^{18}F -FDG PET for Diagnosing Infections in Prosthetic Joints

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KEYWORDS

• ^{18}F -FDG PET • Positron emission tomography • Joint • Prosthesis • Infection

KEY POINTS

- The diagnostic performance of fludeoxyglucose F 18 (^{18}F -FDG) positron emission tomography (PET) in detecting periprosthetic joint infection (PJI) in hip and knee replacements seems sufficiently high for routine clinical application and adds to conventional tests in terms of diagnostic accuracy.
- Iterative metal artifact reduction of computed tomography data improves PET image quality around prostheses.
- Location rather than intensity of ^{18}F -FDG uptake is critical in diagnosing hip and knee PJI.
- ^{18}F -FDG uptake at the middle portion of the femoral shaft at the bone-prosthesis interface is highly suspicious for hip PJI.
- ^{18}F -FDG uptake at the bone-prosthesis interface has been consistently reported as diagnostic criterion for knee PJI.

INTRODUCTION

In 2010, a little more than 2% of the US population were living with a hip or total knee replacement, which corresponds to approximately 7 million people.¹ Given the increasing number of individuals who choose elective joint replacements to maintain active lifestyles² and increasing life expectancy of the general population, the prevalence of hip and knee replacements will continue to increase. Hip and knee replacements can improve function and quality of life of individuals with severe arthritis.^{1,3} A major disadvantage, however, is that approximately 6% of all hip and knee replacements need to be revised after 5 years, which rises to as many as 12% after 10 years.⁴ More than 25% of revisions are attributed to periprosthetic joint infection (PJI), which is a severe complication and associated with substantial morbidity⁵ and high costs.^{6,7} Other causes for revisions are

polyethylene wear and aseptic loosening, fractures, and dislocations. Whereas fractures and dislocations can readily be distinguished by radiography or computed tomography (CT), it may be difficult to differentiate PJI from aseptic loosening. Accurate preoperative diagnosis of PJI is highly desirable, however, because it determines the method of treatment. Aseptic loosening is treated in a 1-stage revision procedure (prosthesis removal and direct implantation of a new prosthesis), whereas a 2-stage revision procedure (prosthesis removal and delayed reimplantation of a new prosthesis)⁵ is considered the current gold standard treatment of PJI.⁸

PATHOGENESIS OF PERIPROSTHETIC JOINT INFECTION

A majority of PJIs occurring within 1 year of surgery are caused by introduction of bacteria at the

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time of prosthesis placement, which can occur either through direct contact or aerosolized contamination.⁹ Once in contact, bacteria colonize the prosthetic surface.⁹ Contiguous spread from an adjacent site is the second mechanism by which PJI can be initiated. This can occur either in the early postoperative period (spread of superficial surgical site infection through incompletely healed superficial and deep fascial planes) or also many years postoperatively (if the normal tissue plane is disrupted again by trauma or surgery).⁹ The third mechanism, although less frequent, is hematogeneous spread from a remote infection site.⁹ Biofilms are complex communities of bacteria embedded in a protective extracellular matrix that forms on prosthetic surfaces.^{9,10} Their formation is intrinsic to the pathogenesis of chronic PJI and is beneficial to bacterial survival and antibiotic resistance.^{9–11}

DEFINITION OF PERIPROSTHETIC JOINT INFECTION

In 2018, an updated evidence-based and validated definition for PJI was published.¹² This definition is based on major and minor criteria¹² (Table 1). Major criteria include 2 positive cultures or the presence of a sinus tract.¹² Minor criteria include results from preoperative serum and synovial fluid analysis.¹² For patients with inconclusive minor criteria, operative criteria can be used to fulfill the definition of PJI.¹²

DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION

The typical clinical presentation of PJI is a patient with a painful, warm, stiff, and swollen joint. Clinical presentation, however, frequently is atypical, especially in chronic and low-grade infections, and there are no clinical signs that achieve both high sensitivity and high specificity in diagnosing PJI. A painful joint is the most sensitive but least specific clinical finding in PJI.¹¹ Signs of deep tissue involvement (ie, sinus tract, purulence, abscess, and extensive necrosis) are the most specific signs and, when present, justify the condition of major criteria for the diagnosis of PJI.^{11,12} Clinical findings differ based on the type of joint involved (hip or knee) as well as on the timing and presentation of PJI (ie, early postoperative, acute hematogenous, and chronic).¹¹ Preoperative synovial fluid culture and serum and synovial fluid analysis for infection markers may be helpful to rule in or rule out PJI (see Table 1). An important limitation, however, is the considerable percentage of dry taps, that is, cases in which no fluid can be aspirated despite appropriate anatomic location within the prosthetic hip or knee joint capsule. This percentage has been reported to be as high as 23% and it does not imply that PJI is not present.¹³ Other limitations of synovial fluid culture are false-negative results when bacteria are embedded in a biofilm¹⁰ and false-positive cultures when synovial fluid samples are contaminated. Even when using the updated

Table 1 Proposed scoring-based definition for periprosthetic joint infection			
Major Criteria (at Least One)			Decision
Two positive cultures of the same organism			Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis			
Minor Criteria, Preoperative		Score	Decision
Serum	Elevated CRP or D-dimer	2	≥6 infected
	Elevated ESR	1	2–5 possibly infected
Synovial	Elevated white blood cell count or leukocyte esterase	3	0–1 not infected
	Positive α-defensin	3	
	Elevated polymorphonuclear	2	
	Elevated CRP	1	
Operative Criteria ^a		Score	Decision
Preoperative score		—	≥6 infected
Positive histology		3	4–5 inconclusive
Positive purulence		3	≤3 not infected
Single positive culture		2	

^a For patients with inconclusive minor criteria.
Adapted from Parvizi J, Tan TL, Goswami K, et al. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. J Arthroplasty. 2018 May;33(5):1309-1314.e2. <https://doi.org/10.1016/j.arth.2018.02.078>. Epub 2018 Feb 26; with permission.

evidence-based and validated major and minor criteria for PJI,¹² there are patients in whom a diagnosis of PJI cannot be established with certainty preoperatively.¹² Moreover, there are conditions (adverse local tissue reaction, crystalline deposition arthropathy, inflammatory arthropathy flare, and infection with slowly growing organisms [such as *Propionibacterium acnes* and coagulase-negative Staphylococci]) in which the criteria may be inaccurate.¹²

ROLE OF IMAGING, INCLUDING FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY

The diagnostic approach in patients with suspected PJI is variable from center to center.¹⁴ It depends on local experience and availability of technological equipment.¹⁴ Also, there currently are no published evidence-based guidelines to guide the diagnostic work-up of PJI.¹⁴ **Table 2** provides a global, descriptive overview of the accuracy of different imaging modalities.

Radiography usually is the initial imaging modality to evaluate possible PJI.^{5,15} Its sensitivity and specificity are low: osteolysis and periosteal reaction are late findings and also may occur in aseptic loosening.^{5,15} CT¹⁶ and magnetic resonance imaging (MRI) using metal artifact reduction sequences may be more accurate, because they can detect soft tissue abnormalities associated with PJI, included among which are periarticular fluid collections, joint effusion, synovitis, lymphadenopathy, and sinus tracts.^{17–19} The accuracy of these cross-sectional imaging modalities, however, has not yet been widely validated. Granulomatous reactions to wear, the concurrence of adverse local tissue reaction and PJI, and

