Quantitative in vitro magnetic resonance imaging characterization of calcified and lipid-laden blood clot

Spencer Christiansen
Supervisor: Dr. Maria Drangova

Introduction: Thrombotic occlusion is the underlying cause of a number of common and devastating pathologies including heart attack and stroke. Knowledge of thrombus composition may provide highly useful clinical information for the treatment of such conditions, including predicting the efficacy of thrombolytic agents and mechanical thrombectomy procedures, and possibly determining the etiology of the occlusion. Current MR methods for inferring thrombus composition rely on a qualitative “susceptibility vessel sign” obtained in late-echo gradient echo (GRE). This measurement is sensitive only to red blood cell (RBC) concentration and capable only of global assessments of composition, rendering invisible other informative components that may be present within thrombus such as calcium and fat. The objective of our work is to evaluate a tailored multi-echo GRE acquisition paired with recently developed novel post-processing algorithms to characterize relevant thrombus components in a cohort of in vitro clots of varying composition and throughout clot ageing over a biologically relevant timescale.

Methods: Phantom- Arterial porcine blood was used to create duplicate 1.5mL blood samples of 0, 20, 40 and 60% hematocrit. Samples were clotted inside 1cm diameter polystyrene tubes by the addition of calcium chloride and thromboplatin. To emulate clinically observed emboli with calcified or lipidic components, 2.5mm length pieces of either calcium carbonate or lard were added to clots of each hematocrit. Platelet-poor plasma filled the remainder of each tube. Tubes were kept inside an agar phantom and at 37°C throughout the experiment except while scanning. The phantom was scanned at 2, 6 and 17 hours and daily thereafter up to 9 days post-clotting.

Imaging- Scans were performed at 3T with a 32-channel transmit/receive head-coil using a custom dual echo-train 3D GRE 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 mm³, matrix: 192x192x42, BW: 142.86 kHz, flip angle: 10°). Total scan time for the acquisition was 6 minutes 28 seconds; no acceleration was performed.

Image post-processing- Individual channel phase data were saved and the inter-echo variance channel-combination algorithm was used to create local frequency shift (LFS) maps for QS mapping, and the non-iterative B0-NICE algorithm was used to calculate fat fraction (FF), B0 field and R2* maps.

Data analysis- Threshold-based segmentation and subsequent ROI analysis was performed using Matlab. A one-way ANOVA followed by the Tukey post-hoc test was conducted for every time point. A p ≤ 0.05 was deemed significant.

Results: For lard, a significantly greater mean fat fraction value was found, while for calcium carbonate a significantly greater QS value was found, than the opposing added component and all clots at every time point in the experiment. Clot R2* values showed a parabolic relationship with time, peaking between 48-72 hours. At no point did the 40 and 60% clots significantly differ, but between days 2 to 6 the R2* values of the 0, 20 and ≥40% hematocrit clots were each significantly different. Within late-echo magnitude images, representing the clinical standard, calcium and lard were detectable in fresh, oxygenated clot but presented with an indistinguishable appearance within the clot, while following sufficient clot deoxygenation, after approximately 24 hours of ageing, calcium and lard were undetectable and clots of >0% hematocrit appeared indistinguishably from each other.

Conclusions: With the proposed protocol, clinically-relevant sized lard and calcium carbonate samples were readily differentiated inside blood clot of up to 60% hematocrit aged up to 9 days. Blood clots of negligible (0%), low (20%) and medium to high (40-60%) hematocrit can be differentiated on the basis of R2* values, but only once the RBCs have become sufficiently aged/deoxygenated. This method shows promise for clinical discrimination of calcified and lipidic components within in vivo thrombi, and inferring an approximate clot hematocrit in thrombi that are not extremely fresh; neither task is possible using current clinical methods.
References: