ACR Prostate MR course

Evidence-based Clinical Indications for Prostate mpMRI

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Disclosures

• Consulting agreement – Koelis
• Research support and consulting agreement with Blue Earth Diagnostics
Objective

• To review current indications for mpMRI in the diagnosis and management of prostate cancer.
Prostate Cancer

Screening

Detection

Risk-stratification

Active Surveillance

Staging

Treatment

Recurrence
• **Early detection** increases chance of successful treatment

• **Digital rectal examination (DRE)**
  – 70-80% of the Bx based on DRE are negative

• **Serum Prostate-Specific Antigen (PSA)**
  – Only ¼ of the patients with elevated PSA have PCa
  – up over detection of indolent disease ➔ over treatment

• **Alternative approaches**
  – **PSA density**: PSA/gland volume (> 0.15 – higher risk for csPCa)
  – PSA isoforms (isoPSA), 4K score
PCa Screening

- MRI is currently not considered a screening tool
- Pilot study* (n = 47 unselected men)
- OR for PCa detection:
  - MRI: 2.7, (95% CI 1.4-5.4)
  - PSA: 1.1 (95% CI 0.9-1.4)
- OR for PCa GS ≥ 3+4:
  - MRI: 3.5 (95% CI 1.5-8.3)
  - PSA: 1.0 (95% CI 0.9-1.2)

PCa Screening

MRI-Targeted or Standard Biopsy in Prostate Cancer Screening

- 49118 men invited, 12570 enrolled – 1532 had PSA > 3ng/ml
- MRI + MRI-guided bx (n = 929) vs Standard bx (n = 603)
- GG ≥ 2: 21% vs 18%
- GG 1: 4% vs 12%
- MRI + MRI-guided bx is more cost-effective than Standard bx

Eklund, et al. NEJM. 2021 PMID: 34237810
Hao, e at. JAMA Oncol 2022 PMID: 36355382
Prostate Cancer

Screening → Detection

DRE and PSA
• Transrectal or transperineal ultrasound-guided biopsy
  – **Systematic** but non-targeted
  – Detects a large number of indolent tumors
  – Misses a large number of clinically significant (CS) PCa
PCa Detection

- Transrectal or transperineal ultrasound-guided biopsy
  - Systematic but non-targeted
  - Detects many indolent tumors
  - Misses many clinically significant (CS) PCa
PCa Detection

- Transrectal or transperineal ultrasound-guided biopsy
  - Systematic but non-targeted
  - Detects many indolent tumors
  - Misses many clinically significant (CS) PCa
Multicenter prospective trial; N= 576 biopsy naïve men

1.5 T with PPAC

MRI vs. TRUS-bx for detection of PCa GS ≥ 4 + 3 or ≥ 6 mm

Reference: transperineal template prostate mapping bx

Results:

- Sensitivity MRI: 93% - TRUS-bx: 48%
- Specificity MRI: 41% - TRUS-bx: 96%

If MRI was used for triage:

- 27% men could have avoided a biopsy
- 5% fewer insignificant PCa detected
PCa Detection

Detection of Individual Prostate Cancer Foci via Multiparametric Magnetic Resonance Imaging

David C. Johnson \textsuperscript{a,b,*}, Steven S. Raman \textsuperscript{a}, Sohrab A. Mirak \textsuperscript{c}, Lorna Kwan \textsuperscript{b}, Amirhossein M. Baggiran \textsuperscript{a}, William Hsu \textsuperscript{c}, Cleo K. Machara \textsuperscript{c}, Preeti Ahuja \textsuperscript{c}, Izak Faieina \textsuperscript{b}, Aydin Pooil \textsuperscript{b}, Amirali Salmasi \textsuperscript{b}, Anthony Sisk \textsuperscript{d}, Ely R. Felker \textsuperscript{a}, David S.K. Lu \textsuperscript{d}, Robert E. Reiter \textsuperscript{b,*}

\textsuperscript{a} Cleveland Clinic, Cleveland, OH, USA, \textsuperscript{b} Northwestern University, Chicago, IL, USA, \textsuperscript{c} Memorial Sloan Kettering Cancer Center, New York, NY, USA, \textsuperscript{d} University of Chicago, Chicago, IL, USA

- \( n = 588; 1213 \) tumor foci in RP specimens
- MRI detected:
  - 45\% of all PCa
  - 65\% of csPCa (GG \( \geq 2 \))
    - 83\% solitary; 58\% multifocal
  - 80\% of high-grade PCa
- Size of missed lesions:
  - 61.1\% <1 cm
  - 28.3\% 1-2 cm
  - 10.4\% >2 cm.

