MRI Targeted/TRUS Guided biopsies

Bernard MALAVAUD
«Random systematic» biopsies were first described by Hodge in 1989

The current EAU recommendations are but the continuation of those
Ancillary staining techniques (eg, basal cell staining) and to investigate the possibility of an anterior located PCa, rebiopsy if it occurs multifocally.

Luminal neoplasia (PIN) is only considered an indication for the detection rate uncertain. The later the repeat biopsy is done, the higher persistent PSA, suspicious DRE, and atypical small acinar DRE/TRUS.

Ciprofloxacin superior to ofloxacin if present, should be recorded. The presence of high-grade involvement per biopsy.

Transition zone biopsies are not recommended in the first set of biopsies due to low detection rates. C laterally directed cores are recommended, with perhaps more cores in prostates with a volume >40 ml. Transition zone biopsies are not recommended in the first set of biopsies due to low detection rates. One set of repeat biopsies is warranted in cases with persistent indication (abnormal DRE, elevated PSA, or histopathologic findings suggestive of malignancy at the initial biopsy) for prostate biopsy. Overall recommendations for further (three or more) sets of biopsies cannot be made; the decision must be made based on an individual patient.
Degree of Suspicion → Target → Location

Biopsy

Outcome

Results (pathology) → Accuracy (spatial)

dimanche 26 mai 13
Suspicion/Pathology

1. Can we grade the degree of suspicion?

2. Is it relevant in terms of cancer yield using TRUS-guided Bx?

3. Does it provide an accurate picture of the cancer burden?
Suspicion/Pathology

1. Can we grade the degree of suspicion?

2. Is it relevant in terms of cancer yield using TRUS-guided Bx?

3. Does it provide an accurate picture of the cancer burden?
There was no doubt that some relationships existed between mpMRI and prostate cancer...

Although - numerous- methodological limitations hampered such demonstration

Clear-cut definition of suspicion,
Yes and No or
Score of Suspicion

Robust enough to cover the differences between MRI units
There was no doubt that some relationships existed between mpMRI and prostate cancer...

Although numerous methodological limitations hampered such demonstration.

Clear-cut definition of suspicion,

Yes and No or

Score of Suspicion

Robust enough to cover the differences between MRI units
Prospective comparison of T2w-MRI and dynamic-contrast-enhanced MRI, 3D-MR spectroscopic imaging or diffusion-weighted MRI in repeat TRUS-guided biopsies

YES/NO: sensitivity, specificity, PPV, NPV

Table 2 Sensitivity, specificity, predictive values and accuracy of T2w-MRI, DCE-MRI, MRSI and DWI for per segment prediction of prostate cancer into 408 segments of peripheral zone

<table>
<thead>
<tr>
<th>Peripheral zone</th>
<th>T2w-MRI</th>
<th>DCE-MRI</th>
<th>MRSI</th>
<th>DWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.48</td>
<td>0.29</td>
<td>0.40</td>
<td>0.39</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.87</td>
<td>0.93</td>
<td>0.89</td>
<td>0.96</td>
</tr>
<tr>
<td>Positive predict. value</td>
<td>0.29</td>
<td>0.33</td>
<td>0.25</td>
<td>0.52</td>
</tr>
<tr>
<td>Negative predict. value</td>
<td>0.94</td>
<td>0.92</td>
<td>0.94</td>
<td>0.93</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.83</td>
<td>0.86</td>
<td>0.85</td>
<td>0.90</td>
</tr>
</tbody>
</table>

T2w-MRI T2-weighted magnetic resonance imaging, DCE-MRI dynamic contrast-enhanced MRI, MRSI 3D-MR spectroscopic imaging, DWI diffusion-weighted MRI
Each modality carried an independent weight in the prediction of cancer in a given segment: mpMRI.

