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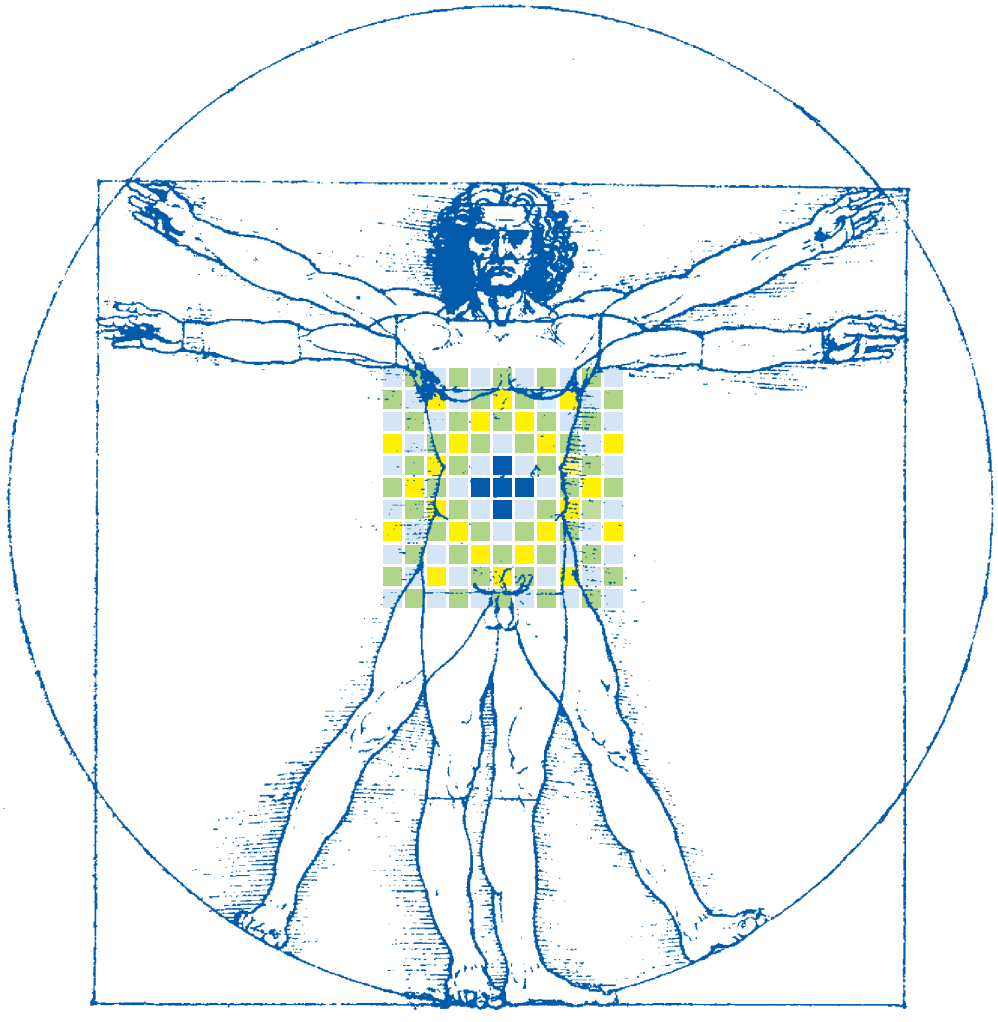

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REVIEW

HYBRID IMAGING IN INFLAMMATION AND INFECTION

Hybrid imaging of musculoskeletal infections

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ABSTRACT

This review article highlights the role of radiological and nuclear medicine techniques in diagnosis of musculoskeletal infections with particular regard to hybrid imaging of osteomyelitis, prosthetic joint infections, sternal infections and spine infections. Authors conclude on the complementary role of the several techniques with indications for an appropriate diagnostic flow chart, in the light of the recent European Association of Nuclear Medicine guidelines on infection.

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Musculoskeletal infections are a serious problem in healthcare. Establishing the correct diagnosis is often difficult, it involves also in a large percentage young people, and may have a huge impact on daily life. Treatment of a musculoskeletal infection often requires a long time and/or multiple surgeries, and may in some cases lead to amputation or can even — in case of dissemination of the infection and sepsis — be life threatening.

Several diagnostic imaging modalities are available for the diagnosis of musculoskeletal infections, but all tests have their limitations, and the imaging techniques used differ in centers based on local experiences, available techniques and costs. In this review we highlight the radiological and nuclear medicine point of view in several musculoskeletal infections: peripheral bone infection, prosthetic joint infection, sternal infections and spondylodiscitis.

The point of view of the radiologist on musculoskeletal infections

Radiological imaging is usually the first modality used to assess patients with suspected musculoskeletal infection and peripheral bone infection (PBI) in particular. Conventional radiographs have been traditionally used as the first diagnostic approach. However, they generally only become positive when at least 30% to

50% bone mass has been lost, making early diagnosis unlikely.[1, 2] Computed tomography (CT) may play a role in anatomically complex zones, such as the shoulder or the pelvis and it is usually confined to patients with chronic osteomyelitis to detect bone sequestra.[3] Magnetic resonance imaging (MRI) has the highest diagnostic performance in diagnosing PBI (88-98% sensitivity, 70-96% specificity, and 81-86% accuracy).[4-6] It does not use ionizing radiation and, in most cases, can be performed without administration of contrast agents. Recent technologic evolution allowed developing new specific imaging sequences (metal artefact reduction sequences, MARS) which allow considerably reducing artifacts related to the presence of metallic implants, which are no longer a limiting factor for MRI examination.