Smaller, low-grade, multifocal, non-index tumors were more likely to be missed.
PCa MRI Visibility

- Histologic and genomic factors affect prostate cancer visibility on MRI.
- Inverse correlation between cancer grade and ADC
- Genes associated with aggressive PCa are overexpressed in aggressive PCa

PCa MRI Visibility

- Histologic and genomic factors affect prostate cancer visibility on MRI.
- Inverse correlation between cancer grade and ADC
- Genes associated with aggressive PCa are overexpressed in aggressive PCa

Correlation between MRI phenotypes and a genomic classifier of prostate cancer: preliminary findings

https://doi.org/10.1007/s00330-019-06114-x
MRI-Detectability of Clinically Significant Prostate Cancer Relates to Oncologic Outcomes After Prostatectomy

Andreas G. Wibmer,¹ Robert A. Lefkowitz,¹ Yulia Lakhman,¹ Joshua Chaim,¹ Ines Nikolovski,¹ Evis Sala,¹,² Samson W. Fine,² Timothy F. Donahue,³ Michael W. Kattan,⁴ Hedvig Hricak,¹,⁴ Hebert Alberto Vargas¹,⁴

- N = 1449 patients with GG ≥ 2 PCa on RP
- MRI invisible cancers were less likely to have BCR (8% vs. 43%), metastasize (0.6% vs. 20%), or lead to PCa mortality (0% vs. 7%) than MRI-detectable cancers (P < .001).

MRI-invisible cancers constitute a prognostically distinct subgroup among higher-grade PCa
Use of prostate magnetic resonance imaging in the risk stratification, diagnosis and treatment pathway of men with prostate cancer is expanding. When quality prostate imaging is obtained, current evidence now supports its use in men at risk of harboring prostate cancer and who have not undergone a previous biopsy, as well as in men with an increasing prostate specific antigen following an initial negative standard prostate biopsy procedure.
Prostate Cancer

- Screening
  - DRE and PSA

- Detection
  - TRUS-Bx
  - MRI and MRI-targeted Bx

- Risk-stratification
Prostate Cancer

Screening

Detection

Risk-stratification

Active Surveillance

(Dlow-risk localized disease)

DRE and PSA

TRUS-Bx
MRI and MRI-targeted Bx

Clinical data, Bx
Active Surveillance

- **MRI can help with the triage**:  
  - Negative MRI: NPV ≥ 96%  
  - Score 5: 87-98% sensitive for upgrading

- **ASSIT trial** – RCT (n = 273)  
- Upgrade from GG 1 to GG ≥ 2  
  - Confirmatory Bx -> SBx arm: 23% vs. MRI arm: 21%  
  - 2-year follow up Bx: SBx arm: 27% vs. MRI arm: 13%


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PCa (GS 3 + 3) on AS  
↑PSA 24.3 ng/dL  
MRI-targeted Bx: PCa 3 + 4  
RP: GS 3 + 4, + ant. EPE
Active Surveillance

- MRI for evaluation of progression
  - Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE)³

MRI-targeted Bx 2015: PCa GG1

MRI-targeted Bx 2016: PCa GG3

Likert | Assessment of likelihood of radiographic progression | Example |
--- | --- | --- |
1 | Resolution of previous features suspicious on MRI | Previously enhancing area no longer enhances |
2 | Reduction in **volume** and/or **conspicuity** of previous features suspicious on MRI | Reduction in size of previously seen lesion that remains suspicious for clinically significant disease |
3 | Stable MRI appearance: no new focal/diffuse lesions | Either no suspicious features or all lesions stable in size and appearance |
4 | Significant increase in **size** and/or conspicuity of features suspicious for prostate cancer | Lesion becomes visible on diffusion-weighted imaging; significant increase in size of previously seen lesion |
5 | Definitive radiologic stage progression | Appearance of extracapsular extension, seminal vesicle involvement, lymph node involvement, or bone metastasis |

