Pulsed near-infrared laser diode excitation system for biomedical photoacoustic imaging

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A pulsed laser diode system operating at 905 nm has been developed for the generation of photoacoustic signals in tissue. It was evaluated by measuring the photoacoustic waveforms generated in a blood vessel phantom comprising three dye-filled ($\mu_a = 1\ \mathrm{mm}^{-1}$) tubes of diameters 120–580 μm immersed to a maximum depth of 9 mm in a turbid liquid ($\mu_s' = 1\ \mathrm{mm}^{-1}$). The system was then combined with a cylindrical scanning system to obtain two-dimensional images of a tissue phantom. The signal-to-noise ratio of the detected signals in both cases and the image contrast in the latter suggest that such a system could provide a compact and inexpensive alternative to current excitation sources for superficial imaging applilcations. © 2006 Optical Society of America

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Photoacoustic (PA) imaging is a new soft-tissue imaging modality, based upon the use of laser-generated ultrasound, that combines the high contrast of optical methods with the high spatial resolution of ultrasound.[1]

To generate PA signals efficiently, laser pulse durations in the range of tens to hundreds of nanoseconds are required. To obtain adequate penetration depth, it is also desirable to use a wavelength in the near infrared (NIR) range (600–1200 nm) where biological tissues are relatively transparent. These requirements can be met, in part, by the Q-switched Nd:YAG laser operating at 1064 nm, which for pulse repetition frequencies (PRFs) of a few tens of hertz, typically provides milijoule pulse energies. This, along with compact size, modest power requirements, and relatively low cost, has led to its widespread use in biomedical photoacoustics. The fundamental disadvantage of the Nd:YAG is that it provides only a single fixed NIR wavelength. It cannot therefore be used for the spectroscopic quantification of specific tissue chromophores such as oxy and deoxyhaemoglobin.[2] Tunable excitation sources, which can provide the necessary tuning range in the NIR, milijoule pulse energies, and nanosecond durations, are available from Q-switched Nd:YAG pumped optical parametric oscillator, dye, and Ti:sapphire laser systems. Although widely used as laboratory tools, their biomedical use, particularly within a clinical environment, is limited by their cost, size, power, and cooling requirements and practical utility (e.g., the need for realignment).

Pulsed laser diodes could overcome these limitations. They are compact, relatively inexpensive and, most important for spectroscopic applications, available in a range of wavelengths in the NIR. The main disadvantage is their low peak output power, which is typically limited to <200 W to avoid catastrophic optical damage at the facet of the diode. This limits the pulse energies available (for nanosecond pulse durations) to a few tens of microjoules compared with the milijoules available from the above sources. For this reason, laser-diode-based excitation systems have found only limited biomedical application. The few studies that have been reported appear to rely upon irradiating small sample areas to provide sufficient energy density, rather than illuminating over an extended region as required for tomographic imaging configurations.[3,4]

Although the limited pulse energy appears to represent a fundamental limitation, there is scope to mitigate this. First, the PRF of a pulsed laser diode can be of the order of kilohertz compared to a few tens of hertz for Q-switched-based excitation systems. With a suitably fast acquisition system this allows several thousand PA signals to be acquired and signal averaged in a fraction of a second, increasing the signal-to-noise ratio (SNR). Further gains in the SNR can be made by optimizing the PA signal generation efficiency and the detection sensitivity: the former by selecting the laser pulse duration in relation to the geometric parameters of the target,[5] and the latter by matching the bandwidth of the ultrasound receiver to that of the generated signal. The low cost of laser diodes and their drive electronics also make it economically viable to combine the outputs of an array of devices to increase total power output. As described in this Letter, by employing a combination of these strategies it then becomes possible to begin closing the SNR gap between Q-switched and laser-diode-based excitation systems.

