The use of simultaneous $^{18}$F-FDG-PET/MRI for the detection of spondylodiscitis

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ABSTRACT

The diagnosis of spondylodiscitis is often challenging. Magnetic resonance imaging (MRI) is quite sensitive, but lacks specificity, and distinction from erosive osteochondritis is often difficult. We sought to assess the diagnostic value of combined 18fluorine-fluorodeoxyglucose positron emission tomography combined with MRI (18F-FDG-PET/MRI) in cases of suspected spondylodiscitis with an inconclusive clinical and/or MRI presentation.

Methods:

In a prospective study, 30 patients with a previous inconclusive MRI and suspected spondylodiscitis underwent combined 18F-FDG-PET/MRI, including standard spine MRI sequences pre- and post-contrast. The image datasets were evaluated on dedicated workstations by two radiology residents and one board-certified nuclear medicine physician independently and then in consensus. Because of severe susceptibility artifacts, only 28/30 image datasets were evaluable with a total of 29 spondylodiscitis-suspicious regions. Standardized uptake value ratios (affected/reference disc) were determined. The imaging results were compared with histopathology or clinical follow-up as reference standards and subjected to statistical analysis.

Results:

The reference standards identified spondylodiscitis in 12 discs, and excluded spondylodiscitis in 17 discs. MRI alone showed a sensitivity of 50%, a specificity of 71%, a positive predictive value (PPV) of 54%, and a negative predictive value (NPV) of 67%. Adding the PET data resulted in sensitivity, specificity, PPV, and NPV of 100%, 88%, 86%, and 100%. In a receiver-operator characteristics analysis, a maximum standardized uptake value ratio threshold of 2.1 resulted in 92% sensitivity and 88% specificity (area under the receiver-operator characteristics curve =
Neither the level of C-reactive protein nor the leukocyte count at the time of PET/MRI was related to the reference standard diagnosis of spondylodiscitis.

Conclusions:

In cases with inconclusive clinical/MRI findings, the use of $^{18}$F-FDG-PET/MRI significantly increases the diagnostic certainty for the detection of spondylodiscitis.

Keywords: Spondylodiscitis; $^{18}$F-FDG-PET/MRI; Positron-Emission Tomography; Magnetic Resonance Imaging; Osteochondritis
INTRODUCTION

Spondylodiscitis, also known as vertebral osteomyelitis, is a rare but serious destructive infection of the vertebral bodies with involvement of the intervertebral discs. The incidence of this disease is increasing, possibly owing to the growing elderly population with chronic and degenerative diseases. Additionally, an increase in spinal surgery and instrumentation and a rising use of immunosuppressive agents and intravenous drug abuse have defined additional risk groups \((1,2)\). Though the mortality from spondylodiscitis has been described as < 5%, the morbidity is high: vertebral infections can result in bone destruction, and the involvement of discs can lead to further instability, chronic back pain, and neurological deficits.

In addition to clinical examination, including a detailed neurological status, blood samples or vertebral biopsies, radiological and nuclear medicine imaging techniques including conventional X-rays, computed tomography (CT), magnetic resonance imaging (MRI), multi-phase bone scintigraphy, leukocyte scintigraphy, or positron emission tomography with \(^{18}\)fluorine-fluorodeoxyglucose positron emission tomography \((^{18}\text{F-FDG-PET})\), and PET/CT have been used. Only recently, PET/MRI has become available, and its usefulness for imaging spondylodiscitis awaits systematic testing \((3–5)\).

Depending on the disease stage, a strict conservative or operative treatment is required for a desirable outcome. Early detection is obviously desirable but often challenging because of nonspecific clinical, laboratory, and radiologic findings.

In the early stages, MRI is currently the method of choice for diagnosing spondylodiscitis with a reported sensitivity of 96\% \((2,6,7)\). MRI can depict the anatomical location and the extent of the disease and allows early detection of disc or bone destruction as well as evaluation of the involvement of neural structures \((8)\). The classic MRI findings of spondylodiscitis are
hyperintense signal alterations on T2-weighted images (T2WI) or turbo inversion recovery magnitude (TIRM) sequences in the disc space (often with fluid collections), appearing in both adjacent vertebrae as bone marrow and paravertebral soft-tissue edema. On T1-weighted images (T1WI), the lesions appear with decreased signal intensity on non-contrast images, with marked contrast enhancement (2,6,9). However, similar findings in the presence of fractures or spinal implants may lead to insufficient specificity. Another well-known MRI problem is the distinction of an infectious spondylodiscitis from an erosive osteochondritis with Modic Type 1 changes, as both entities share similar signal alterations (10,11).

