Measurement of Brain Iron and Calcium using MR QSM and CT: validation using Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES)

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Target Audience: Researchers and clinicians interested in quantitative susceptibility mapping, brain iron and calcium quantification.

Purpose: Hemorrhage and calcification are common pathologic components of many intracranial diseases such as tumor and hemorrhage. Iron products such as met-heme, hemosiderin, and ferritin are strongly paramagnetic with molar susceptibility of $176 \times 10^{-9}\ {cm^3}/{\mu mol}$ [1]. On the other hand, calcification in the form hydroxyapatite (HA, ~40% calcium by mass) is diamagnetic with molar susceptibility of $-2.7 \times 10^{-9}\ {cm^3}/{\mu mol}$ [1]. When both are presence in a pathological site in an unknown proportion, iron concentration maps derived from QSM alone can be underestimating. This study aims at demonstrating the feasibility of correcting calcium susceptibility for more accurate $[Fe]$ maps utilizing both QSM and CT images in brain specimens. The results are compared with ICP-OES results as the golden standard.

Methods: Assuming the presence of iron and calcium were in the form of ferritin and HA respectively, voxel susceptibility measured in QSM can be expressed as

$$QSM = [Fe]\chi_{Fe,mol} + [HA]\chi_{HA,mol} \quad \text{(Eq.1)}.$$

Here $[Fe]$, $\chi_{Fe,mol}$, and $[HA]$, $\chi_{HA,mol}$ are molar concentration and molar susceptibility of ferritin and HA respectively. $[HA]$ can be calculated from CT images according to the definition of Hounsfield unit assuming the attenuation of ferritin is negligible:

$$[HA] = \rho_{HA}\frac{\mu_x - \mu_b}{\mu_{HA} - \mu_b}\ with\ \mu_x = \frac{HU \cdot \mu_{water}}{1000} + \mu_{water} \quad \text{(Eq.2)}$$

Here HU is hounsfield units measured in CT images. μ_x, μ_{water}, μ_{HA}, and μ_b are attenuation coefficient of tissue, water, HA, and background (tissue surrounding calcifications) respectively. ρ_{HA} is the density of HA. Substituting Eq.2 into Eq.1, $[Fe]$ maps with calcium correction can be calculated.

Three brain specimens with calcified tumor, choroid plexus, and pineal gland were prepared for MR (HDxt, GE Healthcare, 8-channel head coil) and CT (Discovery CT750, GE Healthcare) scans. The MRI protocol included a 3D spoiled gradient echo sequence with following parameters: 4 equally spaced echos with TE between 7.4 and 50.7 ms, TR 59.7ms, voxel size 0.32×0.32×0.4 mm. The CT scanning parameters were as followed: peak tube voltage 140kV, tube current 210mA, voxel size 0.32×0.32×0.625 mm. QSMs were generated using the Morphology Enabled Dipole Inversion (MEDI) algorithm[2]. CT images were co-registered and interpolated to the resolution of QSM using FSL FLIRT. $[HA]$ and $[Fe]$ maps were calculated using Eq. 1 and 2. To analyze potential error due to co-registration and inaccuracy ROIs, ROIs were shifted 1mm in all 6 x, y, z directions. Measurements were reported in mean ± stds. ICP-OES was performed on the specimens for $[Fe]$ as the golden standard.

Results: Figure 1 shows tumor $[Ca]$ map calculated from CT and $[Fe]$ maps with/without correction for calcium. Large increase in $[Fe]$ can be appreciated after the correction. Figure 2 compares the total iron mass (μg) in the specimens calculated from QSM / CT images and measured using ICP-OES. Means and stds were calculated from shifted ROIs. The relative difference to ICP-OES results is significantly lower with calcium correction than without (21±5% vs 88±26%, t-test, $p<0.05$).

Discussion: Our prelimary results demostrate that calcium can contribute significantly to susceptibility measured in QSM and need to be corrected for accurate mapping of $[Fe]$ derived from QSM. While ICP-OES and calculated results agree reasonalbly well in choroid plexus and pineal gland specimens, there is a larger disagreement in the tumor sample. This can due to the complex chemical make-up of tumor and require further investigation.

Conclusion: Calcium can contribute significantly to susceptibility measured in QSM and need to be corrected for accurate mapping of $[Fe]$ derived from QSM.

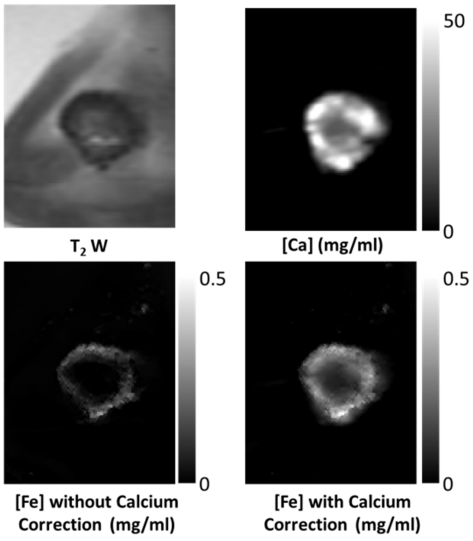

Figure 1: T2w, [Ca], [Fe] maps with/without correction for Calcium.

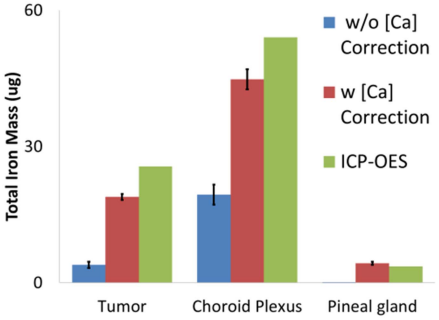

Figure 2: The total iron mass (μg) in the specimens calculated from QSM / CT images with / without correction for calcium and measurements from ICP-OES. Stds shows the potential errors of co-registration and ROI accuracy.

Reference: 1). Wang Y. QSM : MRI of Tissue Magnetism, Jun 2013. 2). Liu T. MRM, 2011;66(3):777-783.