PSMA-PET/(MRI) for Prostate Cancer Imaging

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Content

- Introduction into PSMA-ligand PET
- Comparison of PSMA-PET/CT and PET/MRI
- Nothing is perfect: PSMA negative metastases
- Current research: Additive value of DWI in PSMA-PET/MRI of recurrent prostate cancer
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What is PSMA?

- PSMA = Prostate-specific membrane antigen

- A transmembrane protein physiologically expressed by prostate tissue and significantly overexpressed by most prostate cancer (PCA) cells.

- Increasing PSMA expression with higher tumor stage and grade.

- The recent development of specific PSMA-targeted small molecule ligands allows this trait of PCA cells to be exploited for clinical positron emission tomographic (PET) imaging of PCA
How does PSMA-PET compare to conventional imaging?

PSMA-PET outperforms bone scan.
Radionuclide imaging *and* therapy
Prostate carcinoma with bone metastases

**Evaluation for Radium-223 therapy**
- without PSMA-PET: Indikation for Radium-223 therapy given
- with PSMA-PET: discrepancy between bone mineral turnover (target Ra-223) and tumour in bone marrow
- **Decision against Radium-223 therapy,** instead experimental $^{177}$Lu-PSMA therapy

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How does PSMA-PET compare to conventional imaging?

Value of $^{68}$Ga-PSMA HBED-CC PET for the Assessment of Lymph Node Metastases in Prostate Cancer Patients with

<table>
<thead>
<tr>
<th>Results</th>
<th>Positive</th>
<th>Negative</th>
<th>Diagnostic accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology: LNM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{68}$Ga-PSMA HBED-CC PET rating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>53</td>
<td>3</td>
<td>PPV, 94.6%</td>
</tr>
<tr>
<td>Negative</td>
<td>15</td>
<td>108</td>
<td>NPV, 87.8%</td>
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<tr>
<td>Total</td>
<td>68</td>
<td>111</td>
<td>179</td>
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<tr>
<td>Sensitivity, 77.9%</td>
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<td></td>
<td>Accuracy, 89.9%</td>
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<tr>
<td>Morphologic rating (CT/MR)</td>
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<tr>
<td>Positive</td>
<td>18</td>
<td>1</td>
<td>PPV, 94.7%</td>
</tr>
<tr>
<td>Negative</td>
<td>49</td>
<td>110</td>
<td>NPV, 69.2%</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>111</td>
<td>178</td>
</tr>
<tr>
<td>Sensitivity, 26.9%</td>
<td></td>
<td></td>
<td>Accuracy, 71.9%</td>
</tr>
</tbody>
</table>

$\rightarrow$ PSMA-PET significantly outperforms morphologic CT and MRI concerning lymph node metastases.
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Why should PSMA-PET/MRI be better than PET/CT?
Why should PSMA-PET/MRI be better than PET/CT?
Comparison of hybrid $^{68}$Ga-PSMA PET/MRI and $^{68}$Ga-PSMA PET/CT in the evaluation of lymph node and bone metastases of prostate cancer

Martin T. Freitag¹ · Jan P. Radtke¹ ² · Boris A. Hadaschik² · A. Kopp-Schneider³ · Matthias Eder⁴ · Klaus Kopka⁴ · Uwe Haberkorn⁵ ⁶ · Matthias Roethke¹ · Heinz-Peter Schlemmer¹ · Ali Afshar-Oromieh⁵

Fig. 5 Patient with recurrence of prostate cancer presenting with focal PSMA-positive uptake in the left tuber ischiadicum (rectangle in a, a–c). There is no morphological correlate on the CT images (a, b) probably because the metastasis has not yet sclerized to an osteoplastic pattern. Each of the MRI sequences used shows the metastasis from a different point of view and provides different contrasts that increase the certainty of the radiologist. In this example, all of the MRI sequences used give a definite morphological correlate: d T2-w fat-saturated (fluid and oedema), e T1-w native (infiltration of fatty bone marrow), f T1-w contrast-enhanced (neoangiogenesis), and h DWI and i ADC (cellularity). The diagnostic PET information provided in e and g is equal.
Conclusion

- PSMA-PET significantly outperforms conventional imaging in primary staging and biochemical recurrence of prostate cancer.

- PET/MRI is superior to mpMRI or PSMA-PET alone in imaging of primary prostate cancer.

- PSMA-PET/MRI might be superior to PSMA-PET/CT in biochemical recurrence of PCA.
Introduction into PSMA-ligand PET

Comparison of PSMA-PET/CT and PET/MRI

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PSMA negative PCA – Clinical examples

- Primary Staging of Pat with bone metastases of PCA.
Clinical examples – Heterogeneity of PSMA expression
Clinical examples – PSMA negative metastases
Clinical examples – PSMA negative PCA

7 out of 43 patients (16%) excluded due to low or lacking PSMA expression of PCA lesions

(A) Patient has extensive osseous/marrow and hepatic metastatic disease with low uptake (SUVmax 5). (B) Patient has high PSMA uptake in osseous disease but a site of anterior mediastinal nodal disease with high FDG but absent PSMA uptake.
PSMA negative PCA – Histologic studies

- **Bostwick et al. 1998**: In a study comprising 184 primary prostate-adenocarcinomas PSMA was overexpression by 80% of cancer cells on average.

- **Silver et al. 1997**: PSMA overexpression was found in only 8 out of 18 bone metastases.

- **Mannweiler et al 2009**: No correlation between PSMA positivity of the primary tumor and its metastases.

- **Gorges et al. 2016**: Heterogeneity of PSMA expression demonstrated for circulating tumor cells of prostate cancer
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Additive value of DWI in PSMA-PET/MRI of recurrent prostate cancer

43 patients with biochemical recurrence of prostate cancer
Without previous systemic treatment
examined with PET/MRI

First reading
All lesions suspicious for either bone or lymph node metastases in PSMA and DWI noted

Second reading
Growth tendency of all lesions exclusively detected on DWI evaluated.

PSMA negative but DWI positive lesion with growth tendency
= PSMA negative metastasis
Detection of PSMA negative lymph node metastases with DW-MRI

A) B800 DWI image with focus of high signal intensity
B) Low signal intensity focus on ADC map in corresponding locations
C) T1fs GD depicts a lymph node of 8 x 10 mm size
D) No significant uptake in PSMA Pet.
E) Previous MRI imaging 24 weeks earlier. The lymph node only measured 5 x 8 mm.

+17% more Lymph nodes
Why do we think PET/MRI could detect PSMA negative metastases?
Detection of PSMA-negative bone metastases utilizing DWI?
Thank you for your attention!
How does PSMA-PET compare to conventional imaging?

Benefit of $^{68}$Ga-PSMA-PET/CT in Patients Considered for 223Ra-Dichloride Therapy
Axel Bode, Kambiz Rahbar, Julia Konnert, Martin Bögemann, and Lars Stegger
High detection rates even with low PSA values