Table 3 Per-segment prostate cancer probability of detection in 408 segments of peripheral zone from T2-w MRI results alone or combined with DCE-MRI, MRSI and DWI

<table>
<thead>
<tr>
<th>Probability (%)</th>
<th>T2-MRI</th>
<th>DCE-MRI</th>
<th>MRSI</th>
<th>DWI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unsuspicious</td>
<td>Suspicious</td>
<td>Unsuspicious</td>
<td>Suspicious</td>
</tr>
<tr>
<td>T2-MRI</td>
<td>6.2</td>
<td>5.8</td>
<td>14.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Suspicious</td>
<td>29.4</td>
<td>22.4</td>
<td>44.7</td>
<td>17.8</td>
</tr>
</tbody>
</table>

T2w-MRI T2-weighted magnetic resonance imaging, DCE-MRI dynamic contrast-enhanced MRI, MRSI 3D-MR spectroscopic imaging, DWI diffusion-weighted MRI

![Table](image)

All neg. 6.2% T2+/DWI+ 63.4%
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

Eur Radiol
DOI 10.1007/s00330-011-2377-y
A truly pivotal paper as i) it stated the minimal requirements for mpMRI and ii) proposed to stratify the results in five increments

Table 2  Acquisition protocols: minimum requirements

<table>
<thead>
<tr>
<th>A. Detection protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast &lt;30-min protocol without an endorectal coil (ERC). Images should cover entire prostate, and include T2WI, DWI and DCE-MRI. Imaging can be performed at 1.5 T using a good 8- to 16-channel pelvic phased array (PPA). Anti-peristaltic drugs (Buscopan®, Glucagon®) should be given.</td>
</tr>
<tr>
<td>• T2WI axial=sagittal: 4 mm at 1.5 T, 3 mm at 3 T; in-plane resolution: 0.5–0.5 mm to 0.7–0.7 mm at both 1.5 T and 3 T.</td>
</tr>
<tr>
<td>• DWI axial: 5 mm at 1.5 T, 4 mm at 3 T; in-plane resolution: 1.5–1.5 mm to 2.0–2.0 mm at 1.5 T and 1.0–1.0 mm to 1.5–1.5 mm at 3 T.</td>
</tr>
<tr>
<td>• ADC map should be calculated. At least 3 b-values should be acquired in three orthogonal directions and adapted to quality of SNR: 0, 100 and 800–1000 s/mm². For calculation of ADC, the highest b-value that should be used is 1000 s/mm².</td>
</tr>
<tr>
<td>• DCE-MRI axial: 4 mm at 1.5 T and 3 T; in-plane resolution: 3.0–1.0 mm at 1.5 T and 0.7–0.7 mm at 3 T. Quantitative or semi-quantitative DCE-MRI analysis does not have to be performed. Maximum temporal resolution should be 15 s following single dose of contrast agent with an injection rate of 3 mL/s. For DCE-MRI, imaging should be continued for 5 min to detect washout. Then enhanced T1WI images from this sequence can be used to detect post-biopsy haematomata.</td>
</tr>
<tr>
<td>• MRSI: optionally, MRSI can be added to the detection protocol, but this requires an extra 10–15 min of examination time. For this ERC is mandatory at 1.5 T and optional at 3 T; volume of interest (VOI) aligned to axial T2WI; coverage of the whole prostate in the VOI; field of view at least 1.5 voxels larger than the VOI in all directions to avoid wrap-around or back folding; matrix of at least 8 x 8 x 8 phase-encoding steps with nominal voxel size &lt;0.5 cc; spectral selective suppression of water and lipid signals; positioning of at least six fat saturation bands close to the prostate margin (may be positioned inside the VOI) to conform to the prostate shape as closely as possible; automatic or manual shimming up to a line width at half height of the water resonance peak between 15 and 20 Hz at 1.5 T and between 20 and 25 Hz at 3 T.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Staging protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-min protocol for evaluating minimal extra-capsular extension. Preferably, this examination should be done with an ERC. Images should include entire prostate, with anti-peristaltic drugs.</td>
</tr>
<tr>
<td>• T2WI axial, coronal and sagittal planes, 1 mm at 1.5 T and 3 T; in-plane resolution: 0.3–0.3 mm to 0.7–0.7 mm at 1.5 T and 0.3–0.3 mm to 0.5–0.5 mm at 3 T.</td>
</tr>
<tr>
<td>• DWI and DCE as detection protocol.</td>
</tr>
<tr>
<td>• MRSI optional.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Nodes and bone protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-min protocol, to assess nodal size and bone marrow metastases. Should be performed separately from A and B, as most patients do not require bone or node staging.</td>
</tr>
<tr>
<td>• T1WI coronal of lower lumbar spine plus pelvis (SE or ET SE) 3.0-mm slices</td>
</tr>
<tr>
<td>• DFT ET SE T2WI coronal of lower lumbar spine plus pelvis: 1.0-mm isometric voxels</td>
</tr>
<tr>
<td>• DWI coronal of lower lumbar spine plus pelvis (b-values 0 and 600), slice thickness 3–4 mm, in plane resolution: 2.5–3.0 mm voxels</td>
</tr>
<tr>
<td>• T1WI sagittal cervical and thoracic spine (SE or ET SE)</td>
</tr>
<tr>
<td>• STIR or DWI sagittal cervical and thoracic spine.</td>
</tr>
</tbody>
</table>

