How to Interpret Prostate MRI with PI-RADS

Vikas Kundra, M.D., Ph.D.
Prostate Cancer - Epidemiology

- Primarily a disease of older men
- Highest incidence among all cancers in men and second highest incidence overall in the USA
- Second leading cause of cancer death among men in the USA
- Geographically, prostate cancer is common in North America and northwestern Europe and relatively rare in Asia and South America.

Prostate Cancer - Epidemiology

- Death rates declining since early 1990’s.

<table>
<thead>
<tr>
<th>Survival at all stages</th>
<th>5 yrs</th>
<th>10 yrs</th>
<th>15 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>99%</td>
<td>99%</td>
<td>94%</td>
</tr>
</tbody>
</table>

- Stage
  - Local and regional stages: 100%
  - Distant metastases: 28%

PI-Rads History

- In 2007, AdMeTech Foundation organized an International Prostate MRI Working group (academics and industry) that resulted in PI-RADS version 1
  - European Society of Urogenital Radiology (ESUR) drafted guidelines 2012
  - Limitations
    - American College of Radiology (ACR), ESUR and AdMeTech set up a Steering Committee resulted in PI-RADS v2.

Likert scale, MLS, PIRADS v1
ROC and reproducibility better w/Likert

<table>
<thead>
<tr>
<th></th>
<th>LIKERT</th>
<th>MLS</th>
<th>PIRADS</th>
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<tbody>
<tr>
<td>Expert 1</td>
<td>.81</td>
<td>.77</td>
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</tr>
<tr>
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<tr>
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<td>.81</td>
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> Gleason 7

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<tr>
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</tr>
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Kappa  

|       | .47-.52 | .41-.43 | .38-.44 |

Vache R et al. Radiology 2014
Likert scale, MLS, PIRADS v1
ROC and reproducibility better w/Likert

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Kappa  
.47-.52  .41-.43  .38-.44

Vache R et al. Radiology 2014
PI-Rads v2 vs v1
Change Highlights

- Spectroscopy not included
- For PZ, DWI primary, T2 secondary
- For CZ, T2 primary, DWI secondary
- DCE primarily used in PI-RADS category 3, to see if an equivocal lesion should be upgraded

PI-Rads v2 Purpose

- To promote global standardization and diminish variation in acquisition, interpretation, and reporting. It *needs to be tested and validated* for specific research and clinical applications.

- To improve detection, localization, characterization and risk stratification in patients with suspected cancer **in treatment naïve prostate glands**

PI-Rads – History Needed

- **PSA**
- **Date and Results of biopsy**
  - # of cores, % core involved
  - Locations
  - **Gleason Score**
- **Other relevant clinical history**
  - DRE findings
  - Medications esp. hormones
  - Prior prostate infections
  - Prior radiation therapy
  - Prior pelvic surgery
  - Family history

Hyperintense on T1

May adversely affect interpretation
  - Delay exam if possible
    - ≥ 6 weeks from biopsy

Biopsy related hemorrhage is hyperintense on T1 and hypointense on T2. Hemorrhage can mask an underlying tumor in the prostate and seminal vesicles.
PI-Rads – Patient Preparation

- **No consensus**
  - Enema
  - Positioning
    - Prone vs Supine
  - Use of an antispasmodic
    - Ex. glucagon, scopolamine, butylbromide, or sublingual hyoscyamine sulfate

PI-Rads – Technical Specifications

- **1.5T or 3T acceptable**
  - Most members of the committee preferred 3T
  - 1.5T preferred if implanted device is considered conditional or could cause an artefact

- **Endorectal coil**
  - Pros and cons - *No consensus*
    - At our institution, we prefer ERC
      - Particularly useful for DWI, the menen sequence and for looking at NVB involvement. Can help with T2 and DCE.
      - Nearly all studies have not shown 3T without a coil is better than 1.5T with ERC

