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Ultrasound-enhanced optical coherence tomography: improved penetration and resolution

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Abstract

Increasing penetration remains one of the most important issues in optical coherence tomography (OCT) research, which we achieved with a parallel ultrasound beam. In addition to qualitative improvements of tissue imaging, quantitative improvements in resolution of up to $28\% \pm 2\%$ was noted. At lower frequencies and energies the improvement occurred primarily by altering the detection of multiply scattered light (photon–phonon interaction), which was substantially greater in solids than in liquids (even though the liquid had the higher scattering coefficient). In conclusion, the use of an ultrasound beam with OCT appears the most effective means to date for increasing imaging penetration.

1. INTRODUCTION

Optical coherence tomography (OCT), a rapidly emerging technology for high-resolution biomedical imaging, has demonstrated great potential for medical diagnostics in coronary artery disease, early osteoarthritis, microsurgery, and early cancer detection [1–7]. OCT is analogous to ultrasound, measuring the backreflection of infrared light rather than sound. Several advantages of OCT include its high resolution (4–20 μm), fast acquisition rate, full fiber-optic benefits (small catheter and endoscopes), and flexibility of combining with other spectroscopic techniques.

Increasing imaging penetration is a critical issue for many OCT applications, as it is currently limited to about 2 mm in scattering tissue. The imaging penetration of OCT, which is contrast maintained at depths within the tissue (and not light penetration or sensitivity *per se*), ideally requires recording single-scattering events at a high dynamic range [8–10]. The measurement of multiply scattered light by the detection system leads to inaccurate ranging and loss of contrast. Because light decays exponentially in tissue, increasing power on the tissue substantially increases multiple scattering, with only minor increases in light penetration [11–13]. Therefore, this is not a viable approach to increasing imaging penetration, although photon penetration is increased. In addition, recently popular techniques that use higher-than-average total powers across the spectrum, such as swept source OCT (SS-OCT) or the use of isolators, are expected to have more multiple scattering as a function of depth [14,15].

In previous preliminary work we demonstrated, using a moderately scattering tissue (fish), that an ultrasound beam at 7.5 MHz parallel to the OCT beam reduced multiple scattering at 1 mm by 20% as measured by the pointspread function (PSF) [16]. The presumed mechanism was a photon–phonon interaction, which frequency shifts multiply scattered light with a significant lateral momentum component (sound interacts with light that is not parallel) [16,17]. The frequencies of multiply scattered photons were then outside the bandpass and low-pass filters and were not detected, increasing the percentage of single-scattered events measured. However, critical questions need to be addressed, including the underlying physics, frequency dependency, power dependency, and effects in solids versus liquids, in addition to demonstrating actual improvement of structural identification in an image. Therefore, in this paper, we performed the following: First, we qualitatively demonstrated improved identification of tissue structure in an OCT image of tracheal cartilage, an example tissue with difficult-to-visualize deep structure. Second, quantitative measurements (PSF) were compared in solid tissue (chicken) and highly scattering liquid (Intralipid) of a reflector 1 mm below the surface. Measurements were performed at varying frequencies and intensities. In addition to demonstrating frequency and energy dependence and improved ability to characterize structure, the study suggests two distinct mechanisms for the improved performance. These are the reduction of detected multiply scattered light through photon–phonon interaction and a second mechanism, postulated here to be an increase in the carrier frequency of detected single-scattered events.

