Detection, Screening and Staging with mpMRI

Jelle Barentsz, Radboudumc, Nijmegen, NL
NO CONFLICT OF INTEREST
Paradigm shift

Past
- staging
- TRUS-GBx
- ERC, MRSI
- invasive

Current
- detection aggressive PCa
- mpMRI-directed Bx
- multi-parametric MRI
- minimally invasive
PCa-MRI = multi-parametric MRI

ANATOMY
- T2-Weighted Imaging (T2W)

BIOLOGY
- Diffusion Weighted Imaging (DWI)

VASCULARITY
- Dynamic Contrast enhanced
PCa-MRI = mpMRI
BIOLOGY: DWI

62 yr. PSA 12 ng/ml, 4 negative TRUS biopsies
62 yr. PSA 12 ng/ml, 4 negative TRUS biopsies

BIOLOGY: DWI

MR-GB: GI 4+3
62 yr.  PSA 12 ng/ml, 4 negative TRUS biopsies

BIOLOGY: DWI

MR-GB: GI 4+3
Px: larger tumor
BIOLOGY: DWI

MR-GB and Prostatectomy Gl 4+3

T2W

DWI

Gl 3

Gl 3

Gl 4
DETECTION
DETECTION:

PIRADS=PROBABILITY AGRESSIVE PCA (1-5)
Evidence that mpMRI can early detect significant PCa better than TRUS-Bx
With substantial less insignificant PCa

✓ Two level 1a systematic reviews\(^1,2\)

✓ One level 1a prospective clinical randomised trial\(^3\)

✓ Multiple level 1b studies\(^4,5\)

5. Pokorny Eur Urol 2014
Magnetic Resonance Imaging–targeted Biopsy May Enhance the Diagnostic Accuracy of Significant Prostate Cancer Detection Compared to Standard Transrectal Ultrasound-guided Biopsy: A Systematic Review and Meta-analysis

Ivo G. Schoots, Monique J. Roobol, Daan Nieboer, Chris H. Bangma, Ewout W. Steyerberg, M.G. Myriam Hunink

mpMRI has higher detection rate of significant PCa: 91% vs 71%
More important:

mpMRI has lower detection rate of insignificant PCa: 44% vs 83%
MR-Bx vs TRUS-Bx

mpMRI has much better grading

46%  5%

Undergrading of significant PCa

Gold standard: prostatectomy

Hambrock Eur Urol 2011
DOES mp-MRI MISS SIGNIFICANT PCA?
YES, NO TECHNIQUE IS PERFECT, WE MISS 2-11%
Experts in mp-MRI: “No” = “No”

<table>
<thead>
<tr>
<th></th>
<th>sens</th>
<th>spec</th>
<th>NPV</th>
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<tr>
<td>Villeirs</td>
<td>93%</td>
<td>98%</td>
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<tr>
<td>Thompson</td>
<td>96%</td>
<td>36%</td>
<td>92%</td>
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<tr>
<td>Villers</td>
<td>90%</td>
<td>88%</td>
<td>95%</td>
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<tr>
<td>Pokorny</td>
<td>97%</td>
<td>92%</td>
<td>97%</td>
</tr>
<tr>
<td>Ahmed (PROMISE)</td>
<td>93%</td>
<td>43%</td>
<td>89%/75%*</td>
</tr>
</tbody>
</table>

* 1.5T, no PI-RADS, community radiologists

What is best for a certain patient group?

Balance:

Missing significant PCa vs not finding insignificant PCa

1. Siddiqui JAMA 2015
What is best for a certain patient group?

Balance:

Missing significant PCa or not finding insignificant PCa

mp-MRI + additional TRUS-Bx: 103/1003 additional PCa

1. Siddiqui JAMA 2015
What is best for a certain patient group?

Balance:

Missing significant PCa or not finding insignificant PCa

mp-MRI + additional TRUS-Bx: 103/1003 additional PCa, 83% low risk

1. Siddiqui JAMA 2015
What is best for a certain patient group?

Balance:

Missing significant PCa or not finding insignificant PCa

- 200 TRUS-Bx needed to detect 1 additional significant PCa
- at the cost of over-diagnosis of 17 insignificant PCa

1. Siddiqui JAMA 2015
What is best for a certain patient group?

PI-RADS:

Biopsy naïve / detection:
What is best for a certain patient group?

**PI-RADS:**

**Biopsy naïve / detection:**

- High specificity reading
What is best for a certain patient group?