- **Computer Aided Evaluation**
  - **Not required**
    - May improve workflow
    - May aide less experienced radiologists
    - May facilitate integration with some targeted biopsy systems

PI-Rads – Technical Specifications

Suggestions

- T2
  - Usu. 3 mm, no gap, FOV 12-20 cm, res ≤ .7 x .4 mm; 3 planes
- DWI
  - No strict comment on DWI (or proper b-value) or ADC; axial plane
- DCE
  - No strict comment on rate of acquisition
- At least one pulse sequence with FOV amenable to evaluating pelvic lymph nodes to the level of the aortic bifurcation
  - caveat: one can get metastases/skip metastases above the aortic bifurcation
  - Repeat if any of the above image is compromised/motion

PI-Rads – Technical Specifications

- DWI
  - No set b-value
    - Suggest 750-900 with ADC
      - If two b-values, 1st should be 50-100 sec/mm^2
    - >1400 without ADC may be used and may improve conspicuity
  - ADC value
    - is associated with Gleason score, but considerable overlap
    - Influenced by choice of b-value and are inconsistent among vendors
    - Qualitative assessment is often used
  - Suggested
    - TE: 90 msec, TR: 3,000 msec; Slice thickness: 4 mm, no gap; FOV: 16-22 cm; res. 2.5 mm

PI-Rads – Technical Specifications

- **DCE Suggestions**
  - Acquisition $<10$-$15$ sec, preferably $<7$ sec/acquisition for $\geq 2$ min.
  - 2D or 3D acquisition, 3D preferred
    - TR/TE $<100$msed/$<5$msec, 3mm no gap, FOV covers prostate and SV, res: 2 x 2 mm
  - 0.1 mmol/kg standard GBCA
    - 2-3 cc/sec injection rate with continuous image data acquisition

PI-Rads – Technical Specifications

- **Preferred**
  - Same image plane angle, location and slice thickness to aide synchronized scrolling

- **Computer Aided Evaluation**
  - Not required
    - May improve workflow
    - May aide less experienced radiologists
    - May facilitate integration with some targeted biopsy systems

Prostate Cancer - Anatomy

- Imaging
  - Anatomic
    - % glandular tissue
    - % of prostate cancer in the gland
  - Central
    - Transition
      - 5%
      - 25%
      - Enlarges with BPH
    - Central
      - 20%
      - 5%
  - Peripheral
    - Peripheral
      - 75%
      - 70%
  - Fibromuscular
    - Fibromuscular
      - 0%
      - 0%
  - Stroma
    - Stroma
      - 0%
      - 0%

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Prostate - Anatomy

T2-weighted MR

- Central zone
- Urethra
- Peripheral zone
- Prostate coil
Prostate - Anatomy

- Prostate
- Neurovascular bundle at 5 and 7 o’clock
- Prostate coil

T1-weighted MR

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PI-Rads – Sector Map

- Use encouraged in reporting
- Primarily for the purpose of targeting during interventions
- 39 Sectors/regions
  - 36 for the prostate
  - 2 for the seminal vesicles
  - 1 for the external urethral sphincter

- Each traditional prostate sextant
  - right base, right midgland, right apex, left base, left midgland, and left apex
- is subdivided by six
  - anterior fibromuscular stroma, anterior transition zone, posterior transition zone, anterior peripheral zone, posteromedial peripheral zone, posterolateral peripheral zone
- Anterior and posterior sectors are defined by a line bisecting the prostate into anterior and posterior halves.
- Medial and lateral sectors are defined by a line extending along the junction of the peripheral and transition zones in the anterior-posterior direction.

