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Original Article

Malignant pleural mesothelioma: initial experience in integrated ^{18}F-FDG PET/MR imaging

Benedikt M. Schaarschmidt [a,b,*], Lino M. Sawicki [a], Benedikt Gomez [c], Johannes Grueneisen [b], Mathias Hoiczyk [d], Philipp Heusch [a], Christian Buchbender [a]

[a] University Dusseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, D-40225 Dusseldorf, Germany
[b] University Duisburg-Essen, Medical Faculty, Department of Diagnostic and Interventional Radiology and Neuroradiology, D-45147 Essen, Germany
[c] University Duisburg-Essen, Medical Faculty, Department of Nuclear Medicine, D-45147 Essen, Germany
[d] University Duisburg-Essen, Medical Faculty, Department of Medical Oncology, Essen, Germany

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ABSTRACT

Purpose: This study aims to compare staging results of ^{18}F-FDG PET/computed tomography (CT) and integrated PET/magnetic resonance (MR) in malignant pleural mesothelioma (MPM) patients and to investigate a potential apparent diffusion coefficient (ADC)/SUV correlation.
Materials and methods: Six patients with MPM underwent ^{18}F-FDG PET/CT and PET/MR including diffusion-weighted imaging. Thoracic TNM staging was performed for both modalities. SUV and ADC were assessed in therapy-naive pleural lesions.
Results: In thoracic TNM staging, no differences were found between PET/CT and PET/MR. An inverse correlation was observed between SUV_{mean} and ADC_{min} ($r=-0.63$, $P=.002$).
Conclusion: MPM can be staged using PET/MR. The inverse correlation ADC/SUV indicates that future research on multiparametric therapy response evaluation may be warranted.

1. Introduction

Asbestos exposure is the main cause for malignant pleural mesothelioma (MPM) [1]. Despite the ban of asbestos in many countries, the long latency between exposure and disease onset will lead to a further increase of this currently rare disease in the forthcoming years [2].

The poor prognosis after single modality treatment has led to a multimodal treatment approach that is highly dependent on exact tumor staging and treatment response assessment. Due to its wide availability, computed tomography (CT) is considered the basic tool for MPM staging [3]. Magnetic resonance imaging (MRI), however, is advocated as an alternative that—based on its excellent soft tissue contrast—has been found to be superior to CT in the detection of diaphragmatic invasion and solitary chest wall infiltration [4,5]. Furthermore, functional MRI biomarkers, such as the apparent diffusion coefficient (ADC) derived from diffusion-weighted imaging (DWI) might be used for tumor evaluation [6] and could also improve the detection of tumorous foci in patients suffering from pleural thickening [7].

^{18}F-FDG PET/CT combines the advantages of functional tumor imaging with the precise morphologic information of CT. The functional PET information is useful to differentiate MPM from benign pleural disease [8] and for treatment response evaluation [9,10]. Although PET is advantageous for distant metastases detection, the additional benefit in local tumor and lymph node staging is considered to be low [11,12]. As MRI offers local tumor staging by providing excellent soft tissue contrast, integrated PET/magnetic resonance (MR) combines the advantages of PET and MRI in one single examination. Patients might profit from the superior soft tissue contrast of the MR component in local tumor staging and the possibility of simultaneous acquisition of functional MRI and PET for the differentiation between benign pleural disease and MPM and for therapy response evaluation. Therefore, we compared thoracic MPM staging results of PET/CT and PET/MR and investigated the potential correlation between ADC and SUV in therapy-naive pleural lesions.

2. Materials and methods

2.1. Patients

Six patients (two female and four male patients, mean age: 65.5 years) suffering from histopathologically proven MPM who underwent contrast-enhanced PET/CT and subsequent PET/MR between April 2010

* Corresponding author. University Dusseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, Moorenstrasse 5, 40225 Dusseldorf, Germany. Tel.: +49-2118117752.
E-mail address: Benedikt.Schaarschmidt@med.uni-duesseldorf.de (B.M. Schaarschmidt).

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and February 2015 were included in this retrospective analysis (see Table 1). This retrospective analysis was performed as part of a comparative study between PET/CT and PET/MR. Image acquisition and retrospective data analysis were authorized by the local ethics committee. Before image acquisition, informed consent was obtained from all patients.

2.2. PET/CT

At 74 ± 16 min after injecting a mean ^{18}F-FDG activity of 290 ± 50 MBq, PET/CT scans were performed from the upper thighs to the base of skull on a Biograph mCT (Siemens Healthcare GmbH, Erlangen, Germany). For PET acquisition, seven bed positions were used (2 min per bed position). The contrast-enhanced CT scan was performed 70 s after 100 ml iodine contrast-agent injection (Ultravist, Bayer Schering Pharma, Berlin, Germany). Dose reduction was implemented by CareDose 4D and CareKV to minimize radiation exposure (presets: 210 mAs and 120 kV). Slice thickness was 5 mm. Contrast-enhanced CT images were used for attenuation correction. PET images were reconstructed iteratively using the ordered subset expectation maximization (OSEM) algorithm (3 iterations, 21 subsets, Gaussian filter: 4 mm).

