Use of Quantitative dynamic contrast MR imaging to Monitor Musculoskeletal Sarcomas: Corrlation with FDG PET and Pathology

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Introduction:

The introduction of adjuvant and neoadjuvant chemotherapy has resulted in marked improvement in survival rates in patients with musculo-skeletal sarcomas. A favorable response to pre-operative chemotherapy is generally associated with higher disease-free survival rates and better limb-savaging resection. Accurate evaluation of tumor response to pre-operative chemotherapy is of prime importance, in view of increased morbidity associated with delay in definite surgical treatment. Conventional MRI is currently the choice of modality in solid tumor evaluation primarily based on tumor size and its internal architecture. These morphological criteria, however, correlate poorly with the pathological results following surgical resection. In some hypervascular tumors, such as osteosarcoma, angiography is used. Considering that angiogenesis is a key factor in tumor growth, observation of the changes in tumor vessels on angiography is important but the technique is invasive and the observation is subjective. Metabolic imaging, fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) has been reported to be a sensitive technique in tumor response evaluation in sarcomas. However, it is costly and limited in its availability. Dynamic contrast-enhanced MR imaging (DCE-MRI) using a two-compartment pharmacokinetic modeling can provide non-invasive measures of angiogenesis, e.g. capillary permeability and plasma volume. Using current commercially available low-molecular-weight intravenous contrast, however, absolute measurement of these parameters is still challenging. Other quantitative assessments, such as the "initial area under the time-intensity curve (IAUC)" which reflects extraction and flow components, have also been proposed.

The purpose of this study is 1) to determine the value of IAUC using DCE-MRI in the preoperative evaluation of musculo-skeletal sarcomas and 2) correlate it with the tumor volumes on conventional MRI, glucose metabolism (SUV_{max}) on FDG PET, and histopathological assessment of the degree of tumor necrosis following surgical resection.

Methods and Materials:

A total of 16 patients with various musculo-skeletal sarcomas (10 osteosarcomas, 1 synovial sarcoma, 1 extra-skeletal osteosarcoma, 3 MFH, and 1 liposarcoma) undergoing neoadjuvant chemoradiation were selected. All patients had pretreatment MRI and post-treatment DCE-MRI at the time of completion of chemoradiation, prior to the surgical resection. Ten of these had pre- and post-treatment FDG PET imaging.

Conventional and DCE MRI was performed with a GE 1.5T Signa Echospeed scanner (GE Medical Systems, Milwaukee, WI). The DCE-MRI data were acquired with a very rapid 3D spoiled gradient recalled echo sequence (efgre3d) in conjunction with routine diagnostic imaging. FDG PET was performed using a CTI HR+ PET scanner (Siemens, Inc., Knoxville, Tenn.) and images were aquired approximately 60 minutes after intravenous administration of 15 to 20 mCi of 18-FGD.

Multivariate analysis was performed using following parameters; 1) tumor volume on MRI, 2) IAUC on DCE-MRI, 3) SUV_{max} on FDG PET, and 4) degree of tumor necrosis from surgical specimens. IAUCs were calculated from the first 90 seconds of uptake from the time-intensity curve generated from DCE-MRI and the values were normalized to the plasma AUC. The degree of tumor necrosis on surgical specimens was graded using Slazer-Kuntschik criteria; good response (GR) being greater than 90% of necrosis and poor response (PR) being greater than 10% viable tumor cells.

Results:

Among 10 patients who had conventional MRI, DCE-MRI data, and FDG PET, 5 had GR and another 5 PR on pathology (Table). In 5 patients with GR, mean percent changes in tumor volume, IAUC, and SUV_{max} were -53.6, -80.9, and -83.3, respectively. All 5 patients with PR demonstrated ≥60% decrease in IAUC on DCE MRI and none were with less than 60% demonstrated GR on pathology (Fig 1). On FDG PET, there was a significant difference in mean values of SUV_{max} between the patients with GR and PR and 4 of 5 patients with GR demonstrated ≥60% decrease after treatment. However, there were overlaps in each individual value between these two groups (Fig 2). One of the patients with synovial sarcoma showed little metabolic activity on the pre-treatment FDG PET with little changes after treatment. No significant difference was found between the patients with GR and PR (Fig 3).

Conclusions:

1) The morphologic changes using tumor volume was a poor indicator of tumor response.
2) SUV_{max} on FDG PET was a good indicator but IAUC, a dynamic MR imaging parameter, was the best indicator with all patients with ≥60% decrease showed ≥90% of tumor necrosis.
3) Additional investigation would be necessary using a larger number of patients to validate the IAUC of DCE-MRI further.

Table. Percent changes in tumor volume on MRI, IAUC on DCE-MRI, and SUV_{max} on FDG PET before and after treatment

Pathology	% Change in Tumor volume: MRI		% Change in IAUC: DCE MRI *		% Change in SUV_{max}:FDG PET	
	Mean	Range	Mean	Range	Mean	Range
Good Response (n=5)	-54	-71- 5	-81*	-64 - -90*	-76	-100 - -25
Poor Response (n=5)	-30	-32 - 29	70	-32 -163	-32	-65 - 0

Fig 1. % Changes in IAUC on DCE-MRI vs. tumor necrosis

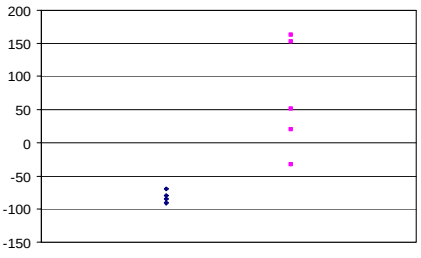

Fig 2. % Changes in SUV_{max} on FDG PET vs. Tumor Necrosis

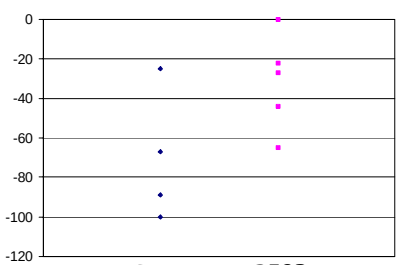

Fig 3. % Changes in Tumor Volume on MRI vs. tumor necrosis