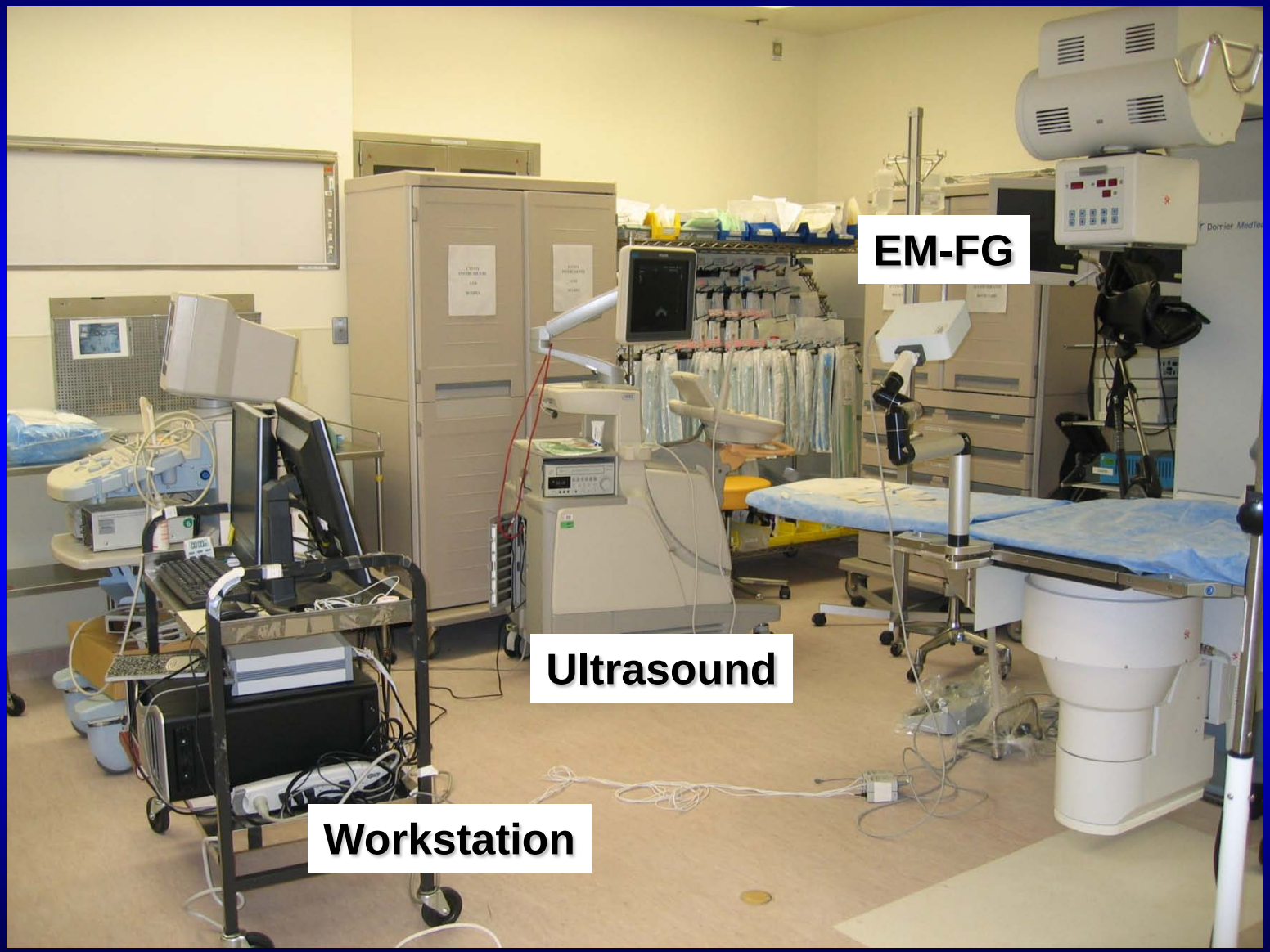
# Image fusion guided prostate bx

- Work here at NIH leads the way in developing this technology with the help of interdisciplinary collaborative efforts
  - Urologic Oncology, Interventional Radiology, Diagnostic Radiology, Pathology, Engineering, Medical Oncology, CIT, Industry (CRADA Philips)

# To Improve current methods of detection / treatment of PCa:

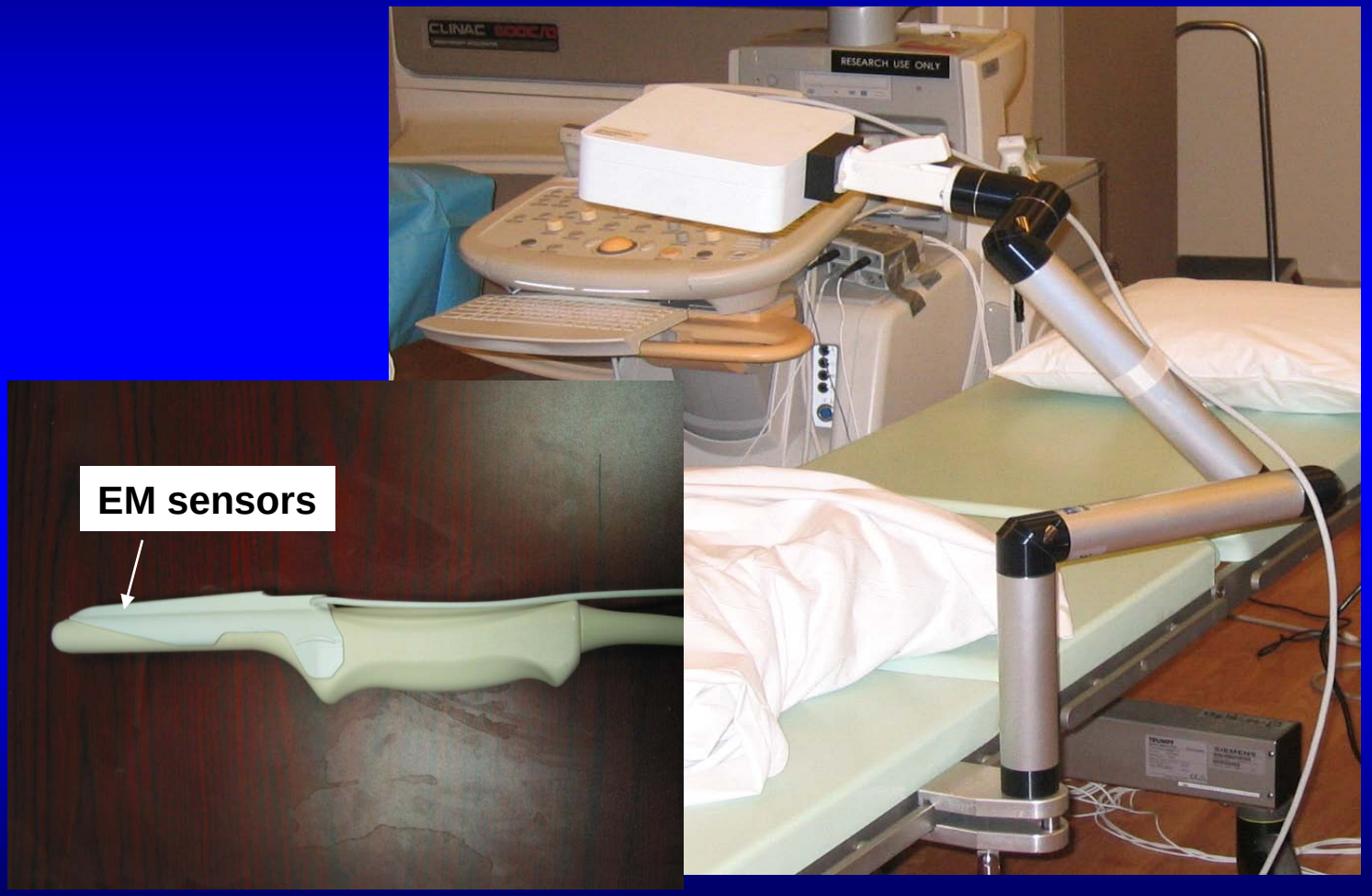
- Diagnostic imaging
  - Improve MR Imaging sequences
  - Other imaging modalities
- **Biopsy devices**
  - **If we can see the tumor in the prostate can we “hit” it**

