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Fabrication and characterization of silicone-based tissue phantoms with tunable optical properties in the visible and near infrared domain

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Abstract

We present a fabrication process for Polydimethylsiloxane (PDMS) tissue simulating phantoms with tunable optical properties to be used for optical system calibration and performance testing. Compared to liquid phantoms, cured PDMS phantoms are easier to transport and use, and have a longer usable life than gelatin based phantoms. Additionally, the deformability of cured PDMS makes it a better option over hard phantoms such as polyurethane optical phantoms when using optical probes which require tissue contact. PDMS has a refractive index of about 1.43 in the near infrared domain which is in the range of the refractive index of tissue. Absorption properties are determined through the addition of india ink, a broad band absorber in the visible and near infrared spectrum. Scattering properties are set by adding titanium dioxide, an inexpensive and widely available scattering agent which yields a wavelength dependent scattering coefficient similar to that observed in tissue in the near infrared. Phantom properties were characterized and validated using a two-distance, broadband frequency-domain photon migration system. Repeatability and predictability for the phantom fabrication process will be presented.

Keywords: optical phantom; tissue spectroscopy; calibration standards; optical properties.

1. Introduction

The use of optical tissue simulating phantoms is a necessary part of the continued development and adoption of optically based clinical techniques. While liquid phantoms may be the easiest to produce and characterize, there are number of phantom applications where a solid, permanent option would be better suited. These include system reference phantoms to improve signal to noise, intersystem and inter-site performance testing phantoms, and technique validating phantoms involving more complex structures. Flow experiments, layered phantoms, and arbitrary phantom geometries would all require the latter.

A tissue simulating phantom is made of a bulk material to which a scattering agent and an absorbing agent are added. To date, a variety of materials and optical agents have been used to produce phantoms and have been recently reviewed.[1] Silicone (PDMS) was chosen for the phantoms discussed in this paper. Vulcanized silicone has several favorable qualities. Most important is its stable, durable nature allowing for ease of transport and use over an extended period of time. Additionally, the deformability of the cured silicone makes it more suitable for contact-based optical technologies than other 'permanent' phantoms such as polyurethane. Finally, the index of refraction for cured silicone is 1.4 which is similar to that of bulk tissue.[2, 3] To introduce scattering and absorption respectively, titanium dioxide (TiO_2) and India Ink were chosen for their price and availability.

Below, a step by step procedure is outlined for the fabrication of silicone phantoms tuned to specific optical properties in the near-infrared spectrum. This process is efficient, repeatable, and controllable. Additionally phantom characterization is reviewed and repeatability and homogeneity is discussed.

2. Phantom Fabrication

2.1 Recipe

Vulcanized silicone requires the addition of a curing agent to bulk PDMS and can be purchased as a commercially available kit (Kit P-4, Eager Plastics). These two ingredients are combined at a ratio of 10 parts PDMS to 1 part catalyst. For our phantoms, we combined 250 ml PDMS and 25 ml of the provided curing agent to make a 275 ml phantom. Scattering was achieved by the addition of rutile TiO_2 powder (Ti-602, Atlantic Equipment Engineers). TiO_2 is a highly effective scatterer due to its high index of refraction[4] and has negligible absorption in the NIR spectrum. An absorber was added in the form of India ink (PRO-4100, Pro Art). At 650nm, approximately 0.07 g India Ink (0.25 g/l) is required to generate absorption of roughly 0.02 mm^{-1}, and approximately 0.2 g TiO_2 (0.73 g/l) is needed to generate reduced scattering of roughly 1 mm^{-1}. These amounts do not significantly change the volume of the phantom. A softball display case (Sports Cube L.P.) was chosen for a mold because the two-piece design allowed for the easy extraction of the cured phantom, and yielded phantom with dimension of 98mm x98mm x ~27mm. We require that the phantom be thicker than the penetration depth of the optical technologies it will be used for, but the exact height was not controlled for in this process. Across the population of newly produced phantoms, the height varied by +/- 2 mm and is the combined result of excess silicone left in the mixing container and some leakage of the softball case mold. TiO_2 and India Ink amounts were always mixed into the 275 ml silicone kit so that concentrations were not affected by the slight size differences of the final cured phantoms.

