

ILLUMINATING SOUND: IMAGING TISSUE OPTICAL PROPERTIES WITH ULTRASOUND

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Introduction

In recent years, the diagnostic imaging community has shown considerable interest in developing techniques for measuring the optical properties of tissue with high spatial resolution.¹ The optical properties governing light propagation through tissue include absorption and scattering. Absorption in the visible and near-infrared wavelength range is related to tissue molecular structure, with the total absorption distributed between several tissue constituents including hemoglobin, water and lipids. Absorption measurements over a broad spectral band can be used to determine tissue composition, and ultimately tissue functional information such as oxygen saturation in blood or increased blood flow. These parameters are associated the metabolic state of tissue and may be used for the detection and diagnosis of tissue abnormalities or to track disease progression. Optical scattering, on the other hand, arises from inhomogeneity in the structure of tissue and associated variations in the index of refraction. Scattering depends on the cellular structure of tissue and may be sensitive to the physiological changes in the cellular architecture associated with tumor formation, for example. It is the strong optical scattering exhibited by biological tissue that makes deep-tissue imaging challenging, particularly when good spatial resolution is desired.

Light propagation through tissue is inherently diffusive; photons follow a random walk in a manner analogous to heat flow. A collimated optical beam incident on a tissue sample is rapidly transformed into a diffuse, isotropic intensity distribution. The rate of decay of the optical fluence is governed by a combination of the absorption, scattering, and scattering anisotropy (angular dependence of the scattering) of a given tissue type. In an unbounded media, light decays exponentially with distance, with the rate of decay given by an effective attenuation coefficient μ_{eff} . The mean optical penetration depth δ , which is defined as the distance over which the optical fluence decays to $1/e$ of the initial value, is given by the reciprocal of the effective attenuation coefficient. The penetration depth of light is a strong function of optical wavelength. At shorter wavelengths, <600 nanometers (nm), the penetration of light is limited by a combination of high scattering and large absorption in blood, while at longer wavelengths (>1300 nm) the scattering coefficient is small but light is strongly absorbed by water. This leaves the near-

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infrared (NIR) wavelength range (600 nm-1300 nm), often referred to as the tissue optical window, available for deep tissue diagnostics. A representative plot of effective attenuation coefficient² in breast tissue as a function of optical wavelength is given in Fig. 1. Note the minimum (approximately 1.5 cm^{-1}) in the 750-800 nm wavelength range, yielding a mean penetration depth of 0.66 cm. The optical fluence rate as a function of depth is shown in the inset of Fig. 1. Although the field decays quite rapidly (e.g., two orders of magnitude at a depth of 3 cm), diffuse

light has been successfully exploited for deep tissue characterization and imaging.

A variety of optical imaging techniques have been developed for high resolution imaging in biological media. Excellent near-surface spatial resolution can be achieved using confocal optical microscopy and optical coherence tomography, but in both cases the image is formed using ballistic (un-scattered) or quasi-ballistic light and thus is limited to depths³ of 1-2 mm. A pure optical imaging technique called diffuse optical tomography (DOT) has emerged as a powerful imaging modality that has been shown to be suitable for deep tissue imaging.⁴ In the frequency domain implementation of this technique, intensity modulated laser light illuminates the media and an array of optical detectors meas-

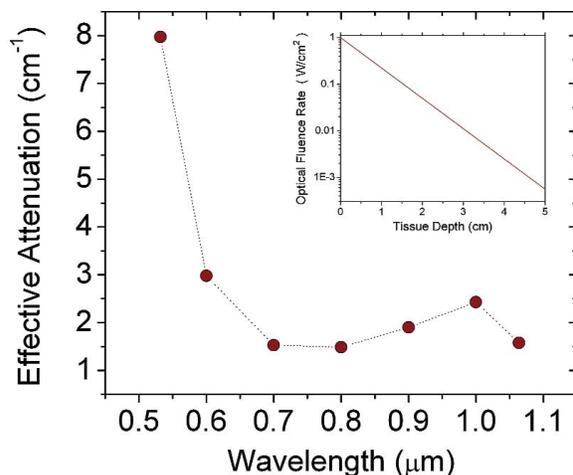


Fig. 1. Effective attenuation coefficient of human breast tissue as a function of optical wavelength. The inset shows the decay of the optical field as a function of depth in the 700-800 nm wavelength range.

ures the magnitude and phase of the diffuse optical field emitted. The modulated laser light propagates through diffuse media with a coherent wave front (referred to as photon density waves) and the dispersion of such waves is highly dependent on the absorption and scattering properties of the media. The media can be illuminated by modulated sources at multiple wavelengths, and a tomographic reconstruction algorithm used to spatially resolve tissue optical properties, from which tissue constituents can be inferred. The main drawback of diffuse optical tomography is its reliance on diffuse light, which propagates along tortuous paths, to create an image of subsurface features. This inherently limits the resolution that can be achieved using the technique to ~ 1 cm.

