PSMA Ligand PET/MRI for Primary Prostate Cancer: Staging Performance and Clinical Impact

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Abstract

Purpose: Primary staging of prostate cancer relies on modalities, which are limited. We evaluate simultaneous [68Ga]Ga-PSMA-11 PET (PSMA-PET) as a new diagnostic method for primary tumor–node–metastasis staging compared with histology and its impact on therapeutic decisions.

Experimental Design: We investigated 122 patients with PSMA-PET/MRI prior to planned radical prostatectomy (RP). Primary endpoint was the accuracy of PSMA-PET/MRI in tumor staging as compared with staging-relevant histology. In addition, a multidisciplinary team reassessed the initial therapeutic approach to evaluate its impact on the therapeutic management.

Results: PSMA-PET/MRI correctly identified prostate cancer in 119 of 122 patients (97.5%). Eighty-one patients were treated with RP and pelvic lymphadenectomy. The accuracy for T staging was 82.5% [95% confidence interval (CI), 73–90; P < 0.001], for T2 stage was 85% (95% CI, 71–94; P < 0.001), for T3a stage was 79% (95% CI, 43–85; P < 0.001), for T3b stage was 94% (95% CI, 73–100; P < 0.001), and for N1 stage was 93% (95% CI, 84–98; P < 0.001). PSMA-PET/MRI changed the therapeutic strategy in 28.7% of the patients with either the onset of systemic therapy/radiotherapy (n = 16) or active surveillance (n = 19).

Conclusions: PSMA-PET/MRI can provide an accurate staging of newly diagnosed prostate cancer. In addition, treatment strategies were changed in almost a third of the patients due to the information of this hybrid imaging technique. Clin Cancer Res; 24(24); 6300–7. ©2018 AACR.

Introduction

Current staging for intermediate- and high-risk prostate cancer includes cross-sectional abdominopelvic imaging with CT or MRI and a bone scintigraphy to rule out metastatic spread (1). In predominantly Gleason pattern 4 prostate cancer, the use of multiparametric MRI can also be used to improve local staging with regard to a nerve sparing surgery (2–4). Multiparametric (mp) MRI has recently confirmed its role in tumor detection and guiding prostate biopsies (5, 6).

Nevertheless, exact local and whole-body staging in a single investigation remains a challenge with standard imaging techniques (7). The clinical value of [18F]fluorodeoxyglucose-PET in local staging is limited due to its reduced sensitivity in primary disease (8), and choline-based PET shows a low local specificity for the differentiation between benign prostatic hyperplasia (BPH) and malignant tissue (9, 10). Nevertheless, this issue might be addressed by the use of combined PET/CT (12) or active surveillance (11) as it was also demonstrated with [18F]fluoroethylcholine in a prospective clinical trial (12). Also other unspecific metabolic radiopharmaceuticals such as [11C]acetate seem to profit by a combined approach with PET/CT and MRI (13, 14).

Unfortunately, the sensitivity of choline-based PET for lymph node staging, in a prospective trial, was 8.2% in a region-based and 18.9% in a patient-based analysis (15), which is too low to be of clinical interest.

But accurate and reliable tumor–node–metastasis (TNM) staging, preferably in a single investigation, is mandatory for surgical planning, disease management, and patient counseling. The aim of a radical prostatectomy (RP) is curative while preserving continence and, whenever possible, potency (16).
In a prospective diagnostic study of 122 patients, $^{68}$Ga-PSMA-11 (PSMA)-PET/MRI demonstrated high staging performance. The treatment was changed accordingly in almost a third of the patients. Whole-body staging with PSMA-PET/MRI can noninvasively provide important information for therapeutic strategies and enables a more personalized concept.

**Materials and Methods**

**Patients and study design**

The investigations were done in the scope of a prospective diagnostic study (clinicaltrials.gov NCT02659527) in 122 patients with biopsy-proven prostate cancer. They were conducted in accordance with the Helsinki Declaration and national regulations. The study was approved by the local Ethics Committee and the national drug authorities. The presented data are reported according to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) criteria (26). Inclusion criteria were biopsy-proven carcinoma of the prostate and scheduled RP. Exclusion criteria were antiandrogen therapy, patient not eligible for 3T MRI, prostate needle biopsy <21 days before PET/mpMRI, known active secondary cancer, endorectal coil not applicable (e.g., anus praetor with short rectal stump), known anaphylaxis against gadolinium-based contrast media, patient’s written informed consent not given, and prostatectomy compound not available for detailed histology (in case of RP).

The presented patient cohort was recruited from April 2014 until July 2017. All patients gave written informed consent and were scheduled for RP. All patients in the high-risk group were additionally staged with bone scintigraphy ≤27 according to the guideline’s recommendations (refs. 1, 2; n = 49, 40.2%), whereas in all other patients, a blinded analysis of the whole-body MRI only data served as cross-sectional imaging reference (n = 73, 59.8%; more details in the Supplementary Section).

**Imaging protocol and analyses**

Imaging was performed on an integrated PET/MRI system (biograph mMR, Siemens Healthineers) with a 3T MRI system. The MRI protocol was performed as multiparametric protocol in accordance with international guidelines. The local PET/mpMRI was followed by a whole-body scan from skull base to upper thigh. All images were interpreted by two experts in hybrid imaging (M. Hartenbach, nuclear medicine; P. Balthes, radiology). The detailed imaging protocol is presented in the Supplementary Methods Section. All MR images were assessed according to the Prostate Imaging Reporting and Data System (PI-RADS) criteria, but according to the protocol, every focal PSMA uptake in the prostate was considered malignant irrespective of the PI-RADS score. For an exact correlation of the main tumor focus between imaging and histology, an identical angulation of the histologic step sections and the MRI slices was assured by initial perpendicularly orientation of the axial MRI sequences to the Denonvillier fascia. Note that 3 mm slicing in histology was assured using a custom-made mounting system. For detection, the PSMA-PET/MRI tumor focus had to match the shape of histology >50%. For local T staging, the position of PET/MRI-suspected extraprostatic spread had to match the position in histology. For T3a staging, T2w MRI assessment of organ edges in the area of the PSMA-positive tumor lesion was the leading modality. For T3b staging, a PSMA focus had to be present in parts of the seminal vesicles.

Every focal uptake, equal or higher than the liver background (27), in locoregional or distant lymph nodes as well as in the bone was considered to be malignant disregarding morphologic criteria. Bilateral pelvic lymphadenectomy up to the iliacal bifurcation was the standard of reference for N staging. Positive lymph nodes in histology were correlated region based according to the surgeon’s description and size in histology with the PET/MRI findings. Focal uptake in visceral organs with corresponding lesion in MRI was considered positive according to the protocol. Nevertheless, that was not the case in the presented cohort.

All results were reported electronically (SAP©), approved, and blocked by the system to “read only” before the initiation of any kind of therapy.

**PET/MRI-adjusted treatment algorithm**

After PSMA-PET/mpMRI and guideline-recommended staging, every case was discussed in the interdisciplinary tumor board, which consisted of experts in urology/uro-oncology, pathology, nuclear medicine, radiology, and radiation oncology. Extralocoregional findings in PSMA-PET/mpMRI were confirmed by biopsies in case they were relevant for TNM staging and treatment decisions. According to the study protocol, in case patients presented with two or more distant metastases, a biopsy was performed in only one of the staging relevant lesions, because a further biopsy in the same patient would not affect the treatment strategy. Patients in the low- or favorable intermediate-risk group (according to the AUA/ASTRO/SUO Guideline; ref. 1), negative staging for metastases, and low/no detectable tumor volume (<0.5 cm) in PSMA-PET/mpMRI were offered to reconsider active surveillance instead of their decision for RP. Patients in the intermediate- or high-risk group with local T2 or T3 stage with or without positive pelvic lymph nodes (N0+N1) in PSMA-PET/mpMRI were referred for RP with extended pelvic lymphadenectomy. Patients with a local T4 stage confirmed by cystoscopy with biopsy regardless of local N stage were referred for RT with androgen deprivation therapy (ADT). In patients with distant lymph nodes (M1a) or bone metastases (M1b), a chemohormonal therapy was initialized. Visceral metastases (M1c) were not detected in our cohort. Within our cohort, all the intended therapeutic changes according to our tumor board have been
really implemented in treating the patients. All surgical specimens were processed according to the institution’s standard pathologic procedures (see Supplementary Methods) in whole mount sections. Tumor lesions were delineated by all three pathologists (M. Susani, P. Mazal, S. Hartenbach). Consensus delineation was then provided by one pathologist (S. Hartenbach). Staging and grading were performed according to the UICC TNM classification and WHO/ISUP 2005 system, respectively (28).

