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Research Article

Reflection-mode multiple-illumination photoacoustic sensing to estimate optical properties

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ABSTRACT

Objectives: We analyze a reflection-mode multiple-illumination photoacoustic method which allows us to estimate optical scattering properties of turbid media based on fitting light-transport models and explore its limits in optical property estimation and depth-dependent fluence compensation.
Background: Recent simulation results show significant promise for a technique called multiple-illumination photoacoustic tomography (MI-PAT) to quantitatively reconstruct both absorption and scattering heterogeneities in turbid medium. Prior to experiments, it is essential to develop and analyze a measurement technique and probe capabilities of quantitative measurements that focus on sensing rather than imaging.
Methods: This technique involved translation of a 532 nm pulsed-laser light spot while focusing an ultrasound receiver on a sub-surface optical absorber immersed in a scattering medium at 3, 4 and 5 mm below the surface. Measured photoacoustic amplitudes for media with different reduced scattering coefficients are fitted with a light propagation model to estimate optical properties.
Results: When the absorber was located at 5 mm below the membrane in media with a reduced scattering coefficient of 4.4 and 5.5 cm^{-1}, the true values were predicted with an error of 5.7% and 12.7%, respectively. We observe accuracy and the ability of estimating optical scattering properties decreased with the increased reduced scattering coefficient. Nevertheless, the estimated parameters were sufficient for demonstrating depth-dependent fluence compensation for improved quantitation in photoacoustic imaging.

1. Introduction

Recently, our group proposed the concept of multiple-illumination photoacoustic tomography (MI-PAT), where optical illumination patterns on the surface serve as sources and signals from sub-surface optical absorbers act as virtual sub-surface detectors [1,2]. Recent simulations show significant promise for using data from combinations of optical source and photoacoustic virtual detector pairs to reconstruct both absorption and scattering heterogeneities [3]. However, no clear technique for experimentally obtaining and fitting such data was presented. In particular, reflection-mode imaging modalities are desirable due to ease of accessibility in thick tissues, and for implementing multiple illumination photoacoustic microscopy (MI-PAM) where penetration depths are within the radiative transport regime. Part of the experimental challenge is to design a probe capable of flexible illumination-pattern delivery (including point-illuminations) and co-linear reflection-mode ultrasound detection with maximal signal-to-noise ratio. As proposed MI-PAT/MI-PAM reconstruction strategies rely on forward light propagation models, the probe should have the capability to sense accurate fluence as predicted by models of light transport at varying depths and varying illumination locations. Accurate estimation of optical properties is required to calculate accurate fluence distribution.

Traditional optical property estimation techniques are limited to surface measurements [4–7]. The majority of current photoacoustic imaging applications rely on optical absorption contrast and much less work, however, has been done on to estimate optical scattering properties [8]. In photoacoustic imaging, we have an ability to effectively measure the relative local laser fluence at sub-surface locations. As such, photoacoustic methods may potentially provide information in addition to surface detectors. Some groups have tried to obtain optical properties of biological tissues using photoacoustic waveform analysis in simple well-controlled situations [9–11]. We recently developed an experimental

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photoacoustic method to effectively estimate the Green's function for light transport in a turbid medium [12]. We translated a pulsed light spot while receive focusing on a fixed sub-surface absorber to obtain a curve of photoacoustic signal amplitude as a function of incremental light translocation distance. We demonstrated that this curve, normalized by its peak value was distinct for different levels of optical turbidity.

We felt it essential to analyze the quantitative capabilities of above method in *homogeneous* turbid media and to this end, we test its capabilities for *sensing* (rather than imaging) of bulk tissue scattering coefficients and demonstrate highly accurate agreement between forward light-propagation models and experimental data. Recovering optical properties from sensing data and understanding the capabilities and limitations of the method will be critical to the success of future MI-PAT/MI-PAM quantitative imaging strategies, and we feel is worthwhile of a dedicated study. While similar to our previous work (which demonstrated scattering differences could be qualitatively observed from photoacoustic data), the present work aims to be much more quantitative and explores the capabilities and limitations of the technique for optical property estimation and depth-dependent fluence compensation. This study provides strong feasibility data for the utility of the proposed probe for future reflection-mode MI-PAT/MI-PAM imaging studies.

