

**PET/MRI versus PET/CT in whole-body staging: results from a unicenter observational study in 1003 subsequent examinations**

**Running title: PET/MRI versus PET/CT in oncology**

Ole Martin<sup>1</sup> and Benedikt M. Schaarschmidt<sup>2\*</sup>, Julian Kirchner<sup>1</sup>, Saravanabavaan Suntharalingam<sup>2</sup>, Johannes Grueneisen<sup>2</sup>, Aydin Demircioglu<sup>2</sup>, Philipp Heusch<sup>1</sup>, Harald H. Quick<sup>3,4</sup>, Michael Forsting<sup>2</sup>, Gerald Antoch<sup>1</sup>, Ken Herrmann<sup>5</sup> and Lale Umutlu<sup>2\*</sup>

1: Department of Diagnostic and Interventional Radiology, University Dusseldorf, Medical Faculty, D-40225 Dusseldorf, Germany

2: Department of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, University of Duisburg-Essen, D-45147 Essen, Germany

3: Erwin L. Hahn Institute for Magnetic Resonance Imaging, University of Duisburg-Essen, D-45141 Essen, Germany

4: High-Field and Hybrid MR Imaging, University Hospital Essen, University of Duisburg-Essen, D-45147 Essen, Germany.

5: Department of Nuclear Medicine, University Hospital Essen, University of Duisburg-Essen, D-45147 Essen, Germany.

\*Both First Authors contributed equally to this work.

**Corresponding Author**

Ole Martin

Resident

University Dusseldorf, Medical Faculty

Department of Diagnostic and Interventional Radiology

Moorenstr. 5, D-40225 Dusseldorf, Germany

Email: Ole.Martin@med.uni-duesseldorf.de

Telefon: +49 211 81 17754

Telefax: +49 211 81 16145

### **Conflict of interest**

All other authors declare that no potential conflicts of interest relevant to this article exist.

### **Word count**

Abstract: words

Manuscript: words

## **Abstract**

### *Purpose*

To investigate differences between positron emission tomography/magnetic resonance imaging (PET/MRI) and PET/computed tomography (PET/CT) in lesion detection and classification in oncological whole-body examinations and to investigate radiation exposure differences between both modalities.

### *Material and methods*

In this observational single-center, study 1003 oncological examinations (918 patients, mean age  $57.8 \pm 14.4$  y) were included. Patients underwent PET/CT and subsequent PET/MRI ( $149.8 \pm 49.7$  min after tracer administration). Examinations were reviewed by radiologists and nuclear medicine physicians in consensus. Additional findings, characterization of indeterminate findings in PETCT, missed findings in PET/MRI including their clinical relevance and effective dose of both modalities were investigated. McNemar's test was used to compare lesion detection between both hybrid imaging modalities ( $p < 0.001$  indicating statistical significance).

### *Results*

Additional information in PET/MRI was reported in 26.3% (264/1003) of examinations compared to PET/CT ( $p < 0.001$ ). Of these, additional malignant findings were detected in 5.3% (53/1003), leading to a change in TNM-staging in 2.9% (29/1003) due to PET/MRI. Definite lesion classification of indeterminate PET/CT findings was possible in 11.1% (111/1003) with PET/MRI. In 2.9% (29/1003), lesions detected in

PET/CT were not visible in PET/MRI. Malignant lesions were missed in 1.2% (12/1003) by PET/MRI leading to a change in TNM-staging in 0.5% (5/1003). The estimated mean effective-dose for whole-body PET/CT amounted to  $17.6 \pm 8.7$  mSv in comparison to  $3.6 \pm 1.4$  mSv in PET/MRI, resulting in a potential dose reduction of 79.6% ( $p < 0.001$ ).

### *Conclusion*

PET/MRI facilitates comparable staging to PET/CT and improved lesion detectability in selected cancers, potentially helping to promote fast, efficient local and whole-body staging in one-step, when additional MRI is recommended. Furthermore, younger patients may benefit from the reduced radiation exposure in PET/MRI.

### **Keywords:**

simultaneous PET/MRI; oncological imaging; lesion detection; PET/CT

## Introduction

Cancer remains one of the leading causes of death worldwide [1]. While morphological imaging techniques to detect and monitor malignant diseases have advanced over the last decades, limitations in their diagnostic accuracy remain. Functional imaging, such as positron emission tomography (PET) has improved the sensitivity and specificity in detecting malignant disease [2, 3]. PET/CT combines high-resolution morphological imaging with the sensitivity of PET, thus improving staging accuracy, optimizing therapy strategies and improving patient outcome [4-7]. Therefore, PET/CT has become a diagnostic cornerstone in various oncological guidelines, most notably in lung cancer and lymphoma [8, 9]. Two disadvantages of PET/CT comprise its low soft-tissue contrast and the additional radiation exposure to the radiopharmaceutical related to the CT component, necessary for morphological correlation and attenuation correction. Both of these disadvantages may be overcome by exchanging the CT as the corresponding partner in hybrid imaging with MRI. Hence, the development of integrated PET/MRI scanners has been a long-term goal of researchers around the world. Despite technical challenges, the three major benefits of this new modality have been postulated:

- MRI-related high soft-tissue contrast
- combination of functional and morphological imaging
- reduction of radiation exposure compared to PET/CT [10-13].

