MRI- 2019

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Uses for MRI

- Cancer detection
- Biopsy guidance
- Management decisions (i.e. as a biomarker)
- Staging and therapy selection, planning and guidance
  - Surgery
  - Radiation
  - Ablative therapies/focal Therapy
- Disease monitoring
  - Active surveillance
  - Ablative therapies/focal therapy

Detection of Individual Prostate Cancer Foci via Multiparametric Magnetic Resonance Imaging

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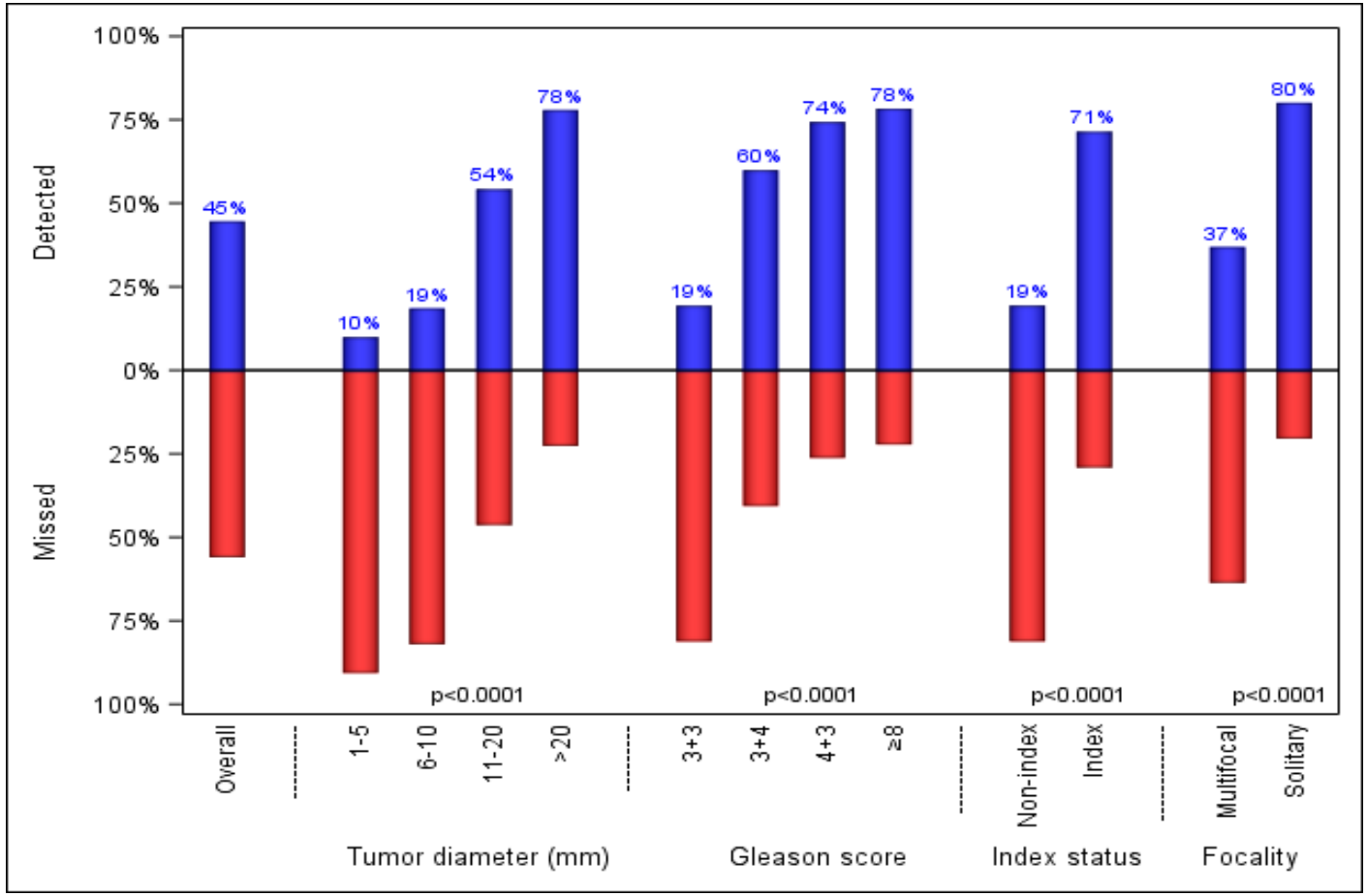

