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Design and Fabrication of Solid Phantoms for NIR Water Fraction Studies

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ABSTRACT

Tissue simulating phantoms provide a valuable platform for quantitative evaluation of the performance of diffuse optical devices. In this paper we report the development of a poly(dimethylsiloxane) (PDMS) tissue phantom that mimics the spectral characteristics of tissue water. We have developed these phantoms to mimic different water fractions in tissue for testing new devices within the context of clinical applications such as burn wound triage. Compared to liquid phantoms, PDMS phantoms are easier to transport and use, and have a longer usable life than gelatin based phantoms. The phthalocyanine dye 9606 was used to provide an absorption feature of in the vicinity of 970 nm. Scattering properties were independently determined by adding titanium dioxide powder to obtain reduced scattering coefficients similar to that of tissue in the near infrared. Phantom properties were characterized using the techniques of inverse adding doubling and spatial frequency domain imaging. Results presented here demonstrate that we can fabricate solid phantoms that can be used to simulate different water fractions.

Keywords: tissue simulating phantoms, diffuse optical spectroscopy, turbid media.

1. INTRODUCTION

Biomedical diffuse optical imaging systems require tissue phantoms that mimic the optical properties of tissue for their development, characterization and calibration. Many phantom systems have been investigated using a variety of host media, scattering particles and absorbers. For an excellent review the reader is directed to Pogue et al¹.

For superficial tissues, such as skin, phantom fabrication efforts have focused primarily on mimicking the absorption characteristics associated with oxy- and deoxy-hemoglobin and melanin. Biomedical problems concerning measuring edema within the context of, for example, burn wounds, infection or simple cosmetic hydration measurements, are likely to benefit from new spectral imaging technologies, however, the means for systematically varying water fraction in a solid phantom in order to test and validate these devices has been difficult to come by.

Water containing phantoms based on liquid fat emulsions have been widely used. In particular Intralipid® (Fresenius Kabi AB, Uppsala, Sweden) has been used extensively²⁻⁴ and significant work has been carried out to determine properties and stability of these phantoms and reliable methods of producing them⁵⁻⁷. It is relatively straightforward to add other chromophores such as blood in order to obtain realistic absorption spectra⁸. Unfortunately, these phantoms have a limited shelf life. The suspended lipid droplets in these phantoms provides the scattering. In order to obtain physiologically relevant reduced scattering coefficients the Intralipid® is typically diluted to a concentration of a few percent. This resulting phantoms are typically >95% water, which leaves little room to vary the water content.

Merritt et al⁹ reported variation of lipid and water content in fat emulsion phantoms, however, the scattering properties of the emulsions were not disclosed. Subsequently Quarto et al.¹⁰ investigated three phantom types that enabled the relative fractions of fat and water to be varied, including the emulsion system described by Merritt et al. They reported that for this recipe the reduced scattering was exceptionally high – almost an order of magnitude larger than skin. It could be reduced somewhat by lowering the amount of the emulsifying agent but this reduced the stability of the emulsions and they would only last a few hours before separating. Furthermore, although the water fraction can be adjusted by changing the fat to water ratio, the scattering is proportional to lipid droplet density. Decreasing the water fraction increases the lipid content thus increasing the scattering.

Water fraction can be varied in agar and gelatin phantoms^{11, 12} and they can also be molded into 3D shapes but again suffer from limited lifespan of a few weeks/months. Phantoms constructed using these materials tend to have fragile mechanical properties and require refrigeration to maintain optical properties and minimize evaporation of the water. As a result their usefulness within a clinical context is somewhat limited.

Michaelsen et al¹³ reported a semisolid animal fat based breast phantom that is capable of reproducing physiologically properties where the water content can be varied over a wide range. These phantoms also require refrigeration and showed stable optical properties for several weeks.

