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Durable optical phantoms with complex geometries and tissue-like mechanical properties

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ABSTRACT

In this paper, we present an approach toward the creation of coronary artery phantoms for optical coherence tomography (OCT). By mixing alumina powder in a matrix of transparent silicone, it is expected that the amplitude of the OCT signal and the soft tissue elasticity can be reproduced. The fabrication process to produce such multiple layer phantoms is presented along with optical and characterization experiments.

Keywords: Optical coherence tomography, phantoms, coronary arteries

1. INTRODUCTION

One of the many applications of optical coherence tomography (OCT) to biomedical optics is the imaging of coronary arteries via catheterized probes. With its high resolution ranging from 5 to 20 μm , OCT is growing as a powerful tool to detect vulnerable plaque. In the development of cardiovascular OCT systems, optical phantoms can find many applications like testing of the OCT hardware, calibration of the OCT system, or evaluating different image processing techniques. There are therefore strong incentives to fabricate phantoms of coronary arteries that can replicate both the optical and mechanical properties.

We obtain similar properties by mixing alumina micro powder in a special mixture of silicone. With that technique, we produce multilayer phantoms of healthy coronary arteries with contrast between layers representing the intima, the media, and the adventitia. Those phantoms are also durable, which makes them very convenient.

In this manuscript, we present the phantoms with characterization experiments and examples of applications. In section 2, the fabrication process is described in details. In section 3, we present how to obtain optical characteristics approaching those of coronary arteries. In section 4, we present results of tensile testing and of scanning electron microscopy imaging. Finally, in section 5, different applications of the phantoms to OCT are presented.

2. FABRICATION

The combination of alumina (Al_2O_3) powder in a room temperature vulcanizing (RTV) silicone as optical phantoms was introduced Bays *et al.* [1]. Silicone is a very interesting matrix material, since it is transparent, inorganic, and elastic. It therefore provides deformable and durable phantoms, with a well defined scattering microstructure. To obtain elastic properties comparable to soft tissues, we use a special mixture of Sylgard 184 and pure PDMS (Dow Corning 200R, 50 cSt viscosity). We mix the PDMS with Sylgard resin and Sylgard catalyst in proportions around 22.5:15:1 and heat at 70 $^{\circ}\text{C}$ for a few hours to allow adequate curing. The group refractive index of this matrix is around 1.4. The alumina is a 1 μm powder kindly provided by Struers. The refractive index of alumina is 1.76 and its specific gravity is 3.97 g/cm^3 .

Obtaining a good dispersion of the powder in the silicone matrix is pretty simple, but the process involves many steps. It begins by weighing the powder and by adding the needed volumes of PDMS and of the resin part of Sylgard 184. The reactive is not added at that point. To insure good incorporation of the alumina, the same volume of hexane is added. Hexane is a very good solvent for Sylgard 184 silicone and PDMS. Therefore, it greatly decreases the mixture viscosity [2]. This mixture is then placed in an ultrasonic bath for about two hours, breaking down most aggregates while efficiently and uniformly dispersing the powder in the silicone matrix. Afterwards, the hexane is evaporated under vacuum for a few hours, leaving the silicone still capable of polymerization. The reactive is finally added to the batch in proper proportion and mixed manually. This mixture can be cast in molds of any shape to obtain complex geometries, but for the specific application of coronary artery phantoms, a different approach is used. First, three mixtures with

different concentrations of alumina are prepared as described above to mimic the intima, the media and the adventitia. They are successively applied on a lathe with desired thicknesses. The lathe is shown in Fig. 1. It is composed of a shaft rotating at 1 Hz close to a razor blade to control and even the thickness of each layer. A heating element raises the temperature to approximately 70 °C for polymerization. Each layer is cured for about one hour before applying the next one. Once all layers are applied and cured, the phantoms are removed from the shaft. An example of coronary artery phantom is presented in Fig. 2.

Fig. 1 : Lathe setup for multilayer phantoms fabrication.

Fig. 2 : Coronary artery phantom.

3. OPTICAL PROPERTIES

The average profile of an OCT signal through depth depends mainly on the backscattering and the total attenuation of the samples. Therefore, these are the properties of each layer of the coronary arteries that the phantoms should reproduce. To match the properties, we characterize the OCT signal for a series of disk shaped phantoms made of different concentrations of alumina, as well as the signal from porcine coronary arteries extracted and cut open for bench top measurements.