2.2 Fabrication Process

Figure 1 illustrates a summary of the process flow which will be described in detail. More than simply mixing the ingredients, we have found that by following a particular process we are able to produce more
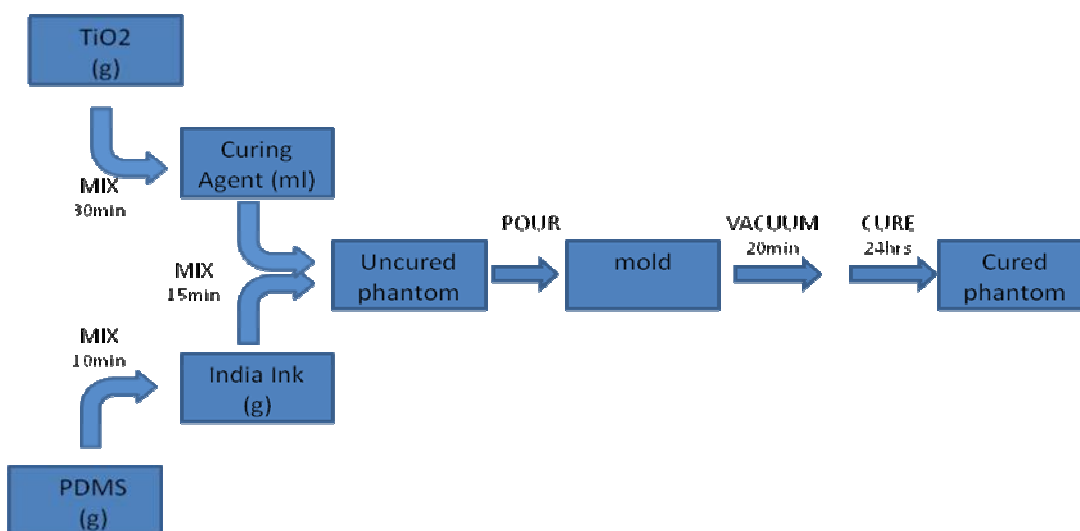

Figure 1 – A summary of the primary steps in the phantom making process.

uniformed phantoms with predictable optical properties in the NIR spectrum.

To begin, 25 ml curing agent is retrieved with a disposable pipette and placed in a 25 ml plastic beaker. TiO_2 is measured by weight and added to the curing agent. This is manually mixed and placed in an ultrasonic bath (BR1200-R-1, Branson) for 30 minutes. This solution should be stirred several times during this period to prevent the TiO_2 from settling. During this 30 minute period the bulk PDMS and India ink can be combined. To make the highly viscous PDMS easier to work with, we transfer it from the original 1 gallon paint can into a plastic container with a pour spout prior to the phantom making process. We have also chosen to measure the PDMS by weight. This allows us to use a disposable plastic mixing dish while still maintaining an accurate measure of volume. Through several volume measurements, we have determined that the PDMS has a density of 0.956 g/cm^3 which equates to 239 g of PDMS to achieve 250 ml. By consistently measuring this amount of PDMS, we can ensure a repeatable and predictable process. Because India ink will stain any plastic it contacts, it can be difficult to determine the amount of India Ink that makes it into the phantom. To ensure the accuracy of our process we measure this absorber by weight. Using a micropipette we can add the required amount if India Ink to a small, 2-3 gram pool of silicone from our batch held in a disposable measuring boat (Figure 2). With the India ink suspended in the silicone, none of the measured amount will be lost due to staining when this suspension is transferred to the larger volume of silicone for mixing. Given the relatively small size of the phantom, hand mixing is effective and uniformity, as judged by eye, can be achieved in about 10 minutes.
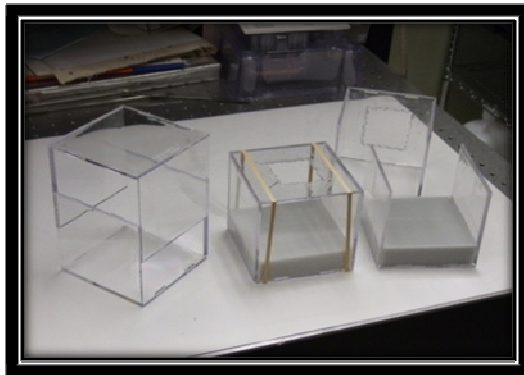