Table 3  PI-RADS scoring system

<table>
<thead>
<tr>
<th>Score</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1. T2WI for the peripheral zone (PZ)</td>
<td>Uniform high signal intensity (SI)</td>
</tr>
<tr>
<td>1</td>
<td>Linear wedge-shaped, or geographic areas of lower SI, usually not well demarcated</td>
</tr>
<tr>
<td>2</td>
<td>Intermediate appearances not in categories 1/2 or 4/5</td>
</tr>
<tr>
<td>3</td>
<td>Discrete, homogeneous low signal focus/mass confined to the prostate</td>
</tr>
<tr>
<td>4</td>
<td>Discrete, homogeneous low signal intensity focus with extra-capsular extension/invasive behaviour or mass effect on the capsule (bulging), or broad (&gt;1.5 cm) contact with the surface</td>
</tr>
<tr>
<td>A2. T2WI for the transition zone (TZ)</td>
<td>Heterogeneous TZ adenoma with well-defined margins: “organised chaos”</td>
</tr>
<tr>
<td>1</td>
<td>Areas of more homogeneous low SI, however well marginated, originating from the TZ/BPH</td>
</tr>
<tr>
<td>2</td>
<td>Intermediate appearances not in categories 1/2 or 4/5</td>
</tr>
<tr>
<td>3</td>
<td>Areas of more homogeneous low SI, ill defined: “erased charcoal sign”</td>
</tr>
<tr>
<td>4</td>
<td>Same as 4, but involving the anterior fibromuscular stroma or the anterior horn of the PZ, usually lenticular or water-drop shaped.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Diffusion weighted imaging (DWI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No reduction in ADC compared with normal glandular tissue. No increase in SI on any high b-value image (b≥8000)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Dynamic contrast enhanced (DCE)-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 enhancement curve</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

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dimanche 26 mai 13
Suspicion/Pathology

1. Can we grade the degree of suspicion?

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ESUR prostate MR guidelines 2012

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

Fig. 1 Algorithm in imaging men referred with elevated serum prostate specific antigen (PSA), abnormal digital rectal examination (DRE), or family history of prostate cancer

First presentation
TRUS-biopsy (10-14 cores)

Biopsy positive
# of cores
% of each core positive

Curative intent
Patient factors: life expectancy, co-morbidities, preference

Staging MRI with bone and node MRI in high risk (PSA>15 or Gleason>7, or DRE T3)

Active surveillance

Staging MRI to confirm grade and extent T2WI, DWI, DCE, (MRSI)

Biopsy negative and clinical suspicion PCa

Detection MRI and then biopsy (TRUS guided by MRI or MR-guided biopsy in some specialist units)

Biopsy negative
Clinical follow up
Re-measure PSA
Validation of the European Society of Urogenital Radiology Scoring System for Prostate Cancer Diagnosis on Multiparametric Magnetic Resonance Imaging in a Cohort of Repeat Biopsy Patients

Daniel Portalez, Pierre Mozer, François Cornud, Raphaëlle Renard-Penna, Vincent Misrai, Matthieu Thoulouzan, Bernard Malavaud

Target definition and Elastic Surface Registration
Post-procedure analysis of DICOM archives
A structured approach for each imaging modality
First validation of the ESUR-S in repeat biopsies patients
With excellent predictive characteristics:

**Fig. 6** – Receiver operating characteristic curves for (A) the European Society of Urogenital Radiology (ESUR) score sum and (B) the Likert scale. CI = confidence interval.
And excellent negative predictive value, suggesting that in case of unsuspicous mpMRI (ESUR-S<9), there is little chance of showing cancer on targeted biopsies.
3rd set of Bx, T1c, prostate volume 32 ml, PSA 9 ng/ml, PCA3 score 101
Does ESUR-S also work in primary biopsies?