*Threshold for size/volume increase has not been set*
Prostate Cancer

Screening

Detection

Risk-stratification

Active Surveillance

Staging

PSA, Bx, MRI

DRE and PSA

TRUS-Bx
MRI and MRI-targeted Bx

Clinical data, Bx

(Low-risk localized disease)
PCa Staging

- EPE and NVBI: affects treatment selection and planning
- DRE: under stages 25-30% of cases
- MRI is appropriate for staging intermediate/high risk PCa

<table>
<thead>
<tr>
<th>Risk</th>
<th>PSA</th>
<th>GS</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&lt;10</td>
<td>6</td>
<td>T1-2a</td>
</tr>
<tr>
<td>Interm.</td>
<td>10-20</td>
<td>7</td>
<td>T2b</td>
</tr>
<tr>
<td>High</td>
<td>≥ 20</td>
<td>≥ 8</td>
<td>≥ T2c</td>
</tr>
</tbody>
</table>

1Akin O, et al. *ACR appropriateness criteria*, JACR 2022 PMID: 37236742
PCa Staging

- Meta-analysis\(^2\)
- 75 studies (9796 patients)
- EPE/SVI sensitivity improved with:
  - T2-WI + DWI/DCE
  - 3 T
- ERC did not improve sensitivity for EPE

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>EPE</td>
<td>0.57</td>
<td>0.91</td>
</tr>
<tr>
<td>SVI</td>
<td>0.58</td>
<td>0.96</td>
</tr>
<tr>
<td>pT3</td>
<td>0.61</td>
<td>0.88</td>
</tr>
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</table>

PMID: 26215604
• Probability of EPE based on MRI features

Assessment of Risk of Extraprostatic Extension of Prostate Cancer at MRI

Mehralivand et al. Radiology 2019 PMID: 30667329
PCa Staging

- **Lymph nodes**¹
  - MRI Sens.: 39%; Spec.: 82%
  - Size (short axis)
    - > 10 mm (> 8 mm if rounded)
  - Borders and signal (subjective)
- **Bones**²
  - MRI Sens.: 95.2%; Spec.: 99%
  - PPV: 86.9–100%; NPV: 99.7%

²Woo S, et al. AJR 2016 PMID: 27043655
PCa Staging

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**PCa Staging**

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2Woo S, et al. AJR 2016 PMID: 27043655

PCa GS 3 + 4, PSA: 70.4ng/mL
Prostate Cancer

Screening
- DRE and PSA

Detection
- TRUS-Bx
- MRI and MRI-targeted Bx

Risk-stratification
- Clinical data, Bx

Active Surveillance
- PSA, Bx, MRI
  (Low-risk localized disease)

Staging
- DRE and Bx, MRI, CT, bone scan

Treatment
MRI-guided PCa Treatments

- Potential for lower morbidity and side effects with comparable functional and oncologic outcomes
- Some alternatives are more attractive to potent patients
- Most patients remain eligible to salvage treatments

<table>
<thead>
<tr>
<th>Prostatectomy</th>
<th>Radiation treatment</th>
<th>Energy ablations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical margin*</td>
<td>Focal boost (FLAME trial**)</td>
<td>Whole gland or focal treatment</td>
</tr>
<tr>
<td>Nerve sparing*</td>
<td>Nerve sparing (POTEN-C)</td>
<td>Nerve sparing</td>
</tr>
<tr>
<td>Partial resection</td>
<td></td>
<td>HIFU, Cryoablation, Laser</td>
</tr>
<tr>
<td>(Hemi-gland or tumor resection)</td>
<td></td>
<td></td>
</tr>
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</table>

*PMID: 36372633
**PMID: 33471548
MRI-guided PCa Treatments
MRI-guided PCa Treatments

Single-port Robotic Transvesical Partial Prostatectomy for Localized Prostate Cancer: Initial Series and Description of Technique

Kaouk et al. Eur Urol 2022 PMID 35970657
Prostate Cancer

Screening

Detection

Risk-stratification

Active Surveillance

(Portrayed as: Low-risk localized disease)