Figure 2 - India Ink measured in a pool of silicone

Figure 3 – Left to right, an empty mold, a curing phantom, and a phantom ready for extraction.

Once the two separate suspensions have been thoroughly mixed, they can be mixed together to begin the curing process. This mixture can be satisfactorily mixed with about 15 minutes of hand mixing. At this time, the mixture is poured into the mold. As stated above, we use a softball award case for this purpose. We have cut a hole in the top so that the mixture can be poured into it and have added two thick rubber bands to strengthen the seal of the two pieces (Figure 3). Because the curing process initially generates gas, the mold is placed in a vacuum chamber for approximately 20 minutes. The majority of the bubbles remaining at the top can be popped through the rapid re-pressurization of the vacuum chamber several times. Any remaining air bubbles should be punctured manually with a sharp object. Removal of bubbles and any other disturbance to the phantom should be concluded shortly after this 20 minute period to ensure that any imperfections do not set in the phantom. The pot life for this silicone kit is 60 minutes. At room temperature the phantom will cure fully in 24 hours.

3. Characterization Methods

3.1 SSFDPM

To characterize the optical properties of our fabricated phantoms we have employed a two-distance steady state frequency domain photon migration (SSFDPM) system. This involves two contact measurements at different source-detector separations using the SSFDPM System (Figure 4). The instrument incorporates six laser diodes at different wavelengths which scans 125 frequencies between 50 and 250 MHz, and a broadband NIR light source.[5] The detection of this combination at two separations is a self-calibrating method[6] and provides fitted absorption and reduced scattering values at discrete points between 650nm and 998nm (Figure 5). Data was taken at a source-detector separation of 9mm and 11mm. The reduced scattering coefficient follows a power law dependance and mimics the scattering behavior of lights seen
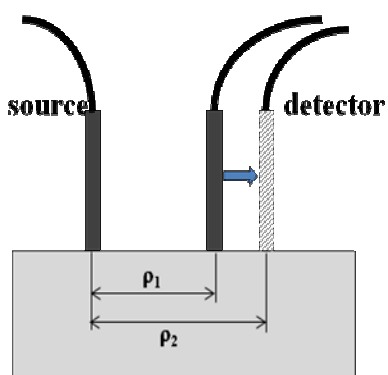
Figure 4 – SSFPDM system. The source contains six laser diodes and broadband NIR source. Measurements are recorded at distance ρ_1 and ρ_2.
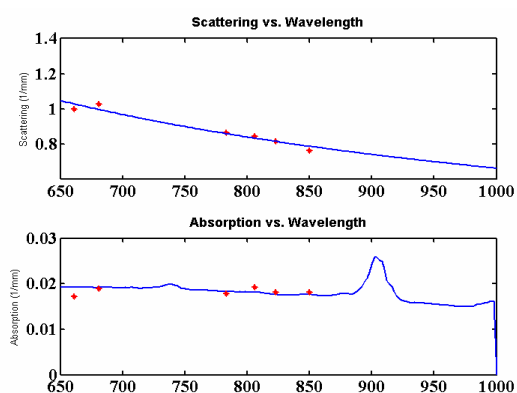
Figure 5 – Sample data generated by the SSFPDM system showing the six points measured by the laser diodes and the fitted broadband scattering and absorption spectra.

