Hematoma Evolution Measured by Quantitative MRI

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TARGET AUDIENCE: Researchers and Clinicians interested in Quantitative Susceptibility Mapping and Intracranial Hemorrhage

PURPOSE: With annual occurrence of approximately 70,000 and 30-day fatality rate of 30-50% in the US, nontraumatic intracranial hemorrhage (ICH) is a serious medical condition[1]. MRI is known to be sensitive to hematoma at various ages as hemoglobin (Hb) degrades progressively from oxyHb to deoxyHb, to metHb, and eventually to hemosiderin. However, hematoma aging has yet to be studied quantitatively, which would provide information important for monitoring and treating ICH patients. A major challenge to hematoma study is that ICH patient is typically very sick and unstable. We propose to investigate the evolution of hematoma in an in vitro model using quantitative MRI including quantitative T1/T2 mapping and the recently developed quantitative susceptibility mapping (QSM).

METHOD: In vitro hematoma experiment. 10 ml venous blood was drawn from healthy volunteers (n=5) and immediately injected into two identical plastic tubes (A and B, 5 ml per tube). Tube A was embedded in 1% agar phantom prior to blood drawing. Both tubes were kept in 37°C water bath except during scanning. Tube B was visually inspected for blood coagulation, upon which tube A was scanned every hour during the first 8 hours, then at 16 hour, 24 hour, and every day until 7 days. Temperatures of the phantom were recorded before and after each scan. Imaging was performed on a 3T GE scanner using an 8-channel brain coil.

Fig. 1: Susceptibility (ppb), T1(ms), and T2(ms) images and plots (mean ±std) of hematoma vs. time (hr).

The imaging parameters were: 1) QSM: 3D multi-echo spoiled gradient echo (SPGR), flip angle = 25°, TR=33.4 ms, first TE=2.1 ms, echo spacing=2.8 ms, voxel size=1x1x1 mm^3, scan time=4 minutes; 2) T1 mapping: 2D IR-FSE with variable refocusing angles, TR=10 s, TI=50, 100, 500, 1500 ms and ∞ (IR pulse turned off), voxel size=1x1x8 mm^3, scan time=3 minutes; 3) T2 mapping: single-echo spin echo, TR=800 ms, TE =9, 50, 100, 250, 500 ms, voxel size=1x1x8 mm^3, scan time=5 minutes. Susceptibility maps were obtained using the Morphology Enabled Dipole Inversion (MEDI) algorithm[2]. T1 and T2 maps were extracted using a three-parameter exponential signal model and the Levenberg-Marquardt algorithm in Matlab.

Human MRI experiment. QSM of one normal volunteer, one acute ICH, and one early sub-acute ICH patients were collected with IRB approval. The stages of ICH were diagnosed by neurologists based on T1 and T2 weighted images.

Fig. 2: Gradient echo magnitude and QSM for (left to right) healthy volunteer, acute ICH, and early sub-acute ICH patients.

RESULT: Blood coagulated in about 9 min after drawing. Hematoma retraction started immediately after coagulation and stabilized within 1-2 hours. An average temperature drop of 6.8°C was measured in the hematoma phantom over the duration of each scan (approximately 15 min). Figure 1 shows sample T1/T2/susceptibility maps and the time course of these parameters. Susceptibility monotonically increased from 456 ppb at start to a plateau of 1500 ppb starting at 96 hours. T1 decreased monotonically from 1600 ms at start to a plateau of 470ms starting at 96 hours (note the large T1 variability during this period). T2 was 16 ms at start, reaching a local maximum of 45 ms at 16 hours, followed by a local minimum of 24 ms at 48 hours, and trending upward afterwards. The mean coefficients of variance (CoV) of all time points are 0.11 for susceptibility, 0.28 for T1, and 0.19 for T2, indicating that susceptibility is a more reproducible MR parameter than T1 and T2 (ANOVA, n=5, p<0.02).

Figure 2 shows the QSM of one normal volunteer, one acute ICH and one early sub-acute patient. The measured susceptibilities were 423 ppb for venous blood in straight sinus of the healthy subject, 980 ppb for the acute phase hematoma consisted of deoxyHb, and 1467 ppb for the early sub-acute hematoma consisted of intracellular metHb, comparable to susceptibility measured in the in vitro model.