Cancers found on repeat biopsies are often located anteriorly of small volume and low Gleason score
Therefore 119 initial biopsies patients were offered mpMRI followed by 12+2 cores if found with suspicious lesion.

119 patients, 1731 cores
And the same threshold values of ESUR≥9 and Likert ≥3

A

ESUR Score 9

Area Under the Curve: 0.89±0.02

B

Likert Score 3

Area Under the Curve: 0.90±0.01

False-positive rate (1-specificity)

True positive rate (sensitivity)
Suspicion/Pathology

1. Can we grade the degree of suspicion?

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119 patients
Normal DRE but PSA 4-20ng/ml
MRI «suspicious»

RSB: 61+/119
51.2%

9 detected only by RSB

PRIIAS criteria: 16/61

26.9%

IGB ESUR < 9
3/32 (9.4%)

1/3

8 detected only by IGB

73.1%

IGB ESUR \geq 9
57/87 (65.5%)

8/57

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Call for project PHRC-INCA 2013

Inclusion: Primary biopsies*

Risk-stratified 1:1 randomization
(PSA, DRE, Family Hx, Ethnicity, Urorisk° model)

Protocol 1.5T mpMRI
(T2w, DCE-MRI, DWI-MRI)

Detection of 1-2 targets
(>7mm, Lickert score >3)

No target detected

2-3 image-guided cores
FDA-approved elastic registration
MRI-3D-TRUS system

Cancer detected
STOP

No cancer detected

12 random-systematic laterally-directed TRUS-guided Bx *

Cancer detected
STOP

No cancer detected

Wait 3-6 months

Protocol 1.5T mpMRI
(T2w, DCE-MRI, DWI-MRI)

Detection of 1-2 targets
(>7mm, Lickert score >3)

No target detected

2-3 image-guided cores
FDA-approved elastic registration
MRI-3D-TRUS system

STOP

* EAU Guidelines, Heidenreich et al., Eur Urol 2011

mardi 7 mai 13

dimanche 26 mai 13
Taken altogether these results strongly support a shift in pradigm from SSB for all to IGB for some...
Location/Spatial accuracy

1. How accurate are transrectal biopsies?

2. What are the limitations of cognitive registration?

3. Are they properly addressed by elastic surface registration?
TWO CONSECUTIVE SETS OF TRANSRECTAL ULTRASOUND GUIDED SEXTANT BIOPSIES OF THE PROSTATE FOR THE DETECTION OF PROSTATE CANCER

MICHAEL A. LEVINE, MICHAEL ITTMAN, JONATHAN MELAMED AND HERBERT LEPOR

From the Departments of Urology and Pathology, New York University Medical Center, and Manhattan Veterans Administration Medical Center, New York, New York

**Table 2. Pathological diagnosis**

<table>
<thead>
<tr>
<th>Pathological Diagnosis</th>
<th>No. Biopsy Set 1 (%)</th>
<th>No. Biopsy Set 2 (%)</th>
<th>No. Both Biopsy Sets (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>89 (65)</td>
<td>84 (57)</td>
<td>78 (57)*</td>
</tr>
<tr>
<td>Intraepithelial neoplasia†</td>
<td>18 (13)</td>
<td>13 (9)</td>
<td>16 (12)‡</td>
</tr>
<tr>
<td>Prostate adenocarcinoma</td>
<td>30 (22)</td>
<td>40 (28)</td>
<td>43 (31)§</td>
</tr>
</tbody>
</table>

* Biopsy sets 1 and 2 benign.
† High grade intraepithelial neoplasia with no cancer.
‡ High grade intraepithelial neoplasia without adenocarcinoma of the prostate in at least 1 of 2 biopsy sets.
§ Adenocarcinoma of the prostate in at least 1 of 2 biopsy sets.
Location/Spatial accuracy

1. How accurate are transrectal biopsies?

2. What are the limitations of cognitive registration?

3. Are they properly addressed by elastic surface registration?
Similar spatial imprecision was observed for radical prostatectomy specimens or autopsy prostates.

