Eight Year Interim Results of a 20-Year Observational Study of Transrectally Delivered, MRI-Guided Laser Interstitial Thermal Therapy of Prostate Cancer in an Outpatient Setting

Prepared for Brigham and Women's, May 8, 2018

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Department of Internal Medicine
Chief Research Officer, Desert Medical Imaging

DMI Desert Medical Imaging®

UCR School of Medicine

Disclosures:

Ms. Greenwood has nothing to disclose

Genomic Classifiers and their Possible Role in Focal Therapy

Topics to be discussed:

- The history of biopsy strategies
- Evolution of mpMRI
- Technical aspects of MRI-guided biopsies
- Rationale for MRI-guided laser focal therapy of PCa
- Update on NCT #02243033 (Phase II clinical trial)

STATE *of* WISCONSIN

OFFICE *of the* GOVERNOR

Proclamation

WHEREAS, on Thursday, June 4, 2015, Milwaukee Area Technical College is hosting a "Wake up and Smell the Coffee – Prostate Cancer Update 2015" session from 11 a.m. – 2 p.m., that is open to the public; and

WHEREAS, in the United States alone, new prostate cancer cases for 2014 were estimated at 233,000 and deaths at more than 29,000; and

WHEREAS, screening can help diagnose the disease in its early stages, increasing the chances of survival; and

WHEREAS, there are no noticeable symptoms of prostate cancer while it is still in the early stages, making screening critical; and

WHEREAS, ongoing research promises further improvements in prostate cancer prevention, early detection, and treatments; and

WHEREAS, educating everyone about prostate cancer and early detection strategies is crucial to saving lives, and preserving and protecting families;

NOW, THEREFORE, I, Scott Walker, Governor of the State of Wisconsin, do hereby proclaim Thursday, June 4, 2015, as

PROSTATE CANCER AWARENESS DAY

throughout the State of Wisconsin, and I commend this observance to all of our citizens.

IN TESTIMONY WHEREOF, I have hereunto set my hand and caused the Great Seal of the State of Wisconsin to be affixed. Done at the Capitol in the City of Madison this 3rd day of June 2015.

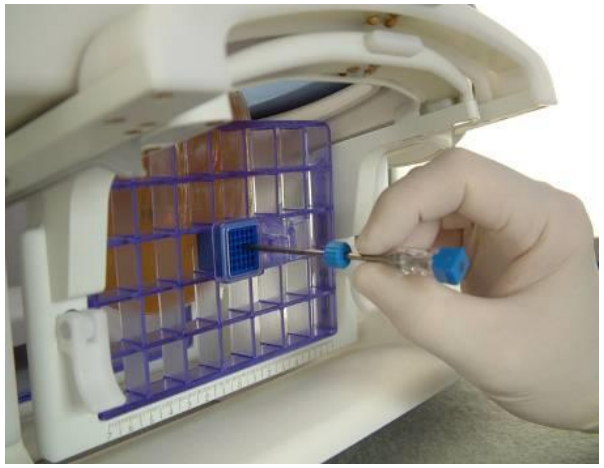
SCOTT WALKER
GOVERNOR

By the Governor:

DOUGLAS LA FOLLETTE
Secretary of State

BREAST MRI

- Complements Mammo / US
- Breast intervention **(do a targeted biopsy under MR)** per ACR practice guidelines
- Mastectomy vs. lumpectomy and focal treatment



PROSTATE MRI

- Complements PSA / DRE /TRUS
- Prostate intervention **(targeted biopsy under MR-guidance)**
- MR/US fusion biopsy
- Focal therapy vs. whole-gland, radical treatment (prostatectomy, XRT, ADT)

Literature Timeline 1920 - present

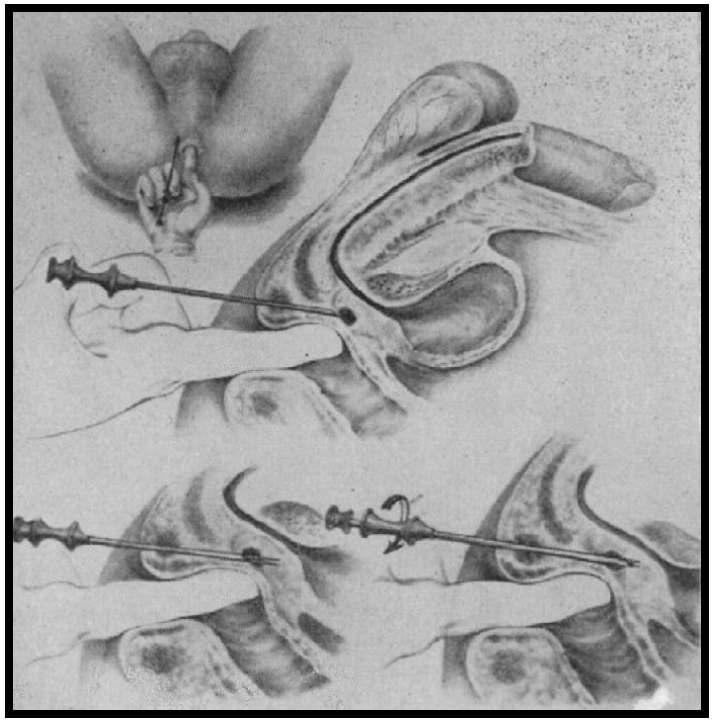
1920's	1922 – Barringer: Transperineal needle biopsy	1926 – Young: Open perineal biopsy	
1930's	1930 – Ferguson: First perineal needle aspiration biopsy	1937 – Astraldi: First transrectal biopsy	
1940's	-----	-----	-----
1950's	-----	-----	-----
1960's	1963 – Takahashi and Ouichi: TRUS to evaluate prostate	1968 – Watanabe et al.: First clinically useful TRUS images	1968 – McNeal: proposes three distinct glandular zones
1970's			
1980's	Mid-1980's – improvements in transducer technology and biopsy capability	1986 – PSA test introduced for prostate cancer screening	1989 – Hodge et al.: modern era of systematic prostate biopsy begins
1990's	1995 – Stamey: modified sextant technique to include laterally directed	1996 – Nash et al.: peri-prostatic nerve blockade used for biopsy pain management	1997 – Eskew et al.: systematic extended biopsy technique
2000's	2004 – Beyersdorff et al.: MRI-guided prostate biopsy at 1.5T		
2010's	2011 – Greenwood et al.: Transrectal MRI-guided laser interstitial thermal therapy of PCa	2011 – Pinto et al.: MRI/US fusion prostate biopsy	2012 – NCCN Guidelines include Multiparametric MRI

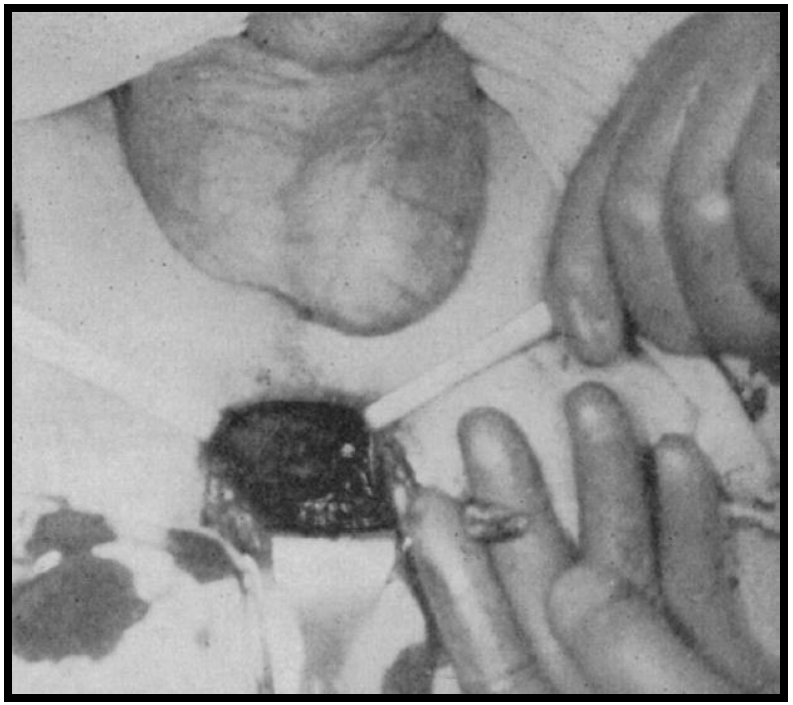
Adapted from Applewhite, Cancer Control 141, March/April 2001, Vol. 8 No.2

Levana Yeo, Dharmesh Patel, Christian Bach, Athanasios Papatsoris, Noor Buchholz, Islam Junaid and Junaid Masood (2011). The Development of the Modern Prostate Biopsy, Prostate Biopsy, Dr. Nabil K. Bissada (Ed.), ISBN: 978-953-307-702-4, InTech, Available from: http://www.intechopen.com/books/prostate-biopsy/thedevelopment-of-the-modern-prostate-biopsy

Prostate Biopsy in the 1920‘s

1920’s	**1922 – Barringer: Transperineal needle biopsy**	**1926 – Young: Open perineal biopsy**

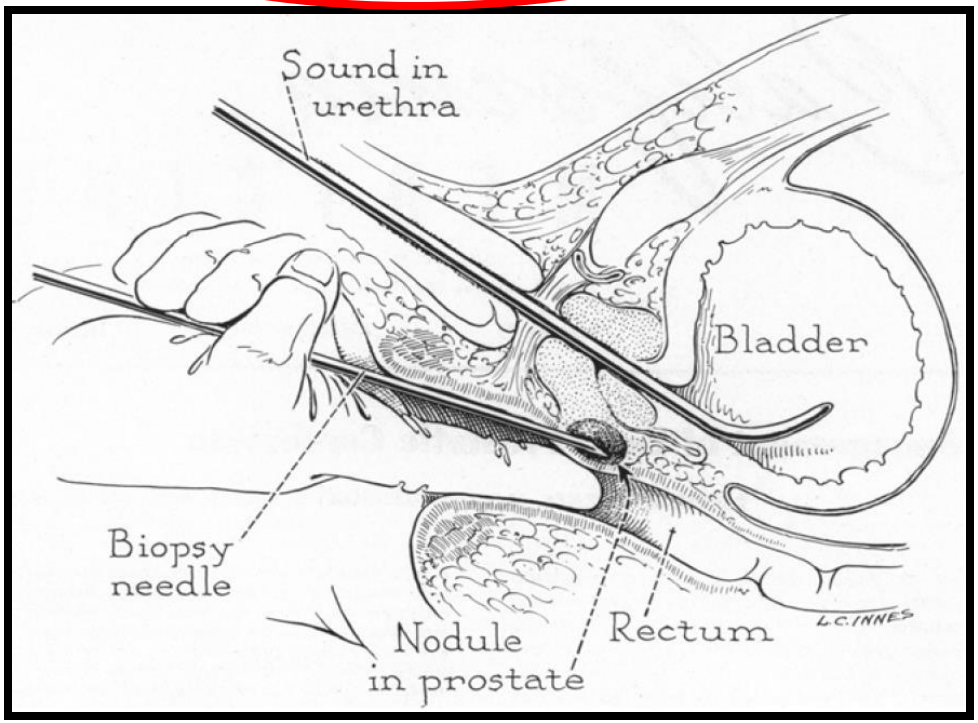




Kaufman, J.J., Rosenthal, M. and Goodwin, W.E.. Needle biopsy in diagnosis of prostate cancer. California Medicine. 1954; 81; 5: 308-313

Prostate Biopsy in the 1930‘s

1930’s	**1930 – Ferguson: First perineal needle aspiration biopsy**	**1937 – Astraldi: First transrectal biopsy**



Astraldi, A. Diagnosis of cancer of the prostate: biopsy by rectal route. Urol Cutan Rev. 1937; 41: 421–427

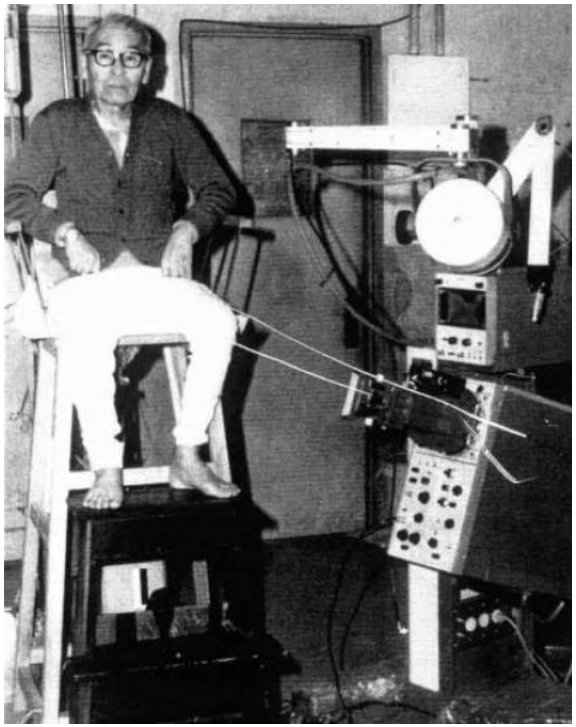
Prostate Biopsy in the 1960‘s

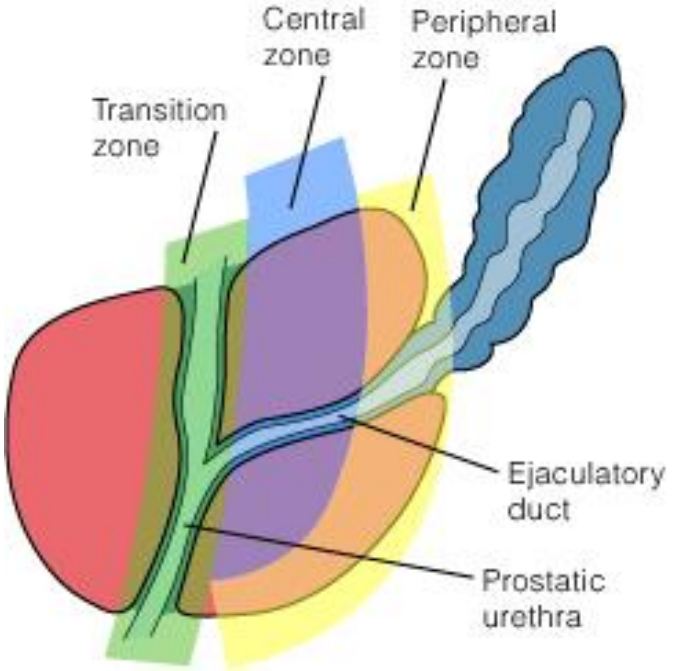
1960’s

1963 – Takahashi and Ouichi: TRUS to evaluate prostate

1968 – Watanabe et al.: First clinically useful TRUS images

1968 – McNeal: proposes three distinct glandular zones





Am J Clin Pathol. 1968;49:347.

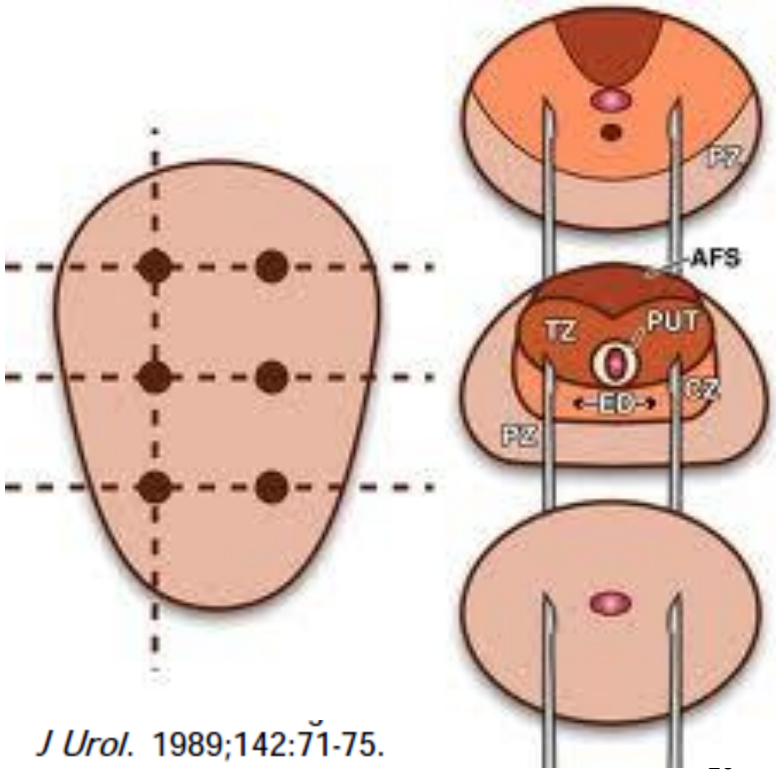
J Clin Ultrasound. **1974;2:91-98**

Prostate Biopsy in the 1980‘s

1980’s **Mid-1980’s – improvements in transducer technology and biopsy capability**

1986 – PSA test introduced for prostate cancer screening

1989 – Hodge et al.: modern era of systematic prostate biopsy begins



J Urol. 1989;142:71-75.

Prostate Biopsy in the 1990‘s

1990’s	1995 – Stamey: modified sextant technique to include laterally directed	1996 – Nash et al.: peri-prostatic nerve blockade used for biopsy pain management	1997 – Eskew et al.: systematic extended biopsy technique

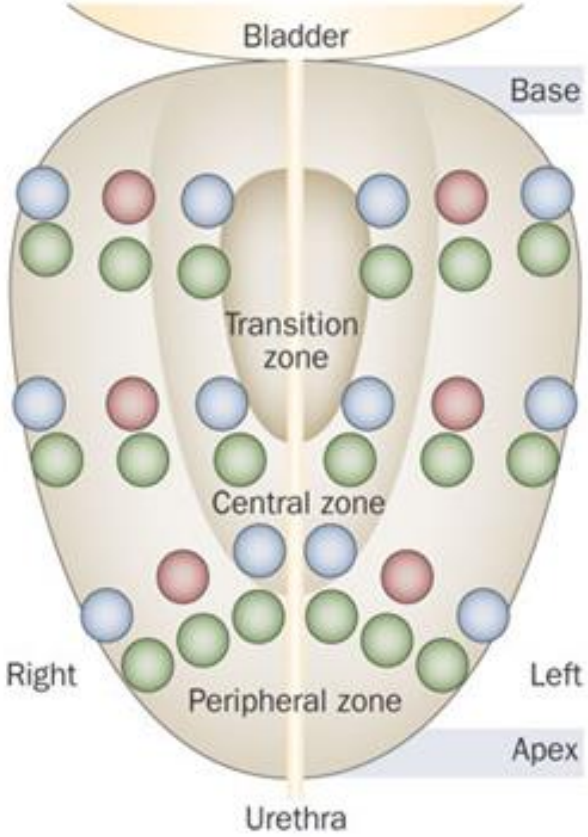
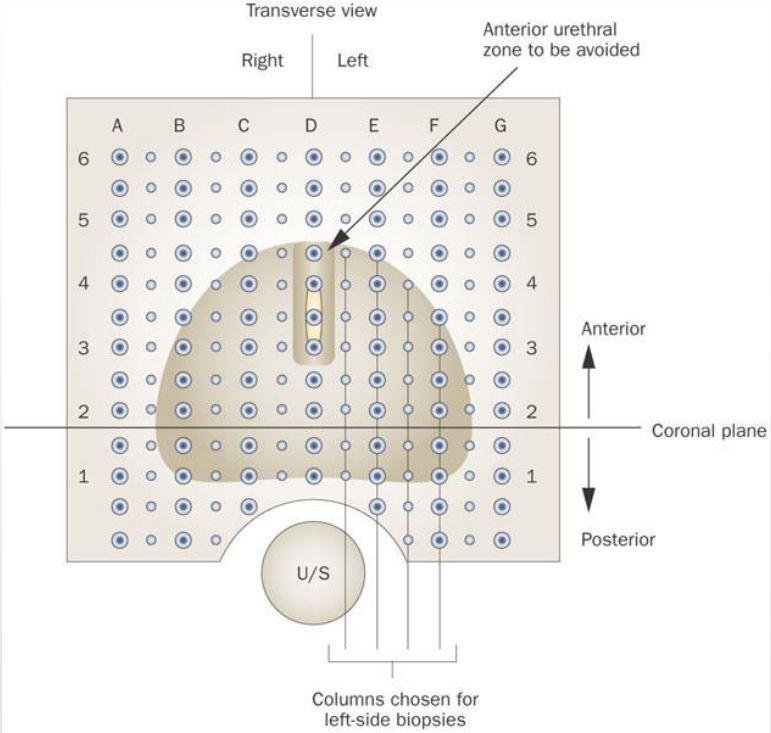


Figure 2 Prostate as seen on transrectal ultrasonography during saturation biopsy



Modified, with permission, from Whitmore, W. F. and Barzell, W. E. (2003) Urology Times, 1 May © Winston E. Barzell.

Andriole GL (2009) The lottery of conventional prostate biopsy
Nat Rev Urol doi:10.1038/nrurol.2009.46

nature REVIEWS UROLOGY

Saturation Biopsy

Photography courtesy of Thomas Polascik. M.D., Duke University

Saturation Biopsy

Saturation Biopsy

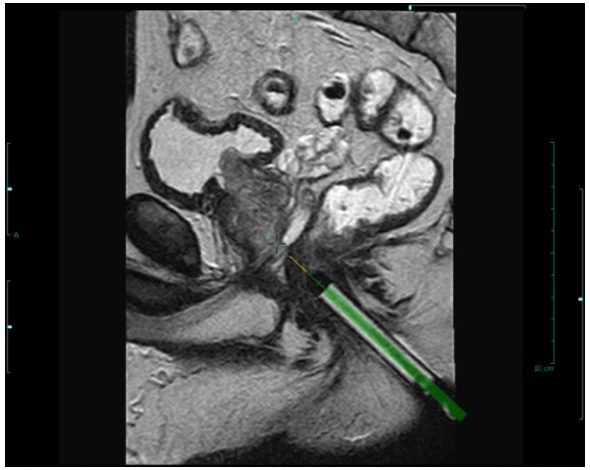
Saturation Biopsy

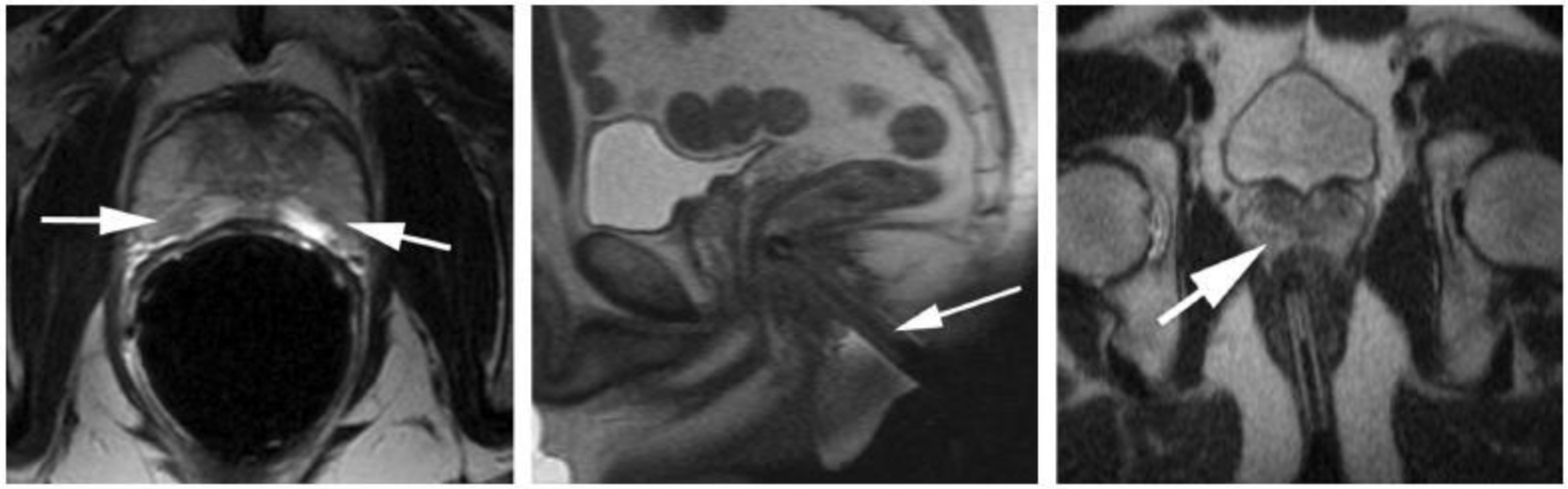
CLOSE TO HOME **JOHN MCPHERSON**

"Good news! The exploratory surgery turned up negative!"

Prostate Biopsy in the 2000‘s

2000’s **2004 – Beyersdorff et al.: MRI-guided prostate biopsy at 1.5T**





Beyersdorff D et al. MR Imaging–guided Prostate Biopsy with a Closed MR Unit at 1.5 T: Initial Results. Radiology 2005; 234:576–581.

