A versatile 3 T phantom for intravoxel-incoherent motion (IVIM) sensitization of microvascular flow

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Introduction: MRI may provide important advancements in characterizing tumor microenvironment properties, such as the degree of angiogenesis. Diffusion-weighted imaging (DWI) has become a standard biomarker for cancer diagnosis. While conventional DWI is sensitive to microstructure (e.g. tumor cellularity) through its restriction of passive water motion [1], DWI can also be sensitized to microvascular flow. Capillary networks can cause intravoxel incoherent motion (IVIM), resulting in a pseudodiffusion coefficient [2]. Here, we use IVIM MRI in a flow phantom model. While other phantom studies have modeled IVIM effects [2,3], many involve advanced DWI in small bore scanners [4,5]. Working in a full-body clinical scanner, our goals are: (1) to develop a phantom to model microvascular flow, (2) to optimize the quantification of IVIM-MRI, and (3) to apply IVIM to anti-angiogenesis cancer treatment studies.

Methods: We manufactured a flow phantom using random flow through cellulose sponges. Fig. 1(top) shows the schematic diagram of two configurations (A, B). Case A used a single sponge channel with a parallel shunt line to decrease flow in the sponge; data was collected for variable input flow speeds to simulate microvascular flow variation. Case B used two parallel sponge lines and different settings of the ball valves (B1: all valves open, B2: valves in one branch constricted) to simulate vascular impedance. Pressure measurements (PowerLab 8/30, AD Instruments) were taken at the proximal and distal ends of each sponge line as a surrogate marker for flow. Tap water was pumped into the phantom using a peristaltic pump. The phantom was enclosed in a reservoir of $CuSO_4$-doped water. Scans were collected in a full body Siemens 3 T Tim Trio, using body and spine receiver arrays. A single-shot, twice refocused spin echo DWI sequence with bipolar diffusion gradients and centric ordered TSE readout (TR / TE =1000/103 ms, iPat = 2, 128 x 80 x 3 matrix, 2.3 x 2.3 x 4 mm) was used at up to 18 diffusion weightings of $0 < b < 500$ s/mm^2, and 3 diffusion directions (x,y,z). A modified, singly refocused SE sequence with bipolar diffusion gradients and TSE readout was used for flow-compensated (FC) DWI [6,7]. Flow speed was quantified by the pressure difference between transducers. DWI data were analyzed with a bi-exponential model:

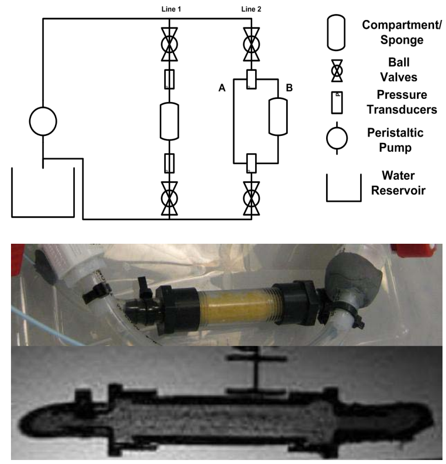

Figure 1: (top) Schematic diagram of phantoms; (middle) photo of sponge compartment; (bottom) 3T MRI.

$$M_i = M_0 \cdot [(1-F_P)\cdot \exp(-b_i \cdot D_t) + F_P \cdot \exp(-b_i \cdot D_p)] \quad (1)$$

where F_p is perfusion fraction, D_p is pseudodiffusivity, and D_t is tissue diffusivity. Image analysis included both region-of-interest (ROI) decay curves in the sponge compartment and parametric maps.

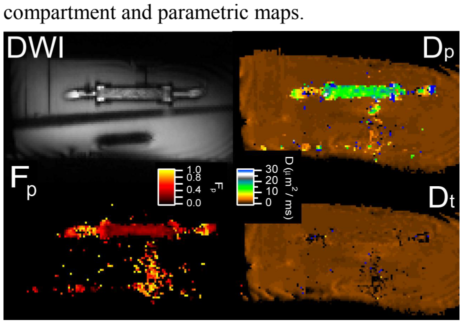

Figure 3: Parametric maps of F_p, D_p, and D_t.

