MRI and PSMA PET scan in PCa
The Game Changers or a Revolution?

Mira Keyes MD FRCPC
Clinical Professor Radiation Oncology
Department of Surgery UBC
Head Provincial Prostate Brachytherapy Program
BC Cancer, Vancouver Canada
mpMRI Use of multiple anatomical and functional parameters

**T2W**
- Bx artefact can overestimate TU volume

**Dynamic contrast-enhanced imaging (DCE)**
- IV gadolinium. Tumours of higher-grade or larger-volume take up contrast (vascularity). The contrast typically leaks out, giving a steep “wash in - wash out” curve. This can be measured.

**Diffusion-weighted imaging (DWI),**
- Assesses the movement of water within a given volume. Higher grade cancer, with its disorganized cellular structure, tends to restrict the movement of water

**Proton spectroscopic imaging (MRSI)**
- high ratio of choline to citrate is suspicious for cancer. Less favoured. Need endorectal coil, not all MRIs have the software
Mp-MRI-defined radiological phenotype includes volume and characteristics of lesions on both anatomical and functional sequences. T2-weighted sequence, Contrast-enhanced sequence, Diffusion coefficient map. T2W, DCE, DWI.
In this scoring system every parameter: T2WI DWI, DCE-MRI and MRSI is scored on a five-point scale.

Each lesion is given an overall score, to predict its chance of being a clinically significant cancer.

- **Score 1** Clinically significant disease is highly unlikely to be present
- **Score 2** Clinically significant cancer is unlikely to be present
- **Score 3** Clinically significant cancer is equivocal
- **Score 4** Clinically significant cancer is likely to be present
- **Score 5** Clinically significant cancer is highly likely to be present.
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Findings</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra-capsular extension</td>
<td>Abutment</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Irregularity</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Neurovascular bundle thickening</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Bulge, loss of capsule</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Measurable extra-capsular disease</td>
<td>5</td>
</tr>
<tr>
<td>Seminal vesicles</td>
<td>Expansion</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Low T2 signal</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Filling in of angle</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Enhancement and impeded diffusion</td>
<td>4</td>
</tr>
<tr>
<td>Distal sphincter</td>
<td>Adjacent tumour</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Effacement of low signal sphincter muscle</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Abnormal enhancement extending into sphincter</td>
<td>4</td>
</tr>
<tr>
<td>Bladder neck</td>
<td>Adjacent tumour</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Loss of low T2 signal in bladder muscle</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Abnormal enhancement extending into bladder neck</td>
<td>4</td>
</tr>
</tbody>
</table>
Fig. 1. Axial T2 weighted (T2W) turbo spin-echo (TSE) images demonstrating examples of the ESUR PI-RADS system for extra-prostatic extension (EPE) outlined in Table 1. 61 year-old patient with confined prostate cancer (PCa) and a PI-RADS score of 1 demonstrates normal peripheral zone (open white arrow) between the tumor (white arrow) and intact capsule in (a). 56 year-old patient with confined PCa and a PI-RADS score of 2, demonstrates tumor (white arrow) that abuts (but does not deform) the prostate capsule (black arrow) in (b). 71 year-old patient with EPE at histopathology and a PI-RADS score of 3, demonstrates tumor (white arrow) that abuts and causes capsule bulge with irregularity (black arrow) in (c). 68 year-old patient with EPE and a PI-RADS score of 4 demonstrates a tumor (white arrow) that bulges and deforms/obscures the prostate capsule (black arrow) in (d). Arrowhead in (d) depicts the normal capsule. 65 year-old patient with EPE and a PI-RADS score of 5 demonstrates gross (measurable) tumor extension through the capsule (white arrow), as well as into the peri-prostatic tissues (black arrow) in (e).
Compared to non-standardized reporting, the PI- RADS system significantly improved the sensitivity of MRI and overall accuracy.
Accuracy of Magnetic Resonance Imaging for Local Staging of Prostate Cancer: A Diagnostic Meta-analysis

Maarten de Rooij *, Esther H.J. Hamoen, J. Alfred Witjes, Jelle O. Barentsz, Maroeska M. Rovers

Radboud University Medical Centre, Radboud Institute for Health Sciences, Nijmegen, The Netherlands
Sensitivity
True positive
Specificity
True negative

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>True positive</td>
<td>True negative</td>
</tr>
<tr>
<td>ECE</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>T3</td>
<td>0.61</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Improved sensitivity for ECE and SVI
1. Functional imaging
2. Higher field strength (3T)
3. Not with endo-rectal coil use.

