Prostate MRI

PARIS, June 7-8, 2013

3rd ESUR Teaching Course on Prostate MRI
Endorsed by the European Society of Urogenital Radiology (ESUR)

MpMRI WHY and WHEN we do it

RECURRENTE
AFTER RP
AND RT

Valeria Panebianco
Prostate Unit
MpMRI INDICATIONS

DETECTION
Early diagnosis, in asymptomatic phase

TUMOUR BIOLOGY
To establish disease aggressiveness

STAGING
Therapeutical planning

DURING TREATMENT
- Biological effects of therapy
- Response assessments
- Residual disease

FOLLOW UP
Effectiveness of therapy
Monitoring response to therapy

From generic to targeted imaging

Biological Correlations

ESUR Guidelines 2012
TREATMENT OPTIONS

Techniques

- Radical Prostatectomy
- External-beam RT + Brachytherapy
- Hormonotherapy
- Watchful waiting
- Ablative Therapies

Cooperberg MR, J Clin Oncol, 2010
THE DAY AFTER TOMORROW

RP: ONCOLOGICAL RADICALITY

IMAGING: EFFECTIVENESS OF THERAPY

- **CR** COMPLETE
- **PR** PARTIAL
- **SD** STABILITY
- **PD** PROGRESSION
THE CLINICAL POINT

PSA is expected to be undetectable within 3 weeks after a successful radical prostatectomy.

A persistently elevated PSA level after radical prostatectomy (RP) means the presence of tissue remained.

- residual cancer (micro-metastases not detected or undetectable)
- residual disease (surgical positive margins)

Schoder H, Clin Cancer Res, 2005
Han M, J Urol 2003
Heidenreich A., EAU Guidelines 2010
THE CLINICAL POINT

In about 30% an increase in (PSA) levels after surgical treatment reveals prostate cancer recurrence

Pts with moderately differentiated tumours, late PSA relapse and slow doubling time (>10-12 months) can be presumed to have local failure only

PSA > 0,2 ng/ml = CUT-OFF

Pound CR, JAMA 1999
Freedland SJ, Urology 2003
Schoder H, Clin Cancer Res, 2005
Stephenson AJ, J Clin Oncol 2006
Heidenreich A., EAU Guidelines 2010
ROLE OF IMAGING

The guidelines of urological and oncological societies do not have significant recommendations regarding the use of specific imaging techniques for the early diagnosis of local recurrence after RP.

The NCCN guidelines provide the use of different imaging techniques as PET, MRI, CT.

AUA guidelines do not have specific recommendations for the use of imaging in patients with biochemical relapse and possibility to have local recurrence after RP.

EAU guidelines indicate PET-CT and MRI as possible tools in patients with PSA recurrence between 1.0 and 2.0 ng/ml, but they are not considered as routine procedures.

We know the importance of a quickly diagnosis in terms of PSA and a sure localization of the recurrence.
MpMRI can influence the RT therapeutical planning. Dose increasing if MR is positive for recurrence (66Gy vs 72Gy).

- Failure of PSA to fall to undetectable
- PSA detectable and rising on 2 or more subsequent determinations

- Bone scan
- CT/MRI
- PSADT
- Prostate bed biopsy

Studies negative for distant metastases

Studies positive for distant metastases

RT + neoadjuvant/concomitant/adjuvant ADT

ADT + RT to site of metastases, if in weight-bearing bones, or symptomatic or symptomatic or Observation

Difficult
Not justified
(Accuracy 54%)

EAU Guidelines 2011
Only if PSA > 1.5 - 2 ng/ml
SENS 83 %

“Detection Rate”
36% PSA <1 ng/ml
43% PSA1<-2 ng/ml
62% PSA 2<-3 ng/ml
73% PSA >=3 ng/ml

Krause BJ

Rinnab L.

PSA cut-off value
1.4 ng/ml


Courtesy by Dr Picchio
Is there a role for $^{11}$C-choline PET/CT in the early detection of metastatic disease in surgically treated prostate cancer patients with a mild PSA increase $<1.5$ ng/ml?

**MpMRI INDICATIONS**

**DETECTION**
Early diagnosis, in asymptomatic phase

**TUMOUR BIOLOGY**
To establish disease aggressiveness

**STAGING**
Therapeutical planning

**FOLLOW UP**
Effectiveness of therapy
Monitoring response to therapy

**ESUR Guidelines 2012**

**Biological Correlations**
- MRI T2-T1
- DWI
- MRP
- MRS
How we do it

TECHNICAL REQUIREMENTS

1. 5T and 3T Magnet

127.8 MHz 3T

ERC MR (MRS)

3

63.9 MHz 1.5 T

1.5

PPA coil

ω = γ B₀

PPA coil at 3T = PPA coil + ERC at 1.5

Is better than...