In these equivocal cases, nuclear medicine imaging techniques may play a useful role. Among the nuclear medicine imaging tools mentioned above, 18F-FDG PET, with a reported sensitivity of 82%, is useful to detect or especially to exclude spondylodiscitis. Thus, the differentiation of active inflammation and degenerative alterations such as erosive osteochondritis can be made with 18F-FDG PET. Combined 18F-FDG PET/CT or 18F-FDG PET in addition to MRI has shown higher diagnostic accuracy than each modality performed alone (12,13), as they can overcome the limited spatial resolution and limited ability of 18F-FDG-PET to differentiate between inflammation and malignant tissue (3,4,14).

The combination of the strengths of 18F-FDG PET and MRI in combined 18F-FDG PET/MRI offers a new type of hybrid imaging by providing highly sensitive metabolic and high-resolution anatomic imaging with excellent soft-tissue contrast. However, this feature has so far not been investigated in spondylodiscitis. The aim of our study was, therefore, to analyze the additive value of MRI performed simultaneously with 18F-FDG PET (18F-FDG PET/MRI) in patients with suspected spondylodiscitis and inconclusive findings on clinical examination and MRI alone.
MATERIALS AND METHODS

Patients

In this prospective single-center study, 34 consecutive patients (14 male, 20 female; mean age ± standard deviation: 72 ± 11 years, range: 49–94 years) with clinically and/or paraclinically suspected spondylodiscitis for less than 4 weeks were enrolled between March 2014 and August 2015. An informed consent for the use of $^{18}$F-FDG and MRI contrast agent gadobutrol (Gadovist®, Bayer HealthCare, Leverkusen, Germany) was obtained from all patients. This study was approved by the Ethics Committee of the Medical Faculty, University of Leipzig, Germany, and all patients gave written informed consent.

All patients had previously undergone MRI with results either inconclusive or “suspicious” for spondylodiscitis. In 30/34 patients, combined $^{18}$F-FDG PET/MRI including whole-spine 3 T MRI with standard sequences pre- and post-contrast, were performed. Four patients interrupted the examination because of severe back pain and restlessness.

Whole-body PET/MRI-imaging protocol

The combined PET/MRI system (mMR - Biograph®, Siemens Healthcare, Erlangen, Germany) used in this study combines a 3 T MRI with an integrated PET scanner. Whole-body sequential PET/MRI scanning was performed from the upper thigh to the skull with a 5-min acquisition time per bed position. Image acquisition commenced an average of 75 min (range 60–105 min) after intravenous administration of $^{18}$F-FDG (4 MBq/kg, range: 149–410 MBq, mean ± SD: 294 ± 64 MBq) after a fasting period of at least 6 h.
PET images were reconstructed using the iterative ordered, subset expectation maximization algorithm with three iterations and 21 subsets, a Gaussian filter with 4-mm full width at half maximum, and a 256 × 256 image matrix. Attenuation correction of the PET data was performed using a four-tissue (fat, soft tissue, air, background) model attenuation map obtained from a Dixon-VIBE MR sequence.

Subsequently, whole-spine MR data were obtained by using the integrated spine coil and two body phased-array coils covering the region from occiput to coccyx in three bed positions: cervical, thoracic, and lumbar. Typical sequences were acquired (Table 1).

For contrast-enhanced MRI, a single dose of 0.1 mmol/kg gadobutrol (Gadovist®) at a rate of 3 mL/s flushed with 10 mL of saline was administered by using a power injector (Spectris Solaris®, Medrad/Bayer HealthCare, Leverkusen, Germany).

Image interpretation

The PET/MRI datasets were evaluated on dedicated workstations (PET/MRI: Syngo.via®, Siemens Healthcare, Erlangen, Germany; MRI only: MagicView 1000®, Siemens Healthcare). Focal 18F-FDG uptake in spinal discs greater than the surrounding tissue (based on visual qualitative analysis) was considered as suspicious for spondylodiscitis. For each affected intervertebral disc identified on the TIRM sequence in MRI, mean and maximum standardized uptake values (SUVmean and SUVmax) were determined by identifying the disc in the fused PET/MRI dataset and by placing a volume of interest (VOI) round the disc (SUVmax threshold 40%). By this method we could determine that only disc tissue was part of the VOI and exclude artifacts by adjacent osseous processes.
SUV_{mean} and SUV_{max} were also obtained for a healthy reference disc and SUV ratios (affected/reference disc) were calculated.