PI-Rads – Benign Findings

- **Hemorrhage**
  - Increased T1 signal

- **Prostatitis**
  - Decreased signal in PZ on T2 and ADC
    - Band-like, wedge-shaped, diffuse
    - Decrease in ADC generally less than cancer

- **Benign prostatic hyperplasia (BPH)**
  - Usually well circumscribed, usually heterogeneous T2
  - Since BPH makes PSA, gland volume allows correlation with PSA level and calculating PSA density (PSA/prostate volume)

- **Atrophy**
  - Wedge-shaped areas of low T2, mildly decreased signal on ADC

- **Fibrosis**
  - Wedge or band-shaped areas of low T2

- **Cysts**

- **Calcifications**

**PI-Rads v2 – Assessment and Reporting**

- mpMRI can detect intermediate to high grade cancers ≥0.5 cc in volume

- Clinically significant cancer definition
  - No universal agreement
  - PI-RADS v2 definition
    - Gleason score ≥ 7 (3+4 or 4+3) and/or
    - Volume ≥0.5 cc and/or
    - Extra-prostatic extension (EPE)

PI-Rads v2– 5 point scale

- 5 point scale based on T2, DWI, DCE only
  - Should not include other factors like PSA, DRE, history, choice of treatment

- Probability of clinically significant cancer to be present
  - PI-RADS 1: Very low
  - PI-RADS 2: Low
  - PI-RADS 3: Intermediate
  - PI-RADS 4: High
  - PI-RADS 5: Very High
  - PI-RADS X: Technically inadequate

- PI-Rads v2 does not make management recommendations such as if to biopsy

PI-Rads v2– 5 point scale

- 5 point scale based on T2, DWI, DCE only

- In PZ
  - Categorization is based
    - Primarily on DWI
    - Secondarily on T2
    - DCE is used when findings are equivocal
      - If focal early enhancement is seen, this may push from 3 to 4

- In CZ
  - Categorization is based
    - Primarily on T2
    - DWI is used when findings are equivocal
      - If focal signal is seen, this may push from 3 to 4

Results: AUROC analysis

DWI meta-analysis

Tan CH, Wei W, Johnson V, Kundra V. AJR, 2012
DCE Meta-analysis

Tan CH, Hobbs BP, Wei W, Kundra V. AJR, 2015
DCE Meta-analysis
Visual analysis performs similar to Quantitative analysis

Tan CH, Hobbs BP, Wei W, Kundra V. AJR, 2015
PI-Rads v2– 5 point scale

Table 1 – PI-RADS Assessment Category for the peripheral zone (PZ)

<table>
<thead>
<tr>
<th>DWI</th>
<th>T2W</th>
<th>DCE</th>
<th>PI-RADS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Any</td>
<td>Any</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Any</td>
<td>Any</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Any</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Any</td>
<td>Any</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Any</td>
<td>Any</td>
<td>5</td>
</tr>
</tbody>
</table>

* “Any” indicates 1-5

Table 2 – PI-RADS Assessment Category for the transition zone (TZ)

<table>
<thead>
<tr>
<th>T2W</th>
<th>DWI</th>
<th>DCE</th>
<th>PI-RADS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Any</td>
<td>Any</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Any</td>
<td>Any</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Any</td>
<td>Any</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Any</td>
<td>Any</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Any</td>
<td>Any</td>
<td>5</td>
</tr>
</tbody>
</table>

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Prostate size

- 3 dimensions (max. AP, RL, SI)
  - Size based on prolate ellipse (AP x RL x SI) x .52
    - May be useful for determining PSA density (PSA/prostate volume)

How to measure prostate size

A: 47.2mm
B: 33.1mm

A: 62.3mm
PI-Rads v2 – Lesion

- Lesions: Up to 4 findings category 3, 4, or 5 - give location
  - All involved sectors should be indicated
  - Lesion size
    - Largest dimension on an axial image
      - Or largest dimension on any plane or sequence that best depicts largest dimension of the lesion
      - Prefer ADC for PZ and T2 for TZ
    - Include image and series number
  - Index or dominant lesion
    - The lesion with the highest PIRADS assessment category
    - If 2 or more with same highest, dominant would be the one with EPE
    - If no EPE, the largest lesion is considered the dominant lesion
      - Usually the largest and is thought to more likely contribute to
        - Highest Gleason score
        - EPE and positive surgical margins
        - Referred to as the index or dominant lesion