Ultrasound vs. MRI

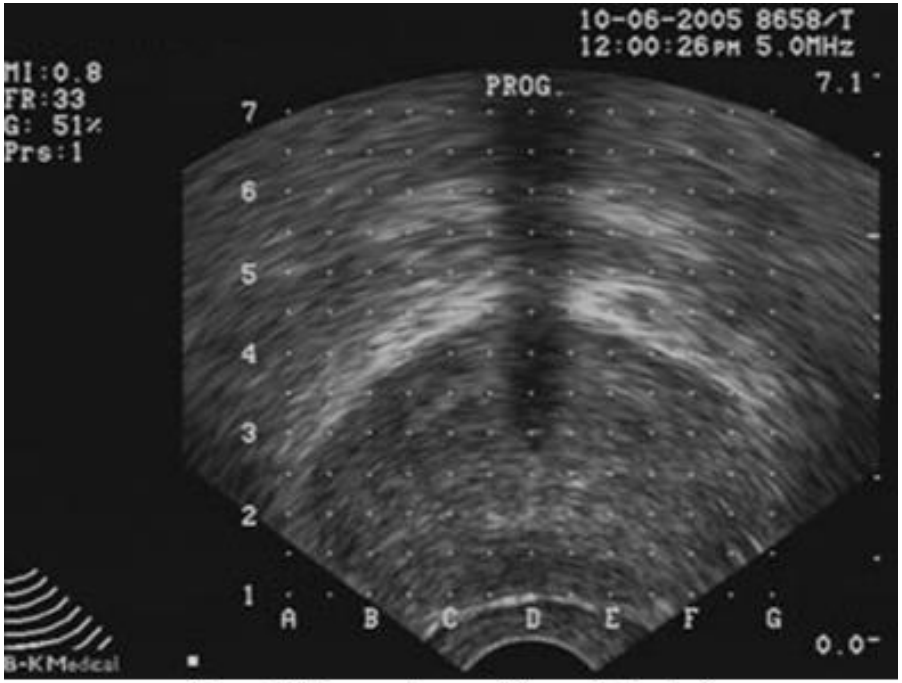
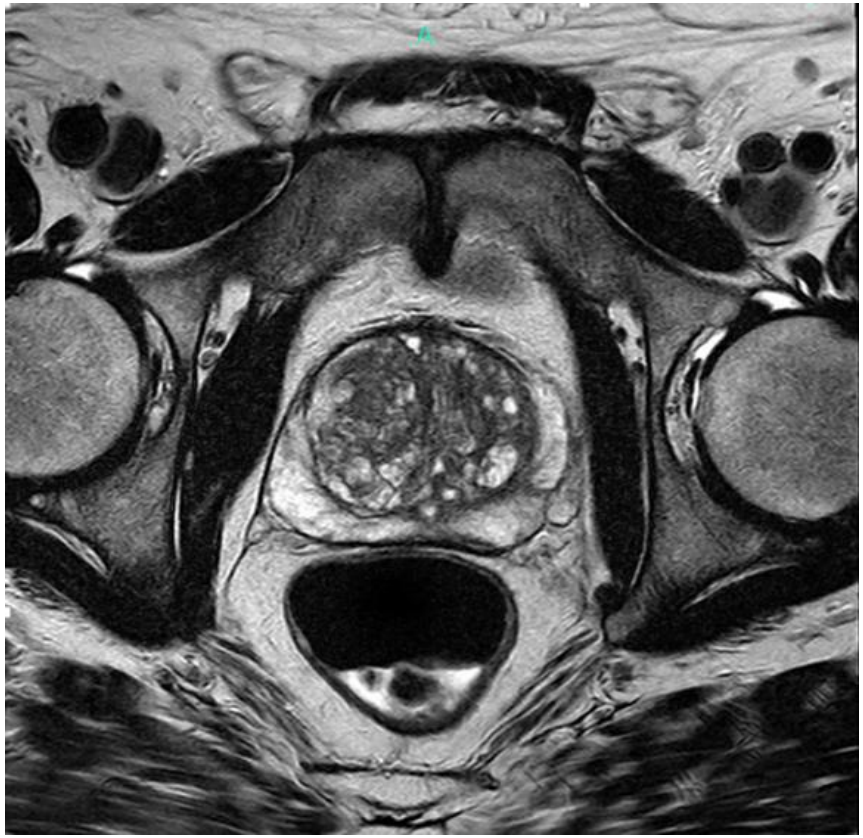
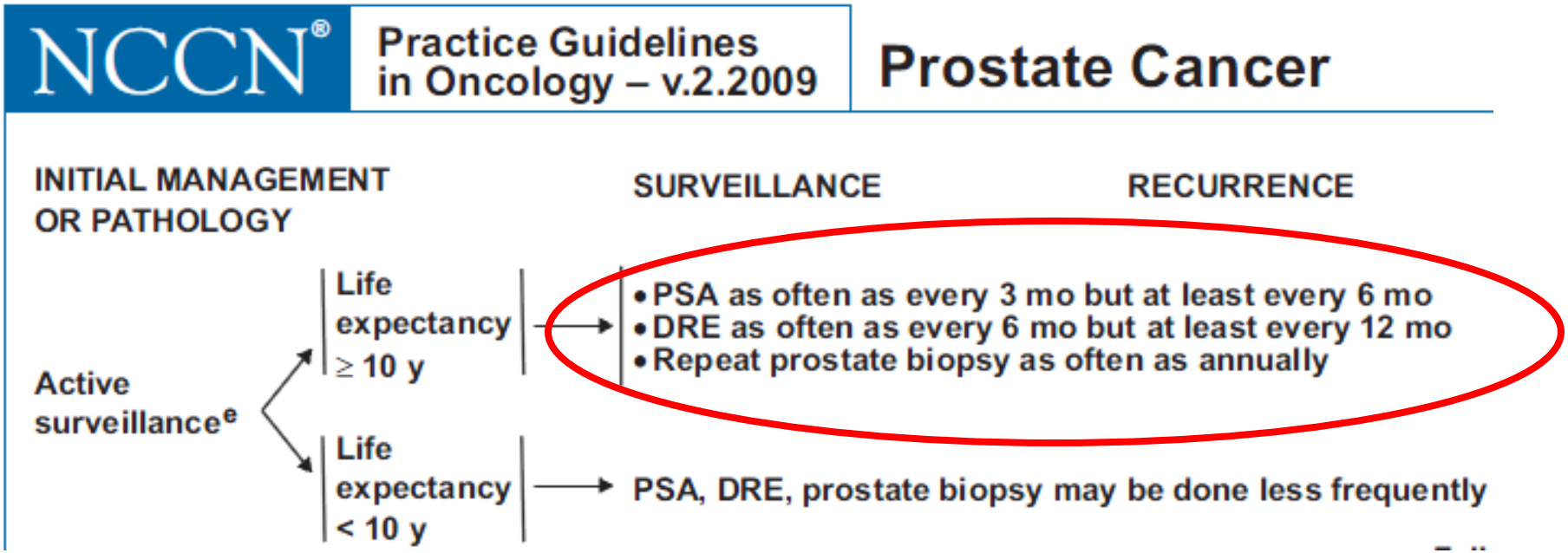


Figure 7: Ultrasound scan of the prostate gland



National Guidelines - 2009



Prostate Intervention in the 2010's

2010's	2011 – Greenwood et al.: Transrectal MRI-guided laser interstitial thermal therapy of PCa	2011 – Pinto et al.: MRI/US fusion prostate biopsy	2012 – NCCN Guidelines include Multiparametric MRI

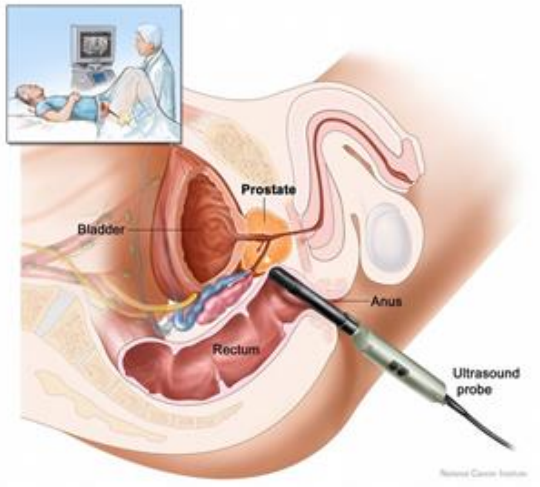
National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2012
Prostate Cancer Early Detection

NCCN Guidelines Index
Prostate Early Detection TOC
Discussion

Repeat Biopsy Technique

Patients with prior negative biopsies, yet persistently rising PSA values should undergo repeat biopsy. Important factors in predicting chance of cancer on repeat biopsy include PSAV and the adequacy of initial biopsy (number of cores, prostate size). Cancer detection rates are higher in men with prior negative sextant biopsies compared to those with prior negative extended biopsies. Yields are highest in the laterally directed cores and the apical cores.[90] Particular attention should be given to apical sampling including the anterior apical horn, which is comprised of peripheral zone.[91] Transition zone biopsies can be considered in repeat biopsy patients. In patients with two negative extended biopsies, yet persistently rising PSA values, a saturation biopsy may be considered.[92] Recent evidence showed that multiparametric MRI (T2 weighting plus functional techniques such as diffusion weighting) can aid in cancer detection in patients with persistent PSA elevation but negative TRUS-guided biopsy (reviewed by Pinto et al.[93]). Additional MRI imaging can be considered in select cases.



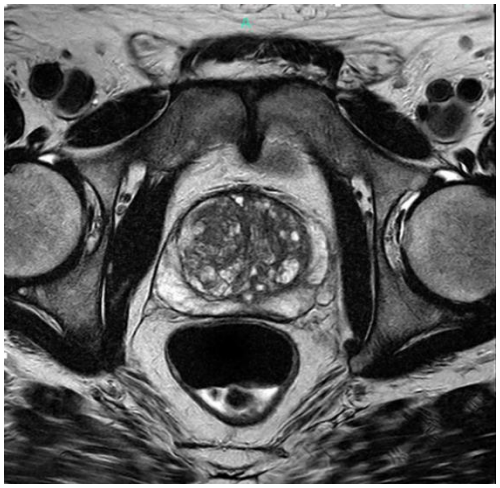
European Guidelines - 2012

Eur Radiol (2012) 22:746–757
DOI 10.1007/s00330-011-2377-y

UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer



PI-RADS v2

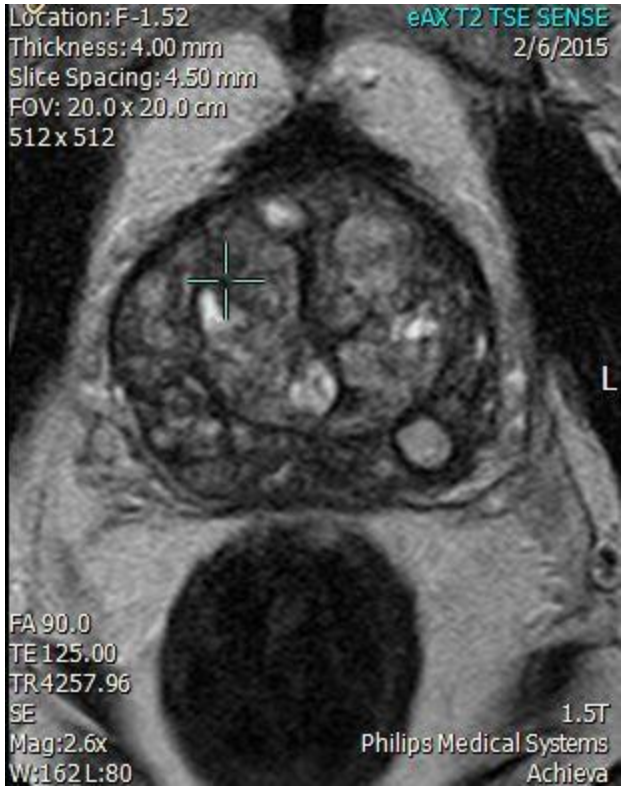
PI-RADS v2 Classification*

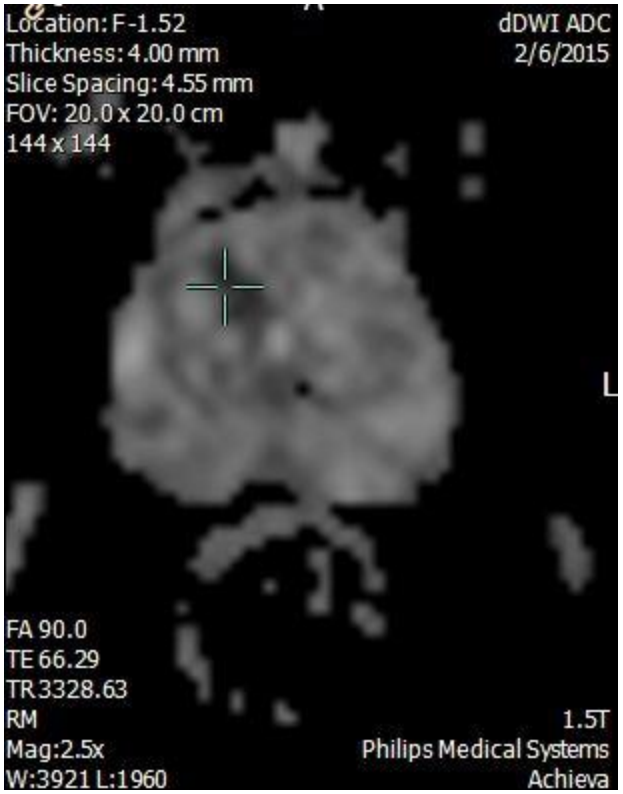
PI-RADS 5	Highly Suspicious for Malignancy
PI-RADS 4	Probably Malignant
PI-RADS 3	Indeterminate
PI-RADS 2	Probably Benign
PI-RADS 1	Most Probably Benign

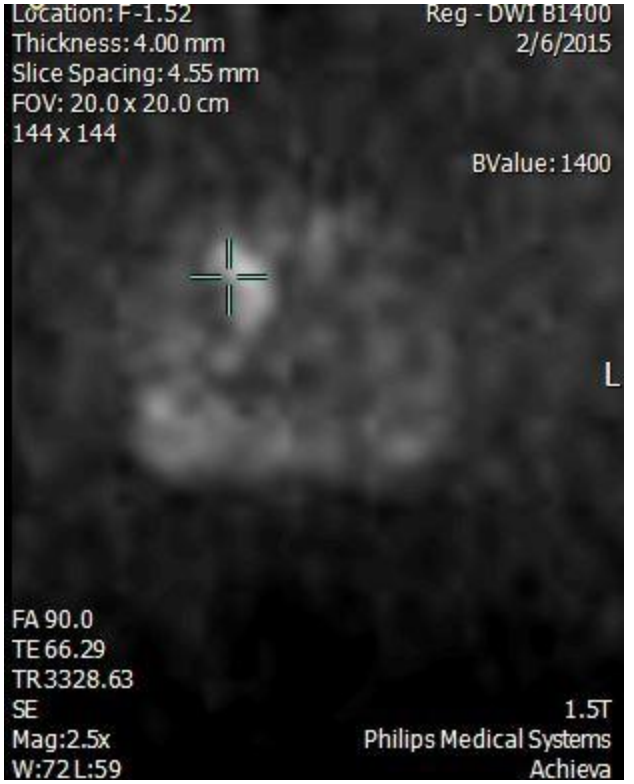
*Based Upon ACR Guidelines January 2015.

http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/PIRADS/PIRADS%20V2.pdf

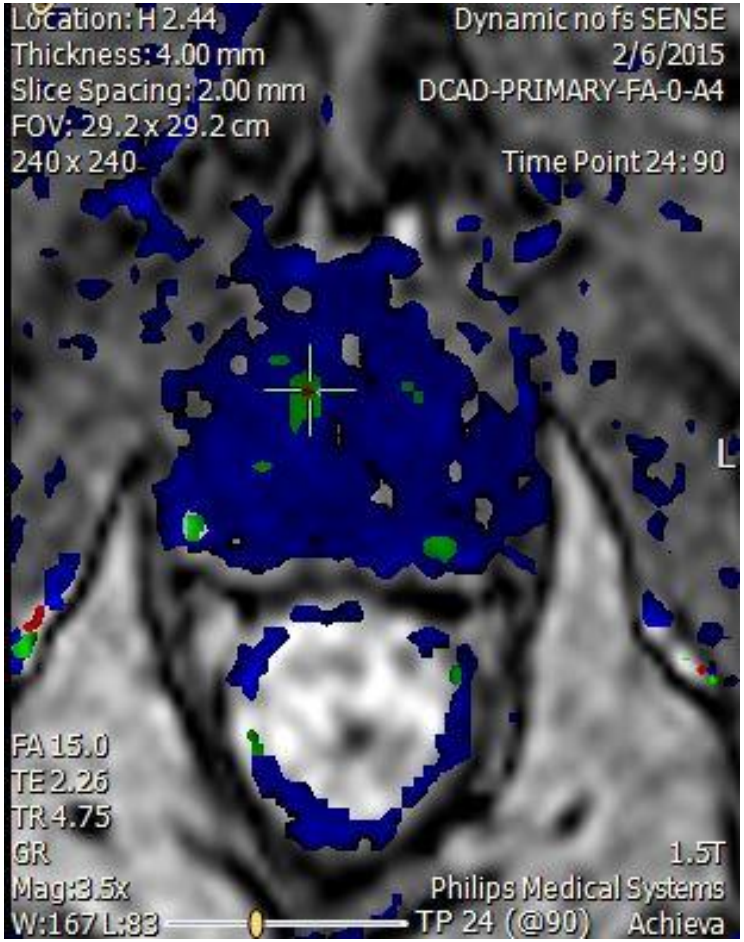
PI-RADS v2

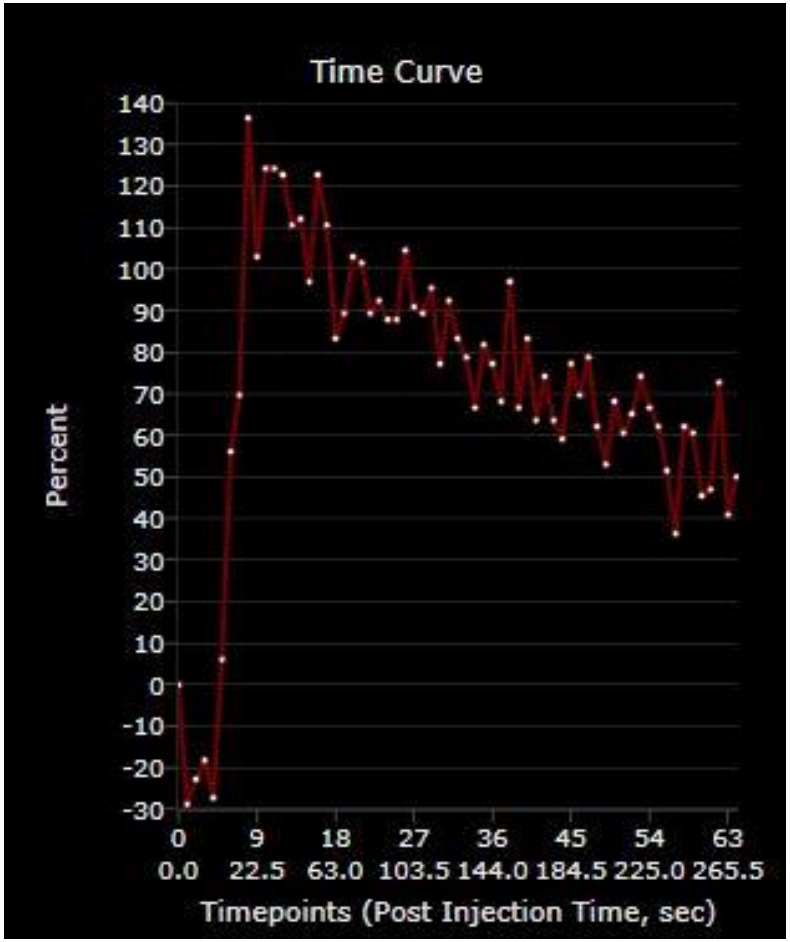

Location: F-1.52
Thickness: 4.00 mm
Slice Spacing: 4.50 mm
FOV: 20.0 x 20.0 cm
512 x 512
eAX T2 TSE SENSE
2/6/2015
L
FA 90.0
TE 125.00
TR 4257.96
SE
Mag: 2.6x
W: 162 L: 80
1.5T
Philips Medical Systems
Achieva


Location: F-1.52
Thickness: 4.00 mm
Slice Spacing: 4.55 mm
FOV: 20.0 x 20.0 cm
144 x 144
dDWI ADC
2/6/2015
L
FA 90.0
TE 66.29
TR 3328.63
RM
Mag: 2.5x
W: 3921 L: 1960
1.5T
Philips Medical Systems
Achieva

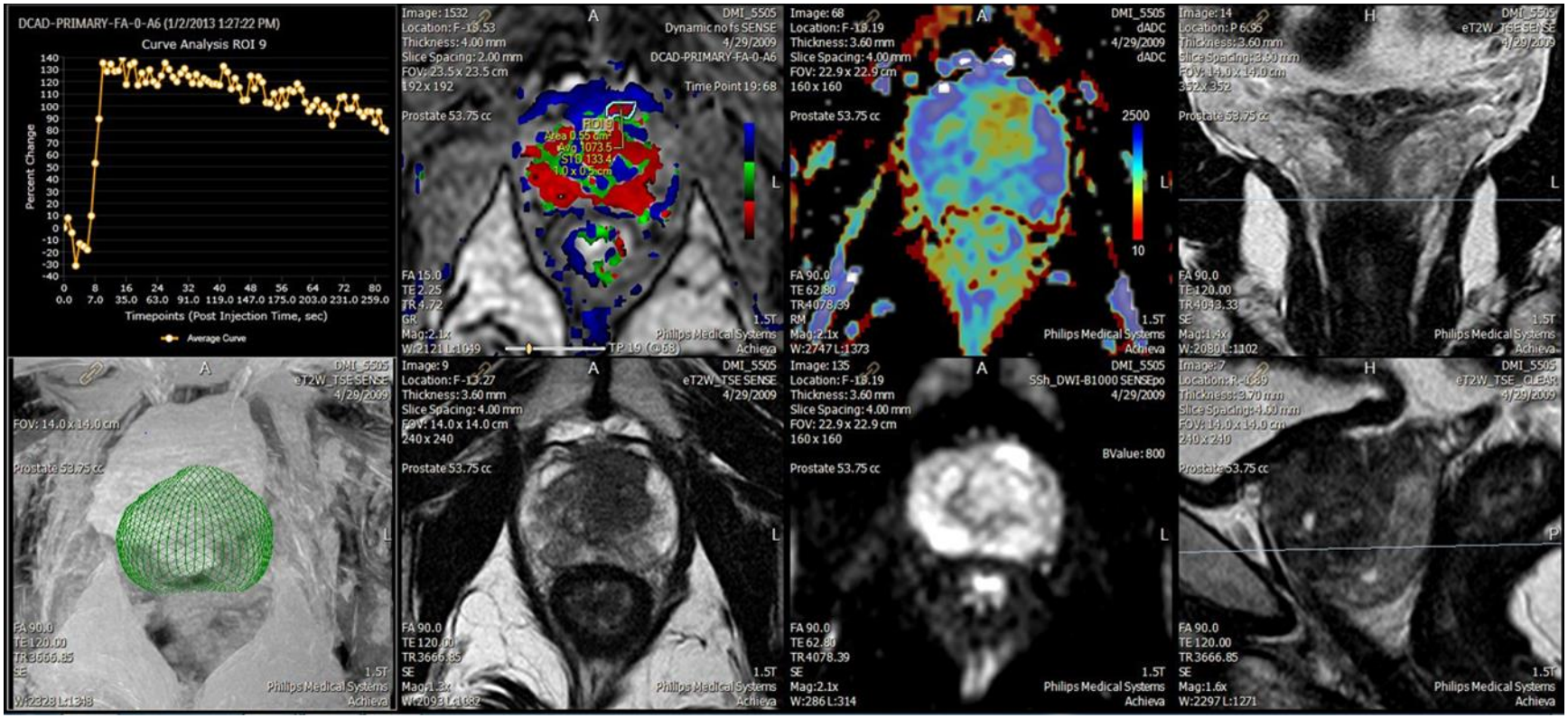

Location: F-1.52
Thickness: 4.00 mm
Slice Spacing: 4.55 mm
FOV: 20.0 x 20.0 cm
144 x 144
Reg - DWI B1400
2/6/2015
BValue: 1400
L
FA 90.0
TE 66.29
TR 3328.63
SE
Mag: 2.5x
W: 72 L: 59
1.5T
Philips Medical Systems
Achieva

PI-RADS v2


Location: H 2.44
Thickness: 4.00 mm
Slice Spacing: 2.00 mm
FOV: 29.2 x 29.2 cm
240 x 240
Dynamic no fs SENSE
2/6/2015
DCAD-PRIMARY-FA-0-A4
Time Point 24: 90
L
FA 15.0
TE 2.26
TR 4.75
GR
Mag:3.5x
W:167 L:83
1.5T
Philips Medical Systems
TP 24 (@90)
Achieva


Time Curve
Percent
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
0 9 18 27 36 45 54 63
0.0 22.5 63.0 103.5 144.0 184.5 225.0 265.5
Timepoints (Post Injection Time, sec)

