

Review Article

[¹⁸F]-FDG-PET for the assessment of major infectious disorders of the musculoskeletal system

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Abstract: Infections of the musculoskeletal system contribute substantially to global morbidity and healthcare expenditure, and conventional imaging frequently falls short of providing the sensitivity and specificity required for early diagnosis in complicated presentations. In this review, we examine the clinical role of [¹⁸F]-fluorodeoxyglucose positron emission tomography paired with computed tomography (FDG-PET/CT) or magnetic resonance imaging (FDG-PET/MRI) in the workup of these infections. Drawing on the published literature, we summarize evidence across osteomyelitis, spondylodiscitis, septic arthritis, and prosthetic joint infection, with attention to reported diagnostic performance and to where each hybrid technique appears to be most useful. Across infection types, FDG-PET/CT consistently shows good diagnostic accuracy, is widely available, and tolerates metallic hardware well, whereas FDG-PET/MRI, though still investigational and confined to a small number of academic centers, offers improved soft-tissue contrast and lower cumulative radiation, which may be advantageous in selected cases such as spondylodiscitis or in patients requiring serial imaging. The available comparative evidence remains limited, much of it drawn from small, single-center cohorts. We therefore emphasize that current data should be viewed as preliminary. Modality choice in practice depends on the clinical question, patient factors, local availability, and cost, rather than on a one-size-fits-all preference.

Keywords: FDG-PET, inflammation, infection, musculoskeletal, orthopedic

Introduction

Worldwide, infections of the musculoskeletal system continue to drive considerable morbidity, lasting functional impairment, and healthcare expenditure [1]. Because these conditions are clinically heterogeneous and frequently progress quickly, prompt and accurate diagnosis matters: it shapes outcomes, limits long-term disability, and helps contain downstream costs of care. Conventional imaging includes plain radiographs, CT, and MRI. Each has its strengths and blind spots. Although these techniques are good at depicting structural pathology, they are less able to separate infectious inflammation from sterile reactive change, and they often miss early disease before macroscopic structural alterations appear [2].

Progress in molecular imaging has brought [¹⁸F]-Fluorodeoxyglucose positron emission tomography (FDG-PET) into clinical workups for the early evaluation of musculoskeletal infections. The technique is sensitive to the heightened glucose metabolism of activated inflammatory cells and precise localization of abnormalities [3]. FDG-PET has high sensitivity, often approaching 94-100% in published series for musculoskeletal infections such as

chronic osteomyelitis and acute and subacute bone and soft tissue infection when used in conjunction with CT (FDG-PET/CT), making this functional imaging modality particularly valuable for detecting early or subtle pathological changes that may otherwise evade conventional imaging with CT and MRI [3]. FDG-PET also has high specificity, reported to be between 75-99% when used to image acute and subacute bone and soft tissue infection [3]. FDG-PET/CT combines metabolic and anatomical data in a single scan, offering rapid whole-body imaging that captures both disease distribution and metabolic activity [4]. FDG-PET/MRI, while similarly leveraging metabolic information, provides superior soft tissue contrast resolution and excels in anatomically complex regions such as the spine, pelvis, and small joints of the hands and feet [5-7].

The objective of this review is to evaluate the role of FDG-PET in the diagnosis and management of infections of the musculoskeletal system. Specifically, this review explores the current applications and emerging roles of FDG-PET/CT and FDG-PET/MRI in infectious disorders such as osteomyelitis, spondylodiscitis, septic arthritis, and prosthetic joint infections (**Table 1**).

Table 1. FDG-PET/CT and FDG-PET/MRI for the assessment of infectious musculoskeletal disorders

Study	Imaging Modality	Condition	Sample Size	Sensitivity (%)	Specificity (%)	Key Findings
OSTEOMYELITIS						
Hulsen et al., 2022 [25]	FDG-PET/MRI	Chronic Osteomyelitis	36	78	100	High specificity; valuable alternative to PET/CT; superior soft tissue characterization
Hulsen et al., 2019 [31]	FDG-PET/MRI	Chronic Osteomyelitis	5	Not reported	Not reported	Prospective case series; PET/MRI more valuable for surgical planning than PET/CT
Wenter et al., 2016 [26]	FDG-PET/CT	Chronic Osteomyelitis & Implant Infection	215	88	76	Large-scale validation; superior to standalone PET; PPV: 76%, NPV: 89%, Accuracy: 82%
Kagna et al., 2012 [29]	FDG-PET/CT	Diabetic Foot Osteomyelitis	39	100 (patient); 100 (lesion)	92 (patient); 93 (lesion)	Accuracy: 95% (patient), 96% (lesion); effectively differentiated from Charcot neuroarthropathy
Xu et al., 2024 [48]	FDG-PET/CT	Chronic Recurrent Multifocal Osteomyelitis (Pediatric)	21	Not reported	Not reported	PET detected 38/131 lesions not visible on CT; per-patient SUV _{max} range 1.2-10.9 overlaps with bacterial osteomyelitis, limiting quantitative thresholds
Familiari et al., 2011 [28]	FDG-PET/CT vs WBC Scintigraphy	Diabetic Foot Osteomyelitis	13	43 (PET/CT); 86 (WBC)	67 (PET/CT); 100 (WBC)	Sequential PET/CT accuracy 54% vs WBC scintigraphy 92%; no reliable SUV _{max} criteria; WBC scintigraphy superior for diabetic foot
VERTEBRAL OSTEOMYELITIS/SPONDYLODISCITIS						
Fahnert et al., 2016 [30]	FDG-PET/MRI	Spondylodiscitis	30	100	88	Selected cohort with previously inconclusive MRI; 28/30 evaluable; PET/MRI superior to MRI alone (sens 50%, spec 71%); diagnostic certainty 93.1% vs 62.1% (P < 0.001)
Kouijzer et al., 2018 [32]	FDG-PET/CT	Vertebral Osteomyelitis	32	100	83.3	Prospective head-to-head vs MRI; PPV: 90.9%, NPV: 100%; detected metastatic infection in 50% of patients
Smids et al., 2017 [35]	FDG-PET/CT	Spondylodiscitis	68	96	95	Superior to MRI (67%/84%); no timing dependency on symptom onset
Treglia et al., 2020 [34]	FDG-PET/CT	Spinal Infection	396 (meta-analysis of 12 studies; 833 in systematic review)	94.8	91.4	Systematic review and bivariate meta-analysis; high accuracy for spondylodiscitis diagnosis and treatment monitoring
Ito et al., 2010 [71]	FDG-PET/CT	Infectious Spondylitis	29	Not reported	Not reported	Altered management in 52% of cases; guided antibiotic therapy, biopsy, and surgical decisions
SEPTIC ARTHRITIS						
Friederichs et al., 2010 [72]	FDG-PET/CT	Shoulder Septic Arthritis	1 (case report)	Not reported	Not reported	Identified shoulder infection and plantar soft tissue infection as entry point
Gorospe et al., 2017 [73]	FDG-PET/CT	Sternoclavicular Septic Arthritis	1 (case report)	Not reported	Not reported	Detected septic arthritis when initial conventional CT imaging was negative
PROSTHETIC JOINT INFECTIONS						
Kwee TC et al., 2008 [43]	FDG-PET	Prosthetic Hip & Knee	635 (meta-analysis)	82.1	86.6	Comprehensive meta-analysis of PJI detection
Roschke et al., 2022 [44]	FDG-PET/CT	Hip or Knee PJI	104	Not reported	Not reported	PET-CT verified PJI in 84.2% of patients preoperatively (87.1% TKR, 81.5% THR); additional infectious foci detected in 53.8% of patients
Kwee RM et al., 2018 [45]	FDG-PET/CT	Hip Prostheses	78	Not reported	Not reported	Adding ¹⁸ F-FDG PET/CT significantly increased diagnostic AUC over conventional tests: radiography (+0.212, P=0.001), aspiration culture (+0.126, P=0.032), aspiration WBC count (+0.191, P=0.035); ESR/CRP (+0.076, P=0.072)
Kiran et al., 2019 [46]	FDG-PET/CT	Painful Unilateral THAs	130	94.87	38.46	High sensitivity for preoperative PJI evaluation; high false-positive rate requires careful interpretation