Prospective study of 612 consecutive men with preoperative MRI and RALP

Lesional analysis

Significant predictors of detection (univariate)

- Larger size
- Higher GS
- Index lesion status
- Solitary tumor

PRECISION: MRI Guided vs Standard Biopsy: Comparison of Cancer Detection between Groups.

Table 2. Comparison of Cancer Detection between Groups.*

Outcome	MRI-Targeted Biopsy Group (N=252)	Standard-Biopsy Group (N=248)	Difference†	P Value
Biopsy outcome — no. (%)			—	—
No biopsy because of negative result on MRI	71 (28)	0		
Benign tissue	52 (21)	98 (40)		
Atypical small acinar proliferation	0	5 (2)		
High-grade prostatic intraepithelial neoplasia	4 (2)	10 (4)		
Gleason score				
3+3	23 (9)	55 (22)		
3+4	52 (21)	35 (14)		
3+5	2 (1)	1 (<1)		
4+3	18 (7)	19 (8)		
4+4	13 (5)	6 (2)		
4+5	7 (3)	2 (1)		
5+5	3 (1)	1 (<1)		
No biopsy‡	4 (2)	3 (1)		
Withdrawal from trial§	3 (1)	13 (5)		
Clinically significant cancer¶				
Intention-to-treat analysis — no. (%)	95 (38)	64 (26)	12 (4 to 20)	0.005
Modified intention-to-treat analysis — no./total no. (%)	95/245 (39)	64/235 (27)	12 (3 to 20)	0.007
Per-protocol analysis — no./total no. (%)	92/235 (39)	62/227 (27)	12 (3 to 20)	0.007
Clinically insignificant cancer — no. (%)	23 (9)	55 (22)	−13 (−19 to −7)	<0.001
Maximum cancer core length — mm	7.8±4.1	6.5±4.5	1.0 (0.0 to 2.1)	0.053
Core positive for cancer — no./total no. of cores (%)	422/967 (44)	515/2788 (18)	—	—
Men who did not undergo biopsy — no. (%)‖	78 (31)	16 (6)	—	—

* Clinically significant cancer was defined as the presence of a single biopsy core indicating disease of Gleason score 3+4 (Gleason sum of 7) or greater, and clinically insignificant cancer as a biopsy sample with a Gleason score of 3+3 (Gleason sum of 6). The Gleason score is composed of a primary (most predominant) grade plus a secondary (highest nonpredominant) grade; the range for a primary or secondary grade is from 3 to 5, with the Gleason sum ranging from 6 to 10, and with higher scores indicating a more aggressive form of prostate cancer.

† Differences between rates are shown in percentage points, and the difference in maximum cancer core length is shown in millimeters. Differences in the percentages of men with clinically significant cancer detected and men with clinically insignificant cancer were calculated with a generalized linear mixed model (with the use of an identity link function with a binomial distribution) that included trial center as a random effect. The between-center variance estimates for the intention-to-treat analysis of the proportion of men with clinically significant cancer was 0.002 and for the proportion of men with clinically insignificant cancer was 0; the 95% prediction intervals for the detection rates of clinically significant and clinically insignificant cancer, incorporating between-center variation, were 14 to 39% and 17 to 28%, respectively, for standard biopsy, and 26 to 51% and 4 to 11%, respectively, for MRI-targeted biopsy. The difference in the maximum cancer core length was calculated with the use of a linear mixed model with trial center as a random effect. The between-center estimate of variance was 2.14; the 95% prediction interval for the maximum cancer core length, incorporating between-center variation, was 3.3 to 9.8 mm for standard biopsy and 4.4 to 10.8 mm for MRI-targeted biopsy.