Multiparametric MRI



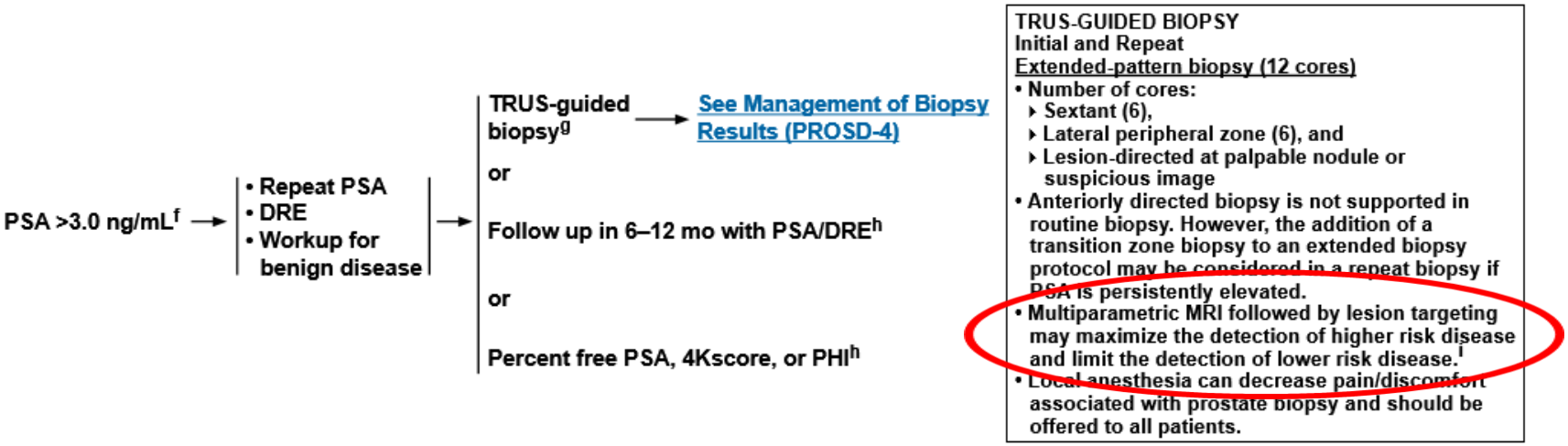
ACR PI-RADS V2, published 2014

http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/PIRADS/PIRADS%20V2.pdf
https://acsearch.acr.org/docs/69371/Narrative/

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2016
Prostate Cancer Early Detection

INDICATIONS FOR BIOPSY



https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf

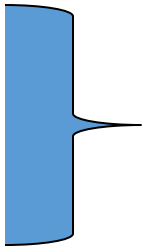
Original Research

Genitourinary Imaging

Prostate Cancer Localization with Dynamic Contrast-enhanced MR Imaging and Proton MR Spectroscopic Imaging

Jurgen J. Fütterer, MD, PhD, Stijn W. T. P. J. Heijmink, MD, Tom W. J. Scheenen, PhD, Jeroen Veltman, MD, Henkjan J. Huisman, PhD, Pieter Vos, MSc, Christina A. Hulsbergen–Van de Kaa, MD, PhD, J. Alfred Witjes, MD, PhD, Paul F. M. Krabbe, PhD, Arend Heerschap, PhD, and Jelle O. Barentsz, MD, PhD

	Accuracy
T2	70%
DWI	86%
DCE	85%
MRS	81%



ROC AUC = 0.91

Radiology 2006;241:449-458

ASCO University
LIFELONG LEARNING

	NPV	NPV - clinically significant CaP	True negative	False negative (3+3)	False negative (G≥7)
Overall (n=53)	64.2%	96.2%	34	17	2
Biopsy naive (n=18)	61.1%	94.4%	11	6	1
Prior negative (n=19)	84.2%	100%	16	3	0
Active surveillance (n=16)	43.8%	93.8%	7	8	1

J Clin Oncol 34, 2016 (suppl 2S; abstr 91)

Radiology

Relationship between Apparent Diffusion Coefficients at 3.0-T MR Imaging and Gleason Grade in Peripheral Zone Prostate Cancer[1]

Thomas Hambrock, MBChB
Diederik M. Somford, MD
Henkjan J. Huisman, MSEE, PhD
Inge M. van Oort, MD, PhD
J. Alfred Witjes, MD, PhD
Christina A. Hulsbergen-van de Kaa, MD, PhD
Thomas Scheenen, PhD
Jelle O. Barentsz, MD, PhD

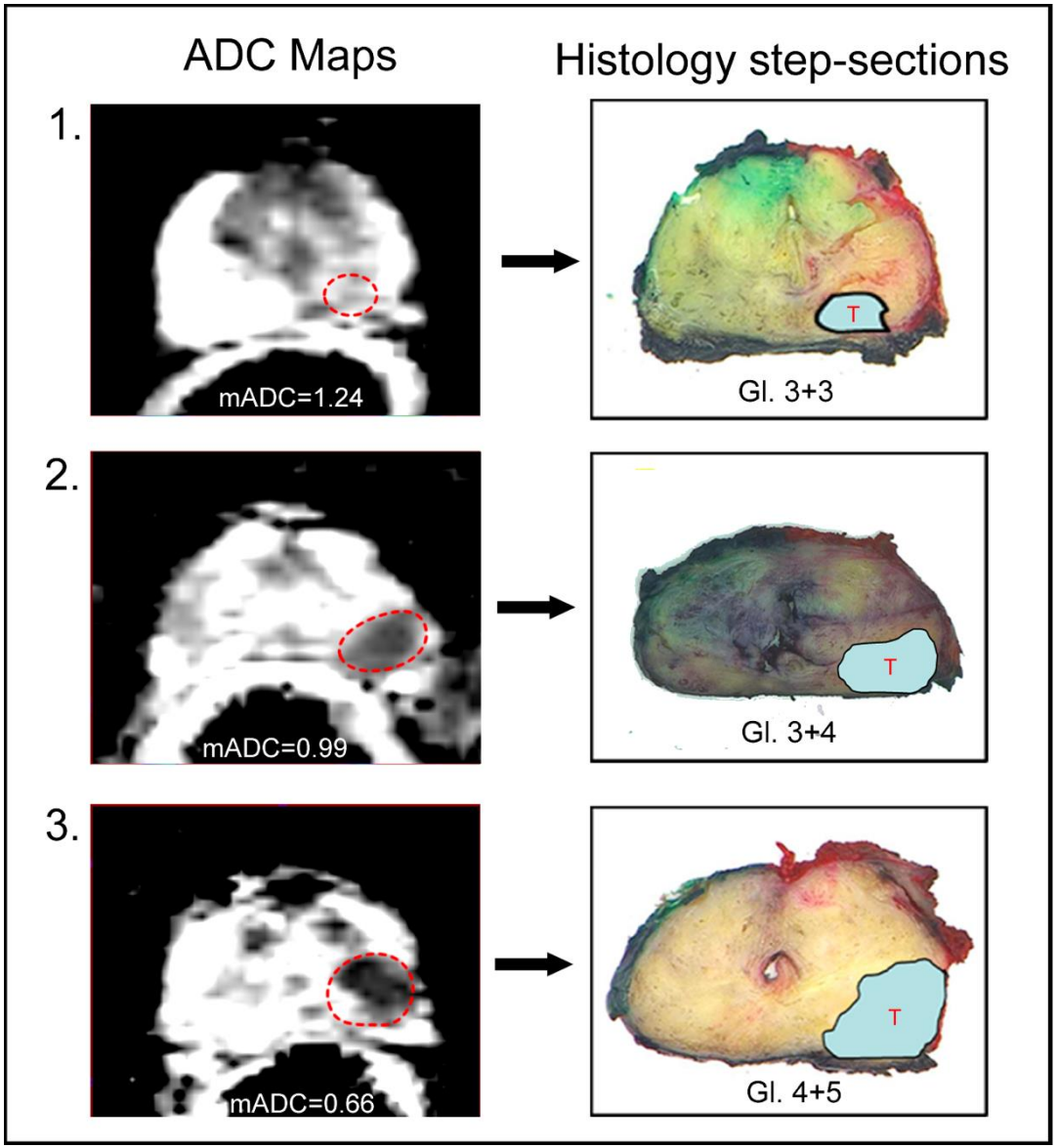
Purpose: To retrospectively determine the relationship between apparent diffusion coefficients (ADCs) obtained with 3.0-T diffusion-weighted (DW) magnetic resonance (MR) imaging and Gleason grades in peripheral zone prostate cancer.

Materials and Methods: The requirement to obtain institutional review board approval was waived. Fifty-one patients with prostate cancer underwent MR imaging before prostatectomy, including DW MR imaging with *b* values of 0, 50, 500, and 800 sec/mm^2. In prostatectomy specimens, separate slice-by-slice determinations of Gleason grade groups were performed according to primary, secondary, and tertiary Gleason grades. In addition, tumors were classified into qualitative grade groups (low-, intermediate-, or high-grade tumors). ADC maps were aligned to step-sections and regions of interest annotated for each tumor slice. The median ADC of tumors was related to qualitative grade groups with linear mixed-model regression analysis. The accuracy of the median ADC in the most aggressive tumor component in the differentiation of low- from combined intermediate- and high-grade tumors was summarized by using the area under the receiver operating characteristic (ROC) curve (A_z).

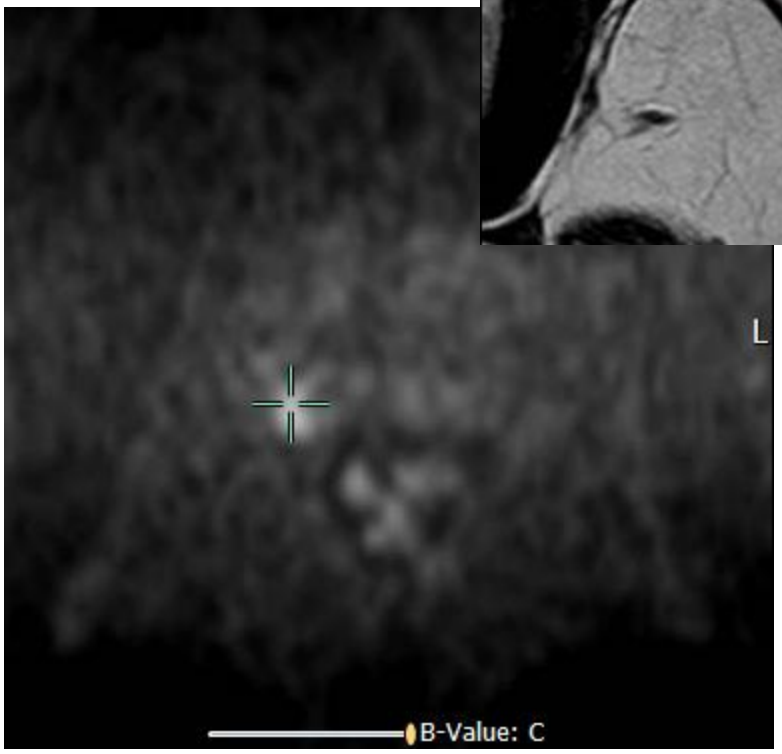
Results: In 51 prostatectomy specimens, 62 different tumors and 251 step-section tumor lesions were identified. The median ADC in the tumors showed a negative relationship with Gleason grade group, and differences among the three qualitative grade groups were statistically significant ($P < .001$). Overall, with an increase of one qualitative grade group, the median ADC (±standard deviation) decreased 0.18×10^{-3} mm^2/sec ± 0.02. Low-, intermediate-, and high-grade tumors had a median ADC of 1.30×10^{-3} mm^2/sec ± 0.30, 1.07×10^{-3} mm^2/sec ± 0.30, and 0.94×10^{-3} mm^2/sec ± 0.30, respectively. ROC analysis showed a discriminatory performance of $A_z = 0.90$ in discerning low-grade from combined intermediate- and high-grade lesions.

Conclusion: ADCs at 3.0 T showed an inverse relationship to Gleason grades in peripheral zone prostate cancer. A high discriminatory performance was achieved in the differentiation of low-, intermediate-, and high-grade cancer.

[1] From the Departments of Radiology (T.H., H.J.H., T.S., J.O.B.), Urology (D.M.S., I.M.v.O., J.A.W.), and Pathology (C.A.H.v.d.K.), University Medical Centre St. Radboud, PO Box 9101, 6500HB, Nijmegen, the Netherlands. Received August 24, 2009; revision requested October 16; revision received February 13, 2010; accepted April 16; final version accepted December 9. Supported by the Dutch Cancer Society (grant KUN 2004-3141) and the European Research Council under the European Community's Seventh Framework Programme (FP7/2007-2013/ERC grant agreement 243115). **Address correspondence to** T.H. (e-mail: *t.hambrock@rad.umcn.nl*).


ADC Maps
Histology step-sections
1.
mADC=1.24
T
Gl. 3+3
2.
mADC=0.99
T
Gl. 3+4
3.
mADC=0.66
T
Gl. 4+5


L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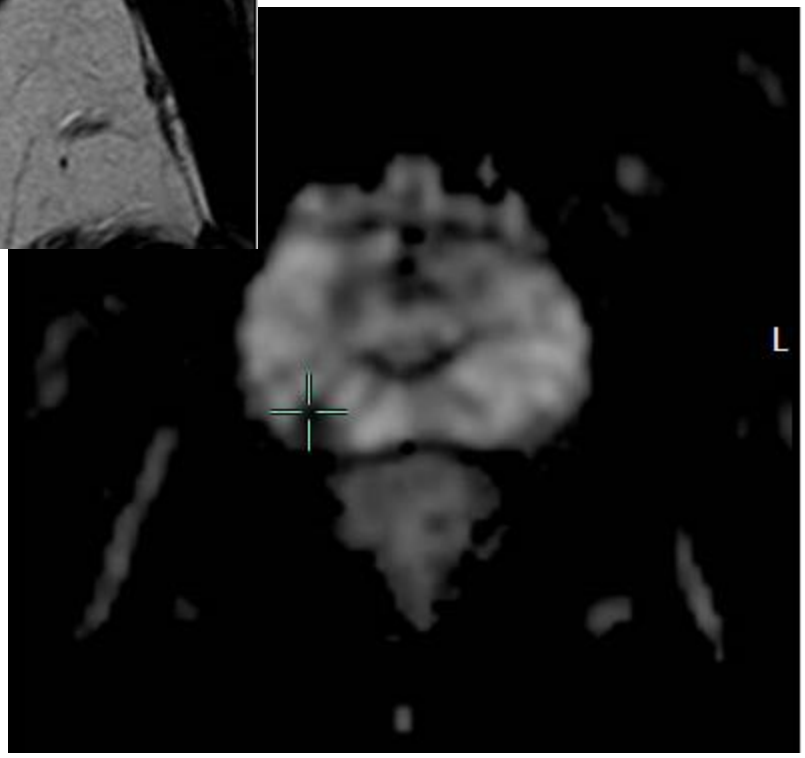
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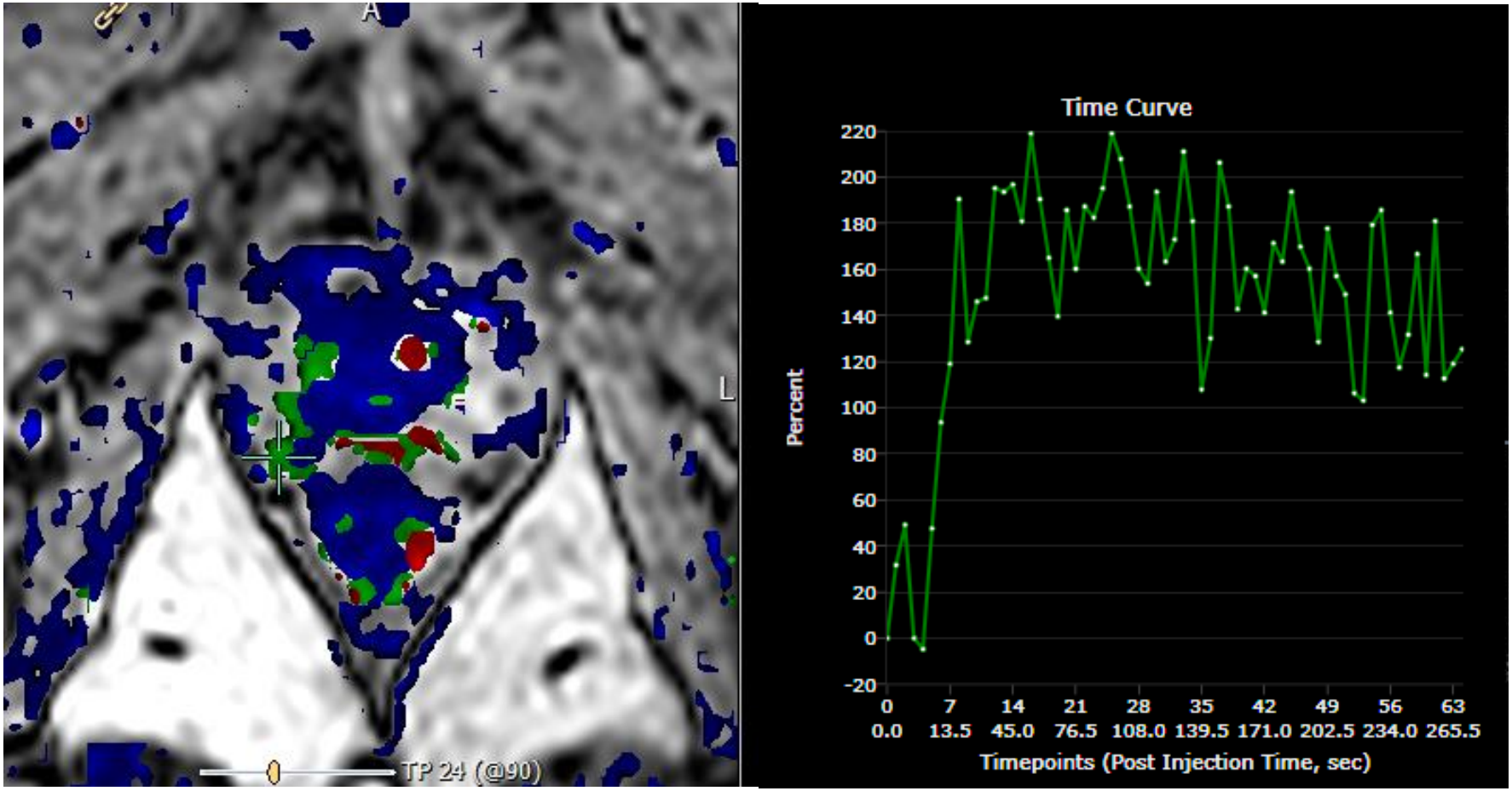
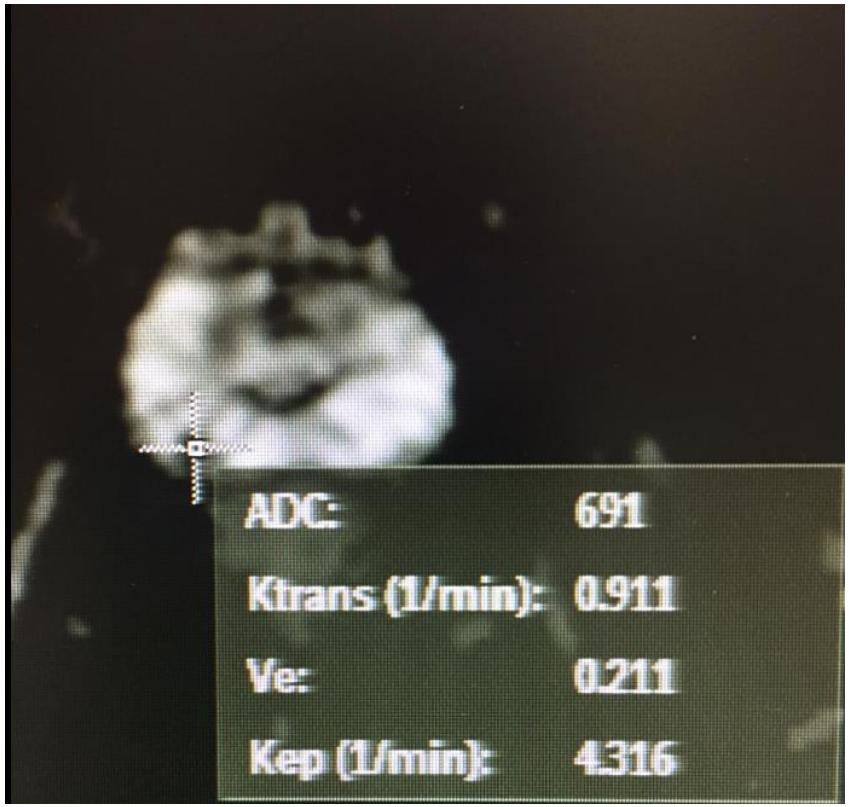
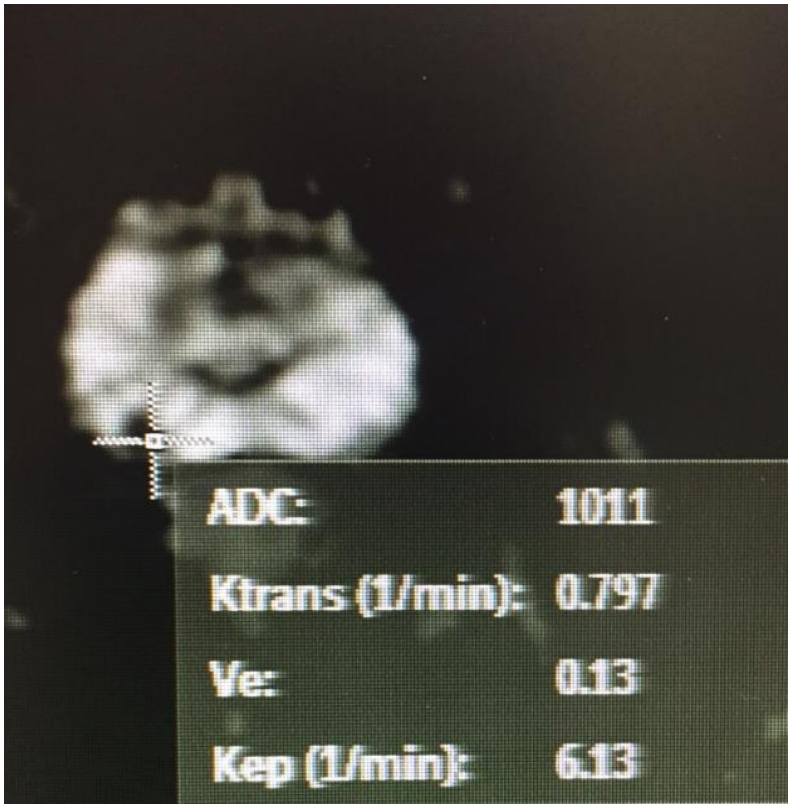
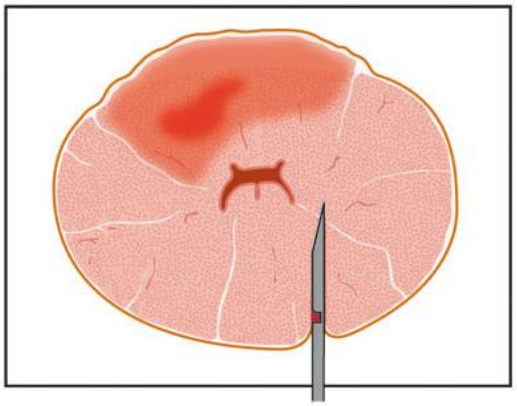

A
L
TP 24 (@90)
Time Curve
Percent
220
200
180
160
140
120
100
80
60
40
20
0
-20
0 7 14 21 28 35 42 49 56 63
0.0 13.5 45.0 76.5 108.0 139.5 171.0 202.5 234.0 265.5
Timepoints (Post Injection Time, sec)

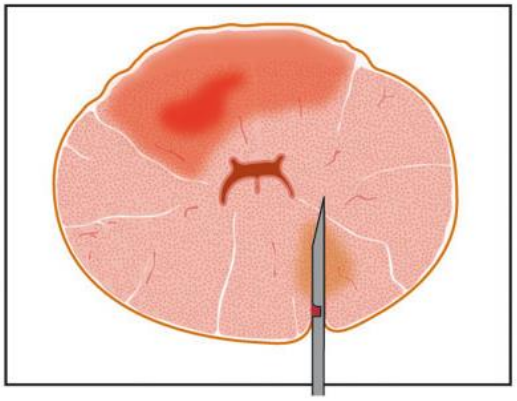

ADC: 691
Ktrans (1/min): 0.911
Ve: 0.211
Kep (1/min): 4.316


ADC: 1011
Ktrans (1/min): 0.797
Ve: 0.13
Kep (1/min): 6.13

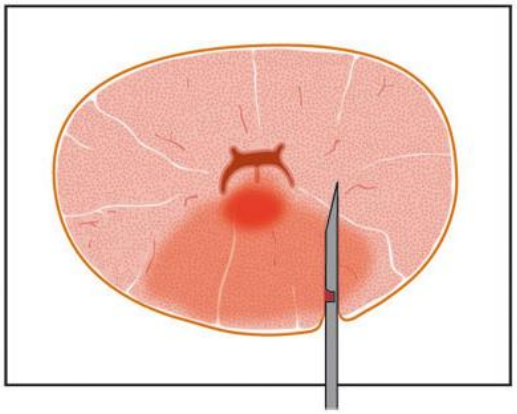
TRUS biopsy



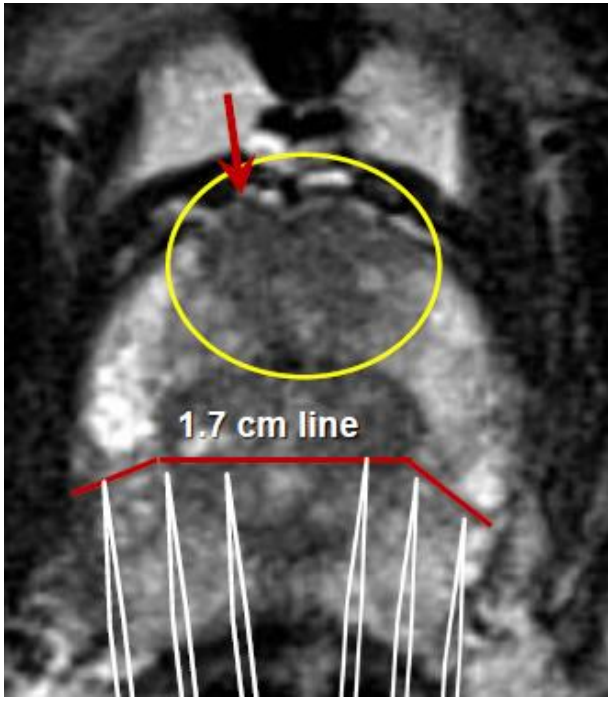
Needle penetrates next to the tumor or does not reach it