Statistical analysis
To assess the diagnostic accuracy of PSMA-PET/mpMRI in clinical staging, contingency tables with the histopathologic finding as standard of reference were used. Statistical significance was calculated according to the Fisher exact or χ² test where appropriate.

ROC analysis was performed, and the AUCs were calculated. Statistical significance was considered at P < 0.05. All tests were two-sided. Statistical analyses were performed using R v.14.1 (R Corporation).

Results
Positivity rate and local T staging
Patient characteristics before and after RP are summarized in Supplementary Table S1 and Table 1. Of all the 122 patients referred for staging before planned RP, 119 patients had a PSMA-positive local finding in PSMA-PET/mpMRI, representing an overall positivity rate of 97.5%. Eighty patients were available for PSMA-PET/mpMRI local T-stage analysis (Fig. 1). All of these patients had a local positive PSMA-PET/mpMRI. The accuracy for the detection of the different T stages was 82.5% [95% confidence interval (CI), 73–90]. PSMA-PET/mpMRI correctly detected organ-confined disease with 85% accuracy [35/41 patients, sensitivity 85.4%, specificity 84.6%, positive predictive value (PPV) 85.4%, negative predictive value (NPV) 84.6%; 95% CI, 71–94], extraprostatic tumor spread with 79% accuracy (14/21 patients, sensitivity 66.7%, specificity 91.5%, PPV 73.4%, NPV 88.5%; 95% CI, 43–85), and invasion of seminal vesicles with 94% accuracy (17/18 patients, sensitivity 94.4%, specificity 95.2%, PPV 84.2%, NPV 98.4%; 95% CI, 73–100; Table 2).

Lymph node staging
RP was performed together with pelvic-extended lymphadenectomy in 80 (65.6%) patients. In 11 (13.8%) patients, positive lymph nodes were diagnosed in the preoperatively performed PSMA-PET/mpMRI. Histopathology revealed negative lymph nodes in 64 (80%) patients, whereas in 16 (20%) patients, positive lymph nodes could be found. A patient-based analysis for prediction of the lymph node status with PSMA-PET/mpMRI assessed an accuracy of 93% (95% CI, 84–98). Sensitivity, specificity, PPV, and NPV were calculated with 68.8%, 100%, 100%, and 91.7%. The AUC for the prediction of lymph node metastasis detected by PSMA-PET/mpMRI was 0.84. A region-based analysis for lymph node staging was not performed. All the 5 patients with lymph node metastases on histopathology and a negative preoperative PSMA-PET/mpMRI for lymph node staging each had only one lymph node metastasis smaller than 4 mm [measured on histologic hematoxylin and eosin (H&E) sections]. The median size of the 11 PSMA-PET/mpMRI-positive lymph node metastases with pathologic confirmation was 8 mm.

Impact on further treatment decisions
Only 81 of 122 patients (66.4%) still underwent surgery after guideline-recommended staging, PSMA-PET/mpMRI, and case discussion in our tumor board (Fig. 1). One patient chose to undergo surgery abroad without providing detailed information on histology, leaving 80 patients for the PSMA-PET/mpMRI staging analysis. In 41 (33.6%) patients, treatment was modified after imaging (Fig. 1). Six of these patients had positive findings on both, conventional guideline-recommended imaging and PSMA-PET/mpMRI. In 35 (85.4%) of these 41 patients, the change in treatment was done because of the exclusive information of PSMA-PET/mpMRI, which represents 28.7% of the total cohort. Fifteen lesions in 14 patients were biopsied, relevant for M1a and/or M1b staging. Extraprostatic lesions without PSMA ligand uptake, suspicious for metastases on mpMRI, did not occur in our cohort. Supplementary Table S2 provides the biopsy and staging characteristics of the 41 patients, in whom the therapeutic management changed. Fourteen (11.5%) patients underwent a primary chemohormonal therapy due to positive distant lymph nodes or the detection of distant metastases (e.g., Fig. 2; of which 5 also got a palliative transurethral resection of the prostate due to obstructive symptoms). 8 (6.5%) patients were referred to primary RT in combination with ADT due to local T4 tumors (confirmed by cystoscopic biopsy), and 19 (15.6%) patients underwent active surveillance due to minimal or no detectable tumor burden in the imaging and initially low or favorable intermediate-risk clinical features (1), with 16 follow-up patients