# Image Fusion Guided Platform

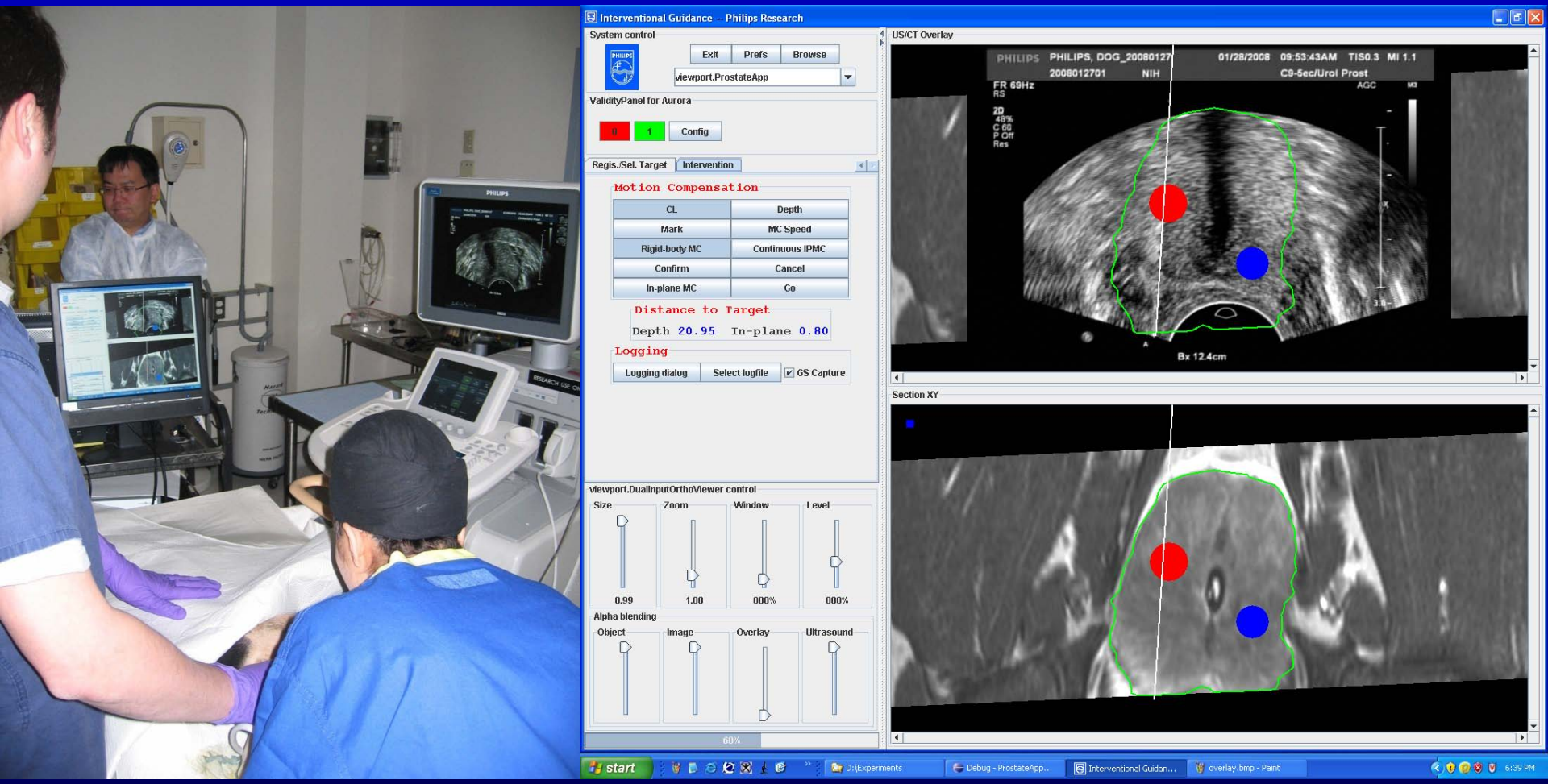


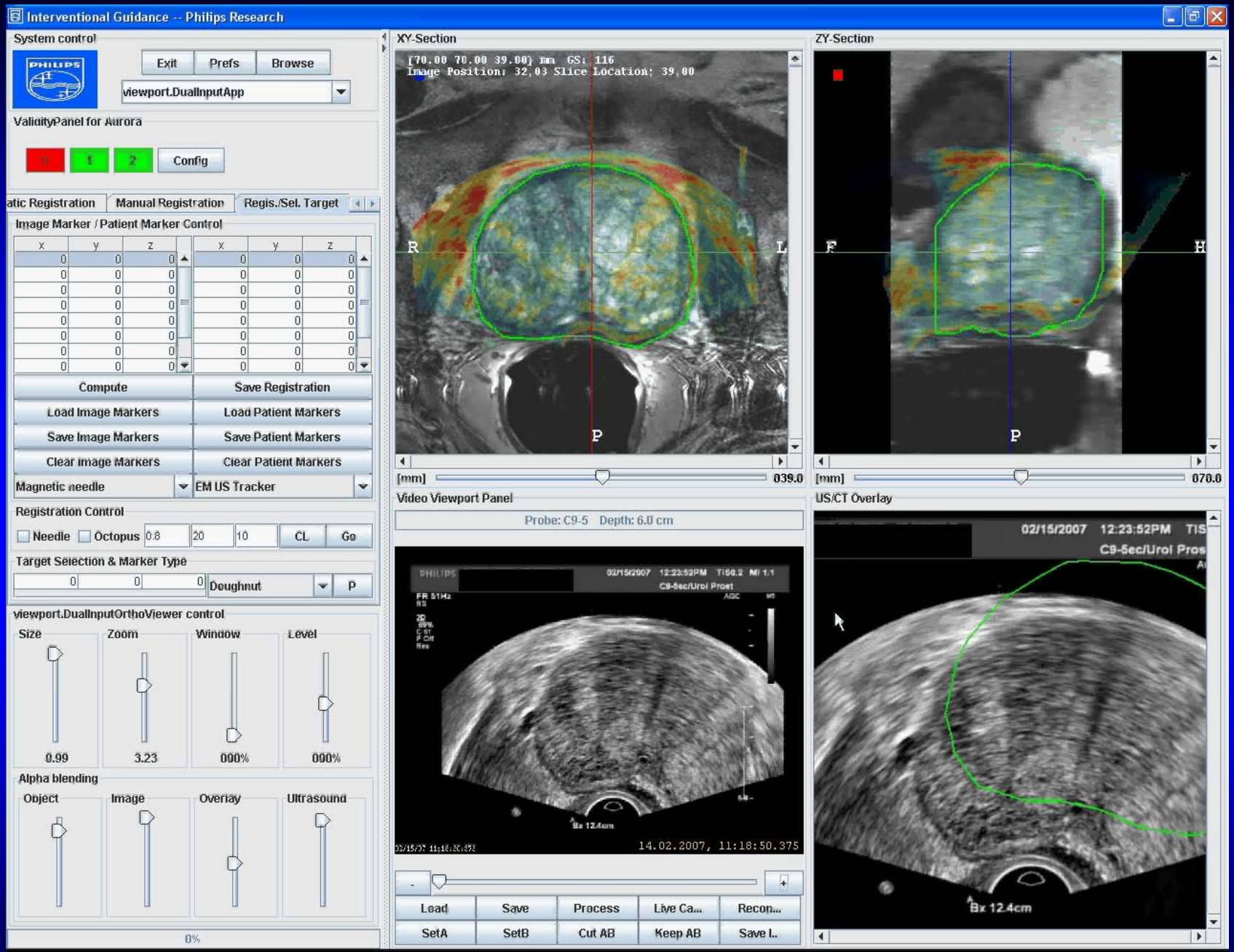

CRADA NIH-Philips medical

# Spatial Tracking System