Although the eventual goal is to develop a multiwavelength system, a single-wavelength system was first developed to demonstrate that PA signals of adequate SNR can be generated. The system (Fig. 1) comprised four high-peak-power pulsed laser diodes,

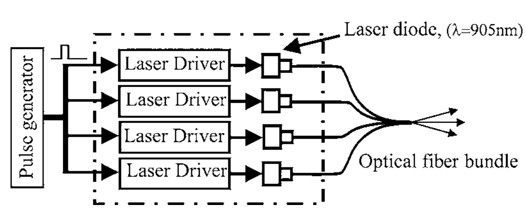

Fig. 1. Laser diode photoacoustic excitation system.

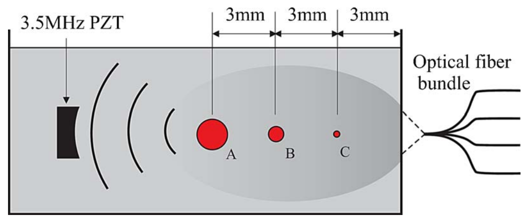

Fig. 2. (Color online) Phantom composed of three dye-filled ($\mu_a = 1\ \mathrm{mm}^{-1}$) capillary tubes (A, Ø120 μm; B, Ø300 μm; C, Ø580 μm) immersed in intralipid ($\mu_s' = 1\ \mathrm{mm}^{-1}$).

each composed of a stack of five active elements, fabricated by using strained InGaAs quantum wells and operating at a 905 nm wavelength. The laser diodes provide a peak optical output power of 175 W when driven with a peak current of 60 A. Their duty cycle was $\delta = 0.1\%$, allowing them to be driven at PRFs of 20 kHz and 2 kHz when driven with pulse durations of 50 and 500 ns, respectively. Each laser diode had a custom-built driver allowing the pulse duration and PRF to be continuously varied from 50 to 500 ns and from 100 to 5 kHz, respectively. The drivers were composed of a capacitor used as a storage element, which was discharged through the laser diode when a fast-switching metal-oxide semiconductor field-effect transistor was triggered by a pulse generator. The output of each laser diode was coupled to an optical fiber of 1.5 mm core diameter to guide the light to the sample.

The high PRF of the system allows the SNR of the detected PA signals to be improved to by rapidly signal averaging many acquisitions. This was implemented by using an oscilloscope (DSO-Tektronix TDS784D) with an on-board segmented memory architecture. This enabled successive PA waveforms to be captured in real time, concatenated in a single segmented record, and then processed by the DSO to provide a single signal-averaged waveform. Thus the significant interacquisition rearm time (~10 ms) of a DSO can be avoided, enabling true PRF-limited signal averaging rates to be achieved. The DSO used had a record length of 50,000 points, enabling the acquisition and averaging of a block of 100 consecutive signals, each with a record length of 500 points in real time. Once the DSO memory was full, the averaged signal was downloaded to a PC where it was averaged with other signals obtained in the same way. Although this meant that signal averaging 5000 signals took approximately 50 s, the majority of this time was due to the process of downloading the signals to the PC via the GPIB interface. The use of a DSO- or PC-based acquisition card with sufficient memory to record all of the acquisitions would enable a true PRF-limited averaging time of 1 s.

To demonstrate the generation of detectable PA signals in a realistic tissue phantom, single point measurements were made in a phantom designed to simulate an arrangement of discrete blood vessels. This phantom was composed of three tubes of diameters 120, 300, and 580 μm, placed in a scattering medium at depths of 3, 6, and 9 mm, respectively (Fig. 2). These tubes were filled with a dye whose absorption coefficient was similar to blood's ($\mu_a = 1\ \mathrm{mm}^{-1}$) and immersed in a 1% solution of intralipid ($\mu_s' = 1\ \mathrm{mm}^{-1}$) to mimic the scattering properties of tissue. The tubes were placed perpendicular to the incident laser beam axis, and the generated PA signals were detected by using a cylindrically focused piezoelectric transducer (PZT, 3.5 MHz) of focal length 33 mm. The recorded signals were amplified (40 dB) and signal was averaged 5000 times. The laser beam diameter was approximately 8 mm.