underlying rheumatoid diseases may impede assessment by CT and MRI.¹⁷

There are several nuclear imaging techniques that can be used to evaluate suspected PJI. Bone scintigraphy with technetium Tc 99m (^{99m}Tc)-labeled diphosphonates or, alternatively, sodium fluoride F 18 PET²⁰ can be used to assess osteoblastic activity around the prosthesis. Because sensitivity is high,^{21,22} normal findings can be considered strong evidence against the presence of PJI.²³ Specificity, however, generally is low^{21,22}; positive findings can indicate either PJI or aseptic loosening. Moreover, a bone scan may be positive for at least 2 years after hip replacement and at least 5 years after knee replacement due to physiologic bone remodeling.²³ Because bone scintigraphy with ^{99m}Tc-labeled diphosphonates is relatively cheap, it may be used as an initial screening test for suspected PJI. Labeled leukocyte imaging has shown superior accuracy for diagnosing PJI compared with bone scintigraphy.^{21,22} A caveat, however, is the normal physiologic accumulation of white blood cells in the bone marrow, which may be variable from 1 person to another.²³ Furthermore, hematopoietically active marrow usually develops around joint prostheses, producing an alteration of the normal bone marrow distribution. This problem may be overcome by late imaging (after 20–24 hours). In PJI, further accumulation of labeled leukocytes is seen in the late images due to increased uptake in infected areas and reduction in background activity.²⁴ Labeled leukocyte scintigraphy has other important drawbacks, including its complexity, high costs, potential hazards due to the direct handling of blood products, and considerable radiation burden.²⁵ Fludeoxyglucose F 18 (¹⁸F-FDG) PET is practically superior, because it is routinely available, provides a completed examination within 1 hour after ¹⁸F-FDG administration (rather than 24 hours for labeled leukocyte imaging), and has a favorable safety profile (lack of pathogens in the final product).²⁵

PRINCIPLE OF FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY IN INFECTION

Activated leukocytes use glucose as an energy source and show increased expression of glucose transporters.^{23,26} In inflammatory conditions, the affinity of glucose transporters for ¹⁸F-FDG is increased by various cytokines and growth factors. ¹⁸F-FDG is transported into cells by glucose transporters and is phosphorylated by hexokinase enzyme to ¹⁸F-FDG-6 phosphate but is not metabolized. The degree of ¹⁸F-FDG uptake is related to

Table 2
Global, descriptive overview of the accuracy of different imaging modalities that may be used to diagnose periprosthetic joint infection

Imaging Modality	Sensitivity	Specificity
Radiography	Low	Low
CT	Unclear ^a	Unclear ^a
MRI	Unclear ^a	Unclear ^a
Bone scintigraphy	High	Low
Labeled leukocyte imaging	Fairly high	Fairly high
¹⁸ F-FDG PET	Fairly high	Fairly high

Note that accuracy may depend, among others, on diagnostic criteria used and joint site.
^a Insufficient data.

the metabolic rate and the number of glucose transporters in leukocytes.²⁶ The uptake of ^{18}F -FDG reflects in vivo labeling of the existing and activated cells at the site of PJI soon after ^{18}F -FDG injection.²⁷ In contrast to labeled leukocyte imaging, ^{18}F -FDG uptake does not rely on leukocyte migration. Therefore, treatment with antibiotics is less likely to affect its sensitivity in delineating the PJI site.²⁷

FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY PROTOCOL

Recommendations with regard to patient preparation and precautions, ^{18}F -FDG dose, and image acquisition have been outlined in detail in the European Association of Nuclear Medicine/Society of Nuclear Medicine and Molecular Imaging guideline for ^{18}F -FDG use in inflammation and infection.²⁸ Simultaneous PET and CT (integrated PET/CT) allows for precise allocation of ^{18}F -FDG uptake.²⁹ CT-based PET attenuation correction is susceptible to errors where artifacts occur, particularly in the vicinity of metal implants.^{30,31} This can result in underestimation and overestimation of ^{18}F -FDG uptake.^{30,31} There has been recent interest in the use of iterative metal artifact reduction of CT data, which improves PET image quality around prostheses.^{30,31}

DIAGNOSTIC PERFORMANCE OF FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY

