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Detection of HIFU lesions in Excised Tissue Using Acousto-Optic Imaging

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Abstract. Real-time imaging of the heating of tissue and lesion formation is a major barrier to the clinical application of HIFU. Tissue necrosis results in a change in the optical properties of the tissue. We have employed the acousto-optical (A-O) interaction to image HIFU lesions formed in excised chicken breast. The tissue was illuminated with infrared light (1064 nm wavelength) resulting in a diffuse optical field throughout the tissue. Simultaneously, the tissue was insonified with a diagnostic ultrasound imager running in B-mode. The photons that passed through the region of tissue where the pulsed 5 MHz ultrasound beam was present were phase modulated by the sound field. These modulated photons were detected by means of an interferometric detector employing a photorefractive crystal (PRC). To first order the amplitude of the output from the PRC is related to the optical absorption of the tissue where the sound was present. By firing multiple acoustic beams along different pathways, the spatially dependent optical absorption coefficient (uncalibrated) within a tissue region of interest is determined and presented in the form of a 2-D image. Images thus generated were recorded in chicken breast before and after HIFU exposure (1.1 MHz, 6 s duration, 6 MPa peak pressure). The acoustic and optical beams were scanned across the tissue, and the waveforms combined to form a 2-D AO image. The imaged lesion size of $9 \times 2 \text{ mm}^2$ agreed well with the measured lesions size $10 \times 3 \text{ mm}^2$.

Keywords: HIFU, lesion detection, Acousto-Optic Imaging

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INTRODUCTION

HIFU-induced tissue lesions show significant optical contrast with untreated tissue. The lesioned tissue has higher optical absorption and scattering [1]. Direct optical imaging of lesions generated at depth is impossible, however, due to the high level of scattering in the intervening tissue. Acousto-optic imaging provides a way to resolve optical contrast within structures with a spatial resolution equal to that of B-mode ultrasound [2]. Acoustic waves induce perturbations in density (and hence in optical index of refraction) as well as periodic translations of optical scattering sites. Photons, whose diffuse random-walk passes through the ultrasound focal zone, will have their paths altered from what they would have been had the acoustic disturbance not been there, resulting in a periodic modulation in phase at the acoustic frequency. If these “tagged” photons can be monitored, then any changes in the tissue optical properties at the focal zone can be sensed and ultimately imaged.

The light emitted from a highly scattering media contains multiple speckle caused by interference of light propagating through different paths in the sample. The phase modulation induced by the interaction of ultrasound and light produces an intensity

modulation of the individual speckle, but this intensity modulation has a random phase across the speckle field. Early schemes for detecting tagged photons involved monitoring the intensity modulation in a single speckle [3]. The sensitivity of detection was later significantly improved by detecting multiple speckles using a CCD camera and summing the intensity modulation measured at each pixel [4]. More recently, the detection of the phase modulated signal using photorefractive crystal based interferometers has been demonstrated [5,6]. This approach allows for the use of a single photodetector and is thus not limited in light collection by the number of pixels on a CCD camera. In this work we apply the PRC-based detection scheme to the problem of detecting HIFU-induced lesions in tissue.

METHODS

Figure 1 depicts the experimental setup. The light source is a 700 mW Nd-YAG laser operating at 1064 nm (IRCL-700-1064-S, CrystaLaser, CA). The light passes through the sample and is collected by a lens and focused onto a GaAs photorefractive crystal (PRC) (MolTech GmbH). A beam-splitter is used to create a reference beam that does not pass through the sample and also illuminates the PRC creating an interference pattern in the PRC. Through the photorefractive effect, the local optical index of refraction changes as a function of the local optical intensity. The 3-D diffraction grating set up in the crystal diffracts the reference beam into a direction parallel to the signal beam, and with the same complex wavefront. These two beams coincide at the photodetector, and constructively interfere. When a perturbation (e.g, due to an ultrasound beam) changes the path of photons which pass through it, the wavefront of the signal beam will change. The signal and reference beams will no longer constructively interfere at the photodetector, and there will be a drop in the output.

Here the pulsed ultrasound field was created using a diagnostic ultrasound array transducer (Model 8802, BK Medical, Wilmington, MA). The scan-head was driven by an Analogic Ultrasound Engine (AN 2300, Analogic, Peabody, MA). The ultrasound system created 5 MHz pulsed ultrasound which had a nominal spatial extent of 1.5mm in the acoustic propagation axis (z-axis in Fig. 1) and 0.8mm in the lateral direction. As an ultrasonic pulse traverses the tissue that is illuminated, the flux of modulated photons increases resulting in an increasing negative voltage from the photodetector. The profile of the A-O signal essentially tracks the local intensity of the illuminated region (typically Gaussian). If the pulse traverses a sub-region of higher optical absorption, such as a HIFU lesion, there will be less local photons available to “tag”. This will diminish the AOI signal, and result in a blip in the overall decrease in photodetector output, giving it a characteristic “W” shape [5]. The ultrasound array is electronically steerable and by firing a sequence of acoustic pulses in different directions it is possible to create a 2D image of the AOI data. However for this study, restrictions in the set-up meant that the multiple lines were achieved by mechanical translating the sample.

