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Multilayer tubular phantoms for optical coherence tomography

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ABSTRACT

We report preliminary results toward making artery phantoms for Optical Coherence Tomography (OCT) that also exhibit mechanical properties similar to arteries for large deformation regimes. A matrix of PVA cryogels is used to obtain the strain hardening effect characteristic of arteries. Means of adjusting the optical properties of PVA cryogels are investigated and the resulting mechanical properties are characterized.

Keywords: Optical coherence tomography, phantoms, poly (vynil alcohol), arteries, atherosclerosis

1. INTRODUCTION

We previously reported a method for the fabrication of coronary artery phantoms for Optical Coherence Tomography (OCT) [1]. When imaged by OCT, coronary arteries show distinctive signal by each of their layers: the intima, the media and the adventitia. The method consists of mimicking the OCT signal for each layer of the arteries and building the phantoms in the shape of multilayer tubes. To match the OCT signal of artery layers, particles of alumina are used to obtain the desired backscattering, and particles of carbon black are used to further adjust the total attenuation. The particles are mixed into a transparent silicone, which insures high durability to the phantoms.

We also demonstrated that by using a specific formulation of silicone, the linear elasticity observed for arteries at low deformation can be mimicked. However, the silicone elasticity is linear for all deformations, whereas arteries, for high deformations, show an important non-linear effect. This effect is called the strain hardening. It translates into a significant increase in stiffness when a certain deformation is reached.

Phantoms that closely mimic both the OCT signature and the mechanical behavior of arteries for large deformations are desirable for the development and testing of different applications such as OCT elastography or OCT monitoring of angioplasty procedures.

In this paper, we present preliminary results toward making phantoms that have mechanical properties that include strain hardening while maintaining the ability to mimic the OCT signal of each layer of coronary arteries. At first, we describe the methods that were considered for the fabrication of the phantoms. Then, we present the optical properties of phantoms that were obtained with each method. Finally, we present preliminary results of mechanical characterization of the phantoms.

2. METHODOLOGY

2.1 Formulations

We investigated a new method to make OCT phantoms with strain hardening using PVA cryogels as the support material, or matrix, of the phantoms. Strain hardening has already been observed in PVA cryogels. For example, it has been used to make prosthetic tissues [2] and mechanical artery phantoms [3]. PVA cryogels are formulated with solutions of varying concentrations of poly(vinyl alcohol), a solid polymer, most commonly dissolved in water to form a thick, liquid hydrogel. These solutions cross-link to become a solid gel when they are successively submitted to freezing and thawing, hence the term "cryogel". The sequence in which the temperature is decreased below freezing point and then thawed, at controlled rates, is called a freeze/thaw cycle (FTC).

Using a matrix of PVA cryogels to fabricate coronary artery phantoms involves adjusting its optical properties to mimic the OCT signal of the 3 different coronary artery layers, but also obtaining a cryogel with mechanical strain hardening similar to arteries. In this paper, we primarily focused on the optical aspect of using a PVA cryogel matrix. Then, we characterized the mechanical properties.

The OCT signal is mostly influenced by the backscattering and the total attenuation of light in a sample. To make phantoms for OCT, a first additive changing the backscattering and a second additive changing the total attenuation would preferably be added to a transparent matrix. This apparently simple process is further complicated for PVA; transparent PVA solutions become translucent, and even opaque, when processed through an increasing number of FTCs, due to the formation of scattering structures in the cryogels [4]. PVA cryogels are thus optical scattering and attenuating structures by themselves.

The final properties of the cryogels are also influenced by several parameters other than the number of FTC. The molecular weight of the PVA, the PVA concentration in solution, the presence of different additives, the duration in the frozen state and the rate of freezing/thawing [2] can impact on the optical and mechanical properties of the resulting cryogel. However, for this preliminary study, we decided to limit the number of variable parameters. All the PVA preparations were made from PVA with molecular weight 146,000 – 186,000 (Aldrich Chemicals). A 10 % w/w PVA/water solution was prepared by heating and mixing with the use of a standard reflux column/flask combination. All the FTCs were processed through freezing and thawing cycles between -20 and +20 °C at 0.1 ^{o}C/min in an environmental chamber with a one hour hold at - 20 ^{o}C.