Figure 3 shows two examples of the PA waveforms generated in the phantom: one for a laser pulse duration $t_p = 65$ ns and pulse energy $E = 24\ \mu$J and the other for $t_p = 500$ ns and $E = 184\ \mu$J. Each waveform is composed of three bipolar signals, one for each of the three tubes, separated by approximately 2 μs and corresponding to the 3 mm separation between tubes. As expected, the SNR is greater for the signals generated using the longer pulse duration (and thus higher energy), although it does not scale proportionately because of the reduced generation efficiency that occurs with increasing pulse duration, a consequence of the stress confinement condition not being wholly fulfilled. The increase in SNR for $t_p = 500$ ns is also accompanied by a temporal broadening of the signals, most obviously for tube A. This is because the signal is given by the convolution of the temporal profile of the laser pulse with the signal that would be generated by an impulsive deposition of the laser energy. These observations highlight the inevitable compromise between SNR and spatial resolution when using a laser diode excitation source; increasing the pulse energy to improve SNR requires a commensurate increase in pulse duration to avoid exceeding the peak power limit of the laser diode and thus a consequent reduction in spatial resolution.

To demonstrate that the system could be used to obtain two-dimensional images, a cylindrical detection geometry similar to that described in Ref. 6 was used (Fig. 4). It comprised a stepper motor that rotates the cylindrically focused PZT (3.5 MHz) detector around a sample under PC control. The detected PA signal was amplified (40 dB) and signal was averaged as described above before being downloaded to a

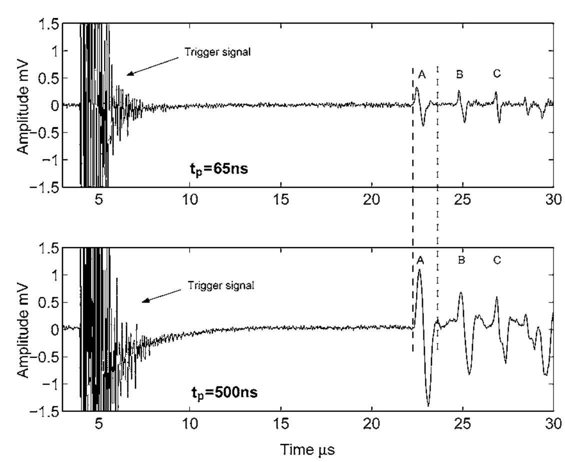

Fig. 3. Photoacoustic signals generated in the phantom shown in Fig. 1 for laser pulse durations $t_p = 65$ ns and $t_p = 500$ ns.

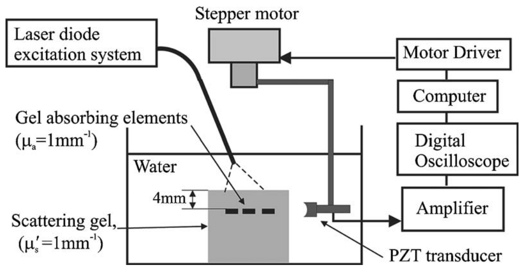

Fig. 4. Cylindrical scanning system.