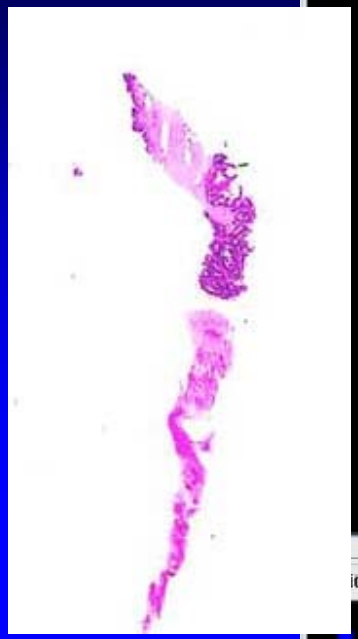


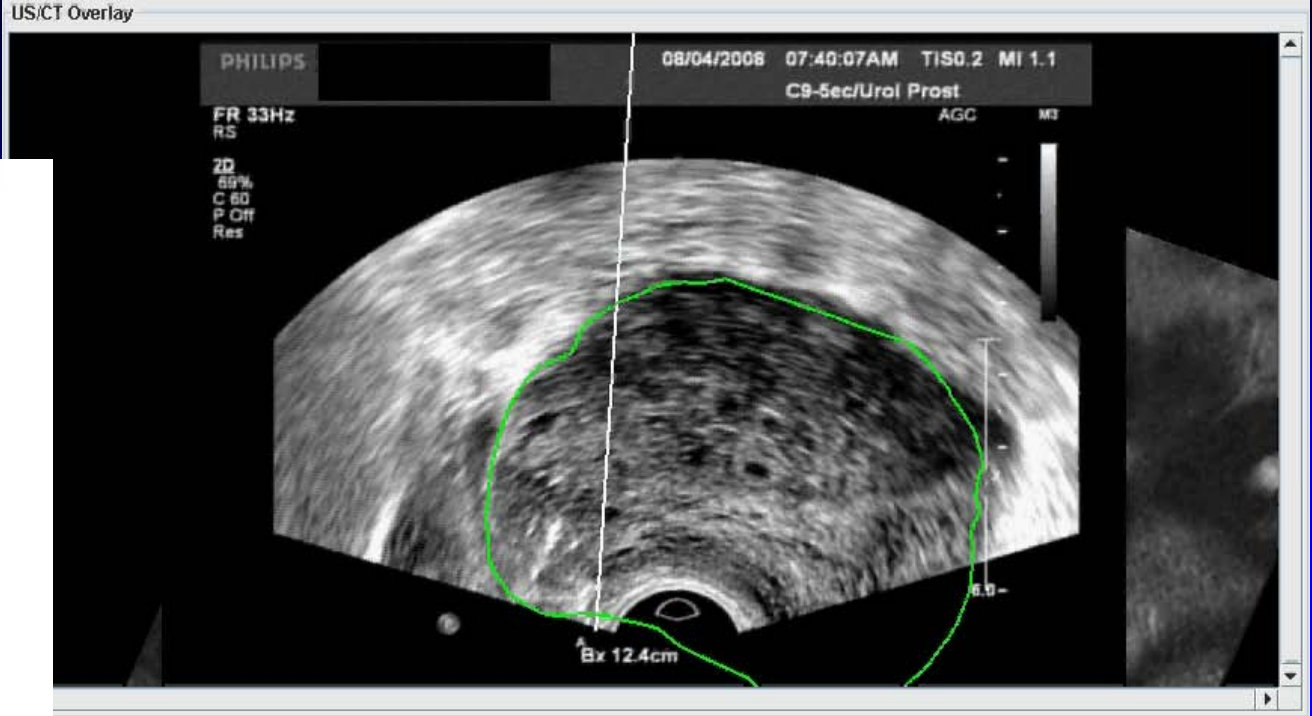
# MR-US prostate image fusion

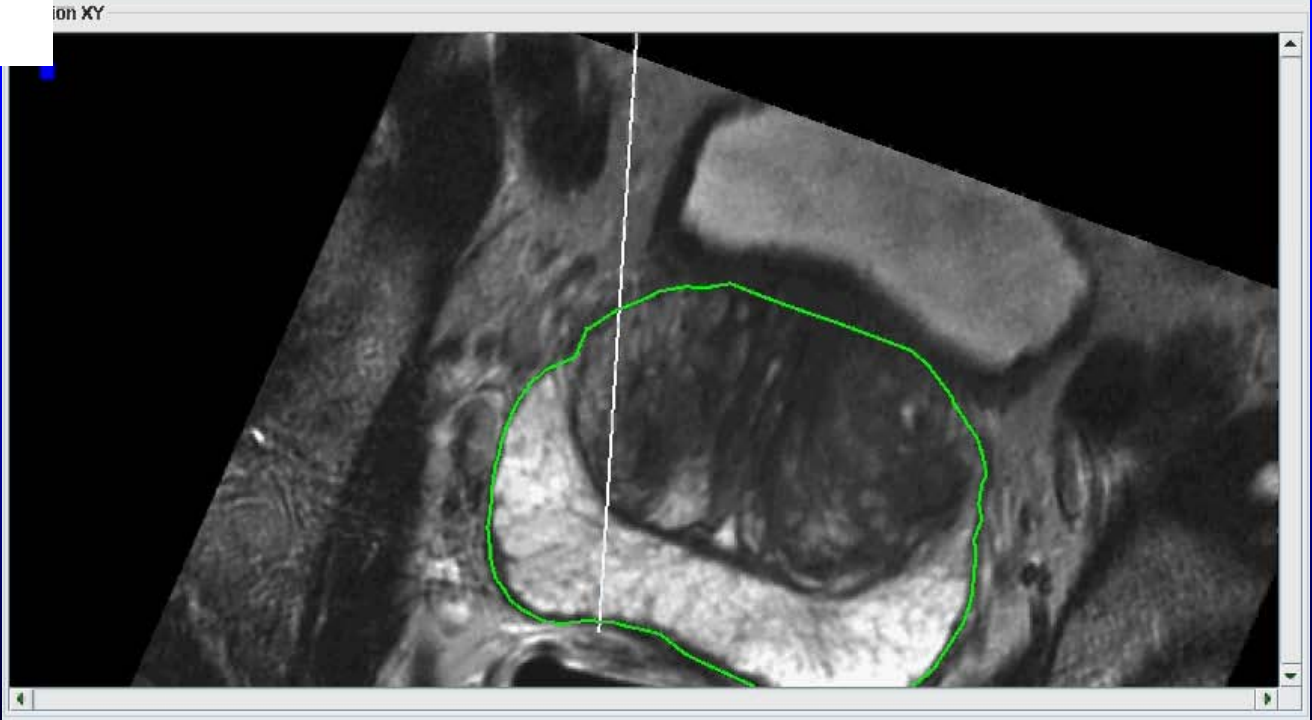





Without motion compensation