Abbreviations: FDG, fluorodeoxyglucose; PET, positron emission tomography; CT, computed tomography; MRI, magnetic resonance imaging; PJI, prosthetic joint infection; PPV, positive predictive value; NPV, negative predictive value; SUV, standardized uptake value; THA, total hip arthroplasty.

FDG-PET for the assessment of infectious musculoskeletal disorders

Most bone and joint infections are caused by *Staphylococcus aureus*, *Streptococcus* species, and gram-negative organisms, and they present clinically as osteomyelitis, septic arthritis, or prosthetic joint infection (PJI) [8, 9]. Timely recognition and treatment matter because delays cost mobility, increase the risk of long-term disability, and can push patients toward rehabilitation or repeat surgery. In the worst cases, an undetected focus seeds bacteremia or sepsis. PJI adds a particular challenge: bacterial biofilms on implant surfaces blunt antibiotic penetration and host defense, so eradication is rarely achieved with antibiotics alone [10, 11]. The downstream cost is substantial, both in dollars and in hospital throughput [12]. Patients themselves report worse function, lower quality of life, and a higher likelihood of needing assisted living after PJI [13]. Plain films still have a role in ruling out tumor or fracture, but bony changes typically take 10 to 21 days to become radiographically apparent, which limits the sensitivity (43-75%) and specificity (75-83%) of radiographs for early disease [14-16]. MRI performs better in the first week of illness, picking up marrow signal change as early as 3-5 days from onset, with reported sensitivity of 82-100% and specificity of 75-96% [14]. When multifocal disease is suspected, bone scintigraphy is warranted [17]. The choice between PET/CT and PET/MRI depends on the type of osteomyelitis, patient-specific factors, the urgency of the clinical question, and what is locally available. PET/CT is well suited to whole-body assessment for distant infectious foci, particularly in bacteremia or multifocal disease, with strong tolerance to metal artifact [18]. This makes it especially useful in periprosthetic and post-surgical evaluation, and benefits from broader institutional availability and more mature interpretation criteria [19]. The CT component additionally provides high-resolution evaluation of cortical bone involvement and sequestra formation. FDG-PET/MRI provides enhanced soft tissue characterization for precise infection delineation and abscess identification, which is particularly valuable in spinal infections where epidural extension influences treatment decisions [20]. PET/MRI also delivers substantially lower radiation exposure than FDG-PET/CT, and superior differentiation between active infection and post-treatment changes through detection of bone marrow edema and fluid collections [21-23].

Patient-specific factors also influence the choice. In pediatric patients, the lifetime radiation risk is greater, making dose minimization a priority [24].

On balance, urgency favors PET/CT for acute presentations requiring same-day answers, while PET/MRI may be more useful in chronic disease and surgical planning where soft-tissue detail matters. Practical caveats include availability (PET/MRI is concentrated in specialized centers), reader expertise, and cost (though comprehensive

single-session imaging may offset some of the higher upfront costs) [21-23].

Chronic osteomyelitis

In selected centers with the necessary infrastructure, FDG-PET/MRI may offer advantages for evaluating chronic osteomyelitis, given its richer soft-tissue contrast and a lower radiation footprint. These features matter when patients are likely to undergo repeated imaging over a prolonged treatment course. We note, however, that the supporting evidence is preliminary and largely confined to small, single-center series. The first quantitative report on FDG-PET/MRI in this setting came from Hulsén and colleagues, who described a sensitivity of 78%, specificity of 100%, and overall accuracy of 86% in chronic osteomyelitis [25].

PET/CT remains a useful tool for chronic osteomyelitis, particularly where PET/MRI is unavailable. Wenter and colleagues demonstrated that FDG-PET/CT has higher sensitivity and specificity compared to stand-alone PET in osteomyelitis diagnosis [26].

Distinguishing Charcot neuroarthropathy from osteomyelitis is one of the harder calls in the diabetic foot, and PET/CT contributes to this discrimination by combining uptake pattern, intensity, and anatomic correlation, though uptake alone is non-specific and must be interpreted in clinical context. In comparative data, FDG-PET achieved sensitivity and accuracy of 100% and 93.8% for this distinction, against 76.9% and 75% for MRI [27].