Multifocal Prostate Cancer

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Lesions:

- Benign findings < 2, need not be reported unless as a guide for biopsy planning
  - In PZ, Mild T2 or DWI signal change suggest prostatitis
  - In PZ, Indistinct, linear, lobar or diffuse morphology suggest prostatitis
  - In PZ, Homogeneous or heterogeneous nodules that are round/oval, well-circumscribed and encapsulated, restrict diffusion and/or focally enhance can suggest BPH
  - Bilaterally symmetric signal abnormalities are usually normal anatomy or benign

Lesions (Malignant):
- In PZ, DWI is the primary determining sequence
  - ADC low signal
  - T2: CA is usually round or ill defined - not specific
- In TZ, T2 is the primary determining sequence (Back to the Future)
  - T2: CA is usually moderately hypointense ill defined “erased charcoal” smudge
    - Others: spiculated margins, lenticular shape, absence of a complete hypointense capsule, and invasion of the urethral sphincter and anterior fibromuscular stroma.
- Category 4 < 1.5 cm
- Category 5 > 1.5 cm or EPE

PI-RADS v2
T2 Categorization PZ

3

5
PI-RADS v2
T2 Categorization TZ

2

5
PI-Rads v2 – DWI characterization

- DWI
  - No set windows
  - Read visually, not quantitatively as ADC values may vary by scanner and vendor
  - ADC value is associated with Gleason score, but there is considerable overlap
  - No clear consensus ADC vs high DWI
  - Malignancy: low B-value focal in PZ, smudge in TZ

PI-RADS v2 ADC Categorization

ADC

T2

3

5
Tumors can have heterogeneous ADC, and can look dark on DWI b-value 700-900 due to T2-shine through...
BPH can have low ADC
PI-Rads v2– DCE Characterization

DCE
- Rapid T1W GRE before, during and after IV bolus injection of low MW gadolinium-based contrast agent.
- “At present, added value of DCE is not firmly established . . . and added value greater than T2W+DWI is modest.”
- Role is secondary to T2 and DWI
- (+) focal, earlier or contemporaneous with adjacent normal prostate
  - Usually enhances within 10 seconds of injection
  - Usually corresponds to T2 and DWI
  - Commonly assessed using visually
    - Others: subtraction, fat suppression, parametric maps, curve typing, pharmacokinetic modeling
- (-) does not enhance early or enhances diffusely so that margins do not correspond to T2 or DWI finding

PI-RADS v2
DCE Categorization
PI-Rads v2– DCE Characterization

- DCE
  - Caveats
    - Always interpret with T2 and DWI
      - Sometimes lesion is only seen with DCE and these tend to be low grade tumors
    - May be helpful with uninterpretable DWI (DWI category X) or prioritizing dominant lesion when multiple lesions are present
    - Diffuse enhancement suggests prostatitis
      - Others: subtraction, fat suppression, parametric maps, curve typing, pharmacokinetic modeling

PI-Rads v2– Category X

Lesions:
- PI-RADS v2 assessment category X

**PZ**
- DWI X,
  - Then T2 with DCE if T2 is 3

**TZ**
- DCE X, No Change,
  - Then T2 with DWI if T2 is 3

### PI-Rads v2– 5 point scale

#### Table 1 – PI-RADS Assessment Category for the peripheral zone (PZ)

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<td>Any*</td>
<td>Any</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Any</td>
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<td>Any</td>
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<td>4</td>
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<tr>
<td>5</td>
<td>Any</td>
<td>Any</td>
<td>5</td>
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Examples of Categories PI-Rads v2
Category 2 PZ or CZ

