Towards Biomimetic Tissue Phantoms for Brain Tumor Detection using Magnetic Resonance Elastography

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Statement of Purpose: Magnetic resonance elastography (MRE) allows for noninvasive determination of the mechanical behavior of human internal organs and can help in tumor detection. It also allows physicians to begin intervention aimed at treating the disease before it progresses to cause irreversible damage. Tissue mimicking phantoms can aid in uncovering potential weaknesses in imaging systems. The more closely a phantom mimics the healthy or pathologic tissue, the more effective the phantom is. This project aims to design biomimetic phantoms, produced by successive freeze-thaw cycles, to mimic the mechanical properties of healthy brain tissues and typical brain tumors. These physically-crosslinked cryogels undergo a crystallization process below freezing temperature. Knowing that the crystallization is a temperature-dependent phenomenon, any temperature gradient within the specimen leads to variations in the level of crystallinity throughout the specimen. This adversely affects the homogeneity of the specimen, as the mechanical properties of a cryogel depend on its crystallinity. In an effort to optimize the freeze-thaw process, by minimizing the temperature gradient throughout the specimens, the Comsol® modeling software was used to predict the heat transfer within the phantoms. The mechanical response of the phantoms was characterized under cyclic compressive loads. In addition we have developed a novel non-local and multi-scaling biomechanical model based on fractional calculus that is able to accurately estimate stiffness values of phantoms from MRE experiments without using any image filtering techniques needed by the classic approaches used so far in the MRE literature.

Methods: Blends of Polyvinyl alcohol (PVA) and Polyvinyl Pyrrolidone (PVP) cryogels were prepared by the freeze-thaw process[1] using an environmental chamber. Aluminum molds were used to reduce the thermal resistance between the mold and the solution during the freeze-thaw cycles. Profiled temperature ramps, featuring multiple isotherms, were input to the chamber and the temperature evolution within the specimens was measured using the mounted thermocouples. A higher number of freeze-thaw cycles were used for preparing tumor phantoms, aiming to mimic the stiffness of typical brain tumors (*i.e.* gliomas). Figure 1a shows a produced phantom that can be used for MRE measurements (100mm×100mm). Disk-shaped specimens (20mm×4mm) were also prepared for mechanical characterization. The samples were subjected to sinusoidal compressive loads at frequencies of 1 Hz – 40 Hz.

Results: Figure 1b shows the typical mechanical response of a cryogel (force and displacement *vs.* time) under the dynamic compression test. These data were used to estimate the storage and loss modulus (E' and E") for the phantoms (Fig. 1c) as a means of comparing their viscoelastic response with that of brain white and gray matters.[2] Figure 2a and 2b show the aluminum mold and the location of the mounted thermocouples, respectively. The Comsol® software was used to predict the 3D heat transfer during the freeze-thaw cycle. The time-dependent boundary condition (preset profile for the chamber) was used as input to the software to simulate the freeze-thaw process. Temperature-dependent specific heat was used to represent the latent heat of freezing/thawing. Figure 2c shows the simulation results for a quarter of the geometry. The evolution of the temperature within the cryogel is plotted in Fig. 2d and is compared with the experimental data. Finally, in Fig.3(a,b) we show the performance of our biomechanical model using an MRE shear test (frequency of 100 Hz) run on a gel phantom (1.5% Agar) containing 4 cylindrical inclusions of stiffer gel (10% B-gel).[3] Our results are compared with the stiffness values estimated using the MRE/Wave software[3] without image filtering (Fig.3c,d).

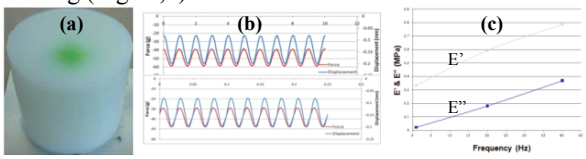

Fig.1. PVA/PVP cryogels as tissue/tumor phantoms (a), dynamic mechanical tests on phantoms at two frequencies (b), and estimated storage and loss modulus (c).

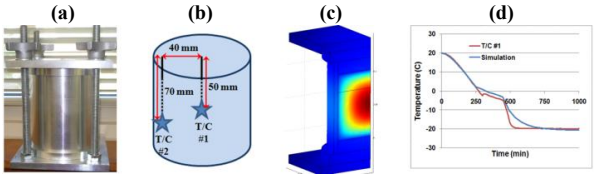

Fig. 2. Simulation of heat transfer inside the phantoms.

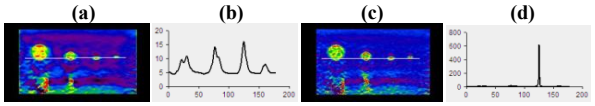

Fig. 3. Elastograms and corresponding 1D profiles using our model (a,b) and MRE/Wave (c,d).

Conclusions: This work aimed at producing homogeneous tissue phantoms by reducing the temperature gradient throughout the tissue phantoms. Our future work will focus on optimizing the freeze-thaw process and the cryogel formulation so as to achieve the target mechanical and Magnetic Resonance Imaging (MRI) properties for brain white/gray matter phantoms as well as tumor phantoms (such as gliomas). Also, we plan to run MRE experiments on these phantoms and use our biomechanical model to estimate stiffness values.

References:

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3. *http://ndc.mayo.edu/mayo/research/ehman_lab/*