2. METHODS

A schematic of the OCT system is shown in Fig. 1 [1,2]. The technique is based on low coherence interferometry, measuring the autocorrelation function and using it to represent backreflection intensity. A wideband infrared light source is split by a fiber coupler, part to the sample arm and part to the reference arm. Light is reflected from within the tissue in the sample arm and off the mirror in the reference arm. It recombines together at the fiber coupler to make an interference signal if the optical group delays in both arms match to within the coherence length. The detected signal is separated from noise and DC signal by a bandpass filter, demodulation, and a low-pass filter. It will be seen that these filters are critical for using ultrasound to improve performance. A broadband superluminescent diode source with a 1300 nm center wavelength and 12mW intensity (AFC, Toronto, Canada) was used. A grating-based delay line was used in the reference arm [1,18,19]. The production of the optical group delay, phase delay, and Doppler shift (carrier frequency) in the reference arm has been described in detail elsewhere [1,18,19]. The OCT imaging optics was scanned across the sample by using a translation stage (Physik Instrumente, Karlsruhe/Palmbach, Germany) with 0.1 μm resolution. The exception was the trachea, which is cylindrical and was imaged with a Lightlab Imagingwire. After conversion from an optical to an electronic signal, transimpedance amplification, bandpass filtration (passive Butterworth filter, ~175 kHz), and demodulation, the signal is low-pass filtered (175 kHz) to remove the carrier frequency (~210 kHz). Therefore, the minimal ultrasound frequency with sufficient energy to shift multiply scattered photons with a momentum vector perpendicular to the OCT beam outside the filters is 120 kHz (assuming perfect coupling). At other angles or with imperfect coupling, higher frequencies would be necessary. The 5–9 MHz ultrasound frequencies are therefore well above this range (discussed below).

For quantitative measurements, the axial PSF was obtained by a PC-controlled digital oscilloscope (TDS 220, Tektronix Int., Beaverton, Oregon) with up to a 1 Gbyte/s sampling rate. The axial PSF is defined here as the full width at half-maximum (FWHM) of the autocorrelation function, as is standard for low coherence interferometry [1–3,20].

An ultrasound transducer (Olympus NDT, Waltham, Massachusetts) was placed approximately in parallel to the OCT beam and driven by a wave-function generator (Hewlett Packard Model HP33120A). Due to the size of the continuous-wave (CW) ultrasound transducer, an angle near 10° existed between the ultrasound and the OCT beam. The ultrasound beam was not brought into direct contact with the tissue surface so that the beam would be in the far field [21]. Instead, it was kept 2 cm from the tissue surface and coupled through a column (6 mm cross-sectional diameter) containing an ultrasound transducing medium (AccuGel; Lynn Medical, Bloomfield Hills, Michigan). The beam diameter was 0.15 cm with a 2.1 cm focal length. Four sets of ultrasound frequencies were compared: 0, 5 MHz, 7.5 MHz, and 9 MHz. In addition, energy on the sample was varied between 0 and 10 V.

For quantitative imaging, the target used was a metal reflector placed 1 mm below the surface of either chicken muscle (scattering coefficient of 2 cm^{-1} at 700 nm) or 20% Intralipid (scattering coefficient of 11.2 cm^{-1} at 700 nm). The scattering coefficients are presented at 700 nm rather than 1300 nm because only the latter was available in the literature for both. However, since scattering is unlikely to cause absorption changes in a continuous manner as the wavelength changes, the relative comparison is applicable, with absolute values unnecessary to illustrate the principles [22]. The general composition of 100 ml Intralipid (Fresenius Kabi, Uppsala, Sweden) is 20 g soybean oil, 1.2 g phospholipids (from powdered egg yolk), 2.25 g glycerin, and water [23].

Chicken was used when measuring the PSF because it is relatively homogeneous and allowed for reproducible results. For demonstrating improved imaging performance in tissue, rabbit tracheal cartilage was examined. The rabbit trachea was used because it is heterogeneous, with structural detail below the tissue surface that often cannot be detected by conventional OCT and that is well known (relatively constant from animal to animal). For imaging of rabbit trachea, tissue was obtained immediately after sacrifice and placed in normal saline. In total, three samples were examined. The trachea was bisected and imaged within hours of sacrifice. Two-dimensional imaging in the presence and absence of a 9 MHz, 10 V ultrasound was performed.

