Novel fibre lasers as excitation sources for photoacoustic tomography and microscopy

T.J. Allen(1), M.O. Berendt(2), J. Spurrell(2), S.U. Alam(2), E.Z. Zhang(1), D.J. Richardson(2) and P.C. Beard(1)

(1) Department of Medical Physics and Biomedical Engineering, University College London, Gower Street, London, WC1E6BT, UK
(2) Optoelectronics Research Centre, University of Southampton, Southampton, SO171BJ, UK

ABSTRACT

Two custom fibre lasers have been developed. One is designed for widefield photoacoustic tomography (PAT) and uses a custom drawn large core diameter fibre (100µm) to provide high pulse energies (5mJ). It also provides a variable pulse repetition frequency (100Hz-400Hz) and pulse duration (10-150ns) and is compact (of comparable dimensions to a desktop PC) and does not require external water cooling. This system was used to acquire *in vivo* images of the subcutaneous microvasculature in the human palm. The second laser is designed for Optical Resolution Photoacoustic Microscopy (OR-PAM) and provides a high quality beam (M^2<1.1), pulse energies >1µJ with a pulse repetition frequency (PRF) up to 2MHz, and a 532nm emission wavelength. The high PRF of this laser was exploited for ultra-fast image acquisition. The compact size and enhanced functionality of these lasers offers a major opportunity to facilitate the translation of photoacoustic imaging to practical applications in medicine and biology.

1. INTRODUCTION

Laboratory based photoacoustic scanners have produced exquisite images of tissue structure and function and in doing so excited a great deal of interest in the biomedical imaging community. The challenge that now lies ahead is to translate the technique to a practical imaging tool that can be used routinely for clinical applications. However, meeting this challenge is seriously compromised by the limitations of existing Q-switched Nd:YAG pumped OPO or dye laser systems typically used in photoacoustic imaging. Laser systems that can provide the mJ pulse energies required for widefield photoacoustic tomography (PAT) are often bulky, require external water cooling and provide low pulse repetition frequencies (<100Hz). For optical resolution photoacoustic microscopy (OR-PAM), the requirement for sub-µJ pulse energies can readily be met by conventional laser sources but achieving the high PRFs required for rapid image acquisition (100's KHz) represents a significant challenge.

Fibre lasers offer an alternative that can overcome these limitations [1]. The long length and small core diameter of the optical fibre that forms the active medium provides high gain, low laser threshold and high gain efficiency. The high surface area to volume ratio provides efficient heat dissipation and allows for compact size. Moreover, the fiberized nature of the laser cavity obviates the need for alignment and regular maintenance. Fibre lasers are not only advantageous in terms of practical utility but also in functionality. The Master Optical Power Amplifier (MOPA) configuration, which amplifies the output of a seed laser (typically a semiconductor device) provides an output that can be arbitrarily modulated over a very wide range of timescales (sub ns-ms). This permits adjustable control of the PRF, pulse duration and shape allowing a wide variety of photoacoustic excitation and signal processing schemes to be implemented.

Fibre lasers have found only limited use in PAT [2] due to the low pulse energy (<1mJ) provided by commercially available systems. These low pulse energies are a consequence of the small core diameter (<25µm) fibres these systems use in order to achieve a high beam quality. For PAT, a high beam quality is not a requirement allowing use of larger core diameter fibres (>100µm) in order to achieve significantly higher pulse energies. It is this approach that has been adopted in this study in order to realise a fibre laser that can provide a pulse energy of 5mJ. This system and its use for *in vivo* imaging in widefield tomography mode is described in section 2. Commercial fibre lasers have previously been used as OR-PAM excitation sources taking advantage of the high beam quality (M^2<1.2) they provide [3]–[7]. However, the PRFs of these lasers have been limited to a few hundreds of kHz thereby limiting image acquisition speed. In section 3 we describe a novel fibre laser that can provide a PRF of 2MHz thus providing significantly reduced image acquisition time.