Less aggressive tumor is biopsied



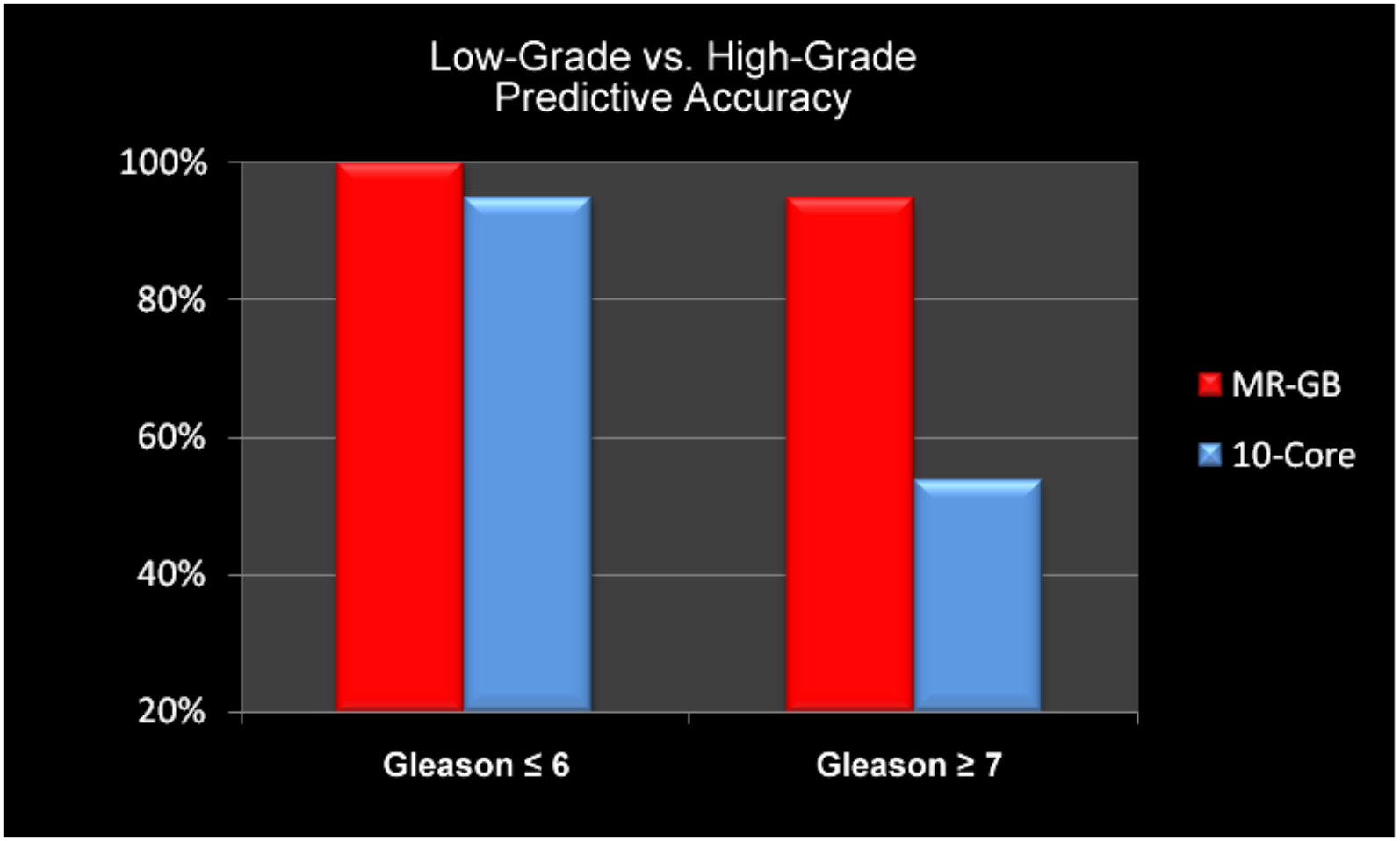
Less aggressive part of the tumor is biopsied



The patient can end up on active surveillance while harboring clinically significant disease

Courtesy Jelle Barentsz, M.D., PhD, Univ. Medical Center, Nijmegen, The Netherlands

TRUS-Biopsy & MR-Biopsy vs. Prostatectomy



Hambrock 2010 SCBTMR “Lauterbur Award”

Trans-rectal interventional MRI: initial prostate biopsy experience

Bernadette M. Greenwood*[a], Meliha R. Behluli[a] John F. Feller[b], Stuart T. May[b] Robert Princenthal[c], Axel Winkel[d], David B. Kaminsky[e]
[a]Invivo Corporation, N27 W23676 Paul Rd., Pewaukee, WI USA 53072
[b]Desert Medical Imaging, 74-785 Hwy 111, Indian Wells, CA 92210
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62

Abdominal Radiology

Abdom Radiol (2016)
DOI: 10.1007/s00261-016-0750-7

In-bore magnetic resonance-guided transrectal biopsy for the detection of clinically significant prostate cancer

Ely R. Felker,[1] Stephanie A. Lee-Felker,[1] John Feller,[2] Daniel J. Margolis,[1] David S. Lu,[1] Robert Princenthal,[3] Stuart May,[2] Martin Cohen,[3] Jiaoti Huang,[4] Jeffrey Yoshida,[5] Bernadette Greenwood,[2] Hyun J. Kim,[1] Steven S. Raman[1]

[1]Department of Radiology, Ronald Reagan-U
[2]Desert Medical Imaging, 1133 N Palm Cany
[3]Rolling Oaks Radiology, 415 Rolling Oaks
[4]Department of Pathology, David Geffen Sch
USA
[5]Newport Urologic Oncology, 1525 Superior

MRI-Guided Prostate Biopsy of Native and Recurrent Prostate Cancer

David A. Woodrum, MD, PhD[1] Krzysztof R. Gorny, PhD[1] Bernadette Greenwood, BSc, BSRS, RT(R)(MR)[2] Lance A. Mynderse, MD[3]

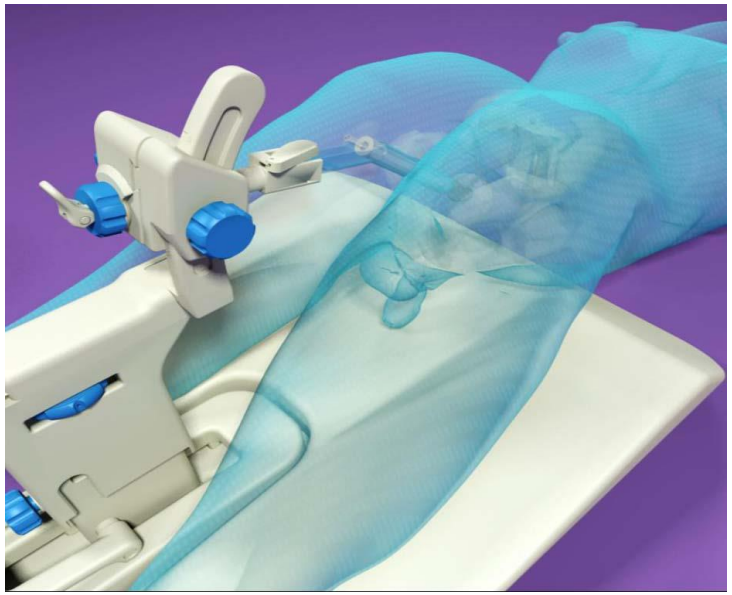
[1]Department of Radiology, Mayo Clinic, Rochester, Minnesota
[2]Desert Medical Imaging, Indian Wells, California
[3]Department of Urology, Mayo Clinic, Rochester, Minnesota

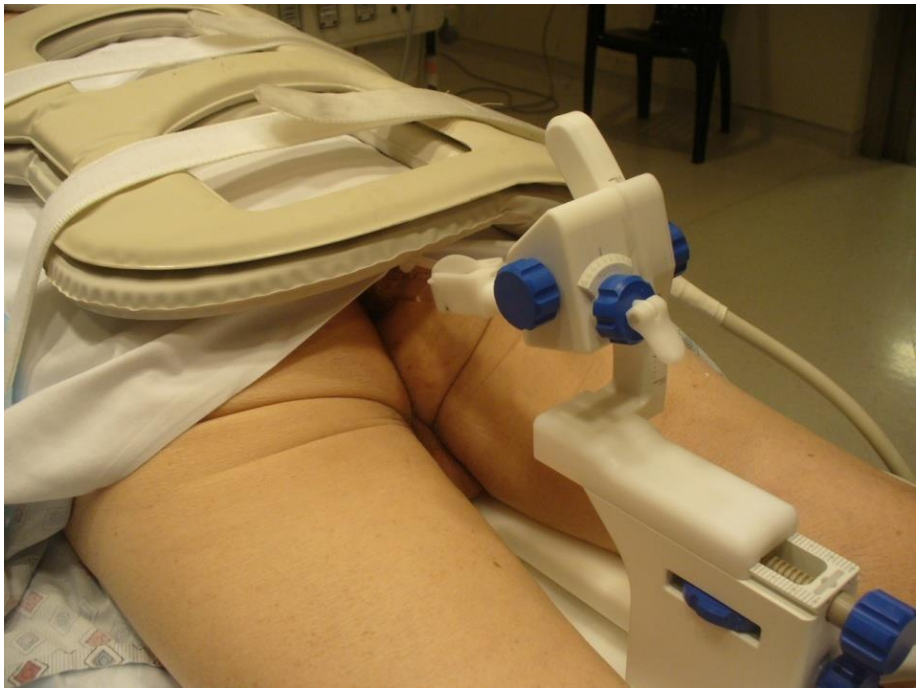
Address for correspondence: David A. Woodrum, MD, PhD, Department of Radiology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (e-mail: woodrum.david@mayo.edu).

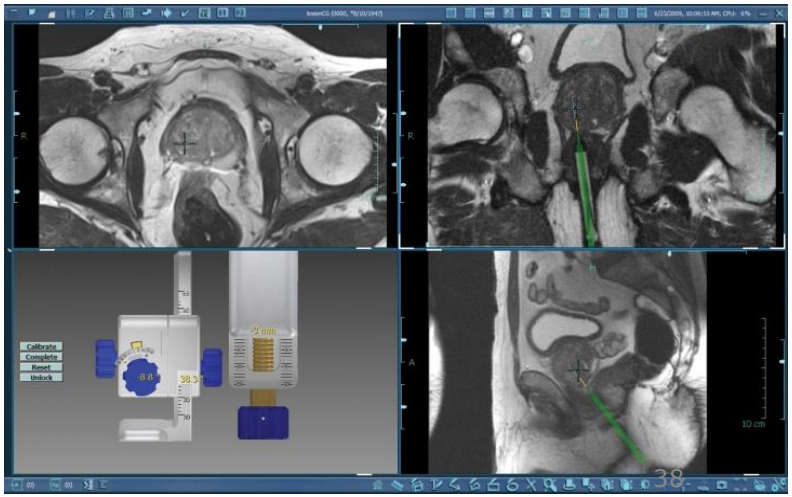
Rationale for Prostate MRI

- Ability to biopsy tumor suspicious regions in the prostate

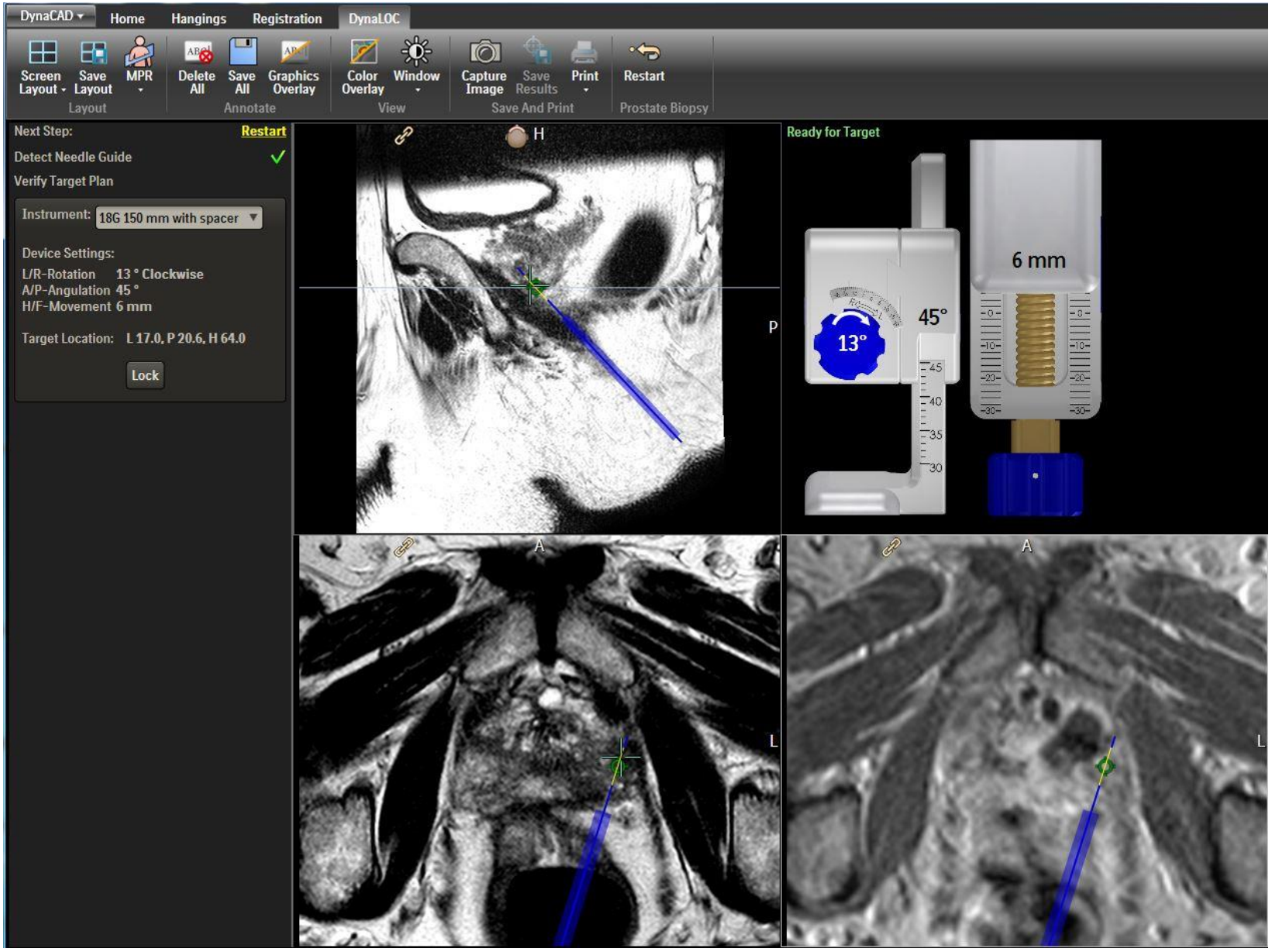
- MRI guidance for biopsy planning to target tumor-suspicious regions (TSRs)







Transrectal Interventional Planning



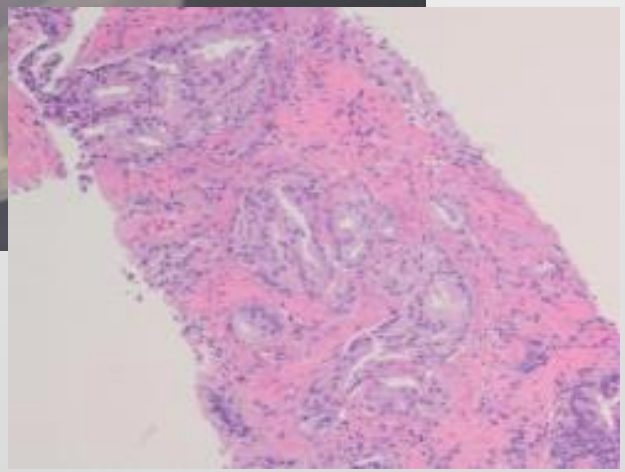
Why MRI for the Prostate Today?

- Easy access to patient for biopsy

1.5T Philips Achieva XR

Why MRI for the Prostate Today?

- Easy access to patient for biopsy



Gleason 4 + 3 = 7

DIAGNOSIS

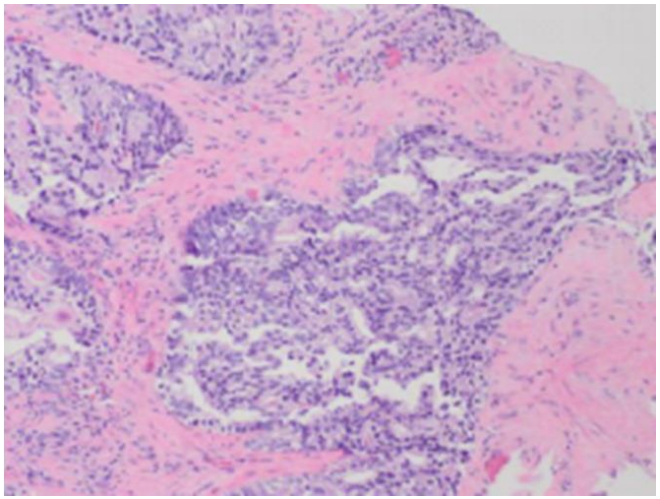
PROSTATE, NEEDLE BIOPSIES:

(A1) Right Peripheal zone Base level: **ADENOCARCINOMA (GLEASON SCORE 4 + 4 = 8) INVOLVING 35% OF THE SPECIMEN (2 OF 3 CORES CONTAIN CANCER). CANCER LENGTH 1.3 cm. PERINEURAL INVASION.**

DIAGNOSIS DESCRIPTION

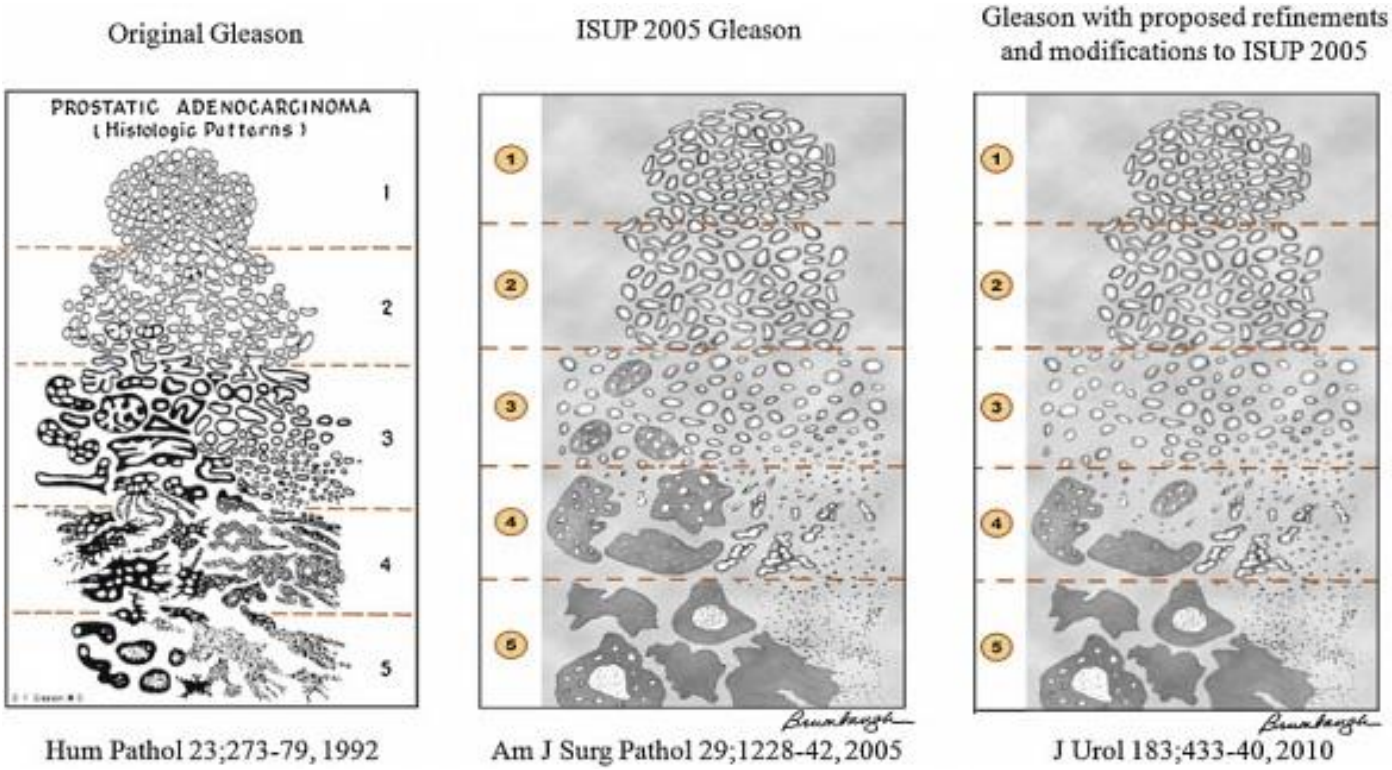
Site	Diagnosis	Core Length	Cancer Length	%Involvement	Gleason Score
(A1)	Malignant	1.5,1.3,0.9	--	--	--
(A1)	Malignant	1.5,1.3,0.9	1.30	35	4 + 4= 8

For a given targeted biopsy location, cores may be combined into one vial. In these instances, the cancer length and percentage of involvement calculations are based on all cores received in the vial for that targeted biopsy location.



What is it? Why does it matter?

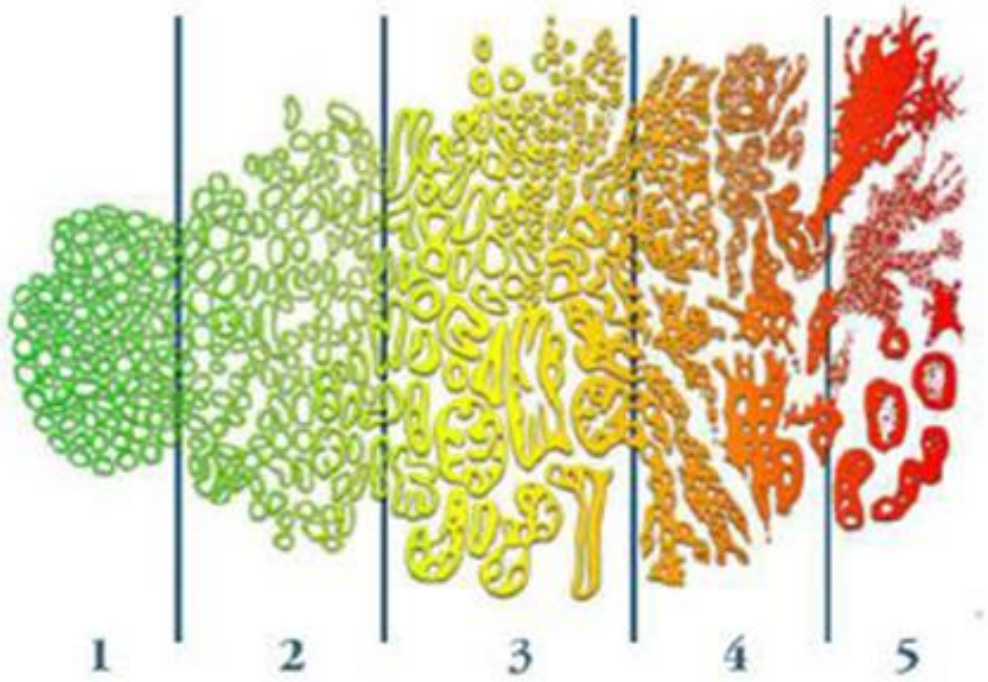
Gleason Grades Determine Gleason Score



http://www.europeanurology.com/article/S0302-2838(12)01234-1/fulltext/contemporary-grading-for-prostate-cancer-implications-for-patient-care-img-src-manager-uploads-europeanurology-com-eur-articles-s0302-2838-12-01234-1-assets-eulogo1-jpg-alt-eulogo1

What is it? Why does it matter?