Solid phantoms fabricated from materials such as epoxy¹⁴, polyurethane¹⁵ and silicone¹⁶⁻²⁰ are more durable, easy to handle and transport and can exhibit stable optical properties for periods extending to several years. This makes them popular for calibration and routine testing of instrumentation. Additionally, they can be molded, machined or 3D-printed²¹⁻²³ into complex three dimensional shapes having homogeneous, heterogeneous and layered optical properties that are useful for more complex tissue models. However, we are unaware of phantoms containing physiological water fractions in the literature. Room temperature vulcanizing poly(dimethylsiloxane) PDMS is a compliant material having a refractive index close to tissue. It is inexpensive, readily available and relatively straightforward to mold into 3D shapes¹⁶. Several groups, including our own, have successfully developed phantoms based on PDMS. These have been used for calibrating and validating various diffuse optical spectroscopy and imaging devices over the years for a range of biomedical applications^{19,20,24}. Unfortunately, the strongly hydrophobic property of silicone makes it difficult to introduce significant amounts of water into phantoms. Since the water fraction of tissue is commonly in the range of 60 – 90% it is not possible to create silicone phantoms having physiological water content. In this paper we describe solid silicone tissue phantoms that incorporate a particular near infrared dye to simulate a variation in tissue water absorption.

2. MATERIALS AND METHODS

The fabrication of the tissue phantoms follows the method described by Ayers et al¹⁷. The base phantom material was room temperature vulcanizing silicone rubber (P4, Eager Plastics Chicago, IL USA). Titanium oxide powder (Titanium (IV) Oxide, anatase 248576, Sigma Aldrich) was used to provide scattering and the near infrared absorption was obtained using the phthalocyanine dye 9606 (Fabricolor Holding Int'l, Paterson, NJ. USA).

Figure 1. Absorption spectra of the 9606 Dye: (a) spectra for the dye dissolved in acetone, (b) variation of absorption at 970 nm with dye concentration in acetone (c) dye in cured PDMS (d) variation of absorption at 970 nm with dye concentration in cured PDMS.

Figure 1(a) shows the absorption spectrum of the dye dissolved in acetone measured using a commercial spectrophotometer. The dye exhibits a broad absorption feature spanning 800 nm to 1100 nm with peak at 972 nm. The absorption spectrum for water²⁵ is reproduced for comparison. Whilst the 9606 dye absorption is broader than that of water, encompassing both the water and lipid peaks at 920nm and 970 nm, it nevertheless is a reasonable approximation. The peak absorption at 972 nm for varying dye concentration in acetone, presented as Figure 1(b), shows a linear relationship between absorption coefficient and concentration. Figures 1(c) shows the absorption spectrum for 5 mm thick cured silicone slabs having no scattering particles measured relative to cured silicone with no dye. The spectra are somewhat broader than the dye in solvent but the peak remains at the same wavelength. The variation of absorption with concentration, presented as Fig 1 (d) is slightly sublinear at higher concentrations.

To make the phantoms, TiO₂ powder was added to the curing component agent (part A) at a concentration of 1 g.kg⁻¹ and the mixture was sonicated for several hours, mixing regularly to break up any clumps. A solution of 9606 dye was made by dissolving dye powder in acetone at a concentration of 1.3% by weight and the dye stock was added to the pdms base component (part B) in amounts ranging from 1.7 ml.kg⁻¹ to 3.4 ml.kg⁻¹ and vigorously mixed using an electric drill with a paint mixing attachment. The two components were then combined in a 10:1 ratio and mixed for ~2 minutes. The mixture was poured into a 100 x 100 mm square mold whose base was lined with sandpaper to reduce specular reflection from the sample surface. The molds were placed in a vacuum chamber and degassed using a rotary pump at a pressure of 30 – 60 mbar for approximately 40 minutes. Thin sheets (1 – 3 mm) of the material were made by removing a small amount of the degassed mixture using a syringe and transferring it to 60mm diameter Petri dishes. All the samples were placed on a level surface and allowed to cure for 24 hr. The phantoms were then removed from the molds and set aside for approximately one week to fully cure before characterizing them.

