Friday, May 6, 2016 1:00 PM-3:00 PM
SDCC: Room 32
Imaging/Radiology: Uroradiology II
Funding: NCI (R01CA195505), Jean Perkins Foundation, Andre Agassi Foundation, Steven C. Gordon Family Foundation, Beckman Coulter Foundation, and the Dream Fund.
PD06-05: **The MRI-Invisible Prostate Cancer: Incidence and Significance**
Jason Wu*, Daniel Margolis, Shyam Natarajan, Alan Priester, Jiaoti Huang, Maria Luz Macairan, Patricia Lieu, Devi Sharma, Frederick Dorey, Leonard Marks, Los Angeles, CA

Abstract: PD06-05

Introduction and Objectives

Targeted prostate biopsy using multi-parametric MRI (mpMRI) guidance results in increased detection of clinically significant prostate cancers (csCaP). However, optimal sensitivity of the new method employs both targeted and systematic template biopsies, as some csCaP lies outside of MRI targets, i.e., is not visualized on MRI. Herein, we examine incidence and significance of the MRI-invisible csCaP.

Methods

322 (23%) of 1385 men with no suspicious lesion on mpMRI (UCLA Grade <3) from 2010-2015 were included in this study. The median age was 65±8, median PSA was 5.15 ng/mL (0.11-67.6) and mean prostate volume was 58.5±33.5 cc. All patients underwent MRI/US fusion biopsy using the 12-point mapping template of the Artemis device within 3 months of MRI. MRI was 3T body coil and interpreted by an expert reader (D.M.); biopsy was performed by an experienced fusion-device operator (L.M.). csCaP was defined as Gleason 3+3 with maximal cancer core length ≥ 4mm or ≥ Gleason 3+4.

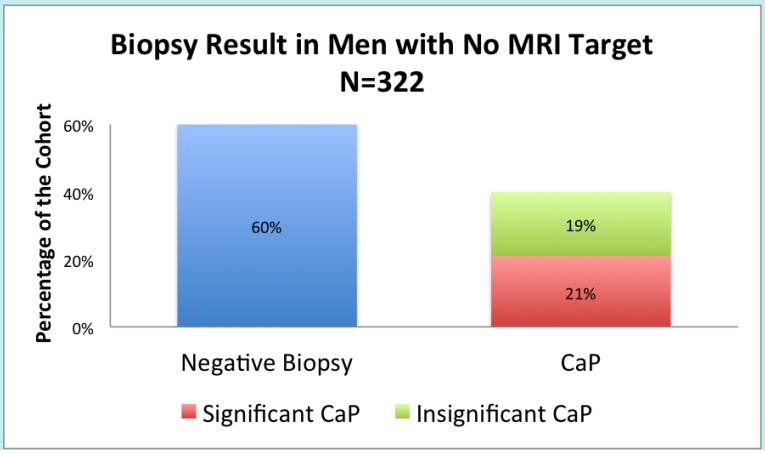
Results

128 patients (40%) were found to have CaP in their biopsies: 61 patients (19%) had insignificant CaP and 67 patients (21%) had csCaP. 52 (78%) of 67 patients with missed csCaP had ≥ Gleason 3+4=7. 105 patients (32%) were in Active Surveillance at the time of their biopsies. Of these, 27 patients (26%) had csCaP with negative mpMRI. Logistic regression indicated that patients with high PCA3, high PSA density, a prior positive biopsy and smaller prostate volume are directly related to having csCaP in the presence of negative mpMRI ($p<0.05$).

Conclusions

Despite recent advancement of MRI technology, negative mpMRI cannot rule out csCaP completely. 40% of men with negative mpMRI were diagnosed with CaP. Of these, 21% of men harbored csCaP. All clinical factors should be considered before eliminating a systematic biopsy because the MRI is unrevealing.

Date & Time: May 6, 2016 1:00 PM-3:00 PM
Session Title: Imaging/Radiology: Uroradiology II
Sources of Funding: NCI (R01CA195505), Jean Perkins Foundation, Andre Agassi Foundation, Steven C. Gordon Family Foundation, Beckman Coulter Foundation, and the Dream Fund.