All values represent means $\pm$ the standard deviation. Data were compared for significant differences established with ANOVA. A p -value of less than 0.05 was considered a significant correlation. For data in Fig. 7, a 95% confidence interval test was performed of the highest frequencies relative to the best fit line.

3. RESULTS

The images Fig. 2 show a section of rabbit trachea, including cartilage, imaged in the presence and absence of ultrasound. Here C is the cartilage, and the shorter arrow is the back wall of the cartilage that is identified in the ultrasound images (bottom) but not when ultrasound was absent (top). The longer arrow identifies a reduction in multiple scattering in the cartilage by the ultrasound.

In Fig. 3, the exponential decays of the backreflected OCT signal in chicken with and without ultrasound are shown. Greater backreflection intensity is noted with ultrasound than without, which was highly statistically significant ($p < 0.005$).

Shown in Fig. 4(a) are representative PSFs with ultrasound exposure at 7.5 MHz and at energies varying from 0 to 10 Vpp (peak to peak). The x axis is distance over a range of 200 μm , rather than the entire 1 mm penetrated, to better examine the PSF. Several points are noted from these data of a reflector 1 mm within chicken. First, increasing ultrasound energy results in a higher resolution or smaller FWHM in the PSF. Second, the reduction in width

does not occur symmetrically, as photons to the left are predominately removed. Photons to the right are ballistic photons, while those to the left are late (longer time of flight), representing multiply scattered light [9,10]. This pattern is seen at lower energies, but as will be shown, slightly different patterns (more symmetric) occur at 10 Vpp for reasons speculated on later. Third, the peak intensity of the PSF decreases as the energy is increased, consistent with the concept that multiply scattered light is removed.

In Fig. 4(b) are shown representative PSFs with energies of 10 Vpp and frequencies of 0–9 MHz. Several points are noted from these data of a reflector 1 mm within chicken. First, there is an improvement in resolution with ultrasound, with a reduction of photons to the left (longer time of flight) consistent with a reduction in multiply scattered light. Second, improvements become less apparent above 5 MHz (it was noted above that the minimal frequency for reducing multiple scattering was 120 kHz, so this result is not surprising). Third, improvements above 5 MHz are associated with more symmetric improvements in the PSF. Fourth, the reasons for which will be discussed, the intensity increases from 7.5 to 9 MHz.

Figure 4(c) uses the same data as in Fig. 4(b) except the fast Fourier transforms (FFTs) are plotted. In addition, data are normalized to a constant intensity [see Figs. 4(b) and 5(a) for intensity variations] to make differences in FWHM more clear. The FWHM clearly improves with ultrasound bandwidth, with a larger Gaussian FWHM corresponding to a smaller PSF.

Figure 5(a) shows a plot of improvement in the PSF as a function of frequency in solid tissue (chicken). PSF increases significantly overall with frequency, although it is relatively flat between 5 and 7.5 MHz. However, a sharp jump occurs at 9 MHz (shaded area), the theory behind which is described below. Briefly, though, it is postulated to have occurred due to an effect on single-scattered photons.

A plot of improvement in the PSF as a function of frequency in liquid (Intralipid) is shown in Fig. 5(b). At the lower energies (<10 Vpp) and frequencies less than 9 MHz, the effect was minimal compared with the chicken. This is in spite of the fact the solid had a substantially lower scattering coefficient than the Intralipid. The exception is in the shaded area, again postulated to be an interaction between sound and single-scattered photons.

Figure 6(a) shows a plot of improvement in the PSF as a function of energy in solid tissue (chicken). PSF increases significantly and almost linearly with lower energy. The significance of the linearity is described below and is consistent with previous studies suggesting a photon–phonon interaction.

A plot of improvement in the PSF as a function of energy in a liquid (Intralipid) is shown in Fig. 6(b). Again, except at the highest energies and frequencies, the effect is very small compared with the solid. The mechanism for this jump in the shaded area is described below.