in tissue. The absorption coefficient has a relatively flat spectra, which is a feature of India Ink. We observe a pronounced peak at 910 nm that is consistent with the absorption of PDMS.
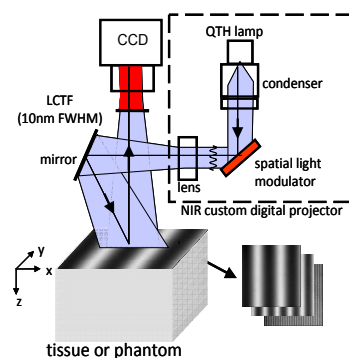
3.2 Modulated Imaging

Figure 6 – Diagram of the modulated imaging system. Sine patterns of varying spatial frequency are projected onto the phantom and the diffuse reflectance is captured by a CCD camera.

Modulated Imaging is a new wide-field spectral imaging modality, based on the principals of diffuse optical spectroscopy and developed by our lab, which relies on spatial frequency domain measurements of diffuse reflectance acquired by a CCD camera to calculate the spatially resolved absorption coefficient and reduced scattering coefficient on a pixel by pixel basis (Figure 6).[7] The imaging capability of this method allows us to simultaneously retrieve the average optical properties over the near infrared spectrum for separate regions of interest on the same phantom. Comparisons of these values were used to test for uniformity of properties across the surface of the phantoms. The system is calibrated using a reference phantom of known optical properties as determined by the above SSFDPM method.

4. Results

Several phantoms were made with varying amounts of TiO_2 and India Ink added. Figures 7 & 8 show the recovered absorption and scattering coefficients plotted against the amount of added absorber and scatterer for nine phantoms at 650 nm. While some variability can be seen, particularly at higher concentrations, the linearity of the two graphs allows for a reasonable prediction of the phantom characteristics. Additionally, the presented populations of phantoms were fabricated over several months while the fabrication process was being improved. To test the repeatability of the fabrication process outlined above, the following experiment was conducted. Two phantoms were made separately by two
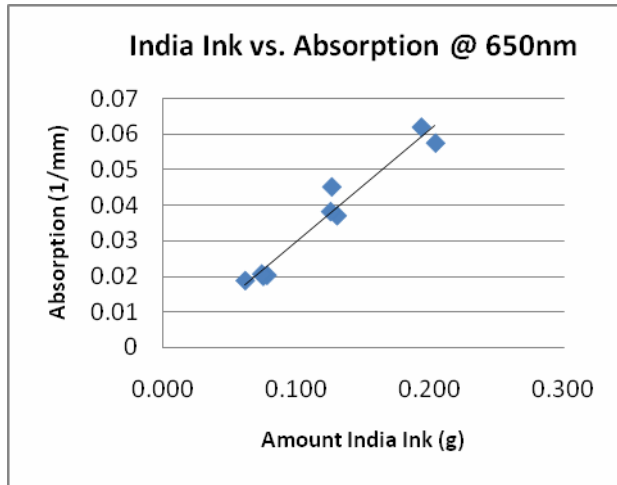

Figure 7 Amount of India Ink added to 275 ml phantoms versus the recovered absorption coefficient.
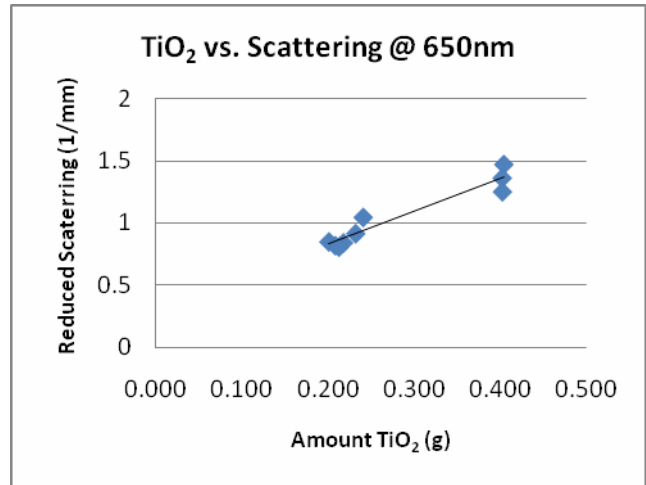
Figure 8 Amount of titanium dioxide added to 275 ml phantoms versus the recovered reduced scattering coefficient.