MRI has high specificity but poor and heterogeneous sensitivity for local PCA staging.
High Specificity reading
Minimize unnecessary exclusion of men from curative treatment. This is probably why the meta-analysis revealed high specificity and low sensitivity for MRI.

High Sensitivity reading
Nowadays, urologists become more interested in high-sensitivity reading to reduce positive surgical margins and preserve neurovascular bundles.
**LR**
- low yield in providing useful information
- role for MRI in active surveillance.

**IR and HR**
MRI has a role in staging and in selecting or tailoring therapy.

**MRI staging accuracy related to reader experience.**
“expert” readers are more accurate in judging ECE compared with “nonexpert” readers (91 vs 56%)
Review of 62 MR studies
95% studies consistently demonstrated upstaging by MRI

Up to 43% of patients are experiencing increased therapy due to MRI staging

The correctness of treatment changes was under-studied.

Overall sensitivity of ~50–60% and specificity of >85%
Use for staging is a reasonable for assessment of EPE in IR and HR (knowledge of EPE will alter management)

Quality assurance
MRI AND EBRT
To evaluate the accuracy of preoperative 3TmMRI for staging of prostate cancer and evaluate its influence on the decision to change the
• **CTV**
• **RTDose**
• **Use of ADT**
N=103 EBRT  
N=47 Prostatectomy

RT treatment (CTV, total dose and hormonal therapy) was initially determined on the basis of the clinical information.

Radiation therapy plan was reevaluated after MRI.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECE</td>
<td>57%</td>
<td>95%</td>
<td>66%</td>
<td>92%</td>
<td>89%</td>
</tr>
</tbody>
</table>

94% modification of Clinical Stage

34% change in RT and ADT
Tumor staging using 3.0 T multiparametric MRI in prostate cancer: impact on treatment decisions for radical radiotherapy

273 pts Final change in stage with MR

<table>
<thead>
<tr>
<th>Type</th>
<th>Baseline</th>
<th>MR</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR</td>
<td>34 vs. 11%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>IR</td>
<td>46 vs. 60%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>19 vs. 29%</td>
<td>29%</td>
<td></td>
</tr>
</tbody>
</table>

ADT added to ~10% (33 vs 42%)
High RT dose ~ 25% (65 vs 88%)
10-30% - Risk group change
20-30% - Change in RT dose, ADT CTV

Literature review table of other published studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of MRI</th>
<th>n</th>
<th>Field strength</th>
<th>Coil</th>
<th>Tumor stage shift (%)</th>
<th>Risk group changes (%)</th>
<th>Change in RT (CTV, doses, HT) (%)</th>
<th>Technique validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panje et al. (2015)</td>
<td>Multiparametric</td>
<td>122</td>
<td>1.5 T &amp; 3 T</td>
<td>PAB</td>
<td>55.7</td>
<td>28.7</td>
<td>30</td>
<td>No</td>
</tr>
<tr>
<td>Horsley et al. (2015)</td>
<td>Morphological</td>
<td>509</td>
<td>1.5 T</td>
<td>PAB</td>
<td>20</td>
<td>9</td>
<td>18</td>
<td>No</td>
</tr>
<tr>
<td>Yamaguchi et al. (2015)</td>
<td>Morphological</td>
<td>157</td>
<td>1.5 T</td>
<td>PAB</td>
<td>25</td>
<td>9</td>
<td>8(^a)</td>
<td>No</td>
</tr>
<tr>
<td>Couñago et al. (2014)</td>
<td>Multiparametric</td>
<td>103</td>
<td>3 T</td>
<td>PAB</td>
<td>94.1</td>
<td>33.9</td>
<td>33.9</td>
<td>Yes</td>
</tr>
<tr>
<td>Chang et al. (2014)</td>
<td>Morphological</td>
<td>115</td>
<td>1.5 T</td>
<td>PAB</td>
<td>68.6</td>
<td>7</td>
<td>20(^a)</td>
<td>No</td>
</tr>
<tr>
<td>Jackson et al. (2005)</td>
<td>Morphological</td>
<td>199</td>
<td>1.5 T</td>
<td>PAB</td>
<td>55</td>
<td>NR</td>
<td>32.6(^b)</td>
<td>No</td>
</tr>
<tr>
<td>Present study</td>
<td>Multiparametric</td>
<td>274</td>
<td>3 T</td>
<td>PAB</td>
<td>90.4</td>
<td>32.8</td>
<td>43.8 or 52.5(^c)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

PAB Phased-array-bodycoil, NR not reported, CTV clinical target volume, HT hormonal therapy

\(^a\) Exclusive assessment of the CTV change

\(^b\) Data from T1–T2 to T3–T4 upstaging

\(^c\) Values according to the HT criteria in intermediate-risk patients
122 pt Clinical staging