However, not all studies support such high diagnostic accuracy for FDG-PET/CT in the diabetic foot. In a pilot study comparing sequential ^{18}F -FDG PET/CT with $^{99\text{m}}\text{Tc}$ -exametazime white blood cell (WBC) scintigraphy in 13 diabetic patients with clinically suspected osteomyelitis, Familiari et al. found that FDG-PET/CT had a sensitivity of only 43%, specificity of 67%, and diagnostic accuracy of 54% for osteomyelitis using quantitative maximum standardized uptake value (SUV_{max}) criteria [28]. In contrast, WBC scintigraphy achieved 86% sensitivity, 100% specificity, and 92% diagnostic accuracy using target-to-background ratio criteria. Even combining visual PET and CT assessment improved accuracy only to 62%. A typical temporal pattern for ^{18}F -FDG uptake could not be defined, and prolonged prior antibiotic therapy (mean 45 days) may have contributed to the low FDG uptake. These findings suggest that WBC scintigraphy remains the nuclear medicine gold standard for diabetic foot osteomyelitis, and that FDG-PET/CT results in this setting should be interpreted with caution (Figures 1, 2).

By contrast, Kagna and colleagues reported per-patient sensitivity, specificity, and accuracy of 100%, 92%, and 95% for FDG-PET/CT in 39 patients with suspected diabetic foot osteomyelitis, with reliable differentiation from Charcot neuroarthropathy [29]. Reconciling the divergent

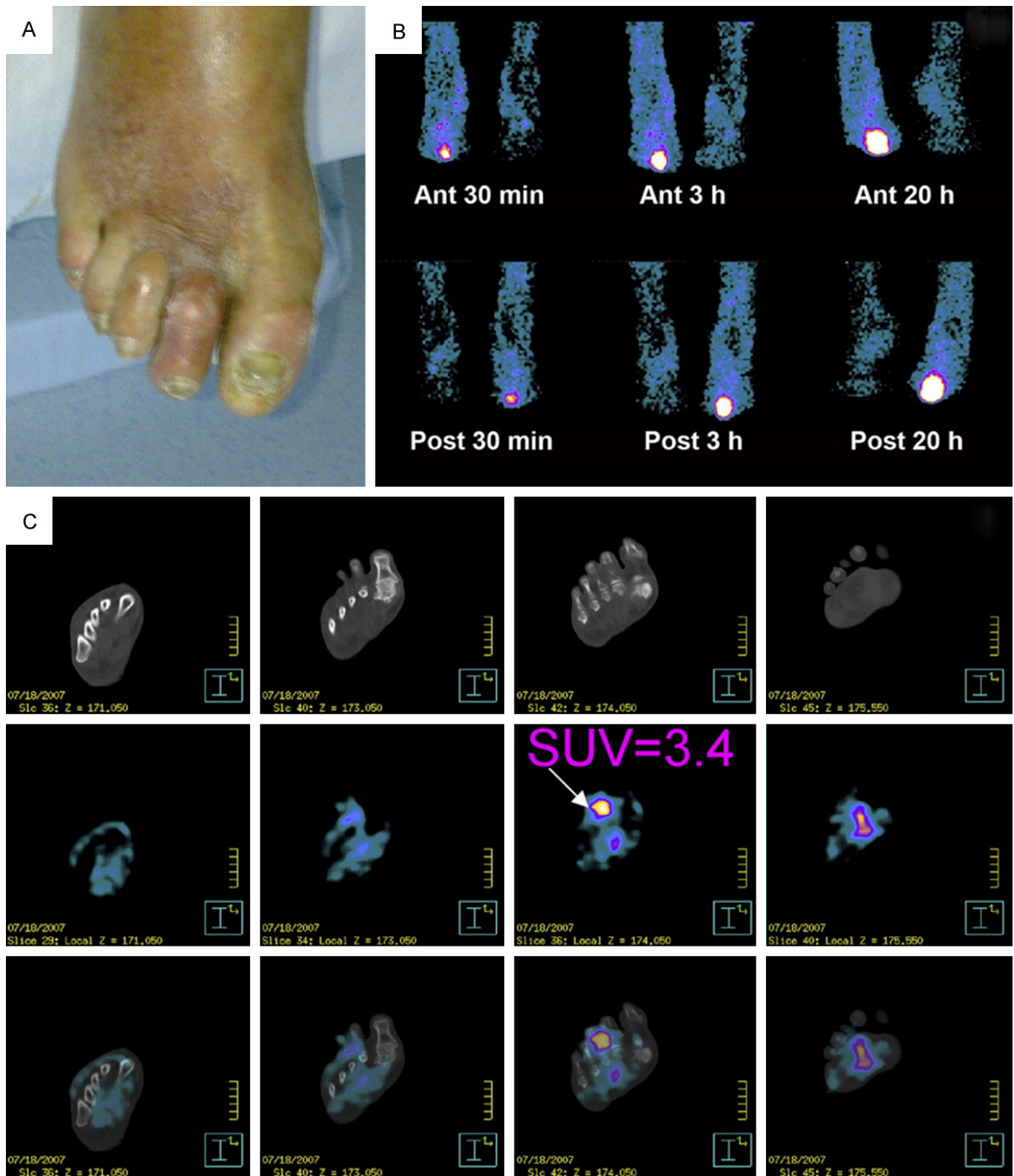


Figure 1. Concordant positive results for osteomyelitis in a diabetic foot patient. (A) Clinical image. (B) Anterior and posterior WBC scintigraphy at 30 min, 3 h, and 20 h showing T/B ratio > 2.0 increasing over time, consistent with osteomyelitis. (C) Transaxial ^{18}F -FDG-PET/CT at 1 h showing $\text{SUV}_{\text{max}} = 3.4$ with CT-confirmed bone localization. Reproduced from [28] © SNMMI.

findings of Kagna et al. and Familiari et al. is important for placing FDG-PET/CT in clinical context for the diabetic foot. Several methodological factors likely account for the gap. First, antibiotic exposure differed in important ways.

Familiari et al. reported a mean prior antibiotic duration of 45 days, with treatment suspended one week before imaging, and explicitly invoked prolonged antimicrobial therapy as a probable explanation for low FDG uptake.