individuals following the same procedures. One of the individuals was involved in the development of this process. The second individual was first exposed to this process for this experiment. The first phantom contains 0.07489 g India Ink and 0.21760 g TiO_2. The second phantom contains 0.07369 g India Ink and 0.23190 g TiO_2. Figure 9 depicts the absorption and scattering spectra for the two phantoms. The error bars reflect a coefficient of variation of $\pm5.98\%$ and $\pm4.39\%$ for absorption and scattering respectively. These values were determined by the average dispersion across the spectra of several measurements taken from the same phantom over a two day period. Given the variability within the measurement, it can be seen that similar phantoms were produced.
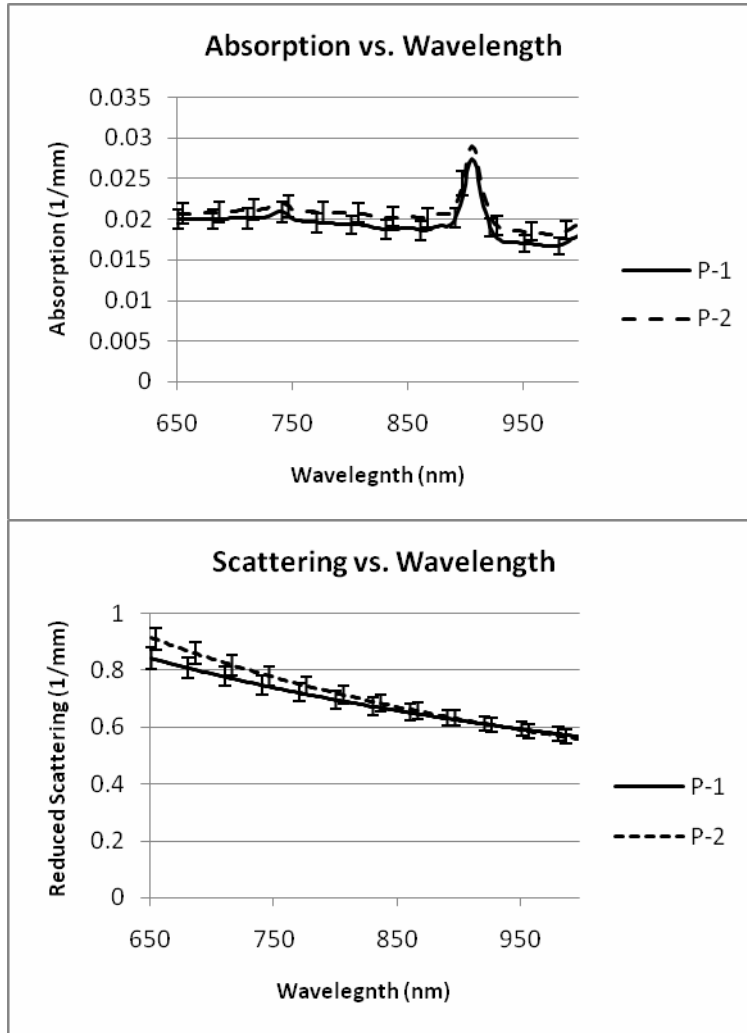
Figure 9 Top: Recovered absorption values for two separately produced phantoms. Phantom P-1 contains 0.07489 g India Ink. Phantom P-2 contains 0.07369 g India Ink. Bottom: Recovered reduced scattering coefficients for the two phantoms. Phantom P-1 contains 0.21760 g TiO$_2$. Phantom P-2 contains 0.23190 g TiO$_2$.