Figure 7 provides further support that two mechanisms are involved. It can be seen that, other than in the shaded zone, intensity decreases with both frequency and energy. However, in the shaded zone, the pattern is reversed both in terms of frequency and light intensity, which was highly statistically significant. We are 95% confident that the mean intensity at 9 MHz and 10 Vpp is between 0.112 and 0.118, and at 9 MHz and 8 Vpp is between 0.112 and 0.116. The comparison was made with best fit data extrapolated from points below 9 MHz. The deviation from the expected values at 9 MHz is consistent with a second mechanism inducing an improved PSF. The dotted line represents the extrapolated line if only one mechanism was operating.

4. DISCUSSION

A. Increasing Penetration

For many applications, such as guiding stent placement or assessing the retina, the penetration of OCT is generally sufficient for diagnostic purposes [24,25]. However, even with an optimized system with maximal noise reduction and perfectly indistinguishable paths (power equal in both arms), for other applications, improved analysis of deeper structures is needed, such as vulnerable plaque components or the gastric mucosa [1,3,26]. Therefore, a need exists for increasing imaging penetration. Imaging penetration with OCT is not the ability to detect increased photons from deep within tissue, but the ability to improve contrast among structures deeper in the tissue as explained in the Introduction [8]. This requires a sustained maximal resolution, a large dynamic range, single-scattered photons that are detected with characteristics similar to those in the reference (e.g., spectrum and polarization), and low multiple scattering to effectively discriminate inherent deep tissue contrast.

Increasing power seems like a logical method for increasing imaging penetration. Increasing power to the maximum safe amount (i.e., ANSI standards) on tissue has several advantages. First, it increases the signal-to-noise ratio (SNR) of the system. Second, and more important, the dynamic range increases up to the limit of the A–D converter [1,8]. However, since contrast is maximal by the detection of the maximum number of single-scattered (backreflected) photons, increased photon detection *per se* may not be beneficial, as it results in increased detection of multiply scattered light, which leads to false ranging information. Furthermore, power decays exponentially in tissue, so increases result only in minimal increases in single-scattered photons returning from deep within tissue but substantially increases the multiple scattering [1,11–13]. Therefore the ability to remove multiply scattered light, particular in the setting of high sample incident powers, would significantly improve performance. This is likely the primary mechanism for ultrasound-induced improvements in resolution within solid tissue.

B. Interaction of Light and Sound (Classical)

The interaction of light with sound can usually be modeled either from a classical or a quantum mechanical perspective due to the correspondence principle, although under certain circumstances the latter is required [27]. It should be noted that the physics of sound in air and in liquid are different from the physics of sound in solids, although both are density waves [27–30]. This is because propagation of sound waves in air or liquid represents randomly moving molecules rather than the regular lattice of a solid (tissue, although not an ideal lattice, can nonetheless be represented as a regularly repeating solid structure) [17,31–33]. Classically, in liquid and gas, the sound wave behaves like a diffraction grating made up of regions of high and low refractive index due to a density wave. In areas where the medium is compressed, the density is higher and the refractive index is higher. When sound and light are parallel, as in the current experiment, the grating effect will be minimum [34]. However, if the light is multiply scattered, it is likely no longer parallel and therefore influenced by the sound-induced grating. Broadly, the potential diffraction patterns are divided into Bragg and Raman–Nath, which are discussed extensively elsewhere and depend on, among other things, the wavelengths of sound and light [21]. With Bragg diffraction, the optical beam is generally split into two separate beams, altered from the incident beam by either the positive or the negative frequency shift [35]. With Raman–Nath diffraction, a large number of modes with different deflection angles and frequencies are typically generated [36]. In general, the regions between the two diffraction patterns can be described by the Klein–Cook parameter [31,32]. The Klein–Cook parameter is