Initial studies investigating the potential advantages of PET/MRI over PET/CT revealed promising results: PET/MRI leads to a markedly reduced radiation exposure [14, 15] and facilitates a high diagnostic performance various oncological diseases such as neuroendocrine tumors [16, 17], prostate cancer [18], gynecological tumors [19, 20], breast cancer [21-23] and lymphoma [14, 20]. However, in head and neck

[24, 25] and lung cancer [26-28], an obvious advantage of PET/MRI has not been demonstrated. Still, these results have to be considered as preliminary, as most studies are based on small patient cohorts (max. 100-150 patients). Furthermore, data pooling is difficult due to heterogeneous study endpoints [29]. Due to the higher operational costs and the technical challenges of PET/MRI, this lack of high quality data hinders a widespread introduction into clinical practice.

Therefore, the aim of this observational single-center study is to evaluate differences of PET/MRI in comparison to PET/CT for the detection and classification of lesions in different oncological diseases.

## **Material and methods**

### **Patients**

**This observational study** was funded by the German Research Foundation (“MR-PET for medical imaging“, grant number AN 397/3-1). The study followed institutional guidelines and was approved by the ethics committee of the Medical Faculty of the University of Duisburg-Essen. Written informed consent was obtained from all patients prior to the examination.

Inclusion criteria were clinically indicated oncological whole-body PET/CT and subsequent whole-body PET/MRI scans, both from skull base to mid-thighs. Exclusion criteria were contraindications to MRI (e.g. pacemakers) or to iodine or gadolinium based contrast media.

### **PET/CT Imaging**

All patients received an oncological, clinically indicated whole-body PET/CT scan from skull base to mid-thighs on a Biograph mCT (Siemens Healthcare GmbH, Forchheim, Germany). Tracers were chosen depending on the clinical indication: <sup>18</sup>F-Fluorodeoxyglucose (FDG) in 71.7% (719/1003, mean activity 258±50 MBq), <sup>68</sup>Gallium-PSMA in 13.2% (132/1003, mean activity 112±26 MBq), <sup>68</sup>Gallium-DOTATOC in 8.3% (83/1003, mean activity 66±16 MBq), <sup>124</sup>Iodine-Miodobenzylguanidine (MIBG) in 3.5% (35/1003, mean activity 47±9 MBq), <sup>124</sup>Iodine in 1.6% (17/1003, mean activity 32±8 MBq), <sup>18</sup>F-Choline in 1.4% (14/1003, mean activity 330±54 MBq) and <sup>18</sup>F-Fluoride in 0.3% (3/1003, mean activity 154±4 MBq). In <sup>18</sup>F-FDG examinations, blood glucose were ensured to be lower than 150 mg/dl.

In case of increased glucose levels, appropriate insulin medication was administered. Low-dose (n=187) and full-dose (n=816) PET/CT scans were performed with automated tube voltage selection (CareKV, preset 120 kV, slice thickness: 5 mm). Full-dose scans were performed with automated tube current modulation (CareDose 4D, preset 190 mAs) 70s after the injection of a weight-dependent dose of contrast agent (Ultravist, Bayer Pharma AG, Berlin, Germany). For low-dose scans, a CareDose 4D preset of 40 mAs was chosen.

PET-data were acquired in up to 7 bed positions (2 min per bed position). Attenuation corrected PET images were reconstructed using a portal venous phase in full-dose scans and low-dose CT-data in low-dose scans. PET-images were reconstructed using an ordered subset expectation maximization (OSEM) algorithm with 4 iterations and 8 subsets. A Gaussian filter kernel with a full width at half maximum of 2 mm was used for post reconstruction filtering.

### **PET/MRI Imaging**

A subsequent whole-body PET/MRI scan was performed on a Biograph mMR (Siemens Healthcare AG, Erlangen, Germany) 149.8±49.7min after tracer injection. PET/MRI scans were obtained from skull base to mid-thighs. All patients in this study received contrast media with administration of macrocyclic gadolinium-based contrast agents for contrast-enhanced imaging (0.05 mmol/kg bodyweight of Gadoterate meglumine, Guerbet Sulzbach/Taunus, Germany or 0.1mmol/kg bodyweight Gadobutrol, Bayer Pharma AG, Berlin, Germany). For each bed position, the following MRI-sequences were performed:

1. For MRI-based attenuation correction, a coronal 3D DixonVIBE sequence.



2. A transverse T1-weighted sequence: until 2015, a T1-weighted fast low angle shot sequence (FLASH) after contrast administration with fat saturation (fs). Following a software update, a transverse T1-weighted volume interpolated breath-hold examination (VIBE) was used due to faster acquisition times and higher soft tissue contrast.
3. A transverse T2 half fourier acquired single shot turbo spin echo sequence (HASTE).
4. For diffusion weighted imaging (DWI), a transverse thoracic echo planar imaging (EPI) sequence with three b-values (0, 500, 1000) in free breathing

In whole-body imaging, only contrast-enhanced T1-weighted sequences were obtained. Depending on the clinical indication, additional high-resolution MRI sequences were acquired for the evaluation of local tumor extent (e.g. in prostate or breast cancer) or metastasis detection (e.g. for the liver in gastrointestinal tumors), where needed. Therefore, additional sequences like dynamic sequences of the liver were added.

PET-data were acquired in list mode without respiratory gating (up to 5 bed positions, 4 min per bed position). 3D-iterative image reconstruction was performed (3 iterations, 21 subsets, Gaussian filter of 4mm).