The profiles are fitted with a model of the variation of the OCT signal amplitude with depth. The OCT signal is the intensity obtained from the product of the fields in the reference and the sample arms. Since the field in the reference arm has nearly constant amplitude, the response is proportional to the field in the sample arm. This field is the summation of the contributions of each scatterer in the coherence volume, a volume defined by area of incident illumination and the OCT resolution. Considering single backscattering events, the contribution of one scatterer is proportional to the incident illumination and the backscattered light collected by the system. The illumination part is the field of a Gaussian beam attenuated through the sample. It has the form: $\exp[-\mu z/(2n)]/\text{waist}$, where z is an optical depth, and is divided by the refractive index of the sample, n , so that the attenuation coefficient, μ , is expressed in geometrical length. The factor 2 at the denominator takes into account that the expression describes a field, but the attenuation coefficient is defined for the intensity. The waist in the expression also varies along the optical depth due to focusing. The field being backscattered from the position of the scatterer, through the sample, and into the system is a situation of mathematical reciprocity. Hence, the previous form multiplies itself to obtain the response of a single scatterer that is proportional to $\exp[-\mu z/n]/\text{waist}^2$.

We consider the contribution of the scatterers to be random phasors. The number of phasors is proportional to the concentration of alumina multiplied by the coherence volume defined by the OCT resolution length and the area of illumination with a radius defined by the waist. Assuming a high density of scatterers and a fully developed speckle field, the discrete sum of phasors leads to an amplitude that is proportional to the square root of the number of contributors [3]. With the cancelation of the waist terms from the coherence volume and the single scatterer response, we are left with the simple form $a \exp[-\mu z/n]/\text{waist}$ used for fitting the profiles, where a is expected to vary with the square root of the concentration [4]. The OCT signal profiles of three phantoms made of 3.8, 13.3 and 34.0 mg of alumina per ml of silicone are shown in Fig. 3. The images were acquired with rather large depth of focus, hence the very weak focusing effect observed in the profiles.

Fig. 3 : Averaged OCT signals of three alumina-silicone phantoms and their fits.

Plotting the fitting parameters a and μ with respect to the concentration for all the phantoms gives characteristic curves of the OCT signal for the alumina-silicone combination. In Fig. 4, the variation of the amplitude with the square root of the concentration is shown, and a linear relation between the attenuation and the concentration is observed. The results are then used to obtain equations characterizing the signal of the phantoms in our system in relation with the concentration of powder. These equations are given in Fig. 4 as well.

The characterization of the signal from coronary arteries is performed in a similar fashion. With a similar experimental setup, OCT cross-sections of extracted porcine coronaries are acquired and their signal is averaged. An example is shown in Fig. 5. Three segments of different amplitude are easily distinguishable. The single peak at optical depth 0 mm

is attributed to the thin layer of endothelial cells also called intima. This layer is thinner than the system resolution, therefore its signal cannot be fitted along depth and its attenuation is neglected. An amplitude factor is then extracted directly from the peak amplitude. The signal following the first peak and decaying until 0.55 mm in depth would come from the media. It has the weaker backscattering of the three. The fit with the model is straightforward. It approximates the profile pretty well. Some discrepancies observed around 0.1 and 0.5 mm are caused by deviations from the constant backscattering through the layer assumed in the model. After 0.6 mm, the stronger signal comes from the adventitia. To fit the profile correctly, the attenuation accumulated in the media is taken into account.

Fig. 4 : Signal amplitude factors and attenuation coefficients of the alumina – silicone combination

Fig. 5 : OCT signal profile of a coronary artery with the optical properties of the multiple layer identified from fits. (Purple – intima, orange – media, green - adventitia)

With both the arteries and the phantoms characterized, we try to find which concentration of alumina in silicone can replicate the optical properties of each layer. For example, to replicate the backscattering of the media, the characteristic

equation of the amplitude in Fig. 4 suggests a concentration of 5 mg/ml. However, the characteristic equation for the attenuation shows that this concentration yields to an attenuation of only 0.84 mm^{-1} , while the media has a coefficient of 4.5 mm^{-1} . Because the phantoms have weaker attenuation than the tissue, it is yet impossible to mimic the whole signal profile of the artery without the addition of an absorbing material. Finding the right absorber is quite a challenge firstly because silicone is only soluble in a few solvent, and secondly because we work at $1.3 \mu\text{m}$. Common choices of absorber like India ink or rhodamine dyes were tried, but they are either immiscible in silicone, or they do not absorb at our wavelength. Many of the absorbers that have been tried even have both incompatibilities.

Even if an attenuator is needed to achieve in-depth profiles similar to arteries, the control we have on the scattering amplitude is already very useful in several applications. For example to have a representative contrast between two layers to test segmentation algorithms.

4. PHYSICAL PROPERTIES

Additional characterization experiments were also performed to assess the mechanical properties, the solidarity of the different layers. We also explored various materials to create inclusions that would allow the replication of features like lipid plaque, calcifications, etc.