Acousto-optic (AO) sensing is a new hybrid technique that combines ultrasound with diffuse light to achieve deep-tissue imaging of optical properties with the spatial resolution of ultrasound. In this technique, the sample is illuminated by a continuous wave (CW) laser source to produce a diffuse optical field. To provide spatially resolved optical information, the sample is simultaneously ensounded by an ultrasound beam. In the acousto-optic sensing volume, defined as the region where the light and sound overlap, the ultrasound modulates the local optical field. The modulated or “tagged” light propagates to the sample boundaries where it is processed and detected. The acousto-optic signal, or intensity of the tagged light, gives an indication of the strength of the acousto-optic interaction. Although the acousto-optic signal in itself is not a direct measure of the optical properties of the sample, it does scale with the optical fluence through the sensing volume and is thus indicative of the local optical properties of the tissue—in particular the local absorption coefficient. By pulsing the ultrasound and scanning the beam across a plane in a manner similar to conventional B-mode ultrasound imaging, a 2-D acousto-optic image can be constructed. One of the key advantages of acousto-optic imaging over diffuse optical tomography, for example, is that the acousto-optic signal is localized by the ultrasound. It originates only from the acousto-optic sensing volume which has a spatial extent given by the ultrasound-pulse used. The net result is a subsurface image of the acousto-optic interaction strength *at depth* and *with a spatial resolution dictated by the ultrasound field*.

Background

The mechanism for the interaction of ultrasound with ballistic light has been well understood for quite some time.⁵ Propagation of an acoustic wave through a homogeneous media will produce a periodic variation in the index of refraction, due to periodic variations in pressure along the acoustic wave path via the piezo-optic effect. Ballistic light incident on this media will scatter or diffract on the index grating. In the case of a moving grating, the diffracted beam will also be frequency-shifted. This phenomenon is used in a wide range of acousto-optic devices including optical frequency and amplitude modulators, switches, and signal processors. The interaction of ultrasound with *diffuse* light, on the other hand, has received considerably less attention.⁶ The treatment of diffuse wave interaction with ultrasound typically involves decomposing the optical field into partial

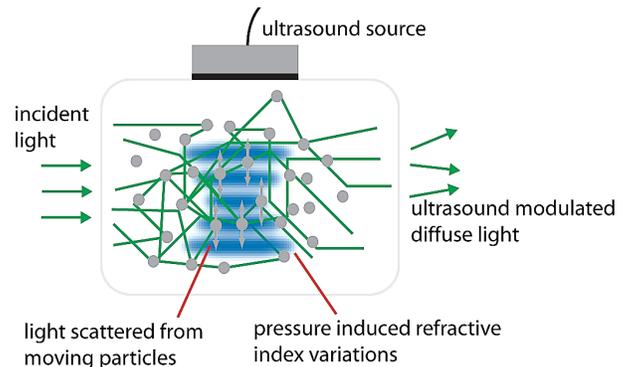


Fig. 2. The primary mechanisms for the ultrasound modulation of light in optically scattering media.

waves, each of which follows a different meandering path through the media (see Fig. 2). Along each path, the light experiences a sequence of scattering events, with the average distance between these events given by the transport mean free path. In the absence of ultrasound, the scattering sites remain stationary less any Brownian motion or physiological motion. In the presence of ultrasound, the scattering sites move with the periodic displacement of the media. The coherent motion of all scatterers along a given partial wave path produces an accumulated phase shift of the light propagating along that path. A second important modulation mechanism results from the periodic variation in the refractive index associated with the ultrasound wave propagation. Again, a change in optical path length is accumulated over each partial wave path leading to a net phase shift. The total phase shift is then given by a combination of both modulation mechanisms, and the net optical field observed external to the sample is given by the sum of partial waves propagating over all paths. In both modulation effects, the optical field is modulated at the ultrasound frequency, and their relative contributions depend on the ratio between the transport mean free path and the acoustic wavelength. If the mean free path is large compared to the wavelength, variations in the index of refraction dominate the response.