100% sens
100% spec

S/N

Futterer JJ, Scheenen TW, Huisman HJ, et al., Invest Radiol 2004
Minimum requirements:

**T2WI** axial and sagittal planes, **4 mm** at 1.5T and **3 mm** at 3T

**DWI** axial: 5 mm at 1.5T, 4 mm at 3T; 3 b-values should be acquired: 0, **100, 800, 1000 s/mm²**. For calculation of ADC, the highest b-value that should be used is 1000 s/mm² (with adequate SNR)

**DCE-MRI** axial, 3-4 mm at 1.5T and 3 mm at 3T. Quantitative or semi-quantitative DCE-MRI analysis does not have to be performed as minimal practice, but if present should be done as optimal practice. Maximum temporal resolution should be 10-15 s following single dose of contrast with an injection rate of 3 ml/s. For DCE-MRI, imaging acquisition should be continued for 5 minutes to detect washout. **For physiological modeling, the maximum temporal resolution should be <5 s.**

**MRSI** CSI sequence with nominal **voxel size < 0.5 cc**; spectral selective suppression of water and lipid signals.

ESUR Recommendations
Comparative analysis of multiparametric magnetic resonance and PET-CT in the management of local recurrence after radical prostatectomy for prostate cancer

Andrea Alfurone, Valeria Paezibianco, Orazio Schilli, Stefano Salciccia, Susanna Cattarin, Gianna Mariotti, Alessandro Gentilucci, Magnus Von Helden, Roberto Passarelli, Vincenzo Gentile, Alessandro Scaia

| Table 2 Characteristics and level of evidence of the different reviewed studies on multiparametric MRI and PET-CT for the diagnosis of local recurrence after RP. |
|---|---|---|---|---|---|---|---|
| Authors | Imaging used | Study | Number cases | Mean PSA | Mean lesion size | Sensitivity, specificity, PPV, NPV, accuracy | Level of evidence |
| Heinrich [29] | 18 F choline PET-CT | Retrospective | 31 | 17.1 ng/ml in positive pts – 3.4 ng/ml in negative pts | Not available | CT-MRI histology, course of disease | 3 |
| Rinnab [30] | Retrospective | 40 | 3.62 ng/ml in positive pts – 0.9 ng/ml in negative patients | Not available | Hystology | Sensitivity 95%, Specificity 40%, PPV 86%, NPV 67%, Accuracy 66% | 2b |
| Cagian [41] | MRI with DCE | Retrospective | 46 | 1.9 ng/ml | 1.5 cm | Hystology or clinical validation with PSA following radiotherapy | Sensitivity 88%, Specificity 100%, PPV 100%, NPV 85%, Accuracy 94% | 2b |
| Sciara [42] | MRSI + DCEMRI | Prospective | 77 (10 pts as control) | 1.26 ng/ml in group A 0.86 ng/ml in group B | 13.3 mm in group A 6 mm in group B | Hystology (group A) or clinical validation with PSA following radiotherapy (Group B) | Sensitivity 87%, Specificity 94%, PPV 96%, NPV 79% | 2a |
| Citlilo [43] | C1-MRI | Retrospective | 72 | 1.23 ng/ml | 1.7 cm | Hystology, choline PET-CT, follow up with PSA | Sensitivity 84.3%, Specificity 89.3%, PPV 92.5%, NPV 78.1%, Accuracy 86.1% | 2a |
| Panachianco [44] | MRSI + DCEMRI and 18F choline PET-CT | Prospective | 84 | 1.1 ng/ml in group A 1.9 ng/ml in group B | 6 mm in group A 13.3 mm in group B | Hystology (group B) or clinical validation with PSA following radiotherapy (Group A) | Sensitivity 92%, Specificity 75%, PPV 96%, NPV 60%, Accuracy 89% | 2a |
## Local Recurrence After RP