### **Image analysis and data evaluation**

All PET/CT and PET/MRI examinations were evaluated by board certified nuclear medicine physicians and board certified radiologists. In the PET/MRI report, the following findings were noted and analysed:

- additional findings by PET/MRI that were missed by PET/CT and their most probable diagnosis
- additional, but indeterminate findings in PET/MRI requiring additional examinations/follow-up
- classification of indeterminate findings in PET/CT by PET/MRI
- missed findings by PET/MRI in comparison to PET/CT

To evaluate the nature of these lesions (benign vs. malignant), clinical and histological reports, characteristic imaging findings in the subsequent PET/MRI examination as well as additional radiological examinations including follow-up examinations were used as reference of standard. According to the reference standard, changes in tumor staging by PET/MRI were analysed. Based on radiotracer activity, effective dose (ED) of the PET part of the examination was calculated using the whole-body ED coefficient recommended by Andersson et al. [30]. Using DICOM structured reports, ED due to the CT part of the PET/CT examination was estimated according to a method described by Christner et al. [31].

## **Statistics**

An explorative data analysis was performed for patient and examination characteristics. All additional findings by PET/MRI, findings that were considered as indeterminate in PET/CT requiring follow-up but could be further classified by PET/MRI, and missed findings by PET/MRI were analysed. Changes in TNM-Staging were evaluated. Differences in lesion detection were compared using McNemar's test. Estimated mean-effective doses were compared using paired t-test.  $p < 0.001$

indicated statistical significance. Statistical analysis was performed using SPSS Statistics 24 (IBM Corp., Chicago, IL, USA).

## Results

### Patient characteristics

Between March 2012 and June 2018, a total of 4949 PET/MRI examinations were performed in our institution in 4659 patients. 3946 examinations were excluded due to various reasons (Figure 1). Therefore, 1003 PET/MRI examinations in 918 patients (mean age  $57.8 \pm 14.4$  y, 400 female, 518 male) were eligible for analysis, resulting in 846 examinations for tumor staging and 157 examination for response assessment. The oncological indications were lung cancer (17.9%, 180/1003), gastrointestinal cancer and neuroendocrine tumors (17.2%, 173/1003), gynecologic and breast cancer (14.8%, 148/1003), prostate cancer (14.8%, 148/1003), lymphoma (12.0%, 120/1003), melanoma (8.7%, 87/1003), head and neck cancer (8.0%, 80/1003), cancer of unknown primary (CUP, 4.3%, 43/1003) and malignant bone disease (2.4%, 24/1003).

### Differences in lesion detection between PET/MRI and PET/CT

According to McNemar's test, significantly more lesions were detected by PET/MRI in comparison to PET/CT ( $p < 0.001$ ). In 15.4% (155/1003) of all examinations, additional lesions were identified by PET/MRI that were not detected in PET/CT (Figure 2). Follow-up imaging was available in 66.5% (103/155). In an additional 11.0% (17/155) of examinations equivocal PET/CT lesions could be clearly classified in PET/MRI without the need for further investigation, providing a reference standard for 120 out of 155 lesions. Among them, PET/MRI enabled a definite classification in 88 out of 120 lesions, comprising a correct classification in 66.7% (80/120; 53 malignant and 27 benign lesions) and an incorrect characterisation in 6.7% (8/120; 7 malignant and

1 benign). In 26.7% (32/120), additionally detected lesions were considered as indeterminate in PET/MRI, requiring further investigation. According to the reference standard, 28.1% (9/32) of all additionally detected but indeterminate lesions in PET/MRI were shown to be malignant and 71.9% (23/32) as benign (supplements).

Overall, in 24.2% (29/120) newly detected lesions in PET/MRI led to a correction in TNM-Staging (T0 to T+ in 9 cases; N0 to N+ in 3 cases; M0 to M+ in 17 cases). In 2/120 (1.7%) patients, an incorrect lesion classification in PET/MRI led to an incorrect upstaging from T0 to T+ in a lung cancer patient and from N0 to N+ in a breast cancer patient.

Overall additional findings were mostly observed in patients with malignant bone disease (33.3%, 8/24), lung cancer (14.4%, 26/180), prostate cancer (12.2%, 18/148), gynecologic and breast cancer (12.2%, 18/148), gastrointestinal cancer and neuroendocrine tumors (11.0%, 19/173) and malignant melanoma (10.3%, 9/87). Additional malignant lesions in PET/MRI were mostly detected in patients with malignant bone disease (12.5%, 3/24), lung cancer (7.8%, 14/180), prostate cancer (7.4%, 11/148) (figure 3) and gastrointestinal cancer and neuroendocrine tumors (6.4%, 11/173).

Additional findings in PET/MRI led to a correction in TNM-Staging in prostate cancer in 5.4% (8/148; upstaging from T0 to T+ in 4 cases and M0 to M+ in 4 cases), malignant melanoma in 4.6% (4/87; upstaging from N0 to N+ in one case and M0 to M+ in 3 cases), and gastrointestinal cancer and neuroendocrine tumors in 3.5% (6/173; upstaging from T0 to T+ in 2 cases and M0 to M+ in 4 cases).