‡ In four participants in the MRI-targeted biopsy group, MRI identified at least one area with a score on the Prostate Imaging–Reporting and Data System, version 2, of 3 or greater (on a scale from 1 to 5, with higher numbers indicating a greater likelihood of clinically significant cancers), but targeted biopsy was not performed. In the standard-biopsy group, three participants declined transrectal ultrasonography–guided biopsy and underwent an MRI. The MRI revealed no areas that were suggestive of prostate cancer, and the participants did not undergo biopsy.

§ These participants did not complete any diagnostic test.

¶ The intention-to-treat analysis included all the participants who underwent randomization, the modified intention-to-treat analysis excluded participants who did not complete a diagnostic test strategy, and the per-protocol analysis included only participants who underwent the randomly assigned testing procedure as specified in the protocol.

‖ Data include men who did not undergo biopsy because they withdrew before undergoing any diagnostic test or because they did not complete the diagnostic strategy.

<u>Biopsy Naïve patients</u>

MRI group: 95/252 = 38% (95/181 biopsied = 52%)
Control group: 64/248 = 27%

Does not address issue of systematic biopsies OR of biopsy in MRI negative patients

The NEW ENGLAND JOURNAL of MEDICINE

JAMA Surgery | Original Investigation

Comparison of Targeted vs Systematic Prostate Biopsy in Men Who Are Biopsy Naive

The Prospective Assessment of Image Registration in the Diagnosis of Prostate Cancer (PAIREDCAP) Study

Fuad F. Elkhoury, MD; Ely R. Felker, MD; Lorna Kwan, MPH; Anthony E. Sisk, MD; Merdie Delfin, RN, NP; Shyam Natarajan, PhD; Leonard S. Marks, MD

- Prospective study of 300 men undergoing systematic and targeted (cognitive and fusion)
- Addresses the following questions:
  - Which technique finds more significant cancers?
  - Is systematic biopsy necessary?
  - Is biopsy necessary in men with negative MRI?
    - 52 men with negative MRI in the study

Systematic and Targeted Biopsies Identify Distinct Tumors

		TARGETED				
		Left	Right	Bilateral*	Negative	Total
SYSTEMATIC	Left	43 (17%)	2 (1%)	7 (3%)	9 (4%)	(61)
	Right	6 (2%)	40 (16%)	0 (0%)	8 (3%)	(54)
	Bilateral	17 (7%)	13 (5%)	2 (0.9%)	3 (1%)	(35)
	Negative	13 (5%)	10 (4%)	1 (0.4%)	74 (30%)	(98)
	Total	(79)	(65)	(10)	(94)	248

1. Overall concordance of targeted and systematic bx = **63.9%**
2. Non-concordance in **36.1%. 20.6%** of men had a tumor detected by systematic biopsy that was missed by targeted biopsy, while **9.7%** had a tumor detected by targeted biopsy that was missed by systematic biopsy.

Cancer Detection Rate in MRI Negative Men in PAIREDCAP

- CDR in the non-targeted cohort 15% (8/52),
  - compared to 70% (174/248) in the group with lesions
- A much greater percentage of the group with targets had elevated PSAD compared to those without targets.
- In men with negative MRI and PSAD > 0.15 ng/mL/cc, 5/14 (36%) had csCaP
- In men with PSAD < 0.15 ng/mL/cc, 3/34 (8%) had csCaP.
  - A negative MRI with a low PSAD yielded an 8% incidence of csCaP.