$$Q=2\pi\lambda_L L/n_o\Lambda^2,$$

where n_o is the refractive index without acoustical stimulation, L is the width of the ultrasound beam, and Λ is the acoustical wavelength. When $Q < 1$, Raman–Nath diffraction typically occurs, and when $Q > 1$, Bragg diffraction occurs. Under the experimental conditions here, Q has a value of approximately 0.1. Two assumptions were made. First, the speed of sound as a function of frequency stays within a factor of 2 over the frequency range used (approximately 1500 m/s used) [33]. Second, the refractive index difference between Intralipid and chicken is within a factor of 2 (R.F. = 1.35 used), an obviously reasonable assumption. It should also be noted that at the ultrasound wavelengths used in this study, between 150 and 300 μm , only a few cycles occur within the tissue (1 mm).

Classical mechanics allows any vibration in an ideal periodic infinite solid to be decomposed into a superposition of normal modes of vibration [37]. We will model solid tissue here for the purpose of analysis as this ideal periodic structure, as has been done previously with OCT [17]. If the periodic structure is rigid, the atoms must be exerting forces on one another, which keeps each atom near the equilibrium position. Therefore classical mechanics does allow some properties of the tissue to be “quantized.” In solids, these sound vibrational modes of molecules occur about their equilibrium position, which alters the optical polarizability and therefore the refractive index. This is again distinct for liquids or gas.

The ultrasound displacement of scatters is another possible classical mechanism for the optoacoustical effect [37–39]. The displacements of scatters, assumed to follow ultrasonic amplitudes, modulate the physical path lengths of light traversing the ultrasonic field. This is not the case here, as shown by Leutz and Maret where this is valid only when the scattering mean free path is much greater than the acoustic wavelength, which is not the case in the current experiments [40].

C. Interaction of Light and Sound (Quantum Mechanical)

From a quantum mechanical standpoint, the light–sound interaction represents a photon–phonon interaction [30]. Sound–light interactions in solids with OCT using this photon–phonon interaction within a periodic structure have been studied previously and found to be effective models, even though tissue cannot be considered an ideal [17,30]. A phonon is a quantized mode of vibration occurring in the periodic structure, such as the atomic lattice of a solid. When these modes are analyzed using quantum mechanics, they are found to possess some “particle-like” properties [30]. When treated as particles, phonons are bosons possessing zero spin. The photon also has zero spin, so spin transfer does not need to be considered in their interaction.

Each phonon is a “collective mode” caused by the motion of every atom in the periodic structure [41]. This may be seen from the fact that the ladder operators contain sums over the position and momentum operators of every atom. The three-dimensional Hamiltonian for an ideal periodic structure is given by

$$\mathbf{H} = \sum_k \sum_{s=1}^3 \hbar \omega_{k,s} (a_{k,s}^\dagger a_{k,s} + 1/2).$$

The a and $a^\dagger$ terms are the creation and annihilation operators, respectively, while the $\frac{1}{2}$ signifies the zero point energy or vacuum fluctuations. The phonon frequency shift from light is given by

$$h\nu = E_{n'} - E_n = \hbar\omega_0 \left(n' + \frac{1}{2} \right) - \hbar\omega_0 \left(n + \frac{1}{2} \right) = \hbar\omega_0(n' - n) = \hbar\omega_0 s.$$

As is standard for the quantum harmonic oscillator model, consecutive energy levels are separated by equal energy spacing unlike, for example, a finite quantum well. Here n and n' represent the infinite number of Fourier modes in the lattice. Each eigenstate for a harmonic oscillator is given by a wave function consisting of a Hermite polynomial and an exponential decay term [27,42]. It is tempting to treat a phonon with wave vector $\mathbf{k}$ as though it has a momentum $\hbar\mathbf{k}$, analogous to photons and matter waves. This is not entirely correct, for $\hbar\mathbf{k}$ is not actually a physical momentum; it is called the crystal momentum or pseudomomentum [38]. This is because $\mathbf{k}$ is determined only up to multiples of constant vectors, known as reciprocal lattice vectors [43].