TRUS-guided biopsies are hardly accurate.
Indeed, the Prostate is a tricky target: Transperineal +phantom approach study

Placement error: $6.5 \pm 3.5\text{mm}$

**Needle deflection** 3.2-8.7 mm

**Misalignment of the needle template**: $1.5 \pm 0.3\text{mm}$

+ **Needle susceptibility artifact** for MRI: $1.6 \pm 0.4\text{mm}$

Blumenfeld, J Magn Reson Imaging 2007
MRI 2D: orthogonal sections

TRUS 2D «endfire» probe: oblique section

Requiring so-called «mental» or «cognitive» registration

Detection of the 302 cancers according to MRI findings, volume, location and targeted biopsies as compared with extended systematic biopsies is modelled in Fig. 4.

SYSTEMATIC VS TARGETED BIOPSIES

Taking both sensitivity and specificity into consideration by integrated discrimination improvement, the detection accuracy of targeted biopsies was better than that of extended systematic biopsies ($P < 0.001$) for significant cancer detection (definition 1). The same analysis for definition 2 showed that neither extended systematic biopsies nor targeted biopsies performed better ($P = 0.312$).

The maximal involvement of cancer in positive cores was 5.56 mm for targeted biopsies and 4.70 mm for extended systematic biopsies ($P = 0.002$). For all 302 cancers, Gleason scores were $\leq 6$ in 54%, 7 in 34% and $> 8$ in 12%, with a median Gleason score of 7 (3 + 4).

Among the 265 patients for whom targeted biopsies were performed in addition to extended systematic biopsies, 25 patients had some pattern 4 cancer (Gleason score $> 6$) on at least one biopsy core, either by targeted biopsy or extended systematic biopsy.
Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging–targeted and systematic biopsy for significant prostate cancer detection

Jérémie Haffner*, Laurent Lemaitre†, Philippe Puech‡, Georges–Pascal Haber§, Xavier Leroy*, J. Stephen Jones§ and Arnaud Villers*

*Department of Urology, †Department of Radiology and ‡Department of Pathology, Université Lille Nord de France, F-59000 Lille, France; INSERM, U703, F-59120 Loois, France; CHU Lille, F-59000 Lille, France, and §Glickman Urological and Kidney Institute CCE, USA

Accepted for publication 26 November 2010

For each patient, cancer was classified as insignificant if only one core was positive with cancer length <5 mm and no Gleason pattern 4/5.

TABLE 5 Comparison between extended systematic biopsies (ESBs) and targeted biopsies (TBs) at MRI for cancer detection of significant cancers in the series of 555 patients

<table>
<thead>
<tr>
<th></th>
<th>ESB</th>
<th>TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.95 (0.92, 0.97)</td>
<td>0.95 (0.92, 0.97)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.83 (0.78, 0.87)</td>
<td>1 (0.99, 1)</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>0.88 (0.85, 0.91)</td>
<td>0.98 (0.96, 0.99)</td>
</tr>
</tbody>
</table>
Location/Spatial accuracy

1. How accurate are transrectal biopsies?

2. What are the limitations of cognitive registration?

3. Are they properly addressed by elastic surface registration?
Prostate biopsy tracking with deformation estimation

Michael Baumann\textsuperscript{a,c,}\textsuperscript{*}, Pierre Mozer\textsuperscript{b}, Vincent Daanen\textsuperscript{c}, Jocelyne Troccaz\textsuperscript{a}

\textsuperscript{a}Université J. Fourier, TIMC Laboratory, CNRS, UMR 5525, Grenoble, France
\textsuperscript{b}La Pitié-Salpêtrière Hospital, Urology Dpt., 75651 Paris Cedex 13, France
\textsuperscript{c}Koelis SAS, 5. av. du Grand Sablon, 38700 La Tronche, France

(a) (b) (c) (d)
41 patients: Mental vs Koelis

To compare the geometry of freehand «mental» biopsies and Elastic-fusion registration biopsies

Cornud & Portalez, manuscript in preparation
Then validated in terms of cancer detection in 101 consecutive patients

<table>
<thead>
<tr>
<th>Mental</th>
<th>Koelis</th>
</tr>
</thead>
<tbody>
<tr>
<td>neg</td>
<td>47</td>
</tr>
<tr>
<td>pos</td>
<td>6</td>
</tr>
</tbody>
</table>

Fisher exact test $p<0.0001$

Cornud & Portalez, manuscript in preparation
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MERCI