To make multilayer phantoms that can mimic the signal from arteries in OCT with this formulation of PVA cryogel, the variation of the signal with the number of FTCs was characterized. The number of FTCs that led to backscattering and attenuation values lower than needed for each artery layer was then chosen as a starting point. The increase in backscattering and attenuation values was obtained by the mixing of additives into the PVA hydrogel, trying to match the values for each layer within the coronary artery. Obtaining a uniform dispersion of the additives is essential because aggregation is easily detected in OCT images. The ability to obtain a uniform dispersion of the additives dictates the choice of additives and the method used for dispersion.

To increase the backscattering in PVA cryogels, the addition of alumina particles to the PVA solution before FTC was studied. A uniform mixture of alumina in the cryogel was obtained by dispersing the particles in the solution using an ultrasonic bath for 5 hours maintained at 60 ^{o}C, which decreases the viscosity of the PVA solution. To increase the total attenuation in PVA cryogels, both carbon black and India Ink were tried, but could not be mixed uniformly in the PVA solutions. A good uniformity was obtained using a block printing ink (brand "Speedball"), an ink that is soluble in water. The uniform dispersion of ink in the cryogel was obtained by mixing the ink manually in the PVA solution at 60 ^{o}C.

To characterize the optical properties of the different PVA formulations, cryogels were moulded into puck-shaped samples according to the following groups:

i. Control: 10% PVA formulation alone (no additives), 1 to 4 FTCs.

ii. Backscatter effect of the alumina: 10% PVA with concentrations of alumina from 0 to 8 mg/ml, 1 and 2 FTCs

iii. Attenuation affect of the ink: 10% PVA with 7 concentrations of ink ranging from 0 to 5 % volume, 1 and 2 FTCs.

2.2 Optical Characterization

All the samples were imaged by OCT to extract values of the backscattering and total attenuation. OCT cross-sectional images were averaged at every depth to obtain the signal profile. The profiles were normalized to a reference reflection and corrected for beam focusing. Then they were fitted for the normalized amplitude, *A*, and the total attenuation, μ_t, with a expression of the form :

$$A \exp\left[-\mu_t z/n\right] \qquad \text{(eq. 1)}$$

where *n* is the refractive index and *z* is the optical depth in the sample. The values obtained were compared with target values from porcine coronary artery layers. These latter values were experimentally obtained with the same type of measurements.

3. RESULTS

3.1 Group i

Optical characterization was performed on samples of PVA without additives. Values for the amplitude of signal and total attenuation were measured on samples for 1, 2, 3 and 4 FTCs. The results are presented in Fig. 1 where they are compared to target tissue values for the different artery layers, the latter being identified as horizontal lines. The figure shows the increase in both the amplitude and total attenuation of the OCT signal in 10% PVA as the number of FTCs is increased. In comparison to the values of the different artery layers, 3 FTCs produces more scattering than the media layer. Therefore, we conclude that a maximum number of 2 FTCs is preferable to allow adjustment of the optical properties to match all the layers of coronary arteries with this formulation of PVA. We further study the effect of the addition of alumina and speedball ink to samples that are submitted to 1 and 2 FTC.