Table 1. Clinicopathologic features of 80 patients after definitive treatment with RP

| Age at RPE (years), median (IQR) | 64 (59–77) |
| PSA at RPE (ng/mL), median (IQR) | 7.63 (5.5–13.4) |
| Pathologic T staging after RP, n (%) |  |
| 2 | 41 (51.2) |
| 3a | 21 (26.3) |
| 3b | 18 (22.5) |
| Positive lymph nodes in histopathology, n (%) | 16 (20) |
| Lymph nodes removed, median (IQR) | 11 (7–16) |
| Positive lymph nodes, n (%) |  |
| 1 | 9 (11.2) |
| 2 | 2 (2.5) |
| 3 | 3 (3.8) |
| 6 | 1 (1.2) |
| 12 | 1 (1.2) |
| Site of positive lymph nodes after RP, n (%) |  |
| Bilateral iliac | 4 (5.0) |
| Left external iliac | 1 (1.2) |
| Left obturator | 3 (3.8) |
| Left pelvis | 2 (2.5) |
| Right iliac | 1 (1.2) |
| Right obturator | 4 (5.0) |
| Not available | 1 (1.2) |
| Positive surgical margins, n (%) | 24 (30) |
| Primary Gleason pattern at RP, n (%) |  |
| 3 | 34 (42.5) |
| 4 | 43 (53.8) |
| 5 | 3 (3.8) |
| Secondary Gleason pattern at RP, n (%) |  |
| 3 | 25 (28.7) |
| 4 | 43 (53.8) |
| 5 | 14 (17.5) |
| Total Gleason score at RP, n (%) |  |
| 6 | 6 (7.5) |
| 7 | 44 (55.0) |
| ≥8 | 30 (37.5) |

Abbreviation: IQR, interquartile range.
still not having primary treatment until July 2018 (follow-up data of the remaining 3 patients were not available).

Discussion

Accurate detection of the tumor location and the local T stage as well as the lymph node and whole-body status is mandatory for patients with biopsy-proven primary prostate cancer before initiation of any kind of therapy or surveillance (29). Unfortunately, with the current guideline-recommended imaging modalities, the exact TNM status is not reliable enough (1, 3–5, 7, 8). In this context, PSMA-PET/CT and PSMA-PET/mpMRI have emerged as a promising imaging technique, as it has already been proven in retrospective studies to be superior in local and distant tumor detection than any other kind of cross-sectional imaging (17–19, 21–25). This prospective clinical trial now evaluates the diagnostic performance of PSMA-PET/mpMRI concerning local and whole-body staging in patients with biopsy-proven prostate cancer. In addition, we elaborated the therapeutic impact of the PSMA-PET/mpMRI in patients before scheduled RP.

Local T staging

We could prospectively confirm that PSMA-PET/mpMRI outperformed all the currently reported guideline-approved imaging modalities for local detection of biopsy-proven primary prostate cancer with an overall positivity rate of 97.5%. As the aim of this study was not the correlation of each lesion in the prostate between the applied methods but rather the local and whole-body staging in primary prostate cancer patients, we simplified the detection approach in this evaluation to the main PSMA-expressing lesion in the prostate. In addition, there is evidence that PSMA expression is a relevant factor for tumor aggressiveness (30). This is supported by a subanalysis of our data, showing significant differences between postoperative low/intermediate-risk patients and high-risk patients concerning PSMA-PET SUVmax taken out of the main intraprostatic tumor region. In this context, cellular density measured via MRI ADCmean values out of the same regions was also able to detect significant differences, but at a lower level of significance (see Supplementary Results; Supplementary Fig. S1 and S2). A retrospective study by Eiber and colleagues (17) revealed a similar overall local tumor localization with PSMA-PET/mpMRI in 98% of the cases. Focusing on local T staging, another retrospective study for primary disease, despite using PET/CT, showed an accuracy of 86% for the detection of seminal vesicle invasion and 71% accuracy for the detection of extraprostatic tumor spread (19). For mpMRI, de Rooij and colleagues (3) could show acceptable rates for the detection of extraprostatic extension (sensitivity 57%, specificity 91%), seminal vesicle invasion (sensitivity 58%, specificity 96%), and overall T3 detection (sensitivity 61%, specificity 88%) in a meta-analysis. Our data are superior in this context with accuracy rates for predicting T2 stage, T3a stage, and T3b stage of 85% (sensitivity 85.4%, specificity 84.6%), 79% (sensitivity 66.7%, specificity 91.5%), and 94% (sensitivity 94.4%, specificity 95.2%), respectively. This especially relies on the sensitivity of PSMA for the T3b stage using integrated methods as has already been demonstrated in a retrospective PET/CT study (19). Therefore, particularly in nonextensively organ exceeding tumors in the prostate base and seminal vesicles as well as in the area of the bladder neck, an exact alignment is needed. This might only be achieved by a simultaneous acquisition of both modalities in the same patient position.