43% Upstaged
12 % Downstaged

30% Changes in CTV: 30.3%
30% change in ADT duration
MRI and Brachytherapy
Post Implant dosimetry

(slides from J. Crook)
Base on MRI
Post implant dosimetry - QA

Dosimetry more accurate
Learning curve shorter
Dose to normal structure accurate
Less inter-observer variability
Higher quality brachytherapy
MRI in Brachytherapy Planning

- More accurate anatomical delineating of prostate, bladder neck, apex and urethra

- Pre-operative or intra-operative US MRI image fusion
Discrepancy between US and MRI volumes and contours

1. Overestimation of the apex in TRUS
2. Overestimation of superior base in TRUS
3. Underestimation of the superior US base and apex
If you know where the tumour is would you not use this information?

**Location of DIL**
- Dose escalation
- Dose de-escalation

MRI contours transferred to US. Green dots are the locations of the planned seeds. - no seeds in the tumour to allow for urethral sparing

MRI can alter intraoperative and pre planning
MRI-guided functional anatomy approach to prostate brachytherapy

Payal D. Soni¹, Alejandro Berlin², Aradhana M. Venkatesan³, Patrick W. McLaughlin¹,∗

¹Department of Radiation Oncology, University of Michigan, Ann Arbor, MI
²Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada
³Section of Abdominal Imaging, Department of Diagnostic Radiology, MD Anderson Cancer Center, Houston, TX
Fig. 2. Dess Classification of Bladder Neck Variants (a) bladder neck intact; (b) bladder neck expansion; (c) bladder neck effacement with prostate protruding into bladder lumen; (d) median lobe (yellow line = bladder neck; yellow arrow = median lobe). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
Fig. 7. Coronal T2-weighted MRI demonstrating variable intraprostatic extension of the external sphincter. TZ = transition zone; PZ = periphery; PB = penile bulb; cm = centimeter.

UG diaphragm
Internal sphincter variations
Anterior venous plexus on MR and CT

10. T2-weighted axial MRIs demonstrating how MRI-based prostate contours differ from CT-based prostate contours. (a) T2-weighted axial MRI slice through midprostate gland, (b) T2-weighted axial MRI slice through prostate apex (blue: dorsal venous plexus, green: MRI-based prostate contour, yellow: CT-based prostate contour, orange dots: true prostate edge). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
Critical Review

Magnetic Resonance Imaging-Guided Adaptive Radiation Therapy: A “Game Changer” for Prostate Treatment?

Angela U. Pathmanathan, MA,* † Nicholas J. van As, MD,* † Linda G.W. Kerkmeijer, PhD, ‡ John Christodouleas, MD, § Colleen A.F. Lawton, MD, ‡ Danny Vesprini, MD, ‡ Uulke A. van der Heide, PhD, ‡ Steven J. Frank, MD, ** Simeon Nill, PhD, * † Uwe Oelfke, PhD, * † Marcel van Herk, PhD, ‡‡‡‡‡ X. Allen Li, PhD, ‡ Kathryn Mittauer, PhD, §§ Mark Ritter, PhD, §§ Ananya Choudhury, PhD, ‡‡‡ and Alison C. Tree, MD* †
Table 1  Magnetic resonance imaging-guided radiation platforms existing or in development