PI-RADS:

Biopsy naïve / detection:

• High specificity reading

Post negative TRUS:
SCREENING?
Manogram®: 8 minutes, no contrast!

T2W axial

ADC axial
Nijmegen study: full protocol vs screen (n=200)
Nijmegen study: full protocol vs screen (n=200)
What is best for a certain patient group?

**PI-RADS:**

**Biopsy naïve / detection:**
- High specificity reading

**Post negative TRUS:**
- High sensitivity reading
• 429 men with PSA > 3 ng/ml
• With or without prior TRUS guided biopsy (up to 4 times)
• Aged median 64.5 years
• AP-MRI identified prostate cancer in 123/429 men

Bruhn, Radiology 2017
T-STAGING

Ghent University Hospital, Belgium

Geert.Villeirs@UGent.be
Inaccurate Nomogram:
- T stage (DRE)
- Untargeted Biopsy
- Unspecific PSA

GP referral
PSA >3 ng/ml

Urologist Advice

Clinical tests (DRE)

TRUS biopsy:
- 40% missed PCa
- 40% overdiagnosis
- 40% aggression underestimation

Old situation

Inaccurate Nomogram:
- T stage (DRE)
- Untargeted Biopsy
- Unspecific PSA

Low risk
Bone scan MRI

i.m. risk
MRI

High risk
Bone scan MRI
New Nomogram:
- T-Stage (mpMRI)
- Targeted Biopsy
- Select MDX
- Advanced PSA
HOW GOOD ARE WE?
M. J. Engelbrecht
G. J. Jager
R. J. Laheij
A. L. M. Verbeek
H. J. van Lier
J. O. Barentsz

Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis
Staging accuracy

Sensitivity
26%-100%

Specificity
0%-100%
Staging accuracy

Accurary 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

Abstract

Context: Correct assessment of tumour stage is crucial for prostate cancer (PCa) man-
Staging accuracy

Sensitivity
14%-91%

Specificity
56%-100%
Staging accuracy

CCO GUIDELINES

Multiparametric magnetic resonance imaging for pre-treatment local staging of prostate cancer: A Cancer Care Ontario clinical practice guideline

Jennifer Salerno, PhD;1 Antonio Finelli, MD;2 Chris Morash, MD;3 Scott C. Morgan, MD;3 Nicholas Power, MD;4 Nichola Schieda, MD;5 Masoom A. Haider, MD6

1McMaster University, Department of Oncology and Program in Evidence-Based Care, Cancer Care Ontario, Hamilton, ON, Canada; 2Princess Margaret Hospital, Toronto, ON, Canada; 3The Ottawa Hospital, Ottawa, ON, Canada; 4Western University, London, ON, Canada; 5Department of Medical Imaging, The Ottawa Hospital, Ottawa, ON, Canada; 6Sunnybrook Health Sciences Centre, University of Toronto, ON, Canada

Cite as: Can Urol Assoc J 2016;10(9-10):E332-9. http://dx.doi.org/10.5489/cuaj.3823 Published online October 13

Introduction
Staging accuracy

Sensitivity: 14%-90%
Specificity: 74%-98%
WHAT IS GOING WRONG?
Staging accuracy

What is wrong?

Sensitivity
14%-91%

Specificity
56%-100%
Staging accuracy

Large variability

Sensitivity: 14%-91%
Specificity: 56%-100%
### Technical parameters

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AUC ECE</th>
<th>AUC SVI</th>
<th>AUC T3</th>
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<tr>
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<td>Without endorectal coil</td>
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<td>With endorectal coil</td>
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<td>Voxel&gt;3.0 mm³</td>
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<tr>
<td>Voxel≤3.0 mm³</td>
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<td>With contrast agents</td>
<td>0.70±0.15</td>
<td>0.74±0.17</td>
<td>0.76±0.12</td>
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<tr>
<td>Without contrast agents</td>
<td>0.55±0.21</td>
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<tr>
<td>Missing value</td>
<td>0.70±0.19</td>
<td>0.85±0.14</td>
<td>0.58±0.08</td>
</tr>
</tbody>
</table>

*Engelbrecht, Eur Radiol 2002;12:2294*
Diagnostic criteria

ECE

Focal contour bulge of capsule nearest the tumor
Abnormality of periprostasric capsular signal tumor
Enhancement of periprostatic veins
Irregular point of neurovascular bundles
Tumor SI within the periprostatic area
Obliteration of periprostatic fat
Contour angulation
Asymmetry of periprostatic fat
Hypointense stranding in periprostatic fat
Thickening of periprostatic veins
Diagnostic criteria