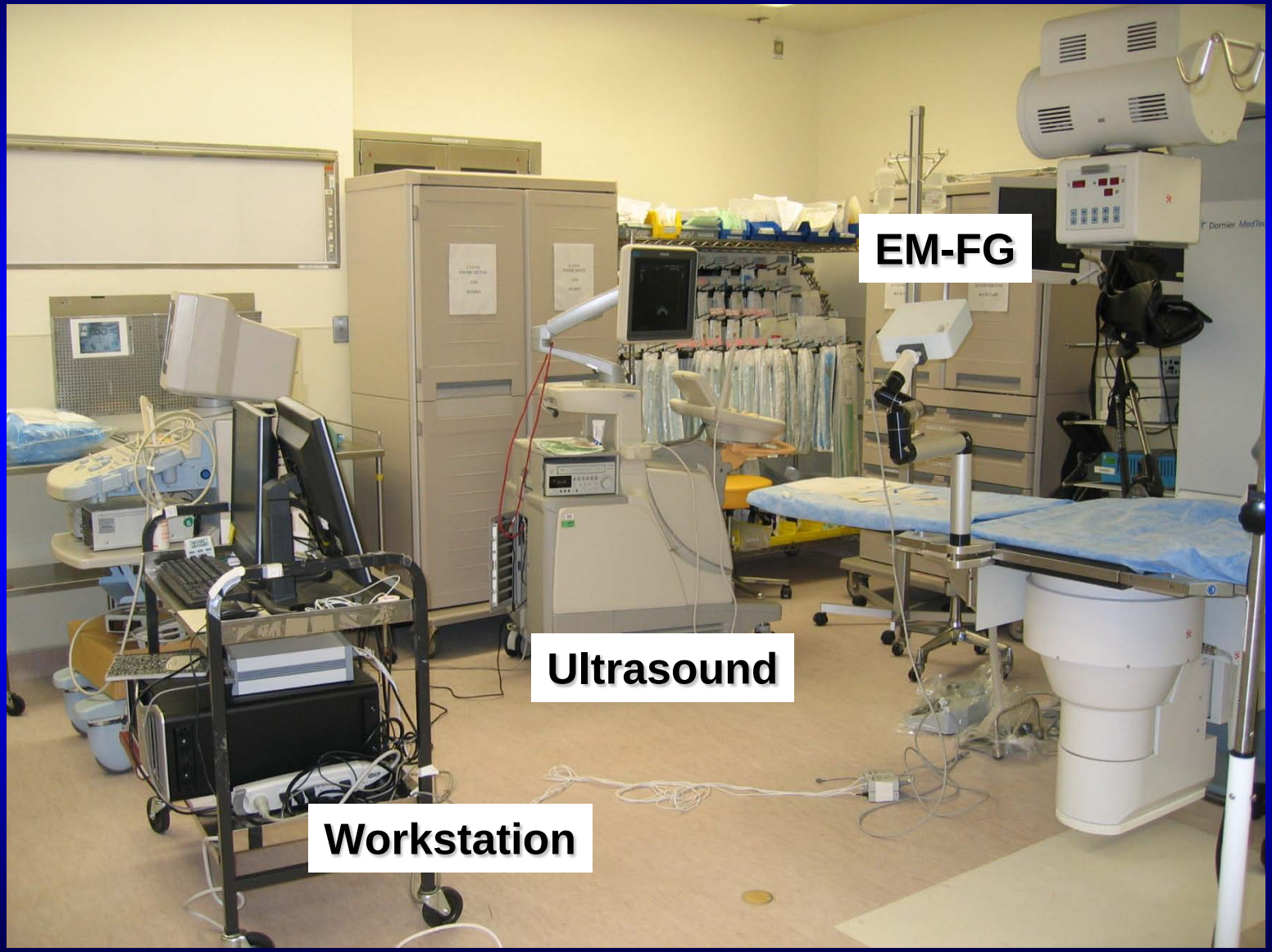

US/CT Overlay
PHILIPS
08/04/2008 07:40:07AM TIS0.2 MI 1.1
C9-5ec/Urol Prost
FR 33Hz
RS
AGC
2D
69%
C 60
P Off
Res
Bx 12.4cm