In case of spondylodiscitis, the role of radiology is to define the correct diagnosis as early as possible, to assist in the percutaneous biopsy, to evaluate the presence of complications and to follow-up the disease.[7-10] Plain radiography is usually the first requested test [11] although it has low sensibility and specificity.[12, 13] It includes antero-posterior and lateral projections of the spine.[12, 13] MRI is, however, the radiological modality of choice for initial diagnososis since its high sensitivity, specificity and accuracy (reported as 96%, 92%, and 94%, respectively). For patient follow-up it is usually not as accurate as for initial diagnosis, MRI findings can sometimes worsen despite clinical improvement.[14-20] MRI is particularly useful in maging diagnosis in early stages of the infection within the first two weeks in more than 50% of cases, when other radiologic imaging modalities are still normal. MRI examinations should include short-tau inversion recovery (STIR) or fat-saturated T2-weighted sequences: they are fluid-sensitive sequences, highly sensitive in detection of inflammatory oedema. In addition, T1-weighted fat-saturated pre- and post-administration of contrast media can be used for more morphological studies and to differentiate between vascularized and non-vascularized lesions and/or necrotic inflammatory components. However, spinal neoplasms may mimic an infectious discitis, especially when they are tubercular in aetiology, since both of them may have low signal on T1W and high signal on T2W. In these cases, the involvement of disc space helps in distinguishing infections from neoplasms as usually tumors do not enter the disk space.[17-19]

A disadvantage of MRI may be related to the over-estimation of the amount of the infected tissue, as some of the signal changes may be only reactive; furthermore, MRI, in presence of severe degenerative disk disease leading to edema-like changes in the endplates and the adjacent disks, may give false-positive results.[20] The signs of healing process consist in the reduction of tissue oedema, loss of contrast enhancement (few weeks to few months after the onset of treatment), progressive bone restoration (seen after a median of 15 weeks as rim of high signal intensity on T1-weighted images at the lesion edges occurring).[20] CT is readily available, easy to perform and faster than MRI. It is the best method to detect bony abnormalities as also minimal erosion of the end plates can be seen.[21] It can be used as a complement of MRI examination or as a substitute of it when MRI cannot be performed.

The point of view of the nuclear medicine physician on peripheral bone osteomyelitis

Bone scintigraphy is known to have high sensitivity but very low specificity and its use is limited to exclude the presence of PBI. After a recent fracture and/or a surgerical procedure or in presence of metallic hardware the role of bone scintigraphy is negligible, although single photon emission computed tomography- computed tomography (SPECT/CT) hybrid imaging can be more accurate than planar or three-phase scans as clearly mentioned in the recent EANM guidelines on bone scintigraphy.[22] Nowadays also the hybrid positron emission tomography- computed tomography (PET/CT) variant ^{18}F-sodium fluoride is available, but its widespread use is still limited due to limited availability and high costs.

White blood cells (WBCs) scintigraphy, preferably acquiring 3 sets of images (30 min, 2-4 h and 20-24 h) with acquisition times corrected for isotope decay and image display in absolute counts, leads to excellent overall diagnostic accuracy.[23] It can be associated to bone-marrow scan for higher specificity. As an alternative radiolabelled antigranulocyte antibodies (AGA) can be used. Typically, planar images allow the diagnosis of the presence of an infection (differential diagnosis between sterile inflammation, osteomyelitis and soft tissue infection), but hybrid SPECT/CT scans are useful to correctly define the extent of the bony infection. This

can be performed at 3-4 h p.i. or at 20-24 h p.i. although some authors have suggested a single time point imaging for osteomyelitis at 6-8 h post injection.

The use of FDG in infectious diseases increased significantly the last years. The main limitation is that FDG is taken up both in inflammatory and infectious lesions and discrimination between them is often difficult, especially when there is metallic hardware *in situ* or if there was a recent fracture and/or surgery. Currently, there are no clear interpretation criteria for declaring a FDG-PET positive or negative for peripheral bone infection, and mostly diagnosis is based on subjective criteria and experience. In the chronic peripheral non-postoperative setting results are equal to WBC scintigraphy.[24] PET/CT to combine (patho)physiology with anatomy is already considered the gold standard, the use of a PET only camera nowadays is considered obsolete.

More recently, the introduction of PET/MRI has emerged as a powerful diagnostic tool, but so far not enough reports have been published on its value in peripheral bone infection. The general advantages of MRI compared to PET/CT will be a better evaluation of soft tissue and the lack of radiation burden.