The use of an endorectal coil at 3T demonstrates comparable results for T3a staging in our cohort (3) but enables exact alignment to whole mount histomorphology due to the very high-resolution T2w multiplanar images (Fig. 3). Although there are data available supporting the use of an endorectal coil at 3T mpMRI (31), one has to discuss its applicability especially in a PET/mpMRI system for a future routine clinical use due to costs and patient comfort.
Primary lymph node staging
We could prospectively confirm the so far published data regarding the detection of lymph node metastases in primary staging before surgery. The sensitivity in retrospective studies ranged from 33% to 84% (18, 21, 25). The only prospective evaluation so far showed a sensitivity of 64% with a specificity of 95% for the prediction of lymph node metastases (23). We could demonstrate similar detection efficacies with a sensitivity of 68.8%, a specificity of 100%, and an accuracy of 93% (AUC 0.84) and therefore, especially with focus on the PPV of 100%, confirmed an important future role of PSMA-PET/mpMRI for lymph node staging in patients with primary prostate cancer. As in our cohort, patients staged N0 in PSMA-PET/mpMRI despite having pN1 status after surgery, presenting only one lymph node smaller than 4 mm each, low metastatic occupation of lymph nodes however seems to remain undetectable.

Change in therapeutic management
mpMRI already demonstrates potential for local risk stratification, alteration of surgical approaches, and guiding active surveillance (4). Nevertheless, whole-body staging with mpMRI only is limited as mentioned above. We found that PSMA-PET/mpMRI, which provides exact modalities for local and whole-body staging, changed clinical treatment decisions in a significant number of patients initially scheduled for RP. Specifically, we could show that in 33.6% of the patients, a treatment modification occurred due to imaging information, and in 28.7%, the treatment modification resulted due to PSMA-PET/mpMRI information only. On the one hand, this was due to the high sensitivity of the PSMA-PET for small distant metastatic spread that is not fulfilling any morphologic criteria of malignancy (example Fig. 2) and/or demonstrates significant uptake in bone scintigraphy.

These patients underwent either chemohormonal therapy or RT due to the detection of distant metastasis, or a local unresectable stage. On the other hand, patients without PSMA-PET-positive findings outside the prostate and also only minimal or no local detectable tumor burden in the imaging (Fig. 4) were counseled to reconsider active surveillance instead of initially preferred prostatectomy by the patient. These 19 patients in our study all presented low- or favorable intermediate-risk clinical features. Remarkably, all 19 patients changed back to active surveillance with the knowledge of the PSMA-PET/mpMRI result with 16 follow-up patients still not having primary treatment until July 2018. This subgroup is of special interest as it is known that a significant number of patients do not want to choose or stay in an active surveillance strategy for several reasons like the anxiety for having or developing metastatic disease (32, 33). Increasing the...
security of not having significant cancer in case of a negative PSMA-PET/mpMRI scan supports clinicians as well as patients and could therefore reduce the costs of potential overtreatment. Nevertheless, a cost-effectiveness analysis was not part of this study and therefore has to be addressed in a dedicated evaluation in this patient group.

Limitations

Our study is limited by the number of patients available for the staging evaluation due to the treatment changes initiated by the information of the PSMA-PET/mpMRI results. The single-center approach precludes robust estimates of reproducibility and repeatability of the method. Nevertheless, our detection results

Figure 3.

A 55-year-old patient with a biopsy-confirmed Gleason 3+4 = 7 adenocarcinoma of the prostate in 6 of 12 cores. PSMA ligand-PET/mpMRI demonstrates a larger tumor in the left lobe with significant PSMA expression (A), hypointense signal on T2-weighted images (B), significant diffusion restriction on ADC (C) and DWI (D), as well as positive Ktrans (E) in parts of the tumor. The patient was staged cN0M0 and underwent RP with suspected T3a stage (red arrows). Histologic whole mount H&E sections confirmed the prostate carcinoma (F), but with predominant Gleason pattern 4 (red delineations) including an area of Gleason pattern 5 (black delineations). International Society of Urological Pathology (ISUP) classification increased from biopsy subgroup 2 to postsurgery subgroup 5. pT3a stage was confirmed on the left organ edge (further color code histology: green = benign prostatic hyperplasia; light blue = low-grade prostatic intraepithelial neoplasia; and dark blue = high-grade prostatic intraepithelial neoplasia).