The single MRI datasets of PET/MRI were analyzed independently and in consensus by two radiologists with 1.5 years’ and 5 years’ experience using a five-point Likert scale ("1: spondylodiscitis definitely absent"); "2: spondylodiscitis probably absent"; "3: neutral"; "4: spondylodiscitis probably present"; "5: spondylodiscitis definitely present"). This was followed by an interdisciplinary analysis of the complete PET/MRI datasets together with a board-certified nuclear medicine physician (8 years of experience in PET image interpretation), which resulted in a consensus decision, dichotomized into “spondylodiscitis” and “no spondylodiscitis”. Except for knowledge of the painful spine level, the readers were blinded to laboratory parameters and histological results.

**Reference standards**

The imaging results were compared with histopathology of surgery/biopsy \(n = 6\) or clinical follow-up \(n = 22\) as reference standards. Spondylodiscitis was excluded by clinical follow-up if symptoms were absent or regressed without antibiotic therapy, and inflammation parameters, including white blood cell count and C-reactive protein were in a normal range (< 5 mg/l) or at a very low level that did not progress during follow-up of at least 6 weeks. Spondylodiscitis was confirmed by clinical follow-up when signs of inflammation and pain regressed after antibiotic therapy or progressed without antimicrobial therapy over at least 6 weeks.

Indications for operative treatment would have been large paraspinal abscesses, sepsis, progressive neurological impairment, deformities due to destruction of the endplates, and
failure of 6 weeks of antibiotic treatment. Conservative treatment was used in the case of an aseptic paraclinical constellation, low pain levels, and no vertebral destructive changes on PET/MRI.

**Statistical analysis**

Non-parametric Mann–Whitney U was performed as indicated. Interrater agreement was established with a linear-weighted Cohen’s kappa coefficient.

Diagnostic certainty was determined as the sum of true positive and true negative patients divided by all patients in percent.

Sensitivity, specificity, positive and negative predictive value (PPV, NPV), and positive and negative likelihood ratios were calculated for both imaging modalities. Sensitivity and specificity were compared using exact McNemar’s test.

Correlations between SUV$_{\text{mean}}$ and SUV$_{\text{max}}$ and laboratory parameters (C-reactive protein, white blood cell count) were calculated using Spearman’s rho. Receiver operating characteristics curve analysis was performed to assess diagnostic performance of PET/MRI, and the maximum Youden Index was determined to define the optimal cutoff value for the SUV ratio.

If not otherwise indicated, data are given as mean ± SD for quantitative variables. Statistical significance for all tests was set at a level of $P < 0.05$. Statistical analysis was done using commercial software (SPSS version 22.0® software package, SPSS Inc., Chicago, IL, USA).
RESULTS

The whole-body PET/MRI examination was successfully completed in 30/34 patients (Table 2). In 5/30 patients, internal fixation material was found at the level of interest, causing susceptibility artifacts on MR. Because of severe susceptibility artifacts in 2/5 cases, the assessment was significantly restricted on MR as well on 18F-FDG PET and final evaluation could not be realized. In the other three cases, MRI images were not evaluable, but a consensus final imaging diagnosis could be made using the PET information.

In total, 28 patients with 29 spondylodiscitis-suspected regions were evaluated. Figures 1 and 2 show typical imaging findings. MRI evaluation of PET/MRI resulted in 6/29 regions in the diagnosis “spondylodiscitis” and in 15/29 regions “no spondylodiscitis” (Supplemental table). Eight of 29 regions remained inconclusive on MRI. Inter-rater agreement between the two MRI readers was moderate with a weighted Cohen’s Kappa of 0.66. Adding the PET information, in 5/8 regions, the inconclusive diagnosis changed into “spondylodiscitis,” and in 3/8 regions into “no spondylodiscitis”. In total, by PET/MRI consensus decision, “spondylodiscitis” was diagnosed in 14/29 regions and excluded in 15/29. There were no inconclusive decisions.