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-F-ChoPET-CT</td>
<td>60 - 95%</td>
<td>40%</td>
<td>84%</td>
</tr>
<tr>
<td>11-C-ChoPET-CT</td>
<td>53 - 93%</td>
<td>36 - 100%</td>
<td>60 - 91%</td>
</tr>
<tr>
<td>ECMRI</td>
<td>95%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>MRI +DCE</td>
<td>84-88%</td>
<td>89 - 100%</td>
<td>86 -94%</td>
</tr>
<tr>
<td>MRI +DCE +MRS</td>
<td>87 – 94%</td>
<td>75 - 100%</td>
<td>89 -94%</td>
</tr>
</tbody>
</table>

- **Depend on size**
- **Size too large**
- **PSA to high**
- **Smaller lesion**
- **PSA lower**

*Heinisch, Rinnab, Vees, Panebianco, Castellucci, Giovacchini, Rinab, Reske, Vees, Sella, Casciani, Cirillo, Sciarra, Panebianco, Alfarone A, Critical Reviews in Oncology/Hematology, 2012*
Normal Changes after surgery

Anterior and caudal bladder shift
Visualization of mm. Int. Obturators & Elevatori ani

Urogenital diaphragm change position

Denonvilliers fascia reconstructed

ESUR Recommendations

T2WI axial+sagittal:
4 mm at 1.5 T, 3 mm at 3 T
Normal Changes after surgery

Increase of soft tissue

After RRP
Normal Changes after surgery

- Normal vesicourethral anastomosis
- Conelike morphology
- Low signal on T2
- No enhancing
Normal Changes after surgery

Normal anastomosis after RRP

Suture after robotic-surgery

Bladder mucosa eversion post-RRP

Right suture passed transversally from left to right through the posterior musculofascial plate

Courtesy of Prof. Gallucci
MpMRI POST RRP: WHY and WHEN we do it

- to detect recurrence in all morphology and sites
- to diagnose smaller lesions
- to distinguish gland residual and/or fibrosis to nodule recurrence (MRS – DWI)
- to determine the aggressiveness of nodule recurrence (MRS – DWI)
DETECTION: imaging T2

Solid Tissue: intermediate signal intensity between pelvic muscle and fat tissue

MORPHOLOGY

- nodular
- lobular
- circumferencial
- thickening
SITE

DETECTION: imaging T2

Perianastomotic

residual glandular or seminal vesicles

neck bladder

surgical margins
DETECTION/LOCALIZATION: DCE-MRI

DCE-MRI axial, 3-4 mm at 1.5T and 3 mm at 3T; maximum TR 10 s, for physiological modeling <5 s

Qualitative / Quantitative analysis
Color Map
SI/T Semi-quantitative
C/T Quantitative

ESUR Recommendations

Imaging Pearls

The typical appearance of recurrence is a soft-tissue nodule in the prostatectomy bed that is isointense to muscle on T1-weighted and slightly hyperintense to muscle on T2-weighted images.

Differential diagnosis: postoperative fibrosis (low signal intensity on images from all sequences) and granulation tissue (may mimic signal intensity of tumor recurrence).

Intravenous contrast material is helpful because tumor tends to enhance earlier and more avidly than do postoperative changes.

Vargas HA, Radiology, 2012
65 y.o. Pt, pT2c R1

PSA
0.3 ng/mL

After 3 months
PSA
0.5 ng/mL
CHARACTERIZATION: 1H-MRS

MRS Analysis

Quali / Quantitative analysis
Color Map
RATIO Spectra Quantification

with nominal voxel size <0.5 cc

No solid tissue/ Empty Fossa : undetectable ratio
Cho + Cr/ C < 0.2 : fibrotic/ scar tissue
Cho + Cr/ C > 0.2 < 0.5: residual healthy prostatic gland tissue
Cho + Cr/ C > 0.5 < 1 : probability recurrence PCa
Cho + Cr/ C > 1 : definitively recurrence Pca

Jung JA, Radiology, 2004
A.PS Kirkam,, Eur Urol 2006

ESUR Recommandations
MRS: when not to do it

ARTIFACTS
DETECTION & AGGRESSIVENESSNESS: DWI

Increasing the b values is obtained by a decay of the signal coming from the normal tissue.

Multiple b values are used, usually in the range of 0–1500 sec/mm$^2$.