Prosthetic joint infections

Because of the increase of life expectancy, the number of patients requiring a prosthetic joint replacement has shown a significant growth in the last decades. The incidence of prosthetic joint infection (PJI) ranges between 2.0% and 2.4% for primary interventions,[25] being up to 20% for revision procedures.[26] In general, the development of an infection significantly affects the patient's quality of life and social costs related to prolonged hospitalization, and it needs antibiotic treatment and repeated surgical approaches (toilette or substitution of prosthesis), especially if the diagnosis of this condition is delayed.[25] A prompt identification of the infection is therefore needed to ensure an earlier and successful treatment for the patients with the aim of preserving joint functionality.

Redness, swelling, local pain, wound leakage and fever are the most common signs and symtoms of an infection that occours "early" after surgery (within three months). If bacteriemia remains unrecognized, a "delayed" (between three months and 2 years after surgey) or a "late" infection (2 years after surgey) can develop.[27, 28] In 30% of systemic symtoms may occur due to the hematogenous spread of the infection to skin, respiratory or urinary tracts; in the remaining 70% of cases the onset is subacute and the symptoms are non-specific.[29] Several microrganisms can be responsible for a PJI: *Staphylococcus Aureus* is generally involved in the development of "early" infection whereas *Streptococci*, coagulase-negative *Staphylococci, Enterococci and Anaerobes* are usually isolated in "late" infections.

It is of pivotal importance to distinguish an infection from an aseptic loosening so the appeal to microbiology is mandatory for a correct diagnosis and appropriate antibiotic treatment as the common laboratory tests for inflammation (erythrocyte sedimentation rate [ESR], C reactive protein [CRP], blood leukocyte count and procalcitonin) are non-specific and they can be altered in both conditions.

The point of view of the nuclear medicine physician in prosthetic joint infections

Nuclear medicine offers several radiopharmaceuticals and techniques able to image infection and inflammation with high sensitivity and specificity.

Autologous radiolabelled WBCs scintigraphy, with both ^{111}-Indium (^{111}In) and ^{99m}-Technetium (^{99m}Tc) is nowadays the gold standard examination when an infection is suspected. This modality is characterized by high specificity because leukocytes progressively accumulate into infected tissue.[30] The diagnostic accuracy of this examination is however deeply dependant to the modality of acquisition and interpretation of the scan. As already mentioned above, imaging at several time points (30', 3 hours, 20 hours) with acquisition time corrected for hisotope decay and image display in absolute counts, is strongly recommended by many authors and by the European Association of Nuclear Medicine (EANM).[23, 31] The diagnosis of PJI can be formulated if an increasing uptake over time, in terms of intensity or extension, is observed in the affected joint compared to contralateral (Figure 1). When qualitative analysis is not sufficient, a semiquantitative assessment can be helpful comparing target to background ratio (T/B) of delayed (3 hours post injection) and late images (20-24 h) drawing region of interests (ROIs) on the uffected and unaffected joint. Despite all these precautions, in some circumstances planar images can be equivocal. An

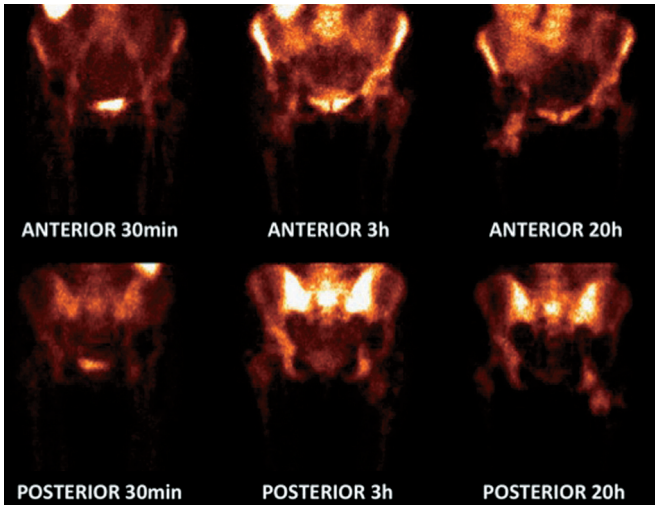

Figure 1.—A case of suspected PJI studied with ^{99m}Tc-HMPAO-WBC. Images were acquired in antero-posterior at 30 min, 3 h and 20 h with acquisition time corrected for isotope decay and displayed in absolute counts. The presence of osteomyelitis with soft tissue involvement is clearly defined in 20 h images without the need of SPECT/CT. Hybrid images, however, can add useful information on the extent of the infection.

increased uptake of WBCs can also be physiologically observed in reticulo-endothelial system of expanded bone marrow and this is the reason why a bone marrow scintigraphy may be performed after WBCs scan.[32, 33]

The role of Monoclonal antibodies (MoAbs) against specific receptors expressed on granulocytes' surface has been extensively investigated in order to overcome the limitations of the *in vitro* procedure of labelling WBCs (risk of contamination with a potentially infected blood, time consuming procedure that requires qualified personnel and adequate laboratory). Image acquisition and interpretation are the same as the WBCs scan. However, also this method has its cons especially considering the possibility to induce human murine antibodies (HAMA) in the patients that make this radiopharmaeutical not useful in the follow-up.

