Effects of realistic vascular networks anisotropy on MR microvascular imaging

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Purpose: To characterize the impact of a realistic distribution of microvasculature structure on susceptibility-related MRI microvasculature imaging.

Background: MRI microvasculature imaging is a powerful tool for characterizing hemodynamic properties in vivo. Different approaches have been proposed for measuring vascular properties such as cerebral blood volume fraction (CBV), vessel size index (VSI), vessel density as well as vessel architecture, though all have used analytical expressions for modeling the imprint of the vasculature on the MR signal. To reduce the complexity of modeling, it was generally assumed that the vessels are straight cylinders isotropically distributed in space. However, the cerebral vasculature is highly structured and its complex architecture generally departs from an isotropic distribution. Here, we explore the impact of the structural complexity of the vasculature, summarized in terms of anisotropy, on CBV and VSI estimations using numerical simulations in conjunction with a realistic vascular network of a mouse brain.

Methods: The microvasculature geometry used for this study was obtained from the Knife-Edge Scanning Microscope (KESM) Brain Atlas which is publicly available at http://kesm.cs.tamu.edu/home. It consists of the whole mouse brain vasculature acquired at 1μm-thick serial slices and imaged at ~0.7μm resolution in plane (Fig.a). This 3D volume was subdivided in 62,921 cubic MRI voxels of 125μm³ (Fig.b). Post-processing was performed using Matlab on a HCP computer equipped with 32 nodes. Haralick image features were used for detecting and removing spoiled slices in the volume. After threshold on the vessels, morphological opening, closing and holes filling operations were applied. Stripes artifacts due to the sectioning were filtered. The vasculature trees were skeletonized and summarized in nodes and segments. For each voxel, CBV and R²KESM were extracted (Fig.c). To further characterize the structural complexity of the vasculature, the preferential orientation of its network was extracted by modeling the spatial distribution of the segments as a tensor and using the eigenvector of the largest eigenvalue as index of the orientational anisotropy (Fig.d). A subset of 4000 high quality voxels was selected based on their connectivity properties for MRI simulation. The MR signal evolution (FID + spin echo, TE=100ms) was simulated using a Fourier-based approach for computing the magnetic field perturbation and a deterministic approach for the water diffusion. The simulations were repeated with an increased magnetic field B₀ along z to mimic the effect of a contrast agent injection. VSI and CBV were computed as described in reference. The simulations were performed for two different orientations of B₀ (along z or y, Fig.d).

Results: For whole brain, the simulations yielded CBV=2.6±0.6% and R²KESM=2.3±0.3μm, in line with previously reported values (e.g., 1). The spatial distribution of the mean radii appears to be uniform across the brain for small vessels while non-uniformity appears in regions with larger vessels (coronal slices, Fig.c). The orientation map of Fig.d illustrates that preferential vessel orientations appear most prominently in the peripheral cortex in agreement with the presence of penetrating arteries. As for the impact of the vessel distribution on MRI, the histograms of Fig. e-f illustrate the variability in CBV and VSI estimations expressed as CBV_MRI/CBV_KESM and VSI_MRI/R²_KESM for B₀ along z. CBV and VSI estimations have similar variability (±4.8% for CBV, ±2.1% for VSI). However, correlation between CBV_MRI and CBV_KESM was higher for VSI (r=0.90) than for CBV (r=0.43) (data not shown). The spatial dependency on vessel orientation is presented on Fig.g-j. A substantial orientation dependent (from z to y) variation in the estimates of CBV_MRI (±15%) and VSI_MRI (±7%), was observed. The vessel orientation dependence of CBV_MRI/CBV_KESM and VSI_MRI/R²_KESM is illustrated in Fig.i-j for B₀ along z. The higher deviation is found for VSI with an overestimation of about 10% when the azimuth is zero and an underestimation of about 12% when the azimuth gets closer to π/2. For VSI, the highest deviation seems to appear for larger CBV (reddish dots).

Conclusion: We characterized the spatial variability of the vasculature network of a mouse brain and computed its vasculature imprint on the MR signal. We found an intrinsic orientation dependent variability of about 20% for CBV and VSI. However, the results may vary depending on MRI spatial resolution, pulse sequence design and contrast agent concentration and thus, requires further investigation. Limit in the slice thickness resolution of the KESM may have further biased vessel segmentation. Additional vasculature indices such as vascular density and fractal dimension could be considered in conclusion, our results indicate that variations in the spatial distribution of vascular networks need to be considered in microvascular MRI for accurate estimations of hemodynamic properties.