In an acousto-optic imaging experiment, the sample is illuminated by a laser source and the scattered light is detected and processed to deduce information regarding the properties of the sample in the region where the optical and ultrasonic fields interact. As discussed above, the optical field at any point in space external to the object is composed of many partial waves, each originating from a different point in the object. The interference of these waves will cause the resulting intensity to be anywhere from fully bright to fully dark, depending on the relative de-phasing between paths. This effect leads to the formation of a speckle pattern. When an ultrasonic beam is introduced, the phase of the light passing through the ultrasound is shifted with respect to the light passing through other regions of the sample. Interference between modulated and un-modulated light leads to the formation of a time varying speckle pattern. However, modulated light emanating from a highly diffuse media has a *spatially random* phase shift. Although the intensity of each individual speckle is modulated at the ultrasound frequency, the phase of this time varying signal is random from speckle to

speckle. A key challenge in acousto-optic imaging is to understand how to detect the phase shift imparted on the modulated light given that the light levels, after passing through an optically diffuse media, are extremely low and come with a strong background of un-modulated light. If the aperture of an optical detector is restricted to detecting a single speckle, then one is left with the detection of a relatively small intensity modulation on an exceedingly weak signal. If the aperture is increased to receive light from multiple speckle, the overall intensity of modulated light is increased, but the modulation depth is reduced owing to the random phase of the intensity fluctuations from speckle to speckle.

The idea of using ultrasound to localize or “tag” diffuse light was first documented twenty years ago in a patent filed by Dolfi and Micheron.⁷ The early 1990’s brought the first experimental results demonstrating that the ultrasound interaction with light in optically scattering media produces a small, but measurable, intensity modulation in the scattered field.⁸ During the mid 1990’s, researchers began using the acousto-optic effect in order to image objects buried in turbid media.^{9,10} Throughout this period, the majority of experiments were performed using a focused, continuous wave ultrasound beam to pump the acousto-optic interaction. The signal was detected using a single element optical detector that was fixed in space and apertured to sample a single speckle (or a small number of speckles) in the optical field. Images of absorbing objects were created by physically scanning the acoustic beam and measuring the intensity modulation of the optical field at each position. Continuous wave ultrasound allows for narrow-band detection techniques, and thus offers substantial improvements in signal-to-noise ratio over systems using pulsed ultrasound. However, since the interaction between light and sound occurs throughout the volume of the ultrasound field, this approach offers limited resolution along the ultrasound axis. To achieve axial resolution from continuous wave exposures, a technique was introduced in which a single optical detector is used and the continuous wave ultrasound source is rapidly chirped over a time frame comparable to the ultrasound propagation time through the region of interest.¹¹ In this way, a specific frequency is assigned to each location along the ultrasonic axis. A 1-D axial scan could then be produced from the time-dependent frequency-domain information of the ultrasound-modulated signals. While acousto-optic imaging systems using single optical detectors have been explored for a number of applications,¹² the extremely low light levels associated with these systems are not conducive to deep tissue sensing and imaging.

A breakthrough in the detection of ultrasound modulated signals came in 1999 with the development of a parallel speckle modulation processing system.¹³ A schematic of the experimental setup is given in Fig. 3. In this approach, the single optical detector is replaced by a charge-coupled device (CCD) array, with the CCD camera positioned such that one speckle grain falls on each pixel. The main technical hurdle associated with this approach is that the speckle intensity modulation is in the MHz range, well beyond the frame rate of a CCD camera. To overcome this, the authors employ a

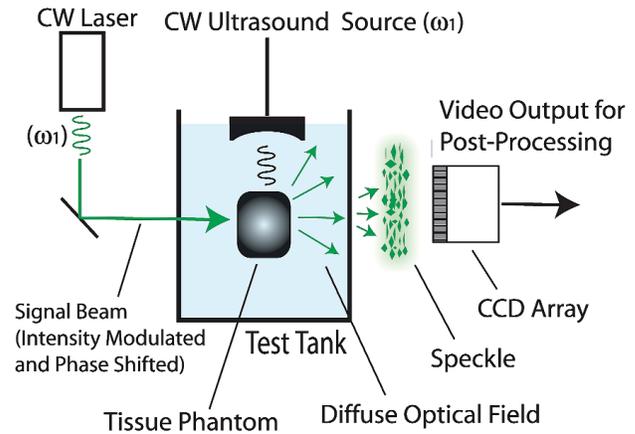


Fig. 3. Acousto-optic imaging system using the charge-coupled device-based parallel speckle modulation processing approach.