The diagnostic performance of ^{18}F -FDG PET in detecting PJI in hip and knee replacements seems sufficiently high for routine clinical application and has not proved inferior to labeled leukocyte scintigraphy.^{21,22,25,27} A meta-analysis reported a pooled sensitivity of 86% (95% CI, 80% to 90%) and a pooled specificity of 93% (95% CI, 90% to 95%) for hip prostheses.²² Another meta-analysis reported a pooled sensitivity of 70% (95% CI, 56% to 81%) and a pooled specificity of 84% (95% CI, 76% to 90%) for knee prostheses.²¹ In addition, ^{18}F -FDG PET has shown useful in

patients with nonspecific clinical presentation (ie, without apparent clinical signs and symptoms, such as absence of a sinus tract).^{32,33} Furthermore, it has additional value to conventional tests (including radiography, erythrocyte sedimentation rate [ESR]/C-reactive protein [CRP] testing, and joint aspiration culture and white blood cell count) in diagnosing PJI (ie, it increases accuracy).³³

FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY EVALUATION

It is important to be aware that ^{18}F -FDG PET uptake in healing bone is normal within 3 months after surgery.³⁴ Differentiating between PJI and inflammation secondary due to foreign body reaction and/or aseptic loosening can be difficult. In noninfected hip prostheses, ^{18}F -FDG uptake is commonly seen around the neck^{35–38} (Figs. 1 and 2), which may be explained by wear of components and an adverse tissue reaction.³⁵ Furthermore, physiologic ^{18}F -FDG uptake also may be present at the lateral and medial sides of the acetabular cup³⁵ (see Fig. 2), at the proximal portion of the femoral component,³⁸ and at the distal tip of the femoral component.³⁶ The level of physiologic ^{18}F -FDG uptake in uncemented hip prostheses is influenced by the age and probably the type of prosthesis.³⁵ In noninfected hip prostheses, there should be no ^{18}F -FDG uptake in the periprosthetic soft tissues, except for the soft tissue near the greater trochanter.³⁵ ^{18}F -FDG PET can identify soft tissue abscesses, which are not apparent on clinical examination (Fig. 3) and, when present, it justifies the condition of major criteria for the diagnosis of PJI.^{11,12} ^{18}F -FDG uptake at the middle portion of the femoral shaft is virtually never seen in asymptomatic patients or in those with aseptic loosening and is highly suspicious for PJI (Fig. 4).^{35,36,38,39} Most studies that have been performed to date have evaluated visual ^{18}F -FDG uptake patterns associated with aseptic loosening or PJI. There is no accepted standardized uptake value (SUV) threshold to diagnose PJI. More importantly, the intensity of

Fig. 1. Nonspecific ^{18}F -FDG uptake in a 66-year-old woman with bilateral asymptomatic total hip prostheses. This patient underwent ^{18}F -FDG PET to evaluate a lung lesion. Coronal PET image (B) shows nonspecific ^{18}F -FDG uptake around the neck of the left hip prosthesis (arrowheads), with corresponding CT image (A).

Fig. 2. Nonspecific ^{18}F -FDG uptake in a 70-year-old man with asymptomatic right total hip prosthesis. This patient underwent ^{18}F -FDG PET to identify the cause of fever of unknown origin. Coronal PET image (B) shows nonspecific ^{18}F -FDG uptake around the neck (arrowheads) and nonspecific ^{18}F -FDG uptake at lateral side of the acetabular cup (arrow), with corresponding CT image (A).