The optoacoustical effect can be viewed as an inelastic scattering phenomenon with the incoming photon absorbing an existing phonon or creating a phonon in the lattice during the process. The exiting photon has gained (or lost) energy and momentum from the lattice vibration (i.e., use of annihilation/creation operators). Since phonons are bosons, any number of identical excitations can be created/destroyed by repeated application of the creation/ annihilation operators. The coherent scattering cross section (inelastic) in terms of the pseudomomentum can be expressed in terms of [33]

$$S_{\text{coh}}(\mathbf{k}, \omega) = \int \frac{dt}{2\pi\hbar} e^{i\omega t} \frac{V}{N} \langle \rho_{\mathbf{k}}(t) \rho_{-\mathbf{k}}(0) \rangle,$$

where V is the volume and N is the number of particles. This is an approximation, as it assumes translational invariance occurs (i.e., infinitely large crystal or a finite crystal with periodic boundary conditions). The $\rho_{\mathbf{k}}(t)$ and $\rho_{-\mathbf{k}}(0)$ represent the density operators in k space, the Fourier transform of the density operator in terms of space and time. The term in brackets is the density–density correlation function, which contains information on the degree of interference. The width of the acoustical resonances are determined by the lifetime of the phonons. It may be possible to use this information to characterize the tissue in addition to the use of the ultrasound wave for reducing multiple scattering.

D. Interpretation of Results

In the present study, the use of combining ultrasound with OCT to better delineate deep tissue microstructure was demonstrated. Rabbit tracheal cartilage was examined, because without ultrasound, the back of the tracheal wall is typically not identified, preventing cartilage width from being assessed. It is also useful because the microstructure is well known, making it relatively reproducible from animal to animal. The back wall of the cartilage could be identified by the combined ultrasound beam, since multiple scattering would be reduced within the cartilage, as marked by the longer arrow in Fig. 2 (bottom). This was not performed in the initial pilot study, which consisted primarily in examining PSF at 7.5 MHz, both CW and pulsed [16]. Similar results were noted in the backreflection curves as a function of depth in chicken (Fig. 3), where an improved signal was noted when combined with ultrasound. From Fig. 7 it can be seen that the PSF does increase dramatically from one mechanism at 7.5 MHz and below (believed to be a reduction in multiple scattering) and a second mechanism above 7.5 MHz.

Several observations were made here in examining the PSF under different ultrasound frequencies and energies. First, the improvement in the PSF was increased with both frequency and energy, reaching $28\% \pm 2\%$ at 9 MHz, 10 Vpp. Second, the ultrasound resulted in a reduction in the photons with greater times of flight. This is shown in Figs. 4(a) and 4(b), which is consistent with multiply scattered light being removed. Third, while PSF increases linearly with power, the increase is more complex with frequency, consistent with the quantum harmonic oscillator model and photon–phonon interaction. For example, between 5 and 7.5 MHz (and possibly at lower frequencies), plots were relatively flat [Figs. 5(a) and 5(b)]. We postulate that it is also analogous with the photoelectric effect (excluding 9 MHz), where a minimal acoustical frequency needs to be achieved, then increasing energy results in a linear increase in the effect on the PSF [17,27,34]. Future experiments examining this phenomenon at more frequencies (both lower and higher) need to be performed to further understand this effect and confirm theory. Fourth, under most conditions, there is essentially almost no effect for liquids when compared with solids. This is consistent again with the hypothesis that photon–phonon scattering represents that primary interaction.

