CHARACTERIZING THE BLOOD OXYGEN LEVEL-DEPENDENT FLUCTUATION IN MUSCULOSKELETAL TUMORS USING FUNCTIONAL MAGNETIC RESONANCE IMAGING

Li-Sha Duan[1], Meng-Jun Wang[1], Feng Sun[1], Zhen-Jiang Zhao[1], Mei Xing[1], Yu-Feng Zang[2], Steven Louis[3], Sheng-Jie Cui[4], Han Zhang[2], and Jianling Cui[1]

[1]*Department of Radiology, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, China,* [2]*Center for Cognition and Brain Disorders and the Affiliated Hospital, Hangzhou Normal University, Hangzhou, Zhejiang, China,* [3]*Physics Department, Oakland University, Rochester, Michigan, United States,* [4]*Department of Anatomy and Cell Biology, Wayne State University School of Medicine, East Canﬁeld Avenue, Detroit, United States*

Target audience: Researchers interested in cancer studies, musculoskeletal radiologists.

Purpose: Distinguishing between malignant and benign musculoskeletal (MSK) tumors is important for clinicians to determine treatment. Vascularization is proposed to be one of the important features for differentiating malignant and benign tumors, which can be detected by dynamic contrast-enhanced imaging and positron emission tomography. However, the drawbacks of these techniques (e.g., radiation hazards, allergic reactions, etc.) may preclude their usage in extensive patient cohort. In current study, we investigate whether the blood oxygen level dependent (BOLD) amplitude fluctuations, a noninvasive and exogenous contrast agent free technique, can characterize the malignant and benign musculoskeletal (MSK) tumors.

Methods: Fifty-two patients with primary MSK tumors (malignant: 38; benign: 14) were examined using 1.5 T MR scanner(Avanto, Siemens, Erlangen, Germany) in this study with following scanning protocol: three-dimensional turbo fast low angled shot (FLASH) T1 weighted images (3D T1WI) (TR/TE, 1900/2.97 ms; flip angle, 15°; slices, 176; slice thickness/gap, 1/0.5 mm; matrix, 256×246; field of view, 220 mm×220 mm) and two-dimensional echo planar imaging (EPI) BOLD fMRI with 20 axial slices (TR/TE, 2000/40 ms; slice thickness/gap, 5/1 mm; field of view, 220 mm×220 mm; matrix, 64×64; voxel size, 3.44 mm×3.44 mm×6.0 mm; dummy scans, 3; scanning time, 6 min, totally 177 scans). 3D T1WI was co-registered BOLD image for setting the regions of interests (ROI). The fMRI data was preprocessed using DPARSFA v2.4 and REST v1.8 based on SPM8 and Matlab 2010a. Three ROIs were chosen in center, periphery of the tumor and normal muscle respectively on T1WI for each patient, and then projected to the BOLD images for time series extraction. The BOLD time series in each ROI was transformed from temporal to frequency domain with a fast Fourier transformation (i.e., frequency power spectrum, where the "power" is the square of the BOLD fluctuation amplitude). This power spectrum was then divided into four frequency bands: band-1, 0.01–0.027 Hz; band-2, 0.027–0.073 Hz; band-3, 0.073–0.198 Hz; and band-4, 0.198–0.25 Hz. The normalized power values for the three ROIs belonging to the same tissue type were further averaged separately for each frequency band for the ANOVA.

Results and Discussion: In the frequency band between 0.073 and 0.198 Hz, the BOLD fluctuations were stronger in the peripheral than that in the central regions of malignant MSK tumors (Figure1, 2) in current study (post-hoc simple-effect analysis, $P < 0.05$, corrected); however, no such a difference was observed for the benign tumors. Vasomotion is an arteriolar phenomenon in normal tissue, which is associated with the rhythmic oscillations in arteriolar diameter which can be observed in vivo by intravital microscopy or laser-Doppler flowmetry. Several frequency components of vasomotion, such as 0.15–0.6 Hz, 0.052–0.15 Hz, 0.021–0.052 Hz, have been indentified to originate from the respiration, vascular myogenic activity in the arteriolar wall, and sympathetic activity respectively by these modalities. The similarity between the intravital microscopy or laser-Doppler flowmetry value for vascular myogenic activity (0.052–0.15 Hz) and our frequency band of interest (0.073–0.198 Hz, band-3) is striking, which mean band-3 may be myogenic origin. Microvascular density and blood supply in the periphery tend to be higher than that in the center of malignant tumors and the more blood supply need of the tissue, the higher myogenic activity according to literatures, which may explain our results.

Conclusion: Our finding provides the first evidence that BOLD fMRI could be utilized to delineate vascularization characteristics in MSK tumors and further provide complementary information to discrimination between malignant and benign MSK tumor.

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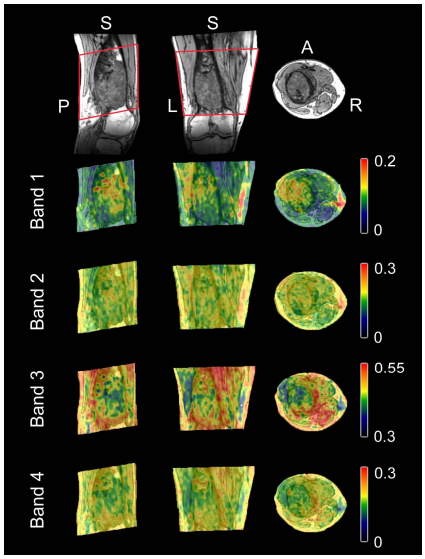

Figure 1. BOLD fluctuation magnitude within and around a malignant MSK tumor from a randomly-selected patient. The first row shows the 3D T1-weighted image of the MSK tumor in the Femur and the BOLD-fMRI field-of-view (within the red rectangular). The second to the last row show the BOLD fluctuation magnitude (normalized power) within frequency bands 1-4, which were rendered onto the T1-weighted image.

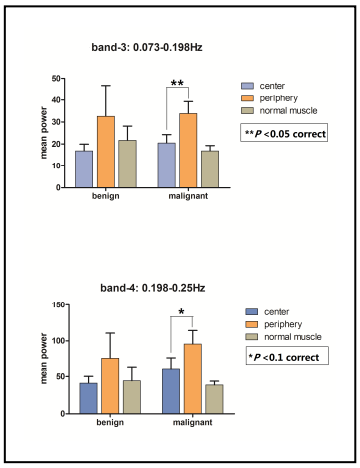

Figure 2 Post-hoc pairwise comparisons analysis with Sidak's adjustment in 2 frequency bands between benign and malignant tumors. ** is $P<0.05$ after correct; *is $P<0.1$ after correct.