Feasibility of quantitative determination of local optical absorbances in tissue-mimicking phantoms using acousto-optic sensing

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We have investigated the application of ultrasound modulation of coherent light for quantitative determination of local absorbances in tissue-mimicking phantoms. An Intralipid-based phantom model, which mimics a blood vessel in human tissue, was used. The detection technique was based on homodyne parallel speckle detection in transmission mode. Based on a comparison of experimental data and Monte Carlo simulations, a quantitative correlation between local absorbances of the phantom and the measured signal has been shown. The use of microsecond pulses of ultrasound and laser light resulted in a spatial resolution of the system of a few millimeters. © *2008 American Institute of Physics*. [DOI: 10.1063/1.2898884]

Often, the state of human health is reflected in the composition of chemical components present in the tissue. To quantify such parameters as total hemoglobin concentration and oxygen saturation, optical sensing methods are widely used. Unfortunately, these methods have inherent drawbacks. For example, coherent anti-Stokes Raman scattering spectroscopy has excellent resolution and potentially can characterize the change in blood oxygenation in individual capillaries. However, the probing depth is restricted to less than 0.5 mm; furthermore, this technique has been demonstrated only on a model system.[1] Diffusive optical tomography (DOT) can measure deep within the tissue, but the resolution decreases severely with increasing pathlength.[2] One way to overcome this difficulty is to combine optics with ultrasound (US), as is done in photoacoustic[3] (PA) and acousto-optic (AO) imaging.[4–8] When we apply AO imaging to human tissue, which heavily scatters light, we obtain an important advantage over DOT: contrary to light, we can focus the US beam in the tissue on a region of interest (e.g., a blood vessel), wherein scattered coherent light is modulated by US; the light that passes through this US focal region will be "labeled" by the US disturbance. We can consider this labeled light as a light source within the tissue; by changing the US focal position, we can freely manipulate the position of this internal light source. By measuring the US modulated light intensity, information is obtained about the intensity of the local light field, which is related to the local absorbance. The advantage of AO imaging over PA imaging is that in AO imaging, we can measure the light fluxes directly, whereas in PA imaging, the information about the absorbance is derived from the detected US.

Until now, AO imaging has been mainly investigated with respect to its *qualitative* imaging abilities;[9,10] in contrast, in this paper, we demonstrate its use for *quantitative* purposes by presenting experimental results for an absorber-containing model system mimicking a tissue with embedded blood vessel.

From our previous experiments with cw US,[11] we found that the AO effect was only slightly dependent on the presence of local absorbers buried in a scattering medium. In this paper, we investigate whether the use of microsecond US bursts combined with a gated optical excitation[12] will result in improved performance.

Consider the central part of Fig. 1, in which a container filled with light scattering medium is shown. In the center, a tube containing light absorbing material and oriented along the Y axis is placed. We now apply a 1 μs US burst along the Z axis. This burst that travels through the medium at a speed of $\sim$1.5 km/s has a length of $\sim$1.5 mm. By firing a microsecond laser pulse that is delayed relative to the start of the US burst, we probe the AO effect only in the volume occupied by the US burst at the instant of the laser pulse. By varying the delay time between the firings of the US burst and laser light pulse, we perform a scan of the medium under investigation. This approach was implemented in the setup depicted in Fig. 1.

High pressure ($\sim$7 MPa) US bursts of $\sim$1 μs length, which were produced by a 5 MHz transducer with a focal zone length of $\sim$8 mm and a focal zone width of $<$1 mm, were fired along the Z axis at 25 kHz repetition rate. Laser light pulses of $\sim$1 μs length were created by deflection of a cw He–Ne laser beam (633 nm, 35 mW) by an AO modula-

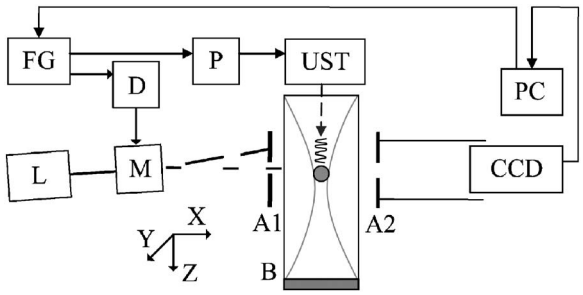

FIG. 1. Schematics of the acousto-optical setup in transmission geometry: FG, two-channel programmable function generator (Tektronix AFG3102); D, delay line; P, metal-oxide-semiconductor field-effect transistor pulser to drive transducer; UST, 5 MHz US transducer (Panametrics V309); L, He–Ne laser, 35 mW at 633 nm; M, acousto-optical modulator (Isomet 1201E-1); A1, aperture to block nondeflected light; A2, aperture for speckle selection system; B, IL-based phantom; and CCD, camera Basler A102f (12 bits, 1392×1040). In the center of the phantom the cross section of an absorber-containing tube is depicted. The US propagation is along the Z direction.