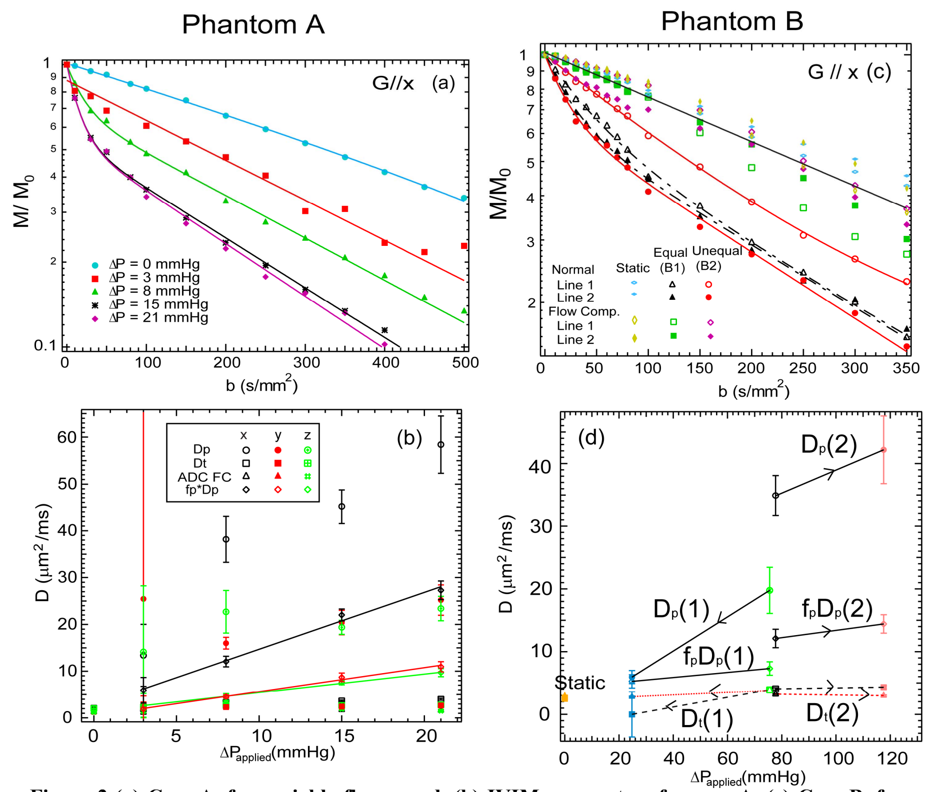

Figure 2:(a) Case A, for variable flow speed. (b) IVIM parameters for case A. (c) Case B, for equal and unequal flow. (d) IVIM parameters for case B. Arrows indicate the direction of change with change in impedance

Results: Fig. 2a show results from Case A (single sponge) with the DWI signal decay curve at various flow speeds. Fig. 2b shows the D_p, D_t, F_p*D_p, and the FC ADC as a function of applied pressure difference. Increased flow values correlated with larger pseudodiffusivity D_p, and linearity was observed between F_p*D_p (total flux) and applied pressure. Pseudodiffusion along the flow direction was nearly triple that along perpendicular axes. Zero-flow and FC results showed equal mono-exponential decay. Fig. 2c displays signal decay curve results from Case B at a fixed flow speed and two impedance settings (B1, B2). In the equal flow case (B1), DWI curves are similar in both branches. In the unequal flow case (B2), signal decays show slower pseudodiffusion in the restricted line (1) versus the open line (2). Fig. 2d shows D_p decreases in the restricted line (1) while D_p increases in the open line (2). The same can be seen for the F_p*D_p. D_t and FC ADC show no change with change in impedance. Fig. 3 shows IVIM maps for a single flow speed in Case A, which shows high pseudodiffusion in the sponge compartment.

Discussion: Our results show that an IVIM flow effect can be observed versus static fluid, and suppressed by a FC diffusion weighted sequence. Biexponential analysis produces IVIM parameters which show an increase in D_p with increasing flow as well as a decrease with increased impedance. IVIM quantification has been historically problematic, particularly for small perfusion fractions [8]. This phantom will allow controlled tests that will strengthen *in vivo* assays of microcirculation.

References [1]Basser PJ. NMR in Biomed. 1995;8(7-8):333-344. [2]LeBihan D. Radiol 1988; 168(2):497-505. [3]Maki JH. MRM 1991;17(1):95 107. [4]Callaghan PT. JMR A 1995;117(1):118-122. [5]Sederman AJ. JMR 2004;166(2):182-189. [6]Gamper U. MRM 2007;57(2):331-337. [7] Fujita Nl. MRM 1992;24(1):109-122. [8] King MD. MRM. 1992;24(2):288-301.