An additional, unexpected effect was also noted. At the highest frequency and energy, a sharp improvement in resolution and PSF intensity occurred. Our most likely explanation for this is due to the interaction of the sound with single-backscattered photons. This would essentially represent an improved detection of single-scattered light due to an increased carrier frequency. An increase in the carrier frequency could be induced in single-scattered events that increase the number of photons available to be measured by the detection electronics (through a bandpass filter). With traditional TD-OCT, in the reference arm, a Doppler shift (carrier frequency) is induced to increase the median frequency of the autocorrelation function to allow detection by the bandpass filter. This allows low-frequency classical noise sources (such as $1/f$ noise) and the DC signal to be removed. However, the maximum induced Doppler shift can be limited by factors, including mechanics of the reference arm such as mirror speed and size. As the ultrasound probe is not exactly in line with the OCT beam and is actually 10° off, this allows some influence on the single-scattered photons. If the ultrasound results in a Doppler shift in these single-scattered photons are sufficient to allow more photons to enter the bandpass filter but not too great to shift them completely out, both resolution and intensity will increase. However, another possibility is that the bandwidth of the single-scattered photon spectrum is increased, resulting in an improvement in resolution through this mechanism. Supporting evidence for this is that the improvement in the PSF was symmetrical, unlike at lower frequencies [Figs. 3(a) and 3(b)]. Future experiments are needed to better understand the physical principles behind the improved resolution through this second mechanism.

It is of note that the ultrasound frequencies used in this experiment were above 5 MHz, while the minimal frequency for generating the effect described above is approximately 120 kHz. One point that needs to be made is that photons that are multiply scattered to such a large degree that they are perpendicular to the incident OCT beam will likely have substantially distorted spectrum and polarization. Thus they have likely already excluded the y axis from the inherent screening properties of OCT. Multiply scattered photons with properties more similar to the single-scattered light but still with the ability to effectively range later would likely require a higher frequency than 120 kHz to be removed. Therefore, frequencies at 1 MHz and below should be examined for potential effects and to define where the major threshold exists.

E. Limitations

There are several potential limitations to the study. First, it is assumed that the ultrasound beam is in the far field. This is not an unreasonable assumption at these high frequencies, as the transducer is 2 cm from the tissue and ultrasound transmitted with acoustical gel. This

assumption could have been more controversial if frequencies below 1 MHz were used. Second, we did not deliver the maximum allowable OCT beam intensity on the sample (ANSI standards). It is conceivable that at higher intensities, such as used with swept sources OCT, multiple scattering would be higher and a shift in the shape of the response curves would take place. Third, tissue is treated as having structure that is highly organized and periodic on a microstructural level from the basis of photon–phonon interaction [17]. In the relatively homogeneous chicken, this is not an unreasonable assumption based on the work of other groups [9,17,40]. The linearity in Fig. 6(a) and the relative lack of effect in scattering liquid further supports the use of this model. Finally, the appearance of a second mechanism for improved resolution was unexpected. While an increase in the carrier frequency or broadening of the spectrum of single-scattered photons are suggested as potential mechanisms, future work is needed to further understand the physical principles.

5. CONCLUSION

This paper demonstrates that the combination of OCT and ultrasound can substantially improve imaging penetration. The improvement is frequency and energy dependent, and data support that it is due primarily to a reduction in multiple scattering. An addition benefit also appears to occur at higher ultrasound frequencies, postulated to be occurring through positive interaction with single-scattered photons. Future studies will examine the interaction of OCT with ultrasound in other medium, at a wider range of frequencies, at higher OCT intensities, and at different angles between the OCT and the ultrasound beam.

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Fig. 1. OCT System. Schematics of the real-time OCT system with a near-parallel ultrasound beam. The system consists of a bandpass and a low-pass filter, which are critical for improving penetration with ultrasound. Ultrasound frequency varies from 0 to 9 MHz, and the energy varies from 0 to 10 Vpp (peak to peak). A gel column (2 cm) is used with the ultrasound transducer to keep the beam in the far field. SLD, Superluminescent diode.

Fig. 2.

Two-dimensional OCT images showing sections of rabbit trachea, including cartilage imaged in the absence (top) and presence (bottom) of ultrasound. C is the cartilage, and the shorter arrow in the ultrasound image marks the back of the cartilage. The longer arrow in both images shows the area of multiple scattering, where it is greatly reduced in the bottom.

