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Synovial sarcoma: dynamic contrast-enhanced MR imaging features

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Abstract *Objective.* To determine whether previously described so-called malignant dynamic contrast-enhanced magnetic resonance (MR) imaging features – early start, peripheral enhancement and early plateau or washout phase – occur consistently in synovial sarcoma.
Design and patients. Dynamic contrast-enhanced MR images of 10 patients with histologically proven synovial sarcoma were reviewed. The start, pattern and progression of tumor enhancement were assessed and correlated with histopathology.
Results. In all patients, the time interval between arterial and early tumor enhancement was less than 7 s (mean 4.40 s, SD 2.09 s). Six synovial sarcomas showed enhancement with a subsequent rapidly progressive linear increase in signal intensity followed by a plateau in one lesion and washout in five. Four lesions showed a late sustained increase in enhancement after the initial rapid increase in enhancement. The pattern of initial enhancement was peripheral in only two lesions, diffuse in four and heterogeneous in four lesions.
Conclusions. Enhancement of tumor within 7 s after arterial enhancement is, of the three parameters described previously, the only sign that occurs consistently in synovial sarcoma.

Keywords Soft tissues, neoplasms · Sarcoma, synovial/di [Diagnosis] · Sarcoma, synovial/pa [Pathology] · Magnetic resonance (MR) imaging, contrast enhancement · Gadolinium/du [Diagnostic Use]

Introduction

Synovial sarcoma comprises approximately 8–10% of all soft tissue sarcomas [1]. Magnetic resonance (MR) imaging has proved valuable in the detection and staging of soft tissue tumors. However, MR features are not tumor-specific [2, 3, 4, 5, 6]. Although synovial sarcoma is a well-defined entity, frequently occurring in the lower extremity in close proximity to joints, tendon sheaths or bursae, it is this soft tissue sarcoma that is radiologically most frequently misdiagnosed as benign [7], perhaps due to its often small size, well-defined margins and slow progression [2, 4, 5, 8, 9].

Dynamic contrast-enhanced MR imaging is a noninvasive method to provide information about microcirculation in tumors. Enhancement characteristics obtained by dynamic contrast-enhanced MR imaging reflect the results of tumor angiogenesis, i.e., increased vessel density and capillary permeability. Recently, it has been shown that, using this technique, malignant soft tissue masses tend to enhance earlier, faster and predominantly in a peripheral fashion compared with benign lesions [10, 11].

Our objective was to determine whether the reported dynamic contrast-enhanced MR features of soft tissue sarcoma such as start, pattern and progression of tumor enhancement occur consistently in synovial sarcoma.

Table 1 Overview of dynamic contrast-enhanced MR features associated with benign and malignant lesions

	Malignant features	Benign features
Start of tumoral enhancement	≤6 s after arterial enhancement	>6 s after arterial enhancement or absence of enhancement
Spatial pattern of enhancement	Peripheral	Diffuse, inhomogeneous, septal or absence of enhancement
Time pattern of enhancement	Type III, IV	Type I, II, V

Materials and methods

Patients

MR images from 10 patients with musculoskeletal tumors who had been referred to our hospital between May 1995 and August 1998 were examined. All patients had histologically proven synovial sarcoma (5 monophasic, 5 biphasic) using appropriate immunohistochemical or molecular-genetic investigations [12]. Some of the data on six patients included in this study group were previously published as part of a mixed population [10]. Three patients presented with local tumor recurrences, developed 7–24 years after resection of the primary tumor. MR studies were obtained prior to intervention, except in two cases; in one, trocar biopsy was taken before imaging, and in the other MR imaging was performed after four cycles of chemotherapy. While chemotherapy can influence enhancement results, the latter patient was included in the study. Radiological findings had indicated that he was a poor responder, despite the fact that no histological confirmation of chemotherapy response was available, as lung metastases had prevented tumor resection. The study group (four males and six females) ranged in age from 15 to 72 years at the time when their initial primary tumors had been diagnosed (mean 43 years). The locations of the analyzed lesions were knee (4), calf (3), upper arm (1), forearm (1) and hand (1).