DISCUSSION: The observed susceptibility time-course of in vitro hematomas directly reflects the underlining Hb degradation pathway as susceptibility increases from oxyHb, to deoxyHb, then to metHb. The observed relaxation times time-courses are mixed effects of hemoglobin degradation and red blood cell changes: Initially cell swells more effectively than Hb degradation, allowing paramagnetic (p) Fe (both deoxyHb and metHb) rapid movement (with Larmor frequency component) that increases 1/T1 (shortening T1) and diluting pFe concentration that decreases 1/T2 (increasing T2). Cell swelling reaches maximal at round 16 hour (approximately a first T1 plateau as Hb degrades slowly and T2 maximum). Then both T1&T2 relaxation rates increase (T1&T2 decrease) as Hb degrades until cell membrane breaks down (lyses around 48hr), which starts to dilute pFe and T2 relaxation rate decreases (T2 increases).

The initial short T2 value at blood coagulation may indicate rapidly increase in pFe concentration during the initial 15 min due to clot retraction, possibly because red blood cells aggregate during coagulation and Hb degrades rapidly in this early phase as indicated by susceptibility time course (Fig.1 top).

CONCLUSION: The temporal evolvement of hematoma can be studied quantitatively using MRI: quantitative susceptibility mapping (QSM) reflects blood degradation, quantitative T1 & T2 mapping + QSM may infer red blood cell swelling and lyses.

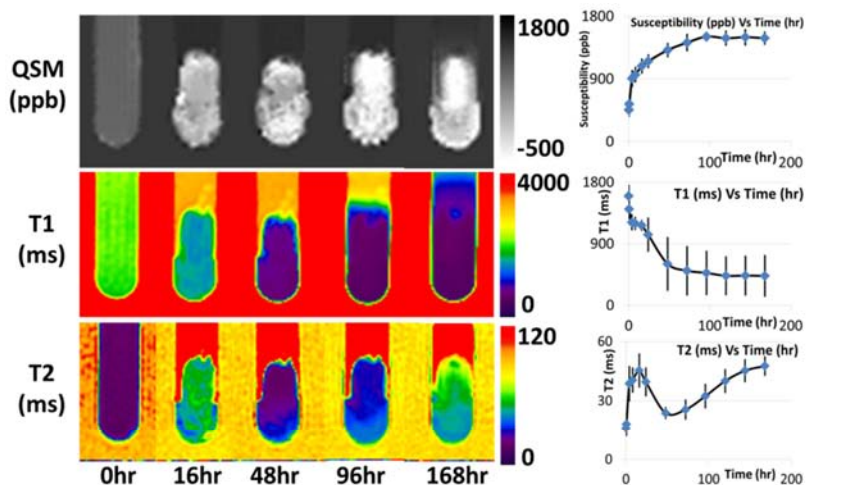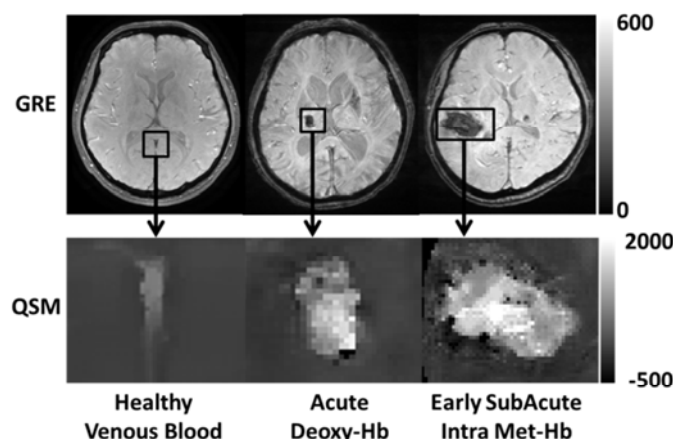**Reference:** 1) Degos, V., et al., Anesthesiology, 2013. 119(1): p. 218-27. 2) Liu, T., et al., MRM, 2011. 66(3): p. 777-83.