Distribution of PI-RADS Scores by Gleason Score

	Solitary				Multifocal			
Gleason score	3+3	3+4	4+3	>=4+4	3+3	3+4	4+3	>=4+4
No MRI lesion (missed)	11	22	6	4	431	152	32	14
PI-RADS 3 (detected)	6	15	5	0	45	46	11	3
PI-RADS 4 (detected)	7	39	14	12	42	88	26	12
PI-RADS 5 (detected)	3	24	27	21	3	48	27	17
Total (from Table 2b)	27	100	52	37	521	340	96	46
	(40)	(22)	(12)	(11)	(83)	(45)	(33)	(30)

72/440 (16%) Gleason 3+4 cancers are associated with a PI-RAD 5 ROI

PI-RADSv2 Category on 3 Tesla Multiparametric Prostate MRI Predicts Oncologic Outcomes in Gleason 3+4 Prostate Cancer on Biopsy

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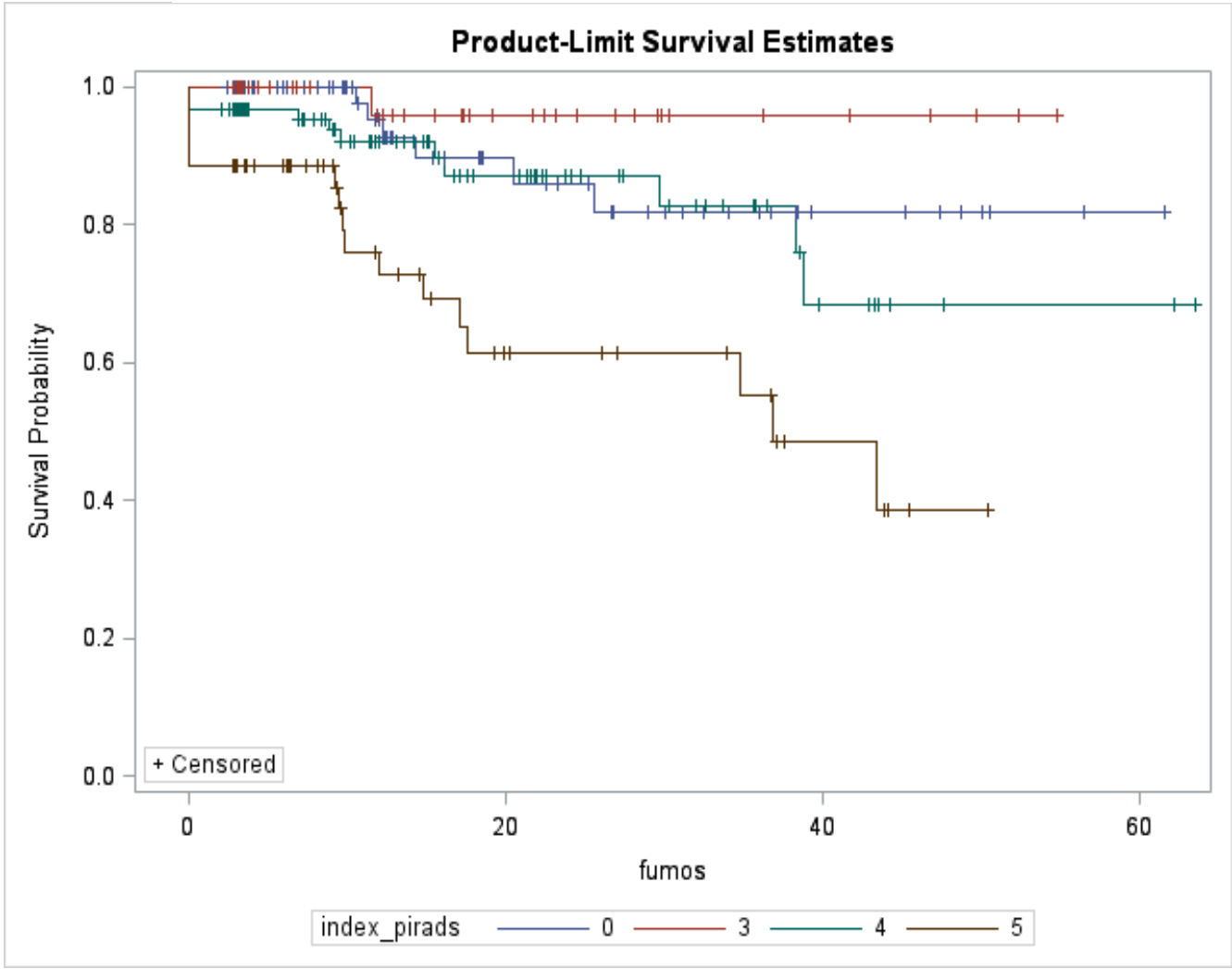

Association of PI-RADS 5 with adverse pathology and BCR is agnostic to biopsy method (systematic OR targeted fusion biopsy)

Molecular Hallmarks of Multiparametric Magnetic Resonance Imaging Visibility in Prostate Cancer.