Friday, May 6, 2016 3:30 PM-5:30 PM
SDCC: Room 30 ABC
Prostate Cancer: Localized: Ablative Therapy
Funding: Jean Perkins, Andre Agassi, Steven C. Gordon Family, and Beckman Coulter Foundations, and the Dream Fund.
MP18-11: **MR-Guided Focal Laser Ablation of Intermediate Risk Prostate Cancer: Phase I Trial**
Shyam Natarajan, Steven Raman*, Alan Priester, James Garritano, Daniel Margolis, Patricia Lieu, Maria Macairan, Jiaoti Huang, Warren Grundfest, Leonard Marks, Los Angeles, CA

Abstract: MP18-11

Introduction and Objectives

Focal laser ablation (FLA) under MRI guidance is a promising method to treat prostate cancer (CaP), but available information is limited. Prior work is largely unpublished and consists mostly of transperineal FLA performed by radiologists in low-risk patients. Herein we describe 6-month results from a prospective Phase I trial of transrectal FLA in an intermediate risk population.

Methods

8 men (58-73 y.o.) with biopsy-proven intermediate risk CaP (all but one Gleason 3+4), located in one MRI target (Fig., A), were enrolled in an IRB-approved clinical trial. FLA was performed under MRI guidance (in bore) transrectally; MRI-compatible thermal probes were also placed into the prostate transperineally under US guidance to determine treatment temperatures at intra-prostatic sites, independent of MR thermometry (MRT) (Fig., B,C). A 980-nm, 15 W fiber-coupled laser system was used to treat each target (4-9 laser applications per patient). Multi-parametric MRI was obtained immediately following treatment to determine ablation effect (Fig., D).

Results

In-bore transrectal FLA was well-tolerated under conscious sedation. All patients were discharged within 4 hours of FLA and have been followed ≥ 6 months without any grade 3 adverse events. The non-perfused tissue, i.e. ablation zone, was confined to the intended region (Fig. D) and measured a median volume of 3 cc (range, 1.9-8.9 cc). Critical structures (rectum, sphincter, capsule, neurovascular bundle) were unaffected, and no differences in IIEF-5 or IPSS were observed at 6-months compared to baseline values. At 6-month follow-up MRI/US fusion biopsy, cancer was not detected in the ablation zone in 5 of 8 men, but tumor foci were often seen outside treatment zone.

Conclusions

In-bore transrectal FLA of the prostate can be performed safely in men with intermediate risk CaP, without serious adverse events or changes in sexual and urinary function. Interstitial thermal probes confirmed the limited extent of laser heat within the prostate. Follow-up biopsy indicates that larger margins may be necessary for effective FLA.

Date & Time: May 6, 2016 3:30 PM-5:30 PM
Session Title: Prostate Cancer: Localized: Ablative Therapy
Sources of Funding: Jean Perkins, Andre Agassi, Steven C. Gordon Family, and Beckman Coulter Foundations, and the Dream Fund.

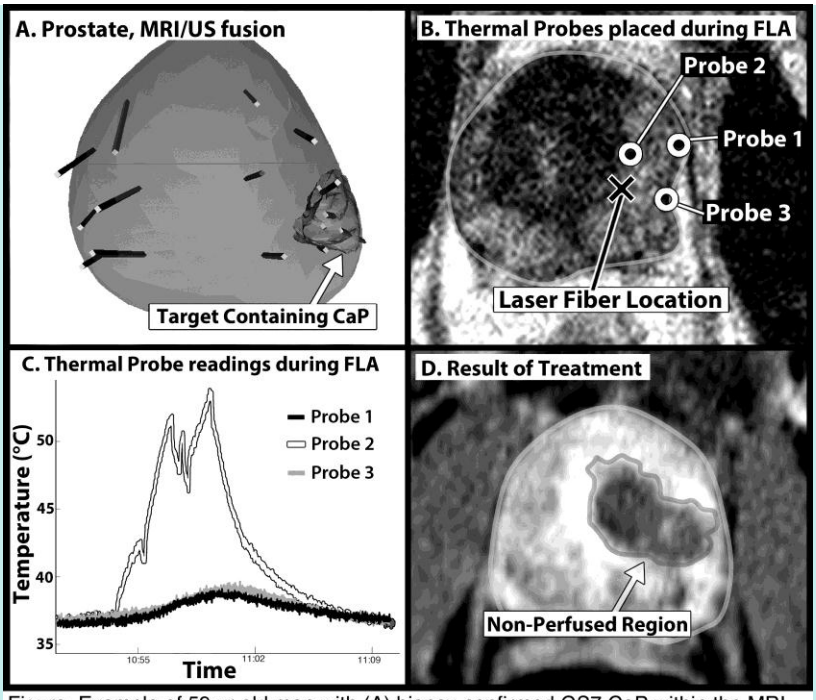


Figure. Example of 59 yr-old man with (A) biopsy-confirmed GS7 CaP within the MRI target. (B) During FLA, MRI-independent thermal probes record real-time temperatures in prostate. (C) Temperature near laser (probe 2) rises to 55 C, but probes away from laser show little change. (D) Post-treatment MRI shows non-perfused area (5 'burns' used) and thermal effect confined within the prostate.