ion XY

# Conclusions

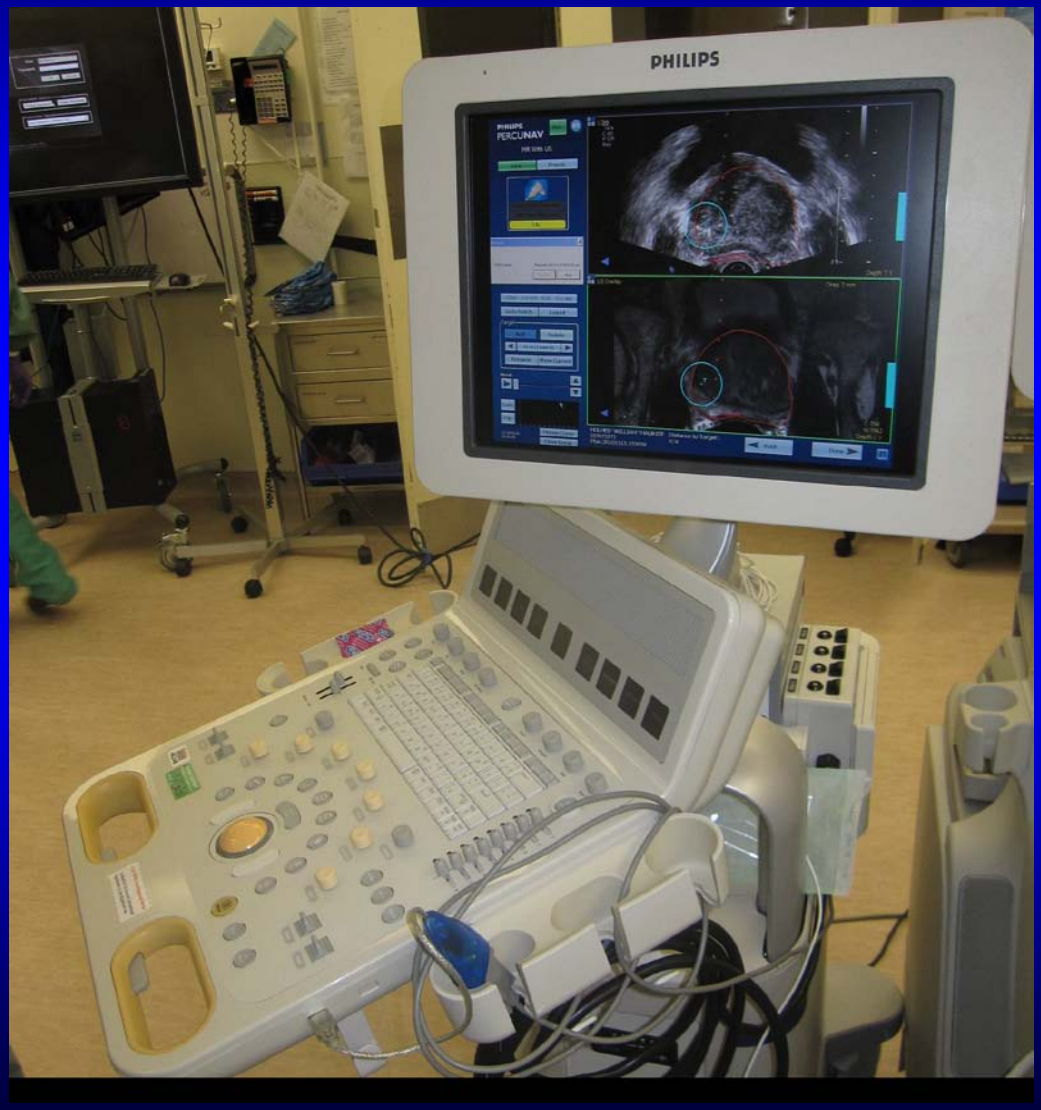
- Feasible to fuse prostate MRI and US in real time
- Real-time electromagnetic tracking enables targeting of MR visible PCa lesions with an office based ultrasound platform, without the need to utilize a hospital MRI suite

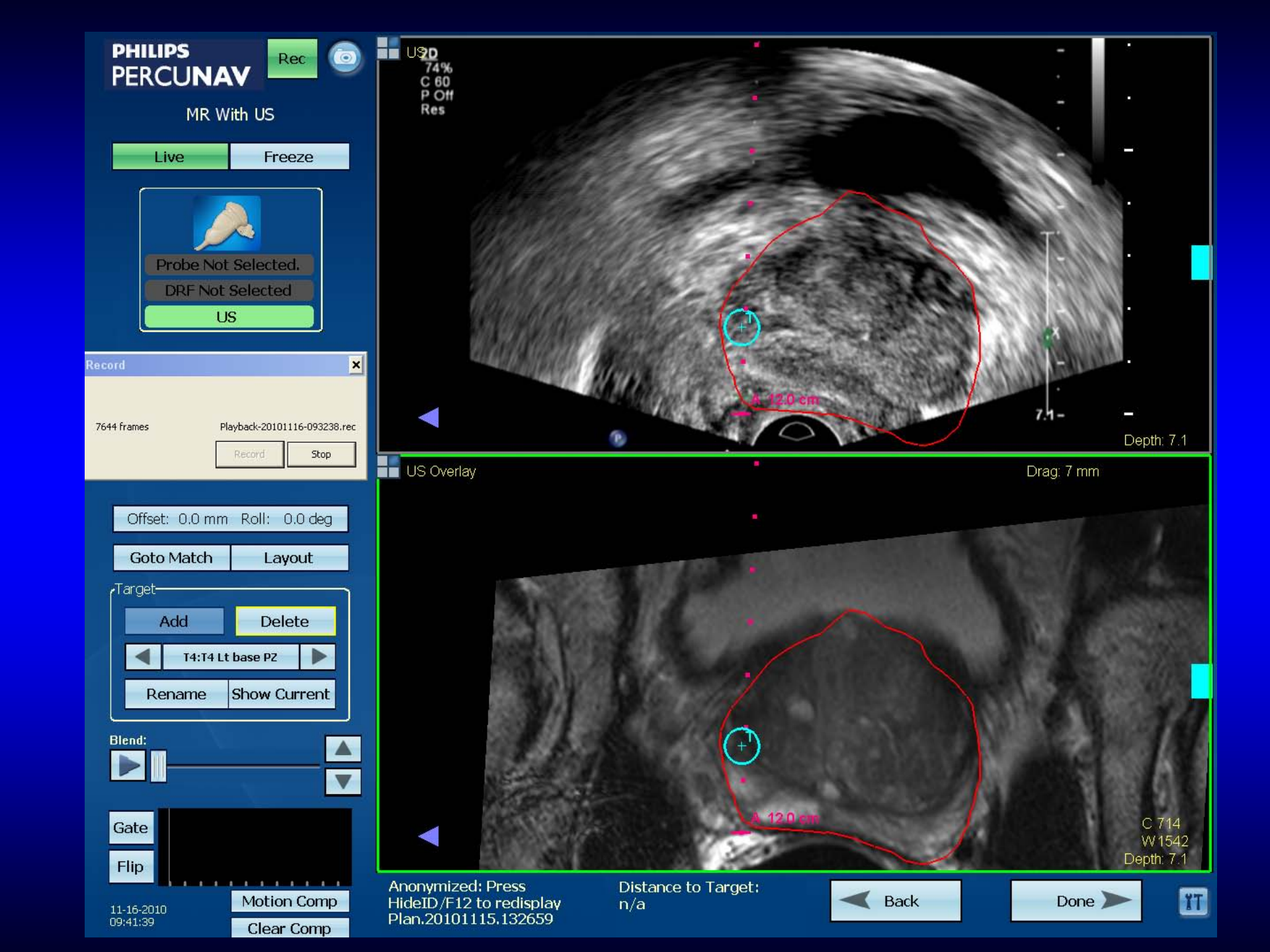
# Research Platform




CRADA NIH-Philips medical

# Commercially Viable Platform




PHILIPS
PERCUNAV
Rec
MR With US
Live
Freeze
Probe Not Selected.
DRF Not Selected
US
Record
7644 frames
Playback-20101116-093238.rec
Record
Stop
Offset: 0.0 mm Roll: 0.0 deg
Goto Match
Layout
Target
Add
Delete
T4:T4 Lt base PZ
Rename
Show Current
Blend:
Gate
Flip
11-16-2010
09:41:39
Motion Comp
Clear Comp
US
74%
C 60
P Off
Res
A 12.0 cm
7.1
Depth: 7.1
US Overlay
Drag: 7 mm
A 12.0 cm
C 714
W 1542
Depth: 7.1
Anonymized: Press
HideID/F12 to redisplay
Plan.20101115.132659
Distance to Target:
n/a
Back
Done