MR imaging

The MR examinations were conducted on a 0.5-T or 1.5-T MR system (Philips Medical Systems, Best, The Netherlands) using T1-weighted [repetition time (TR) ms/echo time (TE) ms: 530–600/12–25, echo train length (ETL): 3] fast spin echo sequences and T2-weighted (TR/TE: 2209–5492/60–150, ETL 5–12) fast spin echo sequences with frequency-selective fat suppression. These studies were followed by a dynamic contrast-enhanced study. For dynamic enhanced MR imaging, a magnetization prepared T1-weighted, gradient-echo sequence was used (TR/TE: 9.5–15/3–6.9, flip angle 30°, preparatory pulse delay time 472–741 ms, number of excitations 1, matrix size 128×256, field of view 250–300 mm, section thickness 7–10 mm). At three levels we obtained sections with a temporal resolution of 3 s. The levels and orientation for the dynamic study were chosen on the basis of the unenhanced T1- and T2-weighted images. The optimal section for the dynamic study contained the largest amount of tumor and an artery. The orientation for dynamic imaging was axial in nine patients and sagittal in one. Data acquisition and manual bolus injection of 0.1 mmol per kilogram body weight Gd-DTPA (Magnevist; Schering, Berlin, Germany) followed by a saline flush were started simultaneously. The total dynamic scan time was 5 min. Contrast-enhanced dynamic images were electronically subtracted from the first pre-contrast image by using standard commercially available software. Regions of interest were drawn in the maximal enhancing area of the tumor, the artery and in muscle, which was used as a baseline reference. The signal intensity values during the dynamic study were plotted against time on time-intensity curves.

On the initial MR images we evaluated the following features: size, margin, signal characteristics, homogeneity, fluid-fluid levels, hemorrhage, septations and calcifications. Tumor margins were categorized as either infiltrating, ill defined, partially defined or well defined, depending on their relation to the surrounding tissues. Signal characteristics were related to adjacent normal fat and normal muscle. Tumor homogeneity was scored as follows: homogeneous, mildly inhomogeneous (<25% inhomogeneity), moderately inhomogeneous (25–50% inhomogeneity) or complex (>50% inhomogeneity) [13].

We studied the diagnostic value of three dynamic enhancement characteristics that have successfully differentiated benign from malignant soft tissue masses (Table 1) [10], all MR images being evaluated by two observers in concert:

Start of tumoral enhancement: The start of tumoral enhancement was defined as the time interval between start of arterial and tumoral enhancement.

Spatial pattern of enhancement: The pattern of initial tumoral enhancement, assessed on dynamic contrast-enhanced subtraction images, was scored as peripheral, diffuse, inhomogeneous, septal or absent. The pattern of vascularization, and thus enhancement, is different for malignant and benign lesions. Malignant lesions have a tendency to outgrow their vascular blood supply and develop a peripheral (neo)vascularized zone with a central area of necrosis. Benign tumors in general do not outgrow their vascular blood supply, and do not have large necrotic areas. Therefore, peripheral enhancement is associated with malignant lesions, whereas diffuse, inhomogeneous, septal, or absent enhancement are features associated with benign lesions [11].

Time pattern of enhancement: The progression of tumoral enhancement was subjectively classified according to the shape of the time-intensity curve (Fig. 1). We distinguished five different

