PET Imaging in Sarcoma

Stephen Becher, MD*, Shervin Oskouei, MD

KEYWORDS

• Sarcoma • PET • PET/CT • Extremity • Soft tissue

KEY POINTS

- PET/CT scanning has evidence that it may be used in biopsy guidance, tumor detection and grading, tumor staging, therapeutic monitoring, and prognostication in sarcoma diagnosis and treatment.
- Currently the evidence does not support the routine use of PET/CT scanning in most sarcoma cases.
- Individual cases of specific histologic subtypes may benefit from PET/CT scanning for staging, biopsy guidance, and/or therapeutic monitoring.

INTRODUCTION

Extremity bone and soft tissue sarcomas are a heterogeneous group of tumors that arise from a mesenchymal origin. They are a rare group of cancers that represent less than 1% of all cancer cases. Approximately 12,000 new soft tissue and 3000 new bone sarcomas were diagnosed in America during 2014.[1] The diagnosis and treatment of extremity sarcomas has guidelines, although the heterogeneity of tumors in this group makes standardization of treatment a difficult proposition. Current guidelines call for a local MRI of the lesion and a computer tomography (CT) scan of the chest before surgery and a core needle biopsy to diagnose the histology of the tumor. Currently use of PET/CT scans is not considered as standard of care in the diagnosis and treatment of extremity sarcomas.[2,3]

PET scanning was originally performed independently from high-resolution anatomic imaging, such as CT. Before 2001 the fusion of PET and CT scanning was done with software fusion techniques and had clinical applicability limited mainly to the brain. Since 2001, however, commercially available combined CT and PET scanners have allowed the advent of combined acquisition of images and use of combined PET/CT scans is common in areas of the body other than the brain. The standard of care is now to use combined PET/CT scan and this article assumes the use of a combined PET/CT scan.[4]

The principle of PET is that proton-rich nucleotides emit positrons via β^+ decay. In this mode a nucleus emits a positron and neutrino while reducing its atomic number by one to a more stable, less proton-rich, nucleus. The neutrino passes through matter without interacting but the positron travels only a few millimeters at most before interacting with an electron in the surrounding matter. Once the positron and electron interact they annihilate each other, giving rise to two photons of equal energy (511 keV) that travel in opposite directions. A ring of detectors around the patient allows for detection of these particular photons traveling in opposite directions with a specific energy. The detection of the dual photon events allows for indirect measurement and localization of the originating positron. The F18 isotope of fluoride is a positron emitter with a relatively long half-life, allowing it to be incorporated into the glucose analog F18-deoxyglucose. F18-deoxyglucose may be injected into a patient, taken up preferentially by abnormal oncologic tissue, and measured using a PET scanner. Doing so allows for detection of primary and metastatic malignant

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Department of Orthopedic Surgery, Emory University, 57 Executive Park South, 160-3, Atlanta, GA 30329, USA
* Corresponding author.
E-mail address: xiaobaidi@yahoo.com

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disease of many differing types.[5] This article evaluates the possible role of PET/CT in diagnosis and treatment of bone and soft tissue sarcomas of the extremities.

AREAS OF APPLICABILITY

PET/CT scanning has been studied in sarcoma detection and grading, biopsy guidance, sarcoma staging, therapeutic monitoring, and prognostication (**Box 1**).

Sarcoma Detection and Grading

This area is the oldest and most researched area for PET scanning in sarcoma. The standardized uptake value (SUV) is a measure of radioactivity in a specific area of interest relative to an idealized even distribution of radioactive material throughout the body. A higher SUV value means the area interrogated by the scan is more metabolically active. In general, higher-grade tumors are more metabolically active than lower grade tumors.[6] However, caution must be taken in such generalizations because high-grade tumors may have a low metabolic activity and not every highly metabolically active tumor is necessarily a malignant entity.[7]

Different studies have used different cutoffs for SUV values to determine if the SUV can predict grade. Folpe and coworkers[8] used an SUV value of greater than 7.5 as a cutoff and found 93% of tumors in this group were high-grade sarcomas, although this means that 7% of benign tumors also were in this group. At the same time 52% of all high-grade malignancies had an SUV value of less than 7.5. There was a correlation between higher SUV values in high-grade tumors and histologic findings of increased mitosis rate and cellularity.[8] Charest and coworkers[9] found that all lesions in their study of 212 bone and soft tissue sarcomas that had an SUV value of greater than 6.5 were of high grade, although many high-grade sarcomas had SUV values of less than 6.5. Meta-analysis performed by Ioannidis and Lau[7] evaluated cutoffs of SUV greater than 2.0 and greater than 3.0 and varying levels of sensitivity and specificity for each cutoff.

Bastiaannet and coworkers[6] performed a meta-analysis of the available literature in 2004 with regards to detection of sarcomas using PET scanning. Overall sensitivity, specificity, and accuracy were found to be 91%, 85%, and 88%.[6]

Using SUV can allow for an estimation of tumor grade before biopsy (**Fig. 1**). A more metabolically active tumor is more likely to be high grade than a less metabolically active tumor, although there are enough outliers that one cannot rely on SUV values alone to determine grade. It remains a supplement to and does not replace biopsy of the lesion and histologic examination by a pathologist to determine the grade. This remains the gold standard for sarcoma grading.

Box 1
Areas PET/CT scanning may be useful in sarcoma diagnosis and treatment

- Sarcoma detection
- Sarcoma grading
- Sarcoma staging
- Biopsy guidance
- Therapeutic monitoring
- Prognostication

Biopsy Guidance

The most interesting application of PET scanning in sarcoma is its use to direct biopsy. There are often areas of necrosis or inhomogeneity seen on MRI in a sarcoma mass. If these areas are sampled the diagnosis is subject to sampling error. This may cause the tumor to be inappropriately graded, delay diagnosis, or if there is not enough clinical suspicion, allow a sarcoma to go undiagnosed. To avoid such scenarios it has been suggested to use PET scanning as a means to determine the most metabolically active area of a tumor

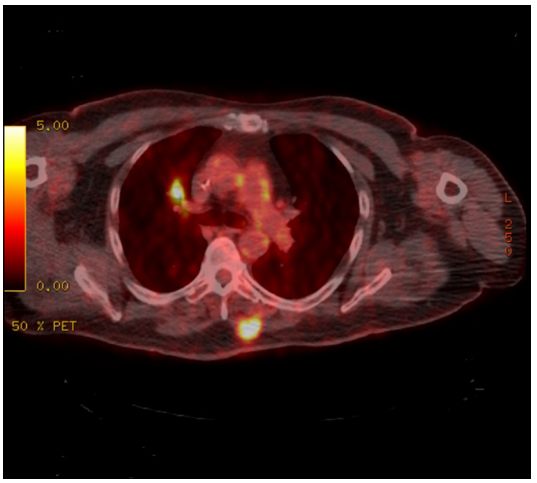

Fig. 1. PET scan of a 58-year-old man with a leiomyosarcoma in the posterior aspect of the spine. Although PET scanning can estimate the grade of a tumor with high accuracy it does not replace the need for accurate histologic diagnosis, which is the gold standard for grading any sarcoma. In addition the exact cutoffs in SUV_{max} values are not standardized across studies and between institutions for which tumors are high grade.

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