Animal imaging using L1-regularized Quantitative Susceptibility Mapping

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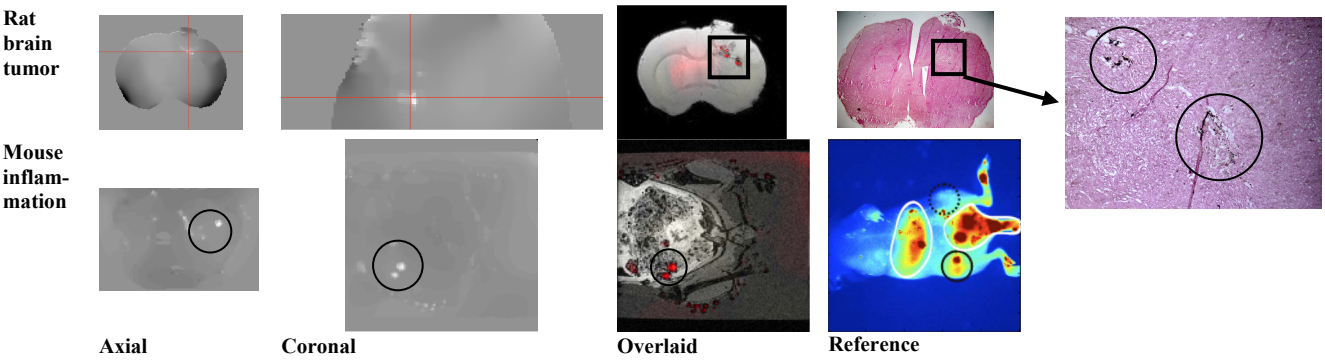
Introduction: Quantitative susceptibility mapping (QSM) is a technique that uses phase data from an MRI image to estimate the susceptibility distribution in the object. It has been demonstrated that QSM is able to correctly estimate the magnetic moment of specimen differing in susceptibility to the surrounding tissue [1]. We would like to exploit this ability to perform quantitative imaging of biomarkers in animal imaging. However, animal imaging presents additional challenges: the need for higher resolution suggests lower SNR; mixes of several tissues can create significant artifacts that impede quantification. In this work, we estimated the susceptibility change induced by SPIO nanoparticles that are targeted to specific cells. In experiment (1), we scan a rat brain after stroke injected with neural progenitor cells (NPCs) incubated in a solution containing a suspension of ferumoxide-protamine sulfate [2]. In experiment (2), we image a mouse injected with SPIO nanoparticles that target the intercellular adhesion molecule ICAM-1, which is induced in response to inflammation. We use total-variation based regularization to circumvent the problems with low SNR and the streaking artifacts.

Materials and Methods: In both experiments, we used a Bruker 7T scanner to obtain high-resolution 3-D T2* images. In experiment (1), the resolution is 0.1μm isotropic. Prussian blue staining was performed for reference in SPIO location. In experiment (2), the MRI resolution was 0.2 μm isotropic. To have reference images, we used the nanoparticles coated with the Alexa Fluor 488 labeled-HA I domain (F265S/F292G), which allows use of fluorescence microscopy to confirm the location of SPIO. The computations were performed in MATLAB.



Results: TV-based computation of the susceptibility map took 7 minutes for the rat brain tumor experiment and 3 minutes for the mouse inflammation case on a 2.4GHz Intel Core 2 Duo Macintosh laptop. In the Figure, we show the computed susceptibility maps in the axial and coronal sections, as well as an overlay of the magnitude image (grayscale) with the susceptibility map in red. In the tumor case, we observe strong susceptibility signal near the location of SPIO as seen on the reference Prussian blue stained image. The total susceptibility change in the region of SPIO is 7503.8. In the mouse inflammation experiment, the reference shows strong signal from the liver, spleen and bladder of the mouse, which has been washed out prior to the MRI; in the MRI reconstruction, we observe intense signal only in the region of the inflammation that matches the corresponding fluorescence image region (black circle). The total susceptibility change is 381.7 and 326.9 for the two red spots.

Discussion and conclusion: We observe a good match between locations of the SPIO particles that target ICAM-1 in a mouse with inflammation, as well as in the tumor in the rat brain. The important advantage of QSM is that the susceptibility maps can be used to quantify SPIO markers. Additional calibration is needed to convert the susceptibility change numbers computed by the algorithm to SPIO iron mass. Another important future research direction is direct validation of the quantitative nature of TV-regularized QSM in animal imaging.

In this study, we have applied TV-regularized QSM to quantify the susceptibility change due to SPIO markers targeted to (1) a tumor in a rat brain (2) an inflammation site in a mouse. QSM-based quantification of biomarkers could be a perfect tool to stratify disease and gauge therapy, becoming an important application of MRI molecular imaging.

Ref: [1] de Rochefort et al. MRM:*in press*; [2] Ali S. Arbab,et al. “Efficient magnetic cell labeling with protamine sulfate complexed to ferumoxides for cellular MRI”, Blood, 15 August 2004.