Reflection-mode time-reversed ultrasonically encoded optical focusing into turbid media

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Abstract. Time-reversed ultrasonically encoded (TRUE) optical focusing was recently proposed to deliver light dynamically to a tight region inside a scattering medium. In this letter, we report the first development of a reflection-mode TRUE optical focusing system. A high numerical aperture light guide is used to transmit the diffrusely reflected light from a turbid medium to a phase-conjugate mirror (PCM), which is sensitive only to the ultrasound-tagged light. From the PCM, a phase conjugated wavefront of the tagged light is generated and conveyed by the same light guide back to the turbid medium, subsequently converging to the ultrasonic focal zone. We present experimental results from this system, which has the ability to focus light in a highly scattering medium with a round-trip optical penetration thickness (extinction coefficient multiplied by round-trip depth) as large as 160. © 2011 Society of Photo-Optical Instrumentation Engineers (SPIE). [DOI: 10.1117/1.3609001]

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In soft biological tissue, photons undergo multiple scattering events and follow “random walks,” which result in a diffusive optical field with compromised spatial resolution for imaging purposes beyond one transport mean free path length (∼1 mm). Hence, the problem of how to effectively focus or deliver light tightly deep into biological tissues has been of particular interest to the optical imaging community. Various schemes, such as adaptive wavefront shaping,1 and optical phase conjugation,2 have been developed to tackle this challenge. These techniques, however, require either time-consuming optimization1 or focusing light through a turbid medium instead of inside it.3

Most recently, a new technique called time-reversed ultrasonically encoded (TRUE) optical focusing3 has been proposed to dynamically focus light to a small volume defined by a focused ultrasound wave inside a turbid medium regardless of the medium’s optical homogeneity. In this technique, photons are multiply scattered inside the experimental sample, the ultrasound (US) wave modulates the propagation of those photons traveling through the region where light and sound coexist, i.e., the acousto-optic (AO) interaction volume,4 and tags photons with an ultrasonic frequency shift. Once the tagged photons (S) have diffused through the sample, they are collected by a photorefractive crystal (PRC), and interfere with a reference coherent optical beam (R) there to form a stationary hologram. The hologram is then read by a conjugated optical beam (R*), resulting in a time-reversed wavefront (S*). S* tracks the same trajectories of S in the reversed directions, and converges back to the AO interaction volume. US focusing enables the AO interaction volume to be much smaller than the broad light distribution inside the turbid medium, achieving good focusing. The feasibility of TRUE optical focusing has been demonstrated3 and further characterized in tissue-mimicking phantoms with optical focusing thicknesses (product of optical extinction coefficient and sample thickness) up to 70.5

The experimental setup implemented in Refs. 3 and 5 employs a transillumination configuration where optical incidence and collection are on opposite sides of an experimental sample. Such an alignment may pose limitations on applications in medical imaging where transmitting illumination leads to an undesirable increase in operative optical penetration. To make this new technique more practical and convenient, a reflection-mode TRUE optical focusing system has been developed, in which the optical input and output modules are installed on the same side of a sample, as reported in this letter.

Figure 1(a) is a schematic depiction of the experimental apparatus. The time sequences of holographic writing and reading, US modulation, and unveiling of the photodiode (by S5) within each system cycle are shown in Fig. 1(b). A continuous-wave laser (Verdi V-10, Coherent) operating at 532 nm was the light source. Its output was split into a sample beam (S), a reference beam (R), and a reading beam (R*). During the first 190 ms of each cycle, R* was blocked, and two acousto-optic modulators (AOMs, 802AF1, IntraAction) were employed in combination to tune the sample beam frequency from f0 to f0 − fa, where f0 represents the frequency of the laser and f0, the net frequency shift due to the AOMs. The resulting sample beam was expanded and directed along the Y direction to illuminate the front surface of the experimental sample with an approximate optical intensity of 880 mW/cm2. Unless otherwise mentioned, porcine gelatin (Sigma) gel-based phantoms doped with intralipid (Fresenius Kabi) (μ′ = 20 cm−1) were used as optical tissue-mimicking samples in the study. Within the sample, light was multiply scattered and phase modulated by the applied focused ultrasonic waves at a frequency of f0. The resultant backscattered light, composed of three spectral components at f0 − fa, f0 − 2fa, as well as f0, was collected from the same side of the sample by an obliquely and closely mounted fiber optical light guide (NT 39-370, Edmund Optics) that had a high optical endude, as illustrated in Fig. 1(a). In a 10 × 10 × 5 mm3 Bi12SiO20 (BSO) crystal (Elan, Russia), the collected signal light interfered with R (30 mW/cm2) at an angle of ∼3.6 deg. Note that only the interference between S(f0) and R at the same frequency f0 could form a stationary hologram inside the crystal.6 To enhance the holographic recording efficiency, a 2.1 kHz, 8 kV/cm

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In the reflection configuration by a photodiode detector (PD1, PDA36A, Thorlabs) outside of the sample.