Photons Plus Ultrasound: Imaging and Sensing 2016, edited by Alexander A. Oraevsky, Lihong V. Wang
Proc. of SPIE Vol. 9708, 97080W · © 2016 SPIE · CCC code: 1605-7422/16/$18 · doi: 10.1117/12.2211733

2. HIGH ENERGY FIBRE LASER FOR WIDEFIELD PHOTOACOUSTIC TOMOGRAPHY

A compact fibre laser system was developed that comprises a superluminescent diode as a seed source and a cascade of 4 Ytterbium-doped fibre amplifier (YDFA) stages, forming an MOPA. A schematic and a photograph of the system are shown in figures 1 (a) and (b), respectively. The final amplification stage used a custom drawn large core diameter (100 µm) fibre to obtain pulse energies up to 5mJ. The system provides variable pulse durations (10 to 150ns) and pulse repetition frequencies (100 to 400Hz) and the emission wavelength was 1064nm. The system was compact (25 × 30 × 30cm) and did not require water cooling.

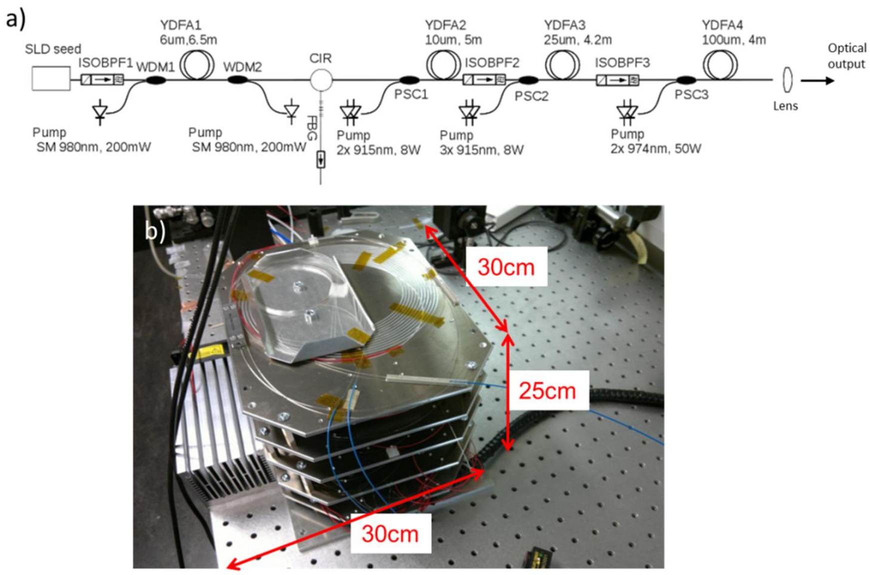

Figure 1: (a) Schematic of the fibre laser (SLD: superluminescent diode, CIR: circulator, YDFA: Ytterbium doped fibre amplifier, ISOBPF: fibre optic isolator with integrated band pass filter, WDM: Wavelength division multiplexer, PSC: pump signal combiner) (b) photograph of the fibre laser

To illustrate the application of the fibre laser to widefield PAT, it was used in conjunction with a photoacoustic imaging system based on a planar Fabry Perot polymer film ultrasound sensor[8] as shown in figure 2(a). This system was used to acquire a 3D image of the vasculature in the human palm (see figure 2 (b)). The photoacoustic signals were recorded over a 12mm by 12mm area in steps of 100µm. The laser beam incident on the sample was 1.7cm in diameter, the PRF was 200Hz and the pulse duration was 20ns. The incident fluence was less than 2.2mJ/cm^2, which is below the Maximum Permissible Exposure (MPE) for skin. A time reversal image reconstruction algorithm [9] was used to form the photoacoustic image which is shown in figure 2 (c). The image acquisition time was approximately 90seconds.