parallel lock-in detection scheme using synchronous excitation, rather than the more conventional synchronous detection approach. The ultrasonic field and laser illumination source are both modulated at the same frequency (2.2MHz), with a fixed relative phase delay. The CCD camera acts as a low-pass filter and records the mean intensity of the field over the measurement time. Four images are recorded, each with the modulation of the laser source delayed by an additional one-quarter period with respect to the ultrasonic source. A linear combination of these images allows one to extract the amplitude and phase of the intensity modulation at each pixel. The amplitudes of the intensity modulations at each pixel are then summed to give the acousto-optic response. This allows for the coherent summation of signals over all detectors in the array and yields a signal to noise ratio improvement on the order of $N^{1/2}$ over single detector schemes, where N is the number of pixels on the CCD. This CCD based approach has seen widespread use in acousto-optic imaging. Over the past several years a number of modifications have been proposed allowing, for example, improved sensitivity through heterodyne detection and operation with pulsed ultrasound for resolution along the ultrasound axis.^{14,15}

More recently, a photorefractive crystal (PRC) based interferometry technique has emerged that has sufficient sensitivity to detect acousto-optic signals generated by short-pulse ultrasound at clinically relevant acoustic exposure levels.¹⁶ Figure 4 illustrates the basic experimental setup used in the photorefractive crystal approach, where the sound source is the beam from a clinical diagnostic imager. The laser source is divided into a signal beam that illuminates the sample, and a reference beam that is sent directly to the photorefractive crystal. Scattered light from the sample is collected and mixed with the reference beam in the photorefractive crystal. The local index of refraction in the photorefractive crystal changes in response to the complex optical interference pattern set up in the crystal, and the reference beam diffracts off of this grating in a process called two-wave mixing. The crystal thus acts as a real time hologram, and the diffracted reference beam is an exact replica of the signal beam, less any high frequency (i.e., ultrasonic) modulation that exceeds the crystal response time. This diffracted reference beam is *in-phase* with the transmitted

signal beam, and the two beams interfere constructively at the detector. In the presence of ultrasound, the phase of the signal beam is shifted with respect to the reference, leading to a *decrease* in the intensity at the detector. This allows for coherent summation of signals detected over a large number of speckles, regardless of the fact that the phase shift imparted on the diffuse optical field by the ultrasound is spatially random. The resulting acousto-optic signal is not at the ultrasound frequency, but rather is manifested as a DC offset signal that tracks the instantaneous flux of modulated light incident on the detector.

A related photorefractive crystal based detection approach has also been presented in which the reference beam to the photorefractive crystal is frequency shifted by an amount equal to the ultrasound frequency and continuous wave ultrasound is employed.¹⁷ Only the ultrasound modulated (frequency shifted) light from the sample forms a static interference grating in the crystal. The strength of this grating thus gives a measure of the amplitude of the acousto-optic interaction. In general, photorefractive crystal-based acousto-optic systems offer a higher étendue, or light collection ability, than previously developed techniques thus making them an attractive option for deep tissue imaging applications. The photorefractive crystal-based detector also accommodates physiological motion as it can respond quickly enough to rewrite the index of refraction grating and automatically adapt to motion-induced changes in the speckle pattern.

The fact that the photorefractive crystal-based system accommodates pulsed acousto-optic sensing at clinically relevant exposure levels is significant for three reasons. First and foremost, the spatial resolution of the measurement is determined by the spatial extent of the acoustic field. By utilizing high-frequency pulsed ultrasound, the lateral and axial resolutions are determined primarily by the width of the beam and the spatial pulse length. Secondly, thermal bioeffects scale with the average intensity of ultrasound exposure,

which is dramatically reduced by utilizing short-pulse, rather than continuous wave ultrasound. Finally, it suggests the marriage of acousto-optic and clinical diagnostic ultrasound imaging, where the clinical ultrasound machine is used to both generate conventional B-mode images *and* pump the acousto-optic signal. Since the same sound field is employed to affect both ultrasound scattering and acousto-optic sensing, the images are automatically co-registered, and multi-mode optical/acoustical imaging is realized. This approach, which has been successfully demonstrated using tissue mimicking phantoms and excised tissue samples,¹⁸ is described in greater detail below.