SVI

Focal hypointense luminal replacement

Asymmetric enhancement within lumen

Enlarged ejaculatory ducts

Non-contiguous areas of low SI within SV

Expanded low SI area of prostate

Focal or diffuse areas of low SI within SV

Focal low SI thickening in both seminal vesicles

Focal low SI within wall thickening

Low SI with wall thickening of SV

Thickening of ducts with low SI

Asymmetric thickening of ducts

Thickening of SV walls only when ducts are positive biopsially

Lack of preservation of ejaculatory ducts at one/both prostatic bases

Obliteration of normal architecture from prostatic base to SV

Nonvisualization of normal architecture in the SV

Direct extension of low SI tumor from prostatic base to SV

Filling defect within root of seminal vesicle

Obliteration of normal prostatic architecture
HOW TO SOLVE THE PROBLEM?
How to solve the problem?

• We need:
  – standardized diagnostic criteria
Diagnostic criteria

Tumor growth timeline
Diagnostic criteria

ECE

Tumor clearly confined to the prostate
Diagnostic criteria

ECE

Broad tumor contact with capsule
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging

![Image showing diagnostic criteria for ECE]

(T refers to the tumor area)
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption

[Image of MRI scan with labeled areas]
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption
- Unsharp margin
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption
- Unsharp margin
- Irregular contour
Diagnostic criteria

ECE

- Broad tumor contact with capsule
- Smooth capsular bulging
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- Irregular contour
- Periprostatic fat infiltration
**Diagnostic criteria**

**ECE**

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption
- Unsharp margin
- Irregular contour
- Periprostatic fat infiltration
- Obliteration rectoprostatic angle
## Diagnostic criteria

### ECE

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<td>Measurable tumor in periprostatic fat</td>
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## Diagnostic criteria

**ECE**

- Broad tumor contact with capsule
- Smooth capsular bulging
- Capsular SI disruption
- Unsharp margin
- Irregular contour
- Periprostatic fat infiltration
- Obliteration rectoprostatic angle
- Measurable tumor in periprostatic fat
Tumor in periprostatic fat

Diagnostic criteria

**ECE**

**Intraprostatic**

- Broad tumor contact with capsule

**Contact**

- Smooth capsular bulging

**Minimal ECE**

- Capsular SI disruption
- Unsharp margin

**Gross ECE**

- Irregular contour
- Periprostatic fat infiltration
- Obliteration rectoprostatic angle
- Tumor in periprostatic fat
# Diagnostic criteria

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Pesapane, Ghent/Belgium, unpublished data
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<td><strong>RPA obliteration</strong></td>
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Pesapane, Ghent/Belgium, unpublished data
UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer

Received: 16 October 2011 / Revised: 23 November 2011 / Accepted: 2 December 2011 / Published online: 10 February 2012 © The Author(s) 2012. This article is published with open access at Springerlink.com

Abstract The aim was to develop clinical guidelines for multi-parametric MRI of the prostate by a group of prostate MRI experts from the European Society of Urogenital Radiology (ESUR), based on literature evidence and consensus expert opinion. True evidence-based guidelines could not be formulated, but a compromise, reflected by “minimal” and “optimal” recommendations was made. The scope of these

Key Points

- This report provides guidelines for magnetic resonance imaging (MRI) in prostate cancer.
- Clinical indications, and minimal and optimal imaging acquisition protocols are provided.
- A structured reporting system (PI-RADS) is described.
# Diagnostic criteria

**ESUR Guidelines**

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<thead>
<tr>
<th>Criteria</th>
<th>Findings</th>
<th>Score</th>
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<tr>
<td></td>
<td>Neurovascular bundle thickening</td>
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<td></td>
<td>Bulge, loss of capsule</td>
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<tr>
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<td>Seminal vesicles</td>
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</tr>
</tbody>
</table>
Diagnostic criteria

SVI

Diffuse wall thickening
Diagnostic criteria
SVI

- Diffuse wall thickening
- Focal wall thickening
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
- Intraluminal mass
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
- Intraluminal mass
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
- Intraluminal mass
- Obliteration of prostatovesicular angle
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
- Intraluminal mass
- Obliteration of prostatovesicular angle
Diagnostic criteria

SVI

- Diffuse wall thickening
- Focal wall thickening
- Intraluminal mass
- Obliteration of prostatovesicular angle
- Destruction
## Diagnostic criteria

### ESUR Guidelines

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Findings</th>
<th>Score</th>
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<td>Extra-capsular extension</td>
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<td>Irregularity</td>
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</table>
How to solve the problem?

