Vessel Size Index MRI: Validation with Micro-CT Angiography

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Introduction. Vessel size index (VSI) MRI uses changes in the ratio of T_2 to T_2* after introduction of an iron oxide contrast agent to determine the mean vessel size within a voxel [1]; this technique may prove to be useful for monitoring the effect of anti-angiogenic agents in tumors. One method by which vessel size measurements of tumors have been done previously is *ex vivo* micro-CT (μCT) angiography [2]. In this work, we seek to validate the MRI VSI measurement by correlating it with μCT vessel size measurements of the same tumors. To account for tumor heterogeneity, we restrict the MRI parameter analysis to the viable tumor tissue as determined with multispectral k-means clustering [3]. Viable-tumor VSI requires no additional MRI scans beyond those used for the standard VSI measurement and can improve accuracy of MRI tumor parameter measurement by eliminating necrotic regions from the analysis.

Methods. *MRI Multispectral Analysis and Vessel Size Index:* The institutional AAALAC-accredited review board approved all animal procedures. MRI scans were performed on a 4.7 T Varian Unity Inova MRI system with a 20 mm two-loop surface coil (Varian Inc, Palo Alto, CA), for 16 mice with HM7 colorectal cancer tumors grown subcutaneously on the leg. A multi-slice FSE sequence with diffusion weighting was used to calculate an apparent diffusion coefficient (ADC) map (6 b-values ranging 300-1100 s/mm^2, TR = 3s, ETL = 4). A multi-slice spin echo sequence was used to calculate T_2 maps (TR = 3s, TE = 5,26,47,68 ms, NEX = 1), and a multi-slice gradient echo sequence was used to calculate T_2* maps (TR = 300 ms, TE = 4,10,16,22,28,34 ms, NEX = 4). ADC and T_2 data were collected as 8 coronal 1-mm-thick slices (FOV = 25.6×25.6mm, 64×64 matrix); T_2* maps were collected with a 128×128 matrix. A USPIO contrast agent (Molday ION, BioPAL) was then injected via a tail-vein catheter (200 μmol/kg), and the SE and GE sequences were repeated to calculate the post-contrast T_2 and T_2* maps.

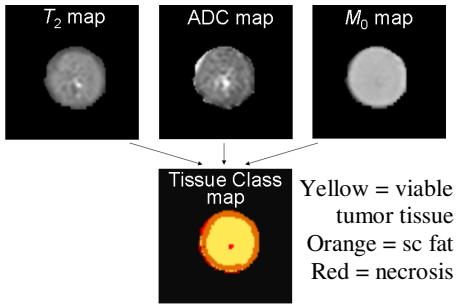

Figure 1. Multispectral analysis done with three source images (T_2, ADC, and M_0), using k-means clustering to segment tumor into four tissue classes. Viable tissue shown in yellow.

A vessel size index (VSI) map was calculated voxel-by-voxel using the ADC map and the pre- and post-contrast T_2 and T_2* maps [1]. Multispectral analysis for tissue segmentation was performed using the ADC and T_2 maps [3]. The tumor was segmented into four classes: viable tumor tissue, subcutaneous fat, necrosis, and necrosis + hemorrhage (Fig. 1). The viable tumor class was used as a mask to calculate VSI parameters only within the viable tissue, excluding regions of fat and necrosis.

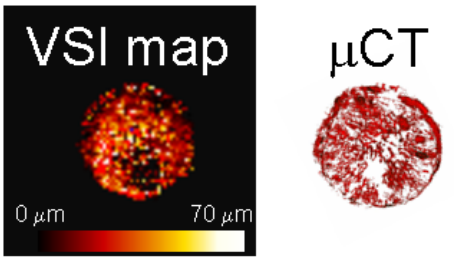

Figure 2. Comparison of MRI vessel size index map with μCT surface rendering for one representative tumor slice.

μCT Angiography: After the MRI scans were completed, μCT angiography was performed by perfusing a lead chromate latex contrast agent (MICROFIL®, Carver, MA) into the vasculature via the aorta at sacrifice of each animal [4]. The tumors were imaged *ex vivo* with a SCANCO μCT40 x-ray micro-computed tomography system. The μCT images were generated with the x-ray tube at an energy level of 45 kV, a current of 177 μA and an integration time of 450 milliseconds, for an isotropic resolution of 16 μm. Vessel size estimates were based on a skeletonization algorithm that employs boundary-seeded and single-seeded distance transform techniques [5].

Results. The mean VSI for each tumor was calculated within the viable tumor tissue as determined by the multispectral analysis. This mean value was compared to the mean vessel radius found from the μCT analysis (see Fig. 3). Out of 16 tumors, two were excluded due to excessive necrosis, which caused errors in the μCT analysis. A linear regression for the remaining 14 tumors resulted in a correlation coefficient of R = 0.83, (p = 0.0002). A linear regression of the mean VSI for the whole tumor, rather than just the viable tissue, yielded R = 0.79 (p = 0.0007); the VSI in the necrotic tissue did not correlate at all with μCT, meaning that it added only noise to the whole-tumor analysis.

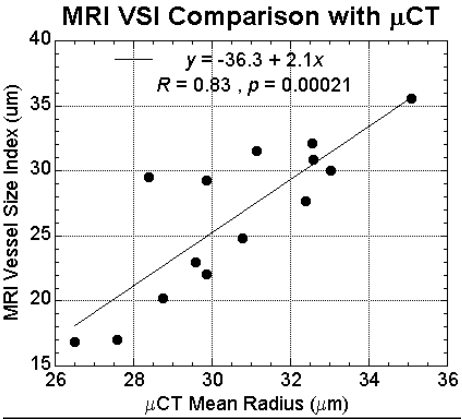

Figure 3. Comparison of mean vessel size calculated by MRI vs. μCT.

Conclusions. We have determined that measuring the vessel size index in viable tumor tissue using MRI yields comparable information to measuring the average vessel radius with *ex vivo* μCT angiography, with the added benefit of repeatable, *in vivo* measurements. Restricting the analysis to viable tumor tissue eliminates necrotic regions which contribute only noise to the analysis. We are currently in the process of further validating our viable-tumor VSI measurement by comparison to histology.

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[3] Carano *et al*.,**MRM** 2004, p. 542-51.
[4] Shojaei *et al*., **Nature** (in press).
[5] Zhou *et al*., **IEEE Trans. Vis. Comp. Graphics** 1999, p.196-209.