It is well known that titanium dioxide will settle in liquid phantoms if the solution is not stirred regularly. This has led to a concern that the TiO_2 might settle in the silicone during the curing process and create a scattering gradient within the phantom. To test for this possibility, the two distance SSFDPM measurement was repeated on the bottom of the phantoms and compared to the recovered properties from the top of the phantom. Figure 10 displays an overlay of the reduced scattering spectra for the top and bottom of two phantoms from our inventory. Again, the similarity in values implies a uniform
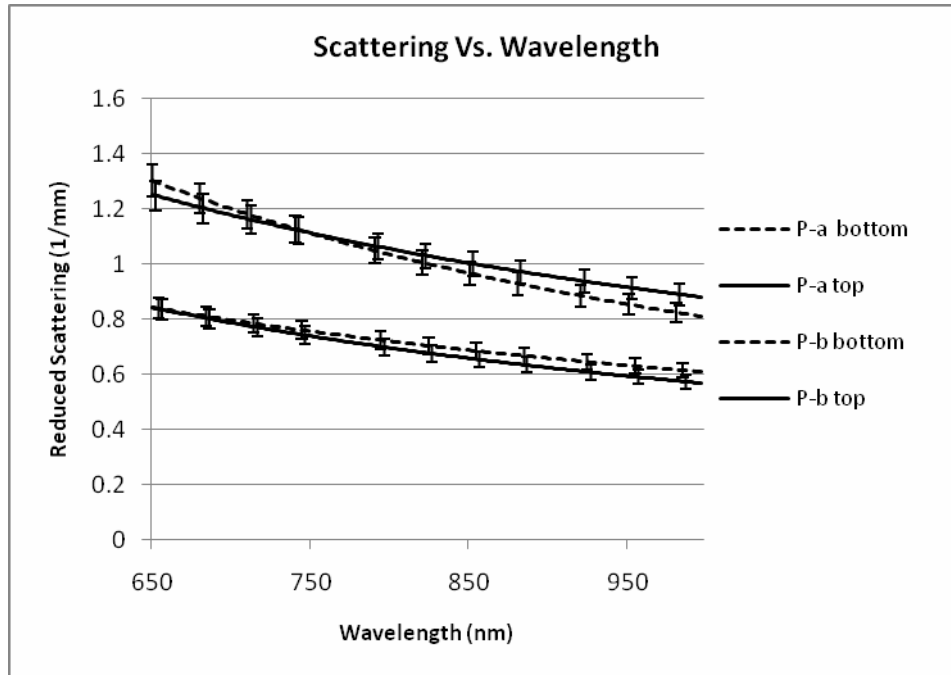

Figure 10 Comparison of reduced scattering coefficients recovered from the top and bottom of a phantom. Two phantoms are shown. Phantom P-a, represented by the top two lines of the graph, contains 0.40267 g TiO_2. Phantom P-b, represented by the bottom two lines of the graph, contains 0.21760 g TiO_2.