Imaging by acousto-optic sensing

The experimental setup, shown in Fig. 4, combines the photorefractive crystal-based optical detection system with a commercially available, PC-based, diagnostic ultrasound scanner (AN2300, Analogic Corp.) employing a 5 MHz, 192 element linear phased array scanhead and a 64 channel beamformer. Light from a frequency-doubled Nd:YAG laser is sent to a variable beam splitter where it is split into signal and reference beams. The reference beam is directed around the test tank and sent to the photorefractive crystal-based interferometer. The signal beam is sent through a beam expander along the Y-axis to the sample. Light scattered from the sample is collected by a lens and directed into the photorefractive crystal, where it interferes with the reference beam. The photorefractive crystal-interferometer employs a bismuth silicon oxide (BSO) crystal ($\text{Bi}_{12}\text{SiO}_{20}$), and a high voltage AC electric field is applied to the crystal to enhance the two-wave mixing process. The signal beam and diffracted reference beam exiting the crystal are collected by an avalanche photodiode (APD), processed using a preamplifier and low-pass filter, and digitized in the oscilloscope.

Figure 5 shows acousto-optic signals observed in a highly scattering tissue phantom using a 3-cycle ultrasound pulse at a center frequency of 5 MHz. As the ultrasound propagates through the phantom, the magnitude of the acousto-optic signal (with respect to the steady-state background) gives a measure of the strength of the acousto-optic interaction and is affected by, among other things, the amount of light in the interaction region, the ultrasound pressure, and the sensing volume. In the case when the ultrasound passes through a homogeneous region of tissue phantom (Traces A and C), the signal tracks the envelope of the background light distribution, with the spatial resolution controlled by the ultrasound beam width and pulse length. If there is an optical absorber embedded in the phantom, the magnitude of the acousto-optic signal decreases when the ultrasound pulse passes the absorber (Trace B). This is because, once the acoustic pulse enters the optical absorber, there is relatively little light available to modulate. In a sense, the acousto-optic interaction region acts like a virtual light sensor that probes the local optical properties of the medium. By using commercial ultrasound imaging technology, this “sensor” can be made to travel along electronically beam-formed trajectories at the speed of sound.

Recall that a primary advantage of photorefractive crystal-based detection of acousto-optic signals is that the sensi-

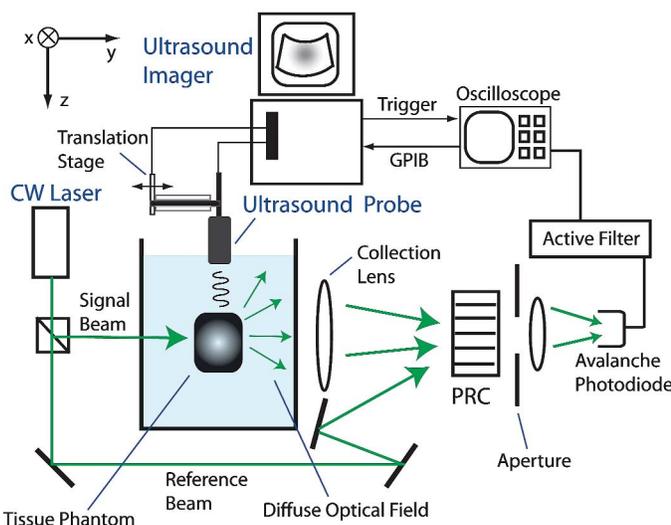


Fig. 4. Experimental setup for acousto-optic imaging using a photorefractive crystal based interferometry system and a commercial ultrasound scanner to pump the acousto-optic response. Electronically scanned images are generated in the X-Z plane. By mechanically scanning along the Y axis, three-dimensional acousto-optic imaging is realized.