<table>
<thead>
<tr>
<th>Variable</th>
<th>Type of system</th>
<th>Magnetic field orientation</th>
<th>Research/clinical status</th>
<th>Adaptive capabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elekta MR-Linac (29)</td>
<td>1.5-T, 7-MV; 70-cm closed bore; single-focused Agility MLC providing 5-mm resolution for nominal 100-cm SSD, projecting to 7 mm at the isocenter</td>
<td>B₀ magnetic field perpendicular to delivery</td>
<td>First patient treated May 2017 in Utrecht as part of First In Man protocol</td>
<td>ART capabilities include 1. Shifting plan to overlay anatomy—simple dose shift 2. Offline ART 3. Library of plans 4. Online ART—segment-weight optimization and full reoptimization available 5. Visual tracking of target response</td>
</tr>
<tr>
<td>ViewRay MRIdian cobalt-60 system (30)</td>
<td>0.35-T Cobalt system, 3⁶⁰Co heads on rotating gantry ring; split magnet 70-cm closed bore</td>
<td>B₀ magnetic field perpendicular to delivery</td>
<td>FDA 510(k) cleared for cobalt systems; treated patients since 2014 on cobalt system</td>
<td>ART capabilities include 1. Shifting plan to overlay anatomy—couch shift 2. Offline ART 3. Library of plans 4. Online ART—segment-weight optimization and full reoptimization available 5. Tracking with exception gating for target</td>
</tr>
<tr>
<td>ViewRay MRIdian Linac system</td>
<td>Newer system with 6-MV linac, split magnet 70-cm bore “Razor” MLC is a double-stacked, double-focused MLC, 8-mm leaf width, providing 4-mm resolution and allowing field sizes down to 2 x 4 mm</td>
<td>B₀ magnetic field perpendicular to delivery</td>
<td>FDA 510(k) cleared for linac system; treated patients since 2017 on linac system</td>
<td>ART capabilities include 1. Shifting plan to overlay anatomy—couch shift 2. Offline ART 3. Library of plans 4. Online ART—segment-weight optimization and full reoptimization available 5. Tracking with exception gating for target</td>
</tr>
<tr>
<td>Sydney Inline Australian MRI-LINAC system (31)</td>
<td>1.0 T 6-MV 82-cm open bore</td>
<td>B₀ magnetic field perpendicular and parallel to delivery</td>
<td>Currently, a research system</td>
<td>NA</td>
</tr>
<tr>
<td>MagnetTx Aurora RT Linac-MR (32)</td>
<td>0.5 T, 6-MV</td>
<td>B₀ magnetic field parallel to delivery</td>
<td>Currently, a research system</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Abbreviations: ART = adaptive radiation therapy; FDA = Food and Drug Administration; linac = linear accelerator; MR = magnetic resonance; MRI = magnetic resonance imaging; MV = megavoltage; NA = not available; SSD = solid-state drive.*
PSMA PET

Challenge to standard target volumes
Challenge to treatment concepts
<table>
<thead>
<tr>
<th>Staging for HR PCa?</th>
<th>PSA Failure</th>
<th>Detection of local and distal failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease volume and locating</td>
<td>Assessment of salvage strategies</td>
<td>Surgical vs. Radiation vs. ADT/CHT</td>
</tr>
<tr>
<td>Assessment of RT volumes</td>
<td>Targeted therapies</td>
<td>Olio Mets?</td>
</tr>
</tbody>
</table>
Location of Recurrence by Gallium-68 PSMA PET Scan in Prostate Cancer Patients Eligible for Salvage Radiation Therapy

51 pts, PSA < 2, post RP, ulR and HR pts

62% had positive scans
- PSA < 1 - 50% scans were positive
- PSA 1-2 - 85% of scans were positive

8 - prostate bed
23 - LN (4 PA, 1 inguinal LN)
11 - bones

Only 40% LN would have been covered by standard pelvic LN
Target Definition in Salvage Postoperative Radiation Therapy for Prostate Cancer: 18F-Fluorocholine PET/CT Assessment of Local Relapse - France

**SALVAGE RT volumes: RTOG and EORTC**
36 pts with local relapse on PET. Post RP, med PSA 4.2

**Relapses:**
50% at anastomosis
30% retrovesical area
10% bladder neck

**CTV PET**
**CTV RTOG** - same volume as CTPET, covered 85% of the disease
**CTV EORTC** - 50% smaller, covered 65% of the disease
Change in RT plans based on PSAM CT
100 pts with PSA recurrence post RP (±RT), med PSA 1
76% had positive PET scan
58% had RT plans changed
32% simultaneous integrated boost Prostate Bed
88% had simultaneous integrated boost to LN
Distribution of prostate nodes: a PET/CT-derived anatomic atlas of prostate cancer patients before and after surgical treatment

Nina-Sophie Hegemann¹*, Vera Wenter², Sonja Spath¹, Nadia Kusumo¹, Minglun Li¹, Peter Bartenstein², Wolfgang P. Fendler², Christian Stief³, Claus Belka¹ and Ute Ganswindt¹
Conclusions: More than one-third of the PET positive lymph nodes in patients with no prior treatment and post RP would not have been treated adequately using the RTOG CTV.
PSMA report: 15mm SVU 16 upper prostate gland near the base lesion - local recurrence, No mets or LN

Prostate Bx: 8 cores and targeted 3 cores form LTZ and base: TZ3 cores: GS4+3=7 80% pattern 4
The rest of the cores benign
Treatment options?

Curative after RP?
Curative after EBRT?
Curative after PB?
LN dissection or RT?
ADT + EBRT
EBRT alone
Palliative
SBRT to LN?

We do not know the answers
Summary

1. Standard post op CTV is wrong (>35%) EORTC and RTOG
2. Pelvic LN RTOG CTV is wrong (>35%)
3. >50% of the plans need to be changed (CTV or dose or both)
4. + Lymph Nodes are everywhere
5. New treatment algorithms
Thank You!