Although well acquired and displayed, planar images of both modalities have an important limitation, as they are not always able to discriminate between bone and soft tissue infection. This distinction is crucial in the optic of the choice of treatment. Even when SPECT is performed in addition to planar images, the anatomic landmarks still lack. The advent of hybrid techniques that are characterized by the fusion of morphological details provided by CT with molecular/functional information of gamma-camera examinations, has substantially changed the way of make imaging improving the diagnostic accuracy of several scintigraphic scans. Hybrid imaging offers the possibility to coregister the CT and SPECT reducing times of acquisition and the artefacts related to patient's change of position. Moreover the use of CT scan allows a precise fusion of the areas of increased uptake with the morphological abnormalities and it is important for another aspect that further improves image quality: the attenuation correction of images.[34]

In the specific clinical setting of PJI, the appeal to SPECT/CT in addition to planar images, allows a correct assessment of the extent of infective process into bone and it allows the evaluation of the eventual involvement of soft tissues aiming to discriminate, with high specificity, between these two conditions.[35-37]

Several papers with encouraging results are available on this argument.[38-43] In the large serie of Kim *et al.* the sensitivity, specificity and diagnostic accuracy of planar images were 82%, 88% and 84% respectively. Adding SPECT/CT increased these values to 93.3%. The CT component resulted more contributory in patients affected with hip prosthesis than for knee prosthesis.[41] In patients studied by Graute *et al.* with ^{99m}Tc-besilesomab, a MoAb, the sensitivity, specificity and diagnostic accuracy of planar images were were 66%, 60% and 61% respectively, wherease adding SPECT/CT these values increased to 77%, 89% and 73%.[43] In the group of patients studied by Filippi *et al.* in 2006, the accuracy of WBCs scintigraphy improved from 64% for SPECT alone, to 100% when SPECT is combined to CT. In the serie of Al-Nabhani *et al.*,[39] bone SPECT/CT was useful in 80% of patients with knee arthroplasty. Van der Bruggen *et al.* performed ^{111}In-labelled WBCs with SPECT and ^{99m}Tc-sulphur colloid reaching a diagnostic accuracy of 95%.[44] From these papers the use of combined SPECT/CT is strongly suggested in addition to planar images of bone, WBCs or MoAb scan.

The role of FDG-PET/CT, in the opinion of some authors, is underestimate.[45] Several authors tried to define interpretative criteria for define a PJI according to qualitative or semiquantitative analysis but a validated method still does not exist.[46-48]

In a meta-analysis performed by Kwee *et al.* in 2008, pooled sensitivity and specificity of FDG-PET for the diagnosis of hip or knee prosthesis infection were

82.1% and 86.6% respectively.[49] Wherease, in the review of Gemmel *et al.*, FDG-PET/CT seems to be more accurate for hip than for knee prosthesis. These authors reported a pooled sensitivity and specificity of 84% of this method.[50] The diagnostic accuracy is influenced by the type of reconstruction method performed for the PET scan and by the type and location of the prostheses. For example in the serie of Reinartz *et al.*, FDG-PET/CT showed an accuracy of 95% in hip prosthesis.[48] In the study of Zhuang *et al.* the diagnostic accuracy is 89.5% and 77.8% for hip and knee prosthesis respectively.[51] Basu *et al.* found a sensitivity and specificity of 81.8% and 93.1% for hip prosthesis and 94.7% and 88.2% for knee arthroplasty.[52]

In the few papers comparing FDG-PET and WBCs scintigraphy [47, 48, 52-54] the results are very variable mainly depending on the acquisition protocols and interpretative criteria. Love *et al.* found a higher diagnostic accuracy of combined WBC scan and bon marrow scintigraphy compared to FDG-PET.[47] On the contrary, Pill *et al.*[54] reported higher sensitivity and specificity for FDG-PET/CT (95% and 93% respectively) compared to combined ^{111}In-labeled WBC and ^{99m}Tc-sulfur colloid (50% and of 95% respectively). In the study of Vanquickenborne *et al.*[55] the two methods showed a similar sensitivity (88%), but WBC scan showed higher specificity compared to FDG-PET (100% *vs*. 78%).

In the joint EANM/SNMMI guidelines for using FDG in inflammation and infection based on expert opinion, this modality retains an overall sensitivity of 95% and specificity of 98% for knee and hip prosthesis, but the general diagnostic accuracy overall was only 78%.[29]

The point of view of the nuclear medicine physician on sternal and mediastinal infections

SPECT/CT, PET/CT and PET/MRI are the most common hybrid imaging modalities used in human diseases. Since 2001 the fusion of the anatomic details of CT with the functional imagings of PET and SPECT allows an instant generation of fused images of PET or scintigraphy and CT data. The clinical data on the use of these systems indicate that this hybrid technology improves the diagnostic accuracy as compared to PET or scintigraphy and CT alone if acquired separately. The improved diagnostic accuracy is reflected by improving image quality of SPECT and PET, detection of more clinically relevant lesions, better localization of disease and differentiation between physiologic and pathologic uptake, characterization of disease by its functional and morphologic appearance before and after therapy and accurate delineation of disease, optimizing biopsy and therapy planning.

This is even more significant and important in the diagnosis of chest and sternum infections where the complexity of mediastinal anatomy structures (heart, large vessels, main airways, esophagus, lymph nodes and skeleton) and related inflammatory pathologies requires a rapid and accurate diagnosis.

