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

Puxiang Lai
Xiao Xu
Honglin Liu
Yuta Suzuki
Lihong V. Wang
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Puxiang Lai, Xiao Xu, Honglin Liu, Yuta Suzuki, and Lihong V. Wang
Washington University in St. Louis, Department of Biomedical Engineering, Optical Imaging Laboratory, Campus Box 1097, 1 Brookings Drive, St. Louis, Missouri 63130

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 diffusely 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.

Keywords: optical imaging; optical focusing, optical phase conjugation; ultrasonic modulation, time reversal; photorefractive crystal; turbid media; reflection mode.

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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, and optical phase conjugation, have been developed to tackle this challenge. These techniques, however, require either time-consuming optimization or focusing light through a turbid medium instead of inside it.

Most recently, a new technique called time-reversed ultrasonically encoded (TRUE) optical focusing 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, and tags photons with an ultrasonic frequency shift. Once the tagged photons 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 demonstrated and further characterized in tissue-mimicking phantoms with optical focusing thicknesses (product of optical extinction coefficient and sample thickness) up to 70.

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 S can be seen 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 − f, where f0 represents the frequency of the laser and f is 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) (µs = 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 f. The resultant backscattered light, composed of three spectral components at f0 − f, f0 − 2f, 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 etendue, 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. To enhance the holographic recording efficiency, a 2.1 kHz, 8 kV/cm
(peak-to-peak) high voltage (square) ac electric field from an amplifier (609E-6-L-CE, Trek) was applied across the crystal. In the subsequent reading phase, when $S$ and $R$ were blocked by the shutters $S_{1,2}$, $R^{*}$ ($\approx 900$ mW/cm$^2$) illuminated the crystal along the direction opposite to $R$, and instantly generated a phase conjugated copy of $S(f_0)$, namely $S^{*}(f_0)$. The copy followed the exact trajectories of $S(f_0)$ back into the medium to converge to the US focal volume, thereby accomplishing optical focusing inside the turbid medium. Part of this time-reversed, low-intensity optical signal was again backscattered, then collected by the shutters. (a) Experimental schematic of the reflection-mode TRUE optical focusing system. The component labels are defined as follows: $f_0$, frequency of laser; $f_a$, frequency of ultrasound; $L_{1-11}$, lenses; $M_{1-5}$, mirrors; $HWP_{1-2}$, half-wave plates; $PBS_{1,2}$, polarizing beam splitters; $S_{1,2}$, shutters; $AOM_{1,2}$, acousto-optic modulators; $PD_{1,2}$, photodiodes; $UT$, ultrasound transducer; $LB$, light block; $FLG$, fiber optical light guide; $FLC$, fiber light condenser; $PRC$, photorefractive crystal; $HV$ ac, high-voltage ac electric field applied across the PRC; $S$, reflectively collected diffused light from the sample; $R$, reference beam; $R^{*}$, conjugate reference beam; $S^{*}$, time-reversed copy of $S$; $XYZ$, system coordinates ($Y$ is the optical illumination direction, and $Z$ is the US propagation axis). (b) Temporal sequences within one system cycle (1 s).

With US modulation, however, $S^{*}$ was generated immediately after $R^{*}$ was allowed to pass [by $S_{1,2}$ in Fig. 1(a)], rendering a sharp peak standing above the background. The difference between these two $PD_1$ signals, shown in Fig. 1(a), 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 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 layer ($\mu_s \approx 0.08 \text{ cm}^{-1}$, $\mu_a = 20 \text{ cm}^{-1}$) was prepared as shown in Fig. 3(a) and sandwiched between two transparent gelatin gels along the $Y$ direction for better acoustic coupling. The sample beam was incident from the left, and $Y = 0$ was set to the front (left) boundary of the scattering layer. On the $XZ$ plane around $Y = 2 \text{ mm}$, i.e., $2 \text{ mm}$ deep in the turbid medium, three absorption inclusions were embedded as illustrated in Fig. 3(b). These inclusions, with dimensions of $1 \times 1 \times 8$ to $10 \text{ mm}^3$ along the $XZ$ axes and separated by 4.5 to 4.8 mm along the $X$ axis, were made of the same material as the turbid background, except that India ink was added to provide optical absorption contrast against the background: $\mu_a = 1 \text{ cm}^{-1}$ for Obj 2, and $0.4 \text{ cm}^{-1}$ 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 $PD_2$ and $PD_1$, respectively, when the AOM tuning and US modulation were turned off. The result of the scan is shown in Fig. 3(c),...
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 \(\mu_{\text{eff}} = \sqrt{3\mu_a(\mu_a + \mu'_s)} \approx 0.219 \text{ mm}^{-1}\) 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 \((\mu_a + \mu'_s) \times 2d \approx 160\) 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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References