Imagerie : IRM dans le diagnostic du cancer de la prostate – ses limites

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What can we expect from targeted biopsies at diagnosis?

• Detection rates

► Comparison to current standard = 10-12 core biopsy

EAU prostate cancer guidelines 2015
MRI targeted vs. randomized: Detection rates

Initial biopsy:

Detection rate (%)

MRI targeted

Van Hove et al., WJU 2014
MRI targeted vs. randomized: Detection rates

Repeat biopsy: Detection rate (%)

MRI targeted

randomized

Van Hove et al., WJU 2014
When should we ask for a prostate MR – and when not?

**Diagnosis**

- Repeat biopsy setting is ideal indication for image guidance

  - Supported by the EAU guidelines:

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before repeat biopsy, perform mpMRI when clinical suspicion of PCa persists in spite of negative biopsies.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>During repeat biopsy include systematic biopsies and targeting of any mpMRI lesions seen.</td>
<td>2a</td>
<td>B</td>
</tr>
</tbody>
</table>

EAU prostate cancer guidelines 2016

**Major achievement for PCa diagnosis**
What can we expect from MRI for active surveillance?

• Patient diagnosed with low volume, low grade disease
• Mostly by systematic biopsy

Selection based on systematic biopsy data to identify non significant prostate cancer (Epstein criteria):
• One core +
• < 3mm cancer per core
• No Gleason 7-10

• < 2 cores +
• <50% of core involved
• No Gleason 7-10

Epstein et al., JAMA 1994
Randomized biopsy

Prostate

Randomized core

Gleason
Protocol inclusion

- Risk of understaging / undersampling
- Need for correct characterization by extended systematic biopsy or imaging
  - MRI helpful to identify lesions and to target biopsies
Targeted vs. randomized cores
MRI targeted vs. randomized biopsy:

Cancer length:

Van Hove et al., WJU 2014
MRI targeted vs. randomized biopsy: “Significance” of cancer

significant cancer / Gleason $\geq 7$ (%)
Protocol inclusion

- MRI targeted biopsy increases the likelihood of correctly sample and grade the lesion
- Better characterization of lesion


▶ Major achievement for the safety in active surveillance
Problem of targeted biopsie

i.e.:

- One core +
- $\leq 2$ cores +

Epstein et al., JAMA 1994

Prostate

5 mm

Gleason

Targeted cores
Problem of targeted biopsie

i.e.:

• < 3mm cancer per core
• < 50% of core involved

Epstein et al., JAMA 1994

5 mm diameter:
\((0.5 \times 0.5 \times 0.5) \times 0.52 = 0.06\text{cc}\)
• Image-targeted biopsy increase the risk attribution if traditional criteria are applied.
• Targeted biopsy strategies need new risk stratification models that account for increased sampling of tumour.”

Robertson et al., EurUrol 2014

The best definition is yet to be found!
Meaning of a “normal” MRI for diagnosis and active surveillance

• How about NPV of mpMRI?

• If NPV is high, a negative mpMRI, may be a tool for ruling out significant disease
  – Tool as a triage test before biopsy
  – Tool for active surveillance

Vargas et al., Radiology 2011
Rastinehad et al., J Urol 2011.
Villers et al., J Urol 2006
Ahmed et al., Nat Rev Clin Oncol 2009
Haffner et al., BJUI, 2011
PROMIS study 2011
How to calculate the NPV?

- NPV = \( \frac{TN}{TN + FN} \)
- TN/FN rate only available on whole mount sections
- TN in prostates diagnosed with PCa?
## Size and grade of prostate cancer missed by mp MRI

Rate of missed high grade cancers = FN:

<table>
<thead>
<tr>
<th>Volume ml</th>
<th>Gleason 7</th>
<th>Gleason 8-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05-0.5</td>
<td>40%</td>
<td>0%</td>
</tr>
<tr>
<td>0.5-2.0</td>
<td>20%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>3%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Bratan et al.; EurRadiol 2013
Prostate cancer missed by mpMRI = FN

Fig. 2 - Rate of tumors detected and missed by multiparametric MRI, as stratified by maximal tumor diameter, Gleason score, index status, and tumor focality for all unique tumor foci (n=283). The index tumor is that with the highest Gleason score; if multiple foci had the same grade, the largest was considered the index lesion.
Pathology of PCa patients with normal preoperative MRI

n= 101: all with insignificant disease?