The most common and often more complex sternal and mediastinal infections to be studied are postoperative interventions of valvular substitutions or aortic vascular prostheses where the presence of metallic sternal keroses prevents or causes artifacts in the MRI study. In these cases, FDG-PET/CT may be a viable alternative to CT, especially in elderly patients with reduced kidney function or hyperthyroidism in which the use of a contrast enhanced CT is contraindicated.[56]

FDG-PET/CT appears to be the most sensitive method of diagnosing endocarditis in valve prostheses. In these cases, mortality is very high and around 30%, and it is essential to reach a diagnosis in the shortest possible time quickly set the most effective therapy. The most serious complications are perivalvular abscesses and metastatic infectious foci that generally affect the lungs, spine, but also the brain in about 30-68% of cases.

FDG-PET/CT is indicated also in localization of origin of a fever of unknown origin (FUO) to guide biopsy and diagnosis: the fusion of PET with CT imaging is essential to distinguish an osteomyelitis of the sternum from a more serious mediastinitis.[57, 58] However, FDG-PET/CT cannot always distinguish infection from inflammation and sometimes cannot distinguish infection from malignancy. A large portion of patients with synthetic vascular grafts will display high FDG accumulation in the graft material or in the line of sternotomy during PET/CT examination, even a long time after surgery, without an infection of the graft or of the bone.

Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants or a response of the organism to a pathogen or a microorganism and in this last case we have an infection. Because the FDG uptake in inflammatory tissues is related to concentra-

tion in granulocytes, lymphocytes and macrophages involved in tissue repair, FDG-PET/CT is not indicated in the first 3 months after surgery for the risk of false positivities.

The positivity criterion of a PET study has been correctly defined in the EANM/SNMMI guideline for FDG use in inflammation and infection and is applicable for both mediastinal and sternal infections. Therefore, a focal uptake (like a fluid collect found in CT) with a standardized uptake value (SUV) higher than 4 is a reliable value to assess the presence of an infection both in soft tissues and in bones.[29, 59]

Hyperglycemia reduces the sensitivity of FDG-PET/CT because the uptake of FDG in malignant and inflammatory cells is affected by the blood glucose level acting as a competitor. Therefore, the patient must be injected with a 6 hour fasting and with a glucose level lower than 1.8 g/L. To increase the diagnostic accuracy of FDG-PET/CT the preparation of the patient is important with a 24 hours diet rich in fat and very low in carbohydrate to minimize myocardial FDG uptake. Because endocarditis is a frequent cause of FUO in our experience we are applying the same diet to all patients with a suspect infection of aortic vascular prosthesis or with an implantable cardiac electronic device.

Another important question is if the antibiotics can affect the sensitivity of FDG-PET/CT: a recent paper Kagna *et al.* reported that antibiotic treatment has no clinically significant impact on the diagnostic accuracy of PET/CT in a large series of patients.[60]

^{99m}Tc-HMPAO-leukocyte SPECT/CT is the best imaging modality to distinguish an infection from a sterile inflammation both in bone and in soft tissues.[61] The positivity criterion of a mediastinal infection is a focal uptake that increases in intensity with time and become more focal. Typically the labelled leukocytes concentrate in cavities or collect around bones, or around vascular prosthesis or around metallic devices like electrodes or ICD implanted in the thoracic wall. A series of planar and SPECT/CT images after 4 and 20-24 hours