Histological confirmation following surgery or percutaneous biopsy was available in 6/28 patients. In the remaining 22 patients, clinical follow-up was used as reference standard to prove or exclude spondylodiscitis.

By the reference standard, 12 cases of spondylodiscitis were finally diagnosed, in 4/12 cases by histopathologic results and in 8/12 cases by follow-up. In one case, the cervical spine was affected; the lumbar spine was involved in the other 11 cases (Table 2). In 17/29
spinal regions, spondylodiscitis was excluded (2/17 by histopathology, 15/17 by clinical follow-up).

Between patients with and without spondylodiscitis there were no significant differences concerning sex, age, CRP, or leukocyte count ($P > 0.05$, Table 2). The MRI showed a sensitivity of 50%, a specificity of 71%, a PPV of 54%, and a NPV of 67%. Adding the PET component, PET/MRI data improved to a sensitivity, specificity, PPV, and NPV of 100%, 88%, 86%, and 100%, respectively (Table 3). With combined PET/MRI there were no false-negative results. Diagnostic certainty was significantly higher in combined PET/MRI vs. MRI alone (93.1% vs. 62.1%, $P < 0.001$).

In a receiver operating characteristics analysis, a $\text{SUV}_{\text{max}}$ ratio threshold of 2.1 resulted in 92% sensitivity and 88% specificity for the correct diagnosis of spondylodiscitis with an area under the curve of 0.95 (Fig. 3). In cases of “spondylodiscitis”, absolute $\text{SUV}_{\text{max}}$ and $\text{SUV}_{\text{mean}}$ in the affected disc were significant elevated compared with cases with “no spondylodiscitis” ($\text{SUV}_{\text{max}}$ 5.07 ± 3.43; $\text{SUV}_{\text{mean}}$ 2.68 ± 1.76 vs. $\text{SUV}_{\text{max}}$ 2.73 ± 1.29; $\text{SUV}_{\text{mean}}$ 1.46 ± 0.67; $P < 0.001$, Fig. 4). There was a significant correlation between level of CRP and $\text{SUV}_{\text{max}}$ of the affected disc with Spearman’s $\rho$ of 0.5 ($P = 0.01$), but not with the $\text{SUV}_{\text{max}}$ ratio ($P = 0.09$).

The MRI of $^{18}$F-FDG-PET/MRI were false positive in five cases, in 2/5 patients owing to osteochondritis, 1/5 owing to spondylitis, 1/5 owing to degenerative disc space narrowing, and in 1/5 patients owing to fracture-associated signal alterations. $^{18}$F-FDG-PET/MRI was false-positive in two cases; in one patient with a spondylitis and the other an erosive osteochondritis was diagnosed by clinical follow-up.
Other main diagnoses in patients without spondylodiscitis were fractures, herniated discs, and spondylolisthesis.

DISCUSSION

The diagnosis of spondylodiscitis usually requires multiple modalities including clinical examination, laboratory tests (including blood cultures), a combination of imaging techniques, and biopsy samples for pathogen detection. Because of a high reported sensitivity of up to 96%, MRI is currently the method of choice for diagnosing spondylodiscitis, especially in its early stages. Furthermore, MRI is widely available and radiation free. Compared with CT, MRI is superior in distinguishing bone marrow, vertebrae, and intervertebral discs, as well as neural structures. Nevertheless, there are limitations, especially in previously operated patients with metallic implants, which may cause severe susceptibility artifacts. Furthermore, differentiation from degenerative processes such as erosive osteochondritis may be difficult with MRI. In these cases, $^{18}$F-FDG-PET has been described as a useful tool to differentiate degenerative from infectious endplate abnormalities found on MRI. However, its lack of anatomic detail and the limited spatial resolution are the main drawbacks of $^{18}$F-FDG-PET (6,7,15,16).