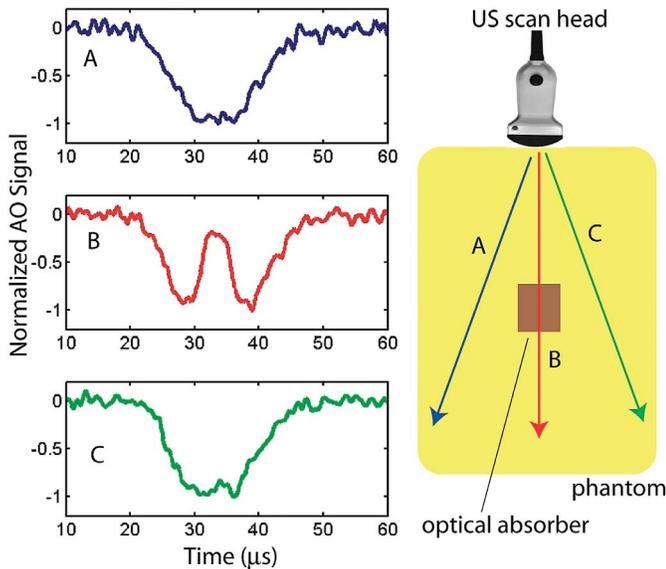


Fig. 5. Acousto-optic signals measured along several scan lines in a tissue phantom with an embedded optical absorber.

tivity afforded by this technique allows one to utilize a conventional ultrasound imaging system to simultaneously generate acousto-optic *and* B-mode ultrasound images. Ultrasound and acousto-optic images of the X-Z plane (see Fig. 4) of the sample are produced as follows. To ultrasonically scan the X-Z plane, the AN2300 beam-former is programmed to fire a set of ultrasonic sector scan lines aligned adjacent to each other. Along the direction of ultrasonic propagation, time is converted to space using the sample sound speed. To display grayscale images (B-mode image), the ultrasound scanner demodulates the received ultrasound echo train associated with a given scan line and converts the signal envelope function to grayscale. Because the envelope of an acousto-optic signal in the time-domain gives a measure of the photon distribution along the ultrasound path, acousto-optic images were built in the exact same manner, and superimposed on top of the B-mode images using a color-scale. As a consequence, B-mode and acousto-optic images are intrinsically co-registered and yield complementary mechanical and optical contrast information. Figure 6 (left) shows a B-mode ultrasound image of a gel-based tissue phantom with optical and acoustic properties similar to breast tissue. Two targets are placed in the phantom with acoustic properties matching that of the surrounding media, and one of the targets was infused with an optically absorbing dye. The target boundaries are seen on the ultrasound image due to a slight impedance mismatch introduced by fabrication process. (The bright spot in the rightmost target is likely due to a microbubble.) The acousto-optic image of the same phantom is given in Fig. 6 (right). In the absence of an absorbing target, this image would be a uniformly illuminated red circle indicative of the background light distribution. The addition of an optically absorbing target (on the right) results in a blue spot that is clearly resolved in the acousto-optic image.

Absorbing objects have also been detected in moderately thick (2 cm) excised biological tissue. In this experiment, a slab of chicken breast was squeezed between two optically

transparent plastic plates. The plates are positioned parallel to each other to keep the thickness of the sample uniform and the signal beam is incident on the center of the sample, perpendicular to the plates. This configuration is roughly similar to that employed for breast examination by X-ray mammography. A small optical absorber, composed of gel infused with India ink, was embedded at the center of the slab. Figure 7 (left) shows a B-mode ultrasound image acquired in the X-Z plane at the center of the target. The acoustically homogeneous, optically absorbing target appears as a dark, uniform region in the middle of the sample; note the lack of detectable reflection from the target interface. The image speckle surrounding the target is caused by acoustic scattering from tissue microstructure, which is noticeably absent in the target. The acousto-optic image of the same target is given in Fig. 7 (right), using a 3-cycle acoustical pulse at 5 MHz. The data has been processed to remove the envelope of the acousto-optic signal observed in the absence of an absorber.

In highly scattering media, the optical field is truly diffuse and the acousto-optic images are *not* the result of the absorber casting a shadow and preventing light from propagating along a given path. In fact, acousto-optic imaging can be used to localize an absorber in three dimensions. Figure 8 shows acousto-optic images taken on the same specimen at several points along the optical (Y) axis, with $Y=0$ roughly corresponding to the center of the inclusion. It is clear from these images that the optical field is sufficiently diffuse that minimal effects of optical shadowing around the target are observed. It is also evident that 3-D acousto-optic volume imaging is possible by mechanically scanning the ultrasound transducer in one dimension.