^{18}F -FDG uptake is less important than the location of increased ^{18}F -FDG uptake to diagnose PJI.⁴⁰ Hip prostheses, which show aseptic loosening, can be accompanied by an intense inflammatory response involving large numbers of leukocytes⁴¹ and, as a result, demonstrate intense ^{18}F -FDG uptake, with SUVs as high as 7.⁴⁰ Therefore, using increased ^{18}F -FDG uptake as the sole criterion to

diagnose PJI in hip prostheses results in false-positive results.⁴⁰ The pattern of ^{18}F -FDG uptake around noninfected knee prostheses has been less well documented than that of hip prostheses. Nonspecific synovial ^{18}F -FDG uptake in knee prostheses has been reported by several studies^{42–45} (Fig. 5). On the other hand, ^{18}F -FDG uptake at the bone-prosthesis interface of the

Fig. 3. PJI in an 80-year-old woman with painful left hip prosthesis. Axial (A, B) and coronal (C, D) CT and PET images are displayed. There is a fluid collection in the left iliacus (arrows [A, C]) muscle, which shows peripheral ^{18}F -FDG uptake and no central ^{18}F -FDG uptake (arrows [B, D]), compatible with an abscess. This abscess was not suspected clinically and extended caudally to the left hip joint. In addition, there is ^{18}F -FDG uptake at the bone-prosthesis interface around the acetabular cup and at the proximal femoral stem (arrowheads [D]).

Fig. 4. PJI in a patient with bilateral prosthesis. Coronal PET image reveals ¹⁸F-FDG uptake at the middle portion of the femoral shaft at the bone-prosthesis interface (arrow), which is highly suspicious for PJI. PJI was confirmed by further assessment. (From Saboury B, Ziai P, Parsons M, et al. Promising Roles of PET in Management of Arthroplasty-Associated Infection. PET Clin 2012; 7:139-50; with permission.)

femoral or tibial component has been consistently reported as diagnostic criterion for PJI in knee prostheses²¹ (**Fig. 6**). The influence of ¹⁸F-FDG uptake, however, at specific bone-prosthesis locations on diagnostic performance has not been reported yet, to the authors' knowledge. **Table 3** summarizes areas of nonspecific ¹⁸F-FDG uptake and criteria for PJI in hip and knee prostheses, based on available evidence.

ROLE OF FLUDEOXYGLUCOSE F 18 POSITRON EMISSION TOMOGRAPHY IN OTHER PROSTHETIC JOINTS THAN HIP AND KNEE

The number of shoulder replacements is growing faster than ever.⁴⁶ The occurrence rate of PJI after total shoulder replacement is approximately 1% to 3.9% and can be even higher in reversed designs due to an increase in dead space and hematoma formation.⁴⁷ Of all revision shoulder operations,

Fig. 5. Nonspecific synovial ¹⁸F-FDG uptake in an asymptomatic knee prosthesis of a 70-year-old man, as shown on coronal (A) and sagittal (B) PET images (arrowheads), with corresponding CT images (C, D).

Fig. 6. PJI in a patient with a left knee prosthesis. Coronal PET image demonstrates a focus of intense ^{18}F -FDG uptake in the medial aspect of femoral component at the bone-prosthesis interface (arrow). Operative findings and histopathology confirmed the presence of infection. (From Saboury B, Ziai P, Parsons M, et al. Promising Roles of PET in Management of Arthroplasty-Associated Infection. PET Clin 2012; 7:139-50; with permission.)

12% are due to PJI.⁴⁷ Because the number of patients who undergo shoulder arthroplasty is growing fast,^{46,47} it can be anticipated that the number of patients with PJI also will increase. The value of ^{18}F -FDG PET in evaluating shoulder PJI, however, has not yet been extensively investigated. The results of a recent study suggested that ^{18}F -FDG PET has poor diagnostic accuracy in diagnosing low-grade PJI of the shoulder.⁴⁸ In addition, the performance and place of ^{18}F -FDG

PET in the diagnostic decision tree of suspected PJI in other less common arthroplasty sites, such as the elbow and ankle, also remains to be investigated. The potential of ^{18}F -FDG PET in evaluating elbow prosthesis already has been demonstrated,⁴⁹ but diagnostic accuracy data are not available yet.