With the recent development of integrated PET/MRI scanners, new possibilities for multimodal molecular imaging have emerged. PET/MRI and the application of the “one-stop-shop” principle enable analysis of simultaneously acquired metabolic and morphological parameters with excellent soft-tissue contrast, and thus may improve diagnostic capabilities in inflammatory processes and other disease entities (3). Besides the improvement in time and patient comfort by a single image examination with simultaneous
PET/MRI (“one-stop-shop”) one of the main advantages over sequentially performed PET and MRI is the added value of excellent soft tissue contrast of MRI. The main drawback of a single PET scan is the lack of anatomical information, thus the distinction between disc and bone tissue is very difficult. Especially in the setting of spondylodiscitis with often nearly completely destroyed discs the distinction between discitis and spondylitis is nearly impossible without the simultaneously acquired MRI dataset. Regarding diagnosis of spondylodiscitis with combined $^{18}$F-FDG-PET and MRI, the scientific literature is still limited. A meta-analysis performed by Prodromuo et al. (14) evaluated diagnostic data on the use of $^{18}$F-FDG PET in spondylodiscitis as provided by 12 studies comprising 224 patients. The combined sensitivity across these studies was 0.97, the specificity was 0.88. The authors concluded that $^{18}$F-FDG PET is a robust diagnostic test when spondylodiscitis is suspected and an excellent tool for the exclusion of infectious spondylodiscitis. Another study by Skanjeti et al. (17) retrospectively included 33 patients with suspected/confirmed spondylodiscitis and evaluated the usefulness of $^{18}$F-FDG-PET in the diagnostic work-up of patients with spondylodiscitis compared with MRI alone. For diagnosing spondylodiscitis, $^{18}$F-FDG-PET showed a sensitivity, specificity, PPV, NPV, and accuracy of 92.9%, 50%, 72.2%, 83.3%, and 75%, respectively, compared with MRI alone with a sensitivity, specificity, PPV, NPV, and accuracy of 100%, 50%, 76.9%, 100%, and 81.3%, indicating similar accuracy of $^{18}$F-FDG-PET and MRI. Thus, the authors recommend the use of $^{18}$F-FDG-PET when MRI is doubtful or unavailable. Similar accuracies of separate MRI and $^{18}$F-FDG-PET/CT for diagnosing spondylodiscitis (81% and 84%, respectively) were also described in a study by Fuster et al. (8). However, this study of 26 prospective patients
demonstrated a very low specificity (38%) of MRI, reflecting the difficulty in exclusion of infectious spondylodiscitis.

Our study, which is, to the best of our knowledge, the first study employing combined $^{18}$F-FDG PET/MRI for the detection of spondylodiscitis, demonstrated a significant improvement of sensitivity, specificity, PPV, and NPV up to 100%, 88%, 86%, and 100% by adding the PET component to MRI assessment. Compared with other studies (2,6,7), our results for sensitivity and specificity (50% and 70.6%) for the assessment of the MRI part of combined PET/MRI seem to be low. According to our patient characteristics with inconclusive findings in previously performed MRI, our study focused on diagnostically difficult cases. Diagnostic certainty was significantly higher with combined PET/MRI vs. MRI alone. However, our results also reflect the difficulty of MRI alone in the exclusion of spondylodiscitis indicated by being false-positive in five cases owing to osteochondritis, spondylitis, degenerative disc space narrowing, and fractures. With combined PET/MRI, there were no false-negative results, indicating that combined $^{18}$F-FDG PET/MRI may be of most use in patients suspected of having spondylodiscitis with inconclusive MRI findings. Simultaneous $^{18}$F-FDG-PET/MRI was false-positive in two patients with spondylitis and erosive osteochondritis. Both patients showed a focally elevated $^{18}$F-FDG uptake and T2WI hyperintense and T1WI hypointense MRI signals. Those MRI signal patterns can equally be found in inflammatory processes and degenerative diseases (11,18,19). Ohtori et al. (12) and Gratz et al. (20) recommended $^{18}$F-FDG-PET for distinguishing between active inflammation of the spine and degenerative changes. These results were confirmed by our study as in 3/4 patients with erosive osteochondritis, active inflammation was correctly excluded with $^{18}$F-FDG PET/MRI. Frequent causes of false-positive findings in $^{18}$F-FDG PET are reported in
healing bone and adjacent tissues after trauma or manipulation after surgery or biopsy (21,22). The induced signal patterns are part of inflammatory processes and can imitate primary infections (23). Nevertheless, in these cases, no histopathologic results were available as a gold standard, so a low level of uncertainty remains.

In contrast to CT and MRI, $^{18}$F-FDG uptake in PET is not or minimally hampered by metallic implant-associated artifacts. Thus, combined $^{18}$F-FDG-PET/MRI may be advantageous in spondylodiscitis patients with susceptibility artifacts. In our study, in five patients, internal fixation material was found at the spine level of interest rendering the MRI data unevaluable. Nevertheless, in 3/5 cases, a consensus final imaging diagnosis was achieved as a result of the additional PET information. In the remaining two cases, a final evaluation could not be realized because of severe susceptibility artifacts in the spondylodiscitis-suspected region.