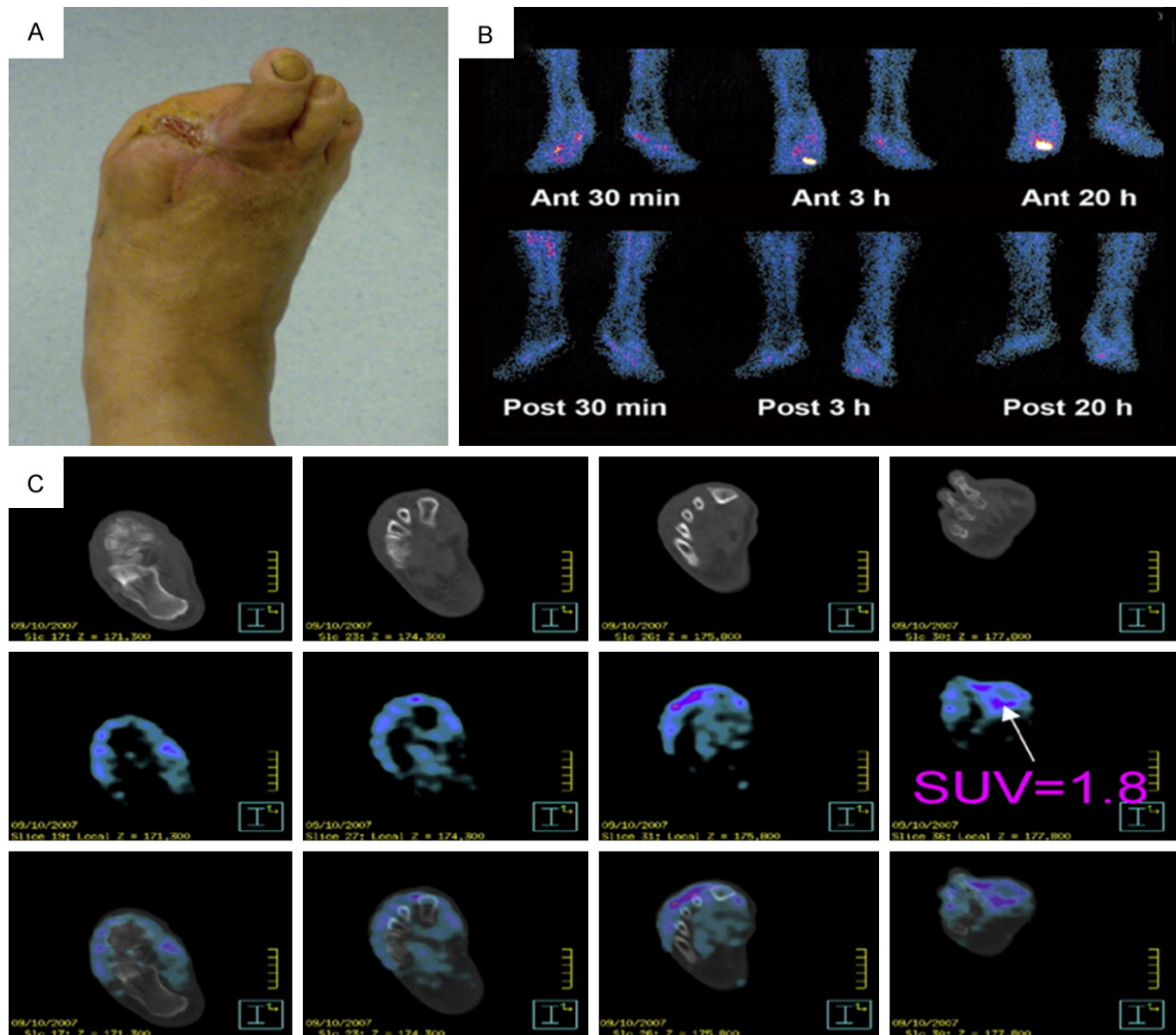


Figure 2. Discordant results in a diabetic foot patient with biopsy-proven osteomyelitis. (A) Clinical image. (B) WBC scintigraphy at 30 min, 3 h, and 20 h shows T/B ratio > 2.0 increasing over time, correctly identifying osteomyelitis. (C) ^{18}F -FDG-PET/CT at 1 h shows $\text{SUV}_{\text{max}} = 1.8$, falsely negative for osteomyelitis. Reproduced from [28] © SNMMI.

Kagna et al. likewise had a substantial proportion of patients on antibiotic therapy at the time of imaging (29 of 39, roughly three-quarters), although the duration of antibiotic exposure was not reported, leaving open whether the two cohorts were truly comparable in this regard [29]. Second, the interpretation mechanisms differed. Familiari et al. applied a quantitative threshold-based approach ($\text{SUV}_{\text{max}} > 2.0$ at 1 and 2 hours, increasing over time) within a sequential acquisition protocol [28]. Kagna et al. instead classified lesions on the basis of focal versus diffuse uptake patterns and anatomic localization on fused PET/CT, with SUV_{max} measured but not used as the primary diagnostic threshold [29]. Third, the reference standards and sample composition differed. Kagna et al. used a composite of histopathology and bacteriology of surgical samples together with clinical and imaging follow-up

across 39 patients with 46 suspected sites [29]. Familiari et al. anchored final diagnosis to biopsy or surgery within one week of imaging in a smaller, highly selected cohort of 13 patients with a high pretest clinical suspicion of osteomyelitis [28]. Fourth, the threshold for what counts as a positive scan, the timing of imaging relative to symptom onset, and the prevalence of confounders such as Charcot neuroarthropathy can all push sensitivity and specificity in opposite directions. Taken together, these differences suggest that the apparent discrepancy reflects methodology and patient selection more than a contradiction in the underlying biology, and they support a cautious, context-dependent role for FDG-PET/CT in the diabetic foot, particularly when interpretation accounts for antibiotic exposure, pattern of uptake, and anatomic correlation. FDG-PET/MRI may be considered



Figure 3. Lumbar spine imaging in a 43-year-old woman on hemodialysis with *S. aureus* bacteremia and back pain. (A) ^{18}F -FDG-PET and (C) ^{18}F -FDG-PET/CT show increased uptake at T12-L1 (score 4). (B) T1-weighted Gd-enhanced MRI shows subtle disc and pervertebral enhancement and subtle interruption of the T12 and L1 anterior endplates (score 4). The initial MRI was reported as false-negative for vertebral osteomyelitis (psoas abscess only), reevaluated PET/CT and follow-up MRI confirmed vertebral osteomyelitis at T12-L1. Reproduced from [32] under Creative Commons Attribution 4.0 International License.

when soft-tissue characterization is critical or when cumulative radiation is a concern, although evidence in this specific setting remains limited.

