Title: Prediction of human thrombus hematocrit from R2* and susceptibility values ex vivo: preliminary results

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Structured Abstract:

Introduction: Knowledge of thrombus composition may aid treatment of ischemic conditions such as stroke and heart attack by predicting efficacy of reperfusion therapies. Current MR-based thrombus characterization methods rely on a qualitative “susceptibility vessel sign” that is unable to distinguish between the effects of red blood cell (RBC) concentration (hematocrit) and deoxygenation (associated with thrombus aging). This work evaluates the ability of measured R2* (=1/T2*) and quantitative susceptibility (QS) values for predicting hematocrit as evaluated by histology of retrieved acute ischemic stroke thrombi ex vivo.

Methods: Specimen collection- 109 thrombi retrieved during mechanical thrombectomy procedures performed on 65 acute ischemic stroke patients at University Hospital were collected and scanned over a period of 21 months.
Imaging- Scans were performed at 3T using a custom dual echo-train 3D gradient echo sequence (TE1/ΔTE/TE5 = 3.20/1.46/9.04 ms, TE6/ΔTE′/TE10 = 16.75/7.15/45.35 ms, TR: 47.6 ms, resolution: 0.94x0.94x1 mm^3, matrix: 192x192x40, BW: 142.86 kHz, flip angle: 10°, scan time = 6 min 10 sec).
Histology- A trial subset of 14 thrombi, selected for varied imaging values, were embedded in paraffin wax, sectioned at 5 μm and stained with hematoxylin and eosin.
Image post-processing- Channel-combined complex data were processed using the B0-NICE and MEDI QS algorithms[1,2] to calculate R2* and QS maps, respectively. House-built Matlab scripts were used to derive mean thrombus R2* and QS values and thrombus hematocrit from MR and histology images, respectively. Equations for predicting hematocrit were derived from previous porcine blood experiments; a linear relation of thrombus QS was used if values were below 0.165 ppm, and a logarithmic relation of R2*/QS ratio was used otherwise.

Results: R2* and QS values from selected thrombi varied between 19 to 205 s^-1 and -0.05 to 1.61 ppm, respectively; histologically-determined hematocrit varied from 5 to 54% (median: 39.0%, IQR: 12.7%). Imaging-derived hematocrit predictions consistently underestimated histologically-determined hematocrit; mean difference between histology and imaging was -26.6 ± 14.9%. Two thrombi with minimal RBCs (5, 10%) as determined by histology were excluded from analysis because histology sections were too shallow to accurately assess composition.

Discussion: Several factors may explain why relationships derived from porcine blood clot R2* and QS values consistently underestimated hematocrit of human thrombi ex vivo. Differences in native R2* and QS values between human and porcine RBCs, as well as clot orientation, retraction and partial volume effects may have each contributed; each effect will be examined and corrected for where possible. Remaining thrombi will be processed and evaluated, and links between imaging values and stroke etiology will additionally be sought.

References: [1] Liu J et al. Magn Reson Med 2015 [2] Liu J et al. NeuroImage 2012