Trans-rectally Delivered, MRI-Guided Laser Focal Therapy of Prostate Cancer: How We Do It

The Prostate Cancer Support Association of New Mexico Albuquerque, NM September 19, 2015

Bernadette Greenwood, BSRS, RT (R) (MR)







Ms. Greenwood has nothing to disclose

STATE of WISCONSIN



OFFICE of the GOVERNOR

rtion

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

MARKEAS; 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, TPEREFORE, 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, 1 have bereanto 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.

ct to SCOTT WALKER GOVERNOR

1. History of Trial #NCT 02243033

- 2. Literature review
- 3. Procedure overview
- 4. Results and conclusions

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Find Studies -	About Clinical Studies	Submit Studies 🔻	Resources	About This Site
Home > Find Studie	s > Study Record Detail			

Laser Interstitial Thermal Therapy of Prostate Cancer

This study is currently recruiting participants. (see Contacts and Locations) Verified August 2015 by Desert Medical Imaging	ClinicalTrials.gov Identifier: NCT02243033
Sponsor: Desert Medical Imaging	First received: September 9, 2014 Last updated: August 14, 2015 Last verified: August 2015
Information provided by (Responsible Party): Desert Medical Imaging	History of Changes



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



•Complements PSA / DRE /TRUS

- Prostate <u>intervention</u> (targeted biopsy under MR-guidance)
- MR/US fusion biopsy
- Focal therapy vs. whole-gland, radical treatment (prostatectomy, XRT, ADT)





Breast vs. Prostate Cancer Research



Ke	search Dollars (Dollars	by Various Ca in Millions)	ancers		
	2007	2008	2009	2010	2011
Total NCI	\$4,792.6	\$4,827.6	\$4,966.9	\$5,098.1	\$5,058.1
AIDS	253.7	258.5	265.9	272.1	270.0
Brain & Central Nervous System	148.2	153.7	151.5	156.8	172.6
Breast Cancer	572.4	586.8	599.4	631.2	625.1
Cervical Cancer	82.4	76.8	70.8	77.0	81.4
Clinical Trials	843.7	853.2	882.8	852.3	877.8
Colorectal Cancer	258.4	273.7	264.1	270.4	265.1
Head and Neck	66.2	76.1	77.1	62.7	61.8
Hodgkin's Disease	16.5	17.5	18.2	14.6	13.4
Leukemia	205.5	216.4	220.5	239.7	227.0
Liver Cancer	67.7	74.2	69.0	72.6	66.2
Lung Cancer	226.9	247.6	246.7	281.9	296.8
Melanoma	97.7	110.8	103.7	102.3	115.6
Multiple Myeloma	32.3	41.5	45.2	48.5	54.9
Non Hodgkin's Lymphoma	113.0	122.6	131.3	122.4	126.4
Ovarian Cancer	96.9	100.0	110.1	112.3	110.8
Pancreatic Cancer	73.3	87.3	89.6	97.1	99.5
Prostate Cancer	296.1	285.4	285.1	300.5	288.3
Stomach Cancer	12.0	12.4	15.4	14.5	13.4
Uterine Cancer	16.6	17.1	18.0	14.2	15.9

http://obf.cancer.gov/financial/attachments/11Factbk.pdf accessed 5/25/14

How did I get here?

PSA

Sensitivity: 34.9% Specificity: 63.1%

DRE

Sensitivity: 27.1% Specificity: 49.0%

http://www.jyi.org/research/re.php?id=931



Current practice

biopsy negative, but high PSA persists – another systematic ultrasound-guided biopsy at urologist



Targeted, Focal or Precision Treatment







Literature Timeline 1920 - present

1920's	1922 – Barringer:	1926 – Young: Open perineal	
	Transperineal needle biopsy	biopsy	
1930's	1930 – Ferguson: First perineal needle aspiration biopsy	1937 – <u>Astraldi</u> : First <u>transrectal</u> 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 – <u>Stamey</u> : 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 — <u>Beyersdorff</u> 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 <u>Multiparametric</u> MRI
	2013 – Oto et al.: Transperineal MRI-guided laser interstitial thermal therapy of PCa	2013 — <u>Amalou</u> et al.: MRI/US fusion prostate biopsy and ablation	2013 – Greenwood et al.: transperineal MRI-guided cryotherapy of PCa

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

Prostate Biopsy in the 1920's

1920's **1922 – Barringer:** Transperineal needle biopsy

1926 – Young: Open <u>perineal</u> 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



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



Am J Clin Pathol. 1968;49:347.

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







Prostate Biopsy in the 1990's



Figure 1 A 36-core saturation biopsy scheme, as used by Delongchamps et al.



Modified, with permission, from Delongchamps, N. B. *et al. Prostate Cancer Prostatic Dis.* doi:10.1038/pcan.2008.38 (2008) © Macmillan Publishers Ltd. All rights reserved.