In 2.9% (29/1003) examinations, PET/MRI **did not detect lesions that were found in PET/CT**. According to the reference standard, which was available in 86.2% (25/29), lesions missed by PET/MRI in 1.2% (12/1003) were considered as malignant and in 1.3% (13/1003) as benign. Missed malignant lesions comprised small lung nodules (n=8, size <10mm, Figure 4), lymph node metastases (n=2), a bone metastasis (n=1) and malignant tissue of the hypopharynx (n=1), leading to an overall change in TNM-staging in five cases (0.5%) due to upstaging in M-Staging (M0 to M+). In all other cases, the malignant lesions **not detected** by PET/MRI did not lead to changes in TNM-Staging due to the presence of diffuse metastatic spread. Missed benign findings comprised lung granuloma (n=8), and unspecific tracer uptake in bone (n=3), liver (n=1) and pharynx (n=1).

### **Classification of indeterminate findings in PET/CT by PET/MRI**

111 findings in 1003 examinations (11.1%) were classified as indeterminate in PET/CT (supplements). Follow-up imaging was available in 62.2% (69/111) and in additional 23.4% (26/111) the lesion could be clearly classified in PET/MRI without the need of further investigation, providing a reference standard for 95 lesions. PET/MRI correctly classified the indeterminate findings in PET/CT in 98.9% (94/95, 29 malignant, 65 benign, Figure 5). In one case (1.1%), an indeterminate lesion in PET/CT was classified incorrectly by PET/MRI: a suspicious liver lesion in a breast cancer patient that was incorrectly classified as a benign haemangioma turned out to be malignant in follow-up PET/CT after 753 days. This finding led to an incorrect TNM-staging (M0 instead of further investigation/follow-up).

In all other cases, PET/MRI led to a correction of TNM-Staging according to the reference standard in 7.4% (7/95, upstaging from T0 to T+ in 1, and M0 to M+ in 2 cases; downstaging from T+ to T0 in 2 and M+ to M0 in 2 cases).

### **Radiation exposure**

Mean effective dose (ED) of all whole-body PET/CT examinations amounted to  $17.6 \pm 8.7 \text{ mSv}$ , with PET accounting for  $3.6 \pm 1.4 \text{ mSv}$  (20.5%). Due to the lack of additional radiation exposure for attenuation correction and morphological imaging in PET/MRI, the radiation exposure could be significantly reduced by PET/MRI by approximately 83.2% in comparison to full-dose PET/CT ( $\text{ED}_{\text{PET/MRI}} 3.5 \pm 1.4 / \text{ED}_{\text{PET/CT full-dose}} 20.8 \pm 7.0 \text{ mSv}$ ) and 36.1% in comparison to low-dose PET/CT ( $\text{ED}_{\text{PET/MRI}} 3.9 \pm 1.3 / \text{ED}_{\text{PET/CT low-dose}} 6.1 \pm 1.6 \text{ mSv}$ ; both  $p < 0.001$ ).

## Discussion

The results of this first unicenter observational study in over 1000 subsequent PET/CT and PET/MRI examinations carry three important messages:

1. PET/MRI improves lesion detection in selected cancers and potentially reduces the need for additional examinations in comparison to PET/CT.
2. The amount of missed malignant lesions, in particular lung metastases in PET/MRI is negligibly small (0.8%), contradicting previous beliefs in the need for additional CT imaging of the chest.
3. Our results confirm and underline the potential for a clinically relevant reduction of radiation exposure in PET/MRI when compared to PET/CT, which is of particular interest for younger patients considering the cumulative radiation dose for staging, therapy monitoring and aftercare.

Integrated PET/MRI systems have been successfully introduced into scientific and clinical applications over the past 8 years, leveraging hybrid imaging onto a new platform of simultaneous acquisition of complementary metabolic, functional and morphologic information based on simultaneously acquired PET and MR datasets. Most early clinical PET/MRI studies put the focus on the assessment of its diagnostic performance in comparison to PET/CT or conventional imaging (MRI), and demonstrated its potential benefits in tumor staging and therapy management for various tumor entities [11, 12, 27, 32-36]. The exceptional soft-tissue contrast and the inherent multifunctionality of MRI, in terms of the potential for multiparametric MR imaging, were shown to facilitate superior lesion detection and improved diagnostic accuracy [18, 37-39]. However, these promising, preliminary findings were based on small patient cohorts. Especially a preliminary study by Catalano et al. detected



changes in clinical management of up to 18%, although these results were based on a highly selected patient cohort, on 18F-FDG examinations alone as well as a considerable number of non-contrast enhanced PET/CT examinations [13]. Our results support and validate these results in revealing a higher detection rate for additional malignant lesions by PET/MRI, mainly in prostate cancer, head and neck cancer, gynecologic and breast cancer as well as gastrointestinal cancer and neuroendocrine tumors most likely due to the enhanced soft-tissue contrast of MRI. In these tumor entities, primary lesions and recurrences can be detected more reliably by PET/MRI than by PET/CT. Additionally, multiparametric MRI protocols lead to a significantly better evaluation of suspicious abdominal lesions in these patients [40]. In prostate cancer imaging, the advantages of local tumor staging by MRI and distant metastases detection by 68Ga-PSMA PET/CT could be combined into a “one stop shop” PET/MRI examination, leading to enhanced patient comfort and a considerable speed up of the diagnostic work-up by including local MRI and whole-body PET-staging in one examination [41, 42]. Apart from detecting additional lesions, PET/MRI also improves classification of lesions rated as indeterminate in PET/CT, hence potentially reducing the need for additional imaging procedures. As demonstrated in previous investigations [32, 43, 44], this was particularly true for small lesions in liver, kidney and prostate due to the higher soft tissue contrast of T2 and contrast-enhanced T1 imaging as well as the additional diagnostic value of DWI. Thus, due to the higher diagnostic certainty **in selected cancers and lesions**, PET/MRI bears the potential to reduce the number of additional examinations in comparison to PET/CT.

