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Ultrasonic encoding of diffused light: from optical imaging to light focusing in turbid media

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ABSTRACT

In optical scattering media such as biological tissue, light propagation is randomized by multiple scattering. Beyond one transport mean free path, where photon propagation is in the diffusive regime, direct light focusing becomes infeasible. The resulting loss of light localization poses serious challenge to optical imaging in thick scattering media. Ultrasound modulated optical tomography (UOT) combines high optical contrast and good ultrasonic resolution, and is therefore an ideal imaging modality for soft biological tissue. A variety of detection techniques have been developed in UOT in an effort to discriminate the ultrasonically encoded diffused light as the imaging signal. We developed a photorefractive crystal based detection system, which has the ability to image both the optical and acoustic properties of biological tissues. With the improved photorefractive crystal based detection, tissue-mimicking phantom samples as thick as 9.4 cm can be imaged. We further exploit the virtual source concept in UOT and combine it with optical time reversal to achieve diffusive light focusing into scattering media. Experimental implementation of this new technology is presented.
Keywords: Optical Imaging, Tissue Optics, Photorefractive Detection, Ultrasound-modulated Optical Tomography, Diffusive Light Focusing.

1. ULTRASONIC ENCODING OF DIFFUSED LIGHT FOR OPTICAL IMAGING

1.1 Ultrasound-modulated optical tomography

Optical imaging of soft biological tissue is a non-invasive, nonionizing, and functional imaging modality, which makes it highly desirable in the biomedical field[1]. The photon energy used in optical imaging is typically ~2 eV for $\lambda = 500$ nm, which is safe for biological molecules as compared with the photons used in X-ray imaging which is ~50 KeV. Because its contrast is based on optical properties (i.e., absorption and scattering) of the tissue, optical imaging can provide better soft-tissue contrast than the ultrasound imaging which is based on mechanical contrast. The optical absorption and scattering properties in the visible and near infrared wavelengths are intrinsic indicators of tissue abnormalities and functions since they are determined by the molecular constituents of tissues and the electronic and/or vibrational structures at the molecular level[2-4]. For example, cancerous tissues manifest significant architectural changes at the cellular and sub-cellular levels, which result in changes to the optical scattering properties[5]. Angiogenesis and hyper-metabolism, which are characteristic of cancers, result in changes to the optical absorption properties[6]. Therefore, optical imaging holds great promise for early cancer detection. Other important physiological parameters can also be measured by optical imaging such as the oxygen saturation of hemoglobin, which makes optical functional imaging possible[7].

However, pure optical imaging lacks good spatial resolution in deep tissue because of strong optical scattering in the visible and NIR wavelengths. For imaging modalities that detect ballistic or quasi-ballistic photons as imaging signal, such as time-gated imaging[8-10] and optical coherence tomography[11,12], the detected photons experience minimal scattering inside tissues and carry spatial information, but the signal strength decays exponentially with increasing tissue thickness. These imaging modalities are therefore not suitable for deep tissue imaging. For diffuse optical imaging modalities that collect diffused photons transmitted through thick tissues as imaging signal, the diffused light decays more slowly with thick tissues, but the spatial information is lost in diffuse photons because multiple scattering randomize light propagation after several scattering mean free paths. At $\lambda = 500$ nm the mean scattering free path $l_S = 0.1$ mm in human breast, while $l_S = 50$ mm for photons at X-ray wavelength used in medical diagnosis. In diffuse optical imaging, convoluted image reconstruction is needed to recover the spatial distribution of the relevant optical properties. Since this is usually an ill-posed inverse problem, the image resolution and the image quality is not good enough.

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Ultrasound-modulated optical tomography (UOT) is a hybrid imaging technique for biological tissue[13]. In UOT, a focused ultrasonic wave is used to modulate the diffused coherent light inside the biological tissues. The ultrasonically modulated or encoded photons are frequency shifted by the ultrasonic frequency and can be discriminated from the un-modulated background light. The ultrasonic focus carries the spatial information and determines the spatial resolution for the ultrasonically modulated photons. Thus UOT provides the combined optical contrast and ultrasonic resolution.