2. Method

2.1. Experiment

We used a custom built probe for our study [12]. This probe consists of a 10 mm × 40 mm right angle prism (P), optical index-matching fluid (IML), and an ultrasound transducer (UT) (Fig. 1). The index matching liquid (Cat# 19569, Cargille-Labs, Cedar Grove, NJ, USA) was kept underneath the prism by attaching a ∼25 μm-thick plastic (Saran wrap) membrane to an acrylic holder which was attached to a *XYZ* positioning stage. The index-matching fluid which has a reflective index similar to the fused silica prism (n = 1.46), enabled light to be delivered down to the sample and collected from the sample without significant loss, refraction, or inter-medium reflection. For the present study, we selected a single-element focused ultrasound transducer (10 MHz, f = 19.05 mm, F#3.1, spherical focus G series immersion type transducer, CD International Technology, Santa Clara, CA, USA) which was mounted horizontally to capture photoacoustic signals deflected from index matching fluid and prism interface. In future MI-PAT/MI-PAM imaging studies, we plan to substitute this single element transducer by a linear array transducer. We used a laser (SureLite III, Continuum Inc., Santa Clara, CA, USA) with a pulse repetition rate of 10 Hz. For simplicity, all measurements were done using 532-nm light. We place a thin glass slide in the beam path to reflect a small amount of light onto a high speed photo diode to capture laser pulse intensity variation. A small light spot was focused at the membrane interface by translating the probe vertically relative to lens L. A human hair was used as an optically absorbing target, and was mounted on an acrylic holder submerged in the medium with a 25 mm × 55 mm opening. Initially, the absorber was mounted on a *XZ* positioning stage and immersed in a water bath for alignment purposes. Our pulser-receiver (5703PR, Panametrics, Waltham, MA, USA) was set to pulse-echo mode and the ultrasound signal of the human hair was captured by a digital oscilloscope (DPO 7054, Tektronix, Beaverton, OR, USA). While observing the ultrasound signal, the hair sample was translated along the z-axis to position the hair at the required depth below the membrane. This depth was a parameter which was varied in our experiments.

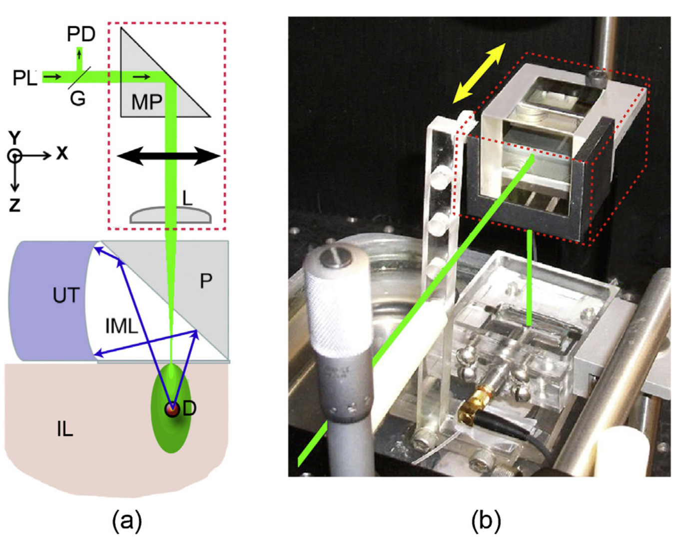

Fig. 1. (a) Schematic and (b) photograph measurement configuration of photoacoustic probe and light delivery. The mirror prism (ML) and the focusing lens (L) in the dashed box were translated along the *x*-axis to move the light spot. PL: pulsed laser input; G: glass slide; PD: photo diode; UT: ultrasound transducer; IML: index matching liquid; M: membrane; IL: intralipid; D: absorbing dye in a thin tube.

To mimic scattering of human tissue, we diluted 20% Intralipid in water to obtain reduced scattering coefficients of $\mu_s' = 4.4, 5.5$ and 11 cm^{-1}. Note that we performed independent measurements of the reduced scattering coefficient and absorption coefficient of our Intralipid stock-solution using the Oblique-Incidence Diffuse-Reflectance (OIR) technique [5]. We set the absorber at depths of 3, 4 and 5 mm below the membrane for each Intralipid concentration. The light spot was translated relative to the absorber by translating top prism (MP) and focusing lens (L) horizontally without moving other parts. The photoacoustic signal by the absorber was recorded by the digital oscilloscope. We plotted photoacoustic signal vs. light spot translation distance. This curve is effectively a measure of a segment of the Green's function of radiative light transport. To minimize the effect of source intensity variation, each photoacoustic signals is normalized by a corresponding photodiode signal. To demonstrate the ability to compensate for depth-dependent fluence for quantitative imaging, we created a phantom consisting of a silicone tube (ID = 0.8 mm; OD = 1.5 mm) filled with varying concentrations of Crystal Violet dye, immersed in a diluted Intralipid bath. For a selected Intralipid concentration, we fixed the absorber depth and obtain photoacoustic signal for different concentrations of dye. Note that the tube was flush with water before and after filling it with the dye. We used a fixed focus transducer for this study and its response varies with the absorber depth. We obtained the amplitude response of the transducer along the axial direction by measuring ultrasound signals of a human hair immersed in the water at different depths. The amplitudes of this depth-dependent ultrasound signal were applied to normalize the photoacoustic signals at different depths. The multiple-illumination photoacoustic sensing technique was used to obtain the optical properties for the Intralipid concentration. The results were applied in a forward Monte Carlo simulation to estimate the laser fluence at the absorber to normalize photoacoustic signals.

2.2. Optical property estimation

Our data was fit to light transport models. First, we considered Monte Carlo simulations because it accurately estimates fluence rate at any given location for a medium with any given optical properties. We used a steady state Monte Carlo simulation