FUTURE PERSPECTIVES

Although diagnostic performance of ^{18}F -FDG PET in detecting hip and knee PJI seems sufficiently high for clinical use, results from several individual studies were heterogeneous.^{21,22} Importantly, the definition of PJI has evolved over the years with the most recent updated evidence-based and validated definition for PJI published in 2018.¹² Most ^{18}F -FDG PET studies performed so far, however, used various other/older definitions of PJI, which may have been an important source of heterogeneity. Standardization of ^{18}F -FDG PET acquisition protocols, diagnostic criteria, and reference standard is required to further explore potential causes of heterogeneity (including type and age of prosthesis) and to further validate this method, preferably by multicenter studies. Large prospective studies comparing the diagnostic performance of ^{18}F -FDG PET and labeled leukocyte imaging for PJI are anticipated.¹⁴ Simultaneous PET and MRI (integrated PET/MRI) has high potential to improve the noninvasive diagnosis of PJI in 1 single examination, because it combines the functional information gathered from PET and the excellent anatomic detail and soft tissue contrast from MRI.⁵⁰

SUMMARY

Diagnosing PJI can be a challenge, especially for chronic and low-grade infections. The diagnostic performance of ^{18}F -FDG PET in detecting PJI in hip and knee replacements seems sufficiently high for routine clinical application and adds to conventional tests. Location rather than intensity of ^{18}F -FDG uptake is critical in diagnosing hip and knee PJI. ^{18}F -FDG uptake at the middle portion of the femoral component and ^{18}F -FDG uptake at the bone-prosthesis interface can be considered positive criteria for PJI in hip and knee prostheses, respectively. The role of ^{18}F -FDG PET in other prosthetic joints remains to be investigated.

DISCLOSURE

All authors have no disclosures to declare.

Table 3
Areas of nonspecific fludeoxyglucose F 18 uptake and criteria for periprosthetic joint infection in hip and knee prostheses, based on available evidence

	Areas of Nonspecific Fludeoxyglucose F 18 Uptake	Criteria for Periprosthetic Joint Infection
Hip	• Around the neck of the prosthesis • Lateral and medial sides of the acetabular cup • Proximal portion of the femoral component • Distal portion of the femoral component	• ^{18}F-FDG uptake at the middle portion of the femoral component
Knee	• Synovium	• ^{18}F-FDG uptake at the bone-prosthesis interface

