In-vitro and in-silico porous phantoms for investigating the relationship between microvascular architecture and ultrasound-contrast-agent kinetics

***In-vitro* and *in-silico* porous phantoms for investigating the relationship between microvascular architecture and ultrasound-contrast-agent kinetics**

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Background, Motivation and Objective

As a recognized hallmark of cancer, tumor-driven angiogenic microvasculature is characterized by increased microvascular density (MVD), smaller vessel diameter (d_v), and higher vessel tortuosity, leading to complex blood flow patterns [1, 2]. Analysis of the dispersion kinetics of an ultrasound contrast agent (UCA) in the tumor vasculature has shown promise for prostate cancer (PCa) diagnostics [1, 2], but the link between UCA kinetics and underlying microvascular architecture is still under investigation. In previous work, modeling the microvasculature as a porous medium, we developed *in-vitro* phantoms and imaged their perfusion by contrast enhanced ultrasound. The experimental results were consistent with our *in-vivo* findings [3]. In this work, we developed a simulation framework to further advance our understanding of the UCA kinetics through porous media that mimic microvascular networks.

Statement of Contribution/Methods

The *in-silico* model of a porous phantom was realized using a 3D sphere-packing algorithm. Thousands of mono-sized spheres were uniformly distributed inside a cylindrical space. Spheres were then separated iteratively until no overlapping was present. For each 100 iterations, random motion was applied to all the spheres mimicking a shaking process. In agreement with our previous *in-vitro* measurements, we simulated porous phantoms with sphere diameters of 3.1, 2.5, and 1.6 mm. The distribution of the radial porosity within the cylinder was obtained by calculating the void fraction in each concentric layer of 0.04-mm thickness. Moreover, Delaunay triangulation was applied to the simulated phantoms, enabling us to measure the pore size represented by the size of the inscribed spheres of each connected tetrahedron. Furthermore, the MVD was reflected by the number of pores. Dynamic simulations of bubble transport flowing through the porous phantoms are being tested by COMSOL.

Results/Discussion

The simulated porous phantoms are shown in Fig. 1. The pore size and density distribution demonstrate that the pore size decreases while the density increases as the bead size decreases, representing smaller d_v and higher MVD. This result confirms our hypothesis that porous phantoms with smaller beads can mimic angiogenic microvasculature.

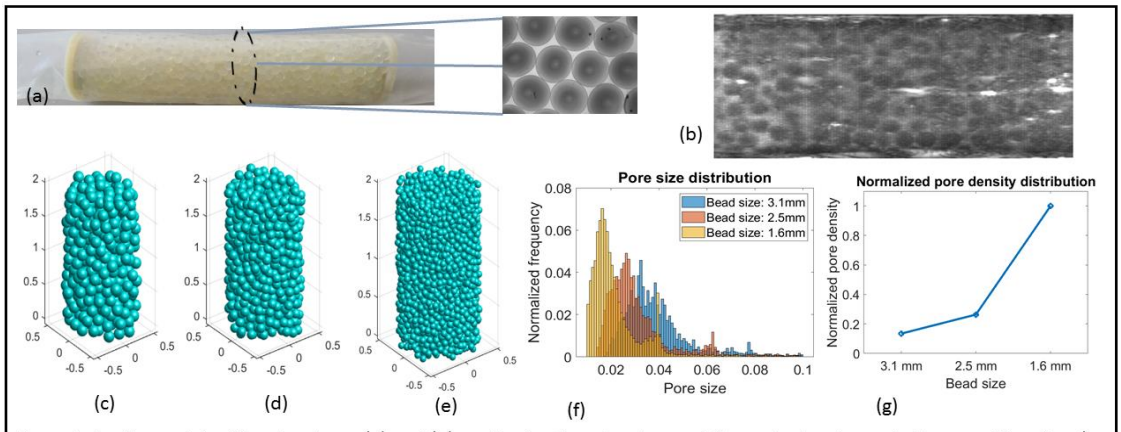

Figure 1. *In-vitro* and *in-silico* phantoms: (a) and (b) are the *in-vitro* phantom and its contrast enhanced ultrasound imaging; (c-e) are the *in-silico* phantoms with sphere size of 3.1, 2.5 and 1.6 mm, respectively. The diameter of the tube is 20 mm and the length of the tube is 40 mm. In (c-e), all the dimensions are scaled up by a factor 50 only for visualization. (f) is the pore size distribution. (g) is the normalized pore density distribution.

[1] Kuenen et al., IEEE TMI, 2011. [2] van Sloun et al., Med. Image Anal, 2016. [3] Chen et al., IEEE IUS, 2019.