In the experiments reported here the tissue sample consisted of store-bought chicken breast, cut into a 4 cm x 4 cm x 2 cm sample and then degassed for 40 min. in phosphate buffered saline (PBS). It was then transferred and mounted in the

experimental tank, all under PBS. Before HIFU treatment the sample was imaged with AOI. To obtain sufficient signal-to-noise ratio it was necessary to average the AO signals for 10^4 acoustic pulses, however we believe that this figure can be significantly reduced by using long-pulsed lasers [7] and a more optimal wavelength. The sample was also imaged with the ultrasound scanner in standard B-mode.

Figure 1. Experimental setup. The sample is placed in a tank of water to allow acoustic coupling of the HIFU transducer and ultrasound probe. The light passes through optically transparent walls into and out of the tank.

Single HIFU lesions were made in the center of the tissue sample, along the x-axis in Fig. 1. The lesions were made with a 1.1 MHz transducer (Model H-102, Sonic Concepts, 73 mm diam., 64 mm focal length.). The source was driven continuously for 6 s and pressure measurements in water yielded $p_+ = 6$ MPa, $p_- = 4.32$ MPa and $I_{SPTA} = 880$ W/cm². The depth of the HIFU focus into the tissue was 16 mm. After HIFU treatment the sample was re-imaged with AO and B-mode ultrasound.

RESULTS

Figure 2 shows time waveforms from the photodetector for a scan line through the center of a lesion. The width of the pre-lesion AOI dip, shown in Fig. 2(a), is $5 \mu\text{s}$ which, based on the speed of sound in the tissue, corresponds to a physical distance of 7.7 mm. This is the optically illuminated region and comprises the effective field of view of our current AO setup. Fig. 2(b) is the post-lesion waveform, showing a central region where the AOI effect is less. The width of the central blip is proportional to the width of the lesion region of increased optical absorptivity. By subtracting the two waveforms the resulting trace, Fig. 2(c), is essentially a 1-D line plot of the optical property contrast through the lesion. A 2-D image can be constructed by stacking the individual lines scanned across the sample (just as is done to create a B-mode ultrasound image). The result is an optical image of the interior of a diffuse medium, with a resolution determined by spatial extent of the acoustic pulse (typically of order 1 mm).

Figure 2. Photodetector waveforms for acoustic pulses directed through the center of HIFU lesion in chicken. (a) pre-lesion, (b) post-lesion, (c) difference.

Figure 3 shows the resulting image for one lesion. The white dotted line shows the location of the HIFU focal region, as determined by -6 dB pressure contours. The AO image indicates that the lesion “grew” toward the HIFU source—a phenomenon commonly reported in the literature. Shown at right is a B-mode image taken of the same sample, within five minutes post sonication. The dashed line indicates the region of the AOI image at left, and a similar oval marks the focal region. No evidence of the lesion can be seen, consistent with the known difficulty in detecting HIFU lesions with standard ultrasonic imaging. Any gas bubbles that may have been created during the HIFU insonation have dissolved by the time the B-mode image was taken.

Figure 3. Left: AOI image of HIFU lesion in chicken breast. The HIFU focal zone is shown by the white dashed oval. The tissue was scanned in increments of 1/3 mm in the horizontal dimension. Right: A standard B-mode ultrasound image of the same tissue where the dashed rectangle represents the area of the AOI image shown at left. The lesion was not visible in the B-mode image.

The experiment was repeated on three separate chicken breasts. After AO imaging a "post-mortem" measurement was made by partially freezing the chicken samples, cutting them into 2 mm slices with a razor blade, and observing where the lesion occurred. For the three lesions the AOI measurements yielded lengths of 9, 14 and

8 mm and the "post-mortem" measurements 10, 17 and 9 mm. The location of the start of the lesion was within 1 mm for the two methods. The agreement between the AO and the measured properties of the lesion, both the position and length, are within the uncertainty of the measurements.

CONCLUSION

We have shown that HIFU lesions in ex-vivo chicken breast can be detected using AO imaging. The imaging technique exploited the changes in the optical properties of the lesions and the resolution was governed by the ultrasonic B-mode imaging (~ 1 mm). These lesions were invisible in standard B-mode images, due to the absence of the persistent gas bubbles typically produced by cavitation or boiling. For these experiments a 57-line scan took 40 minutes, the speed being limited by signal to noise ratio. Recently Rousseau et al. [7] greatly increased the speed of AO imaging by using a high power pulsed laser source, which increased the optical intensity without exceeding the maximum permissible exposure. They were able to use AO imaging to depths of 6 cm.

We note that in addition to post-treatment imaging described here, continuous monitoring of lesion growth during HIFU is possible. In this case the acoustic field of the HIFU transducer would be used to excite the AO signal. Because HIFU uses long tone bursts rather than pulses the temporal resolution (vertical axis in Fig. 3) is forfeited. As the tissue starts to form a lesion, the increase in both the acoustic and the optical absorption will cause a decrease in the magnitude of the AOI signal, providing real time feedback on the formation of lesions in tissue.

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