Validation of EPSI Angiography by Image Co-registration

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Introduction: High spectral and spatial resolution (HiSS) data, acquired with EPSI (echo-planar-spectroscopic imaging) can be used to acquire water and fat spectra from each small image voxel, and images can be constructed from various features of the water lines. These images are extremely sensitive to changes in local susceptibility caused by super paramagnetic iron oxide particles (SPIO), and therefore we proposed that images derived from HiSS data are very sensitive to tumor neo-vasculature. To test this hypothesis we have developed accurate image registration methods that allow precise correlation of MR images, microCT images of tumor vasculature, and CD31 stained tissue slices.

Methods: Athymic nude mice and Copenhagen rats were inoculated with Dunning AT6.1 prostate tumor cells in the right hind limb. A dental impression material cast was made around the tumor bearing leg of each mouse to facilitate image co-registration. Water fiducials are inserted into the dental material before it cures. Animals had physiological monitoring under isoflurane anesthesia during all procedures. High resolution spin echo images (137 µm in-plane in 0.6 mm thick slices) anatomic images were acquired with a 4.7 T Bruker scanner to provide anatomic reference for image co-registration. The tumor region was imaged using EPSI (TR = 800 ms) pre- and post- I.V. injection of paramagnetic particles (Bangs Labs), with spatial resolution of ~150 µm in-plane in ~500 µm thick slices and spectral resolution of ~3 Hz. After MRI, rats were sacrificed and a 10% Barium solution was injected into the femoral artery while blood was removed from the femoral vein. This provided high contrast for microCT images of tumor vasculature – as shown in Figure 1. For histological comparisons, a home-built slicing device was used to cut the leg of each into 3 mm thick slices. The two faces of each slice were scanned optically to facilitate co-registration of MRI and histology. The water fiducials seen in MRI were manually co-registered with the holes from the fiducials seen in the optical image of the cast/leg. Each slice was then further cut into 5 µm thick slices for histology and alternating slices were stained with H&E and CD31.

Using a mutual information based, manual image co-registration program written in Matlab, 3D assemblies of the CD31 stained slices were co-registered with MR images. Similarly, the microCT images were co-registered with EPSI.

Results: Regions containing high vascular density on MRI were identified based on changes in image intensity following contrast media injection. The average distance between regions of high vascular density on MRI and CD-31 stained regions on histology was 200 µm, indicating excellent spatial correlation. Figure 1shows typical co-registration of the microCT image of the barium vascular cast, and MR images showing vasculature. The 'bone colored' areas near to or overlapping blue and red on EPSI show where large changes in MR image intensity following contrast injection coincide with vasculature in the microCT image. An example of these regions are indicated by the red boxes in the figure. As suggested by the image registration, there was strong agreement between microCT and HiSS images regarding location of dense vasculature.

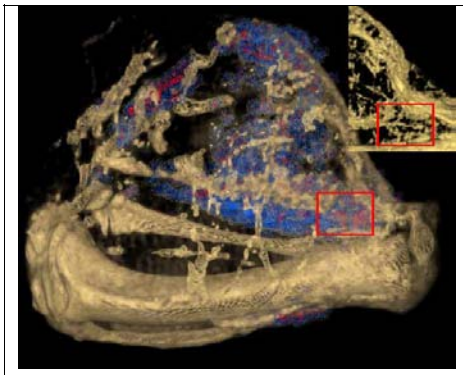

Figure 1 MicroCT/EPSI co-registered fusion image. Bone color is microCT. The foot would be to the right and the tumor encompasses most of the upper portion of the image. Blue and red denotes decreased and increased EPSI contrast after Bangs particle injection. The inset is microCT alone.

Conclusions: The data demonstrate strong correlation between tumor vasculature on MRI and the gold-standards: microCT and histology. This suggests that HiSS data are highly sensitive to tumor vasculature. The image registration methods described here have broad applications. They could be used, for example, to correlate MR images with immunohistochemical staining for a variety of important bio-markers such as VEGF, Hoechst, pimonidazole, etc.

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