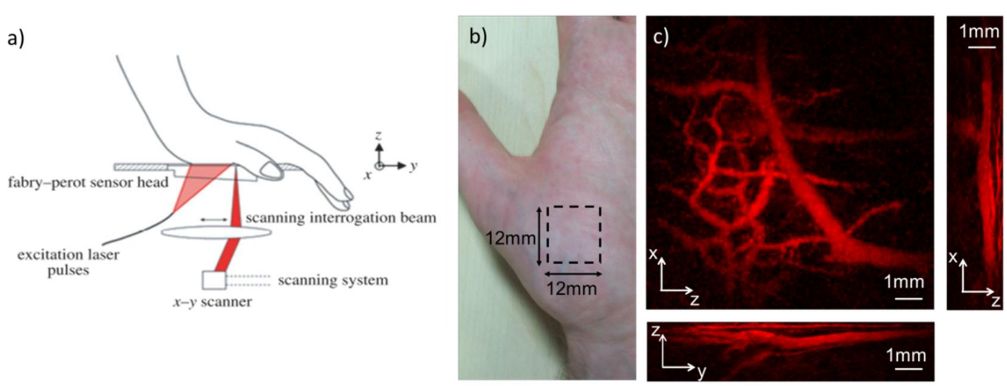

Figure 2: (a) Schematic of FP planar scanner[8] (b) photograph of a human palm (the dotted box indicates the imaged area) (c) x-y maximum intensity projection (MIP) of 3D image data set. (Below and right) y-z and x-z MIPs respectively.

3. HIGH PRF FIBRE LASER FOR OPTICAL RESOLUTION PHOTOACOUSTIC MICROSCOPY

The fibre laser developed for OR-PAM employed an injection locked Fabry Perot laser diode as the seed and a two stage fibre amplifier (see figure 3 (a)). Small core (<25µm) diameter Ytterbium-doped fibres were used to achieve a high quality beam ($M^2<1.1$). The output was frequency doubled using a Lithium triborate (LBO) crystal to obtain an excitation wavelength of 532nm. The pulse duration was 2ns, the pulse repetition frequency (PRF) was variable between 250kHz to 2MHz and the pulse energy was in the range 1 to 4µJ depending on PRF.

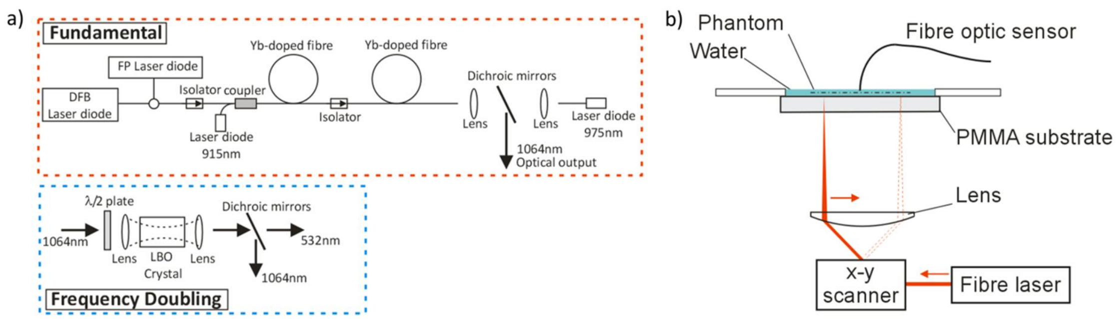

Figure 3: (a) Schematic of frequency doubled fibre laser system for OR-PAM (b) Experimental OR-PAM imaging setup[10]

To evaluate the laser, it was combined with a laser scanning optical resolution photoacoustic microscopy (LS-ORPAM) system [10] (see figure 3 (b)). The scanner comprised a pair of x-y galvanometers, which were used to continuously raster scan the focused excitation beam over the sample which was placed on a PMMA substrate. A fibre optic sensor [11], [12], comprising a Fabry Perot polymer film interferometer deposited on to the tip of an optical fibre, was used to detect the generated photoacoustic signals. The small active area (<10µm) of this type of ultrasound sensor provides a significantly larger angular detection aperture than conventional piezoelectric receivers. This enables large areas to be imaged without mechanically scanning either the detector or sample. As a consequence, high image acquisition rates limited only by the PRF of the excitation laser and the acoustic transit time can be achieved. The lateral resolution of the system was approximately 7µm, as defined by the spot diameter of the focused excitation beam light [10].

