Quantification of contrast agent in human brain using quantitative susceptibility mapping

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Introduction:

An accurate *in vivo* quantification of contrast agent concentration [CA] is critical to dynamic contrast enhanced MRI for computing tissue blood flow or endothelial permeability, parameters important for evaluating stroke and tumor. However, current T1/T2/T2* based methods for estimating [CA] may subject to many error sources including the relaxation quenching caused by limited surrounding free water, the flip angle profile, the ill-condition of the signal equation, and other effects in the pulse sequence [1-3]. These problems are avoided in the signal phase based analysis such as quantitative susceptibility mapping (QSM) [4], which is sensitive to paramagnetic contrast agents including both superparamagnetic iron oxide (SPIO) nanoparticles and gadolinium (Gd) solutions. Here, we report the use of QSM to quantify [CA] *in vivo*.

Materials and Methods:

Ex vivo validation. Three C57BL6J adult male mice were euthanized and their brains were immediately removed and microinjected with various amounts of SPIO. The MRI imaging was performed on a 7T small animal scanner using a quadrature RF coil for transmission and reception, a 3D gradient echo sequence, 104μm isotropic resolution and 8 signal averaging. QSM was performed using the morphology enabled dipole inversion method [5]. The total susceptibility (proportional to the magnetic moment) was calculated by summing the susceptibility values from all voxels in regions containing SPIO and was subsequently converted to SPIO mass by scaling with its molar susceptibility 6.5×10^3ppmL/mol [6].

In vivo study. Contrast enhanced MRI was acquired in 6 patients with brain tumors including meningioma and glioblastoma multiforme before and a few minutes after injection of 0.1mmol/kg gadolinium agent (Magnevist). Data were collected on a 3T MR Scanner using an 8 channel birdcage head coil and a 3D multi-echo gradient echo sequence with 12 TEs, 3ms uniform TE spacing, 45ms TR, and ~1×1×3 mm^3 voxel size at no signal averaging. QSM was reconstructed. Susceptibility values were converted to [Gd] by scaling with its molar susceptibility 326ppmL/mol [7].

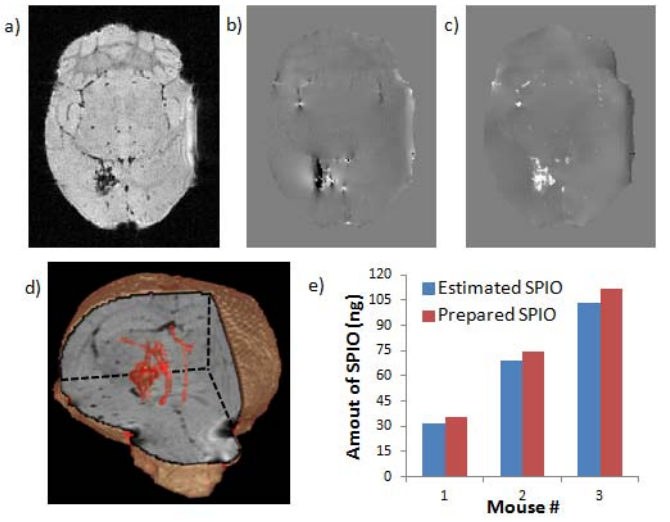

Fig. 1. QSM quantification of SPIO in mouse brains. A section of a brain injected with 112ng SPIO is depicted in (a) T2* magnitude image where SPIO appears hypointense, (b) local field map where susceptibility sources create dipole patterns with positive and negative values, and (c) QSM measuring susceptibility in each voxel. A volume-rendered view of QSM (d) shows the injected SPIO as a pseudocolored map with the magnitude image as the background. (e) The QSM estimated amounts of SPIO were in good agreement with the amounts of the injected SPIO in all three brains tested.

Results:

In the *ex vivo* experiment, the T2* hypointensity on the magnitude image and the dipole pattern on the local field map indicated the presence of paramagnetic substance. This impression was quantified on QSM, where the obtained SPIO masses in the three mouse brains were 31.8, 69.4 and 103.6 ng, respectively, corresponding to 10%, 7.1% and 7.5% underestimation possibly due to the loss of contrast agent during needle withdrawal.

In the *in vivo* data, [Gd] in a voxel, which is linearly proportional to the susceptibility of that voxel, was higher preferentially at the tumor periphery (<[Gd]>=0.22mM) than at its center (<[Gd]>=0.017mM), demonstrating peripheral hypervasculature of the tumor (Fig. 2). The magnitude image showed intensity enhancement of the tumor with less periphery-to-center contrast (CNR=6) than QSM (CNR=31), likely caused by the saturation in the nonlinear relationship between [Gd] and signal intensity.

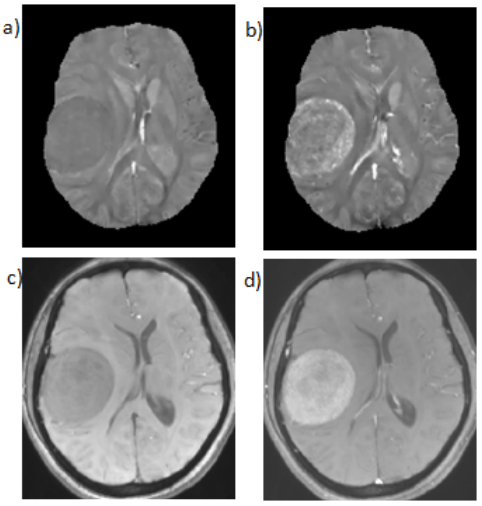

Fig. 2.in vivo quantification of [Gd] in MRI. Compared to (a) pre-Gd injection QSM of a brain tumor, (b) post-Gd QSM demonstrates Gd accumulation preferentially at the outer periphery of the tumor possibly due to hypervasculature. The (c) pre- &(d) post- Gd magnitude images show intensity enhancement of the tumor with less periphery-to-center contrast than that of QSM.

Discussion:

QSM offers a new approach to [CA] quantification. QSM is based on the signal phase ϕ that linearly related to the local magnetic field δB induced by contrast agents. Currently, the measurement of ϕ is accurate on modern magnets, but δB is the convolution of the known dipole kernel with the susceptibility distribution χ. QSM deconvolves δB to obtain χ, which is then scaled to [CA] by the molar susceptibility. Therefore, the problems in the traditional T1/T2/T2* approach are circumvented in QSM. This QSM [Gd] map has potential to increase the accuracy and reliability in estimating kinetic parameters including tissue blood flow and vessel wall permeability, which are valuable for tumor diagnosis and prognosis.

Conclusion:

QSM can be applied for in vivo quantification of contrast agents, such as SPIO and Gd..

References:

[1] Terreno et al. MRM 55(3):491-7; [2] Zurkiya et al. MRM 59(6):1225-31; [3] Schabel et al. PHYS MED BIOL 53:2345-73; [4] Liu et al. MRM 61(1):196-204; [5] Liu et al. MRM:66(3):777-83; [6] Jung et al. MRI 13(5):661-74; [7] de Rochefort et al. MRM 60(4):1003-9.