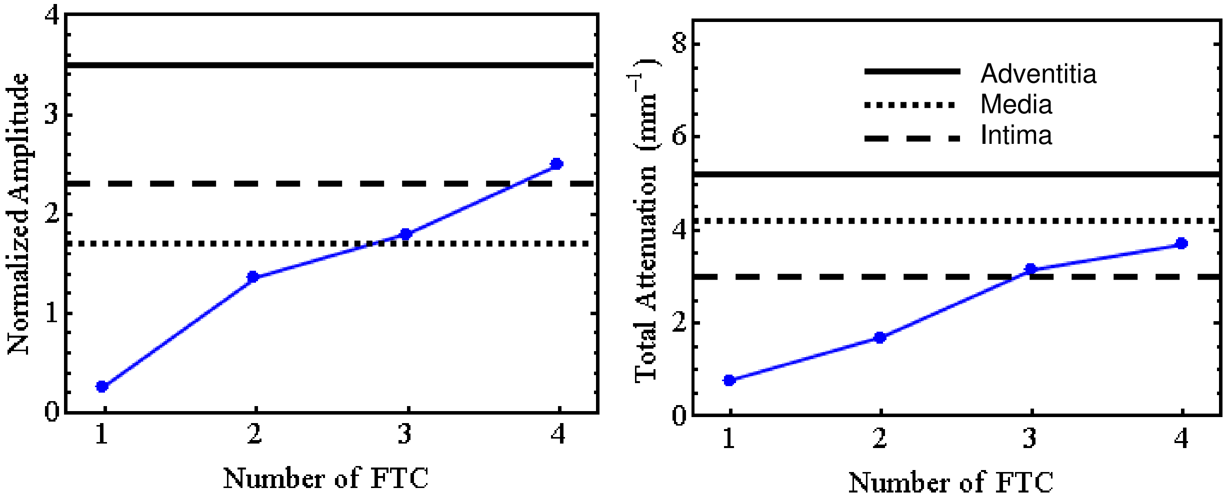

Fig. 1 : Values of normalized amplitude (left) and total attenuation (right) of the OCT signal for 10% PVA samples after various numbers of FTC. The target values for the different artery layers are identified as horizontal lines.

3.2 Group ii

The resulting normalized amplitude and total attenuation of 10% PVA samples with different alumina concentrations and submitted to 1 and 2 FTC are plotted in Fig. 2. Both properties show an increase in their values with the concentration of alumina. Compared to target values for arteries, the normalized amplitude of the 2 FTC samples reaches the range desired for both the media and the intima layers. Obtaining the desired value for the adventitia should be possible with higher concentrations of alumina. However, the concentrations that provide the required normalized amplitudes to mimic artery layers do not also provide the required attenuations. This highlights the need for ink to obtain additional attenuation.