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



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





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







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



"Fast is fine, but accuracy is everything."



Why MRI for the Prostate Today?









Gleason 4 + 3 = 7

Gleason Grades Determine Gleason Score



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

Gleason Grades Determine Gleason Score







Gleason Grades Determine Gleason Score

Original Gleason System Versus 2005 ISUP Modified Gleason System: The Importance of Indicating Which System Is Used in the Patient's Pathology and Clinical Reports

By: Rodolfo Montironi^a * ⊠, Liang Cheng^b, Antonio Lopez-Beltran^c, Marina Scarpelli^a, Roberta Mazzucchelli^a, Gregor Mikuz^d, Ziya Kirkali^e and Francesco Montorsi^f European Urology, Volume 58 Issue 3, September 2010, Pages 369-373

Published online: 01 September 2010

http://www.europeanurology.com/article/S0302-2838(10)00422-7/fulltext/original-gleason-system-versus-2005-isupmodified-gleason-system-the-importance-of-indicating-which-system-is-used-in-the-patient-s-pathology-and-clinicalreports

Genomic testing results



ProstaVysion



Oncotype Prostate



Prostate Intervention in the 2010's

2010's	2011 – Green Transrectal N laser interstit therapy of PC	wood et al.: /IRI-guided tial thermal Ca	2011 — Pinto et al.: MRI/US fusion prostate biopsy	2012 – NCCN Guidelines include <u>Multiparametric</u> MRI
NCCN	National Comprehensive Cancer Network®	NCCN Gui Prostate C	delines Version 2.2012 ancer Early Detection	NCCN Guidelines Index Prostate Early Detection TOC Discussion

Repeat Biopsy Technique

Patients with prior pegative biopsies, yet persistently rising PSA values should undergo repeat biopsy. Inportant 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 bionsy may be considered.92 Recent evidence showed that multiparametric MRI 2 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.



Adoption of Prostate MRI

- MRI Volumes Reached 34.9M in 2014
 - The two highest volume categories of MRI imaging were Spine (23%) and Brain (22%) procedures.
- Prostate
 - From 2013 to 2014, the biggest percentage increase in MR procedure volume is for prostate procedures which more than doubled from 0.2 to 0.5 million
 - Though the volume of prostate procedures is only 1% of 2014 MR procedures, growth of 150% shows application adoption
- Other Growth Areas
 - Pelvis & abdomen procedures grew 28% from 2.5 to 3.2 million
 - Chest procedures grew ~ 25% from 0.8 to 1.0 million procedures.



New Standards in MRI: PI-RADSv2

Leading International Scientists Announce New Guidelines for Improved Prostate Cancer Diagnosis

Scientific Cooperation Aims to Accelerate Transfer of High Quality Prostate MRI from Laboratories to Clinics

 The Joint Steering Committee of the American College of Radiology (ACR), AdMeTech Foundation and the European Society of Urogenital Radiology (ESUR) today released new clinical imaging guidelines to assist early detection and treatment of prostate cancer. The new guidelines were announced at the meeting of AdMeTech's International Prostate MRI Working Group (AdMeTech's Group) held in conjunction with the Annual Meeting of the Radiologic Society of North America (RSNA).

The Joint Steering Committee developed Prostate Imaging Reporting and Data System Version-2, (PI-RADSv2) as global guidelines for high quality multi-parametric prostate MRI service. This work has built on the initial PI-RADS standardization, which was recommended by AdMeTech's Group in 2010 and created by ESUR in 2011. PI-RADSv2 has defined minimum technical requirements for creating images and in coordination with RSNA's Radiologic Lexicon Committee, set standards for communicating the risk and location of aggressive prostate cancer. These clinical guidelines were established in order to expedite wide-scale transfer of the high quality clinical service from the few leading research centers to the international medical community.

<section-header> PJ-RADS v2 prostate Imaging and Reporting and Data System: Version 2 prostate Imaging and Reporting and Data System: Version 2 protuction inical Considerations and Technical Specifications CECTION II Cinical Considerations and Technical Specifications Section VI Constant Anatomy and Benign Findings Section VI Constant Anatomy and Benign Findings

INTRODUCTION

Magnetic Resonance Imaging (MRI) has been used for noninvasive assessment of the prostate gland and surrounding structures since the 1980s. Initially, prostate MRI was based solely on morphologic assessment using T1-weighted (T1W) and T2-weighted (T2W) pulse sequences,

1

National Guidelines - 2009



National Guidelines - 2012

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2012 Prostate Cancer Early Detection

NCCN Guidelines Index Prostate Early Detection TOC Discussion

Repeat Biopsy Technique

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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