Resolution, sensitivity, and the role of the sound field

The greater the interaction volume between the light and the sound, the greater the fluence of modulated photons and the better the signal to noise ratio. This fact argues for a continuous wave approach to acousto-optic sensing, where photons are modulated along the entire length of the acoustic beam. What you sacrifice, however, is spatial resolution along the ultrasound axis. Pulsed ultrasound provides axial resolution, albeit at the expense of sensitivity. Pulses also allow you to work at somewhat greater peak acoustic pressure levels, as the risk of thermal bioeffects are minimized. One is still lim-

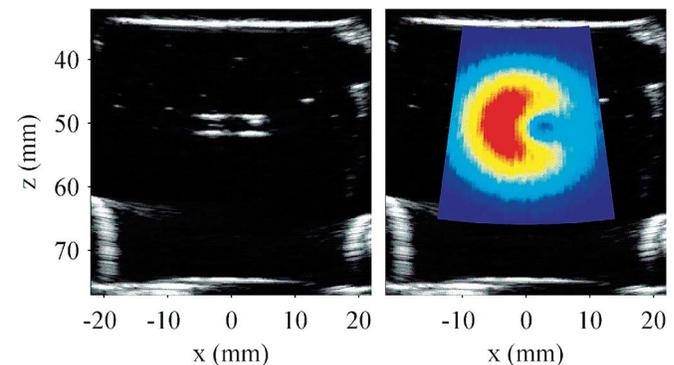


Fig. 6. B-mode ultrasound (left) and acousto-optic images of a tissue phantom with two embedded inclusions. The inclusion on the right has been infused with an optically absorbing dye.

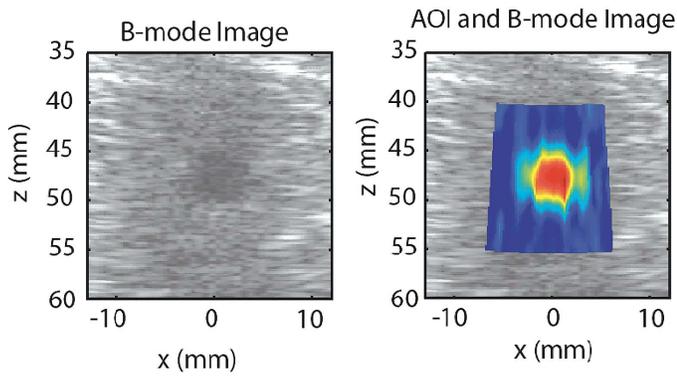


Fig. 7. B-mode ultrasound (left) and acousto-optic images of a gel based optical absorber embedded in a chicken breast sample.

ited by a need to avoid mechanical bioeffects, however, and as such clinical implementation will still be bound by the same Food and Drug Administration (FDA) exposure limits that are currently applied to imaging ultrasound.¹⁹ Regardless, greater pressures will yield a greater average acousto-optic phase shift and enhanced sensitivity.

Another advantage of acousto-optic imaging using photorefractive crystal-based sensors is that they are inherently very broadband. One could utilize high acoustic frequencies (order 10-50 MHz) to achieve enhanced spatial resolution. However, increased absorption will limit high frequency scans to shallow depths and increased resolution comes at the cost of both a reduced interaction volume and a reduced acousto-optic phase shift due to smaller particle displacements, which scale as $1/f$. On the other hand, FDA limits on maximum peak negative pressure amplitudes scale with $f^{1/2}$; therefore the actual decrease in maximum particle displacement should scale as $1/f^{1/2}$. The relationship between acoustic pressure amplitude, peak particle displacement and the average phase shift encountered in the acousto-optic interaction zone will vary with tissue mechanical and optical properties, as there are multiple interaction mechanisms at play. It suffices to say that, when it comes to both acousto-optic and ultrasound imaging, one is motivated to use as high a pressure amplitude as possible while maintaining an adequate margin of safety *re* both thermal and mechanical bioeffects.

The implementation of the acousto-optic sensing paradigm described above is a simple one; a combination of light and sound is used to augment B-mode imaging. It need not stop there. For example, one could use B-mode to image a tumor and then launch a single A-line in the target region to assess, or even monitor, changing optical properties in response to therapy. One could use the acousto-optic interaction between light and high intensity focused ultrasound (HIFU) to assess real time changes in tissue optical properties during the formation of thermal lesions. Indeed, the very same sound field that generates the lesion also pumps the acousto-optic interaction. Multiple optical wavelengths can be used to image blood oxygenation levels and otherwise do functional tissue imaging. By employing absorbing particles targeted to tissue types, one can realize targeted contrast imaging. Of course, in all of this, one is limited to shallow penetration depths and/or relatively transparent tissues, such as breast and brain.