Gleason Grades Determine Gleason Score



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Home > Find Studies > Study Record Detail

Phase II Laser Focal Therapy of Prostate Cancer (LITT or FLA)

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2016 by Desert Medical Imaging

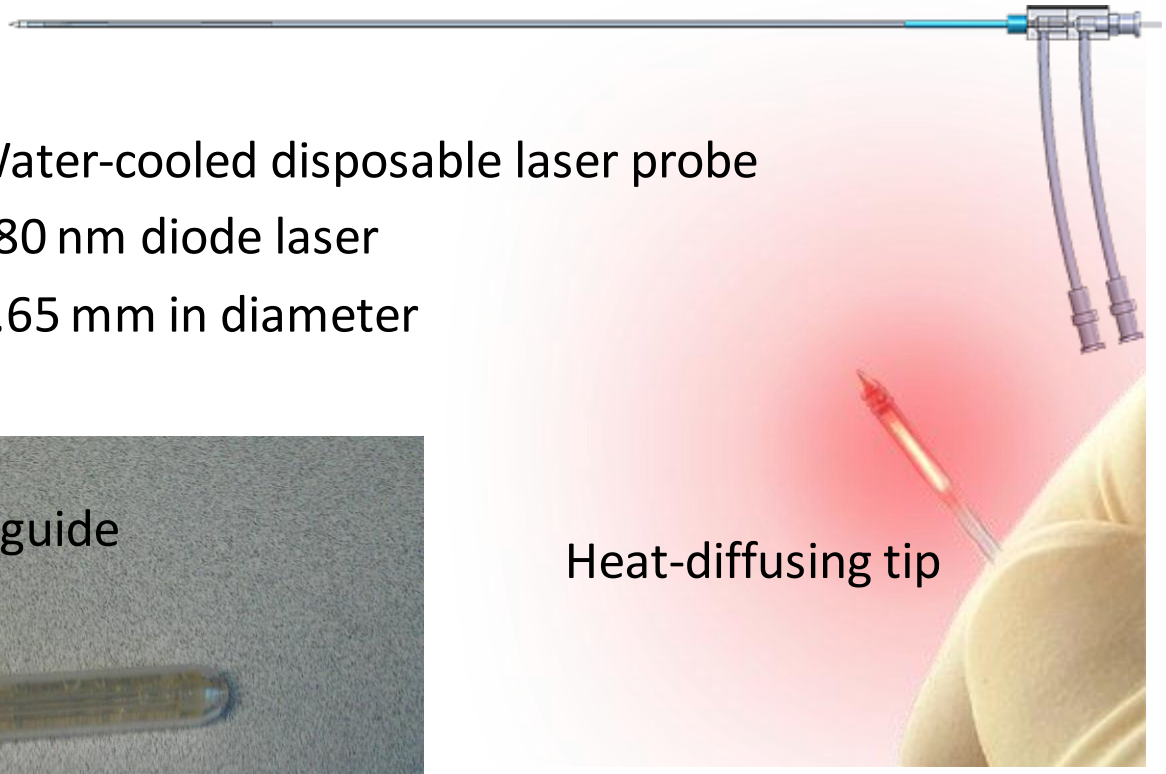
Sponsor:
Desert Medical Imaging

Information provided by (Responsible Party):
Desert Medical Imaging

ClinicalTrials.gov Identifier:
NCT02243033

First received: September 9, 2014
Last updated: May 28, 2016
Last verified: May 2016
History of Changes

MR-guided Laser Focal Therapy



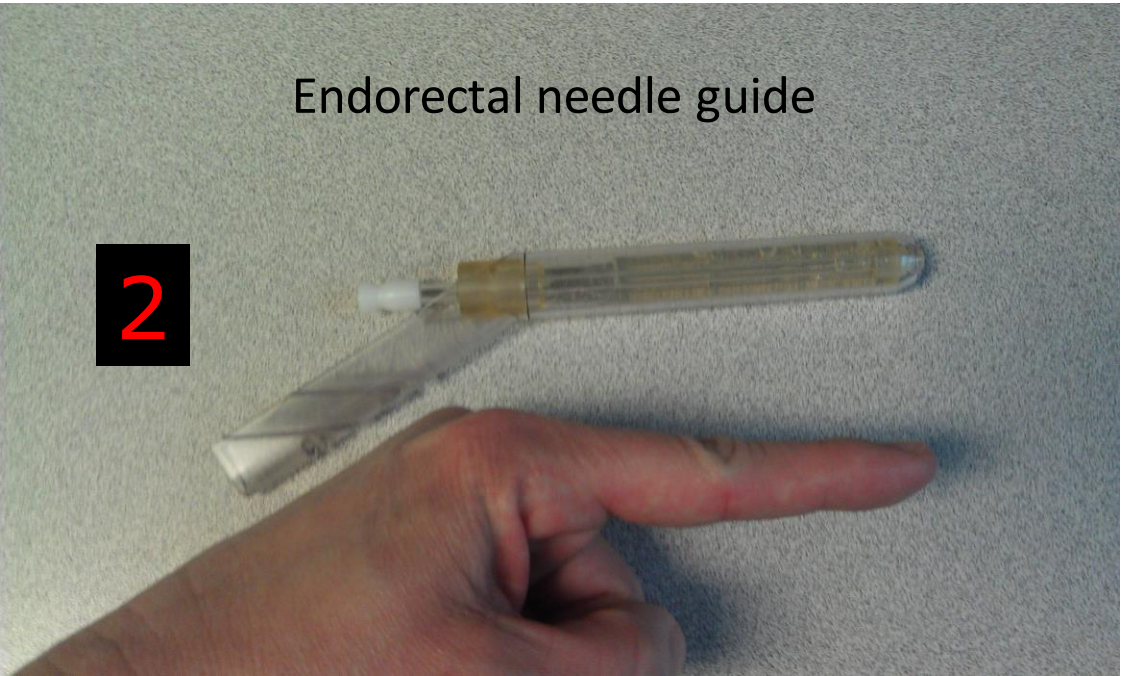
1

Water-cooled disposable laser probe

980 nm diode laser

1.65 mm in diameter

Heat-diffusing tip



Endorectal needle guide

2

3

14 G titanium coax needle

Laser Workstation

- 15 Watt laser * (Fiberoptic)
- Standard power plug
- Integrated to MR (Ethernet)
- Software: real-time prediction model; MR thermometry; safety control features
- FDA 510(k) clearance Sept 10,2008

*The catheter and fiber are MR compatible up to 1.5T

Medtronic Indications, Safety, and Warnings Visualase Thermal Therapy System. http://www.medtronic.com/for-healthcare-professionals/products-therapies/neurological/laser-ablation/visualase/indications-safety-warnings/index.htm. Accessed March 9,2016

FDA cleared with broad, general indications

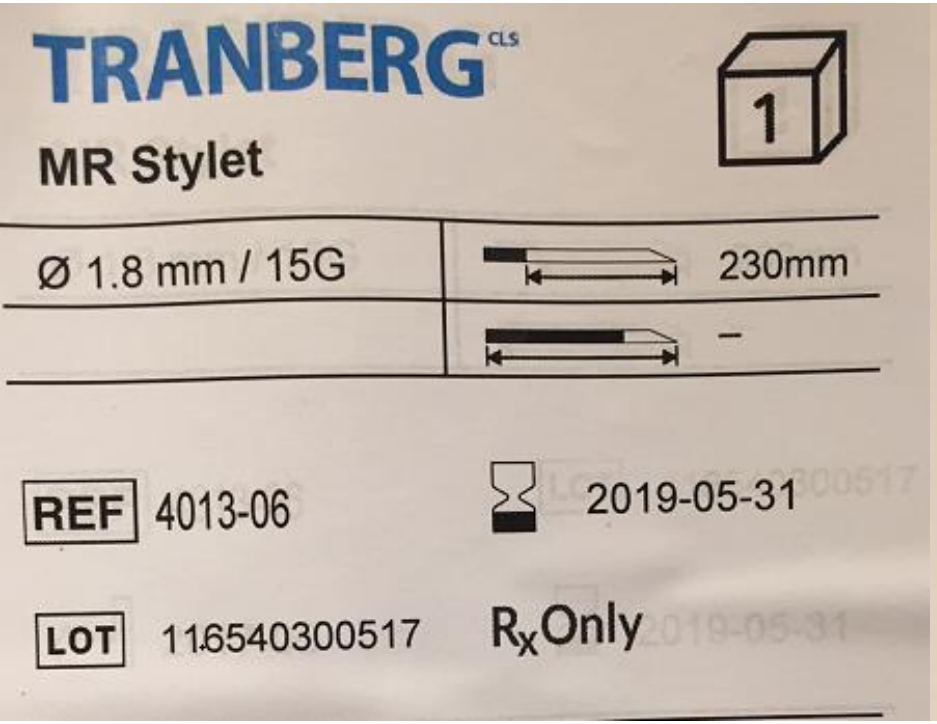
"for use to necrotize or coagulate soft tissue through interstitial irradiation or thermal therapy. . . in neurosurgery, general surgery, urology. . ." and multiple additional named specialties.

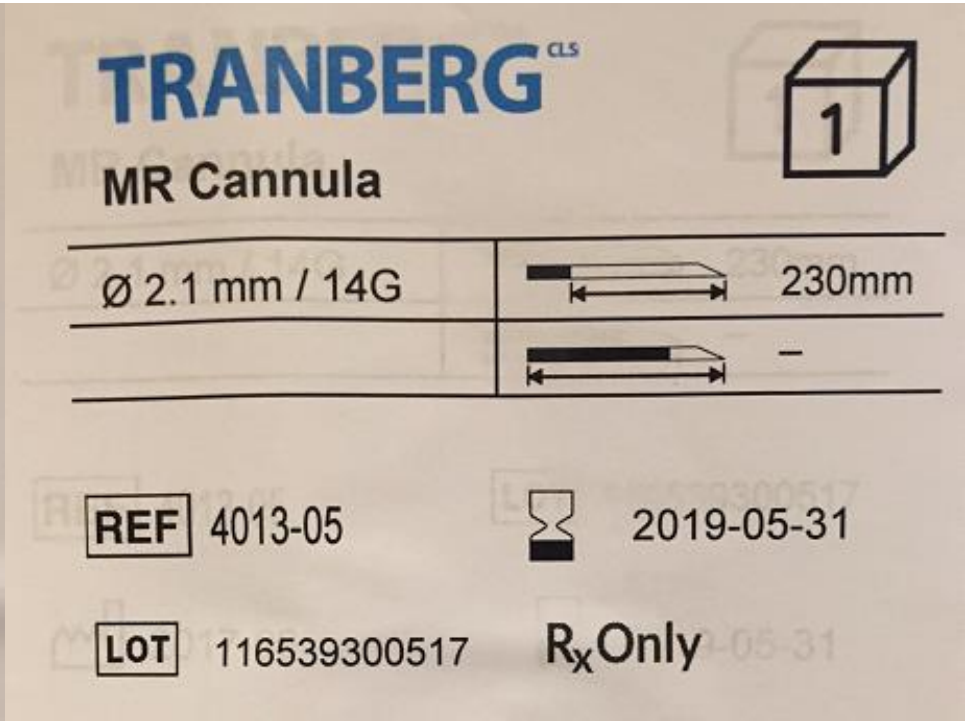
Technology is FDA cleared for commercialization in the US:

30 Watt Diode Laser

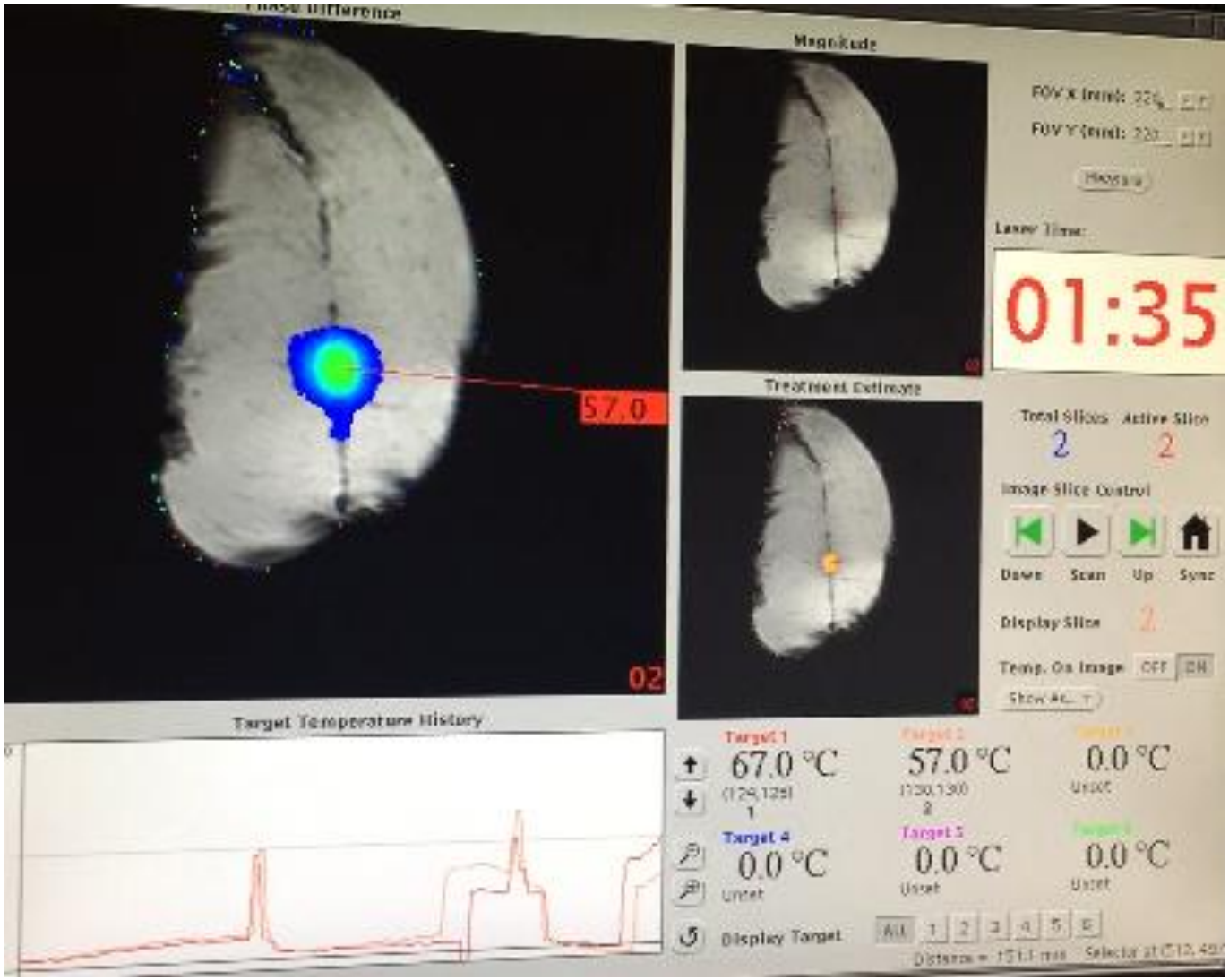
• Laser Applicator	K053087 (March 2006)
• Laser System	K060304 (March 2006)
• Workstation Software	K063505 (December 2006)
• Visualase Thermal Therapy System	K071328 (August 2007)
	K081656 (September 2008)
• 30 W Laser System	K092197 (November 2009)

Materials and Methods:





TRANBERG cannula ***retracted*** in sagittal and axial planes:


Magnitude
57.0
02
Treatment Estimate
01:35
Total Slices
Active Slice
2
2
Image Slice Control
Down
Scan
Up
Sync
Display Slice
Temp. On Image
OFF
ON
Target Temperature History
Target 1
67.0 °C
Target 2
57.0 °C
0.0 °C
Target 4
0.0 °C
Target 5
0.0 °C
0.0 °C
Display Target

Dissection:

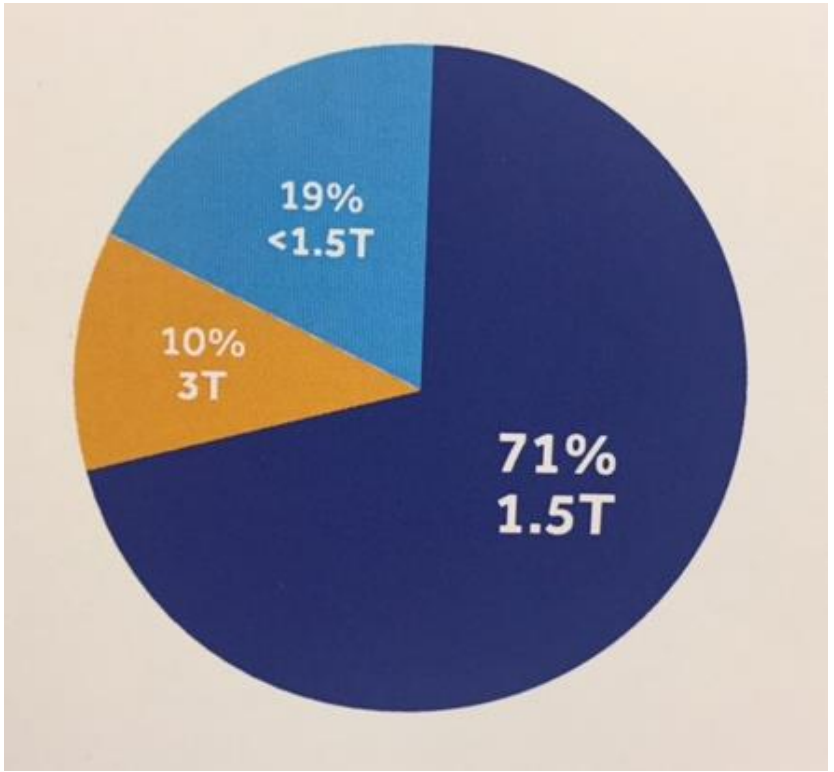
The Team:

Alan Weinberg - CLS
Bernadette M. Greenwood, PG Cert., BSc. – DMI
Dr. John F. Feller – DMI
Thomas Noah - CLS

Rationale for 1.5T

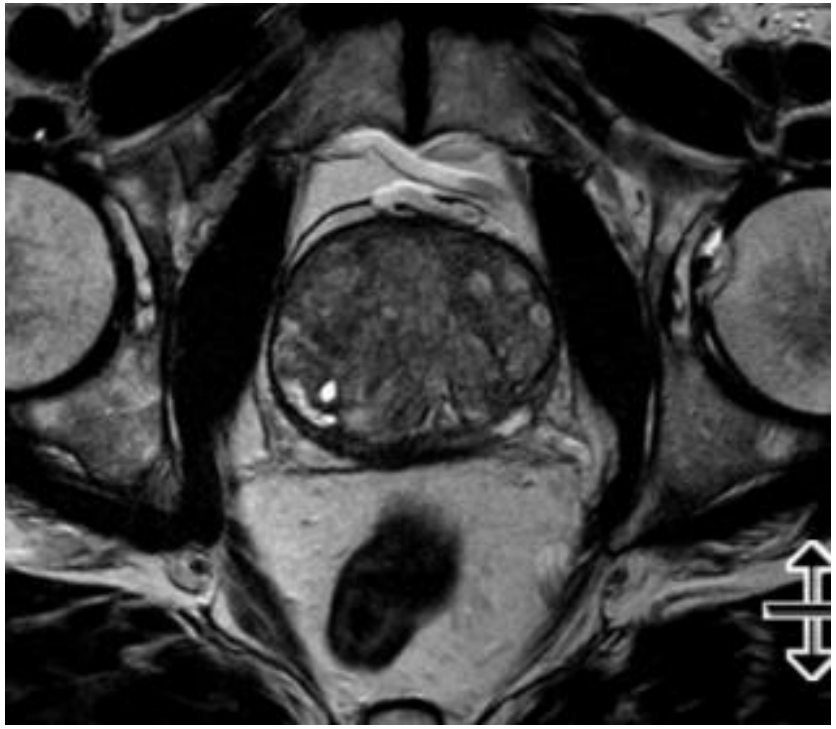
- Operator: Credentialed, experienced MRI technologist familiar with mpMRI protocol
- Software: modern, state-of-the art (ability to perform high b-value diffusion)
- Coil choices: high channel-count surface coils
- Patient preparation: NPO, glucagon, etc.
- Interpreter: Experienced Radiologist

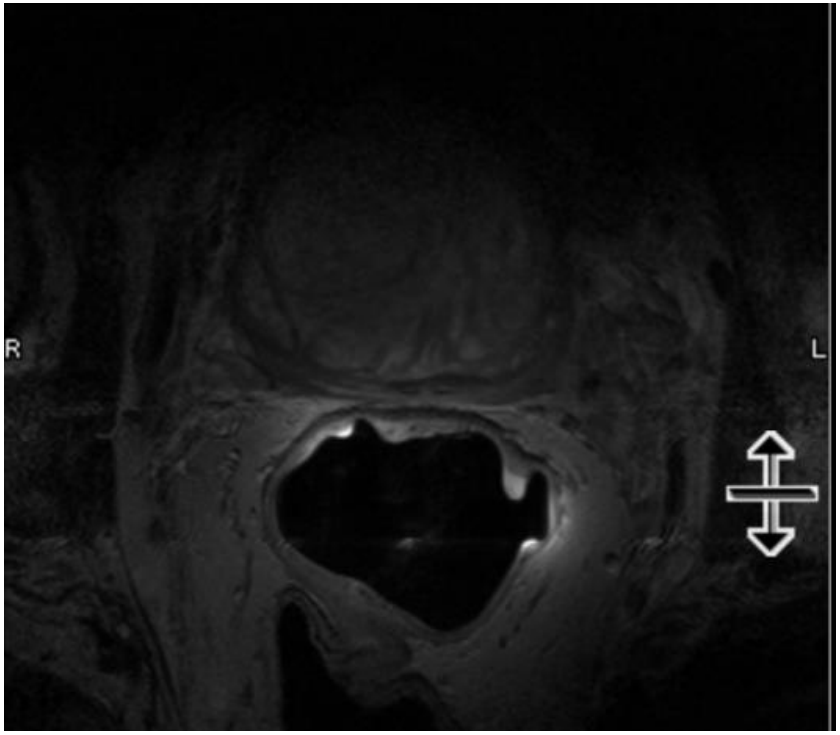
IMV Benchmark Report MR 2013; IMV Medical Information Division, Inc., 2013