Table. Median characteristics of patients who received FLA (n=8) as part of a Phase I trial.

	Pre-treatment	Post-treatment	P Value
PSA (ng/ml)	7.5	3.3	<0.01
IPSS	4	3.5	NS
IIEF-5	19.5	20	NS
Prostate Volume (cc)	35.5	32.5	0.03
PSA Density (ng/cc^2)	0.22	0.08	0.05

Friday, May 6, 2016 3:30 PM-5:30 PM
SDCC: Room 30DE
Prostate Cancer: Localized: Active Surveillance III
Funding: None
PD08-07: **Molecular Progression of Gleason 6 Prostate Cancer: Tracking of Specific Clones by Image-Guided Biopsy**
Ganesh Palapattu*, Andi Cani, Daniel Hovelson, Rohit Mehra, Jeffery Montgomery, Todd Morgan, Simpa Salami, Scott Tomlins, Ann Arbor, MI, Shyam Natarajan, Leonard Marks, Los Angeles, CA

Abstract: PD08-07

Introduction and Objectives

Magnetic resonance imaging/ultrasound (MRI/US) fusion biopsy may be used to follow men during active surveillance (AS). Repeat sampling of the same biopsy site (within a few mm) is theoretically possible (Natarajan, 2011). However, the ability to sample the same clonal focus of cancer over time is unknown. Using next generation sequencing (NGS), we sought to determine if a clonal focus can be tracked serially and if so, is there evidence that cancer progression at the molecular level can occur.

Methods

31 men with Gleason 6 prostate cancer (CaP) were enrolled in an IRB-approved registry for AS. Subjects underwent MRI/US fusion biopsy at study entry and re-sampling of the tracked biopsy site 1 year later. Immunohistochemistry (IHC) and targeted RNA/DNA NGS on routine formalin-fixed paraffin-embedded (FFPE) prostate biopsy tissues obtained at both time points were performed. ETS gene fusion status, a marker of CaP clonality and common oncogenic alterations associated with human cancer were assessed.

Results

In 96% of subjects (25 of 26 men with evaluable specimens), we found ERG expression concordance between targeted biopsy samples assessed over 1 year from the same site. Of the 11 men (35%) who progressed to higher grade cancer on targeted surveillance biopsy at 1 year, 100% (10/10; 1 not evaluable) displayed ERG concordance between initial and subsequent biopsy. Among these men, a driving mutation in IDH1 and SPOP was detected, in one patient each, in both the early (low grade) and late (higher grade) sample. In one case with progression to Gleason 8 disease, a TP53 mutation was detected in the late but not the early sample. In 2 out of 20 cases that did not progress, driving mutations in SPOP and BRCA2 were detected in the late sample only (Table 1).

Conclusions

In this first of its kind study, employing sophisticated molecular techniques, we found that MRI/US targeted biopsy permits serial sampling of the same clonal focus of CaP over time. Furthermore, while molecular progression of low risk CaP appears to be uncommon over the course of 1 year, a proportion of high grade CaP appear to originate from low grade cancers and that de novo mutations in potential driver genes can occur. These findings provide a rationale for employing MRI/US fusion biopsy technique in monitoring men on AS for CaP and importantly imply that not all Gleason 6 CaP may be indolent.

Date & Time: May 6, 2016 3:30 PM-5:30 PM
Session Title: Prostate Cancer: Localized: Active Surveillance III
Sources of Funding: None

Open Attachment

Saturday, May 7, 2016 10:30 AM-
SDCC:
Science & Technology Posters
Funding: Jean Perkins Foundation
S&T-13: **Informing Focal Therapy Margins through MRI-Pathology Correlation**
Alan Priester*, Khoshnoodi Pooria, Shellee Ogawa, Jesse Le, James Garritano, Bryan Radosavcev, Daniel Margolis, Robert Reiter, Jiaoti Huang, Warren Grundfest, Shyam Natarajan, Leonard Marks, Los Angeles, CA

Abstract: S&T-13

Introduction and Objectives

Multi-parametric MRI (mpMRI) appears to be a robust method for imaging prostate cancer (CaP) and guiding targeted interventions. However, the spatial relationship between MRI-visible regions of interest (ROIs) and areas of known CaP is incompletely understood. We aimed to clarify that relationship and characterize the treatment margins necessary for effective focal therapy.