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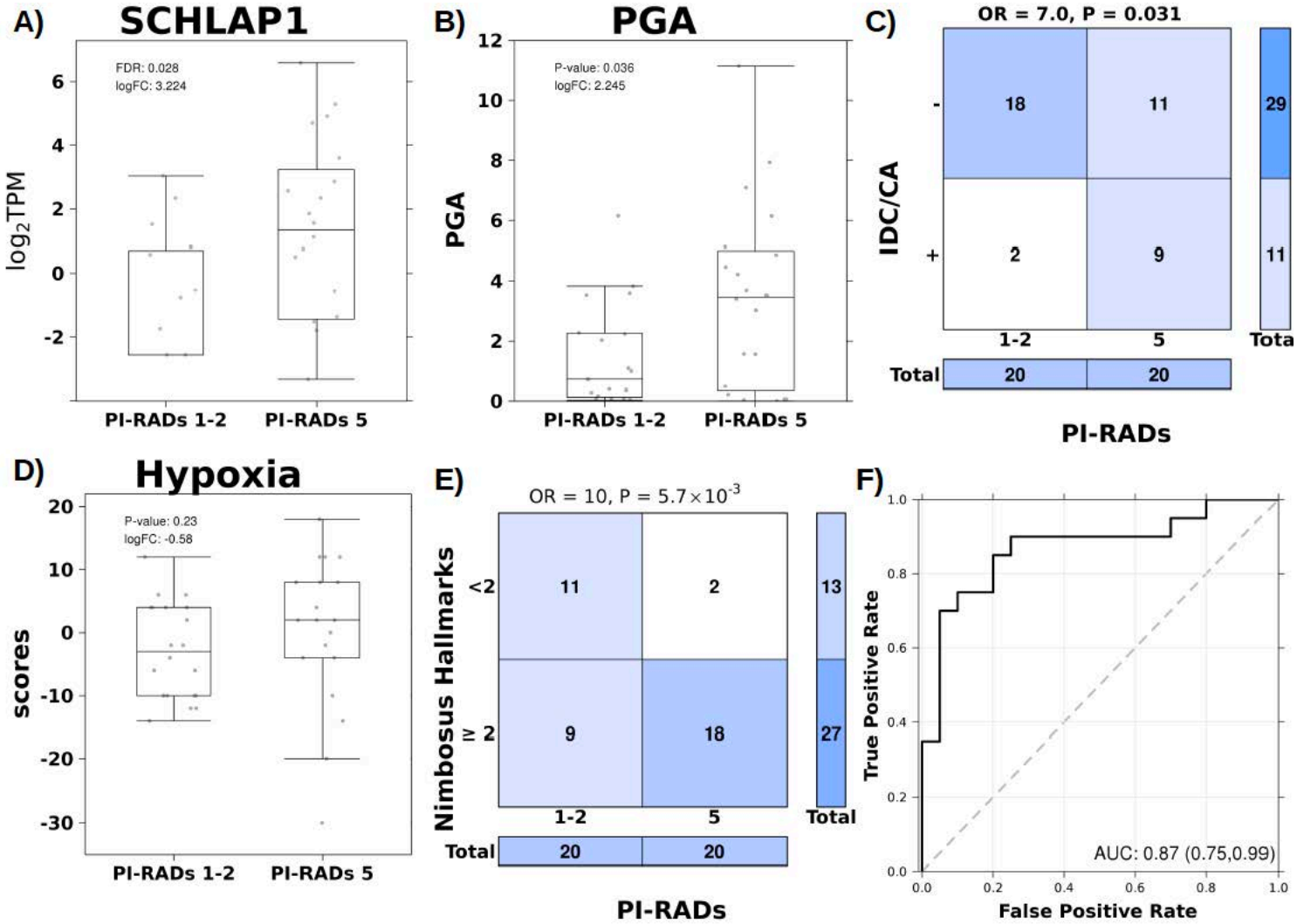