Discussion and conclusions

It is important to point out that the contrast observed in acousto-optic images is not a direct measure of the distribution of optical absorption within the sample, but rather it depends on both the photon distribution in the light/sound interaction region, and the probability that the modulated photons will be acquired by the detection system. These parameters, in turn, depend on the characteristics of the source and detection system and the spatial distribution of optical properties. Three-dimensional acousto-optic images can potentially be used to determine the quantitative optical absorption or scattering distribution through the use of an inversion algorithm similar to those currently employed for diffuse optical tomography. This may be particularly important in the development of multi-wavelength acousto-optic systems for functional imaging.

To date, the majority of acousto-optic imaging experiments have been done using tissue phantoms or *ex-vivo* tissue samples. While the optical and acoustic properties of these samples can be representative of those observed *in-vivo*, a key difference is that *in-vivo* measurements are made in a dynamic environment. Physiological motion alters the optical field passing through tissue, resulting in the formation of a time varying speckle pattern. The characteristic timescale over which the speckle can be considered stationary, or so called speckle decorrelation time, is on the order of milliseconds. The CCD based parallel processing approach requires the acquisition of several images to determine the amplitude of the modulated signal at each pixel. All of these

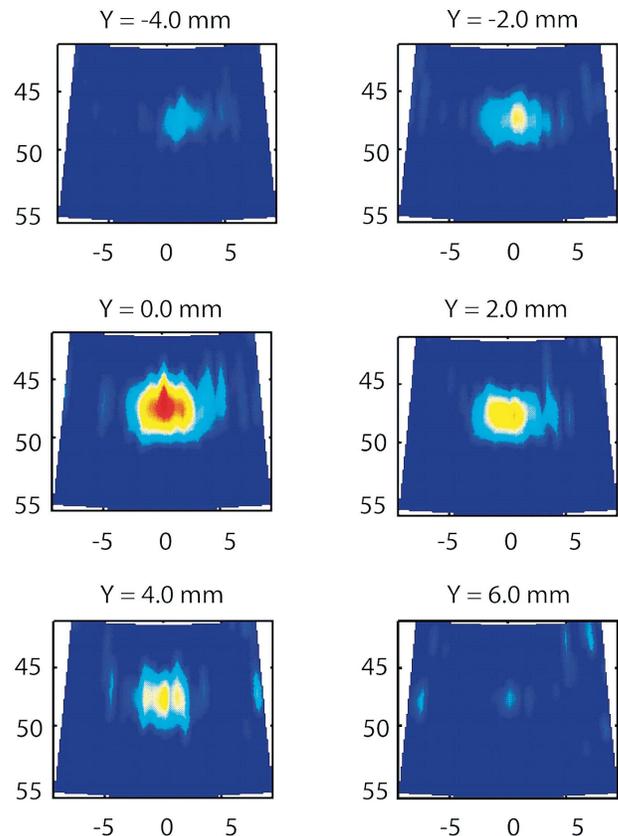


Fig. 8. X-Z scans of the chicken breast sample at several positions along the optical (Y) axis. The absorber is located at approximately $Y=0$.

images must be acquired within the speckle decorrelation time in order to achieve high sensitivity detection. In the case of photorefractive crystal-based detection, the crystal response must be fast enough to follow the speckle decorrelation, i.e., the crystal must be capable of rewriting the index grating on the order of 1.0 ms, such that the diffracted reference beam is held in a fixed phase relationship with the transmitted signal beam. Fortunately, semiconductor photorefractives, operating in the near-infrared wavelength band, possess response times in the desired range.

In summary, acousto-optic imaging is a promising new modality that could fuel improvements in the detection and characterization of any tissue abnormalities that exhibit concomitant changes in optical properties. One target application is in the diagnosis of breast cancer, where a dual mode ultrasound/ acousto-optic imaging system may provide improvements in the ability to differentiate benign from malignant lesions. Technical challenges in the transition from a laboratory to a clinical setting are primarily associated with the sensitivity limitations imposed by the low photon flux and overcoming the effects of physiological motion on the diffuse optical field. Recent advances in the detection of acousto-optic signals, however, offer hope that dual-mode ultrasound/ acousto-optic imaging *in vivo* may be just over the horizon.

Acknowledgments

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