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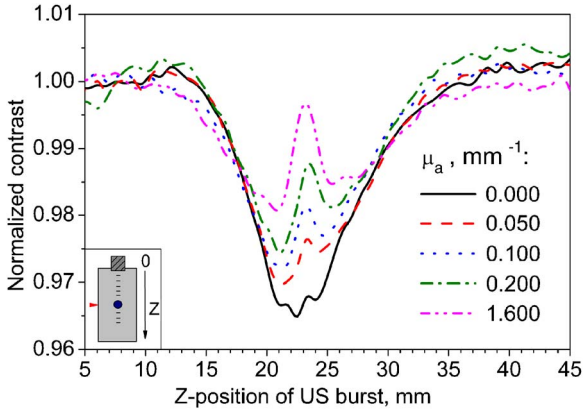

FIG. 2. (Color online) Dependence of contrast profile on Z position of US burst for some concentrations of absorber. Contrast profiles are normalized to their respective background contrast levels and are spline interpolated.

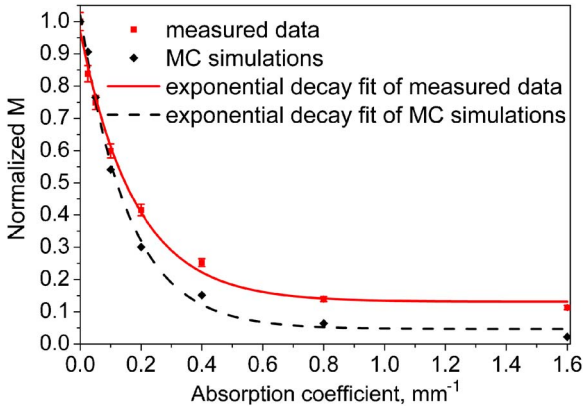

FIG. 3. (Color online) Dependence of modulation depth on the absorber concentration, normalized to its value at zero concentration, both for experimental data and simulation data. Each simulated data point is the result of 10^4 detected photons.

tor and delayed in the range of 3–30 μs relative to the start of the US burst. These pulses illuminated a tissue-mimicking phantom along the X axis. The light transmitted through the phantom produced a speckle pattern, which was detected by a charge coupled device (CCD) camera. The camera and a 0.6 mm diaphragm were positioned such that approximately one speckle illuminated one pixel.[13] Laser beam, diaphragm, and camera axis were positioned approximately in line. Several hundreds of light\US pulse cycles were accumulated to yield one image with a sufficient signal-to-noise ratio (SNR). For each probed position of the US burst, a camera exposure time of ~80 ms was required.

To analyze the images, we adopted an approach[10] in which the change in contrast of the CCD image is a measure of the AO effect. Because the US period is short compared to the CCD exposure time, the US-induced oscillating speckle pattern as detected by the camera is time averaged and results in a blurring of the speckle contrast C, which is defined as

$$C = \frac{\sigma}{\mu}, \tag{1}$$

where σ is the standard deviation of pixel values in an image and μ is the image mean pixel value.

The phantom used in the experiments was a Perspex container (XYZ dimensions of $\sim 15 \times 45 \times 40$ mm^3) filled with Intralipid (IL) solution in an agar matrix ($\mu_s' \approx 1.5$ mm^{-1}, similar to the reduced scattering coefficient of tissue). US-absorbing material was placed on the bottom of the container. A silicone rubber tube (inner diameter of 3 mm, similar to the size of a typical human artery) was mounted in the center of the container with its axis along the Y axis (cf. Fig. 1). This tube contained solid IL of a predefined absorbance, prepared by mixing IL with the appropriate amounts of ink.