Fig. 3.
 (Color online) Decay curves in tissue. A-scans of chicken in the presence and absence of ultrasound are demonstrated. The x axis is distance, while the y axis is intensity. The use of 9 MHz ultrasound led to a statistically significant increase in backreflected OCT signal ($p < 0.005$).

Fig. 4.

Representative OCT PSF at varying energies and frequencies. (a) Example PSF at varying energies. Shown are representative PSFs with ultrasound exposure at 7.5 MHz and at energies varying from 0 to 10 Vpp. Several points are noted from the image of a reflector 1 mm within chicken. First, increasing ultrasound energy results in a higher resolution or smaller FWHM in the PSF. Second, the reduction in width does not occur symmetrically, as photons to the left are predominately removed. Photons to the right are ballistic photons, while those to the left are late, representing multiply scattered light. This pattern is seen at lower energies, but as will be shown, slightly different patterns (more symmetric) are seen at higher frequencies for reasons discussed later. Third, the peak intensity of the PSF decreases as the energy is increased, consistent with a reduction in multiply scattering photons. (b) Example PSF at varying frequencies. Shown are representative PSFs with energies of 10 Vpp and frequencies of 0–9 MHz. Several points are noted from the image of a reflector 1 mm within chicken. First, there is an improvement in resolution with increasing frequency. Second, improvements become less apparent above 5 MHz. Third, improvements above 5 MHz are associated with less shift to the right than from 0 to 5 MHz [or in (a)]. Fourth, a point that is discussed in the text, the intensity increases from 7.5 to 9 MHz. (c) The same data used in (b) are used here, except the fast Fourier transforms (FFTs) are plotted. In addition, data are normalized to a constant intensity [see Figs. 4(b) and 5(a) for intensity variations] to make differences in FWHM more clear. The FWHM clearly improves with ultrasound bandwidth, with a larger Gaussian FWHM corresponding to a smaller PSF.

Fig. 5.

(a) Plot of ultrasound frequency versus modification in the PSF for chicken. This figure shows a plot of improvement in the PSF as a function of frequency in solid tissue (chicken). PSF increases significantly with frequency. However, a sharp jump occurs at 9 MHz (shaded area) that it will be argued is due to an effect of the ultrasound beam on single-scattered rather than multiply scattered light. This is the same reason as for the intensity increase in the previous figures from 7.5 to 9 MHz. (b) Plot of ultrasound frequency versus modification in the PSF for Intralipid. The effect in Intralipid is minimal except at the highest frequencies and energies (shadow area as in Fig. 4). This is in spite of a high scattering coefficient for the Intralipid.

Fig. 6.

(a) Plot of energy versus modification in the PSF for chicken. This figure shows a plot of improvement in the PSF as a function of energy in solid tissue (chicken). PSF increases significantly and almost linearly with energy. The rate almost doubles between 6 and 10 V, consistent with this linear dependence. (b) Plot of energy versus modification in the PSF for Intralipid. This figure shows a plot of improvement in the PSF as a function of energy in a liquid (Intralipid). It can be seen that up to 8 MHz, the increases are linear but substantially less than those in solid. A sharp increase occurs in the shaded area for the reason described in the text.

Fig. 7.

(Color online) Plot of frequency versus peak intensity for chicken. In this figure it can be seen that, other than in the shaded zone, intensity decreases with both frequency and energy. However, in the shaded zone, the pattern is reversed both in terms of frequency and power. This again illustrates that at least two distinct mechanisms are occurring. We are 95% confident that the mean intensity at 9 MHz and 10 Vpp is between 0.112 and 0.118, and at 9 MHz and 8 Vpp is between 0.112 and 0.116. The deviation from the expected values at 9 MHz is consistent with the second mechanism inducing an improved PSF. The dotted line represents the best fit comparison used for analysis.