Figure 4.

A 75-year-old patient with a biopsy-proven Gleason 3+4 = 7 prostate adenocarcinoma in 5 of 24 cores but a PSA level of 32 ng/mL. PSMA ligand-PET/mpMRI demonstrates a PSMA-expressing tumor in the left apex (A) in a T2w faintly hypointense lesion (B) with a diameter of approximately 5 mm. Significant diffusion restriction is shown on ADC (C) and DWI (D) with a focus of increased Ktrans on DCE (E). Representative needle biopsies illustrate the predominant Gleason 3 pattern (F, red arrow) and the second common pattern 4 (G, black arrow). PSMA-PET/MRI whole-body staging was cN0M0. The patient chose active surveillance instead of RP as proposed by the interdisciplinary tumor board after PSMA-PET/MRI. MRI-derived prostate volume was 110 mL, which might be one explanation for the higher PSA level.
of primary prostate cancer and primary lymph node metastases are comparable with previously published retrospective results. A further limitation is the biased detection rate of primary prostate cancer due to the previously positive needle biopsy result. The cohort was also already scheduled for RP so that it does not represent a normally distributed cohort of primary prostate cancer patients. Therefore, the results have to be seen in the context of this patient population, which nevertheless represents a larger group in daily clinical routine. We also simplified the tumor detection approach in this prebiased patient cohort to the detection of increased focal 68Ga-PSMA 11 uptake in the prostate. A lesion-based analysis of all histologically detected tumor and non-tumor lesions in RP specimens according to PI-RADS v2 ± PSMA-PET is part of a separate “stand alone” analysis as the presented evaluation is focused on staging and clinical impact. However, with the limitation of a biopsy-proven tumor cohort, PSMA positivity provides already a high detection rate of the main tumor focus. A blinded T staging between PET/mpMRI and mpMRI alone was not part of the study protocol. Nevertheless, referring to the literature for local staging of larger mpMRI-only cohorts might be more suitable in this regard due to possible interobserver biases in our comparatively smaller cohort. A region-based analysis of the lymph node staging performance was also not planned in the protocol due to logistic reasons. In addition, the number of positive lymph nodes after surgery was small. Due to ethical reasons, it was only allowed to gain biopsy confirmation of staging-relevant, PSMA-positive metastases. So we are not able to report confirmed data of all PSMA-positive lesions. But applying the described definition of focal PSMA uptake, we did not discover any false positive findings in our cohort. Anyhow, for a future whole-body staging approach with PSMA-PET/mpMRI in a biopsy-proven cohort, the mpMRI whole-body protocol might be improvable to provide confirmatory information for PSMA-positive lesions (e.g., WB DWI) substituting some local mpMRI sequences. PSMA-PET/mpMRI still has limited access worldwide, but prospective trials as ours are ongoing, ultimately leading to the approval of this outperforming radiopharmaceutical, and might enable a broad distribution of this highly sensitive and predictive method.

Conclusions

This study prospectively demonstrated that simultaneous PSMA-PET/mpMRI provides a reliable TNM staging in patients with primary prostate cancer. This resulted in a direct clinical impact regarding a change in the therapeutic management for almost one third of the patients.

Disclosure of Potential Conflicts of Interest

W. Wadsak reports receiving commercial research grants from BSM Diagnostica GmbH. J. Babich has ownership interests (including patents) at Noona Therapeutics Inc. M. Hacker reports receiving speakers bureau honoraria from Bayer Schering Pharma, GE Healthcare, Siemens Healthineers, and reports receiving commercial research grants from Bayer Schering Pharma, Eckert & Ziegel Radiopharma, Ipsen, ITG, GE Healthcare and Siemens Healthineers. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The funding organizations had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data; preparation, review, or approval of the article; and decision to submit the article for publication.

Authors’ Contributions


Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): B. Grubmüller, G.M. Goldner, W. Wadsak, S. Pfaff, M. Mitterhauser, T. Balber, M. Grahovac, J. Babich, M. Susani, P. Mazal, L. Kenner, S.F. Shariat, M. Hacker, M. Hartenbach

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Other (supervision and organization of radiotracer preparation): W. Wadsak, M. Mitterhauser

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