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# Preliminary results for a novel in vitro MRI-based approach to quantify blood clot permeability

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Blood clots are a complex heterogeneous porous matrix primarily composed of platelets, red blood cells, and fibrin. This matrix composed of micron and sub-micron scale components results in pores on the order of microns, which causes high flow resistance through the clot in occluded vessels [1]. Elevated flow resistance in these occluded vessels, as occurs in cases of stroke or heart attack, results in poor blood perfusion, reduces fibrinolytic protein transport to the clot, and limits the clot lysis rate during thrombolytic therapy. Quantifying blood clot permeability in both statically and dynamically formed clots, which may vary significantly [2], is critical to understanding thrombolytic efficacy and vessel reperfusion. Although previous studies have quantified permeability [2,3], a thorough understanding of blood movement through the porous clot structure remains elusive. This study aims to quantify blood clot permeability using two methods: an established method and a novel MRI-based method.

The first method followed the benchtop permeability experiments detailed by Wufsus et al. [3]. Briefly, a test chamber was occluded with clots of reconstituted platelet rich plasma formed over 24 hours. A saline solution reservoir was attached to the test chamber, and fluid was allowed to permeate through. Flow rate was calculated using a camera to track fluid velocity in tubing downstream of the clot. Permeability was calculated using the Darcy equation and the known fluid viscosity, flow rate, and pressure gradient across the clot. The second method used magnetic resonance imaging (MRI) to track fluid permeation (Fig. 1A). The occluded test chamber was attached to a saline solution reservoir with MRI contrast agent Gadavist® (Bayer HealthCare) at a 1000:1 dilution and placed inside a 14 Tesla MRI scanner (Bruker). Three-dimensional scans of the test chamber were taken using a FLASH pulse sequence with echo and repetition times of 3 and 30 ms, respectively, resulting in a 100 x 100 x 200 microns squared voxel resolution and 3.5 minute scan time. This scan time was sufficiently low to prevent significant signal loss due to fluid motion. Sequential scans were taken over the course of an hour. Avizo was used to generate volumetric reconstructions of the high-intensity fluid domain and calculate flow rate (Fig. 1B).

Results from both methods produced similar average permeability measurements. The average permeabilities from the camera tracking and MRI methods were 5.87E-2 microns squared and 3.86E-2 microns squared, respectively. Although average results were similar, variability between clots were relatively high. These permeability values were slightly higher in magnitude compared to previously reported results by Wufsus et al. for platelet rich plasma clots with low platelet volume fractions (1.2E-2 +/- 0.6E-2 microns squared) [3]. The MRI method had the added benefit of tracking the entire fluid volume through the clot to observe any significant permeation heterogeneities. The fluid moved uniformly through the clot across the entire cross-sectional area, which indicates in this fully occlusive state where fluid motion is primarily governed by Stokes flow, a homogeneous porous media modeling approach may still be appropriate in macroscopic-scale modeling.

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### References

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