# MR/Sono 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**

National Cancer Institute

# *Cancer Detection Rates of MR/US Fusion Guided Prostate Biopsies Directly Correlate with Suspicion on Multiparametric MRI*

Paul H. Chung[1], Ardeshir R. Rastinehad[1], Angelo A. Baccala[1], Jochen Kruecker[5], Sheng Xu[5], Baris Turkbey[3], Julia K. Locklin[2], Stacey P. Gates[2], Joanna Shih[4], Neil D. Glossop[5], Peter L. Choyke[3], Bradford J. Wood[2], and Peter A. Pinto[1*]

[1] Urologic Oncology Branch,
[2] Department of Radiology and Imaging Sciences,
[3] Molecular Imaging Program,
[4] Biometric Research Branch,
National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

[5] Philips Research North America, Briarcliff, NY, USA

National Cancer Institute

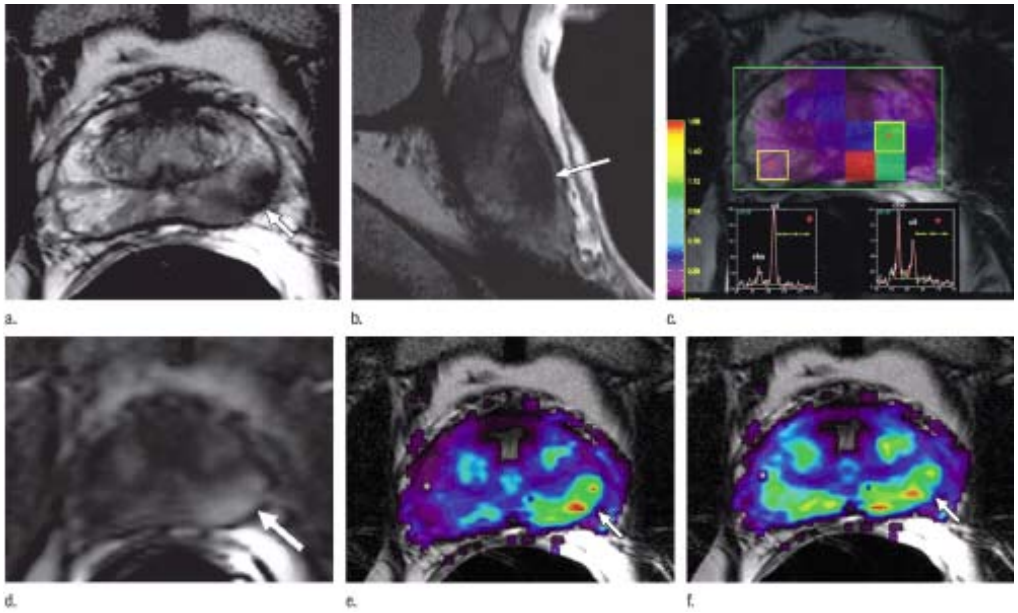
# Objective

- To determine the cancer detection rates of our MR/US fusion guided biopsy protocol

National Cancer Institute

# MR/US Fusion Guided Biopsy Workflow

1) 3T Multiparametric MR Scan
   - T2 weighted
   - Dynamic contract enhanced
   - MR spectroscopy
   - Diffusion weighted imaging




Turkbey et al. Radiology, 2010.

National Cancer Institute

# MR/US Fusion Guided Biopsy Workflow

1) 3T Multiparametric MR Scan

2) MRI Lesions are Assigned PCa Suspicion Levels
   - Low → 1 or 2 modalities
   - Medium → 3 modalities
   - High → 4 modalities

National Cancer Institute

# MR/US Fusion Guided Biopsy Workflow

1) 3T Multiparametric MR Scan

2) MRI Lesions are Assigned PCa Suspicion Levels

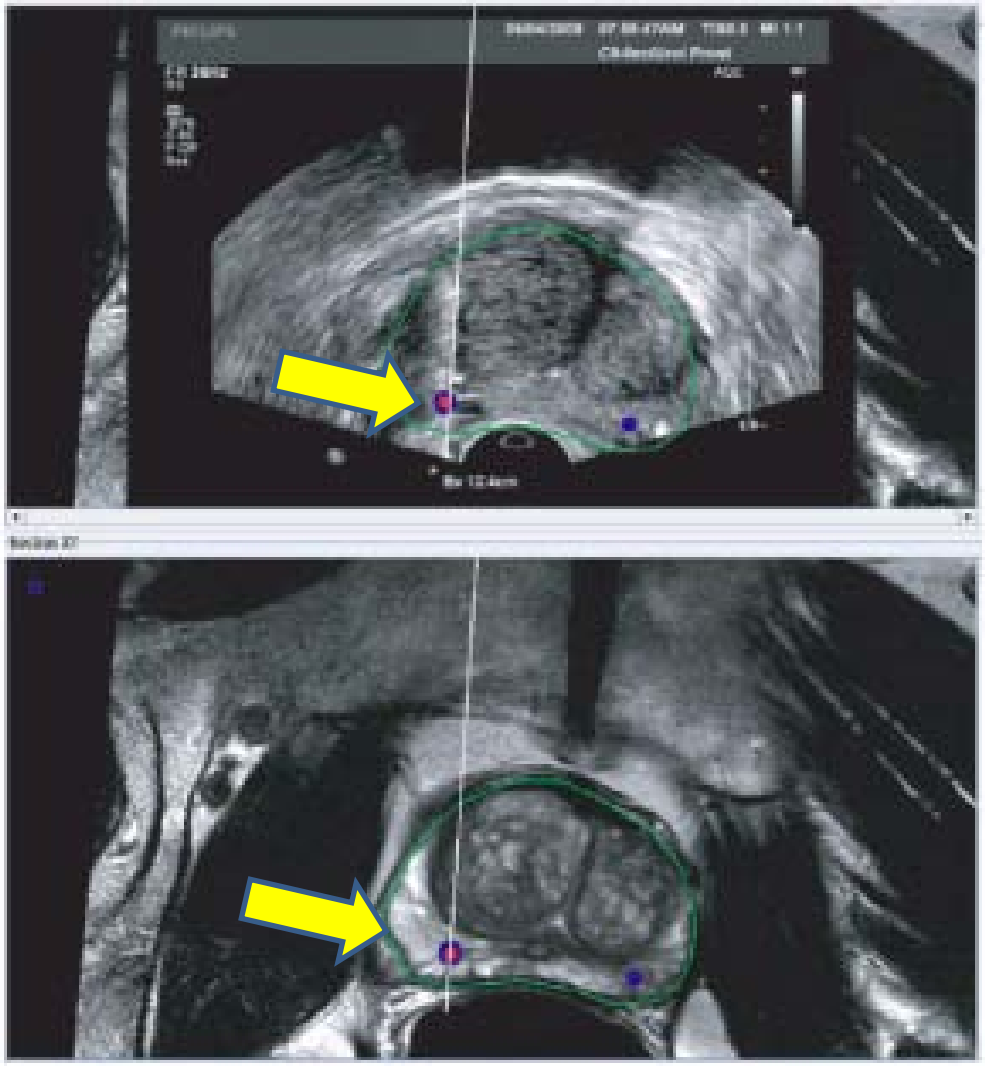
3) Biopsy Protocol
   - 12 Core Standard Biopsy
   - MR/US Fusion Guided Biopsy