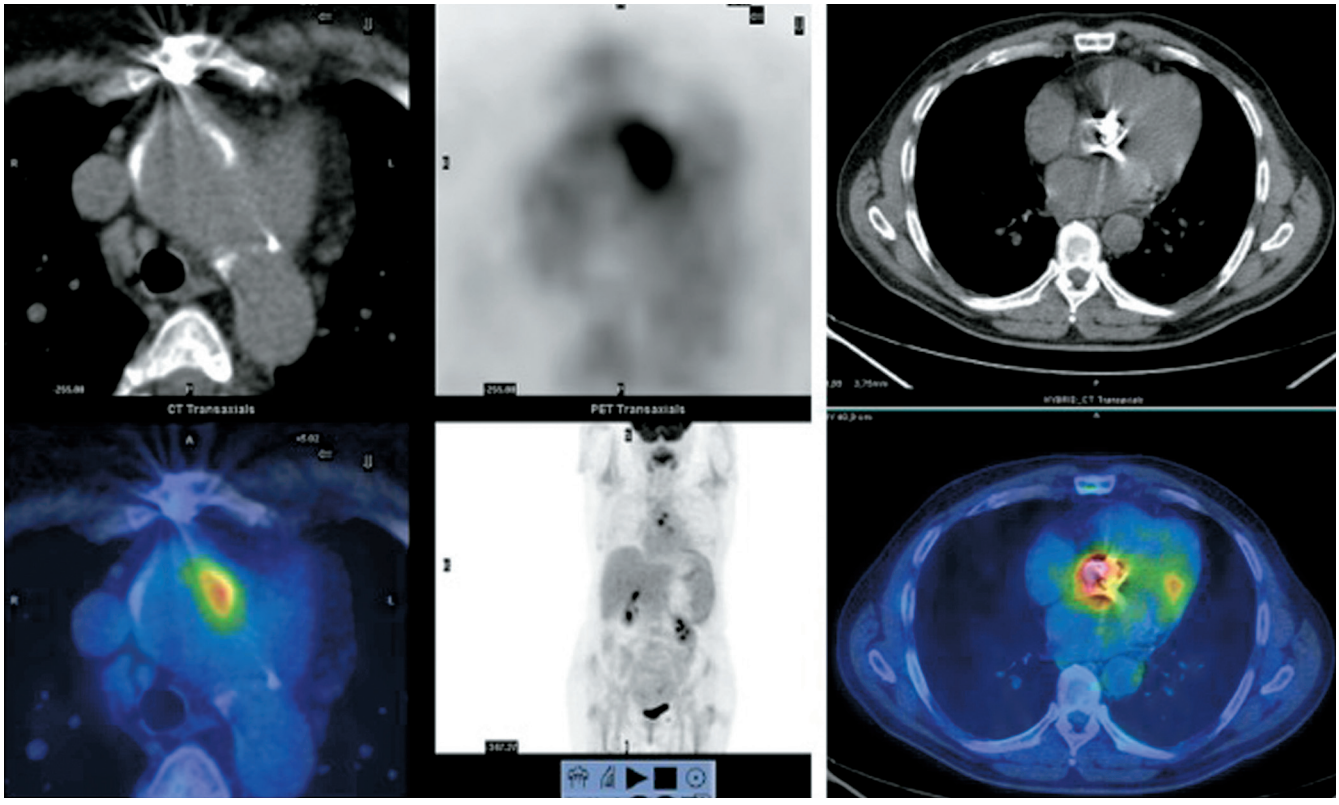

Figure 2.—[^{18}F]FDG PET/CT in infection of the aortic arc and of the valvular prosthesis without involvement of the sternum.