Spinal infections (vertebral osteomyelitis and spondylodiscitis)

Early experience with FDG-PET/MRI in musculoskeletal infection, including vertebral osteomyelitis, is encouraging, although the data remain limited and largely investigational. By coupling the soft-tissue contrast of MRI with the metabolic information from PET in a single acquisition, the technique can in principle reduce radiation exposure relative to PET/CT and, in selected patients, broaden the diagnostic field to include disseminated foci, an attractive feature in systemically ill or complex cases [25, 30, 31].

Where PET/MRI is unavailable, PET/CT remains a workable substitute. Kouijzer and colleagues conducted a prospective head-to-head comparison of PET/CT and MRI alone in 32 patients with suspected vertebral osteomyelitis, performing both scans within 48 hours of each other and using blinded, independent readers [32]. FDG-PET/CT sensitivity, specificity, positive predictive value, and negative predictive value for diagnosing vertebral osteomyelitis were 100%, 83.3%, 90.9%, and 100%, respectively. This was comparable to MRI alone, which had a sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 91.7%, 95.2%, and 100%, respectively. FDG-PET/CT can serve as a complementary or even corrective imaging modality. In one patient, the initial MRI identified only a psoas abscess and was false-negative for vertebral osteomyelitis (**Figure 3**). FDG-PET/CT demonstrated hypermetabolism at T12-L1, prompting reevaluation with follow-up MRI that confirmed vertebral osteomyelitis. In another patient, MRI demonstrated Modic

type 1 changes at multiple levels (**Figure 4**). FDG-PET/CT argued against infection, a finding corroborated by long-term follow-up. This case highlights the specificity of FDG-PET/CT in preventing unnecessary treatment based on false-positive MRI findings.

In the Kouijzer comparison, although PET/CT and MRI both achieved excellent sensitivity (100%) and negative predictive value, they offered different strengths [32]. MRI was better at picking up small epidural or paraspinal abscesses, whereas PET/CT uniquely identified metastatic infectious foci in roughly half of the patients, reflecting its whole-body field of view, which is particularly relevant when bacteremia is suspected. PET/CT also tolerates metallic hardware, an asset in spinal practice where instrumentation is common.

Turning to spondylodiscitis specifically, a related condition complicated by dual involvement of the vertebral body and the adjacent disc, preliminary data suggest that FDG-PET/MRI may also be useful in this setting. Fahnert and colleagues, using simultaneous FDG-PET/MRI in a prospective cohort of 30 patients (28 evaluable) with previously inconclusive MRI and suspected spondylodiscitis, reported diagnostic performance (sensitivity 100%, specificity 88%, PPV 86%, NPV 100%) that exceeded that of MRI alone (sensitivity 50%, specificity 71%) in the same patients [30]. **Figure 5** demonstrates a use case of FDG-PET/MRI for the diagnosis of spondylodiscitis when MRI alone was not sufficient.

The improvement appears to come from the complementary information captured by the two modalities: the MRI component picked up bone-marrow edema, endplate erosions, and epidural extension in all confirmed cases, while the PET signal remained detectable in both acute and subacute disease, even in patients who had been on anti-