REFERENCES

- Maradit Kremers H, Larson DR, Crowson CS, et al. Prevalence of total hip and knee replacement in the United States. *J Bone Joint Surg Am* 2015;97:1386–97.
- Lam V, Teutsch S, Fielding J. Hip and knee replacements: a neglected potential savings opportunity. *JAMA* 2018;319:977–8.
- van der Wees PJ, Wammes JJ, Akkermans RP, et al. Patient-reported health outcomes after total hip and knee surgery in a Dutch University Hospital Setting: results of twenty years clinical registry. *BMC Musculoskelet Disord* 2017;18:97.
- Labek G, Thaler M, Janda W, et al. Revision rates after total joint replacement: cumulative results from worldwide joint register datasets. *J Bone Joint Surg Br* 2011;93:293–7.
- Kapadia BH, Berg RA, Daley JA, et al. Periprosthetic joint infection. *Lancet* 2016;387:386–94.
- Alp E, Cevahir F, Ersoy S, et al. Incidence and economic burden of prosthetic joint infections in a university hospital: a report from a middle-income country. *J Infect Public Health* 2016;9:494–8.
- Kurtz SM, Lau E, Watson H, et al. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty* 2012;27(8 Suppl):61–5.
- Charette RS, Melnic CM. Two-stage revision arthroplasty for the treatment of prosthetic joint infection. *Curr Rev Musculoskelet Med* 2018;11:332–40.
- Tande AJ, Patel R. Prosthetic joint infection. *Clin Microbiol Rev* 2014;27:302–45.
- Gbejuade HO, Lovering AM, Webb JC. The role of microbial biofilms in prosthetic joint infections. *Acta Orthop* 2015;86:147–58.
- Amanatullah D, Dennis D, Oltra EG, et al. Hip and knee section, diagnosis, definitions: proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019;34:S329–37.
- Parvizi J, Tan TL, Goswami K, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. *J Arthroplasty* 2018;33:1309–14.
- Ali F, Wilkinson JM, Cooper JR, et al. Accuracy of joint aspiration for the preoperative diagnosis of infection in total hip arthroplasty. *J Arthroplasty* 2006;21:221–6.
- Signore A, Sconfienza LM, Borens O, et al. Consensus document for the diagnosis of prosthetic joint infections: a joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement). *Eur J Nucl Med Mol Imaging* 2019;46:971–88.
- Li C, Renz N, Trampuz A. Management of periprosthetic joint infection. *Hip Pelvis* 2018;30:138–46.
- Cyteval C, Hamm V, Sarrare MP, et al. Painful infection at the site of hip prosthesis: CT imaging. *Radiology* 2002;224:477–83.
- Fritz J, Lurie B, Miller TT, et al. MR imaging of hip arthroplasty implants. *Radiographics* 2014;34:E106–32.
- Fritz J, Lurie B, Potter HG. MR imaging of knee arthroplasty implants. *Radiographics* 2015;35:1483–501.
- Koff MF, Burge AJ, Koch KM, et al. Imaging near orthopedic hardware. *J Magn Reson Imaging* 2017;46:24–39.
- Grant FD, Fahey FH, Packard AB, et al. Skeletal PET with 18F-fluoride: applying new technology to an old tracer. *J Nucl Med* 2008;49:68–78.
- Verberne SJ, Sonneg RJ, Temmerman OP, et al. What is the accuracy of nuclear imaging in the assessment of periprosthetic knee infection? A meta-analysis. *Clin Orthop Relat Res* 2017;475:1395–410.
- Verberne SJ, Rajmakers PG, Temmerman OP. The accuracy of imaging techniques in the assessment of periprosthetic hip infection: a systematic review and meta-analysis. *J Bone Joint Surg Am* 2016;98:1638–45.
- Glaudemans AW, Galli F, Pacilio M, et al. Leukocyte and bacteria imaging in prosthetic joint infection. *Eur Cell Mater* 2013;25:61–77.
- Signore A, Jamar F, Israel O, et al. Clinical indications, image acquisition and data interpretation for white blood cells and anti-granulocyte monoclonal antibody scintigraphy: an EANM procedural guideline. *Eur J Nucl Med Mol Imaging* 2018;45:1816–31.
- Kwee TC, Basu S, Alavi A. The ongoing misperception that labeled leukocyte imaging is superior to 18F-FDG PET for diagnosing prosthetic joint infection. *J Nucl Med* 2017;58:182.
- Love C, Tomas MB, Tronco GG, et al. FDG PET of infection and inflammation. *Radiographics* 2005;25:1357–68.
- Basu S, Kwee TC, Saboury B, et al. FDG PET for diagnosing infection in hip and knee prostheses: prospective study in 221 prostheses and subgroup comparison with combined (111)In-labeled leukocyte/(99m)Tc-sulfur colloid bone marrow imaging in 88 prostheses. *Clin Nucl Med* 2014;39:609–15.
- Jamar F, Buscombe J, Chiti A, et al. EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. *J Nucl Med* 2013;54:647–58.
- von Schulthess GK, Steinert HC, Hany TF. Integrated PET/CT: current applications and future directions. *Radiology* 2006;238:405–22.
- van der Vos CS, Arens AIJ, Hamill JJ, et al. Metal artifact reduction of CT scans to improve PET/CT. *J Nucl Med* 2017;58:1867–72.
- Schabel C, Gatidis S, Bongers M, et al. Improving CT-based PET attenuation correction in the vicinity of metal implants by an iterative metal artifact reduction algorithm of CT data and its comparison to

