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Perfusion MR imaging at 3-Tesla: Can it predict tumor grade and histologic necrosis rate of musculoskeletal sarcoma?

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KEYWORDS
Magnetic resonance imaging (MRI);
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Musculoskeletal sarcoma;
Neoplasm grading;
Tumor necrosis

Abstract
Purpose: To identify quantitative perfusion parameters that are best associated with tumor grade and tumor necrosis at magnetic resonance (MR) imaging at 3-Tesla.
Methods: MR perfusion studies of 31 patients with a musculoskeletal sarcoma were retrospectively evaluated by two readers. There were 18 men and 13 women with a mean age of 34.9 ± 24.4 (standard deviation [SD] years) (range: 6—87 years). All patients underwent carcinologic tumor resection less than 3 months after MR imaging. For all patients six perfusion parameters (three semi-quantitative and three permeability parameters) were analyzed. The percentage of tumor necrosis was estimated using MR imaging. Perfusion data were compared between groups of tumors with different grades and necrosis ratios. Interobserver variability was calculated using intraclass correlation coefficient (ICC).

Abbreviations: FNCLCC, Fédération nationale des centres de lutte contre le cancer; MSK, Musculoskeletal system; INI, Imaging necrosis index; ROI, Region of interest; FSE, Weighted fast spin-echo; NEX, Number of excitations; FOV, Field of view; HPF, High power field; SPGR, Spoiled gradient-echo; AIF, Arterial input function; ICC, Intraclass correlation coefficients; EES, Extravascular extracellular space; CER, Contrast enhancement ratio; AUC, Area under the curve; Max Slope, Maximum slope of increase; K^{trans}, Transfer constant from the plasma to the extravascular extracellular space; k_{ep}, Backflux constant; V_e, Extravascular extracellular space volume.

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Results: Interobserver variability among the perfusion parameters was good to excellent (ICC: 0.72—0.9). The area under the curve and maximum slope values showed a significant association with the degree of tumor necrosis ($P = 0.02—0.04$). When tumors with low necrosis ratios were compared to those with high ratios the former parameter was 80% lower. In the same groups, the imaging necrosis index was 56.9—59.8% higher in patients with grade 2 necrosis ($P = 0.01$). Extracellular space volume (V_e) was 31.4% to 55.8% lower in tumors with high grade while the backflow constant (K_{ep}) was 33.6% to 40.1%% higher in tumors with high grade.
Conclusion: Semi-quantitative MR perfusion parameters have an excellent reproducibility and are associated with the degree of histologic tumor necrosis in musculoskeletal sarcomas. The utility of permeability parameters for determining tumor grade needs further investigations.

Introduction

Tumor histological grading is an important prognostic factor for patients with musculoskeletal sarcomas and is related to the likehood of metastatic disease and overall survival [1—4]. Studies have suggested an association between tumor grade and surgical margin status, which is another strong prognostic indicator [3]. Treatment-induced histological necrosis is reported to be an independent predictor of overall survival and recurrence rates in patients with high grade soft-tissue sarcomas [5—8]. Tumor grading is more accurately performed on a whole tumor or surgical biopsy specimens [9]. Grading based on core biopsy material remains controversial due to tumor sampling issues and difficulties in evaluating tumor necrosis and mitotic indexes [1].

Magnetic resonance (MR) imaging obtained after intravenous administration of a gadolinium chelate is currently used for musculoskeletal tumor characterization, local staging and post-treatment follow-up [10—13]. Contrast-enhanced MR perfusion can non-invasively help assess tumor capillary density and vessel permeability [14,15]. Perfusion characteristics of viable and necrotic tumors areas are fairly different, making necrotic tissue assessment possible with this technique [16]. Although MR perfusion parameters have been shown to be associated with tumor grading in brain gliomas and liver tumors, there is scarce information regarding the correlation with tumor grade in musculoskeletal sarcomas [17,18]. Non-invasive tumor grading may help optimize patient imaging evaluation, surgical planning and the evaluation of treatment response.

Musculoskeletal sarcomas are frequently heterogeneous tumors with different zones of viable and necrotic tissue, which makes imaging post-processing difficult, most notably for selecting regions of interest (ROI) for analysis. Moreover, post-processing and measurements in MR imaging tend to be performed in the original acquisition plane for simplicity and to avoid reconstruction-related image quality loss. While there are no guidelines to determine the perfusion acquisition plane, macroscopic histopathological sectioning (which determines the zones to be evaluated microscopically) is performed by convention in the largest tumor diameter, which increase the discrepancies between imaging and histologic analysis [19].

The objective of this study was to identify quantitative perfusion parameters that are best associated with tumor grade and tumor necrosis at MR imaging.

Materials and methods

Patients

The medical and imaging files of 74 patients, who underwent MR imaging in our institution from May 2014 to January 2017 for the evaluation of bone or soft-tissue tumors, were initially retrospectively evaluated. A total of 43 patients with a tumor other than sarcoma or who underwent surgical resection of their tumor more than three months after MR imaging were excluded.

The study population consisted of 31 patients with a histopathologically proven sarcoma who underwent curative surgical resection less than three months after MR imaging. There were 18 men and 13 women with a mean age of 34.9 ± 24.4 (standard deviation [SD] years) (range: 6—87 years). At the time of MR imaging, nine patients presented with native tumors not being treated, 18 patients were under chemotherapy and four patients had received radiotherapy. Due to the retrospective data analysis, institutional review board exemption was granted.

Pathological analysis

The surgical specimens of all tumors were analyzed by a pathologist specialized in musculoskeletal tumors. At least one section per centimeter in the plane of the largest tumor diameter was performed considering tumor heterogeneity along with surgical margins sampling according to international recommendations [19]. Soft-tissue tumor grading was performed according to the French system of the Cancer Centers (Fédération nationale des centres de lutte contre le cancer [FNCLCC]) while the grading of bone sarcomas was performed according to Broder's system [5,19]. The following parameters were extracted from these reports:

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