National Cancer Institute

# MR/US Fusion Guided Biopsy

TRUS

MRI



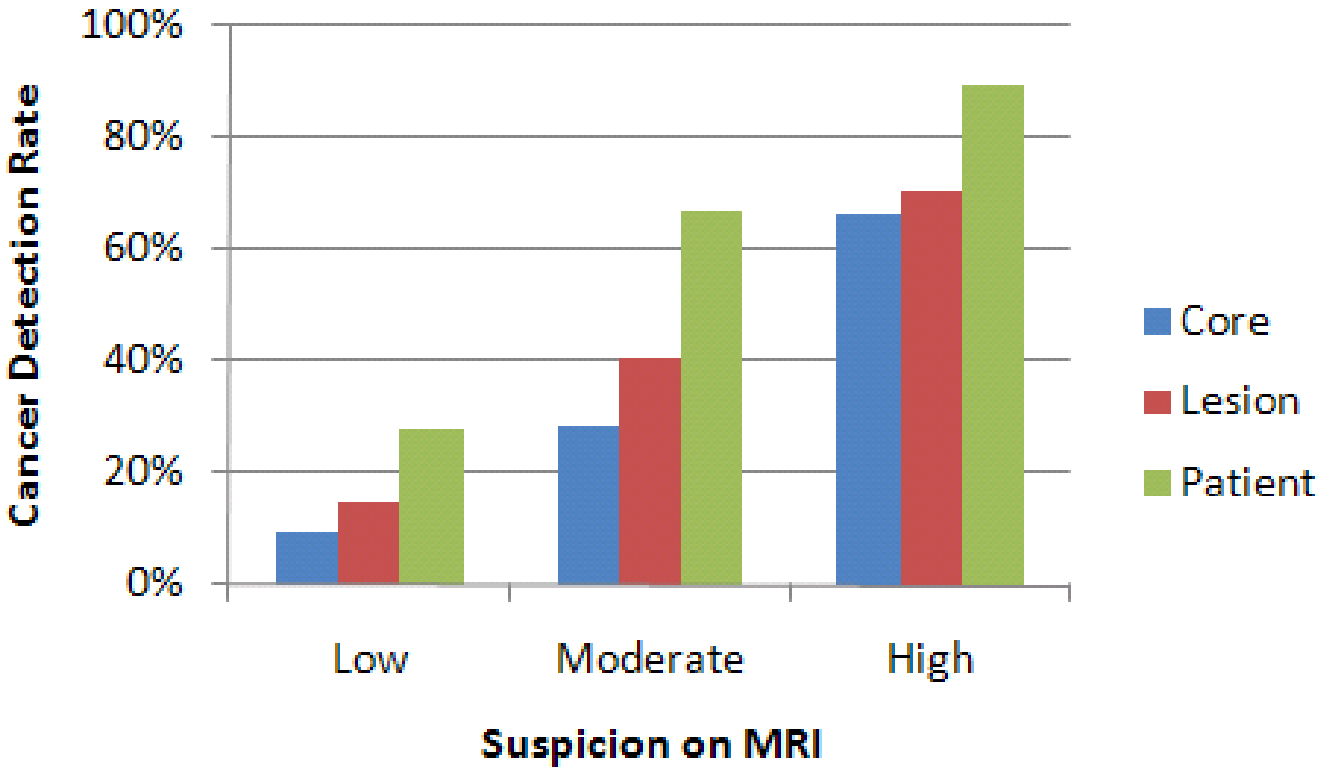
National Cancer Institute

# Patient Characteristics

| | |
|---|---|
| Total No. patients | 101 |
| Mean age, yrs (range) | 63 (41-82) |
| Mean PSA, ng/mL (range) | 8.3 (0.2-103) |
| Median PSA, ng/mL | 5.8 |
| Biopsy History | |
| No Prior | 36 |
| Negative | 29 |
| Positive | 36 |
| Mean No. lesions suspicious for cancer on MRI (range) | 2.6 (1-7) |
| Median No. lesions suspicious for cancer on MRI | 3 |
| Mean No. cores per lesion (range) | 2.2 (1-8) |
| Median No. cores per lesion | 2 |

National Cancer Institute

# Cancer Detection Rates

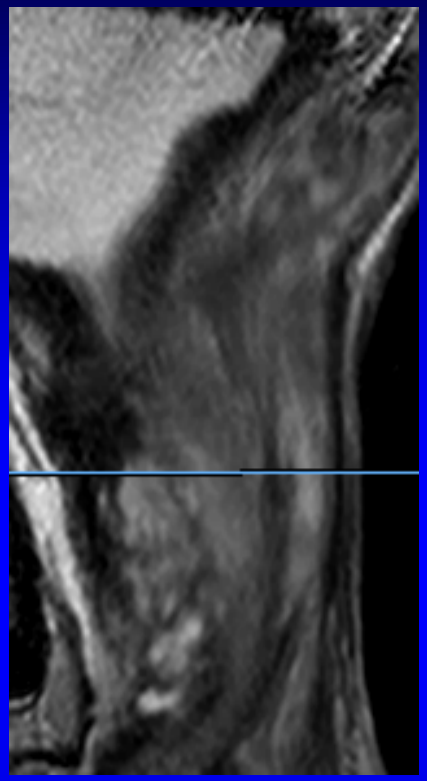


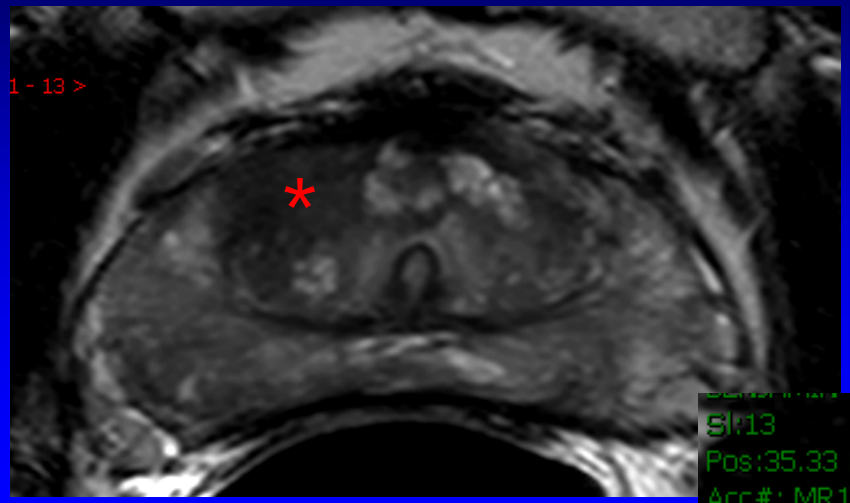

| | | |
|---|---|---|
| Core | n = 588 | p<0.0001 |
| Lesion | n = 264 | p<0.0001 |
| Patient | n = 101 | p<0.0001 |