One major concern that has limited the utilization of PET/MRI as an alternative to PET/CT for whole-body staging, has been the awareness towards the inferiority of MRI in lung nodule detection [45, 46]. Previous investigations in smaller patient

cohorts (up to 121 patients) showed the comparable diagnostic competence of PET/MRI and PET/CT for lung lesions >10mm and inferiority of PET/MRI in lesions <10mm [45]. Nevertheless, further investigations by Raad et al. and Sawicki et al. showed that the vast majority (97%) of lung nodules missed by PET/MRI either resolved or remained stable on follow-up, indicative of their benignity and leaving the potential effects on therapeutic management changes questionable [46, 47]. Amplifying prior study cohorts by an eight- to tenfold to 1003 PET/MRI examinations, the number of missed malignant lung nodules in our study cohort amounted to a total of 8 lesions (0.8% of all examinations), hence, underlining the high diagnostic potential of PET/MRI as an alternative to PET/CT considering the negligibly low number of undetected lung metastases. Furthermore, new MRI sequences, such as ultrashort echo time (UTE) sequences, are expected to improve lung nodule detection in comparison to established lung imaging MRI protocols, which will improve the sensitivity of PET/MRI even further [48]. Another demerit that had a negative impact on the clinical implementation of PET/MR imaging was the misconception of excessively long examination times rendering PET/MRI as an “ineffective” research tool, incompatible for clinical utilization. However, this misconception has been proven wrong in a considerable number of studies, demonstrating the comparability of PET/MRI to PET/CT for whole-body staging when specific fast protocols are used [49-52], although further research is needed to elucidate the significance of whole-body DWI as well as contrast agent administration in whole-body PET/MRI protocols.

One major benefit of PET/MRI for patient care is the significant reduction of radiation exposure. Similar to previous publications on smaller cohorts, our results confirm the potential for a mean dose reduction of 83.2% when compared to full-dose PET/CT imaging. Although possible genotoxic effects of MRI have been discussed by various

researchers, the quality of most studies has been a serious matter of concern [53]. Furthermore, a recent negative study by Fatahi et al. in 2016 on individuals repeatedly exposed to examinations on 7T MRI published seem to indicate that the clinical relevance of genotoxic effects by MRI is negligible [54]. Hence, considering the high diagnostic accuracy of PET/MRI, it may be particularly beneficial in pediatric patients and adolescents considering the cumulative radiation dose for multiple examinations for staging, therapy monitoring and aftercare [9]. Acknowledging the advantages of PET/MRI for pediatric patients, the German Society of Pediatric Oncology and Haematology recently introduced PET/MRI as an alternative to PET/CT for imaging patients with Hodgkin's lymphoma [55].

Therefore, PET/MRI might be considered as an important supplement to PET/CT. Although PET/CT will still be considered the oncologic "work horse", patients might profit from the diagnostic advantage due to the improved soft tissue contrast of MRI as well as the improved diagnostic workflow in certain cancers. Furthermore, pediatric patients and young adults may profit from the markedly reduced radiation exposure, especially in oncological diseases requiring repeated PET imaging such as lymphoma.

This study has some limitations. To reduce radiation exposure, PET/CT and PET/MRI were performed subsequently after a single radiotracer injection in this study. Therefore, PET/MRI examinations had a later acquisition timepoint than PET/CT, resulting in an increased sensitivity for metastases at the expense of specificity, e.g. in small lymph nodes [56]. Furthermore, PET/MRI protocols evolved during the course of the study as new software updates by the vendor provided more advanced MRI sequences which were implemented to guarantee the best possible image quality.

In conclusion, our results demonstrate the comparability and potential benefit of PET/MRI towards PET/CT with an improved detection rate in selected cancers and overall reduced radiation exposure, which may be particularly beneficial in pediatric and adolescent patients. Future studies addressing the technical and operational challenges of PET/MRI as well as involving different vendors and even larger cohorts will hopefully further pave the way for a widespread introduction of PET/MRI into clinical patient care.

## **Key points**

**Question:** Are there differences between positron emission tomography/magnetic resonance imaging (PET/MRI) and PET/computed tomography (PET/CT) in lesion detection and classification in oncological imaging?

**Pertinent findings:** In this 6-year observational study with over 1000 investigated examinations, PET/MRI improves lesion detection and classification in comparison to PET/CT in oncology, thus changing TNM staging. Furthermore, PET/MRI significantly reduces ionizing radiation in comparison to PET/CT.

**Implications for patient care:** PET/MRI reduces the need of additional examinations in tumor staging. The radiation exposure reduction may be highly beneficial in particularly for pediatric and adolescent patients.