distribution of scatterer in the phantom. Phantom P-a has almost twice the amount scattering agent as phantom P-b suggesting that this result does not change with an increase in concentration. Of less concern is the possibility that the scattering and absorbing agents will not distribute evenly in the phantom across the x-y plane. We have opted to test for this uniformity by measuring the phantoms with the Modulated Imaging System. As stated in the Characterization Methods section, Modulated Imaging allows the recovery of average optical properties for individual regions of interest at discrete wavelengths. Figure 11 shows the average absorption and reduced scattering coefficients at discrete wavelengths for four regions of interest on the surface of a phantom. Here, uniformity is clearly demonstrated by the overlapping spectra of the separate areas of the phantom.
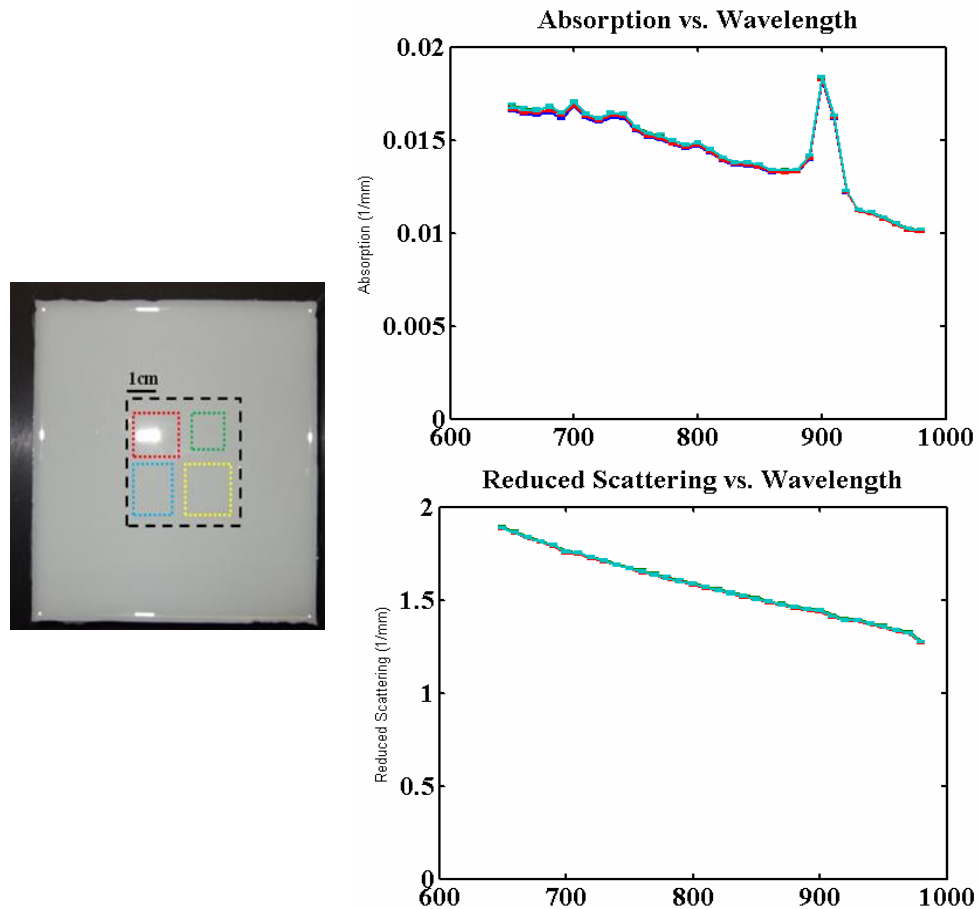
Figure 11 Left: Color photograph depicting the four selected regions of interest within the field of view. **Right Top:** Absorption versus wavelength was plotted for the four regions of interest and shows high precision in values recovered. **Right Bottom:** Reduced scattering versus wavelength was plotted for the four regions of interest, with the four data sets appearing nearly indistinguishable.

5. Conclusion

Tissues simulating optical phantoms play a central role in the development, validation, and application of optically based biomedical technologies. An inventory of well characterized phantoms will be useful to many labs. In these proceedings we have outlined an efficient fabrication process that is easy to follow and can produce phantoms with predictable and repeatable optical properties in the near-infrared spectrum. This has been demonstrated through the comparisons outlined above. In the future, additional phantoms with a wider variety of optical properties will be produced and characterized. The characterization process itself was effective in determining the optical properties of the phantoms. However, inter-measurement variability should be investigated further with the goal of refining the data acquisition process. We have also begun to leverage the characteristics of the silicone by making thin-layered phantoms in the 100 micron range and phantoms with depth dependent inclusions.

Acknowledgements

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