Similar to the data of Fuster et. al. (8), which demonstrated a statistically significant difference in mean SUV$_{\text{max}}$ between infected and non-infected spondylodiscitis patients (SUV$_{\text{max}}$ 6.5 and 3.6, respectively), semiquantitative assessment of $^{18}$F-FDG-PET in our study demonstrated significant differences of absolute SUV$_{\text{mean}}$ and SUV$_{\text{max}}$ in the affected disc compared with cases with “no spondylodiscitis.” Additionally, a SUV$_{\text{max}}$ ratio threshold of 2.1 resulted in 92% sensitivity and 88% specificity for the correct diagnosis of spondylodiscitis. For further evaluation of spondylodiscitis patients, these data may help to improve discrimination between infected and non-infected spinal discs. As described by Nakahara et al. (13), accurate delineation of areas of active spondylodiscitis infection may also be useful to narrow the surgical field.
In our study, absolute values of $SUV_{\text{mean}}$ and $SUV_{\text{max}}$ were significantly correlated with CRP. However, there was no significant difference in leukocyte count or CRP between patients with and without spondylodiscitis. Clinical and paraclinical course as well as imaging patterns of degenerative diseases and low-grade infections can be very similar (11). It is well known that inflammatory markers do not serve as pathognomonic parameters in diagnosing spondylodiscitis (24,25).

One limitation of our study needs to be mentioned: histopathology was not available in all patients because surgery/biopsy was only performed in six cases. Some uncertainty remains in the cases with clinical follow-up.

Future spondylodiscitis imaging research should also focus on a possible role of $^{18}$FDG PET/MRI for early response assessment of the response towards antibiotic therapy. As demonstrated by Skanjeti et al. (17), $^{18}$F-FDG-PET is more accurate and more specific than MRI in the treatment assessment of spondylodiscitis, suggesting that $^{18}$F-FDG-PET should be preferred over MRI for determining when treatment can be safely discontinued. Similar results were found in a study by Nanni et al. (26) analyzing 34 spondylodiscitis patients and determining $SUV_{\text{max}}$ of a baseline $^{18}$F-FDG PET/CT ($SUV_{\text{1}}$) and of a second $^{18}$F-FDG PET/CT after 2–4 weeks of therapy ($SUV_{\text{2}}$). $^{18}$F-FDG PET was found to be a useful tool in identifying responders, in which the use of delta-$SUV_{\text{max}}$ provided the highest sensitivity and specificity (82%) for identifying responders compared with the change of CRP level during therapy, which only showed a sensitivity of 67%. According to these results, a decrease in $SUV_{\text{max}}$ of at least 34% is strongly predictive of a complete response. This may have a strong impact on the clinical management of spondylodiscitis patients because initial CRP is known to be false-negative in a significant percentage of patients.
CONCLUSION

The use of combined $^{18}$F-FDG-PET/MRI significantly increases the diagnostic certainty for detection of spondylodiscitis, especially in cases with inconclusive MRI findings. Combined $^{18}$F-FDG-PET/MRI showed 100% sensitivity and may be most relevant in the detection of early cases of spondylodiscitis. With this “one-stop-shop” approach, the improved diagnostic certainty and—if needed—the possibility for a prompter initiation of the proper treatment are the main benefits for spondylodiscitis patients.
REFERENCES