UOT holds promise for broad applications in biomedical imaging and diagnosis, such as early detection of breast cancer and skin cancer. However, there remain challenges in UOT's theoretical understanding and practical applications. For example, in real practice, the sample thickness in breast cancer diagnosis will be 5-10 cm. For UOT imaging in such thick tissue, signal detection becomes a critical bottleneck. New development is required to improve the sensitivity of the signal detection techniques. In addition, the detection configuration should be modified to meet the requirement of convenience for practical applications.

The signal-to-noise ratio (SNR) of UOT is limited by several factors. First, due to the small ultrasonic focal region relative to the light diffusion volume, the part of the diffused photons that get modulated by a focused ultrasound beam is overwhelmed by the un-modulated, background diffuse photons. Second, as a coherent light beam gets multiply scattered through a turbid medium, the wave front of the diffused light becomes speckled and this limits the detection efficiency[14]. Furthermore, due to their independent statistical nature, the two speckled wave fronts—the ultrasonically modulated and un-modulated—do not coincide with each other. Third, the speckled wave front of the diffused light through a biological tissue is not stationary due to various internal motions, such as Brownian motion and internal transportation of the micro structures. This usually imposes a speckle decorrelation time τ_C of less than several hundred milliseconds to the UOT signal, which further deteriorates the signal-to-noise ratio.

1.2 Photorefractive detection in UOT

In recent years, photorefractive crystal (PRC) based detection has been applied to UOT, which effectively improves the etendue of the imaging system because of PRC's real time holography feature in a two wave mixing (TWM) or four wave mixing (FWM) scheme. Several variations of the PRC based UOT system have been implemented and the relevant theories developed by various groups[15-18].

The photorefractive crystal $Bi_{12}SiO_{20}$ (BSO) is a cubic oxide crystal of the sillenite family. It belongs to the cubic noncentrosymmetric crystal point group 23, i.e., the crystal structure is symmetric for 180° rotations about the crystal axis and 120° rotations about the diagonals of the cube. It is piezo-electric, electro-optic, elasto-optic, and optically active[19].

In comparison to other commonly used PRC's, such as $BaTiO_3$ and GaAs, BSO has much smaller electro-optic coefficient, similar mobility, and smaller dielectric constant. However, it has larger photoconductivity, which leads to better sensitivity. Table 1 lists the relevant physical parameters of BSO at three wavelengths.

Table 1. Physical parameters of BSO[20]:

Parameter	λ = 488 nm	λ = 514.5 nm	λ = 632.8 nm
Refractive Index n	2.650	2.815	2.530
Absorption α (cm^{-1})	7.0	2.8	0.6
Optical rotatory power ρ (°/mm)	45.5	38.6	21.4
Photon ionization energy E ($\times 10^{-12}$ erg)	4.07	3.88	3.14
Dark resistivity R (Ω-cm)	5×10^{13}		

We have developed a BSO-based UOT system with a quasi-CW ultrasound modulation scheme, where a one-millisecond long focused ultrasound burst was applied to the sample and the time dependent change of the detected optical signal was recorded to image both the optical and acoustic properties of the sample[21]. The benefits of using a millisecond long ultrasound burst are twofold: it improves the SNR; it also enables the detection of the acoustic radiation force effects, which happens in millisecond time scale and can be related to the acoustic properties of the sample. This was demonstrated by imaging two segments of nude mouse tail (dimensions=3×10 mm (dia.×Z) and 8mm separation) embedded in a tissue-mimicking gelatin ($\mu_s' = 10cm^{-1}$, and dimensions=10×4×10 cm (X×Y×Z)). The UOT images (Fig. 1) acquired at T=0.1ms and T=1.1 ms after the onset of a one-millisecond long ultrasound burst show markedly different contrast. Owing to the higher optical absorption of the mouse tails, they appear dark in the T=0.1 ms image, although the

contrast is low. On the other hand, due to the large acoustic impedance mismatch between the bone structures of the nude mouse tail and the background gelatin phantom, the radiation force effect induces much stronger ultrasonic modulation of light at T=1.1 ms from the mouse tails, resulting in two corresponding bright spots on the second UOT image.