Vargas HA, Radiology, 2012

ESUR Recommendations
MpMRI POST RRP: WHY and WHEN we do it

- to detect recurrence in all morphology and sites
- to diagnose smaller lesions
- to distinguish gland residual and/or fibrosis to nodule recurrence (MRS – DWI)
- to determine the aggressiveness of nodule recurrence (MRS – DWI)
66 y.o with PSA value of 0.8 ng/mL

At 18F-choline PET-CT
No pathological uptake

5 mm nodule recurrence
<table>
<thead>
<tr>
<th>TECHNIQUE</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MR Spectroscopy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient group A (7.6 – 19.4 mm)</td>
<td>84 (26/31)</td>
<td>88 (14/16)</td>
<td>93 (26/28)</td>
<td>74 (14/19)</td>
</tr>
<tr>
<td>Patient group B (5.0- 7.2 mm)</td>
<td>71 (10/14)</td>
<td>83 (5/6)</td>
<td>91 (10/11)</td>
<td>56 (5/9)</td>
</tr>
<tr>
<td><strong>DCEMR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient group A (7.6 – 19.4 mm)</td>
<td>71 (22/31)</td>
<td>94 (15/16)</td>
<td>96 (22/23)</td>
<td>63 (15/24)</td>
</tr>
<tr>
<td>Patient group B (5.0- 7.2 mm)</td>
<td>79 (11/14)</td>
<td>100 (6/6)</td>
<td>100 (11/11)</td>
<td>67 (6/9)</td>
</tr>
<tr>
<td><strong>MRSI+DCEMR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient group A (7.6 – 19.4 mm)</td>
<td>87 (27/31)</td>
<td>94 (15/16)</td>
<td>96 (27/28)</td>
<td>79 (15/19)</td>
</tr>
<tr>
<td>Patient group B (5.0- 7.2 mm)</td>
<td>86 (12/14)</td>
<td>100 (6/6)</td>
<td>100 (12/12)</td>
<td>75 (6/8)</td>
</tr>
</tbody>
</table>

In a previous experience MRS combined with DCEMR
MpMRI POST RRP: WHY and WHEN we do it

- to detect recurrence in all morphology and sites
- to diagnose smaller lesions
- to distinguish gland residual and/or fibrosis to nodule recurrence (MRS – DWI)
- to determine the aggressiveness of nodule recurrence (MRS – DWI)
MRS to distinguish gland residual to nodule recurrence

A 69 y.o. with PSA value of 1, 4 ng/mL
In a more recent experience MRS combined with DCE

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients number</th>
<th>PSA serum level (mean)</th>
<th>Maximal transverse dimension of local recurrence (mean)</th>
<th>Features and standard validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>28 patients</td>
<td>0.8–1.4 ng/mL (1.1 ng/mL)</td>
<td>5–7.2 mm (6 ± 0.5 mm)</td>
<td>Patients in which the PSA level modification after radiation therapy was used as validation of MR results.</td>
</tr>
<tr>
<td>B</td>
<td>56 patients</td>
<td>1.3–2.5 ng/mL (1.9 ng/mL)</td>
<td>7.6–19.4 mm (13.3 ± 4.5 mm)</td>
<td>Patients in which a TRUS-biopsy of the post-prostatectomy prostatic fossa was performed as control.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR Group A</td>
<td>92%(22/24)</td>
<td>75%(3/4)</td>
<td>96%(22/23)</td>
<td>60%(3/5)</td>
<td>89%(25/28)</td>
</tr>
<tr>
<td>Group B</td>
<td>94%(49/52)</td>
<td>100%(4/4)</td>
<td>100%(49/49)</td>
<td>57%(4/7)</td>
<td>94%(53/56)</td>
</tr>
<tr>
<td>PET-CT Group A</td>
<td>62%(15/24)</td>
<td>50%(2/4)</td>
<td>88%(15/17)</td>
<td>18%(2/11)</td>
<td>60%(17/28)</td>
</tr>
<tr>
<td>Group B</td>
<td>92%(48/52)</td>
<td>33%(1/3)</td>
<td>98%(48/49)</td>
<td>43%(3/7)</td>
<td>91%(51/56)</td>
</tr>
</tbody>
</table>

Prostate cancer: 1H MRS-DCEMR at 3 T versus [(18)F]choline PET/CT in the detection of local prostate cancer recurrence in men with biochemical progression after radical retropubic prostatectomy (RRP)

Valeria Panebianco*#, Alessandro Sciarra##, Danilo Lisi##, Francesca Galati##, Valeria Buonocore##, Carlo Catalano##, Vincenzo Gentile##, Andrea Laghi##, Roberto Passariello##
58 y.o. Pt PSA: 0.39 ng/mL