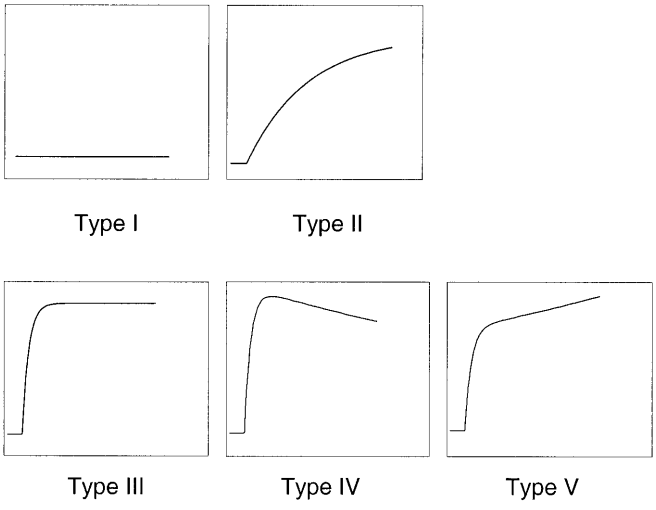

Fig. 1 Classification for subjective assessment of time-intensity curves: Type I, no enhancement; type II, gradual increase in enhancement; type III, rapid initial enhancement followed by a plateau phase; type IV, rapid initial enhancement followed by a washout phase; and type V, rapid initial enhancement followed by sustained late enhancement