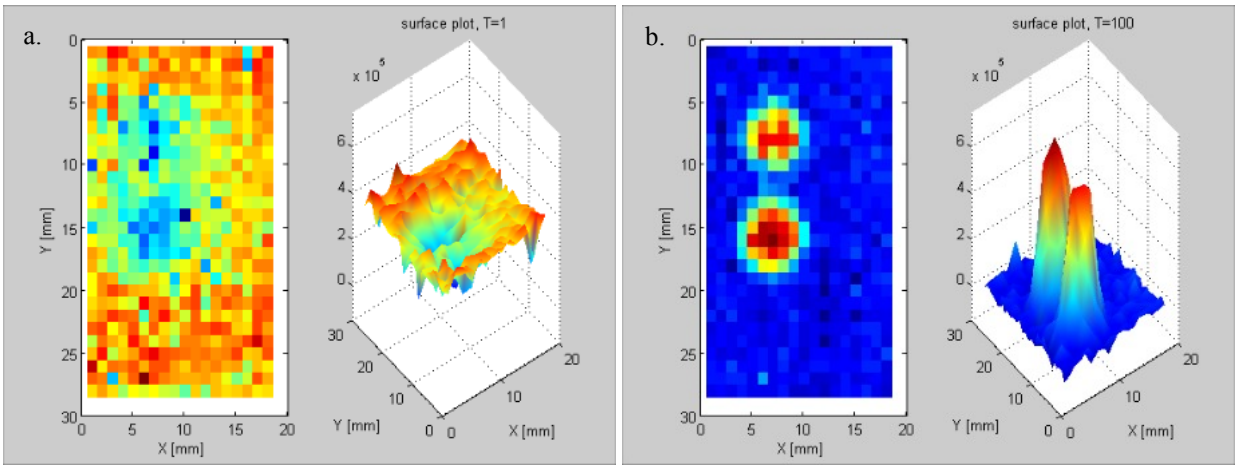

Figure 1. UOT surface maps of two mouse tails embedded in a tissue-mimicking phantom, at (a). T=0.1ms and (b). T=1.1ms after the start of a 1-ms long ultrasound burst.

The BSO-based photorefractive detection system was further optimized in terms of the diffused light collection efficiency and the photorefractive two-wave-mixing gain. A schematic of the improved system was shown in Figure 2. With the help of a large etendue optical light guide (aperture=0.5 inch, NA=0.55) to couple more diffused light from the sample onto the BSO and a high TWM gain (gain coefficient=0.81 cm^{-1} when the intensity of the reference beam R=30mW/cm^2, and S=200mW/cm^2). We were able to image tissue-mimicking samples as thick as 9.4 cm[22].