- dual-energy-based strategies: a phantom study. *Invest Radiol* 2017;52:61–5.
32. Zajonz D, Zieme A, Prietzel T, et al. Periprosthetic joint infections in modular endoprostheses of the lower extremities: a retrospective observational study in 101 patients. *Patient Saf Surg* 2016;10:6.
33. Kwee RM, Broos WA, Brans B, et al. Added value of 18F-FDG PET/CT in diagnosing infected hip prosthesis. *Acta Radiol* 2018;59:569–76.
34. Zhuang H, Sam JW, Chacko TK, et al. Rapid normalization of osseous FDG uptake following traumatic or surgical fractures. *Eur J Nucl Med Mol Imaging* 2003;30:1096–103.
35. Gelderman SJ, Jutte PC, Boellaard R, et al. 18F-FDG-PET uptake in non-infected total hip prostheses. *Acta Orthop* 2018;89:634–9.
36. Zhuang H, Chacko TK, Hickeson M, et al. Persistent non-specific FDG uptake on PET imaging following hip arthroplasty. *Eur J Nucl Med Mol Imaging* 2002;29:1328–33.
37. Vanquickenborne B, Maes A, Nuyts J, et al. The value of (18)FDG-PET for the detection of infected hip prosthesis. *Eur J Nucl Med Mol Imaging* 2003;30(5):705–15.
38. Aydin A, Yu JQ, Zhuang H, et al. Patterns of 18F-FDG PET images in patients with uncomplicated total hip arthroplasty. *Hell J Nucl Med* 2015;18:93–6.
39. Verberne SJ, Temmerman OPP, Vuong BH, et al. Fluorodeoxyglucose positron emission tomography imaging for diagnosing periprosthetic hip infection: the importance of diagnostic criteria. *Int Orthop* 2018;42:2025–34.
40. Chacko TK, Zhuang H, Stevenson K, et al. The importance of the location of fluorodeoxyglucose uptake in periprosthetic infection in painful hip prostheses. *Nucl Med Commun* 2002;23:851–5.
41. Palestro CJ. Radionuclide imaging of musculoskeletal infection: a review. *J Nucl Med* 2016;57:1406–12.
42. Love C, Marwin SE, Tomas MB, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. *J Nucl Med* 2004;45:1864–71.
43. Delank KS, Schmidt M, Michael JW, et al. The implications of 18F-FDG PET for the diagnosis of endoprosthetic loosening and infection in hip and knee arthroplasty: results from a prospective, blinded study. *BMC Musculoskelet Disord* 2006;7:20.
44. Van Acker F, Nuyts J, Maes A, et al. FDG-PET, 99mTc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties. *Eur J Nucl Med* 2001;28:1496–504.
45. Mayer-Wagner S, Mayer W, Maegerlein S, et al. Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants. *Arch Orthop Trauma Surg* 2010;130:1231–8.
46. Kim SH, Wise BL, Zhang Y, et al. Increasing incidence of shoulder arthroplasty in the United States. *J Bone Joint Surg Am* 2011;93:2249–54.
47. Pinder EM, Ong JC, Bale RS, et al. Ten questions on prosthetic shoulder infection. *Shoulder Elbow* 2016;8:151–7.
48. Falstie-Jensen T, Daugaard H, Søballe K, et al, ROSA Study Group. Labeled white blood cell/bone marrow single-photon emission computed tomography with computed tomography fails in diagnosing chronic periprosthetic shoulder joint infection. *J Shoulder Elbow Surg* 2019;28:1040–8.
49. Balasubramanian Harisankar Natrajan C, Mittal BR, Bhattacharya A, et al. Interesting image. Aseptic loosening of elbow prostheses diagnosed on F-18 FDG PET/CT. *Clin Nucl Med* 2010;35:886–7.
50. Ehman EC, Johnson GB, Villanueva-Meyer JE, et al. PET/MRI: where might it replace PET/CT? *J Magn Reson Imaging* 2017;46:1247–62.