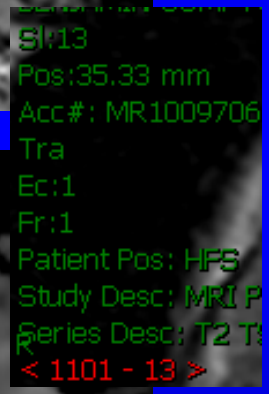
# Conclusions

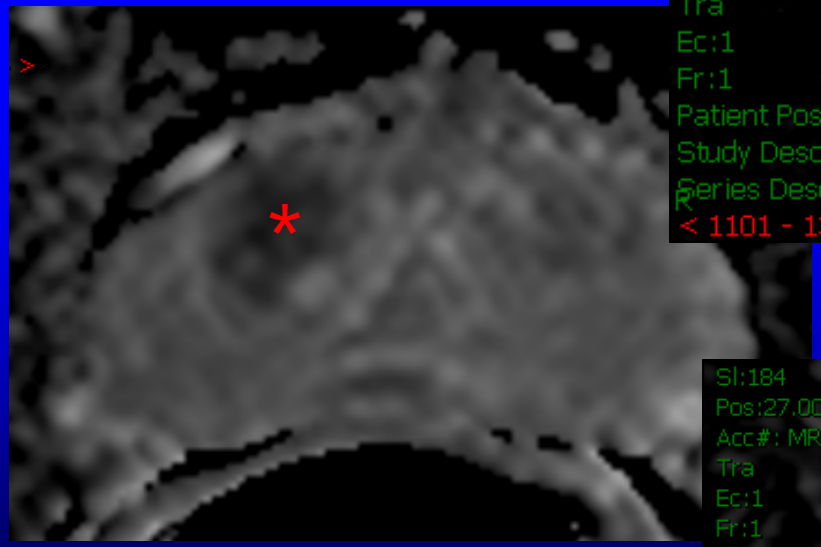
- Degree of suspicion on MR imaging directly correlates with incidence of cancer detected on biopsy
- 55% overall cancer detection rate
- 90% of patients with high suspicion on MR imaging were diagnosed with cancer
- This platform may have a future role in active surveillance and image guided focal therapy

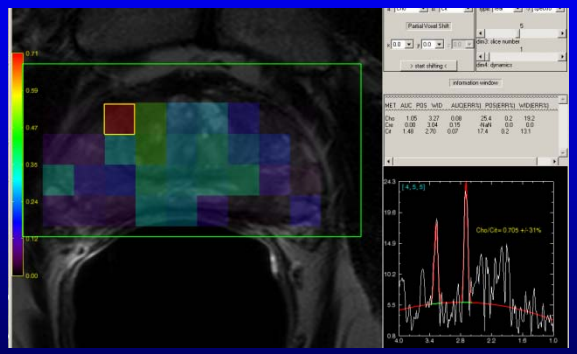
# 68 yo with rising PSA, annual bx x 7 including saturation bx

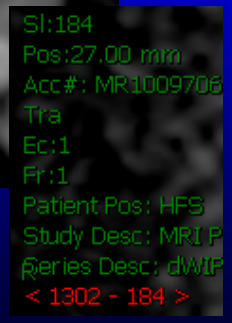









Right mid anterior central gland lesion

T2 +

DWI +

DCE +

MRS +

High suspicious

# Summary

- Multiparametric MR prostate imaging may be the platform for image guided biopsies
- Continued research is necessary to determine its role in the care of our patients with prostate cancer, especially for image guided focal therapy

# Era of Image Guided Focal Therapy for Prostate Cancer

# PSA Screening Effects on Prostate Cancer

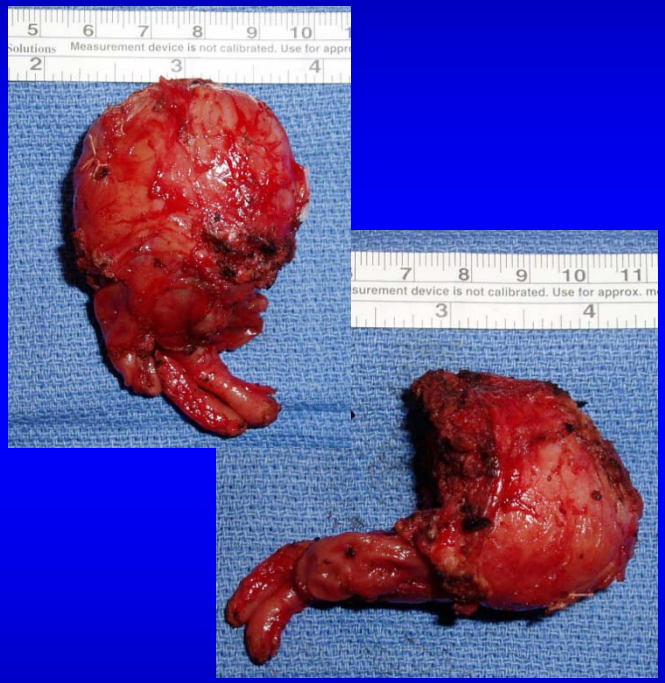
- Shift toward localized disease
- Shift toward lower volume disease
- Shift toward moderately differentiated disease

YET…

- Treatment remains directed at whole gland

# Methods of Treating Localized Prostate Cancer

- Surgery
  - Retropubic Prostatectomy
  - Perineal Prostatectomy
  - Laparoscopic Prostatectomy
  - Robotic Assisted Prostatectomy
- Radiation Therapy
  - External Beam
  - Interstitial Seed Implantation
- Active Surveillance
- Ablation



# What is best for our patients?

- High incidence of significant morbidity associated with whole gland therapy.
  - Impotence
  - Incontinence
- Patients and physicians are seeking less morbid treatment modalities
  - Image guided focal therapy

# Summary

- Localized prostate cancer is the new challenge of the PSA era
- Requires rethinking of our diagnostic and treatment strategies
- MRI is a promising diagnostic tool.
- Further research in this field is required.

# Acknowledgements


- Molecular Imaging
  - Peter Choyke, M.D.
  - Baris Turkbey, M.D.
  - Marcelino Bernado, Ph.D.
  - Vijay Shah, Ph..D
  - Tom Pohida, Ph.D.
- Pathology
  - Maria Merino, M.D.
  - Haresh Mani, M.D.
  - Vladimir Valera, M.D.
- Interventional Radiology
  - Bradford Wood, M.D.
  - Jochen Krueker, Ph.D.
  - Sam Kadoury, Ph.D.
  - Sheng Xu, Ph.D
  - Julia Locklin, R.N.
  - Stacey Gates, R.N.
  - Carey Buckner, R.N.

# Urologic Oncology Branch, NCI