To illustrate the potential for fast acquisition, a leaf skeleton dyed with ink was imaged over an area of 1cm × 1cm in steps of 2.5µm. Carbon fibres (Ø7µm) were also placed in the imaging plane to illustrate the high spatial resolution. The PRF of the fibre laser was 1 MHz, enabling 16×10^6 A-lines (4000 × 4000 points) to be acquired in 16 seconds and the pulse energy was keep below 400nJ. The photoacoustic image is shown in figure 4 (a) and clearly shows the large features of the leaf structure as well as the 7µm carbon fibres.

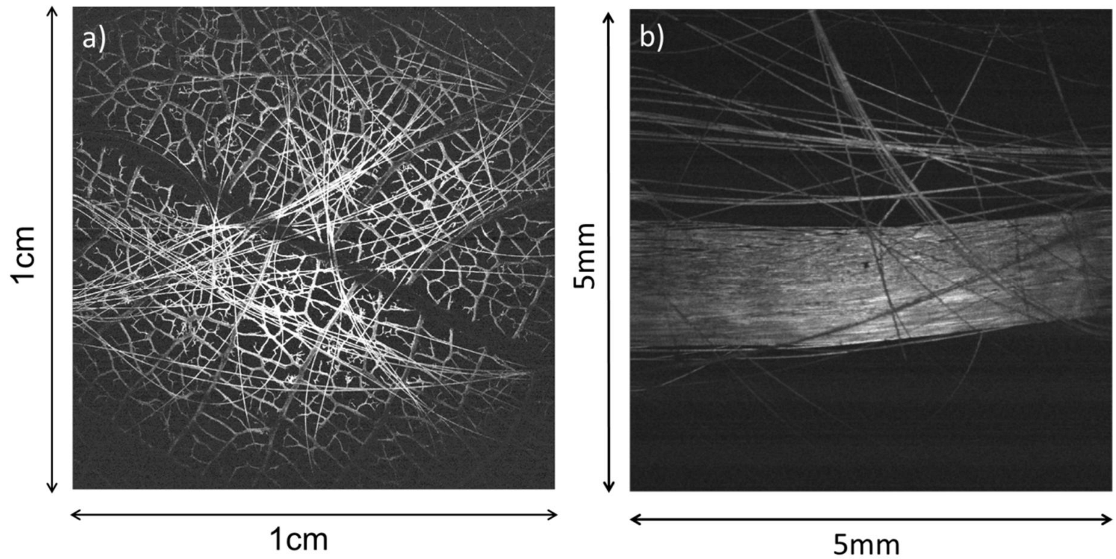

Figure 4: OR-PAM imaging. (a) Photoacoustic image of a phantom composed of a leaf skeleton dyed black and Ø7µm carbon fibres obtained using a PRF of 1MHz. The image comprises 4000×4000 detection points which were acquired in 16 seconds (b) photoacoustic image of Ø7µm carbon fibres obtained using a PRF of 2MHz. This image comprises 2000 × 2000 detection points which were acquired in 2 seconds.

To demonstrate the acquisition of an image with the fibre laser operating at a PRF of 2MHz, a second phantom composed of carbon fibres (Ø7µm) was imaged over an area of 5mm × 5 mm in steps of 2.5µm. The pulse energy was kept below 100nJ. The photoacoustic image is shown in figure 4 (b); this image consists of 4×10^6 A-lines which were acquired in 2s.

4. DISCUSSION AND CONCLUSION

A compact fibre laser system that can provide a pulse energy of 5mJ, a PRF of up to 400Hz and variable pulse durations in the range 10ns-150ns has been developed. These output parameters are broadly consistent with those required for *in vivo* widefield PAT as illustrated by figure 2. However the 1064nm output wavelength of the laser is not optimal for most biomedical applications. Future work will therefore focus on increasing the pulse energy, frequency doubling the output and integrating the system with an OPO in order to access biologically relevant wavelengths in the visible and near-infrared.