TRIM Compared to 2nd or 3rd TRUS Bx



^{*}Based on 71 patients

Ultrasound vs. MRI



5

ACR Appropriateness Criteria[®] ACR PI-RADS V2, published 2014

Prostate Cancer - Pretreatment Detection

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



TRUS biopsy

Needle penetrates next to the tumor or does not reach it



Less aggressive tumor is biopsied

1.7 cm line

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



Less aggressive part of the tumor is biopsied

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

Prostate Intervention in the 2010's





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 MR Guidance Device



Interventional Device

Interventional Instruments 18 G MR compatible

TRUS-Biopsy & MR-Biopsy vs. Prostatectomy



Hambrock 2010 SCBTMR "Lauterbur Award"

MR-guided Laser Focal Therapy



Water-cooled disposable laser probe 980 nm diode laser 1.65 mm in diameter



Heat-diffusing tip



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

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:



- Laser Applicator
- Laser System
- Workstation Software

• 30 W Laser System

• Visualase Thermal Therapy System

K053087 (March 2006) K060304 (March 2006) K063505 (December 2006) K071328 (August 2007) K081656 (September 2008) K092197 (November 2009)

30 Watt Diode Laser

Thermometry interface



MR Thermometry and Image Generation



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

MR Thermometry and Image Generation

Proper parameter selection allows for exploitation of tissue properties:

Tissue contrast Flow quantification Perfusion Diffusion Phase shifts

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



Contouring and Safety Controls



Real Time MR Thermometry

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

Treatment Dose 12W (80%) 90 sec



Irreversible Damage Estimate



Laser interstitial thermal therapy margins

Precision and Control

Sharp transition zone between dead and viable tissue



US-guided HIFU lesion

Necrotized tissue

Technical aspects – ECR 2011



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

Poster No.:	C-1045
Congress:	ECR 2011
Туре:	Scientific Paper
Authors:	<u>B. M. Greenwood</u> 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

Results: NCT 02243033, as of Sept. 2015

- 45 patients
- 4 salvage patients for BCR
- 62 cancer foci treatments
- Age range: 50-81 years
- Initial PSA
 Range = 0.9 28
 Mean = 7.12
- MRI tumor volume Range = 0.1 – 4.1 cc Mean = 0.88 cc

Results: Treatment Naïve

Gleason Score*	Patients	Cancer Foci
3+3	15	18
3+4	20	26
4+3	10	12

Zone†	Cancers
PZ	36
TZ	22
CZ	3

* Four patients had GS6 and GS7 lesions, one had both 3+4 and 4+3

+ Seven patients were treated for multifocal cancer

Results: Salvage

Therapy	Cancer Foci	Patients
Brachytherapy	3	2
Proton beam	1	1
Cryotherapy	1	1

Gleason Score	Cancer Foci	Patients
3+3	0	0
3+4	1	1
4+3	3	2
4+4	0	0
4+5	1	1

Results: Treatment Naïve

- Total procedure time = 1.5-4.0 hours
 Goal of eliminating T2W / ADC map attained initially in 80%
 MRI vol. of coagulation necrosis 1.2-11.8 cc
- No serious adverse events, no morbidity!

2 cases of asymptomatic periprostatic necrosis

3 cases of retention cyst

13 patients with positive biopsy at treatment site consistent with residual/recurrent cancer

- Positive margin rate = 26%
- Incidence cancer rate = 6%
- 10 patients retreated with laser focal therapy

Results - PSA



47% decrease of mean PSA 1 year after laser focal therapy

Results - IPSS



Results - SHIM



Results: Patient Withdrawal

- 1 patient expired from metastatic melanoma
- 1 patient withdrew for personal reasons
- 1 patient withdrew after negative 6 month bx (GS 3+3) because of travel
- 5 patients went on to whole gland therapy (11%)
 4 incidence cancer patients (2 GS 4+4, 1 GS 4+3 multifocal,1 3+4)
 elected RP*

Importantly, no additional technical difficulty reported with RP

1 GS 3+3 elected PBT before 6 month Bx

*One 4+4 was downgraded to 4+3 at surgery

Small Series Conclusions

- 1. Outpatient MR guided transrectal laser focal therapy of prostate cancer is feasible and safe
- 2. Positive margin rate = 26%
- 3. Whole gland therapy rate = 10%
- 4. Incidence cancer rate = 6%
- 5. Patients are still re-treatment viable (focal or whole gland therapy)
- 6. Continuity of imaging modality:

Multiparametric MRI >> MR Guided Bx >> MR Guided Focal Therapy

Take Home Message

Establishing an MRI based prostate laser focal therapy program is a multi-disciplinary team sport!



MRI Program for Detection and Treatment of Prostate Cancer

- I. Multi-parametric MRI of the prostate
- II. MR guided biopsy
- III. MR guided focal laser ablation of prostate cancer (Investigational)

MRI is the GPS for detecting and localizing prostate cancer!

Acknowledgements

DMI RESEARCH TEAM

- John Feller, MD
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- Axel Winkel (Invivo-Germany)
- Wes Jones

- Andrew Farrall, PhD
- Elda Railey, Co-founder Focus on Research

Thank you for your attention!

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Research Advocacy Network



