PET in the Diagnostic Management of Soft Tissue Sarcomas of Musculoskeletal Origin

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KEYWORDS

• Positron emission tomography • Liposarcoma • Malignant fibrous histiocytoma • Pleomorphic undifferentiated sarcoma • Malignant nerve sheath tumor • Rhabdomyosarcoma • Synovial cell sarcoma • Angiosarcoma

KEY POINTS

- A soft tissue sarcoma (STS) is relatively rare. (18) Fluorine-2-fluoro-2-deoxy-D-glucose (FDG) PET–computed tomography (CT) offers complementary information in the management of an STS.
- Additional research is needed to strengthen the current evidence and to elaborate on the application of FDG PET-CT, particularly for rare subtypes of STS.
- Though FDG PET-CT cannot replace direct tissue sampling, it can significantly enhance the biopsy diagnostic yield by targeting the hypermetabolic part of lesion.
- FDG PET-CT can be used to detect malignant transformation of a benign lesion into an aggressive lesion.
- Because classic size-based assessment of treatment response is inadequate, metabolic FDG PET data is valuable in posttreatment evaluation of cancer, including STS.

INTRODUCTION

Soft tissue sarcomas (STSs) are a relatively rare group of heterogeneous tumors derived from mesenchymal tissue elements. An STS can occur at any age, accounting for less than 1% of all adult solid tumors and about 7% of pediatric malignancies. As a result, STSs are the cause of 2% of all cancer-related deaths.[1,2]

Typically, the clinical manifestation of an STS is of a heterogeneous soft tissue mass that grows over time. Symptoms usually develop due to the mass effect on nerves, vessels, and other adjacent structures. The anatomic locations at which STSs of musculoskeletal origin most often occur are the extremities (70%), followed by the thoracic wall.[3] Within these locations, the muscular compartments are the most common spaces. Distinguishing between the more than 50 discrete histologic subtypes of STSs is possible through tissue biopsy. In adults, the most common histologic subtypes are liposarcoma, malignant fibrous histiocytoma (MFH), and leiomyosarcoma. In children, almost all STSs are rhabdomyosarcomas at 40%.[4,5] Prognosis of disease is subsequently determined

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through the combination of the histologic subtype, the tumor's grade, the size and depth of the primary tumor, the stage of the disease at its initial presentation, and the patient's age. Following treatment, additional indicators of prognosis are incorporated, including the presence of disease at the margins of the resected specimen and the recurrence of disease on successive follow-up imaging studies. Treatment protocols often focus on surgical resection with the addition of adjuvant chemotherapy and radiotherapy. With current management strategies, the resulting 5-year survival for patients with an STS is 50% for adults and 71% for pediatric patients.[3]

With the advent of PET–computed tomography (CT), many clinicians and researchers have explored the use of (18) fluorine-2-fluoro-2-deoxy-D-glucose (FDG) PET imaging to improve the management of STSs. This article reviews the current evidence for use of FDG PET-CT in the general diagnosis, staging or prognosis, and treatment monitoring of STSs. Additionally, a brief overview of several of the most common histologic subtypes of STS are discussed with more specific information regarding the use of FDG PET-CT in the management of each subtype.

VALUE OF PET IN THE DIFFERENTIAL DIAGNOSIS OF PRIMARY SOFT TISSUE MASSES

FDG PET-CT is rarely the modality of discovery for a mass concerning for a STS. However, FDG PET-CT may be used for specific patient populations as a method for detecting malignant transformation of benign lesions into biologically aggressive lesions. One example of this is the case of plexiform neurofibroma transformation into a malignant peripheral nerve sheath tumor (MPNST).[6,7] On finding a suspected malignancy, evaluation proceeds with tissue sampling and histologic grading. Though FDG PET-CT cannot replace a direct tissue sampling, it can significantly increase the diagnostic yield of the biopsy by targeting the hypermetabolic part of a heterogeneous lesion.[3]

Grading a tumor is the most reliable predictor of a tumor's biological behavior and the patient's ultimate clinical outcome. The most commonly used grading system for STSs is the French Federation of Cancer Centers Sarcoma Group (Fédération Nationale des Centers de Lutte Contre le Cancer [FFNLCC]) grading system. The FFNLCC system categorizes tumors based on the mitotic rate, cellularity, and degree of differentiation. Recently, many studies have explored the complementary role of FDG PET-CT in the grading of STSs.[8–11] Benz and colleagues[12] analyzed 120 subjects with 12 different STS subtypes. Their study revealed a significant relationship between the standard uptake value (SUV) at maximum SUV (SUV_{max}) of a lesion and the histologic grade given by the 3-tiered FFNLCC system when using a cutoff of 6.6 g/mL. On a meta-analysis examining a total 441 tumoral lesions that attempted to distinguish malignant STSs from benign lesions with FDG PET, Ioannidis and Lau[13] reported a sensitivity and specificity of 87% and 79% using an SUV_{max} threshold of 2.0, and 70% and 87% using an SUV_{max} threshold of 3.0, respectively. In their study, 100% of the intermediate and high-grade sarcomas were detected, whereas 74% of lower grade sarcomas and 39% of benign lesions were correctly characterized. Furthermore, several additional studies have shown similarly high sensitivities in distinguishing high-grade sarcomas from lower grade tumors.[14,15] Another meta-analysis, which included 341 subjects with STSs, revealed a sensitivity and specificity of 88% and 86%, respectively, when using the mean SUV to discriminate between low-grade sarcomas and high-grade sarcomas.[16]

Several recent studies have attempted to achieve better performance in STS and benign tumor differentiation by examining the lesion FDG kinetics. Lodge and colleagues[17] reported that malignant STSs achieve the maximal FDG uptake 4 hours following the radiotracer injection, whereas benign lesions reached peak uptake after only 30 minutes. They found that these indices had a sensitivity and specificity of 100% and 76%, respectively. In another approach, Dancheva and colleagues[18] studied the method of dual time point imaging for the detection of recurrent tumor in restaging FDG PET-CT studies. They reported that an increase in SUV greater than 10% on delayed imaging could detect high-grade sarcomas with a sensitivity and specificity of 100% and 80%, respectively.

With the many potential benefits of evaluating a primary tumor with FDG PET-CT, it is important to know its limitations. Though FDG PET-CT has shown the ability to differentiate between high-grade and benign tumors on multiple studies, there is lack of evidence of its ability to differentiate between low-grade and benign soft tissue lesions.[3] One study found that false-negative interpretations of low-grade sarcomas was found to be primarily related to their low metabolic rate, whereas false-positive results of benign lesions were often the result of associated inflammation.[16]

PET IN INITIAL STAGING OF SOFT TISSUE SARCOMAS

Staging a patient's STS is among the most important prognostic indicators for a patient's clinical