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ABSTRACT

Experiments directed towards a clinically useful optical imaging system use long-pulse near-infrared lasers and a correlation time gate based on degenerate four-wave mixing in a nonlinear medium.

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Introduction

In the past several years much effort has been applied toward the development of optical tomography for applications such as mammography and brain imaging, motivated by the possibility of eliminating the use of ionizing radiation. The challenge results from the fact that tissues are strongly scattering, and the scattering coefficient can be a factor of 100 greater than the absorption coefficient in the near infra-red (NIR). For two-dimensional imaging, a variety of schemes have been investigated for time gating to selectively detect ballistic photons (i.e. photons that are not scattered) and quasi-ballistic, or "snake" photons (photons that undergo very little scattering and stay on a predominantly straight path between the source and the detector).

In addition to the conceptually-straightforward electronic gating of the detector, Kerr-gate shuttering, collimation and spatial filtering, and coherent, nonlinear-optical, time-gating techniques such as stimulated Raman scattering (SRS) and coherent anti-Stokes Raman spectroscopy (CARS) are among several methods that have been proposed for this purpose.[1] While many of these methods rely on ultrafast lasers, a few are based on correlation gates (which may be implemented, for example, for SRS or CARS). A correlation gate can be formed by the interference of two signals originating from the same laser. The length of the gate is determined by the coherence time of the laser. Therefore, methods employing correlation time gates can use longer laser pulses, even continuous wave (cw), and broad bandwidth light. Technically, this allows for lower-cost, more reliable systems.

Fundamentally, a potential advantage of long pulses or cw illumination is that for each exposure more light may illuminate the tissue since the peak powers are lower. This can be very important when a basic question is whether there are sufficient ballistic and snake photons to form an image, regardless of the noise rejection efficiency. The method described here, resonant degenerate-four-wave-mixing (DFWM), was first suggested by Feinberg [2], but to our knowledge no experimental demonstrations have been published to date. DFWM covers a variety of nonlinear-optical phenomenon, and may be used as a correlation time-gate to produce an effective, ultrafast optical gate. DFWM can take advantage of optical processes occurring on or very near resonant transitions in atoms or molecules, thus providing signal amplification. DFWM also offers, theoretically, the highest possible rejection of the diffuse light component. However, in practice, a variety of experimental issues determine the lower limits for the noise, which generally are considerably in excess of the theoretical limits.

Results and Discussion

With DFWM the signal is proportional to the induced nonlinear index in the medium, which can be a resonantly enhanced process. The general layout for our experimental approach is shown in Figure 1. In preliminary experiments [3], a frequency-doubled Nd:YAG laser, with a coherence length of a few millimeters, was used as the laser source, and a dilute dye solution provided the phase conjugating medium. The path lengths of the forward pump beam, E_f, and the straight-through probe beam, E_p, are made equal, so that only ballistic and quasi-ballistic photons along the path of E_p arrive coherently with E_f. Where E_f and E_p cross in the medium a Bragg grating is formed by the interaction of the interference pattern with the medium. The backward-propagating pump beam, E_b, scatters off this grating directly back along the probe beam path, forming the signal, E_s, which is the phase conjugate of the probe beam, E_p. The backward pump need not arrive at the same time as the two beams that formed the grating, nor does it have to be coherent with them, in order to "read out" the "hologram", as long as the grating is still present. In our preliminary experiment, the backward pump is actually delayed about 2 ns with respect to the beams that form the grating. (If E_b is timed to arrive coincident with E_p, then those two will generate a different volume grating, from which E_f can scatter, creating another signal that has a phase front identical to the phase-conjugate wave from the first combination.). The amplitude of E_s can be greater than the original probe beam, since the counter-propagating pump beams are much more powerful than the probe; thus, amplification is achieved. Light delayed by multiple scattering in the phantom cannot form a grating with the either pump, and therefore produces no periodic index variations from which the backward pump can scatter. Moreover, the consequent quasi-random scattering is predominantly omni-directional and can be substantially rejected by solid-angle restriction of the detector.