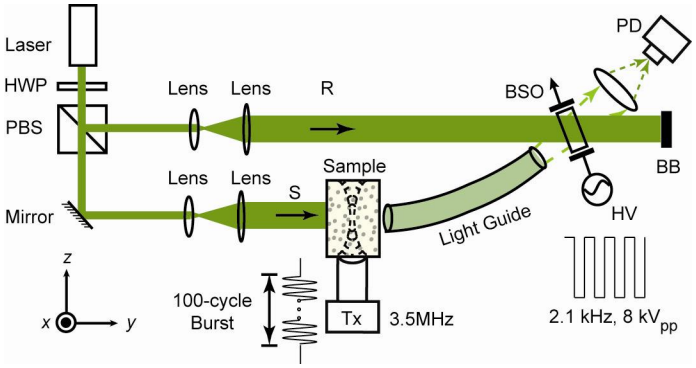

Figure 2. Experimental setup of the BSO-based photorefractive detection for UOT

2. THE LEAP FROM UOT TO LIGHT FOCUSING

2.1 Ultrasonic encoding as a virtual source

In UOT, it is the ultrasonic encoding of the diffused coherent light that provides the spatial resolution for imaging. The phase modulation shifts light frequency by the ultrasonic frequency, thus enables spectral discrimination of the ultrasonically encoded photons from the dominant background of the un-modulated photons. In other words, the ultrasonic encoding mechanism can be regarded as providing a virtual source to UOT. This is illustrated in a simulated diffusive light propagation through a scattering slab, as shown in figure 3. The various detection schemes developed so far explored different routes to differentiate the signal light from this virtual source and extract the useful imaging information. If all the un-modulated light (background light) were filtered in the signal detection process, then only the light emanating from the virtual source can be detected, resulting in a very high signal-to-background ratio.

Unfortunately, this ideal elimination of the background seems to be un-attainable with current detection schemes in UOT.

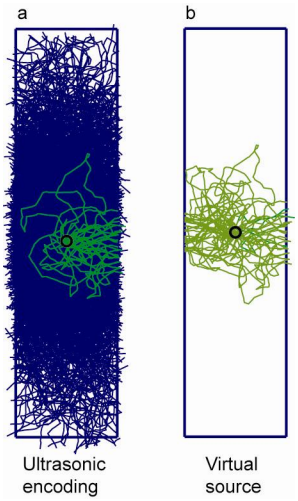

Figure 3. Monte Carlo simulation of diffusive light propagation through a scattering slab in UOT. (a). a focused ultrasonic wave shift the frequency of the diffused photons by the ultrasonic frequency, creating a virtual source of the modulated light. (b). in ideal detection scheme, all the un-modulated photons are filtered; only light from the virtual source is detected.

2.2 Ultrasonic encoding plus optical time reversal

The task of eliminating the background and keeping the light from the virtual source, while seems to be a formidable assignment, can in fact be accomplished as an inverse problem. With the help of optical phase conjugation, the ultrasonically encoded light can be selectively time reversed. We designed the following experiment to prove the feasibility of this concept, as shown in figure 4 and figure 5. In the forward process, a signal light beam illuminates a USAF resolution chart, and gets modulated by a focused ultrasonic wave inside a clear gelatin sample before transmits through a diffuser, then its scrambled wavefront S is mixed with a reference beam R and record a hologram inside the photorefractive BSO. The frequency of R and the ultrasonically encoded light S is synchronized, so that the only stable hologram recorded results from the interference from these two beams. In the time reversal process, shutter S1 is closed and shutter S2 opened. A reference beam R* (counter propagating as R) read out the hologram, and produce a wavefront S*, which is the phase conjugate of S. By principle of optical phase conjugation, S* retraces the trajectory of S, and forms a real image of the USAF resolution chart at its conjugate position. If we scan the ultrasonic beam across the signal light beam inside the gelatin phantom, so that only part of the signal light beam is modulated, then in the phase conjugation process, only that part of the signal light beam is recovered, resulting in the partial reconstruction of the USAF resolution chart, which can be imaged by a CCD.

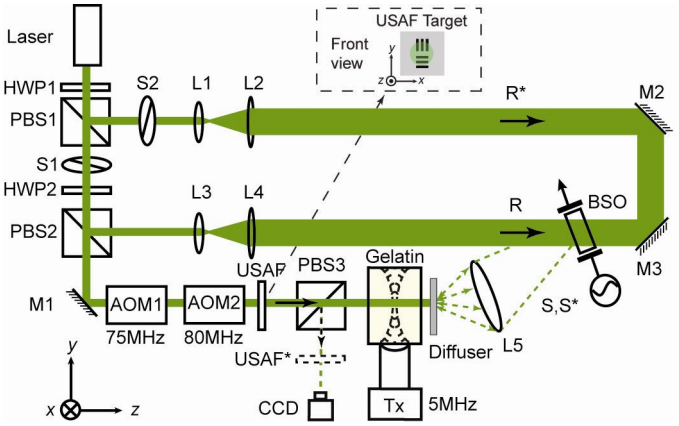

Figure 4. Ultrasonic encoding plus optical time reversal.