3. RESULTS AND DISCUSSION

Measurements of the optical properties of these homogenous phantoms were taken using two methods. The thin discs were measured using the technique of inverse adding-doubling (IAD)²⁶. The samples were placed at the entrance port (for transmission measurements) or at the exit port (reflection measurements) of an 8-inch diameter integrating sphere and a collimated beam from a broadband light source was incident on the sample. A fiber-coupled cooled CCD spectrometer having a wavelength range of 450 – 1000 nm and a resolution of ~1 nm was used to measure the transmitted and reflected spectra relative to a diffuse reflection standard (Labsphere SRS-99-020, 99%). These data were processed using Matlab® code incorporating the IAD code written by Scott Prahl²⁷ to obtain the reduced scattering and absorption coefficient spectra. This technique is calibration free in the sense that the determination of the reduced scattering and absorption does not require the measurement of a sample having known μ_a and μ_s . For these calculations a scattering anisotropy of 0.9 and a refractive index 1.43 were selected.

Figure 2 shows the calculated reduced scattering and absorption spectra for three phantoms containing stock dye concentrations of 1.7, 2.55 and 3.4 ml.kg⁻¹. The absorption spectra are similar to the measurements of the non-scattering samples displayed in Figure 1 that were made using the spectrophotometer. The peak at 915 nm corresponds to an absorption peak arising from the PDMS itself that is not apparent in the spectrophotometer measurements because a matched sample of silicone without dye was placed in the reference arm. The peak absorption varied linearly with concentration as shown in Fig 2(c). The scattering monotonically decreases with increasing wavelength, with a value of approximately 1mm⁻¹ at 700 nm which is consistent with our experience of phantoms using this concentration of TiO₂.

Figure 2. (a) Absorption and (b) reduced scattering spectra obtained using the technique of inverse adding-doubling for thin sheets of phantom for three concentrations of dye. (c) peak absorption versus concentration.

The 3 cm thick phantoms were characterized using the technique of spatial frequency domain imaging (SFDI) that we have described in detail elsewhere^{28, 29}. Our SFDI measurement system employed broadband illumination from a quartz–tungsten halogen lamp and narrowband detection using a camera fitted with liquid crystal tunable filter³⁰. Measurements were taken from 650 - 1000 nm at 10 nm intervals. A look-up table method²⁹ was used to calculate the reduced scattering and absorption coefficients from measurements of the reflectance at 0 mm⁻¹ and 0.15mm⁻¹.

Figure 3. Spectra of (a) absorption and (b) reduced scattering coefficients for 3cm thick PDMS phantoms incorporating different concentrations of 9606 dye measured using spatial frequency domain imaging (mean of central 100 x 100 pixels).

The mean absorption and reduced scattering coefficients for a 100 x 100 pixel central regions of three samples having different dye concentrations are presented as figure 3. -The measurements broadly agree with those obtained for the thin specimens that were made using the integrating sphere and inverse adding-doubling method. Since SFDI is a wide-field imaging technique we were able to image the surface of each phantom in order to assess the homogeneity of the optical

properties across the sample. The phantoms showed good uniformity across the central 90% of their area. The full width at half maximum (FWHM) of the histograms of the reduced scattering were 4% of the mean value for all samples and the FWHM of the absorption coefficient was less than 7% of the mean value.

4. CONCLUSIONS

We have described the fabrication and measurement of poly(dimethylsiloxane) PDMS tissue simulating optical phantoms having independently controllable absorption and scattering. The phantoms incorporate a near infrared dye to provide absorption that mimics water absorption at 970 nm. Whilst the dye absorption spectrum is not identical to that of water, these phantoms are expected to serve as useful test samples to characterize the ability of diffuse optics systems such as SFDI to determine tissue water fraction.

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