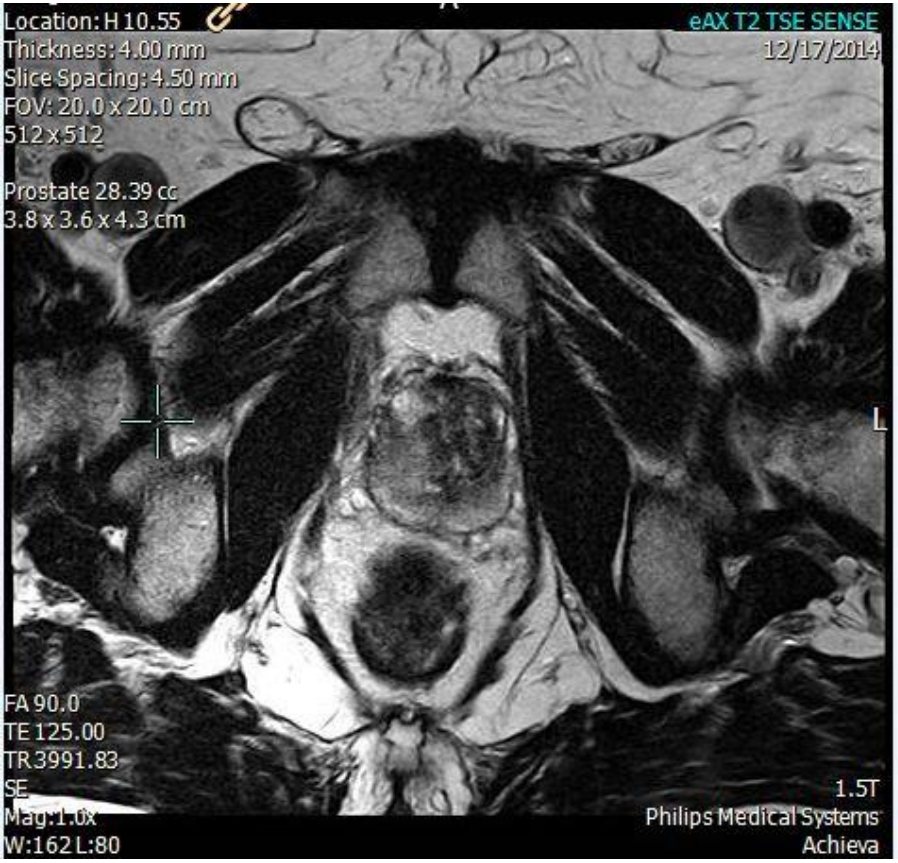
U.S. 1.5T Scanners 2013

1.5 Tesla vs. 3 Tesla ERC





1.5 Tesla vs. 3 Tesla



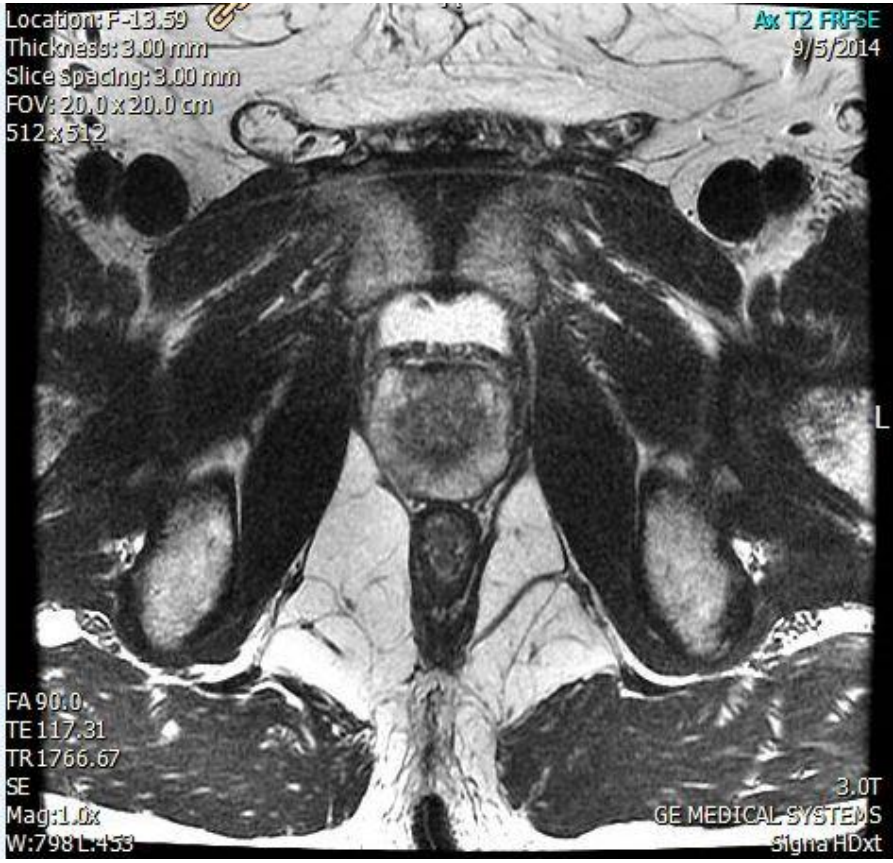


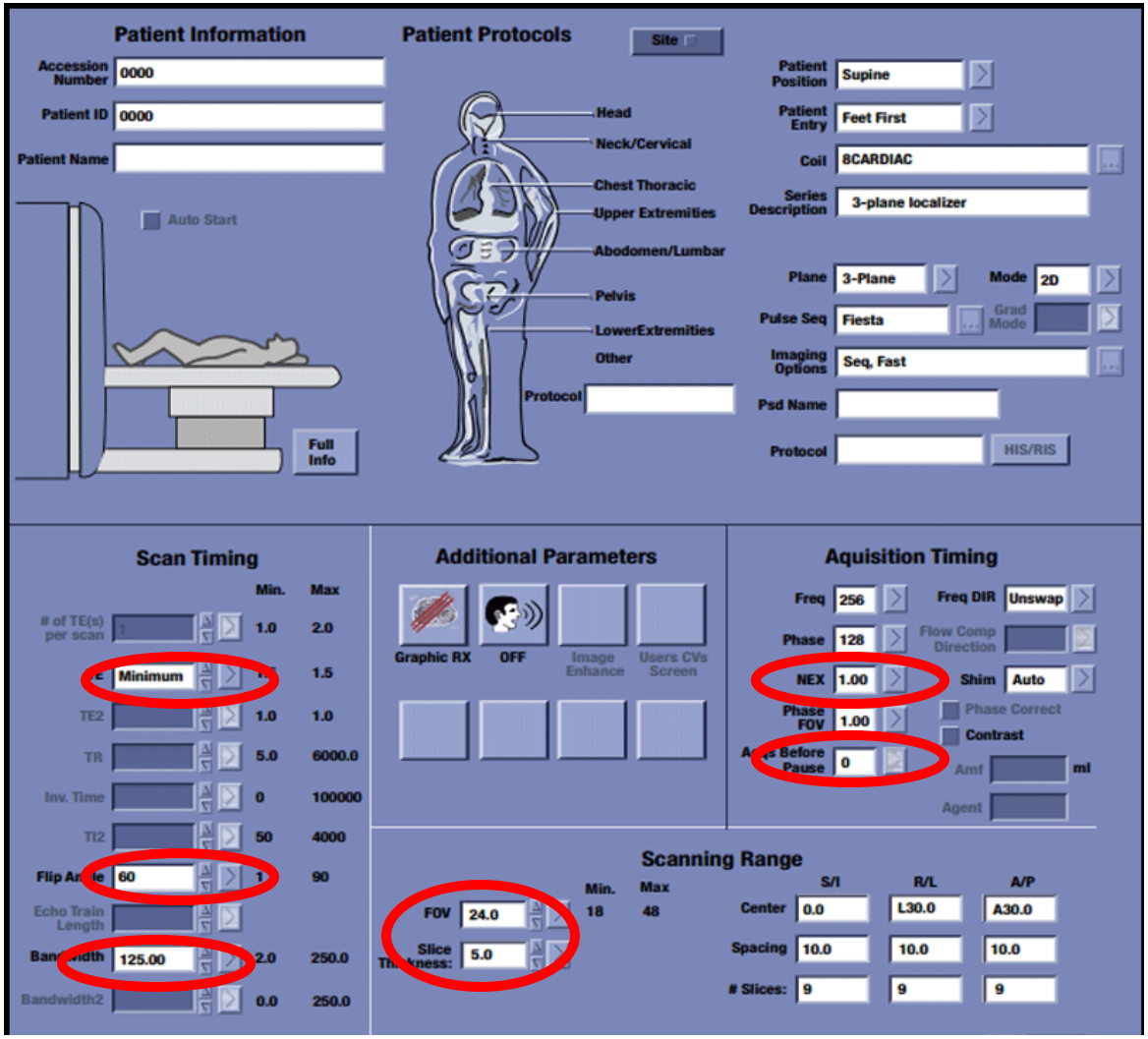
Image Generation and MR Thermometry

MRI Parameter selection allows for exploitation of tissue properties such as:

- Tissue contrast
- Flow quantification
- Perfusion
- Diffusion
- Phase shifts

Parameters include:

- Echo Time
- Repetition Time
- Flip Angle
- Bandwidth
- Signal Averages
- Matrix



MR Thermometry and Image Generation

Gradient recalled echo sequences allow measurement of phase shifts

Damage to tissue can be modeled as an Arrhenius rate process:

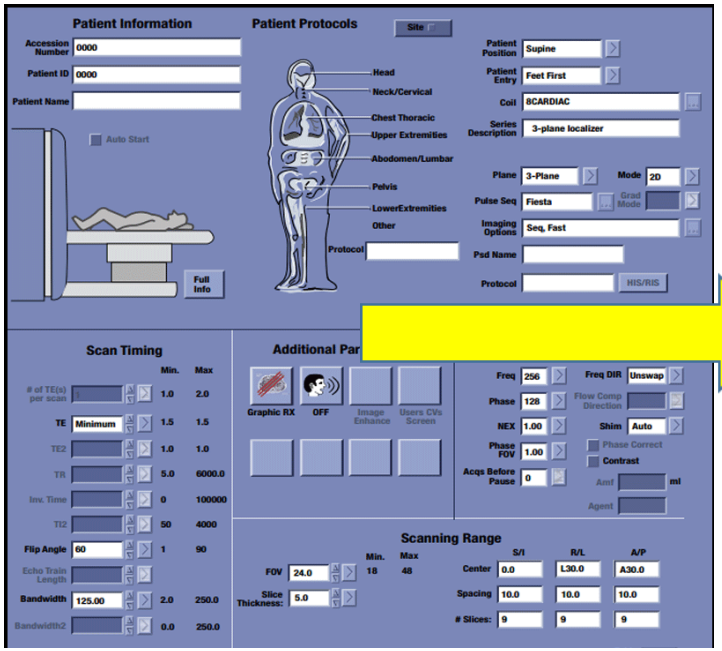
$$\Omega = A \cdot \int_0^t e^{-E_a/RT(\tau)}\, d\tau$$

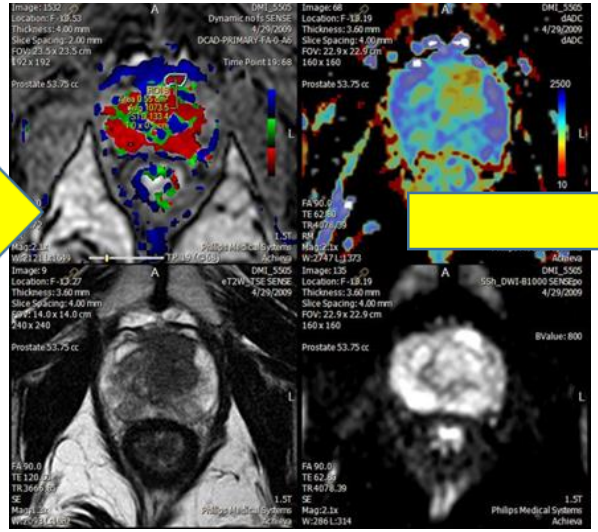
A = frequency factor (3.1×10^{98} s^{-1})

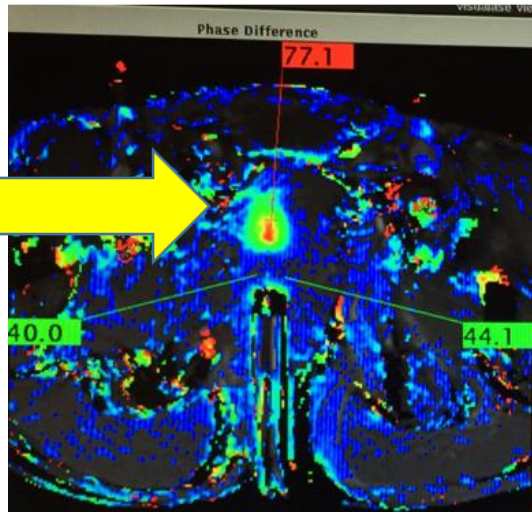
E_a (6.25×10^5 J/mol) = activation energy

R = universal gas constant

T(τ) = absolute temp. in °K as a function of time

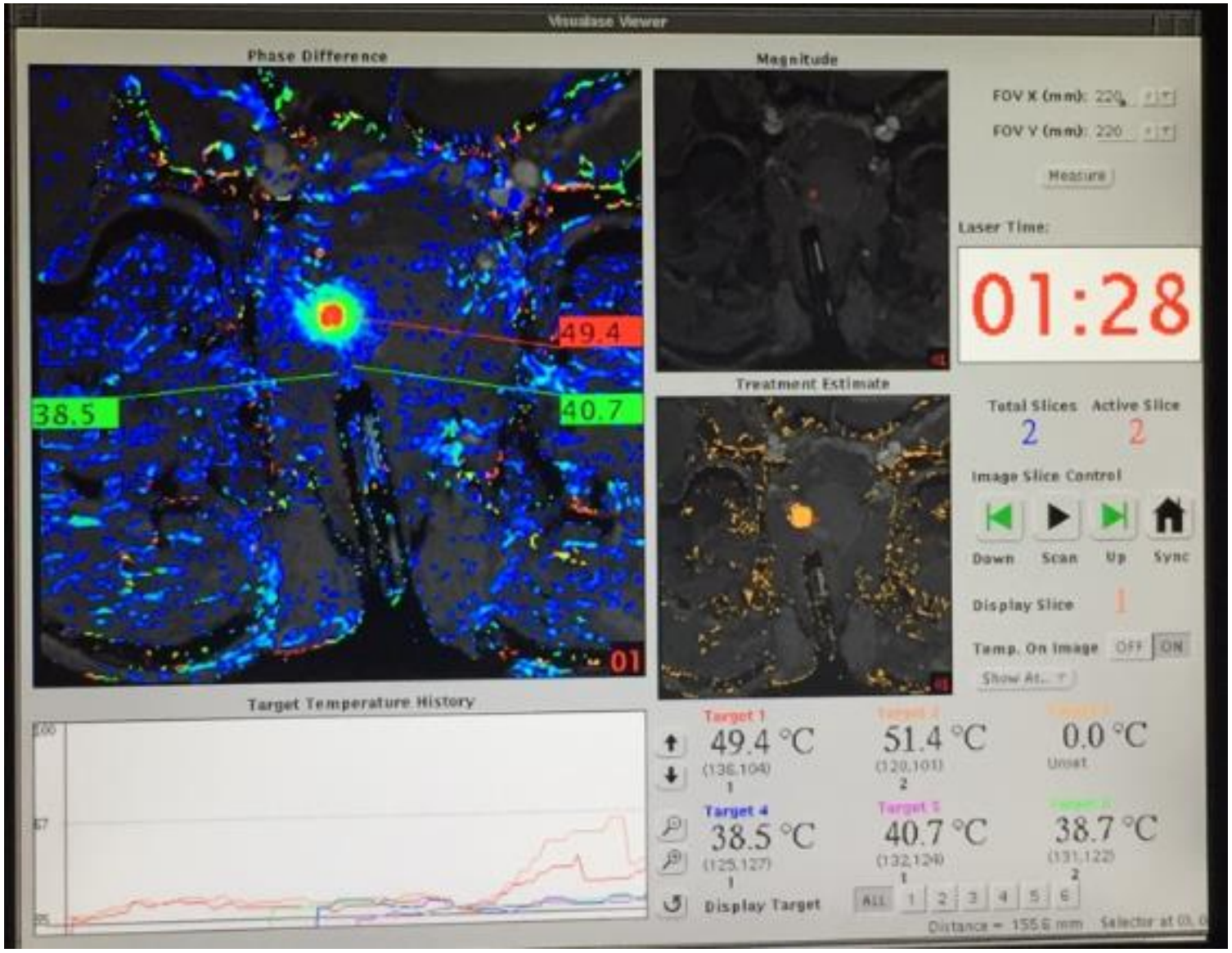




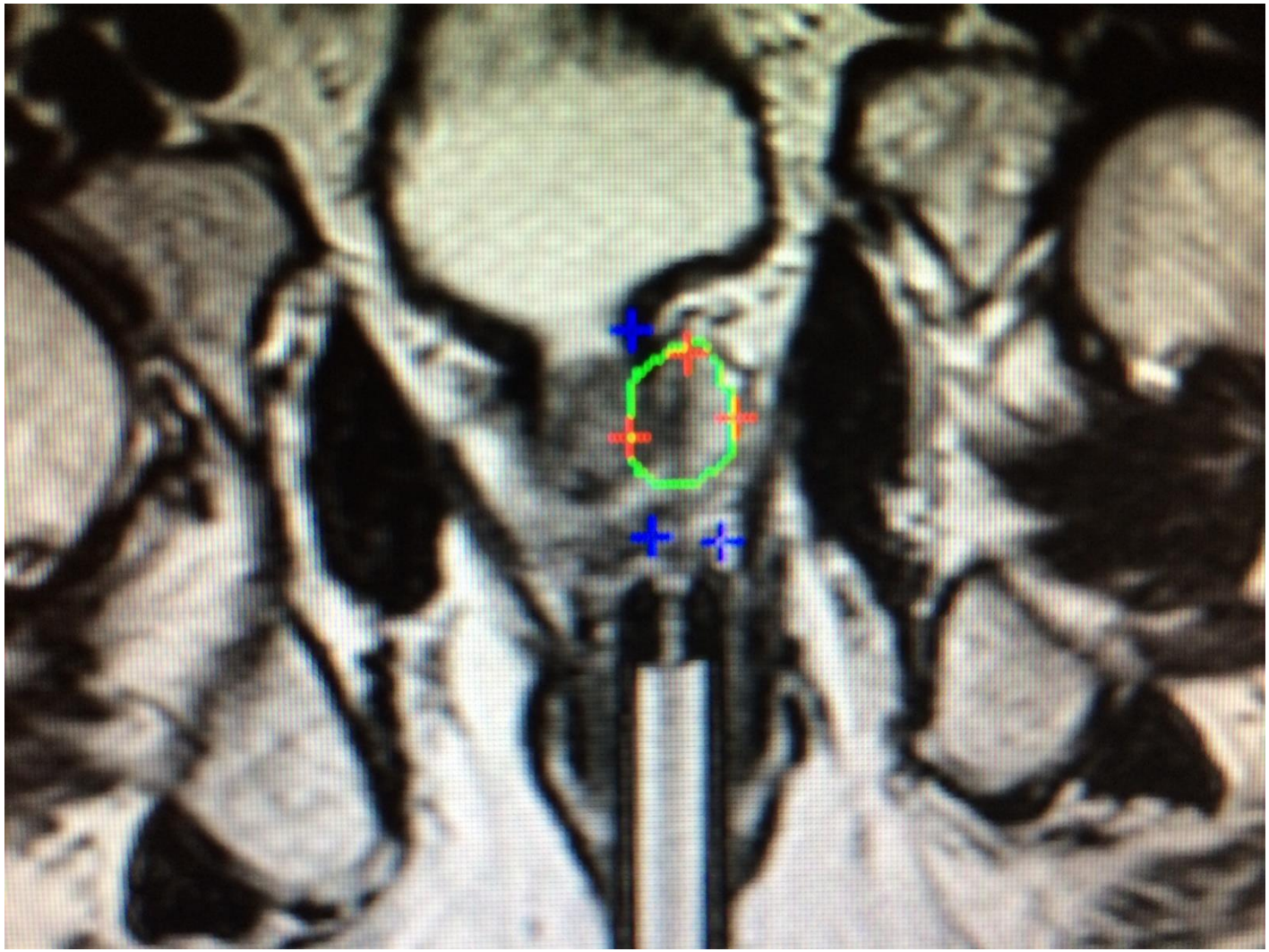


https://www.bing.com/images/search?q=baking+a+cake&view=detailv2&&id=E0619BA4C321DB343BDA407A101E9D9E45BB0B6C&selectedIndex=4&ccid=v6Af2VQj&simid=607992663429939575&thid=JN.t2FcJIB1rEYOUIBkmlLvLg&ajaxhist=0

Thermometry interface - Proton resonance frequency (PRF) shift thermometry



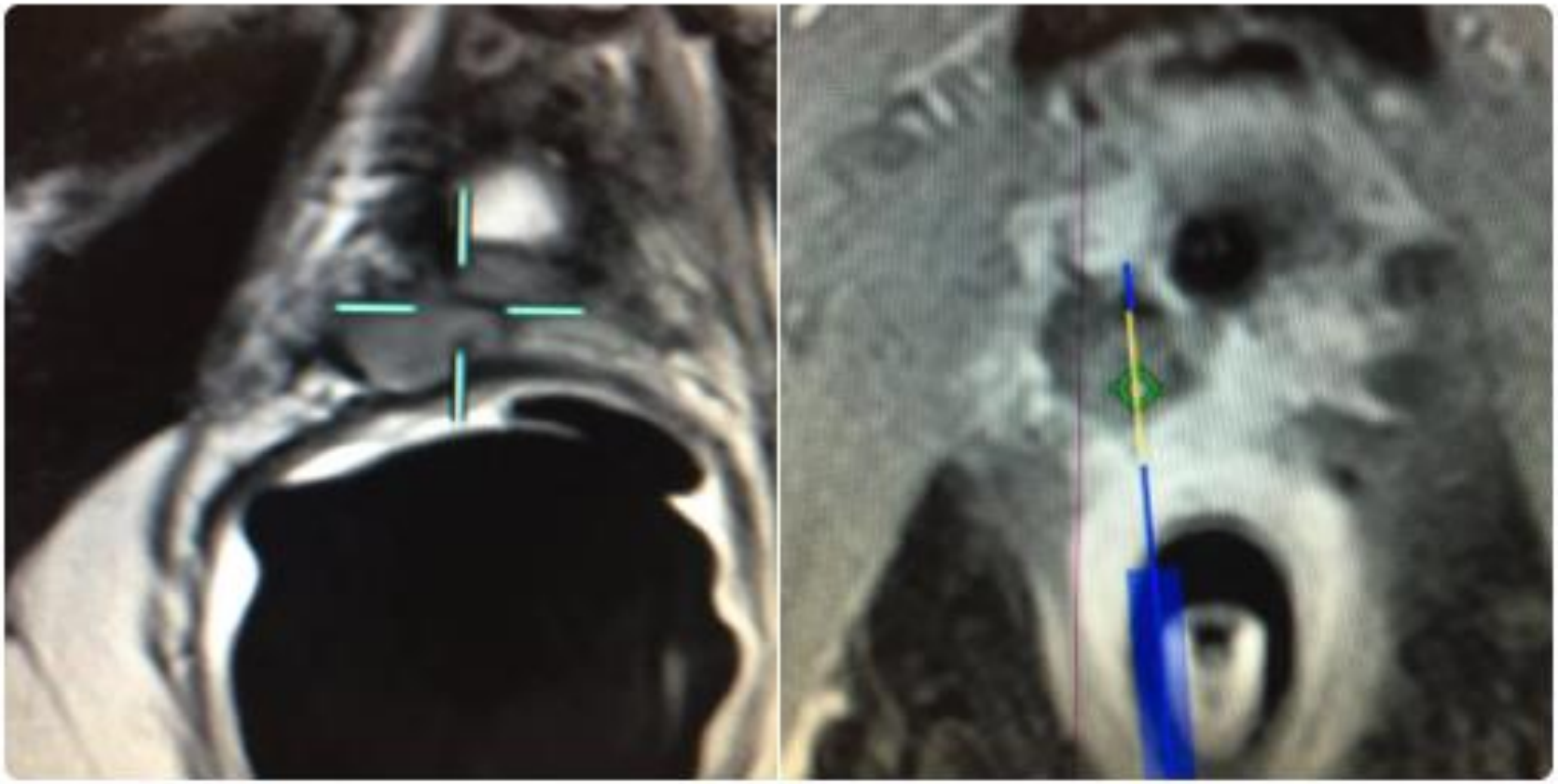
Contouring and Safety Controls



Salvage post-prostatectomy April 5, 2018

Bernadette Greenwood @multiparametric · Apr 5

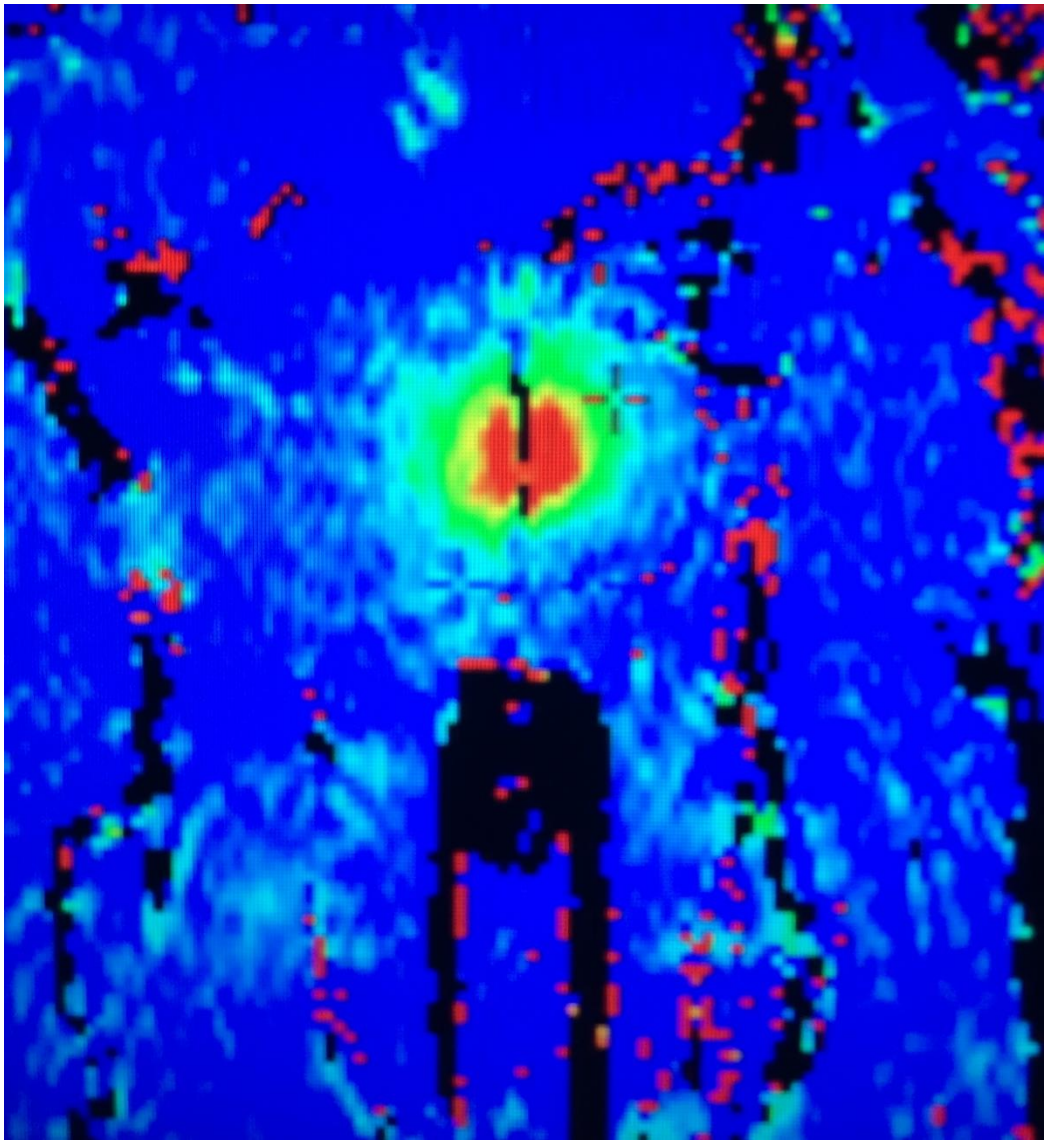
Before and after. Tricky!