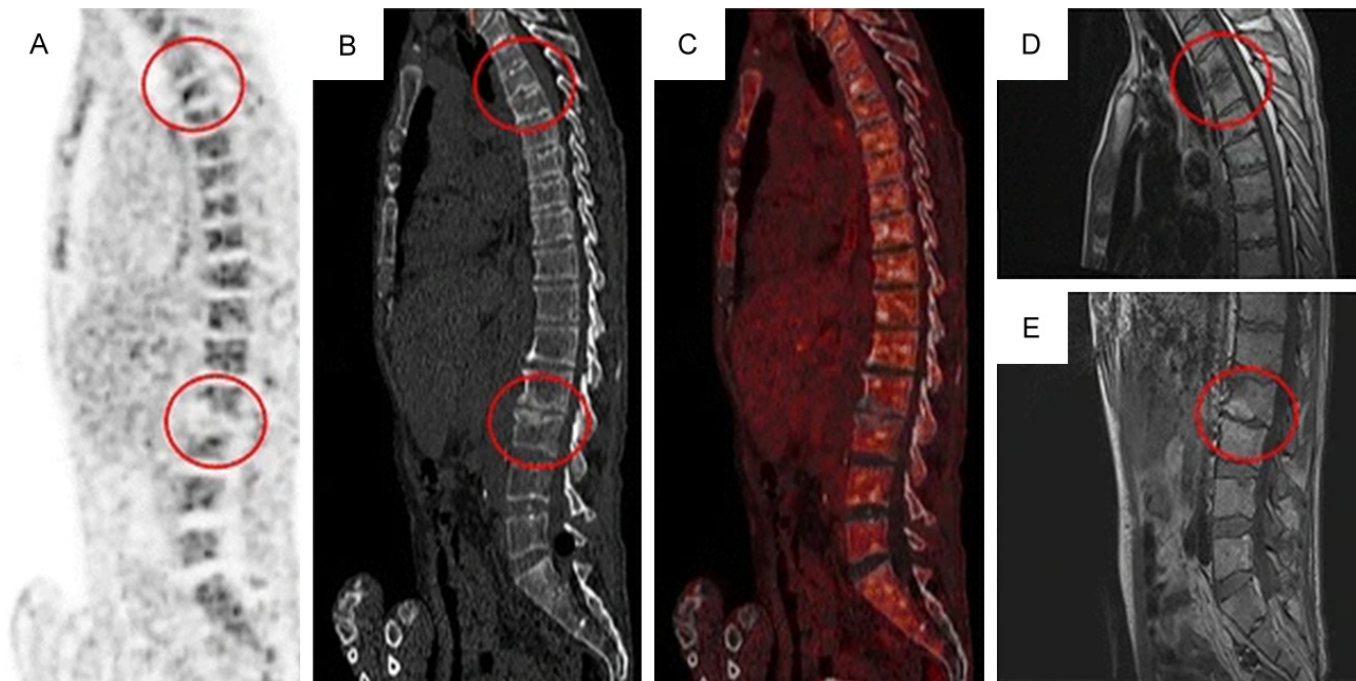


Figure 4. Spinal imaging in a 61-year-old man admitted with *S. aureus* endocarditis and back pain. (A) ^{18}F -FDG-PET, (B) CT, and (C) ^{18}F -FDG-PET/CT show degenerative changes at T3-T4 and L2-L3. (D, E) Pre- and post-contrast T1-weighted Gd-enhanced MRI show Modic type 1 changes at the same levels. Initial MRI reported vertebral osteomyelitis at T3-T4 and L2-L3, while PET/CT was negative. On reevaluation, both modalities were negative, and long-term follow-up indicated that the back pain was attributable to degenerative changes. Reproduced from [32] under Creative Commons Attribution 4.0 International License.

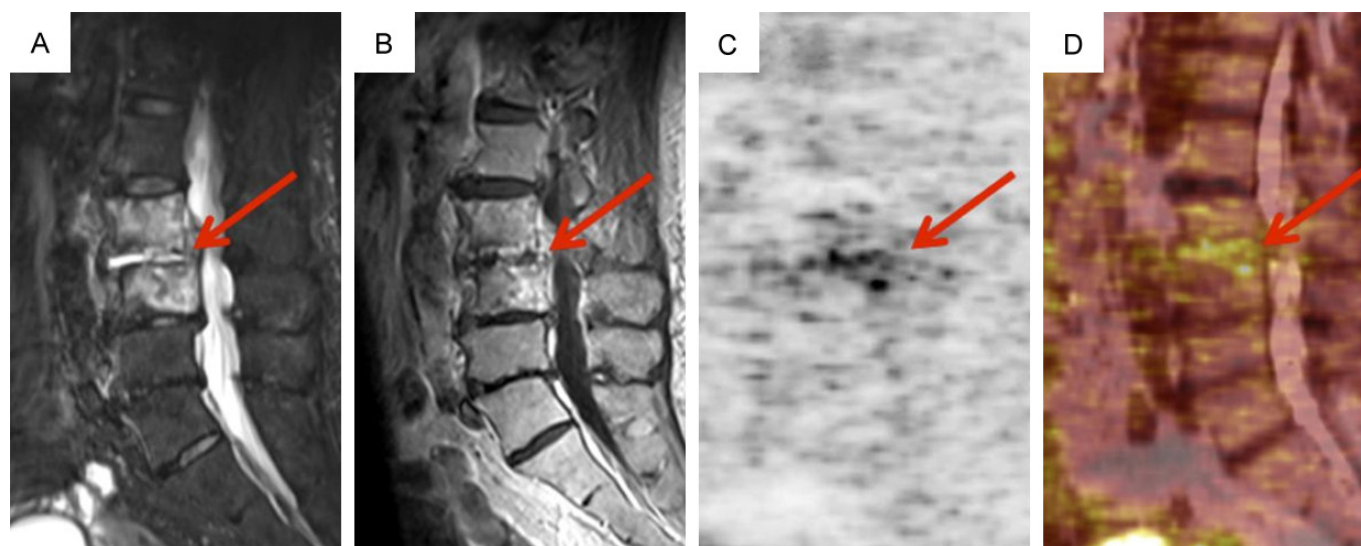


Figure 5. Simultaneous ^{18}F -FDG-PET/MRI in a 71-year-old woman with a final diagnosis of spondylodiscitis after inconclusive MRI. (A) Turbo inversion recovery magnitude (TIRM) shows the typical hyperintense signal at L4-L5 (arrow). (B) T1-weighted MRI shows moderate contrast enhancement (arrow). (C) ^{18}F -FDG-PET and (D) combined ^{18}F -FDG-PET/MRI reveal focally elevated uptake in the affected disc ($\text{SUV}_{\text{max}} = 8.14$, $\text{SUV}_{\text{mean}} = 3.99$), indicating active inflammation. Reproduced from [30] © SNMMI.

biotics for up to 14 days before imaging. The authors used a standardized protocol with dedicated spine coils and Dixon-based attenuation correction to limit susceptibility artifact at the bone-disc interface.

These refinements improved localization of infection foci and, in the cohort studied, yielded significantly higher dia-

gnostic certainty than MRI alone (93.1% versus 62.1%, $P < 0.001$), with histologic confirmation available in 6 of 28 evaluable patients and clinical follow-up serving as the reference standard for the remainder. While these findings are promising, it is important to emphasize that they come from a small, single-center cohort ($n=30$). FDG-PET/MRI should therefore be regarded as an investigational

tool that may offer advantages in selected centers and selected patients with pyogenic spondylodiscitis, rather than an established first-line modality, particularly in the context of prolonged antibiotic courses (typically 6-12 weeks) and possible surgical intervention [33].

PET/CT, used in tandem with conventional MRI when clinically indicated, also has a role in the diagnostic work-up of pyogenic spondylodiscitis. It can complement inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein, particularly during early therapy-response assessment when these markers remain unrevealing. A bivariate meta-analysis by Treglia and colleagues, pooling data from 12 studies (396 patients) drawn from a systematic review of 26 articles (833 patients), reported pooled sensitivity and specificity of 94.8% and 91.4% for PET/CT in spinal infection [34].

PET/CT also extends into spinal pathology that overlaps with septic arthritis, including facet-joint involvement and related forms of spondylodiscitis. In a comparative study by Smids and colleagues, MRI achieved an overall sensitivity of 67%, specificity of 84%, and accuracy of 72%. Notably, MRI accuracy fell to 58% when performed within two weeks of symptom onset and improved to 82% when performed later. PET/CT, by contrast, achieved 96% sensitivity and 95% specificity, with no clear dependence on the timing of imaging relative to symptom onset [35].

Septic arthritis

Septic arthritis is an emergency in rheumatology and orthopedics, driven by direct bacterial colonization of the joint space, most often by *Staphylococcus aureus* [36].

