Title: Quantitative MR characterization of hematocrit and etiology in human stroke thrombi

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Structured Abstract:

Ischemic stroke is a common and devastating disease caused by the occlusion of an artery within the brain by a thrombus (blood clot). Currently, the only treatments available for acute stroke are tissue plasminogen activator (tPA) and mechanical thrombectomy. Both treatments entail non-negligible risk of potentially fatal hemorrhage, and the decision to treat is based only on patients’ level of impairment and time since stroke onset. However, evidence suggests that thrombus composition (fraction of red blood cells (RBCs); hematocrit) influences each treatment’s efficacy.[1,2] Furthermore, thrombus composition has been linked to etiology (large artery atherosclerosis (LAA) or cardioembolism (CE)),[3] a characteristic which remains unknown in approximately 1/3rd of strokes, greatly limiting clinician’s ability to mitigate recurrence. MR imaging offers the potential to non-invasively infer thrombus hematocrit through sensitivity to hemoglobin’s paramagnetic iron atoms, and thereby predict response to treatment and inform etiology. Past MR characterization methods rely on a qualitative "susceptibility vessel sign" to signify high RBC content, but are only able to detect deoxygenated RBCs, where hemoglobin’s susceptibility is largest, and have proven inconsistent at predicting etiology. The goal of this work is to apply quantitative susceptibility (QS) and R2* mapping to quantitatively predict hematocrit and etiology in human stroke thrombi.

To first define the relationship between MR imaging parameters and RBC content, porcine clots of varied hematocrit were created and scanned over time (as deoxygenation occurs). An equation linking a clot’s R2*/QS ratio to its hematocrit was derived, yielding a prediction error of 8±5% when tested on an independent porcine clot group.

This relationship was then applied ex vivo on a cohort of 109 thrombi retrieved from ischemic stroke patients. Twelve thrombi were initially selected for histological analysis, and MR predictions were compared against histological hematocrit, producing a prediction error of 23±14%. Separately, a published radiomics method was repurposed to differentiate between LAA and CE thrombi,[4] and tested on the subset of retrieved thrombi scanned within 6 h of excision where etiology was known (39/109; 9=LAA, 30=CE). A random forest classifier classified LAA from CE thrombi with an accuracy of 79%. Ongoing work includes histological analysis of remaining thrombi as well as the collection of additional thrombi to increase sample size and confidence in these preliminary results.

This work represents the first quantitative MR characterization of hematocrit and etiology in human stroke thrombi. Such a technique, while still being refined, offers potential for improving the efficacy of both acute treatment and chronic prevention of ischemic stroke.