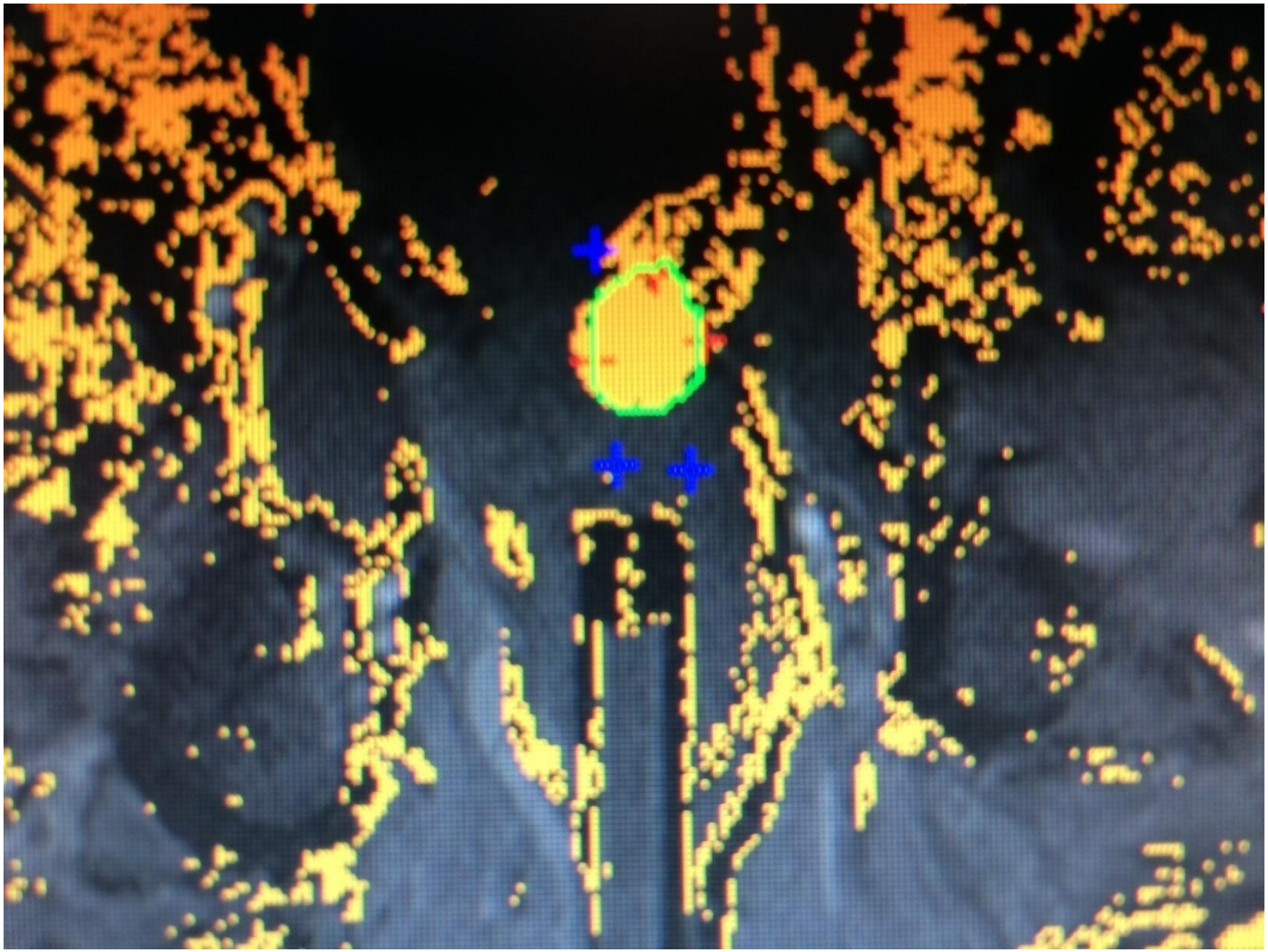
Real Time MR Thermometry

Test Dose
4W (27%)
~100 degrees F

Treatment Dose
12W (80%)
90 sec



Irreversible Damage Estimate



Technical aspects – ECR 2011

EPOS™
Electronic Presentation Online System

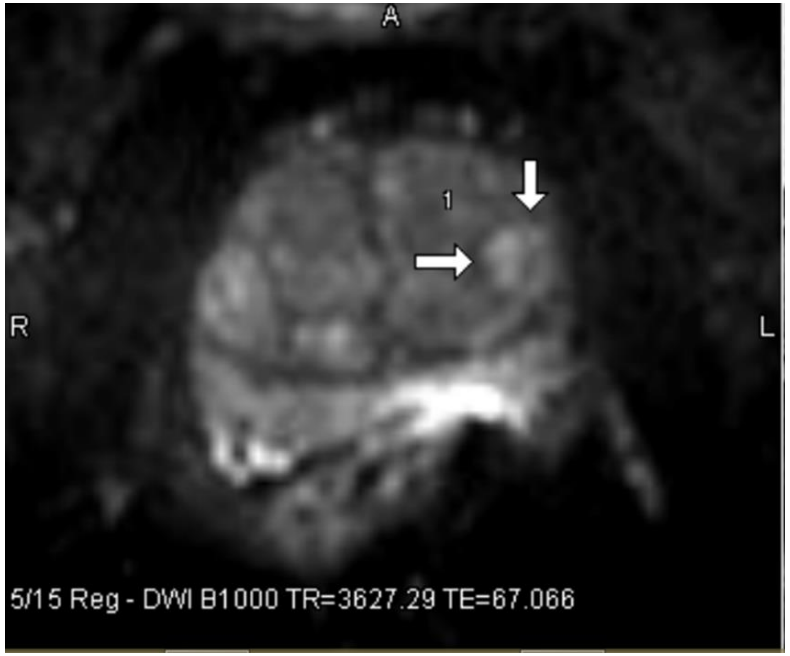
ESR
European Society of Radiology

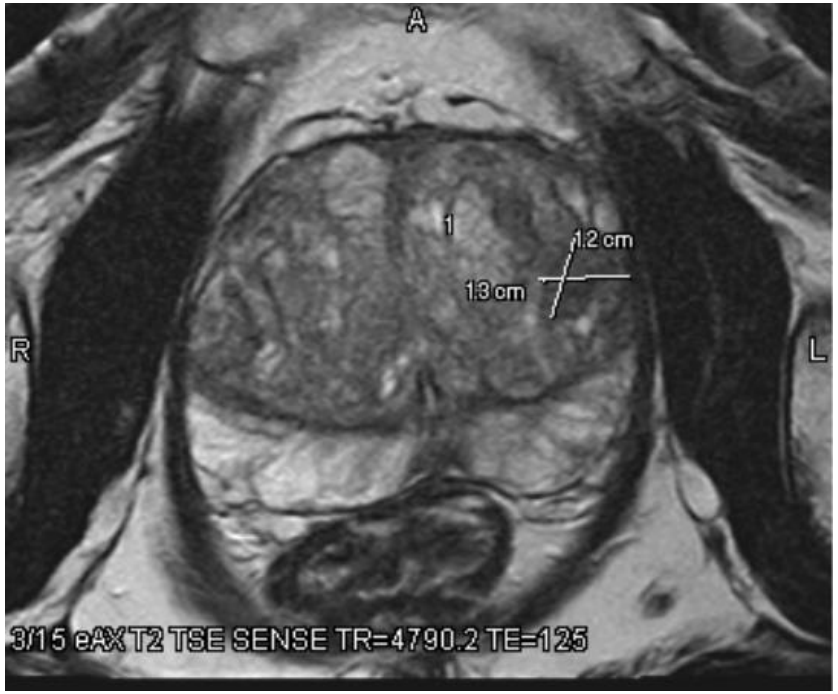
Technical aspects of trans-rectally delivered, MRI-guided laser therapy of prostate cancer

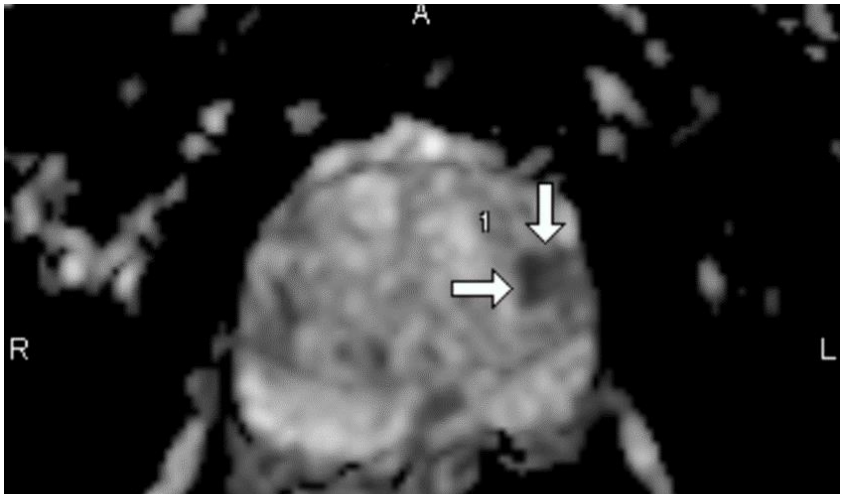
Poster No.:	C-1045
Congress:	ECR 2011
Type:	Scientific Paper
Authors:	B. M. Greenwood[1], J. F. Feller[2], R. McNichols[3]; [1]Pewaukee, WI/US, [2]Indian Wells, CA/US, [3]Houston, TX/US
Keywords:	Genital / Reproductive system male, Oncology, Pelvis, MR, CAD, Image manipulation / Reconstruction, Ablation procedures, Laser, Computer Applications-General, Tissue characterisation
DOI:	10.1594/ecr2011/C-1045

Patient J.D.

GS 3+4=7

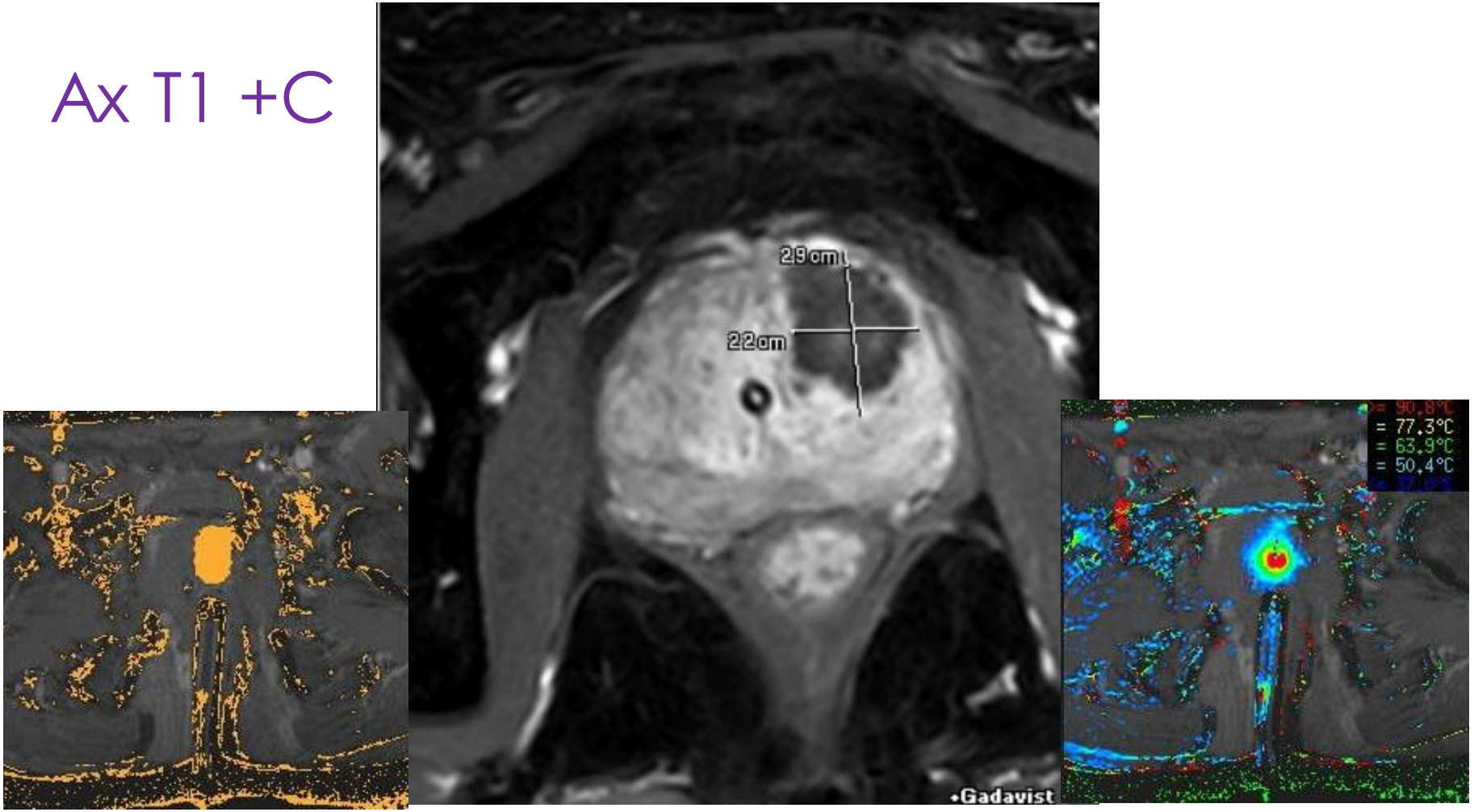






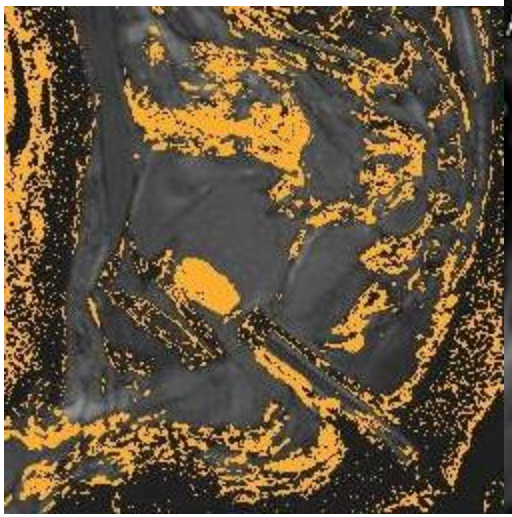
Patient J.D. – MRG Laser focal therapy 8/2014

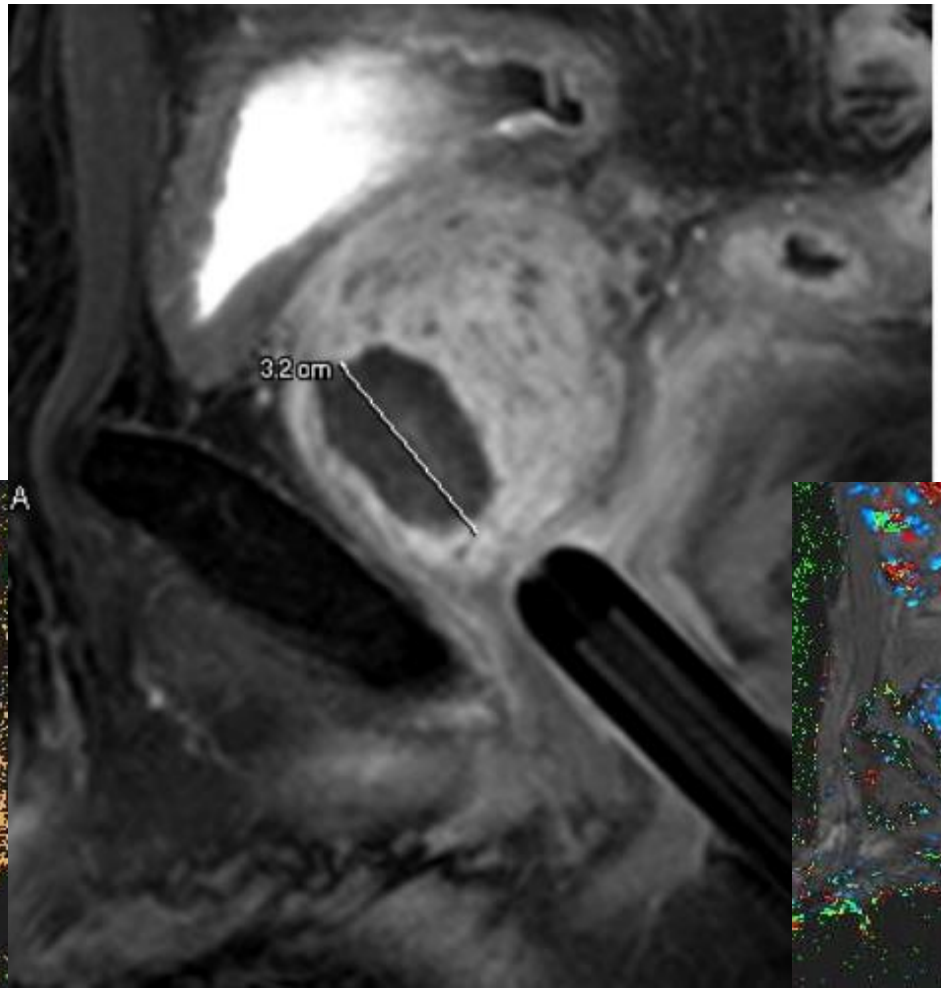
Ax T1 +C

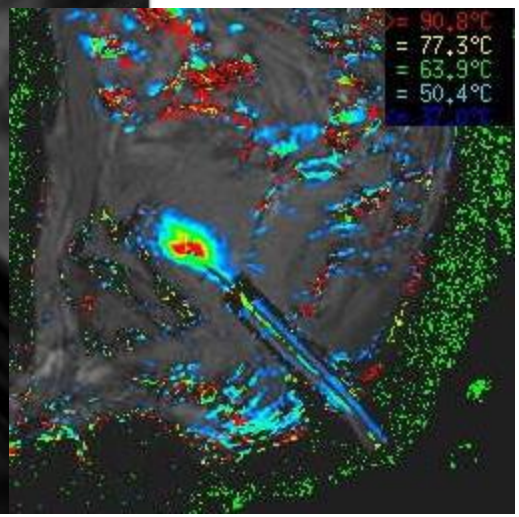


Patient J.D. – MRG Laser focal therapy 8/2014

Sag T1 +C

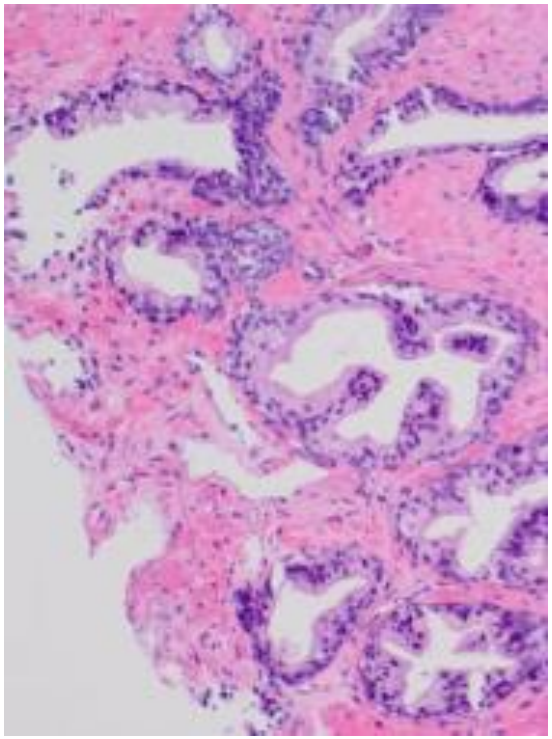






Patient J.D.

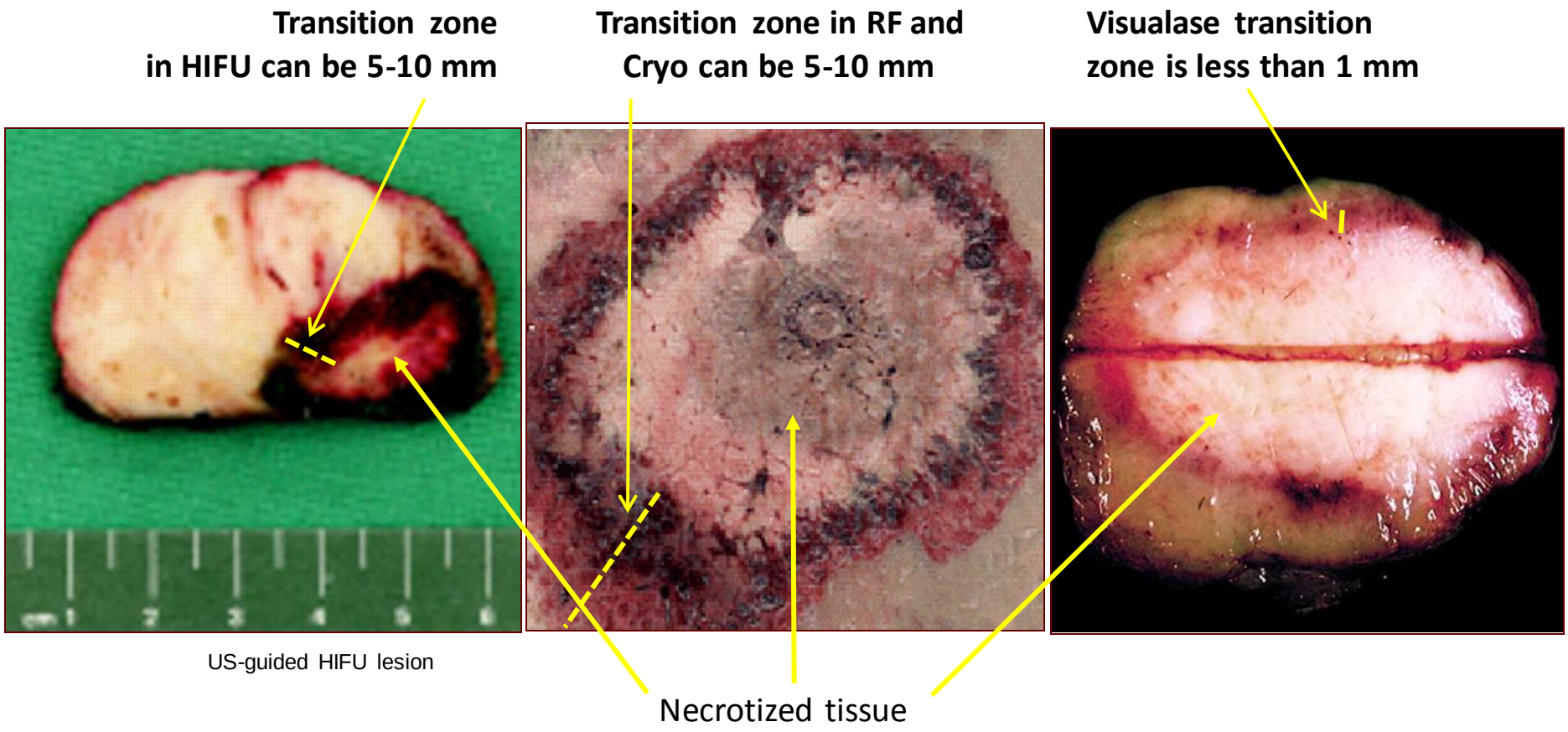
Negative bx at 6 mo. f/u focal laser



Laser interstitial thermal therapy margins

Precision and Control

Sharp transition zone between dead and viable tissue



Source
http://jcp.bmjjournals.com/content/53/5/391/F1.expansion

* Photos at different scales

Methodology

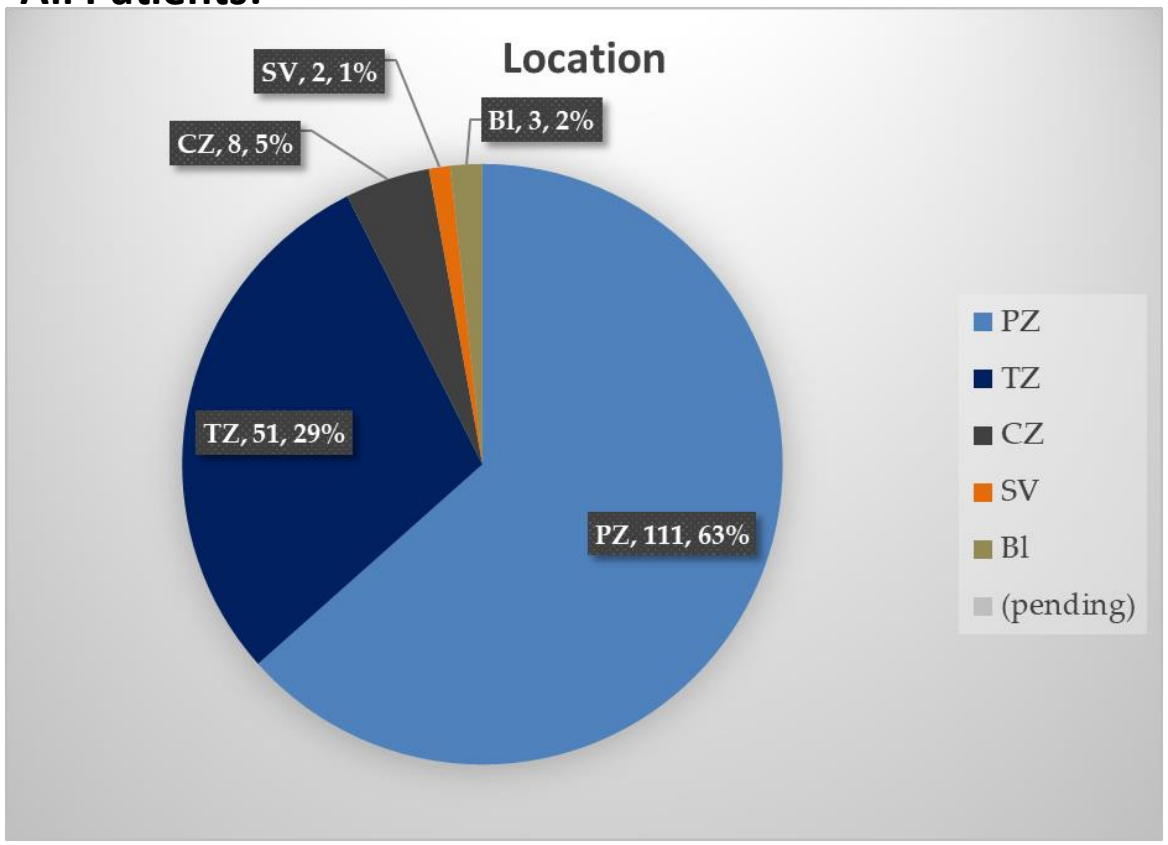
- IRB approved, 510k cleared technology
- NCT# 02243033
- Outpatient trans-rectal laser therapy (15W, 980 nm diode laser) guided with 1.5T MRI system (image acquisition & real-time thermometry)
- True focal therapy
- Goal to eliminate MRI abnormality + 1cm
- 175 cancer foci treated in 119 patients from 2010 – 2018
- 6-Month biopsies performed with MRI active surveillance follow-up
- Evaluation of PSA, PSAD, mpMRI, recurrence rates (marginal, incidence), IPSS, SHIM, PHQ-9