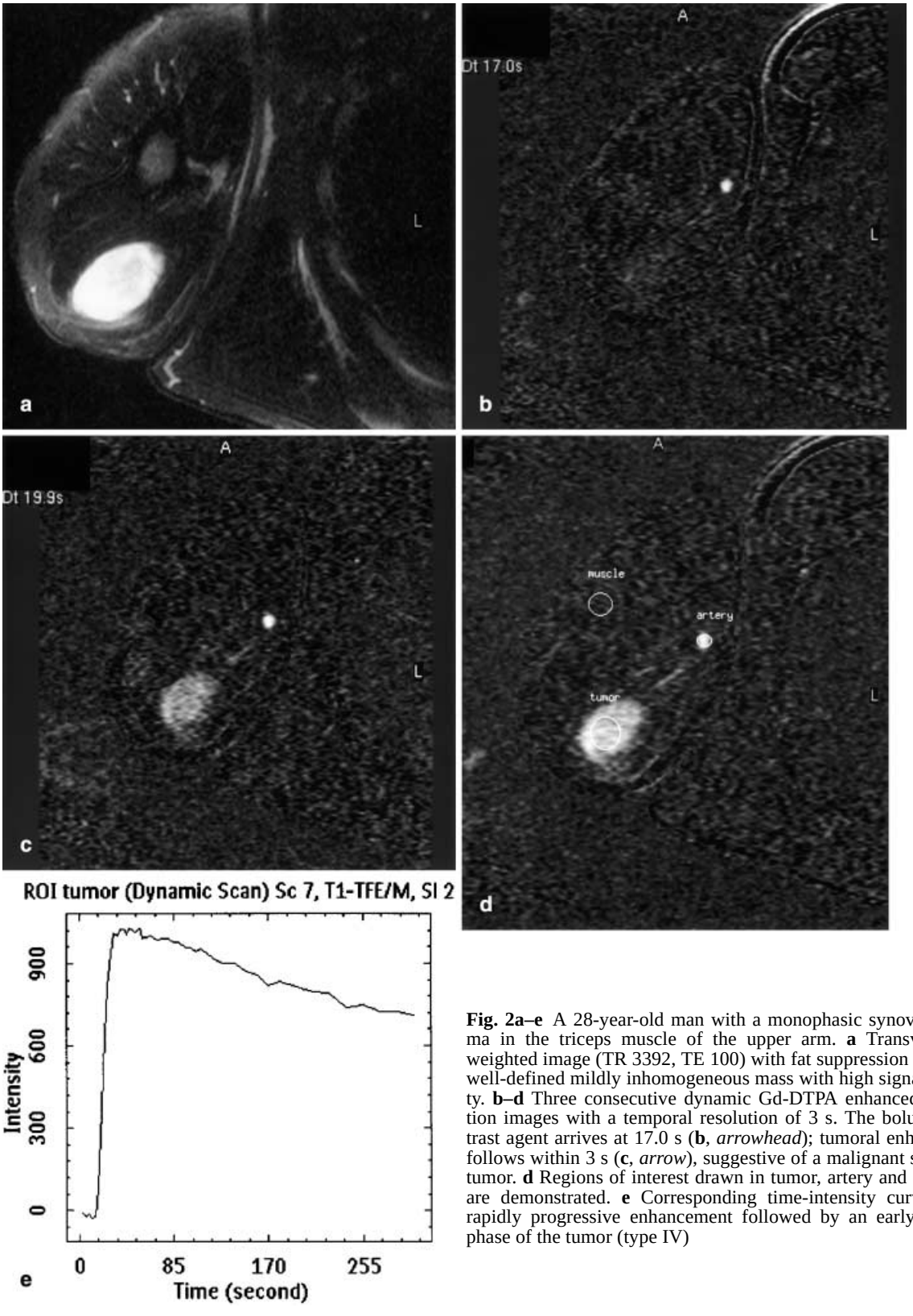

Fig. 2a–e A 28-year-old man with a monophasic synovial sarcoma in the triceps muscle of the upper arm. **a** Transverse T2-weighted image (TR 3392, TE 100) with fat suppression exhibits a well-defined mildly inhomogeneous mass with high signal intensity. **b–d** Three consecutive dynamic Gd-DTPA enhanced subtraction images with a temporal resolution of 3 s. The bolus of contrast agent arrives at 17.0 s (**b**, *arrowhead*); tumoral enhancement follows within 3 s (**c**, *arrow*), suggestive of a malignant soft tissue tumor. **d** Regions of interest drawn in tumor, artery and in muscle are demonstrated. **e** Corresponding time-intensity curve shows rapidly progressive enhancement followed by an early washout phase of the tumor (type IV)

time-intensity curves: absence of enhancement (type I); gradual increase (no steep slope and a continuous increase in signal intensity over a period of 5 min) of enhancement (type II); rapid initial enhancement followed by a plateau phase (arterial-like steep slope, maximum signal intensity being reached within 120 s followed by signal intensity that does not change for 180 s) (type III); rapid initial enhancement followed by a washout phase (initial part of curve as type III, but a decrease in signal intensity after maximum has been reached) (type IV); or rapid initial enhancement and sustained late enhancement (signal intensity increases further after the early maximum has been reached) (type V) [10, 14].

The biopsy specimens of the primary tumors were reviewed for histological analysis. Resection specimens were not usable because all but one of the patients were treated with isolated limb perfusion or systemic chemotherapy before surgery.

Results

The largest tumor diameter ranged in size from 0.8 to 18.0 cm (mean 7.5 cm, SD 5.6 cm). Six lesions were equal to or larger than 5.0 cm. Two of the smaller lesions were recurrences. The signal intensities were isointense (n=2), slightly hyperintense (n=7) or hyperintense (n=1) to muscle, but lower than fat on T1-weighted images and high on T2-weighted images. Six synovial sarcomas displayed mildly inhomogeneous to complex signal characteristics on T1- and T2-weighted images. Low-signal intratumoral septations were seen in four patients and hemorrhage in one. Fluid-fluid levels, calcifications and a triple signal pattern on T2-weighted images as described by Jones et al. [4], consisting of a combination of high, intermediate and low signal intensity, were not seen. Nine lesions were relatively well demarcated from adjacent tissues by a pseudo-capsule.

In all patients, the time interval between arterial and tumoral enhancement was less than 6.6 s (mean 4.40 s, SD 2.09 s). Six synovial sarcomas demonstrated enhancement with an immediate rapidly progressive linear increase in signal intensity, followed by a plateau in one, and washout in five lesions (Fig. 2). The time needed to reach the plateau phase was 90 s after initial tumoral enhancement in this single case. The washout phase started on average 46 s (range 15–70 s) after initial tumor enhancement. One synovial sarcoma displayed a gradual increase in enhancement (type II) (Fig. 3), and the remaining three showed during the entire scan time of 5 min a late sustained increase in enhancement after the initial rapid increase (type V). The pattern of initial tumoral enhancement was peripheral in only two lesions, diffuse in four and heterogeneous in four. The pattern of tumoral enhancement was independent of tumor size.