MRI visibility associated with adverse genomic and pathologic features

PGA= percent genome alteration

Do Contemporary Imaging and Biopsy Techniques Reliably Identify Unilateral Prostate Cancer? Implications for Hemiablation Patient Selection

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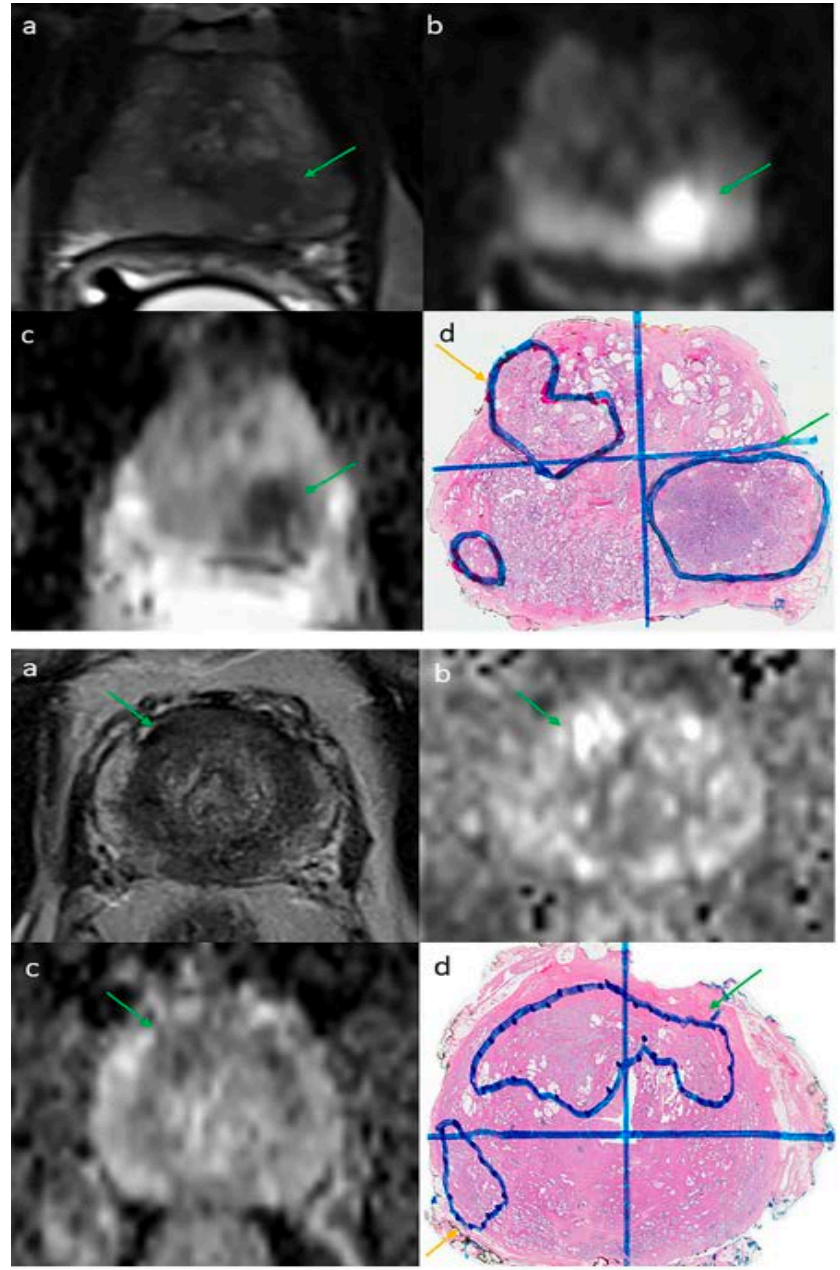
- 44/92 (48%) candidates for hemiablation ineligible on prostatectomy
  - 41 patients had discordant laterality of csCaP
    - 21 with tumor crossing midline
    - 20 with undetected distinct contralateral tumors
    - 3 with ipsilateral upgrading (GS 4+3 with tertiary pattern 5 [n=1], GS 4+4 [n=1] and GS 4+5 [n=1]).
  - 10/41 (24%) patients with unidentified contralateral csCaP had tumors containing ≥GS 3+4 with tertiary pattern 5 pathology