Methods

Prior to radical prostatectomy, 65 men underwent mpMRI, from which a radiologist contoured the prostate capsule and regions suspicious for CaP. A custom mold was then 3D printed from the patient&[prime]s MRI and used for precise sectioning of the surgical specimen. This mold facilitated accurate matching of the delineated slides (Fig 1A) with preoperative mpMRI (Fig 1B). All tumors found on pathology were digitally reconstructed in 3D and matched to corresponding MRI targets (n = 71). The geometric features of all surfaces and the maximum distance between each MRI target and matched tumor were determined using custom software.

Results

Spatial features of ROIs and tumors are summarized in Table 1. The mean volume and longest axis of the prostate capsule corresponded closely with MRI measurements, yet the mean volume of CaP was 2.7 times greater than the ROI predictions. The mean longest axis on MRI was found to be 16.8 mm, whereas the mean longest axis on pathology was 27.5 mm. Due to tumor asymmetry, CaP extended an average of 15 mm beyond the ROI along at least one axis (Fig 1C). Retrospectively, only a minority of these tumor extensions was identifiable on MRI.

Conclusions

MRI underestimated CaP volume by a factor of 2.7 (0.9 cc on MRI vs 2.4 cc on pathology). Using MRI targeting alone, effective focal therapy would need to include substantial margins around the ROI (median 15 mm). In practice, this margin could be reduced using tracked biopsy information or better imaging to characterize tumor asymmetry.

Date & Time: May 7-10, 2016 10:30 AM-
Session Title: Science & Technology Posters
Sources of Funding: Jean Perkins Foundation

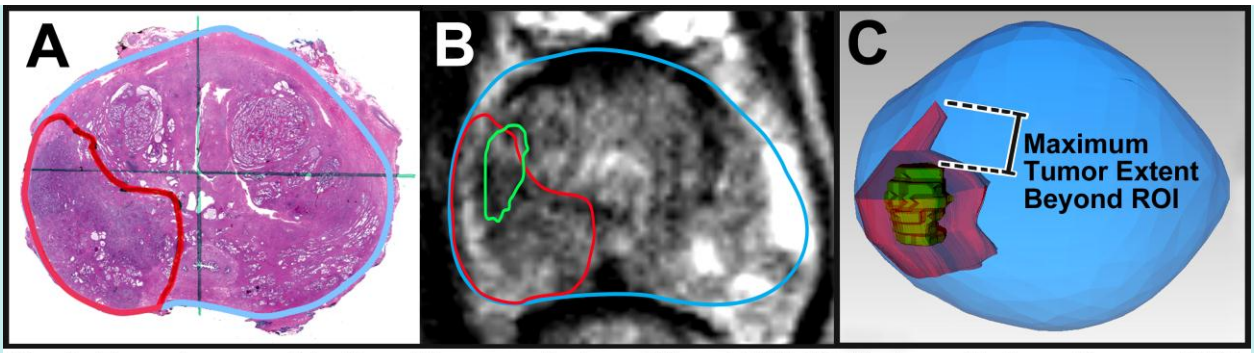


Fig. 1. Example co-registration of tumor pathology (A) and MRI (B). Red = pathology, Green = MRI. In C, the irregular contour and maximum extent of the tumor beyond a matched ROI is shown. Significant MRI underestimation of both tumor volume and longest axis is apparent.

	MRI	Pathology	P value
Prostate Gland (mean ± SD)			
Volume (cc)	39.7 ± 16.9	43.1 ± 15.5	< 0.01
Longest Axis (mm)	50.5 ± 6.4	49.4 ± 6.7	NS
Tumor (mean ± SD)			
Volume (cc)	0.9 ± 1.4	2.4 ± 2.6	< 0.01
Longest Axis (mm)	16.8 ± 7.6	27.5 ± 10.8	< 0.01

Table 1. Spatial parameters of prostates and matched tumors as determined by MRI vs whole mount pathology sections (N=71 tumors, 65 prostates). MRI significantly underestimated tumor volume and longest axis (matched pair t-test, $p<0.01$).