- pT3 = 17%
- Primary Gleason 4: 14%
- Secondary Gleason 4-5: 48%
- Volume > 0.5cc: 71%
- Volume > 2.0cc: 22%

= FN

Branger et al., BJUI 2016 in press

► NPV of >90% possible with these rates?
Pathology of PCa patients with normal preoperative MRI

pT3a, Gleason 3+4, 40% Gleason 4
### Influence of the expertise

<table>
<thead>
<tr>
<th>Pathological stage</th>
<th>Extern mpMRI n=72 (72%)</th>
<th>in house mpMRI n=29 (28%)</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT2</td>
<td>78%</td>
<td>97%</td>
<td>0.02</td>
</tr>
<tr>
<td>pT3</td>
<td>22%</td>
<td>3%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary pGleason (%)</th>
<th>Extern mpMRI</th>
<th>in house mpMRI</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>82%</td>
<td>97%</td>
<td>0.05</td>
</tr>
<tr>
<td>4</td>
<td>18%</td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Global tumor volume (mL)</th>
<th>Extern mpMRI</th>
<th>in house mpMRI</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range)</td>
<td>1.10</td>
<td>0.67</td>
<td>0.05</td>
</tr>
<tr>
<td>≥ 0.5 mL</td>
<td>76%</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>≥ 2 mL</td>
<td>27%</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

Branger et al., BJUI 2016 in press
Influence of expertise on MRI performance

Prostate cancer detection (ROC):

- General Radiologist: 0.66
- Uro-Radiologist: 0.88

Scheidler et al., ROFO 2012

- Before training: 0.74
- After training: 0.88

Garcia-Reyes et al., Abdom Imaging 2015
Need of standardized MRI protocols

- MRI protocol for mpMRI:
  
  EMRI was conducted with a standardized protocol at a single MR scanner at 1.5 T (Magnetom Sonata; Siemens Medical Solutions, Erlangen, Germany). For signal reception, a combination of the manufacturer standard multi-channel body and integrated spine phased array coils with an endorectal coil (Medrad Inc., Indianola, PA, USA) was used. Before insertion of the endorectal coil, a digital rectal examination was performed. To reduce potential bowel motion, body-weight adjusted 20–40mg butyl-scopolamine (Buscopan®, Boehringer Ingelheim, Germany) was administered intravenously in fractions (one fraction before insertion of the coil and the other before application of the T2w TSE sequences) in patients with no contraindications. After insertion, the endorectal coil was inflated with 40–60 ml air. EMRI comprised T2w half-fourier acquisition turbospin-echo (HASTE) sequences for prostate localization and planning of slice angulations of the T2w TSE sequences. Transversal T2w TSE slice orientation was defined perpendicular towards the rectum wall to assure best standardization of slice orientation in T2w imaging and for the preparation of the whole-mount sections. For lymph node staging and detection of haemorrhage, a 3DT1wgradient echo sequence (fast low angle shot; FLASH) was used. Sequence parameters for the axial/coronal T2w TSE sequences were: TR 9820/7720 [ms], TE 121/121 [ms], FoV (169×200)/(169×200) [mm2], Matrix size (216×512)/(216×512) [Px2], number of slices 30/24 [n], slice thickness 3/3 [mm], averages 3/3 [n], resulting acquisition time (TA) 7:22/7:20 [min:sec]; the resulting voxel size was (0.8×0.4×3) [mm3] for transversal and coronal T2w TSE, respectively. Turbo factor was 23 each and no parallel imaging techniques were applied. To reduce the total rooming time, the numbers of slices could be reduced depending on prostate volume and the conducting technicians were allowed to reduce the resulting TR down to 5000 [ms]. Voxel sizes and TE were fixed in all cases.

  Roethke et al., EurRadiol 2010
Need of standardized MRI protocols

N = 126 patients with repeat MRI due to referral
► very poor level of agreement
► significant difference in PI-RADS score

Müller et al.; Abstract Nr 504, EAU 2016
Need of standardized MRI report

Recommended standard vs. improvable
“Widespread trust in mpMRI of the prostate and its incorporation into clinical guidelines will require not only the ability to obtain high-quality images and perform accurate interpretations, but also to show that the entire community is able to perform these tasks consistently.”
The results from PROMIS: not yet published, but.....

It works if you:

- do not expect it to find every millimetre of significant disease
- quality assure and control every scanner
- optimize the sequences iteratively
- have robust training for radiologists

H. Ahmed, editorial BJUI 2016
The results from PROMIS: not yet published, but….

It works if:

- You accept that results depend on your definition of clinical significance.
- All centres evaluate their own data to determine where their own negative predictive value sits.
- All centres strive to improve upon this through a constant iterative dialogue between urology and radiology.

H. Ahmed, editorial BJUI 2016