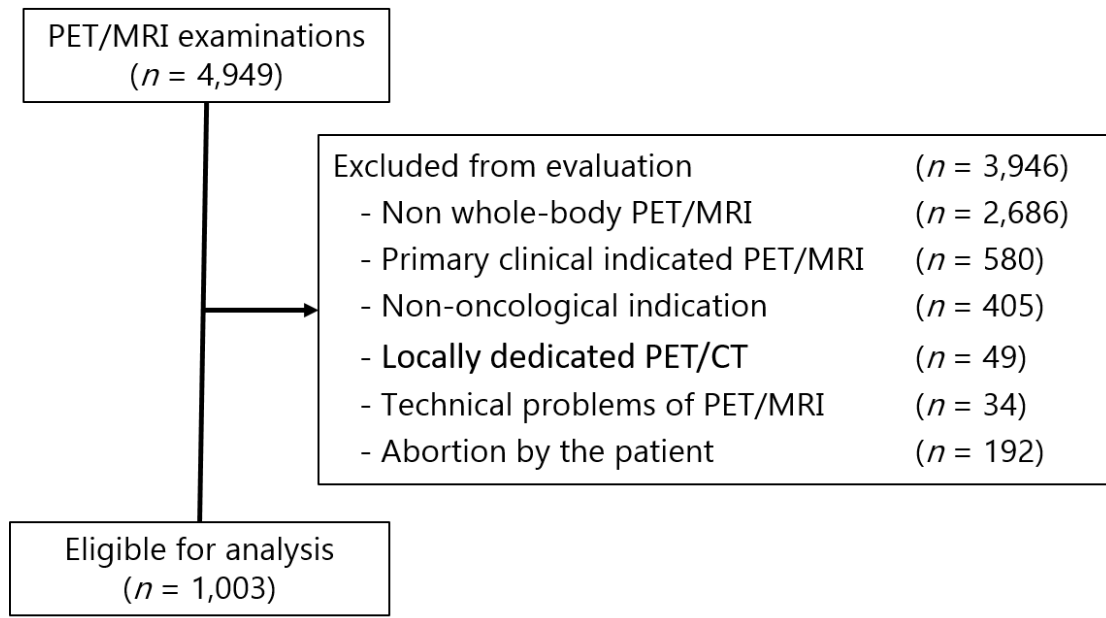
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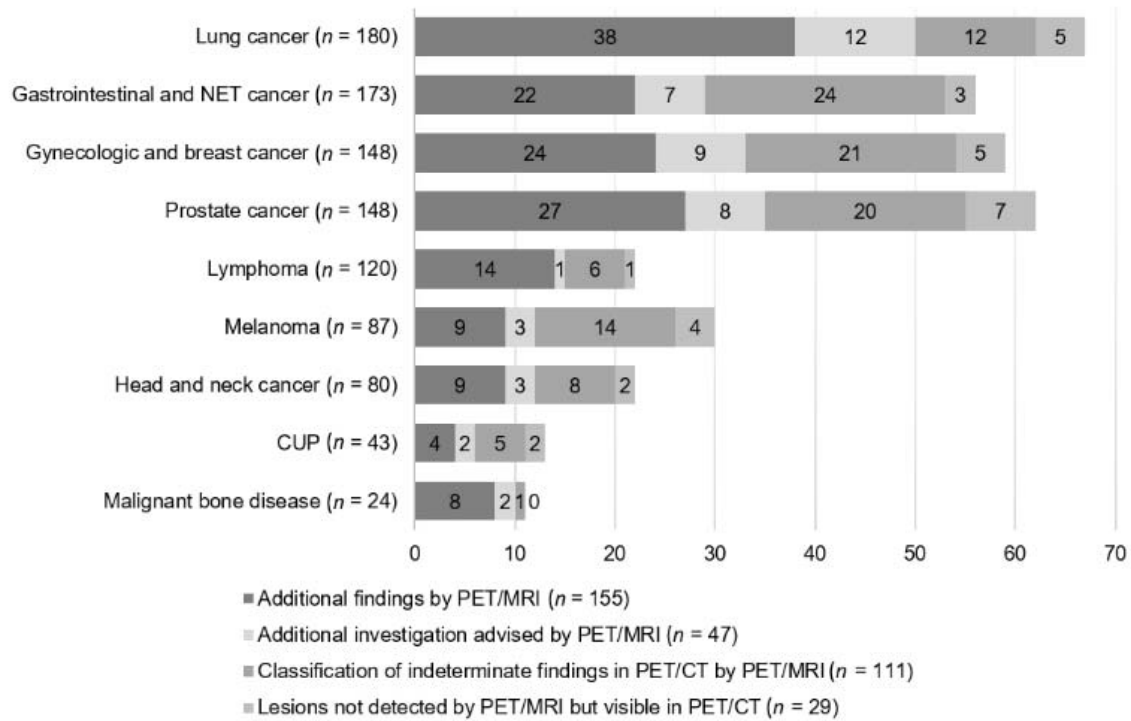