TABLE 2. Details of Missed Contralateral Tumors (N = 41)

	No.	Mean Size, cm	Whole-Mount Tumor Pathology	Index Tumor Location on Biopsy/MRI, No.	Location of Crossover csCaP, No.
Crossover	21	2.6	GG2 (≤10% pattern 4): 6 GG2 (20%-40% pattern 4): 9 GG3: 4 GG3 (tertiary 5): 1 GG4: 1	Zone PZ only: 10 PZ plus AFS: 1 PZ plus TZ: 6 PZ plus CZ: 1 CZ only: 1 TZ only 2 Location Apex: 18 Midline: 16 Base: 7	Anterior: 11 Posterior: 8 Anterior plus posterior: 2 Crossover from: Right to left: 13 Left to right: 8
Distinct	20	1.4	GG2 (≤10% pattern 4): 9 GG2 (20%-40% pattern 4): 7 GG2, tertiary 5: 1 GG3: 3	Zone PZ only: 16 PZ plus AFS: 1 PZ plus TZ: 1 TZ only: 1 CZ only: 1 Location Apex: 9 Mid: 15 Base: 2	Laterality of missed csCaP Left: 11 Right: 9

Abbreviations: AFS, anterior fibromuscular stroma; csCaP, clinically significant prostate cancer; CZ, central zone; GG, Gleason grade group; MRI, magnetic resonance imaging; PZ, peripheral zone; TZ, transition zone.


a
b
c
d
a
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Whole Mount/ mpMRI Tumor Volume and Diameter Correlations

Table 3: Mean size of tumors and matched Regions of Interest

	All Matches (N = 118)	Gleason = 3+3 (N = 22)	Gleason = 3+4 (N = 61)	Gleason ≥ 4+3 (N = 32)	3+4 vs. ≥ 4+3 p Value
Tumor Volume (cc)	2.49 ± 0.26	1.1 ± 0.5	2.6 ± 0.3	3.2 ± 0.5	0.57
ROI Volume (cc)	0.84 ± 0.11	0.31 ± 0.07	0.7 ± 0.1	1.2 ± 0.2	0.01
Tumor Diameter (mm)	28.4 ± 0.9	19.2 ± 2.3	30.0 ± 1.1	31.9 ± 1.3	0.38
ROI Diameter (mm)	17.0 ± 0.7	12.8 ± 1.0	16.5 ± 0.9	20.5 ± 1.3	0.01
Hausdorff Max** (mm)	14.8 ± 0.7	10.9 ± 1.5	16.3 ± 0.9	15.2 ± 1.0	0.54

Tumor size exceeded ROI size in each GS category and overall ($p<0.05$). GS categories were significantly different from one another ($p<0.05$). However, no difference was seen in tumor size, comparing GS = 3+4 and GS ≥ 4+3 (last column).

**The Hausdorff maximum is the greatest distance between matched tumor and ROI surfaces.

Priester et al. Jurol 2016

Summary

- MRI identifies most men with prostate cancer but misses 20-30% of tumors on a lesion by lesion basis
- Targeted and systematic biopsies are additive—they do not always detect the same lesions
- Don't ignore men at high risk with negative MRI
- MRI PIRAD 5 is a predictor of adverse pathology and BCR and is associated with adverse genomic features
- MRI insufficient (even with systematic biopsy) to determine unilaterality of significant cancer—implications for focal therapy and hemiablation
- MRI underestimates tumor size and must be taken into account for therapy planning