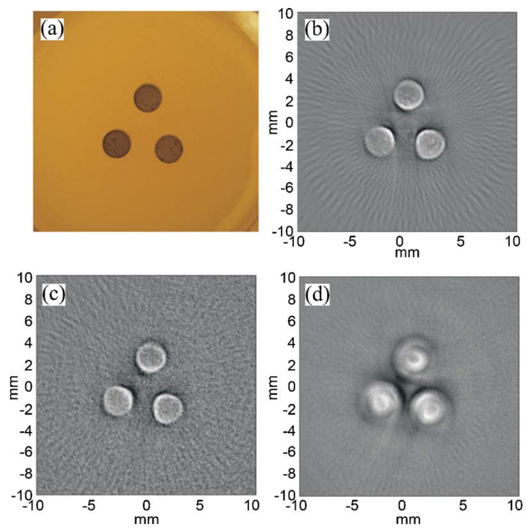

Fig. 5. (Color online) (a) Photograph of the phantom used in Fig. 4 before adding the top layer of the scattering medium. (b) Reconstructed PA image obtained using the Q-switched Nd:YAG laser, $t_p = 7$ ns. (c) and (d) Images obtained using the laser diode system with $t_p = 65$ ns and $t_p = 500$ ns, respectively.

PC at each angular increment of the scan. The signals were then used in a modified backprojection algorithm[6] to reconstruct a two-dimensional image. The phantom was composed of three cylindrical absorbing elements (diameter 2.7 mm and thickness 1 mm). These elements were formed out of gelatine and mixed with a dye whose absorption coefficient is similar to blood's ($\mu_a = 1\ \mathrm{mm}^{-1}$). Figure 5(a) shows these three elements as they were in the phantom, before a gel mixture containing 1% intralipid ($\mu_s' = 1\ \mathrm{mm}^{-1}$) mimicking the scattering properties of tissue was poured on top, immersing the absorbing elements to a depth of 4 mm. The detector was scanned through 306° in 3.6° steps, and the scanning radius was 25 mm.

An image was first obtained by using a Q-switched Nd:YAG laser operating at 1064 nm for comparison purposes. The pulse energy was 10 mJ, $t_p = 7$ ns, and the detected signals averaged over 20 shots. The reconstructed image is shown in Fig. 5(b) and correlates well with the photograph of the phantom [Fig. 5(a)]. Figures 5(c) and 5(d) show the images obtained using the laser diode excitation system for $t_p = 65$ ns and $t_p = 500$ ns, respectively, and signal averaging over 5000 pulses. These images illustrate the SNR spatial resolution compromise referred to above. For the longer pulse duration the SNR is approximately a factor of 5 higher, but the spatial fidelity of the reconstructed image is relatively poor, with the absorbing cylinders being barely distinguishable from each other. For the shorter pulse duration the resolution is much improved and, although the SNR is significantly reduced, the objects are clearly identifiable and compare well with the image in Fig. 5(b) that was obtained with the Nd:YAG laser.

In general, identifying the optimum pulse duration requires careful consideration of the mechanisms limiting spatial resolution. For example, when imaging relatively deep anatomical features, spatial resolution may be limited by the bandlimiting effect of the frequency-dependent acoustic attenuation in tissues. There may then be a SNR advantage in using a relatively long pulse duration as,[5] despite the lower generation efficiency, the frequency content of the signal will be shifted to lower frequencies that are attenuated less. If spatial resolution is limited by the detector, the pulse duration should be such that it produces a signal frequency content that lies within the detector bandwidth. In some cases the trade-off is less obvious. For example, although increasing pulse duration downshifts the acoustic frequency spectrum, the pulse energy can be increased proportionately to remain within the peak-power limitation of the laser diode. Under these circumstances the absolute amplitudes of the high-frequency components for the longer pulse duration may be comparable with or exceed those generated by a shorter pulse. The retention of the higher frequency components (assuming they are above the noise floor) offers the prospect of deconvolving the detected signals with the temporal shape of the laser pulses to improve spatial resolution in an image such as in Fig. 5(b).

In summary, it has been shown that a laser diode system has the potential to be used for short-range imaging applications such as visualizing superficial vascular anatomy in the small animal brain or the skin.[1] Future work will focus on adding laser diodes with different NIR wavelengths for spectroscopic applications. It is considered that this work represents the first step in developing a new generation of compact, inexpensive NIR multiwavelength excitation systems that provide a realistic alternative to existing sources.

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