The basis for using FDG-PET in this setting is straightforward: FDG, a glucose analogue, accumulates wherever glycolytic activity is high, and activated neutrophils and macrophages at sites of bacterial invasion upregulate glucose transport substantially [37-39]. As a result, FDG uptake at sites of septic arthritis tends to exceed that seen in normal bone and marrow or in routine degenerative or healing bone change. PET/CT also tolerates metallic implants better than CT or MRI alone, which is a meaningful practical advantage when imaging patients with prostheses or other hardware where conventional modalities are degraded by artifact [40, 41].

For septic arthritis, PET/CT is generally the more practical option than PET/MRI, both because it picks up coexisting osteomyelitis well and because its faster whole-body coverage helps identify metastatic infectious foci during bacteremia [32].

Prosthetic joint infection

Prosthetic joint infection (PJI) is one of the most consequential complications of joint replacement. It involves microbial colonization of the tissues immediately sur-

rounding the implant, typically presenting with chronic pain, loosening, and progressive functional decline. Treatment usually requires some combination of implant removal, prolonged antibiotic therapy, and staged revision [42]. Much of the diagnostic difficulty stems from the limited ability of conventional imaging and laboratory tests to separate septic from aseptic causes of implant failure, particularly in early or low-grade infection.

Standard tools, including radiographs, CT, MRI, and joint aspiration, each fall short for different reasons. Radiographic changes lag behind tissue destruction. MRI is degraded by metal artifact in the periprosthetic region. Culture-negative aspirates do not exclude infection. FDG-PET/CT helps fill some of these gaps by mapping the metabolic activity of inflammatory infiltrates around the implant. A meta-analysis covering 635 prosthetic hip and knee arthroplasties reported pooled sensitivity and specificity of 82.1% and 86.6% for FDG-PET in PJI detection [43].

PET/CT is generally favored over PET/MRI for PJI workup because of its tolerance to metallic artifact, given that metal-induced signal distortion is the dominant technical constraint in periprosthetic imaging. The combined assessment of hardware position, loosening, and metabolic activity in a single examination is useful for revision planning. PET/MRI may be considered in younger patients who require repeated imaging where cumulative radiation dose is a particular concern, and in selected cases where detailed soft-tissue assessment, for example of pseudotumor formation or neurovascular involvement, directly informs the surgical strategy.

Roschke and colleagues retrospectively analyzed FDG-PET/CT in 104 patients with periprosthetic infection of the hip or knee, focusing on confirmation of local infection and identification of additional infectious foci [44]. They reported that PET/CT successfully verified local PJI in 84.2% of patients when performed preoperatively, with comparable yield in total knee replacement (87.1%) and total hip replacement (81.5%). Pattern of uptake matters for interpretation: in total hip replacement, focal FDG uptake at the middle portion of the femoral component or in the periprosthetic soft tissues is suspicious for infection, while uptake around the prosthesis neck or near the greater trochanter is more often non-specific; in total knee replacement, uptake at the bone-prosthesis interface or in the periprosthetic soft tissues suggests infection, whereas synovial uptake is less specific. In a separate analysis of 78 patients with non-specific clinical presentation of suspected hip prosthesis infection, Kwee and colleagues showed that adding ^{18}F -FDG PET/CT to conventional tests significantly increased diagnostic accuracy as measured by area under the ROC curve: adding PET/CT to radiography increased AUC by 0.212 ($P=0.001$), to aspiration culture by 0.126 ($P=0.032$), and to aspiration white blood cell count by 0.191 ($P=0.035$), supporting its complementary role particularly when aspiration cultures are falsely negative [45].

Beyond initial diagnosis, PET/CT contributes to surgical planning and treatment selection. Whole-body coverage identifies previously unrecognized distant infectious foci in a substantial proportion of patients (53.8% in the Roschke cohort, most commonly in other joints, the lungs, the ENT or dental region, the spine, and the musculoskeletal tissues), with direct implications for antibiotic choice and the operative plan. Kiran and colleagues reported high sensitivity (94.87%) for preoperative PJI evaluation but a notable false-positive rate (specificity 38.46%), which means that a positive scan needs to be interpreted carefully against the rest of the clinical picture [46, 47].

Limitations and considerations of FDG-PET/CT & FDG-PET/MRI

Although both PET/CT and PET/MRI perform well across many of the indications discussed, both have important limitations that should be kept in mind. The most consistent issue is the non-specificity of FDG uptake: tracer accumulation occurs with inflammatory processes of any cause, with post-surgical change, and with healing fractures, all of which can produce false-positive readings. Xu et al. illustrated this challenge in 21 pediatric patients with chronic recurrent multifocal osteomyelitis (CRMO), a sterile autoinflammatory bone disease that can mimic bacterial osteomyelitis clinically and radiologically [48]. Of 131 lesions identified, 38 (29%) were visible on PET but unremarkable on CT, and per-patient SUV_{max} values varied widely (range 1.2-10.9), overlapping substantially with values reported for pyogenic osteomyelitis. The data therefore underscore that FDG uptake alone cannot reliably distinguish sterile inflammatory bone disease from infection, and that strict numeric SUV_{max} thresholds are unreliable. Sensitivity also depends on timing: PET sensitivity falls in early-stage infection with low metabolic activity, particularly during the first 7-10 days of symptoms, before substantial inflammatory cell infiltration [28, 32]. As discussed earlier, Familiari and colleagues found that sequential ^{18}F -FDG PET/CT had significantly lower diagnostic accuracy (54%) compared to WBC scintigraphy (92%) for diabetic foot osteomyelitis, with no reliable SUV_{max} criteria identified for differentiating soft-tissue infection from osteomyelitis [28].

PET/CT has its own technical constraints. The examination typically requires 10-15 minutes of patient immobility, making motion artifact a recurring problem. CT-based soft-tissue resolution is also less than that of MRI. A typical study delivers 5-15 mSv of radiation, depending on scanner and protocol, with the CT component accounting for most of the dose [49-51]. This dose budget meaningfully limits serial imaging, particularly in children and in chronic conditions requiring repeated assessment. Pediatric protocols are bound by published dose-optimization frameworks, including the North American Consensus Guidelines for Pediatric Administered Radiopharmaceutical Activities and the 2016 EANM Pediatric

Dosage Card [52]. Total-body PET systems represent an important development in this regard: their substantially higher sensitivity allows meaningful reductions in injected tracer dose, although the radiation contribution from the CT component is largely unchanged [53]. The clinical positioning is also setting-specific: in acute osteomyelitis, combined WBC plus bone marrow scintigraphy reaches roughly 90% accuracy and may be preferred for straightforward presentations. PET/CT is most useful in chronic osteomyelitis, particularly in patients with prior documented infection and suspected recurrence, or in those whose symptoms have been present for more than six weeks.

