Novel Pore Size-Controlled, Susceptibility Matched, 3D-Printed MRI Phantoms for Double Diffusion Encoding Methods

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Synopsis

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We report the design concept and fabrication of dimensionally stable, uniformly oriented blocks or modules that can be assembled into large-scale MRI phantoms. We present the bundled capillary in an aqueous emulsion to create random orientation. This phantom can be used to vet and calibrate various MRI methods, such as DTI, AxCaliber MRI, MAP-MRI, DEXSY, and various multiple pulsed field gradient (PFG) or multiple diffusion- encoded microstructure imaging methods

Abstract

There is a drive to develop diffusion-based MRI methods that can enable the characterization of the shape, size, and orientation of complex tissue. Of particular interest is the identification of morphological features within a single voxel, such as highly anisotropic but randomly orientated tissue or multicompartment tissue within a voxel that presents as isotopic when characterized by traditional diffusion tensor imaging methods.

Groups often have no choice but to transition from theory to tissue application because of the lack of widely distributed phantoms that control the distribution of shape, size, orientation, and exchange. Several notable MRI phantoms have been fabricated to represent microscopically anisotropic but macroscopically isotropic grey matter tissue. Phantoms that control the morphological feature and the exchange rate between these microcompartments are rare. These phantoms, although functional, often suffer from susceptibility contrast between phantom material and water when compared to biological tissues, material robustness, safety issues, and transportability.[2] To address this, we have utilized advanced 3D Printing technology with +/- 100 nm accuracy to produce MRI phantoms that provide model systems mimicking the anisotropic capillary structure found in the grey matter of the brain as well controlling both orientation and exchange between these compartments.

We 3D-printed phantom of bundled capillaries with controlled diameters at The Center for Nanophase Materials Sciences (CNMS) at Oak Ridge National Laboratory (ORNL). Scanning electron microscopy images were used to further validate the ground truth size. The bundles were randomly distributed via an aqueous emulsion. We further characterize these phantoms using a combination of double diffusion encoding methods to quantify microscopic anisotropy and compartmental exchange. We employed custom analysis code to estimate both microscopic anisotropy, diameter size, and exchange rates from this phantom.[1,3,4]

We first optimized 3D printing conditions to yield uniformly solid walls and confirmed the size of the uniform bundle capillaries phantom via scanning electron microscopy as shown in Figure 1. We then distributed these bundles into an aqueous solution for the measurement shown in Figures 3 and 4. We designed a ‘flower’ arrangement of two distinct diameters as shown in Figure 2, where the scanning electron microscopy images show two compartments with consistent spacing throughout the entire 3D printed structure. We used the knowledge gained from printing the first phantom to systematically control wall permeability.

3D printing with high resolution is an opportunity for phantom fabrication as additive manufacturing methods are highly reproducible with precise control of structure and composition. Here we have shown two types of phantoms fabricated for calibration of microscopic anisotropy and DEXSY double diffusion encoding methods. We plan to use these phantoms to vet current and developing methods in our lab to robustly identify distributions of shape, size, orientation, and exchange in our lab.

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References

References:

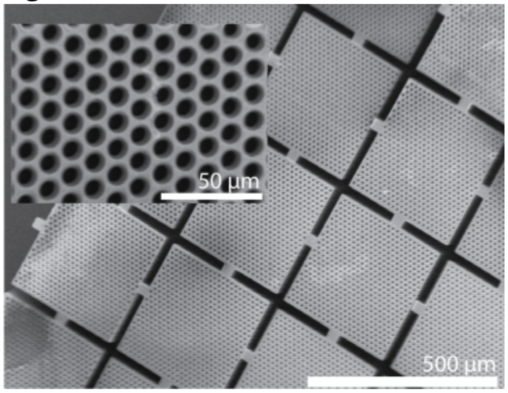
[1] V.J. Witherspoon, M.E. Komlosh, , D. Benjamini, E. Özarslan, N. Lavrik, P.J. Basser Novel Pore Size-Controlled, Susceptibility Matched, 3D-Printed MRI Phantoms bioRivx: doi: https://doi.org/10.1101/2022.10.10.511634

[2] K. E. Keenan, M. Ainslie, A. J. Barker, M. A. Boss, K. M. Cecil, C. Charles, T. L. Chenevert, L. Clarke, J. L. Evelhoch, P. Finn, et al., Quantitative magnetic resonance imaging phantoms: a review and the need for a system phantom, Magnetic resonance in medicine 79 (1) (2018) 48–61

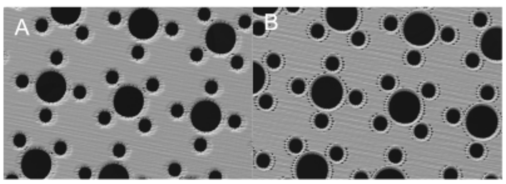
[3] D. Benjamini, M. E. Komlosh, P. J. Basser, U. Nevo, Nonparametric pore size distribution using d-pfg: Comparison to s-pfg and migration to mri., Journal of Magnetic Resonance 246 (2014) 36–45. doi:10.1016/j.jmr.2014.06.017

[4] C. Yolcu, M. Herberthson, C.-F. Westin, E. Özarslan, Magnetic resonance assessment of effective confinement anisotropy with orientationally-averaged single and double diffusion encoding, in: 27 E.¨Ozarslan, T. Schultz, E. Zhang, A. Fuster (Eds.), Anisotropy Across Fields and Scales, Mathematics and Visualization, Springer Nature, Cham, 2021, pp. 203–223

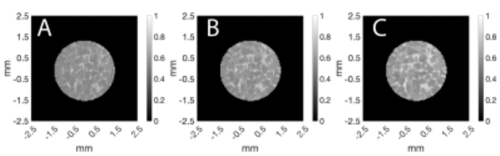
Figures



Scanning electron microscopy images of 3D printed single-sized bundled capillaries.



Scanning electron microscopy images of 3D printed dual-sized bundled capillaries with varying wall permeability.



Echo planar imaging acquisition of the same axial slice with the number of segments varied from 2 (A),4(B), and 6(C) segments, with TE = 54 ms. voxel size is 50 μm^3. The relative structural similarity indexes SSIMs of images B and C to the first image A are 0.9984 and 0.9661, respectively

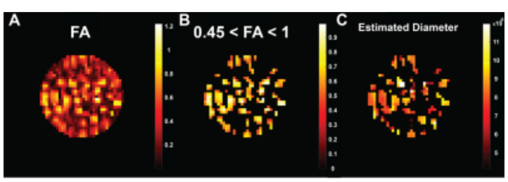


Figure 4. 100μm isotropic resolution images, showing (A) fractional anisotopy(FA), (B) FA with an applied threshold of FA>.45, and (C) the calculated diameter map using the framework from Benjamini et al.