FIGURE LEGENDS

FIGURE 1. Simultaneous $^{18}$F-FDG PET/MRI in a 71-year-old female patient with final diagnosis of spondylodiscitis. MRI was inconclusive: (A) TIRM with typical hyperintense signal alterations in the intervertebral disc level L4/5 (arrow) and a moderate post-contrast MRI T1-WI signal (B). $^{18}$F-FDG PET and combined $^{18}$F-FDG PET/MRI (C,D) show a focally elevated uptake in the affected disc (arrow; SUV$_{max}$ 8.14 and SUV$_{mean}$ 3.99) as a sign of active inflammation. TIRM turbo inversion recovery magnitude.
FIGURE 2. Simultaneous $^{18}$F-FDG PET/MRI in a 59-year-old female patient with suspected spondylodiscitis in level L2/3 and final diagnosis of “no spondylodiscitis” but post-fracture changes. Single MRI was inconclusive: MRI, TIRM (A) with typical hyperintense signal alterations in intervertebral disc level L2/3 (arrow) but poor post-contrast signal in MRI T1-weighted (B). $^{18}$F-FDG PET and fused $^{18}$F-FDG PET/MRI (C,D) show no elevated tracer uptake in the suspected disc (arrow, SUV$_{\text{max}}$ 3.08 and SUV$_{\text{mean}}$ 1.77), thus active inflammation was excluded. TIRM turbo inversion recovery magnitude.
FIGURE 3. Receiver operating characteristics analysis for SUV$_{\text{max}}$ ratio for differentiation of “spondylodiscitis“ and “no spondylodiscitis“ in combined $^{18}$F-FDG PET/MRI. SUV$_{\text{max}}$ ratio threshold of 2.1 resulted in 92% sensitivity and 88% specificity for the correct diagnosis of spondylodiscitis (area under the curve=0.95).
FIGURE 4. $^{18}$F-FDG PET SUV$_{\text{max}}$ and SUV$_{\text{mean}}$ values depending on reference standard diagnosis. The ends of the box represent the 25th and 75th percentiles (or 1st and 3rd quartiles), while the center line represent the median. The 75th minus the 25th percentile equals the Interquartile Range (IQR), and the ends of the whiskers are placed at 1.5 times the IQR. Any values lying outside these boundaries are considered outliers.
TABLES

Table 1. MRI sequence parameters used in combined whole-body PET/MRI

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Orientation</th>
<th>TR [ms]</th>
<th>TE [ms]</th>
<th>TA [min]</th>
<th>Voxel size [mm]</th>
<th>Remarks</th>
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<tr>
<td>TIRM</td>
<td>Sagittal</td>
<td>3500</td>
<td>43</td>
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<td>1.1 x 0.8 x 4.0</td>
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<tr>
<td>T1WI TSE</td>
<td>Sagittal</td>
<td>523</td>
<td>10</td>
<td>1:45</td>
<td>0.8 x 0.6 x 4.0</td>
<td>pre and post</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>contrast</td>
</tr>
<tr>
<td>T2WI TSE</td>
<td>Transverse</td>
<td>4000</td>
<td>116</td>
<td>3:22</td>
<td>0.8 x 0.6 x 4.0</td>
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<tr>
<td>T1WI TSE</td>
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<td>12</td>
<td>2:42</td>
<td>0.7 x 0.6 x 4.0</td>
<td>fat-saturated</td>
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*TIRM* turbo inversion recovery magnitude, *TR* repetition time, *TE* echo time, *TA* acquisition time, *T1WI/T2WI* TSE T1-/T2-weighted turbo spin-echo
Table 2. Patient characteristics

<table>
<thead>
<tr>
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<th>Spondylodiscitis</th>
<th>No spondylodiscitis</th>
<th>P value</th>
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<tr>
<td>No. of suspected regions</td>
<td>12</td>
<td>17</td>
<td></td>
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<tr>
<td>Localization</td>
<td>1/0/10</td>
<td>1/4/12</td>
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<tr>
<td>CRP, mean ± SD (mg/dL)</td>
<td>51.0 ± 60.8</td>
<td>20.2 ± 22.5</td>
<td>0.053*</td>
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<td>Leucocyte count, mean ± SD (x10^9/L)</td>
<td>8.1 ± 2.3</td>
<td>8.1 ± 2.6</td>
<td>0.817*</td>
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SD standard deviation, CRP C-reactive protein (normal: < 5 mg/l), * Mann–Whitney U-test
Table 3. Diagnostic Comparison of MRI only and of combined $^{18}$F-FDG PET/MRI for the diagnosis of “spondylodiscitis”.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>MRI</th>
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<tr>
<td>Spondylodiscitis</td>
<td>TP: 6</td>
<td>TP: 12</td>
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<tr>
<th>Characteristics</th>
<th>MRI</th>
<th>PET/MRI</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>50.0</td>
<td>100</td>
<td>0.031*</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>70.6</td>
<td>88.2</td>
<td>0.025*</td>
</tr>
</tbody>
</table>

TP true positive, FP false positive, TN true negative, FN false negative; *Exact McNemar’s Test
The use of simultaneous $^{18}$F-FDG-PET/MRI for the detection of spondylodiscitis

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