Residual Glande
MpMRI POST RRP: WHY and WHEN we do it

- to detect recurrence in all morphology and sites
- to diagnose smaller lesions
- to distinguish gland residual and/or fibrosis to nodule recurrence (MRS – DWI)
- to determine the aggressiveness of nodule recurrence (MRS – DWI)
60 y.o. Pt  PSA: 0.8 ng/mL

GS 7(3+4)
MpMRI POST RRP: WHY and WHEN we do it

- PSA increase (0.2 to 1.5 ng/ml)
  PET-TC is not recommended in values lower than 1.5 ng/ml)

- Imaging is requested to guide therapeutical planning (RT)

- to change the patient management
MRS POST RRP: clinical relevance

The early detection of loco-regional prostate cancer recurrence post RRP in patients with low increasing of PSA value improves therapeutical planning

A correct characterization (residual gland vs nodular recurrence) of pathological tissue in the prostatic fossa can guide Radiation Therapy planning, dose reducing

Distinction therapy injury from recurrent disease based on characteristics of tissue

MpMRI could be use as problem solving in difficult cases (smaller lesions, other techniques borderline)

Panebianco V, Eur Rad 2013
About 25% of patients with prostate cancer undergo RT as definitive treatment.

Biochemical failure after RT occurs in about 20%-60% within 5 years.

PSA levels decrease slowly after radiation and may never reach undetectable levels. To determine RESPONSE to therapy and to distinguish RECURRENCE.

The time to reach Nadir (lowest PSA value) after RT is variable and depends on different factors (dose, prostate size, and pretreatment PSA level).

**PSA NADIR at least 2.5 ng/ml** (better if tending to 0 value)

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D'Amico AV., Cancer 2002
Cooperberg MR., Urology 2003
Kuban DA., Int J Radiat Oncol Biol Phys 2003

Cooperberg MR, J Clin Oncol 2010
Sheinbein C, Urology 2010
Hurwitz MD, Cancer 2011
## MR-Techniques and RT Effects

<table>
<thead>
<tr>
<th>MR Technique</th>
<th>RT Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>Diffuse low signal intensity on T2; no detectable zonal anatomy. Reduction in size of gland and tumor (Atrophy &amp; Fibrosis)</td>
</tr>
<tr>
<td>MRS</td>
<td>Metabolities decrease, especially Ci (“metabolic atrophy”)</td>
</tr>
<tr>
<td>DCE-MRI</td>
<td>Vascularization: decrease in blood flow. From inflammation to fibrosis</td>
</tr>
<tr>
<td>DWI</td>
<td>ADC map modifications</td>
</tr>
</tbody>
</table>

Coakley FV, Radiology 2004
Pucar D., Radiology 2005
Antonio C. Journal of Endourology 2008
Lucy E., Radiotherapy and Oncology 2009
Song I, AJR 2010
MRI
- Diffuse low signal intensity on T2;
- no detectable zonal anatomy
- Reduction in size of gland and tumor
  (atrophy and fibrosis)

MRS
- Metabolities decrease, especially Ci (metabolic atrophy")
DCEMR

Vascularization decrease in blood flow
from inflammation to fibrosis
EBRT: Complete response
### MR-Patterns as BIOMARKERS

<table>
<thead>
<tr>
<th>MR TECHNIQUE</th>
<th>RT EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>Nodular lesion of lower signal intensity than the adjacent normal prostate, in the same location as the pre-RT tumor. Growth of the lesion and progressive bulging of the prostatic capsule</td>
</tr>
<tr>
<td>MRS</td>
<td>Increase of metabolic ratio (cho+Cr/Cr)</td>
</tr>
<tr>
<td>DCEMR</td>
<td>Rapid contrast agent uptake and washout</td>
</tr>
<tr>
<td>DWI</td>
<td>Restricted diffusion</td>
</tr>
</tbody>
</table>

Lucy E., Radiotherapy and Oncology 2009  
Song I, AJR 2010  
Vargas HA, Radiology 2012  
Coakley FV, Radiology 2004  
Pucar D., Radiology 2005
The combination of MRGB and diagnostic MR imaging of the prostate was a feasible technique to localize PCa recurrence after EBRT.

Yakar D., Invest. Rad., 2010
Hurwitz MD, Cancer 2011
Cardone G., RSNA 2011
CLINICAL RELEVANCE

Monitoring response to therapy depicting physiological effects of therapy to establish responsive patterns (predictive value)

Recurrence detection and residual disease

Distinction therapy injury from recurrent disease
THANK YOU

valeria.panebianco@uniroma1.it