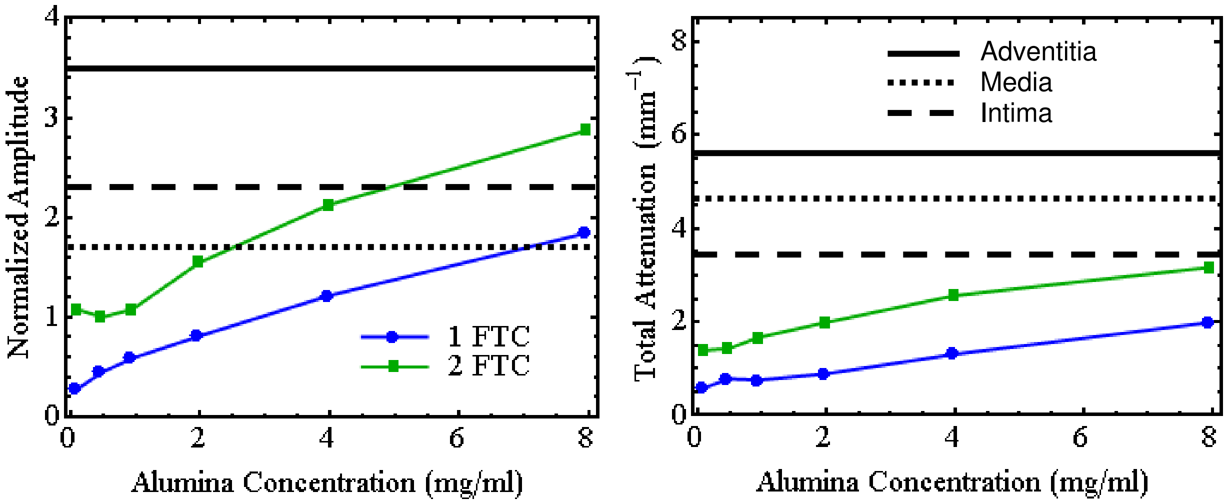

Fig. 2 : Values of normalized amplitude (left) and total attenuation (right) of the OCT signal for 10% PVA-1FTC and 10% PVA-2FTC samples with various concentrations of alumina. The target values for the different artery layers are identified as horizontal lines.

3.3 Group iii

The resulting normalized amplitude and total attenuation of the PVA samples with different ink concentrations and submitted to 1 and 2 FTCs are plotted in Fig. 3. Both properties also show an increase in their values with the concentration of ink. However, the total attenuation shows a larger increase with concentration for ink than for alumina; easily reaching the values targeted for artery layers. Although ink was considered mainly to increase attenuation, Fig. 3 shows that it also contributes to the normalized amplitude.

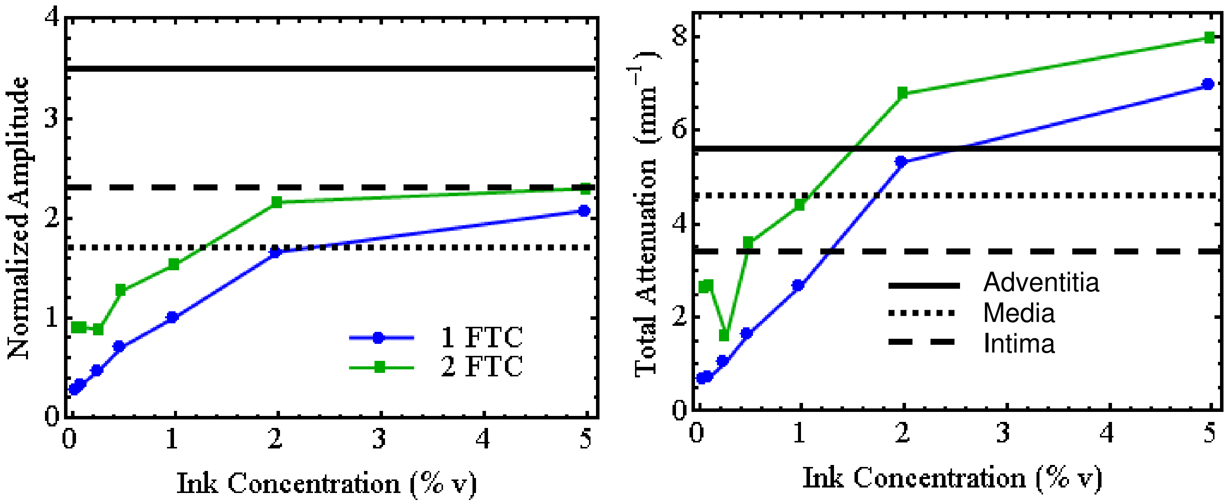

Fig. 3 : Values of normalized amplitude (left) and total attenuation (right) of the OCT signal for 10% PVA-1FTC and 10% PVA-2FTC samples with various concentrations of ink. The target values for the different artery layers are identified as horizontal lines.

These experiments show that the number of FTCs, the concentration of alumina and the concentration of ink all affect the optical properties of PVA cryogels. They also demonstrate that the range of values required to mimic the optical properties of the different artery layers can be obtained with a combination of these parameters.