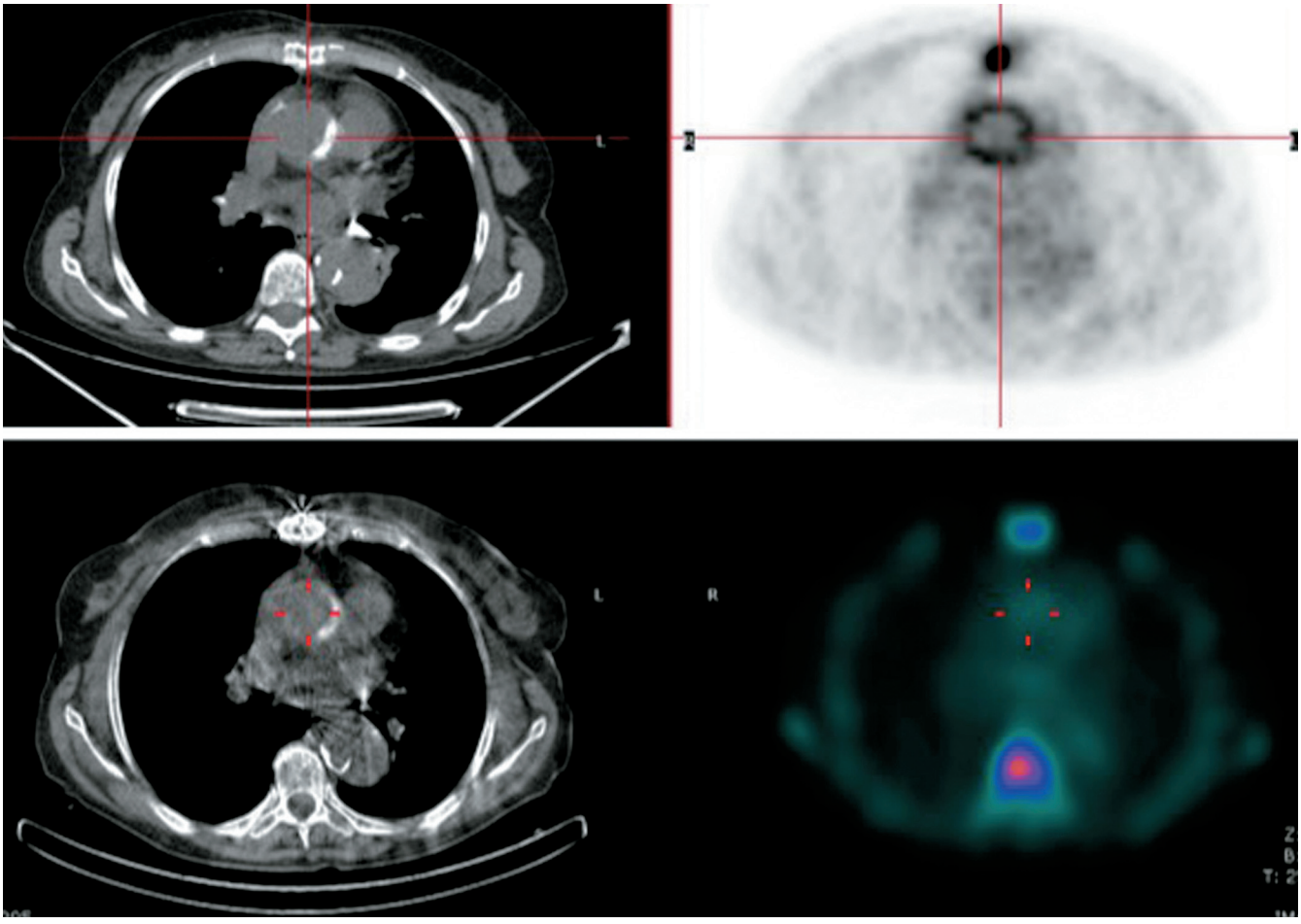

Figure 3.—Upper images: [^{18}F]FDG PET/CT in a patient refered for fever of unknown origin. Images show a diffuse uptake of FDG both in the aortic wall and in the recent sternotomy.
Lower images: [^{99m}Tc]-HMPAO labelled WBC with SPECT/CT acquisition at 20 h post injection in the same patient, showing no uptake in the aortic valve and moderate, physiological uptake in the sternotomy (false positive of [^{18}F]-FDG PET/CT).

must be taken to follow the accumulation of labelled WBCs to infected areas.[62]

In chronic sternal infections often a cold area is observed because of the presence of necrotic bone into the physiological uptake of normal bone marrow: in this contest a peripheral faint uptake of leukocytes could be the only sign that confirms a bone infection.

Considering the specificity of ^{99m}Tc-HMPAO-leukocyte SPECT/CT, higher than FDG-PET/CT this imaging modality can be applied in all cases with inconclusive findings of PET and other modalities or after recent cardiac surgery (Figures 2, 3).

In conclusion for sternal and mediastinal infections, FDG-PET/CT is a reliable method to start in the search of the location, diffusion and intensity of a suspected infection like in FUO whereas ^{99m}Tc-HMPAO-leukocyte SPECT/CT has to be preferred in patients with recent surgery, inconclusive findings of other modalities and high suspicion of bacterial infections.

The point of view of the nuclear medicine physician on spinal infections

Spinal infections include vertebral osteomyelitis (infection of the vertebral body), discitis (infection of the intervertebral disk) and spondylodiscitis (SD) (infection of two adjacent vertebral bodies and their intervertebral disk).[63] Incidence of SD in developed countries ranges

from 4 to 24 per million per year.[64] It occurs at any age but is most frequent in the fifth to seventh decades. Men are affected more frequently than women.[64] The most frequent site of infection is the lumbar spine (45%) followed by the dorsal (35%) and the cervical tract (20%).[64]

The diagnosis of SD can be challenging and includes laboratory, microbiology, radiology, and nuclear medicine examinations.

Differential diagnosis includes others spine diseases like erosive osteochrondrosis, osteoporotic and pathological fracture, bone metastasis, ankylosing spondylarthritis, Scheuermann's disease and post-surgical changes.

Bone scintigraphy with ^{99m}Tc-MDP/HDP and ^{67}Ga-citrate have a sensitivity of 81.4% and a specificity of 40.7% and of 86.3% and 35.8%, respectively.[65, 66] A combination of ^{99m}Tc-MDP bone scintigraphy with ^{67}Ga-citrate can be used to increase the diagnostic accuracy, but does not increase specificity too much.[67-69]

[^{18}F]FDG has been extensively investigated in SD. Histopathologic and autoradiographic analysis of an experimental soft tissue abscess model showed that the [^{18}F]FDG is mainly uptaken by neutrophils in the acute phase and by macrophages in the chronic phase of infections.[70]

PET or PET/CT with [^{18}F]FDG showed a very high sensitivity with relatively low specificity in diagnosing spine infections (Figure 4).

Fuster *et al.* have evaluated the usefulness of FDG-PET/CT in comparison to ^{99m}Tc-MDP bone scan and ^{67}Ga-citrate scintigraphy in the diagnosis of spondylodiscitis in 34 patients showing the best diagnostic accuracy of PET/CT (Sens 89%, spec 88%, accuracy 88%) (69). Similar results have been confirmed by many other studies.[63, 71]

The pattern of activity is critical to accurate interpretation.[72] Hungenbach *et al.* proposed a four different patterns (score 0-4) of FDG uptake:[73, 74]