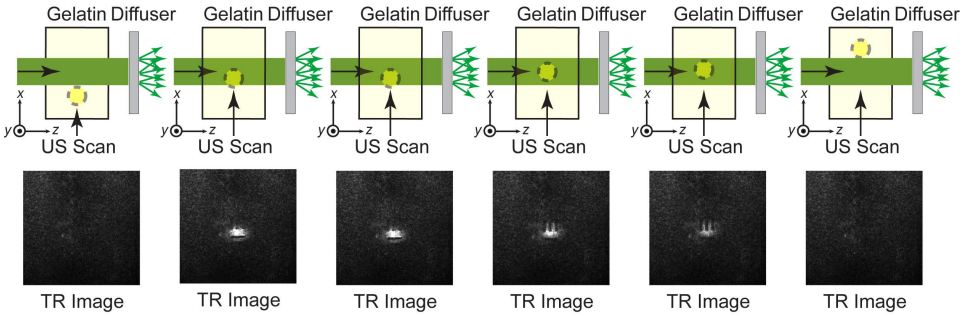

Figure 5. As a focused ultrasonic beam scan through the signal light beam inside a clear gelatin phantom, only partial recovery of the USAF target will result.

2.3 Time-reversed ultrasonically encoded (TRUE) optical focusing

In the above experiment, the virtual source, i.e., the ultrasonic encoding of the coherent light takes place in a clear medium. In a more general setting, such as in UOT, the virtual source is embedded in a scattering medium, e.g., soft biological tissue. It is therefore more useful to implement the experiment in a scattering medium, as shown in figure 6. By reproducing the virtual light source in such a scattering medium while eliminating all the un-modulated light background, localization of diffused light is achieved inside the medium. Unlike conventional optical focusing in a clear medium, where geometric optics predicts the concentration of ballistic photons, this process—time reversed ultrasonically encoded (TRUE) optical focusing—localize diffuse photons in a scattering medium. It can therefore be called a diffusive light focusing technique. The experimental validation of TRUE focusing can be done by an imaging experiment. Since the first implementation of this technology[23], we have developed TRUE focusing in transmission and reflection mode, and into thick soft biological tissue and tissue-mimicking phantom samples[24-25].

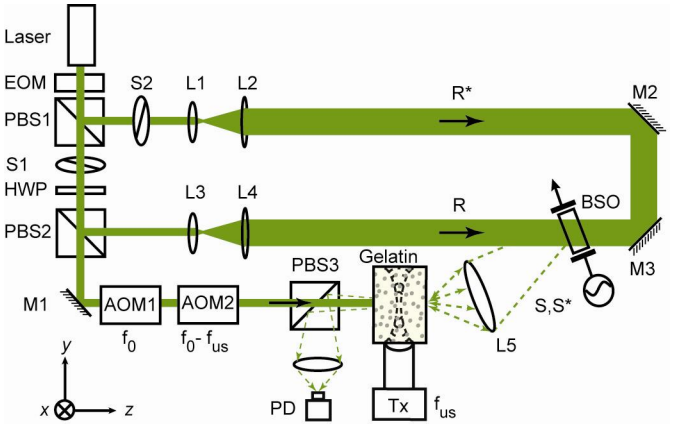

Figure 6. Schematic of a transmission mode TRUE experimental system.

3. OUTLOOK FOR PRC-BASED UOT AND TRUE FOCUSING

The photorefractive BSO crystal used in our experiment operates outside of the optical window in biological tissue. It photorefractive response time is on the order of ~100 ms, which is two orders of magnitudes longer than the decorrelation time in live biological tissue. Therefore, it is important, for en vivo UOT or TRUE focusing application, to find a photorefractive material that operates in the optical window and has a response time less than one millisecond.

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