For each concentration, we measured a contrast profile $C=C(z)$, where z is the position of the US packet. All contrast profiles were normalized to their respective background contrast levels C_b, which were determined by measuring the average contrast in the region $z \leqslant 12$ mm, where there is a very low probability of US modulated photons reaching the detector. In Fig. 2, the measured normalized contrast profiles are shown for various values of the absorption coefficient μ_a.

We observe a larger decrease in image contrast as the US burst approaches the optical axis at $z \approx 23$ mm. However, when the US burst enters the tube with absorber, the AO effect decreases appreciably, as is apparent from the increase in contrast. The minimum US disturbance is found at $z \approx 23$ mm, and the half width of the "positive" peak is ~3 mm, i.e., close to the position and the width of the tube, respectively.

We interpret these results as follows: when the US burst approaches the tube, an increasing number of photons undergo US modulation. Moreover, in view of the chosen detection geometry, photons in this area have a larger probability to be detected. However, when the US burst is propagating inside the tube with absorber, the photon flux undergoing AO modulation will be reduced and, as a result, the contrast blurring becomes smaller. In the figure, we observe a progressively smaller US effect in the tube as the absorber concentrations increase; it even goes down to almost zero when the photon flux is completely absorbed within the tube.

From the experimental contrast profiles, we extracted a measure of the fraction of the light absorbed within the tube. To this end, we determined the modulation depth M, at the position where the US packet is within the tube ($z \approx 23$ mm). M, defined here as the ratio of US modulated to unmodulated light intensity, can be determined according to Ref. 10,

$$M(z) = \frac{\Delta C(z)}{C(z)}, \tag{2}$$

where $\Delta C = C_b - C$ and C is the contrast value in the region of interest.

In Fig. 3, M, normalized to the value at $\mu_a = 0$, is depicted as a function of absorber μ_a. Because the positions and sizes of the absorbing zone and US focus remained constant throughout the experiments, changes in M are expected to correspond to the change of the photon flux through the US pressure zone in the absorbing structure. To evaluate this statement, we utilized a Monte Carlo (MC) software package[14] in a way similar to that in Ref. 15, which has been shown as a reasonably accurate approach.

This program has the option to "tag" photons that traverse a predefined volume V_l with specific μ_s' and μ_a inside the medium. In our case, these tagged photons mim-

icked the US modulated photon flux. We copied the values of the various experimental parameters to the input parameters of the MC model and determined the ratio of tagged to nontagged photons that reach the detector. When we select V_l such that it is situated in the center of the tube and with the dimensions of the US burst, we obtain the MC simulation result shown in Fig. 3.

The overall good correspondence between the experimental results and the MC simulation confirms that, indeed, the changes in measured AO modulation mainly stem from changes in photon flux that has passed through the tube. We attribute the presence of an experimental AO modulation at high absorbances to the presence of acoustical shear waves, which can also contribute to the speckle contrast,[12] and of residual pressure outside the −6 dB border of the US focal zone.

If we assume that the average photon light path through the US zone remains approximately constant for all measurements, we can apply a Lambert–Beer (LB) model to the data depicted in Fig. 3. As seen from this figure, this results in good-quality fits, both for simulation and experimental data. Apparently, a LB law also holds for a scattering medium, provided we define an effective optical pathlength. The exponent for both fits corresponds to an effective pathlength $l_{\mathrm{eff}} \approx 6$ mm, which is reasonable in view of the employed tube diameter, US focal zone size, and μ_s'.

This finding strongly points to the feasibility of solving the inverse problem, i.e., the determination of a local absorption coefficient in a scattering medium for a known tube diameter, which is a highly relevant application in a biomedical environment.

In conclusion, we have provided the proof of principle that acousto-optics can be used for quantitative absorbance measurements in light scattering media. The obtained spatial resolution is comparable to other resolving techniques[16] (x-ray and magnetic resonance imaging) and is sufficient for local interrogation of the blood oxygenation of arteries, which are situated at depths of $\leqslant 2$ cm below the tissue surface. However, it has to be added that in a living tissue, the contents of a blood vessel is highly mobile, whereas in our model system, it is much less mobile.

By extending our approach to multiple wavelength experiments, we expect that we can determine local absorbances without solving the transport equation for a scattering medium. Apart from a necessary decrease in required US energy to become compliant with FDA regulations, the main experimental problem that yet has to be solved is in obtaining data with sufficient SNR in *mobile* media, wherein the speckle decorrelation time is much shorter than that of the present medium.

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