Sunday, May 8, 2016 1:00 PM-3:00 PM
SDCC: Room 24
Prostate Cancer: Detection & Screening VII
Funding: NCI (R01CA195505)
MP53-07: **Cancer Detection Rate of Conventional vs 3D Template Prostate Biopsy in a MRI/US Fusion Device**
Shyam Natarajan*, Jiaoti Huang, Leonard Marks, Los Angeles, CA

Abstract: MP53-07

Introduction and Objectives

Targeted prostate biopsy devices include a 3D digital template grid for systematic biopsy, but the value of following the template (vs conventional systematic biopsies) has not been established. Theoretically, following a template would result in biopsy sites with spatial symmetry and increased sampling extent, possibly increasing the cancer detection rate (CDR) beyond targeting alone. Thus, we determined cancer detection rates (CDR) obtained by conventional systematic sampling vs 3D sampling using the digital template of an MRI/US fusion device.

Methods

3677 men underwent prostate biopsy at UCLA between 2006-14; 1500 met criteria of no prior biopsy or treatment and ≥10 cores. 1161 had conventional systematic biopsy (CB). 339 had template biopsy (TB) performed using an MRI/US fusion and tracking device (Artemis, Eigen, Figure); in the TB group, any cores taken from targets were excluded from analysis. Data were collected retrospectively in an IRB-approved protocol. CDR found in the 2 groups (CB, freehand systematic and TB, template-guided) was compared.

Results

Age, PSA, and # of systematic cores were essentially same in both groups (Table). TB detected any CaP in 190/339 men (56.1%), and CB detected CaP in 458/1161 (39.5%), $p<0.01$. Clinically significant cancer (csCaP), i.e. Gleason ≥7, was found in 206/1161 men by CB (17.7%) and 90/339 men by TB (26.6%), $p<0.01$.

Conclusions

Template biopsy via 3D sampling in a biopsy tracking/fusion device yields a significantly higher CDR, including csCaP, than conventional systematic sampling ($p<0.01$) in biopsy naïve men. Improved spatial symmetry of biopsy sites may be obtained when the template is followed, and sampling extent increased. Increased CDR via the 3D template may explain the continued need to obtain systematic as well as targeted biopsy cores, when MRI/US fusion biopsy is performed.

Date & Time: May 8, 2016 1:00 PM-3:00 PM
Session Title: Prostate Cancer: Detection & Screening VII
Sources of Funding: NCI (R01CA195505)

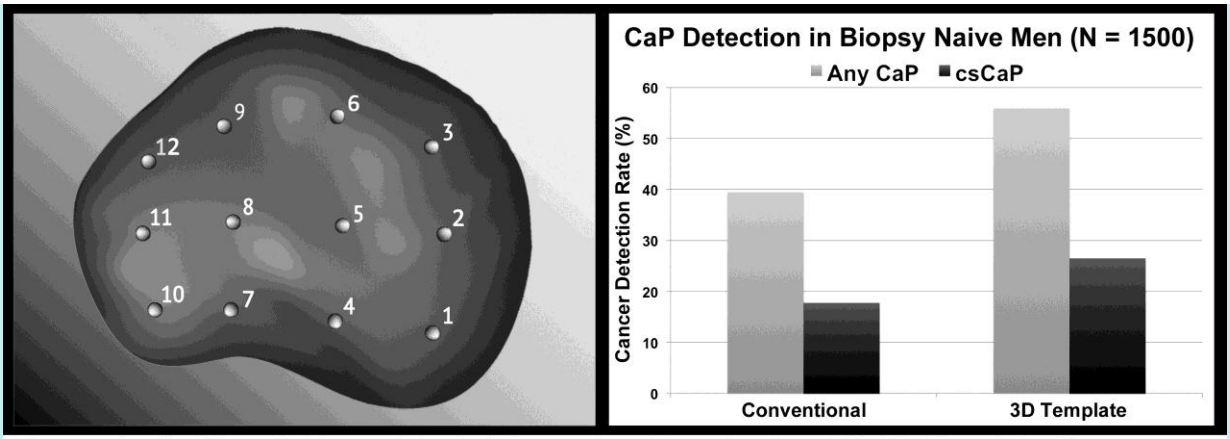


Figure. Left: 12-point template in biopsy tracking device. Right: Prostate Cancer Detection Rate (CDR) among biopsy-naïve men undergoing conventional vs 3D template systematic sampling. Both differences are statistically significant ($p<0.01$).

Table. Comparison of conventional and template biopsy cohorts

	Conventional	3D Template	p Value
N	1161	339	—
Median Age (years old)	65 (38-90)	64 (36-82)	NS
Median PSA (ng/ml)	5.5 (.03-74.6)	5.6 (0.27-80.9)	NS
Median N Cores	12 (10-24)	12 (10-18)	NS
Any Cancer (%)	458 (39.5)	190 (56.1)	<0.01
csCAP (%)	206 (17.7)	90 (26.6)	<0.01