INVITED COMMENTARY

Is There a Role for FDG PET in the Diagnosis of Musculoskeletal Neoplasms?

The approach to a patient with a suspected tumor typically includes diagnosis, staging, therapy decisions, and evaluation of response and follow-up. Imaging is essential for these steps and is traditionally based on conventional radiography and CT or on MRI, which is, at present, the method of choice (*1*). During the past 5 y, assessment by FDG PET has been added for several tumors, and consensus has been reached on its usefulness for staging disease, detecting recurrences, and evaluating treatment.

The diagnosis and management of malignant musculoskeletal tumors have changed since the introduction of new-generation imaging techniques and new chemotherapeutic agents. For example, because of better characterization of sarcomas and the possibility of reducing the tumor mass before surgery, radical resection has become infrequent and limited to recurrent high-grade sarcomas (*2*). State-of-the-art imaging can now noninvasively provide information on the presence, site and extension, and nature of the tumor and on the response of the tumor to treatment and follow-up. These variables can then be used for staging the disease.

DIAGNOSIS OF PRESENCE

The first step in detecting a suspected bone or soft-tissue tumor in a symptomatic patient is clinical and radiologic evaluation. Radiographs provide important information about the appearance, intraosseous extent, and internal characteristics of bone tumors, but usefulness in the evaluation of soft-tissue tumors is questionable. MRI is more accurate for the detection of soft-tissue tumors (*3*). At present, no role for FDG PET can be foreseen in this application, because radiography and MRI are usually adequate.

DIAGNOSIS OF SITE AND EXTENSION

Tomographic imaging methods have, in general, an advantage over planar imaging in that their better resolution affords greater sensitivity in detecting small lesions in deep structures, such as the pelvis. CT can be useful in assessing the extent to which a bone tumor involves the soft tissue and marrow or in assessing for the presence of cortical erosions and fractures. However, MRI is the technique of choice for defining the intra- and extraosseous extent of a bone tumor, the involvement of a joint, and the presence of skip metastases, which are defined as neoplastic foci distant from the principal tumor mass but in the same anatomic compartment.

Schulte et al. (*4*), in this issue of *The Journal of Nuclear Medicine*, provide extensive data on the accuracy of FDG PET in the evaluation of local and distant spread of bone neoplasms. The high sensitivity of FDG PET (93%) allows detection of small lesions and skip metastases and accurate evaluation of the local extension of a tumor mass.

The value of detecting metastases to local lymph nodes is limited for musculoskeletal tumors, because local metastases are rare and have the same poor prognosis as distant metastases. Metastases to the chest (the most frequent site of secondary lesions from bone tumors) are usually detected with CT. Bone scintigraphy with ^{99m}Tc–methylene diphosphonate (MDP), because of its relatively high sensitivity but low specificity, is used for the detection of polyostotic bone disease or bone metastases.

FDG PET, by providing whole-body tomographic metabolic imaging, appears particularly useful in evaluating for distant metastases to bones and other tissues. Recent observations indicate that PET with either ^{18}F-ion (*5*) or FDG (*6*) appears to be more accurate than ^{99m}Tc-MDP bone scanning, at least for osteolytic lesions (C Landoni, unpublished data, 2000).

DIAGNOSIS OF NATURE

The last step in the evaluation of patients with bone and soft-tissue tumors is the histologic examination of biopsy specimens. If the tumor is found to be malignant, the grade is estimated on the basis of cellularity, nuclear atypia, mitotic activity, and necrosis. Difficulties in selecting a representative tumor sample and disagreement in defining the histopathology of some lesions, such as soft-tissue sarcomas, limit the accuracy of biopsy.

Imaging may be helpful by suggesting malignancy through the size and depth of a tumor. When malignancy is suspected, patients are usually referred for biopsy (*2*). Schulte et al. (*4*) suggest that integrated FDG PET and MR images of bone tissue may help target the tissue more accurately for biopsy. In addition, Schulte et al. pose the question of whether a role exists for FDG PET as an integrated method in, or an alternative to, biopsy for grading bone tumors.

Several FDG PET studies have shown a correlation between FDG uptake and grading (*7–9*) and have suggested the possibility of discriminating between benign and malignant lesions using standard cutoff values for uptake (*10*). However, false-positive findings for non-neoplastic lesions, such as os-

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teomyelitis and Paget's disease (*11*,*12*), have also been reported. In a study by Kole et al. (*13*), performed with a full kinetic analysis of FDG dynamic data for tissue and plasma, no differentiation between low- and high-grade bone tumors could be found.

Schulte et al. (*4*) report that the counterpart to the high sensitivity observed is the relatively low specificity (66.7%). This is caused by false-positive findings not only for all benign aggressive lesions but also for lesions that are not considered aggressive, such as fibrous dysplasia. The incidence of false-positive findings of bone tumors with FDG limits the application of this PET technique for grading tumors and does not allow one, at present, to avoid biopsy before initiating therapy.

However, even if the correlation with grading is poor, a correspondence exists between FDG uptake and lesion aggressiveness. The value of information on tumor aggressiveness (i.e., its impact on patient management) has yet to be established for bone tumors. It may be important in determining prognosis, as has already been shown for tumors of the brain. In bone tumors, benignity, as defined histologically, does not necessarily imply conservative surgical resection. Indeed, bone lesions that are benign but locally invasive and recurrent (stage 3 by Enneking) are treated with wide operative resection, similarly to high- and low-grade sarcomas of the bones or soft tissues.

ASSESSMENT OF RESPONSE TO TREATMENT AND FOLLOW-UP

In musculoskeletal tumors, ^{201}Tl, ^{99m}Tc–methoxyisobutyl isonitrile, and FDG PET have been reported to be more accurate than CT and MRI in the follow-up of patients with treated bone and soft-tissue sarcomas, by helping in the differentiation of fibrosis from recurrence (*14*). FDG PET, because of its higher spatial resolution and quantification capabilities, is considered the method of choice. FDG PET measurement of tumor response early after adjuvant chemotherapy has been shown to be fairly accurate for soft-tissue and bone sarcomas (*15*–*17*).

In general, the importance of any diagnostic procedure is measured by its impact on patient management and therapeutic strategies, by the information it provides that cannot be learned conventionally, and by its cost-effectiveness. FDG PET is now established for staging lymph node metastases in patients with non–small cell lung carcinoma (*18*,*19*), for evaluating patients with breast cancer (*20*–*22*), and for detecting distant metastases and recurrences of many tumors, such as those of the gastrointestinal tract (esophagus, pancreas, colon, and rectum), thyroid, and brain (*23*).

For musculoskeletal tumors, recent scientific evidence suggests that FDG PET is clinically indicated for detecting distant metastases; evaluating, in conjunction with MRI, local tumor extension for guiding biopsies of large and heterogeneous neoplasms; detecting recurrences during follow-up; and evaluating treatment responses, although this last needs to be better standardized. Another potential use for FDG PET is as a noninvasive tool to assess malignancy or aggressiveness of musculoskeletal tumors. However, this application requires further research, including prospective longitudinal studies of aggressive "benign" tumors, and a clinical and pathologic consensus on the definition of benign and malignant musculoskeletal neoplasms and their aggressiveness.

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