Staging

Treatment

Recurrence

DRE and PSA

TRUS-Bx, MRI and MRI-targeted Bx

Clinical data, Bx

PSA, Bx, MRI

DRE and Bx, MRI, CT, bone scan
PCa Recurrence

• Occurs in 10-53% of patients, depending on risk group and treatment modality

• Typically detected by elevation in PSA levels after treatment, which can precede symptoms by months to years

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Biochemical recurrence (BCR) criteria</th>
</tr>
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<tbody>
<tr>
<td>Radical Prostatectomy (RP)</td>
<td>Two consecutive PSA levels $&gt; 0.2$ ng/mL</td>
</tr>
<tr>
<td>Radiation therapy (RT)</td>
<td>PSA level $\geq 2.0$ ng/mL above nadir</td>
</tr>
<tr>
<td>Tissue ablation treatments</td>
<td>No consensus, but some use same as RT</td>
</tr>
</tbody>
</table>
MRI after RP – Expected Findings

- **Fibrotic tissue** develops in the prostatectomy bed and vesicoureteral anastomosis
  - T2-WI: symmetric non-mass like tissue with low signal
  - DWI/ADC: no restricted diffusion
  - DCE: delayed and progressive enhancement
MRI after RP – Expected Findings

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  - T2-WI: symmetric non-mass like tissue with low signal
  - DWI/ADC: no restricted diffusion
  - DCE: delayed and progressive enhancement
MRI after RP – Recurrence

- Locations: perianastomotic, retrovesical, or in the SV bed
- MRI features:
  - T2-WI: focal mass-like lesion with intermediate SI
  - DWI/ADC: focal mass-like lesion with markedly restricted diffusion
  - DCE: focal mass-like lesion with early enhancement

77 y.o man s/p RP for GS 3+4 stage T2b PCa presents with BCR (PSA: 2.6ng/mL)
### MRI after RP – Recurrence

**Prostate Magnetic Resonance Imaging for Local Recurrence Reporting (PI-RR): International Consensus -based Guidelines on Multiparametric Magnetic Resonance Imaging for Prostate Cancer Recurrence after Radiation Therapy and Radical Prostatectomy**

<table>
<thead>
<tr>
<th>Score</th>
<th>DCE Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No enhancement</td>
</tr>
<tr>
<td>2</td>
<td>Diffuse heterogeneous enhancement</td>
</tr>
<tr>
<td>3</td>
<td>Focal or mass-like <em>late</em> enhancement</td>
</tr>
<tr>
<td>4</td>
<td>Focal or mass-like <em>early</em> enhancement not at the site of primary tumor tumor site unknown</td>
</tr>
<tr>
<td>5</td>
<td>Same as 4 but <em>at the site of primary tumor</em></td>
</tr>
</tbody>
</table>

![Diagram showing DCE and DWI scoring system](image-url)
MRI after RT—Expected findings

- **T2-WI:** diffuse low signal and loss of zonal anatomy
- **DWI/ADC:** no restricted diffusion
- **DCE:** decreased and delayed enhancement except for urethra and residual BPH
• Local recurrence often occurs in the site of the original disease

• MRI features:
  - T2-WI: nodular lesion with intermediate/low signal
  - DWI/ADC: may have restricted diffusion
  - DCE: early enhancement

72 y.o. man s/p Brachytherapy for GS 3+4 PCa detected by TRUS biopsy of left sided sextants, now with BCR (PSA 6.1 ng/mL)
MRI after RT—Recurrence

- Local recurrence often occurs in the site of the original disease
- MRI features:
  - T2-WI: nodular lesion with intermediate/low signal
  - DWI/ADC: may have restricted diffusion
  - DCE: early enhancement

75 y.o man s/p brachytherapy for GS 4+3 detected by TRUS in right sided sextants, now with BCR (PSA 3.5ng/mL)
In summary

Prostate MRI:

a. Accurate method for detection of PCa, especially those that are likely to be significant
b. Helps identity men who are suitable for active surveillance
c. Provides important information that can assist with staging and treatment planning
d. Detects recurrent PCa, usually at the site of original disease and using DCE
Thank you!