All patients displayed at least one dynamic contrast-enhanced MR feature associated with malignancy, seven cases demonstrated at least two features, whereas only one case demonstrated all three dynamic contrast-enhanced MR features associated with malignancy.

No differences were noted with regard to specific imaging findings between primary and recurrent synovial sarcoma.

Discussion

Synovial sarcoma typically presents as a well-defined, often inhomogeneous soft tissue mass (on conventional MR imaging). The MR findings are often not characteristic for malignancy. Dynamic contrast-enhanced MR imaging has been used to differentiate between benign and malignant soft tissue masses, and thus used to narrow the differential diagnosis.

On dynamic contrast-enhanced MR images, early enhancement, i.e., within 7 s after arterial enhancement, was the only pharmacokinetic feature associated with malignancy consistently observed in all synovial sarcomas. We anticipated that we would observe this finding because the early start of tumoral enhancement reflects the rich (neo)vascularization present in soft tissue sarcoma. An early start of tumoral enhancement has previously been shown to be valuable in differentiating benign from malignant soft tissue tumors [10]. However, only one case exhibited all three dynamic contrast-enhanced MR features associated with malignancy, i.e., an early start of tumor enhancement, peripheral tumoral enhancement and rapid initial enhancement followed by a plateau or washout phase.

Instead of these features previously associated with malignancy, we observed in four lesions a late sustained increase in signal intensity during the total scan time, after initial rapid enhancement (type V). In an attempt to explain this, we reviewed the previously described physiological and pharmacokinetic two-compartment models [15]. According to Tofts et al. [15], a mixed flow- and permeability-limited model is the most suitable model for the signal enhancement of soft tissue sarcoma. During first pass, contrast agent diffuses from the intravascular into the extravascular spaces, until equilibrium is reached. The time interval of this process depends on vessel density, vessel permeability for contrast agents and the amount of the extravascular extracellular space (EES). Only highly vascularized tumors with a small EES and highly permeable vessels will display the rapid washout or plateau phase that we found in six of 10 synovial sarcomas [16]. The late sustained increase in enhancement we found in our study group may be explained by a large EES and decreased vessel permeability.

The third dynamic contrast-enhanced MR feature we evaluated was the spatial pattern of tumor enhancement. Peripheral enhancement has been previously related to malignancy [11]. However, only two of 10 synovial sarcomas demonstrated peripheral enhancement. The absence of peripheral enhancement in eight lesions (four