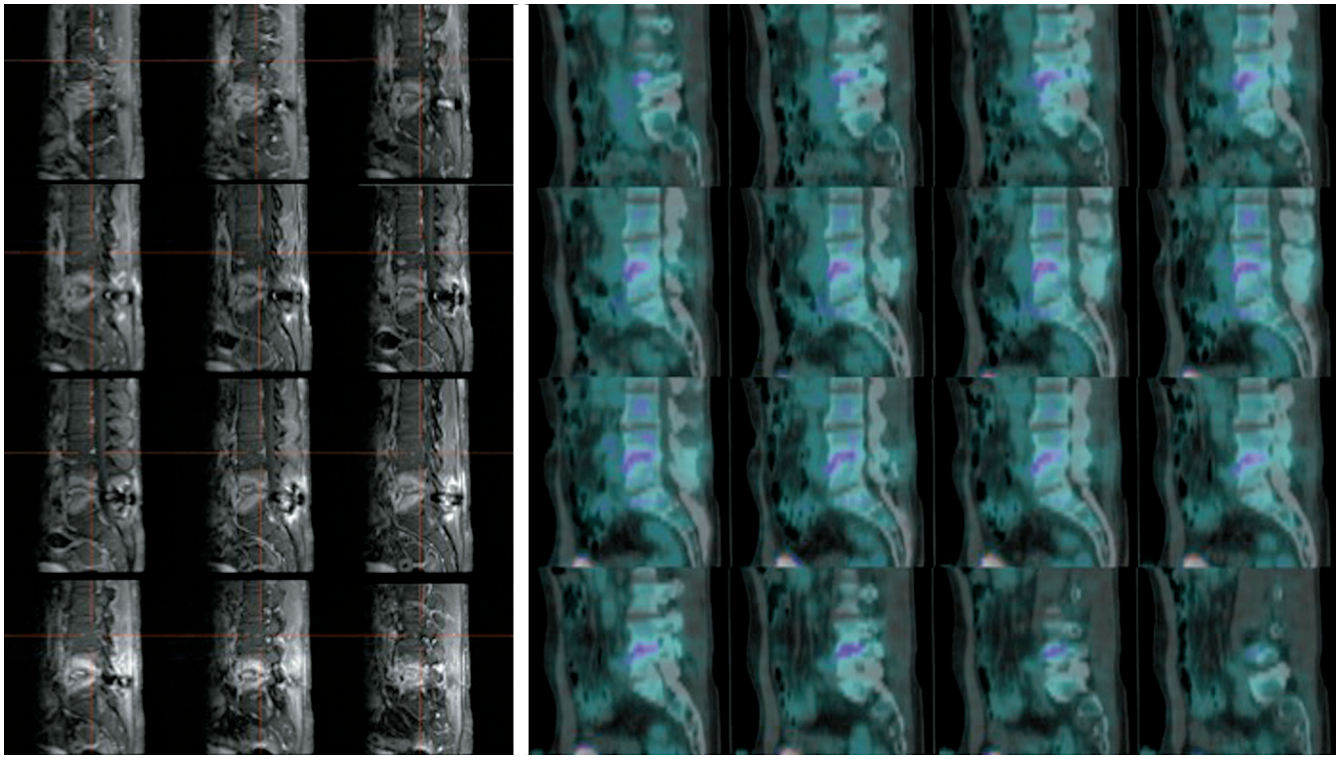

Figure 4.—A case of suspected SD. Left panel: sagittal MRI images showing oedema of L4-L5 highly suggestive of spondylodiscitis. Right panel: same patient studied with [^{18}F]FDG PET/CT showing very moderate uptake of the radiopharmaceutical in L3-L4, this excluding the presence of an infectious process.
Patient performed a CT guided bone biopsy with microbiological culture, showing the absece of bacteria (false positive MRI scan).

— score 0: normal findings and physiological FDG distribution (consistent with no infection);

— score 1: slightly elevated uptake in the inter or paravertebral region (consistent with no infection);

— score 2: clearly elevated uptake of a linear or disciform pattern in the intervertebral space (consistent with discitis);

— score 3: clearly elevated uptake of a linear or disciform pattern in the intervertebral space and involvement of ground or cover plate or both plates of the adjacent vertebrae (consistent with spondylodiscitis);

— score 4: clearly elevated uptake of a linear or disciform pattern in the intervertebral space and involvement of ground or cover plate or both plates of the adjacent vertebrae+surrounding soft-tissue abscess (consistent with spondylodiscitis).

Gemmel *et al.* proposed a diagnostic algorithm for non-violated spine and for post-surgical/post-traumatic SD. In the first case, the diagnostic method of choice is MRI followed by ^{99m}Tc-MDP bone scintigraphy with ^{67}Ga-citrate or FDG-PET when MRI is not readily available and/or when there is a contra-indication. In post-surgical/post-traumatic SD the diagnostic choice is based on the presence or not of metallic implant: the algorithm recommends FDG-PET in patients with metallic implant (to overcome the artefacts problems of MRI) and, in case of absence of metallic implant, MRI or FDG-PET with similar accuracy.

This algorithm should nowadays be upgraded due to wide availability of SPECT/CT, PET/CT and PET/MRI.[75-78] In the joint EANM/ESNR guidelines with the endorsement of ESCMID the diagnostic method of choice is MRI in suspected SD of hematogenic origin while in suspected post-surgical SD the proposed diagnostic method of choice is FDG-PET/CT.

Conclusions

Concluding, nuclear medicine and radiological imaging are complementary techniques for the study of patients with musculoskeletal infections. MRI plays a crucial role, and is often the first method applied, easy to perform and radiation free. Nuclear medicine, with labelled leukocytes or monoclonal antibodies or FDG, provides a further help in correctly defining the site and extent of infection and, particularly, for patient follow-up. In this view, hybrid imaging is contributing to a further improvement of the diagnostic accuracy of pre-existing methods. More recently, the introduction of PET/MRI is emerging as a powerful diagnostic tool in several infective and inflammatory diseases, and, considering the high quality images provided by MRI in the study of soft tissues and bones, in the near future a possible use for imaging ostomyelitis and spondylodiscitis may be speculated.[79]

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