The elasticity of the phantoms was evaluated by uniaxial traction testing of blank samples of silicone with various proportions of the different components. Specialty silicones are often sold in kits of a resin part and a reactive part to be mixed in a 10 to 1 ratio. This ratio can be changed to vary the elasticity of the resulting polymer to some extent [5]. The addition of PDMS to a specialty silicone was also reported to produce phantoms with stiffness similar to soft tissues [6]. Results of traction tests on samples of Sylgard 184 with ratios of resin to reactive from 10:1 to 20:1, as well as sample of various proportions of pure PDMS added to a 15:1 Sylgard mixture are compared to the results from soft porcine tissues in Fig. 6.

Fig. 6 : Elasticity of different compositions of silicone compared to porcine aorta and a porcine left circumflex artery (LCX).

We can observe that there is a decrease in stiffness with the increase of the resin to reactive ratio of Sylgard 184. However, a ratio higher than 15:1 does not further decrease the stiffness and leads to very sticky samples while still being quite stiffer than soft tissues. A further decrease in stiffness can be obtained by the addition of pure PDMS. From Fig. 6, we can see that the proportions up to 22.5:15:1 of PDMS:Sylgard Resin:Sylgard Reactive can produce samples as soft as tissues in their linear regime. Samples of such compositions no longer cure at room temperature, but do polymerize within 2 to 3 hours at a temperature of 70°C .

To further investigate the resulting phantoms, we also looked at cross-sections of the multilayer phantoms with scanning electron microscopy (SEM). One of these images is presented at Fig. 7. On the SEM images, there is no evidence that

successive layers of silicone were applied. In our opinion, this means that uncured silicone can cross link to some extent with cured silicone, creating attached layers. This is a very interesting aspect because when applying stress to the samples, joined layers will undergo continuous deformations. This solidarity resulting from successive applications of silicone combined with the ability to adjust the backscattering and the elasticity of each mixture gives the alumina in silicone combination great potential to create even more complex phantoms.

Fig. 7: SEM image of a cross-section of a multilayer cylindrical phantom.

With this same objective in mind, we also looked at stiffer materials that could be incorporated into the artery phantoms. Fig. 8 shows a SEM image of a high density polyethylene (HDPE) wire embedded in an alumina-silicone phantom. As opposed to the silicone-on-silicone layers, the presence of the wire is very obvious and the HDPE-silicone interface is discontinuous. Therefore, this kind of inclusions remains interesting for elastography experiments because its behavior under stress should be much different than the behavior of a phantom made with linked inclusions.

Fig. 8: HDPE wire in an alumina and silicone phantom.

5. APPLICATIONS

The proposed phantoms can have multiple uses in the development of cardiovascular OCT. One major aspect is in system tuning and testing. Electronic connections, source power and optical alignment are just a few potential tuning parameters of a system under development. An appropriate tissue phantom provides a very good validation tool to be used before any critical measurements such as in-vivo trials to insure the system is optimized. The fabrication of OCT catheters is also challenging and artery phantoms are very useful in testing probe prototypes or catheter designs. Not only are they much less cumbersome to measure than real tissues, their scattering properties won't change in time so that they provide a constant basis of comparison. This is of course not the case from one artery sample to another. An example of probe testing is presented in Fig. 9. The difference between the images acquired with two different probe prototypes is striking. On the left, scattering signal from the phantom is practically absent, while on the right, the whole phantom is observed, and contrast between all the layers is evident. On top of the second image, we also detect reflections from the table under the phantom.

Fig. 9: On the left, an OCT image of a multilayer artery phantom taken with a broken or dirty probe. On the right, an image taken with a functional probe.

Another field of application to these phantoms is the testing of various processing techniques like segmentation and elastography. In segmentation, we can use the phantoms to test the ability of different algorithms to automatically identify features. For example, in Fig. 10 the outer diameter of the guiding catheter and the arterial wall are detected using filtration and peak detection along the OCT A-scans. Such an algorithm can be used for example to track the luminal area during a pullback through a stenosis and evaluate the obstruction. With control on the backscattering, different contrasts can also be used to determine the limits of detection of such algorithms.

Fig. 10: Segmentation of the lumen in an OCT image of a multilayer phantom. The dashed lines show the automatic identification of the catheter outer diameter and of the arterial wall.

6. CONCLUSION

In this paper, we presented an approach toward the creation of coronary artery phantoms for optical coherence tomography. By mixing various concentrations of alumina powder in a matrix of transparent silicone, the amplitude of backscattering can be reproduced for all three layers of healthy coronary arteries. In addition, by adjusting the proportions of pure PDMS and Sylgard components, the elasticity of the phantoms can be modified to replicate soft tissue elasticity in the linear regime. The materials and fabrication process provide layers that are attached. We also investigated some materials to create unattached inclusions. The phantoms are already of great utility in fields like system tuning, systems testing, and testing of segmentation algorithms. However, because the attenuation of the signal from the phantoms is weaker, the whole OCT profile of coronary arteries cannot be duplicated yet. Future work will therefore consist in finding a proper absorbing component to add to the actual combination, or to investigate other combinations to further improve the currently obtained properties.

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