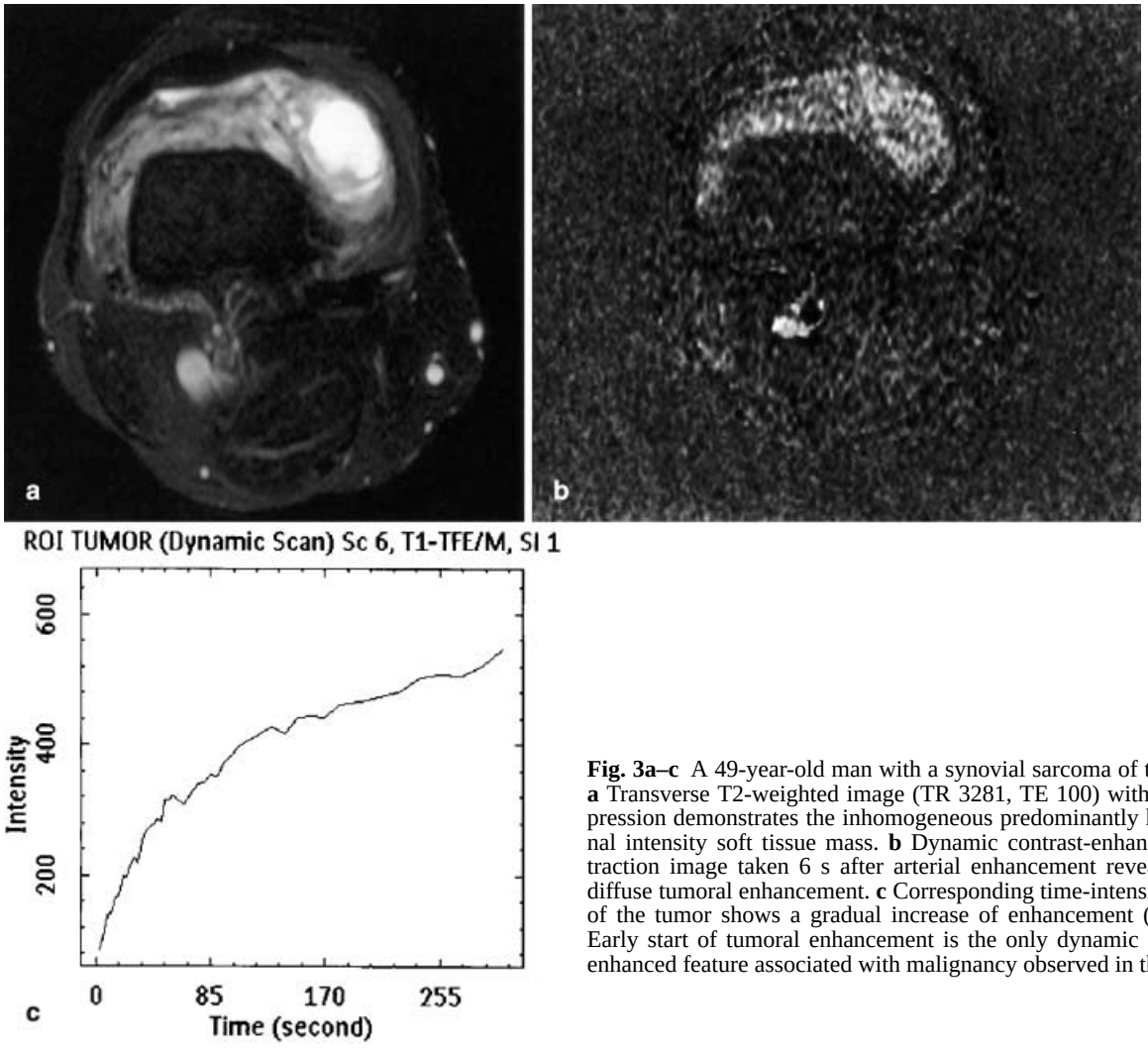

Fig. 3a–c A 49-year-old man with a synovial sarcoma of the knee. **a** Transverse T2-weighted image (TR 3281, TE 100) with fat suppression demonstrates the inhomogeneous predominantly high signal intensity soft tissue mass. **b** Dynamic contrast-enhanced subtraction image taken 6 s after arterial enhancement reveals early diffuse tumoral enhancement. **c** Corresponding time-intensity curve of the tumor shows a gradual increase of enhancement (type II). Early start of tumoral enhancement is the only dynamic contrast-enhanced feature associated with malignancy observed in this case

diffuse, four heterogeneous) may be explained by slow growth and increased vascularization of the whole tumor without large areas of necrosis.

In conclusion, early enhancement is the only dynamic contrast-enhanced MR feature associated with malignancy that we consistently observed in synovial sarcoma. When a nonspecific or small well-defined benign-appearing mass, located in close proximity to joints, tendon sheaths or bursae, displays early enhancement on dynamic contrast-enhanced MR images, synovial sarcoma needs to be included in the differential diagnosis. Absence of peripheral enhancement and sustained progression of tracer uptake can not be used to exclude synovial sarcoma from the differential diagnosis. Despite the use of imaging characteristics to try to suggest a specific diagnosis, histological examination remains necessary to differentiate between benign and malignant soft tissue tumors.

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