With US modulation, however, $S^*$ was generated immediately after $R^*$ was allowed to pass [by $S_{3,4}$ in Fig. 1(a)] rendering a sharp peak standing above the background. The difference between these two PD1 signals, shown in the inset, provides the TRUE optical response, whose peak value is defined as the TRUE signal intensity in the study.

Since the US modulation depth is related to the local optical properties within the US focus, so are the consequent hologram contrast and TRUE signal intensity. Therefore, the TRUE signal intensity can be used to gauge the efficacy of optical focusing in turbid media. To validate this experimentally, a single-element focused transducer (A381S, Olympus) that had a central frequency at 3.5 MHz and a full-width at half maximum (FWHM) of 0.87 mm at focus was used as the US modulation source. In our study, focal pressures at 1.0 MPa (peak-to-peak) were used. The US propagation axis was aligned perpendicular to the incident sample beam, so that the focal point intersected with the center of the laser beam. A 6-mm thick highly scattering medium with and without US modulation. Their absorption contrast against the background: $\mu_a = 1$ cm$^{-1}$ for Obj 2, and 0.4 cm$^{-1}$ for Obj 1 and 3.

In the experiments, the transducer was first moved along the $Y$ direction to position the US focal point 2 mm deep in the scattering layer (the same $Y$ plane where the inclusions were embedded). Both the light and the ultrasound were kept stationary, while the phantom was scanned along the $X$ direction with a step size of 0.127 mm. At each position, a TRUE signal was obtained as discussed in Fig. 2. A dc signal and a time-reversed direct current (TRDC) signal were also recorded at PD2 and PD1, respectively, when the AOM tuning and US modulation were turned off. The result of the scan is shown in Fig. 3(c),
where the normalized signal intensities are plotted as a function of $X$. The dc and TRDC images have spatial resolutions of 3.3 and 2.8 mm, respectively, based on the FWHM of their Gaussian fits, and thus lack the ability to resolve the three objects due to the light diffusion. For TRUE, however, the embedded objects are evident against the background. Their fitted widths, based on the Gaussian fit, measure 1.0, 1.1, and 1.0 mm, respectively, agreeing well with the actual widths of the objects. Spacings between the adjacent objects are also consistent with the actual positions. In addition, Obj 2 produced a lower TRUE signal intensity than the other two targets due to its higher absorption coefficient, suggesting less light was focused back to the US focus at Obj 2’s position. Finally, the spatial resolution of the TRUE image, computed from the FWHM of the Gaussian fit, was 0.63 mm, which is approximately $1/\sqrt{2}$ of the US focal width and consistent with the square law. All of these findings lead us to conclude, although indirectly, that the reflection-mode TRUE focusing system was able to focus light back to the US focal zone within a turbid medium.

Figure 3(d) shows the TRUE signal intensity as a function of US focus depth in the sandwiched turbid layer. Measurements were performed by scanning the transducer along the $Y$ direction, with the US focus away from the three objects in the $X$ direction, while the phantom and the optical incidence/collection were kept fixed during the scan. From Fig. 3 we can see that the measured TRUE signal intensity (squares) decays approximately exponentially when the US beam moves deeper into the scattering layer and fits quite well with a model (curve, the fitting coefficient of determination $R^2 = 0.98$) $Y = 92.92 \cdot \exp(-0.432 \cdot d)$, where $d$ is the $Y$ position of the US focus in millimeters. Considering that light was collected in a reflection configuration, the actual optical depth for penetration was $2d$. Therefore, the TRUE signal intensity had an exponential decay rate of $0.432/2 = 0.215$ mm$^{-1}$, close to the effective attenuation coefficient of the medium ($\mu_{a,eff} = \sqrt{3}\mu_a(\mu_a + \mu_s^\prime) \approx 0.219$ mm$^{-1}$) that governs the decay of fluence rate for diffused light. It should be noted that the measured values deviate more from the fitted results at depths around 2 mm, which may be due to the slight mismatch in acoustic impedance and index of refraction since the layers of turbid media on the right and on the left of the $Y = 2$ mm plane were solidified separately in the process of phantom fabrication to embed the three absorption objects. Nevertheless, the overall consistency once again validates that TRUE optical focusing converged diffused light tightly back to the US focus and created a virtual light source within the turbid media. The maximum focusing depth with our current setup, as shown here, is more than 4 mm into such a highly scattering medium. The round-trip optical penetration thickness of $(\mu_a + \mu_s^\prime) \times 2d \approx 160$ is equivalent to 16 mm in tissue-mimicking phantoms that have an optical extinction coefficient of 10 mm$^{-1}$.

In summary, this letter presents the development of the first reflection-mode TRUE optical focusing system, with demonstrated the ability to dynamically focus diffused light into a tight volume guided by ultrasound focus within turbid media. Compared with previous schemes in transmission mode, the reported reflection-mode configuration using a light guide for back-scattered diffused light collection and transition is more convenient and practical, and a round-trip optical penetration thickness as much as 160 was reached. As a new technique, TRUE optical focusing is not mature yet. However, further improvements, especially with regard to penetration depth and time-reversed signal gain, together with tests in tissues, will undoubtedly make this innovation more attractive.

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