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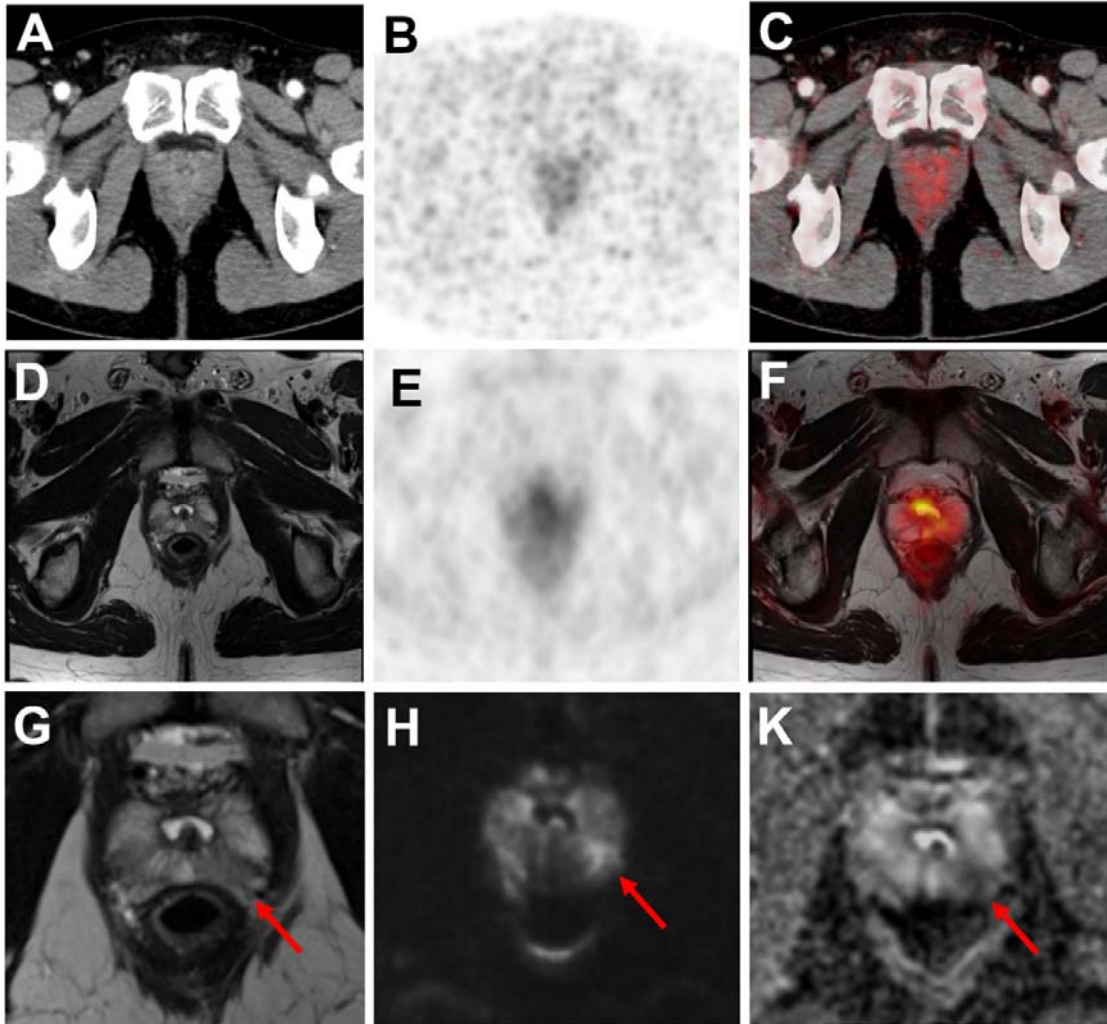