T2
ADC
DCE
Examples of Categories PI-Rads v2
Category 4 PZ

T2
ADC
DCE
Examples of Categories PI-Rads v2
Category 5 PZ

T2
ADC
DCE
Examples of Categories PI-Rads v2
Category 4 CZ, 3 Right PZ

T2
ADC
DCE
Examples of Categories PI-Rads v2
Category 5 CZ

T2
ADC
DCE
Examples of Categories PI-Rads v2

Category 5 PZ and CZ

Tan C. Wang J Kundra V. Eur Rad 2011
PI-Rads v2: No focal lesion
Diffuse Gleason 9
Elevated PSA, 4 negative biopsies

T2

ADC

First dynamic

Maximum slope
PI-RADS v1 vs v2

- Retrospective study, 65 consecutive biopsy-naïve or biopsy-negative patients suspicious for PCa referred for biopsy (caveat: may increase sensitivity and decrease specificity)

<table>
<thead>
<tr>
<th></th>
<th>v1</th>
<th>v2</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Kappa</td>
<td>.81</td>
<td>.71</td>
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<tr>
<td>Overall sensitivity</td>
<td>94/94</td>
<td>100/97</td>
<td></td>
</tr>
<tr>
<td><strong>Overall specificity</strong></td>
<td>68/56</td>
<td>31/37</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>PZ sensitivity</td>
<td>100/100</td>
<td>100/100</td>
<td></td>
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<tr>
<td><strong>PZ specificity</strong></td>
<td>62/43</td>
<td>12/18</td>
<td>p&lt;.001</td>
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<td>TZ sensitivity</td>
<td>75/75</td>
<td>100/88</td>
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<tr>
<td>TZ specificity</td>
<td>75/68</td>
<td>50/56</td>
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Authors suggest v2 preferable for TZ and v1 for PZ, but definitive stats for differences in sensitivity not presented

(Polanec S et al. Eur J Radiol 2016)
Reproducibility

- **PI-RAD v 2**
  - Polanec S et al. Eur J Radiol 2016 .81, .71
    - Single institution
  - Muller BG et al. Radiology 2015 .46
    - Single institution
    - Using local system (kappa was .56)
  - Kasel-Seibert M et al. Eur J Radiology 2016 .68
    - Single institution
  - Park SY et al. Radiology 2016 .80
    - Single institution
  - Baldisserotto M et al. JMRI 2016 .53
    - Single institution
  - Rosenkrantz AB et al. Radiology 2016 .52 (category ≥ 4)
    - **Multi-institution**

- Example Local systems
  - Muller BG et al. Radiology 2015 .56
    - Using local system (kappa was .56)
  - Vache R et al. Radiology 2014 .47-.52
PI RADS v 2 Detection Rate at MR-UTS fusion Biopsy

- 116 lesions in 62 patients underwent MR and then underwent fusion MR-US biopsy
- Cancer detection rate at fusion biopsy

<table>
<thead>
<tr>
<th>Category</th>
<th>(All Gleason score) detection rate</th>
<th>(Gleason &gt;3+4) detection rate</th>
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<tbody>
<tr>
<td>2</td>
<td>22 %</td>
<td>6 %</td>
</tr>
<tr>
<td>3</td>
<td>16 %</td>
<td>0 %</td>
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<tr>
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<td>30 %</td>
<td>21 %</td>
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<tr>
<td>5</td>
<td>78 %</td>
<td>75 %</td>
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(Mertan et al. J Urol. 2016)
158 patients

Biochemical recurrence rate of 13%

Upon multivariate analysis, PI-RADS categorization independently predicted biochemical recurrence after radical prostatectomy

- 2 year BCR-free survival
  - ≥ 4 85%
  - < 4 100%

(Park SY et al. Eur Radiol. 2016)
MR-Ultrasound Fusion Directed Biopsy Can Improve Detection of Higher Risk Disease, but Systemic Biopsy can also Aide Detection.
Thank you

Vikas Kundra, M.D., Ph.D.