- We need:
  - standardized diagnostic criteria
  - standardized technical parameters
ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg ·
Richard Clements · Peter Choyke · Sadhna Verma ·
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Jurgen J. Fütterer

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Abstract The aim was to develop clinical guidelines for multi-parametric MRI of the prostate by a group of prostate MRI experts from the European Society of Urogenital Radiology (ESUR), based on literature evidence and consensus expert opinion. True evidence-based guidelines could not be formulated, but a compromise, reflected by “minimal” and “optimal” requirements, has been made. The purpose of these

Key Points
• This report provides guidelines for magnetic resonance imaging (MRI) in prostate cancer.
• Clinical indications, and minimal and optimal imaging acquisition protocols are provided.
• A structured reporting system (PI-RADS) is described.
Technical parameters

- Optimal T2-weighted MRI
  - thin slices (preferably 3 mm)
  - high in-plane resolution (preferably $512^2$) and small field of view (preferably 0.3 mm$^2$)
  - transverse images perpendicular to posterior prostate margin

- Functional imaging: mpMRI

De Rooij, Eur Urol 2016, Bittencourt, Radiology 2016
Technical parameters

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  – transverse images perpendicular to posterior prostate margin

• Functional imaging: mpMRI

De Rooij, Eur Urol 2016, Bittencourt, Radiology 2016
DIAGNOSTIC THRESHOLD
Diagnostic threshold

iT3a

iT3b
Diagnostic threshold

Slight capsular irregularity
Slight capsular undulation
Local staging: EPE?

We need:

3 Categories:
Local staging: EPE?

We need:

3 Categories: 1. No
Local staging: EPE?

We need:

3 Categories: 1. No

2. Possible or minimal
Diagnostic threshold

- **Intraprostatic**
  - Broad tumor contact with capsule

- **Contact**
  - Smooth capsular bulging

- **Minimal ECE**
  - Capsular SI disruption

- **Gross ECE**
  - Unsharp margin
Local staging: EPE?

We need:

3 Categories:

1. No
2. Possible or minimal
3. Yes
Diagnostic threshold

- **Intraprostatic**
  - Broad tumor contact with capsule
  - Smooth capsular bulging
  - Capsular SI disruption
  - Unsharp margin
- **Contact**
  - Irregular contour
  - Periprostatic fat infiltration
  - Obliteration rectoprostatic angle
  - Tumor in periprostatic fat
- **Minimal ECE**
- **Gross ECE**
Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

1. Somford, J Urol 2013,
2. Park, J Urol 2014,
Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

27% influence of surgical plan \textsuperscript{2,3}

Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

27% influence of surgical plan \textsuperscript{2,3}

- 60% more NSS (appropriateness 91%)

Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

27% influence of surgical plan \textsuperscript{2,3}

- 60% more NSS (appropriateness 91%)
- 40% more non-NSS

Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

27% influence of surgical plan \textsuperscript{2,3}

- 60\% more NSS (appropriateness 91\%)
- 40\% more non-NSS
- NSS: 0\% positive margins

Local staging: mpMRI

Accuracy 74%\textsuperscript{1,2}

27% influence of surgical plan \textsuperscript{2,3}

- 60% more NSS (appropriateness 91%)
- 40% more non-NSS
- NSS: 0% positive margins
- non-NSS: 7% positive margins

TAKE HOME MESSAGES
Take home messages

• For staging, use MRI to assess capsular perforation and/or seminal vesicle invasion
  – Technical standardization needed
  – Reporting standardization needed
Not all radiologists can do it well!
Diagnostic threshold

- A doubtful MRI should not change the therapy plan
Diagnostic threshold

• A doubtful MRI should not change the therapy plan

• Talk to the surgeon:
  – active surveillance good option?
  – broader margin at site of potential ECE → more R0!
And,....
mpMRI shows the aggressive tumor, but..
mpMRI shows the aggressive tumor, but..

Raise your finger to the Radiologist
When he is wrong!
Stimulate Radiologists to work on certification
And,.... non-radiologists need to learn PI-RADS and staging as well.

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