2.3. PET/MR

Thoracic PET/MRI was performed subsequently to PET/CT (mean time after tracer injection: 163 ± 56 min) on a Biograph mMR (Siemens Healthcare GmbH, Erlangen, Germany). The thoracic MR protocol comprised the following sequences:

- T1 3D-Dixon-VIBE for four class segment attenuation correction in inspiration [coronal orientation; TR: 3.6 ms, TE1: 1.23 ms, TE2: 2.46 ms, flip angle: 10°, slice thickness: 3.12 mm, matrix size: 96×96, field of view (FOV): 500×500 mm^2].
- T2 BLADE turbo spin echo sequence in free breathing (transverse orientation; TR: 4360 ms, TE: 160 ms, slice thickness: 5 mm, matrix size: 384×384, FOV: 400×400 mm^2)
- T2 half-Fourier acquired single-shot turbo spin echo sequence in inspiration (coronal orientation; TR: 649 ms, TE: 51 ms, slice thickness: 6 mm, matrix size: 320×288, FOV: 330×330 mm^2)
- T2 steady-state free precession sequence in inspiration (coronal orientation; TR: 3.75 ms, TE: 1.64 ms, slice thickness: 6 mm, matrix size: 320×272, FOV: 330×330 mm^2)
- Nonenhanced T1 fast low-angle shot (FLASH) in inspiration (transverse orientation; TR: 1510 ms, TE: 2.15 ms, slice thickness: 5 mm, matrix size: 320×256, FOV: 400×325 mm^2)
- Contrast-enhanced transverse T1 FLASH sequence in free breathing (transverse orientation; TR: 1700 ms, TE: 3.33 ms, slice thickness: 7.5 mm, matrix size: 256×205, FOV: 400×366 mm^2)
- DWI in free breathing (transverse orientation; TR: 17,900 ms, TE: 78 ms, slice thickness: 5 mm, FOV: 450×383 mm, matrix size: 160×120, voxel size: 3.8×2.8×5.0 mm, two averages) was performed in free breathing using five *b* values (0, 100, 500, 1000, 2000).

Monoexponential ADC maps were calculated using the vendor-specific software. PET data were acquired simultaneously to MRI in list mode for 20 min in the thorax without respiratory gating. OSEM was used for iterative image reconstruction (3 iterations, 21 subsets, Gaussian filter: 4 mm, matrix size: 344×344, voxel size: 2.01×2.01×2 mm).

2.4. Image analysis

PET/CT and PET/MR images were analyzed in random order by two independent readers on an OsiriX workstation (Pixmeo SARL, Bernex, Switzerland). There was a minimum timespan between the PET/CT and the PET/MR reading sessions of at least 4 weeks to minimize recognition bias. Discrepancies between both readers were resolved in a consensus reading. For both modalities, TNM staging was performed in accordance with the latest edition of the AJCC staging manual [13]. As PET/CT is an accepted method for MPM staging, the staging results from PET/CT were considered as reference standard.

One patient received a shortened PET/MR protocol without DWI and with a decreased PET acquisition time and was therefore excluded from quantitative analysis. In the remaining patients, a maximum of six lesions visible on PET and on the b0 image of DWI were identified per patient on the T2 BLADE images. Twenty-two lesions (20 pleural manifestations, one lymph node metastasis, one sternal metastasis) were detected. All images were resampled to match the voxel size of the ADC map to avoid measurement errors. At the maximum tumor diameter, a freehand polygonal region of interest (ROI) was drawn around the lesion on the T2 BLADE image and this ROI was copied to both, the PET image derived from PET/MR and the ADC map. Automatically, SUV_{max}, SUV_{mean}, ADC_{min}, and ADC_{mean} were calculated.

2.5. Statistical analysis

PET/MR staging results were compared to the reference standard. Pearson correlation coefficients were calculated for any combination of ADC_{mean}, ADC_{min}, SUV_{max}, and SUV_{mean} for therapy-naive pleural lesions. $P<.05$ indicated statistical significance. Statistical analysis was performed using IBM SPSS Statistics 22 (IBM, Armonk, NY, USA).

3. Results

Tumor staging was possible in all six patients based on the data provided by PET/CT and PET/MR (Fig. 1 and Table 1). PET/MR was capable of detecting small pleural nodules without tracer uptake (Fig. 2) and focal thoracic invasion was depicted distinctively (Fig. 3). All lesions were detected by PET/MR as well as PET/CT and there was no discordance between the TNM-stage defined by the two imaging modalities (Table 1). In integrated PET/MR, a statistically significant inverse correlation was observed between ADC and SUV (Fig. 4 and Table 2).

4. Discussion

In this pilot study on ^{18}F-FDG PET/MR in MPM, PET/MR demonstrates staging results equal to ^{18}F-FDG PET/CT in patients with

Table 1
Characteristics of patients undergoing PET/CT and integrated PET/MRI for MPM

Gender	Age	Histopathological subtype	Tumor stage	Prior treatment	TNM stage PET/CT	TNM stage PET/MR
M	73	Epitheloid	IV	Chemotherapy and radiotherapy	T4 N0 M1 (sternal metastasis)	T4 N0 M1 (sternal metastasis)
M	72	Biphasic	III	None	T3 N0 M0	T3 N0 M0
F	37	Epitheloid	III	Chemotheray	T2 N0 M0	T2 N0 M0
M	70	Epitheloid	III	None	T3 N2 M0	T3 N2 M0
M	66	Epitheloid	III	None	T3 N2 M0	T3 N2 M0
F	75	Epitheloid	IV	Chemotherapy and pleurectomy	T4 N3 M1 (lung and cutaneous metastases)	T4 N3 M1 (lung and cutaneous metastases)