PET/MRI carries its own practical drawbacks that deserve explicit emphasis. Acquisition is markedly longer than for PET/CT, with the MRI portion typically taking 20 to 40 minutes compared with roughly 15 seconds to 1 minute for the CT component, and the longer scan can worsen motion artifacts in patients who are unwell, in pain, or unable to hold still [23, 54, 55]. The same prolonged exam time is poorly tolerated by patients with claustrophobia (who may be unable to complete the scan even with anxiolysis) and by acutely ill patients in whom shorter scan times are clinically preferable [56]. Standard MRI safety constraints also apply: many implantable cardiac pacemakers, defibrillators, and certain neurostimulators preclude scanning, and even when a device is labeled MRI-conditional, the necessary workflow may be impractical in busy clinical settings [57, 58]. High-quality musculoskeletal PET/MRI requires dedicated surface coils, and patients with extensive metallic hardware, including multiple prostheses, instrumented spinal fusions, plates and screws, generate susceptibility artifacts that can degrade both the MRI sequences and the PET attenuation correction. This last point is particularly relevant because the population most likely to require these scans (postoperative or revision orthopedic patients) is also the population most affected by these artifacts [7, 59]. For periprosthetic joint infection evaluation, metallic artifact susceptibility remains problematic. One study reported sensitivity and specificity of only 57% and 50%, respectively, in the periprosthetic bone margin region despite metal artifact reduction techniques, with assessment noting that currently, this modality is unlikely to be recommended in clinical practice due to artifacts [60]. Standard MRI contraindications apply to the MRI component of PET/MRI, including certain metallic implants, cardiac pacemakers, and severe claustrophobia [7]. PET/MRI technology remains in development with limited institutional availability, and quantitative performance standardization is still being explored through ongoing scientific projects [61].

Condition-specific factors also affect performance. In PJI, the false-positive rate remains a concern despite good overall accuracy. Kiran and colleagues reported a false-positive rate of 60.21% against MSIS criteria, concluding that PET is most useful for ruling out infection rather than

for confirming it [46]. This issue is most acute in the early postoperative period and in patients with aseptic inflammatory processes: non-specific periprosthetic uptake from foreign-body reaction can persist for years after arthroplasty, and aseptic loosening can produce SUVs as high as 7, making the distinction from infection genuinely difficult [62]. Postsurgical residual inflammation may also remain detectable for an extended time, adding another layer of interpretive complexity [63]. In septic arthritis, PET/CT is sensitive for inflammatory change but the uptake is non-specific. Familiarity with characteristic uptake patterns is needed to narrow the differential [64]. Tracer uptake is also high in non-infective inflammatory arthropathies, including rheumatoid arthritis, psoriatic arthritis, and other rheumatic conditions, so all readings need to be correlated with the clinical and laboratory picture [65]. Combined with the relatively limited literature on PET in septic arthritis specifically, and with cost and availability constraints, this restricts routine PET use in emergency presentations where rapid diagnosis is the priority.

Beyond technical limitations, several practical and economic considerations shape how these tools fit into real-world workflows. FDG-PET/MRI is concentrated in a small number of academic centers worldwide [66]. Even in well-resourced healthcare systems, scanner availability, qualified technologist support, and reader expertise remain bottlenecks. FDG-PET/CT is far more widely deployed but is still expensive on a per-study basis, and reimbursement for musculoskeletal infection indications varies by jurisdiction and is often more restrictive than for oncologic indications [67]. Neither modality is positioned as first-line in current major guidelines for osteomyelitis, spondylodiscitis, septic arthritis, or prosthetic joint infection [63, 68, 69]. Conventional MRI and white blood cell scintigraphy retain central diagnostic roles, with FDG-PET typically reserved for cases that remain unresolved after standard workup or that require whole-body assessment [68]. In low- and middle-income settings, the absence of cyclotron infrastructure, the cost of FDG production, and limited PET capacity mean that radiographs, ultrasound, MRI where available, and microbiological sampling continue to anchor practice [70]. These realities should temper expectations about how broadly FDG-PET imaging can be deployed, and they argue for a stepwise diagnostic strategy in which hybrid imaging is reserved for clinical questions that conventional modalities cannot resolve.

Conclusion

FDG-PET imaging fills a real gap in the workup of musculoskeletal infections by picking up metabolic change before structural damage is visible on conventional imaging. Across osteomyelitis, spondylodiscitis, septic arthritis, and prosthetic joint infection, FDG-PET/CT has shown good diagnostic performance, and FDG-PET/MRI has shown promise in chronic osteomyelitis and spinal infection, with the choice between them driven by the

clinical question rather than by a blanket preference. FDG-PET/CT remains the more practical option for diabetic foot osteomyelitis, prosthetic joint infection, and acute presentations, on the strength of its tolerance to metallic hardware, its short acquisition time, and its broader availability. FDG-PET/MRI, still investigational and concentrated in a small number of academic centers, may be advantageous in selected patients with chronic osteomyelitis or spinal infection where soft-tissue characterization is paramount or cumulative radiation is a concern. The most important caveats are well known: FDG uptake is not specific, with false-positive rates exceeding 60% in some prosthetic joint series [46]. Sensitivity is lower in early disease before robust inflammatory cell infiltration. Acquisition time, claustrophobia, MRI safety constraints, hardware-related artifacts, cost, and limited reimbursement constrain how widely either technique can be applied. Future work will need to focus on standardized acquisition protocols, validated quantitative thresholds for distinguishing infection from non-infectious inflammation, and prospective multicenter studies, particularly head-to-head comparisons of FDG-PET/CT with FDG-PET/MRI in the same patients, to clarify where each modality belongs in the diagnostic algorithm.

Disclosure of conflict of interest

None.

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