**Figure 1: CONSORT diagram.** From overall 4,949 examinations, 3,946 cases were excluded from analyses, resulting in 1,003 evaluable examinations.

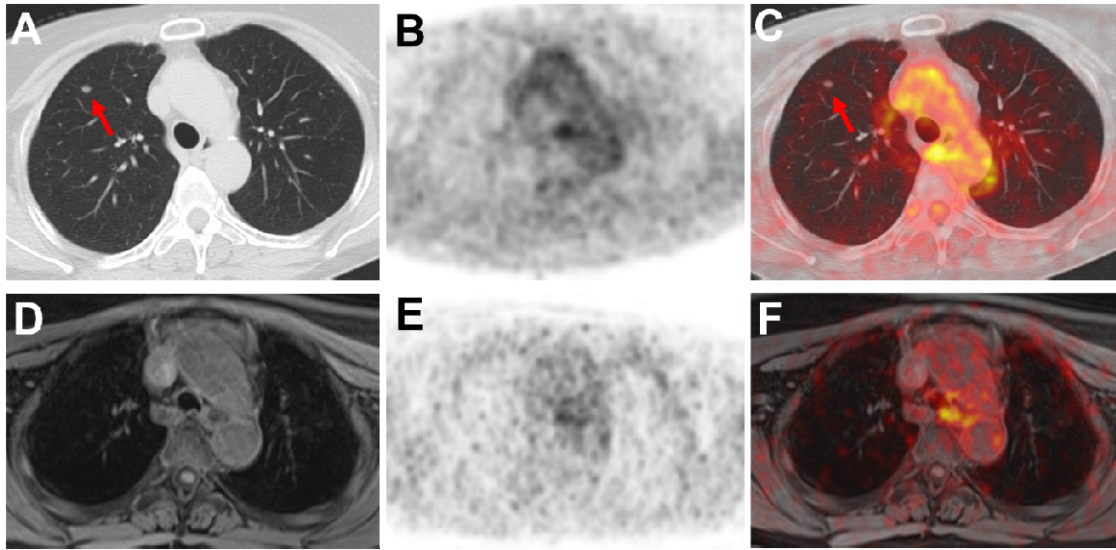


**Figure 2: Additional information in PET/MRI in different cancer entities**

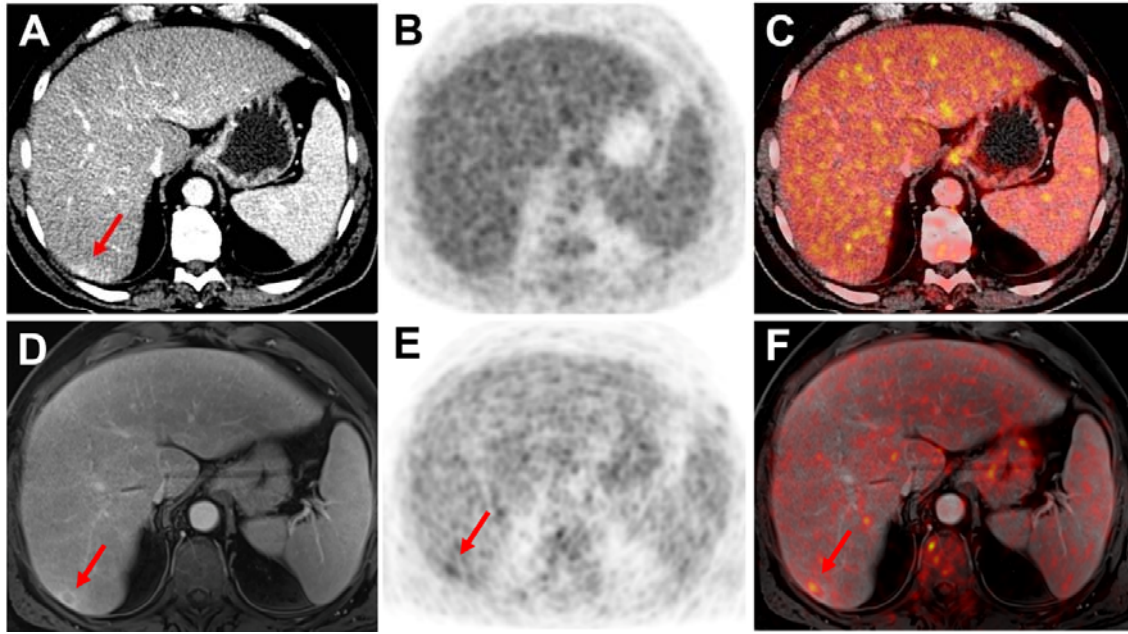
CUP = cancer of unknown primary; NET = neuroendocrine tumor



**Figure 3: Additional finding in PET/MRI:** 51y old male patient suffering from prostate cancer. Contrast enhanced CT (A), PET (B) and fused  $^{68}\text{Ga}$ -PSMA PET/CT images (C) are displayed in comparison to T2 MRI (D, G), PET (E) and fused  $^{68}\text{Ga}$ -PSMA PET/MRI images (F) as well as DWI (b1000: H; ADC-map: K). A suspicious lesion in the left peripheral zone, missed by CT and PET in PET/CT and by PET in PET/MRI due to its small size in homogenous soft tissue. However, restricted diffusion of the soft tissue mass is indicative of malignancy. Additional biopsy confirmed the diagnosis after.



**Figure 4: Missed finding by PET/MRI.** 77y old female patient suffering from ovarian carcinoma. Contrast enhanced CT (A), PET (B) and fused 18F-FDG PET/CT images (C) are displayed in comparison to T1 MRI (D), PET (E) and fused 18F-FDG PET/MRI images (F). A small lung metastasis in right upper lobe that is missed by MRI as well as in PET in PET/MRI and PET/CT due to its small size, is clearly visible in CT. Follow-up CT confirmed malignancy after 78 days.



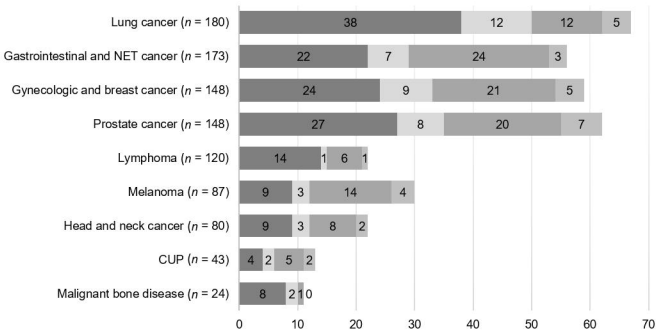
**Figure 5: Indeterminate lesion in PET/CT classified by PET/MRI.** 53y old male patient suffering from lung cancer. Contrast enhanced CT (A), PET (B) and fused 18F-FDG PET/CT images (C) are displayed in comparison to contrast enhanced T1 MRI (D), PET and fused 18F-FDG PET/MRI images (F). In CT (A), the hyperdense, subcentimeter liver lesion in segment VII is suspicious of a transient hepatic attenuation difference or a small hemangioma. As malignancy cannot be excluded, it needs further investigation. In PET/MRI, the lesion is clearly classified as metastasis due to contrast enhancement and tracer uptake due to a later acquisition time point. Follow-up CT confirmed the diagnosis after 78 days.

PET/MRI examinations  
( $n = 4,949$ )

Excluded from evaluation ( $n = 3,946$ )

- Non whole-body PET/MRI ( $n = 2,686$ )
- Primary clinical indicated PET/MRI ( $n = 580$ )
- Non-oncological indication ( $n = 405$ )
- Locally dedicated PET/CT ( $n = 49$ )
- Technical problems of PET/MRI ( $n = 34$ )
- Abortion by the patient ( $n = 192$ )

Eligible for analysis  
( $n = 1,003$ )



■ Additional findings by PET/MRI (n = 155)

■ Additional investigation advised by PET/MRI (n = 47)

■ Classification of indeterminate findings in PET/CT by PET/MRI (n = 111)

■ Lesions not detected by PET/MRI but visible in PET/CT (n = 29)