Patient Population At A Glance:

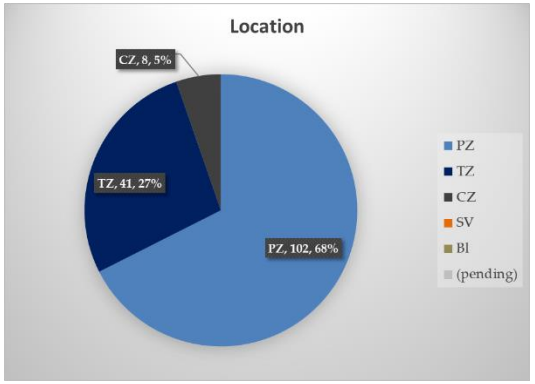
Statistic	Data
# of Patients	119
# of Treatment Naïve Patients	100 / 119 (84%)
# of Salvage Patients	19 / 119 (16%)
# of Total Lesions	175
# of Treatment Naïve Lesions	150 / 175 (86%)
# of Salvage Lesions	25 / 175 (14%)
Mean Initial PSA	7.31
Mean Nadir PSA	3.19 (56% drop)
Min Age	48
Max Age	87
Median Age	67

Tumor Location Statistics

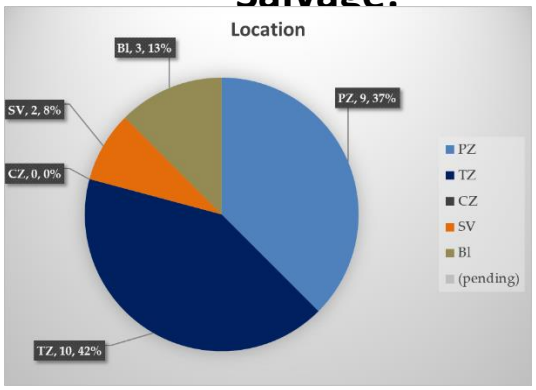
All Patients:



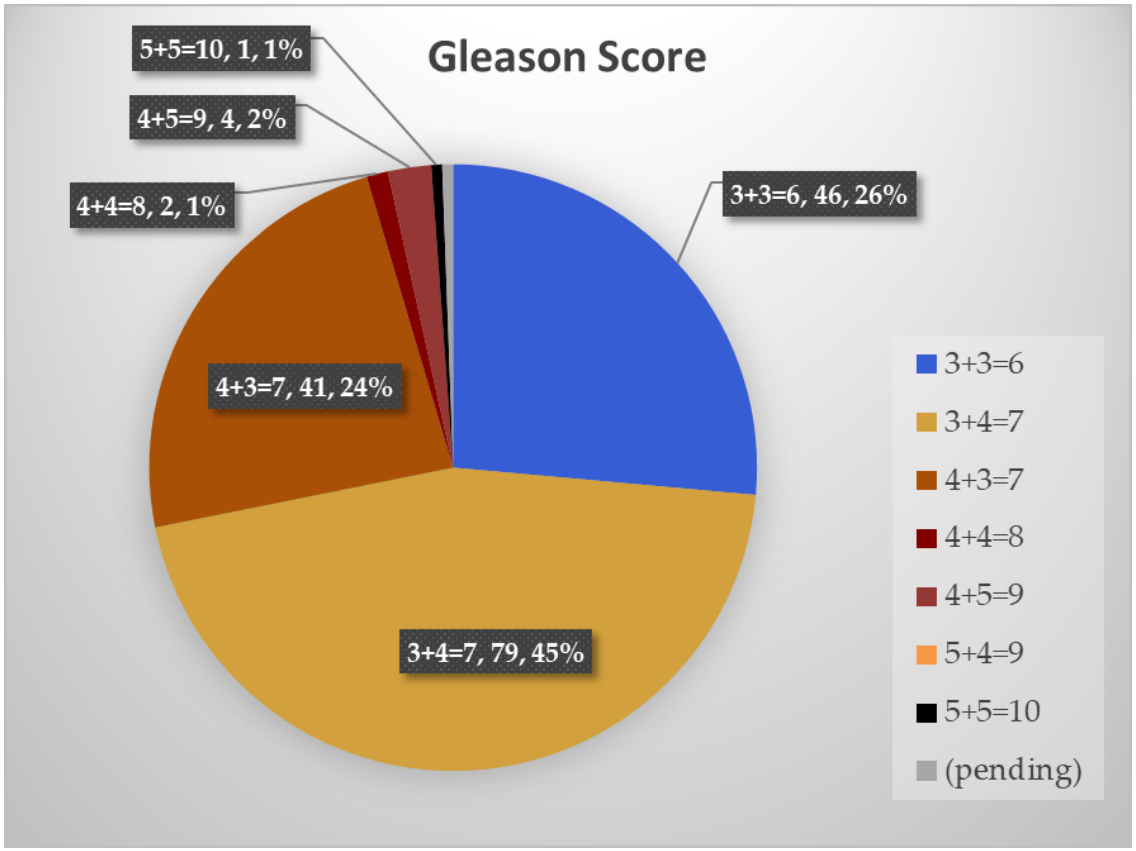
Treatment Naïve:



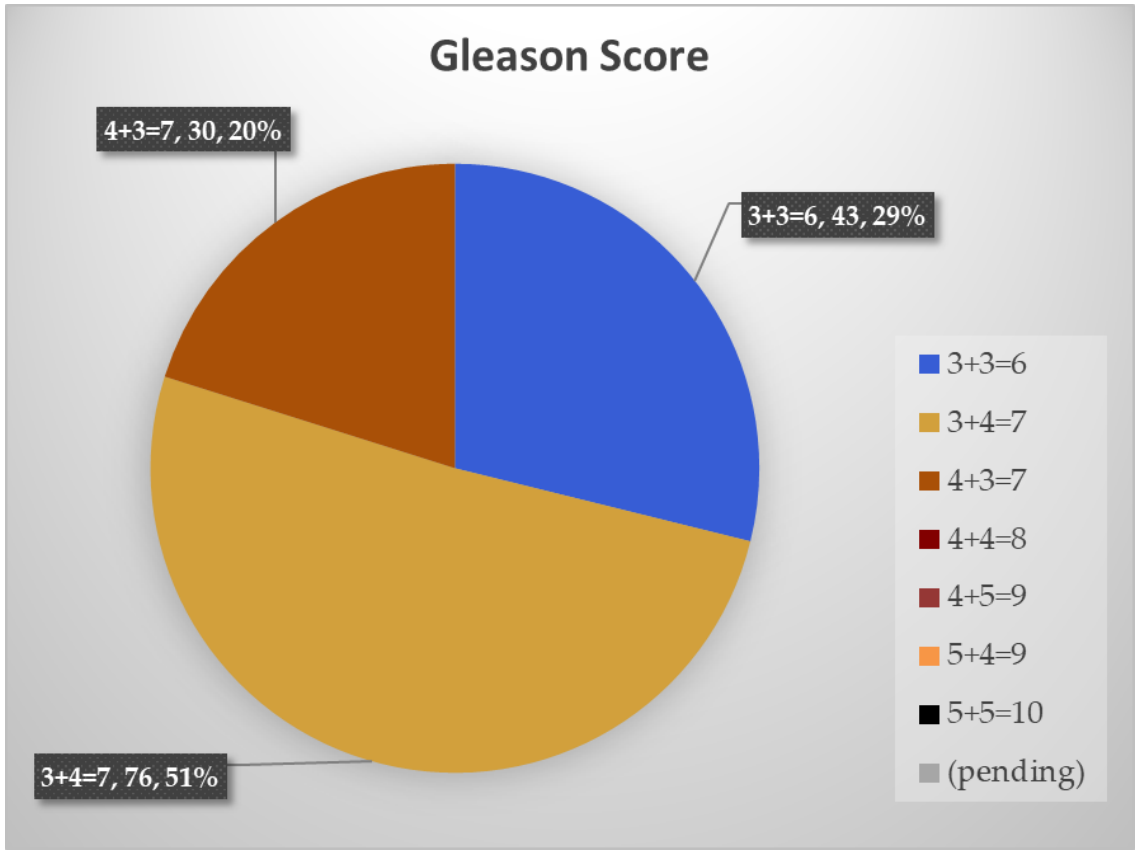
Salvage:



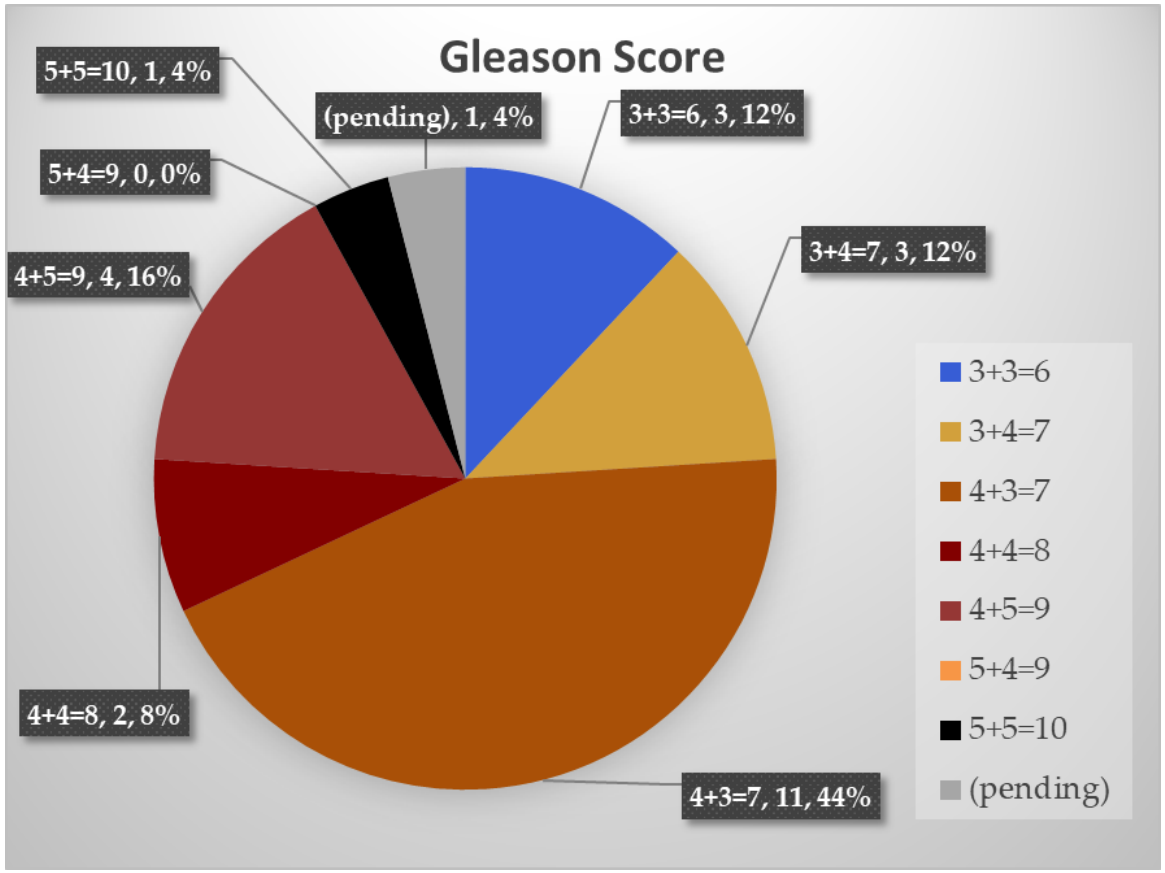
Gleason Score Breakdown – All Patients



Gleason Score Breakdown – Treatment Naïve

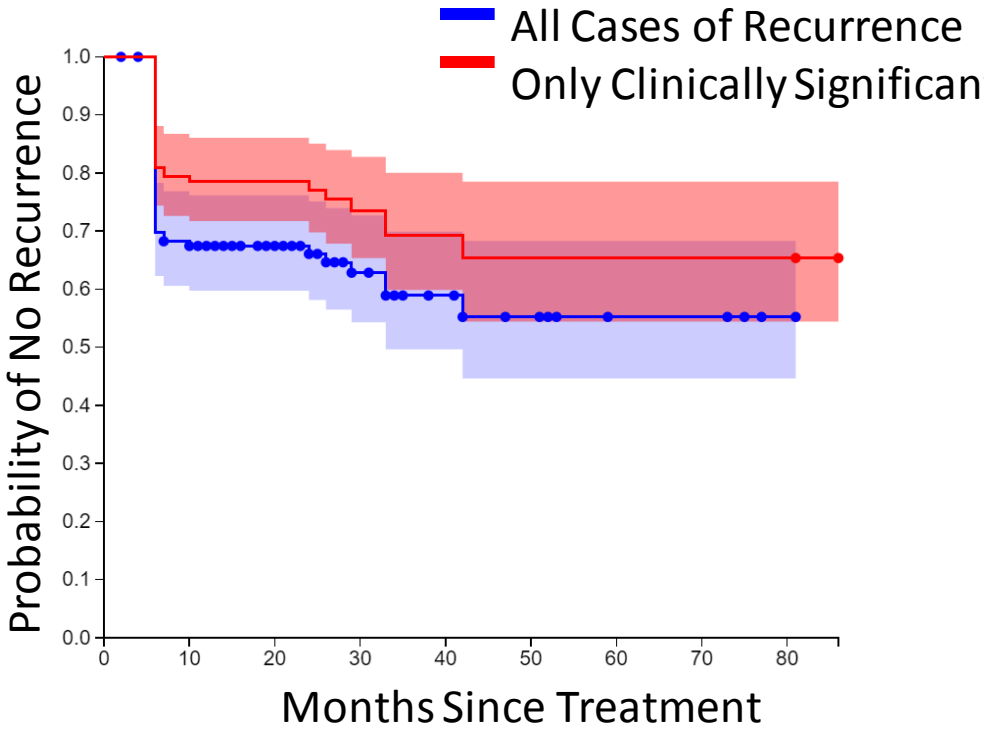


Gleason Score Breakdown – Salvage



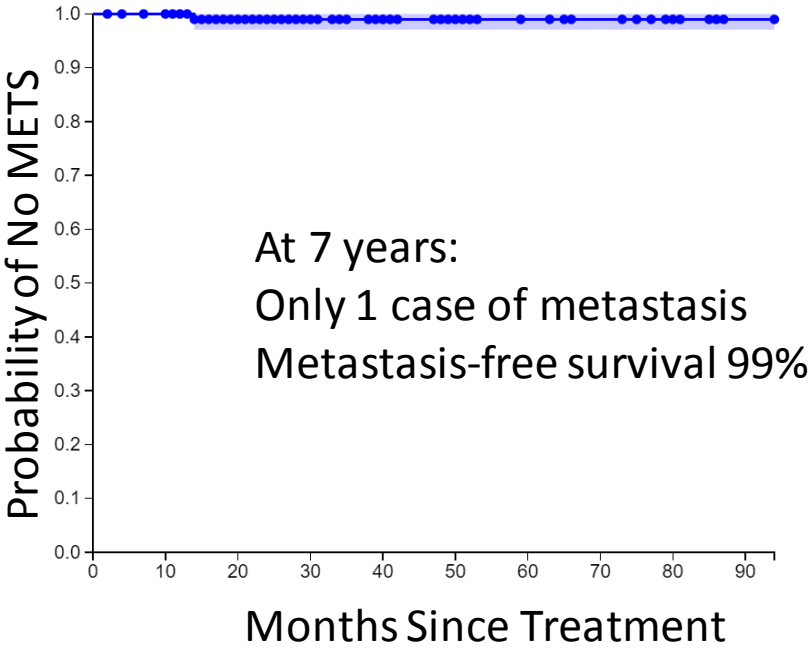
Results – Biopsy Proven Recurrence Statistics

- While **no** prostate cancer-specific deaths have occurred, a Kaplan-Meier Curve of *recurrent* cancer is shown with 95% confidence interval bands.
- The drop at the 6-month mark is due to the protocol with a biopsy being acquired 6-month following treatment to detect marginal recurrence.

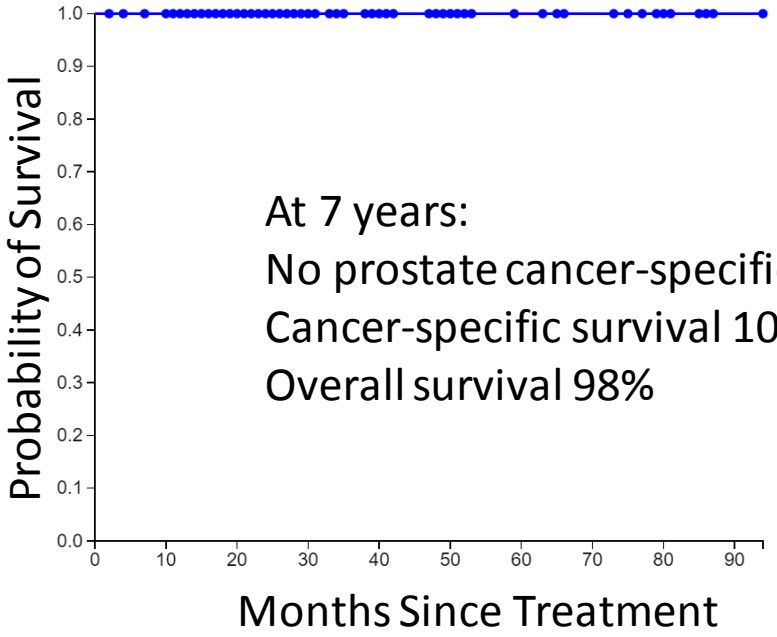


**Excludes 3+3=6 recurrence*

Results – Kaplan-Meier Survival Curves



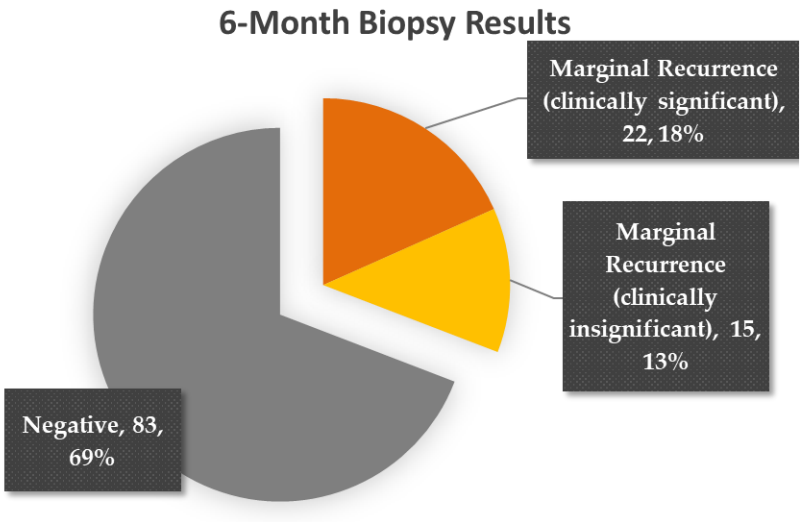
At 7 years:
Only 1 case of metastasis
Metastasis-free survival 99%

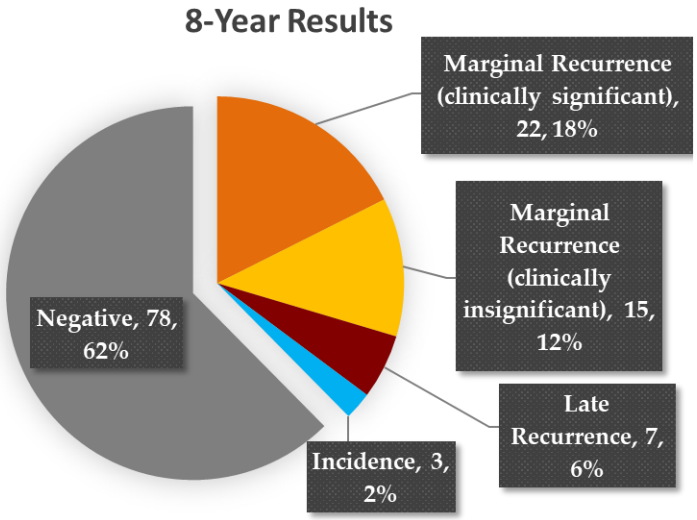


At 7 years:
No prostate cancer-specific deaths
Cancer-specific survival 100%
Overall survival 98%

Results – Biopsies (with significance breakdown)

- Biopsies evaluating treatment efficacy performed at 6 months.
- MRI active surveillance over 8 years.



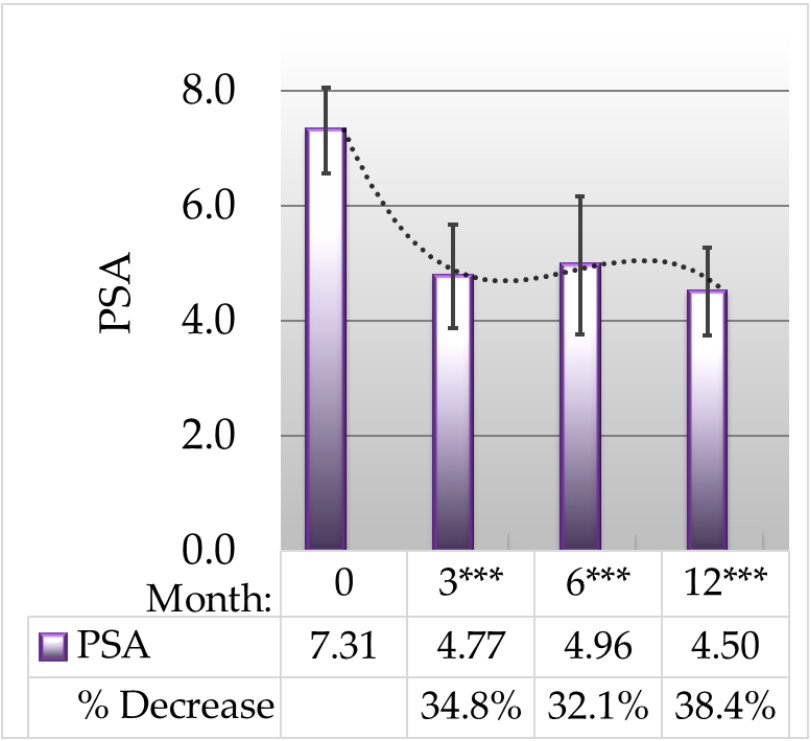


("Clinically Significant" excludes 3+3=6)

Field Cancerization: “WHAC-A-MOLE” Patients

Results – PSA

- Mean PSA dropped 38%, 12 months following treatment
- 95% Confidence Interval shown as error bars
- Compared to the initial PSA (Month 0), paired Student's t-test used to evaluate mean PSA, **p<.001*****



Month:	0	3***	6***	12***
PSA	7.31	4.77	4.96	4.50
% Decrease		34.8%	32.1%	38.4%

Conclusions & Next Steps

- 8 year interim data in over 100 patients indicates outpatient MR-guided trans-rectal laser focal therapy is both safe and feasible.
- No statistically significant erectile dysfunction, or incontinence.
- Favorable results for quality of life without eliminating the possibility of whole-gland therapy or additional laser focal therapy in patient's future.
- Short term and intermediate term oncologic control is achievable in 75% of patients.
- Minimally-invasive outpatient laser focal therapy of prostate cancer may be an attractive option for specific patient populations.
- "Nothing ruins good results like follow-up." >>> 20 year Phase 2 study ongoing.
- International multi-institutional Phase 2 trial through the International Laser Network awaiting IRB approval.
- Ongoing IRB approved clinical trial exploring tissue genomics for risk stratification.
- IND submission completed to FDA for combination therapy awaiting approval.

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Disclosures:

Ms. Greenwood has no financial disclosures

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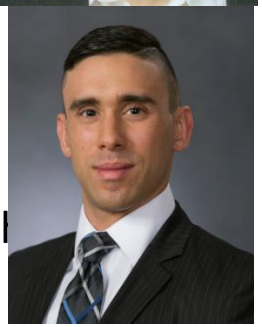

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Thank you for your attention!

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