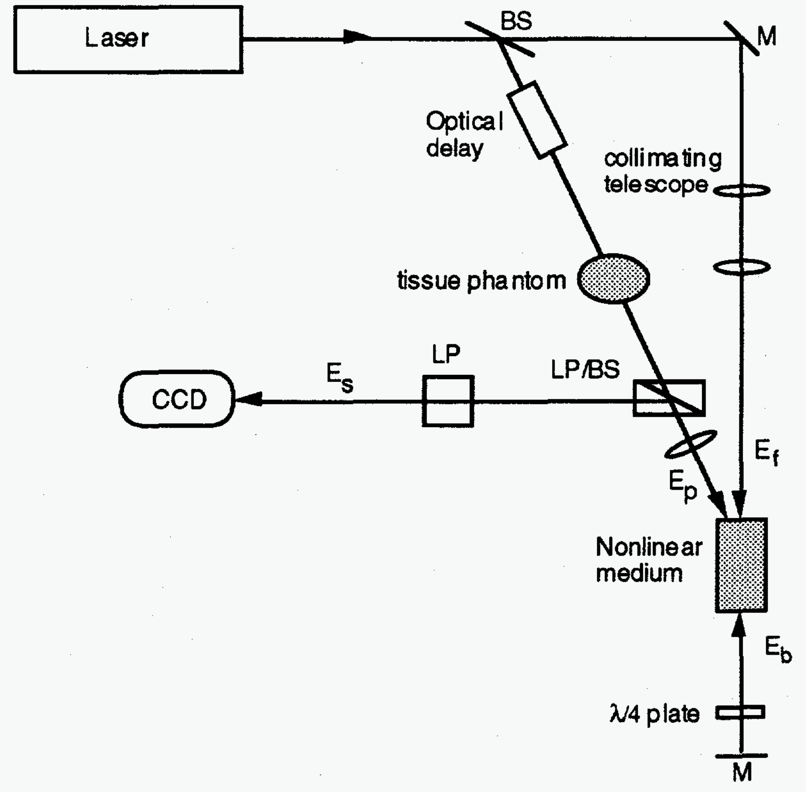

Figure 1, a schematic of the experimental apparatus. M designates mirrors; BS, beam splitters; LP/BS is a polarizing beamsplitter; and E_f, E_b, E_p, and E_s, represent the forward, back-reflected, probe and signal beams, respectively.

Using this apparatus, preliminary results were obtained by imaging a 200-micron-diameter cross-hair (placed before the scattering cell) through a 5-cm-long turbid suspension of 1% whole milk in water, which corresponds to a reduced scattering coefficient, μ_s', of approximately 1.2 cm^{-1}. A coherence time of ≈25 ps was observed, consistent with the laser bandwidth of 1.4 cm^{-1}. Images from these experiments are shown in Figure 2. Proof-of-principle was clearly demonstrated, and suggests that the application of this approach to medical imaging is worth further effort.

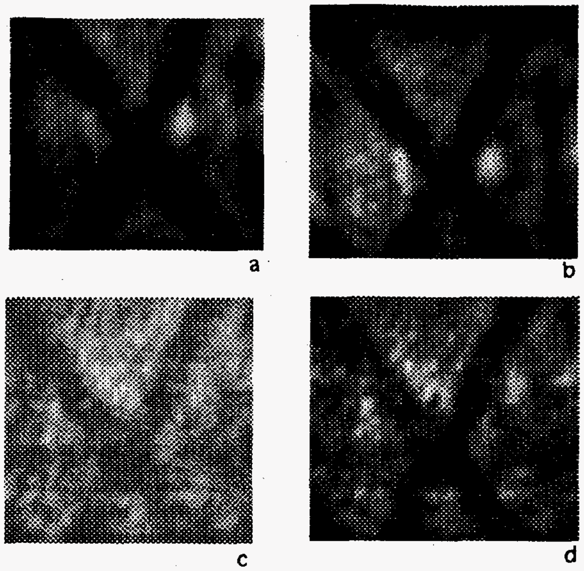

Figure 2. shows four images of a 200 µm crosshair. Image a) has no scattering medium; image b) uses a cell filled with water; image c) is a single shot image through a suspension of whole milk in water; image d) is a fifty shot average through the milk-scattering medium.

In order to investigate the application of this technique to real biomedical imaging, we have redirected our experiments to invoke parameters more relevant to tissue imaging. We are using phantoms that more accurately reflect the scattering and absorption properties of real tissue, and we are working at NIR wavelengths, where the absorption in tissue is minimized.[4] Addressing tissue samples also requires relatively low peak-power laser sources, to obviate tissue damage. Since the ideal source would be a cw laser, we conducted exploratory experiments with a cw Argon-ion laser, using a $BaTiO_3$ photorefractive crystal as the nonlinear medium. The very low power of a cw source for this type of application requires the use of a nonlinear medium with an exceedingly large nonlinear index, making photorefractive media conceptually attractive. Unfortunately, our experiments revealed that intrinsic scattering of the strong pump beams in the $BaTiO_3$ crystal itself, probably due to growth inclusions, acts as a noise source that dominates over any process induced by a weak external probe beam. We intend to explore the use of other high-nonlinearity media with potentially less intrinsic scattering, such as near-resonance metal vapors.

Currently, we are using a Cr^{+3}:Li_2SrAlF_6 laser as the light source for these studies. This laser emits in the optimal spectral region, 800-850 nm, with an easily adjustable bandwidth; and in the gain-switched mode it produces a relatively long duration pulse of 20-30 µsec. (We are examining methods to further reduce the peak intensities of the typical gain-switching spikes.) Among the candidates for nonlinear media being tested are dye solutions, metal-salt solutions and metal vapor cells. Work in progress at the time of this writing appears promising, and latest results will be described in the presentation.

References:

[1] See a variety of papers in OSA Proc. Advances in Optical Imaging and Photon Migration, Vol. **21**, R.R. Alfano, ed., (1994).

[2] J. Feinberg, "Seeing through scatter", presentation at the Optical Society of America Annual Meeting (1992).

[3] A. D. Sappey, "Optical imaging through turbid media with a degenerate four-wave mixing correlation time gate", Appl. Opt., **33**, 8346 (1994).

[4] See, for example, V.G. Peters et al., "Optical properties of normal and diseased human breast tissues in the visible and near infrared", Phys. Med. Biol. **35**, pp. 1317-1334 (1990).