4. MECHANICAL CHARACTERIZATION

Preliminary mechanical characterization was also performed to assess the strain hardening and to investigate the effect of the addition of alumina on the mechanical properties of PVA. Uniaxial tensile testing was performed on samples of PVA that were cross-linked by 2 FTC with and without the addition of alumina. The results are compared with data from tensile tests on silicone and on a porcine coronary artery. The results are shown in Fig. 4. The figure shows that the addition of alumina has low impact on the mechanical properties since the results are within experimental precision. It also shows that the 10% PVA formulation submitted to 2 FTCs does exhibit a strain hardening effect. This is a huge improvement in terms of mechanical properties over the silicone that was used as a matrix in our previous artery phantoms. However, the strain hardening effect is not yet large enough to mimic that of the coronary artery. We will be exploring other means to increase the strain hardening affect.

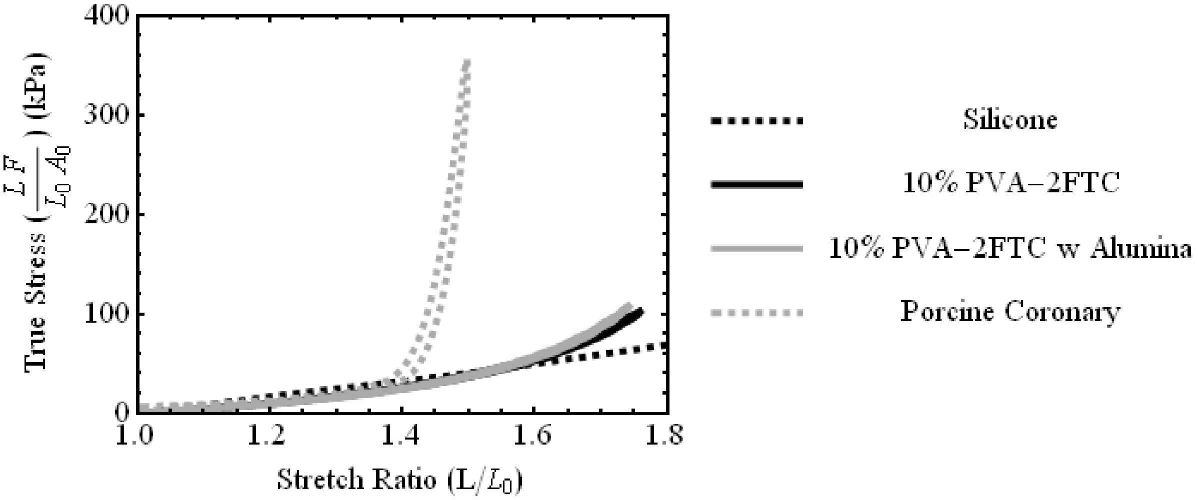

Fig. 4 : Results of tensile tests 10% PVA – 2FTC samples with and without alumina compared to data from a silicone sample and from a porcine coronary artery.

5. CONCLUSION

Preliminary results of using 10% PVA cryogels as a matrix for phantoms that mimic the optical properties and the strain hardening characteristics of coronary artery layers were presented. A specific formulation and processing of PVA cryogels was chosen and the variation of the optical properties with the number of FTCs was characterized. The results suggest that to finely adjust the optical properties, selecting a low number of cycles and adding scattering and attenuating additives would be a suitable method. The range of values desired for artery layers was obtained by adding alumina particules and an ink to PVA cryogels processed by 1 and 2 FTCs. With the PVA processed by 2 FTCs, strain hardening was obtained but was rather small compared to arteries. The strain hardening is known to increase with the number of FTCs. This means that the two goals: mimicking the OCT profile and obtaining representative mechanical properties, appear to be competing against each other. To obtain the desired properties, we will need to either decrease the scattering from the PVA matrix when submitted to large numbers of FTCs, or increase the strain hardening of the PVA matrix with low number of FTCs without increasing its scattering. This represents quite a challenge that will be addressed in our future work. An additional challenge is to deposit the material in layers over a tubular structure to obtain a multilayer artery phantom. This will also be addressed in our future work.

6. ACKNOWLEGMENTS

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