A custom fibre laser suitable for OR-PAM has also been demonstrated. Its distinguishing advantage over commercially available fibre lasers previously used in OR-PAM is the significantly higher PRF (2MHz) it can provide. It was shown that the LS-ORPAM scanner could exploit this capability in order to acquire an unprecedented 2×10^6 A-Lines per second enabling large areas (>1cm) to be imaged within a few seconds. Future work will be directed towards frequency tripling the output of the fibre laser in order to pump an OPO to permit access to visible wavelengths in the 410-650nm range for spectroscopic applications.

In summary, this study has shown that fibre laser technology can provide a range of compact and robust excitation sources with added functionality for photoacoustic tomography and microscopy. It is anticipated, that this will aid the translation of photoacoustic imaging from the laboratory to practical applications in medicine and biology.

ACKNOWLEDGEMENT

This work has been supported by Engineering and Physical Science Research Council (EPRSC) UK, FAMOS (FP7 ICT, Contract 317744).

REFERENCES

[1] D. Richardson, J. Nilsson, and W. Clarkson, "High power fiber lasers: current status and future perspectives [Invited]," *JOSA B*, vol. 27, no. 11, pp. B63–B92, 2010.

[2] T. J. Allen, S. Alam, E. Z. Zhang, J. G. Laufer, D. J. Richardson, and P. C. Beard, "Use of a pulsed fibre laser as an excitation source for photoacoustic tomography," *Proc. SPIE*, vol. 7899, pp. 78991V–1–78991V–6, 2011.

[3] W. Shi, S. Kerr, I. Utkin, J. Ranasinghesagara, L. Pan, Y. Godwal, R. J. Zemp, and R. Fedosejevs, "Optical resolution photoacoustic microscopy using novel high-repetition-rate passively Q-switched microchip and fiber lasers," *J. Biomed. Opt.*, vol. 15, no. 5, p. 056017, 2010.

[4] W. Shi, P. Hajireza, P. Shao, A. Forbrich, and R. J. Zemp, "In vivo near-realtime volumetric optical-resolution photoacoustic microscopy using a high-repetition-rate nanosecond fiber-laser," *Opt. Express*, vol. 19, no. 18, pp. 17143–17150, 2011.

[5] Y. Wang, K. Maslov, Y. Zhang, S. Hu, L. Yang, Y. Xia, J. Liu, and L. V. Wang, "Fiber-laser-based photoacoustic microscopy and melanoma cell detection," *J. Biomed. Opt.*, vol. 16, no. 1, p. 011014, 2011.

[6] H. Kang, S.-W. Lee, E.-S. Lee, S.-H. Kim, and T. G. Lee, "Real-time GPU-accelerated processing and volumetric display for wide-field laser-scanning optical-resolution photoacoustic microscopy," *Biomed. Opt. Express*, vol. 6, no. 12, p. 4650, 2015.

[7] J. Yao, L. Wang, J. Yang, K. I. Maslov, T. T. W. Wong, L. Li, C. Huang, J. Zou, and L. V Wang, "High-speed label-free functional photoacoustic microscopy of mouse brain in action," *Nat. Methods*, vol. 12, no. 5, pp. 407–414, 2015.

[8] E. Zhang, J. Laufer, and P. Beard, "Backward-mode multiwavelength photoacoustic scanner using a planar Fabry-Perot polymer film ultrasound sensor for high-resolution three-dimensional imaging of biological tissues.," *Appl. Opt.*, vol. 47, no. 4, pp. 561–577, Mar. 2008.

[9] B. E. Treeby and B. T. Cox, "k-Wave: MATLAB toolbox for the simulation and reconstruction of photoacoustic wave fields," *J. Biomed. Opt.*, vol. 15, no. 2, p. 021314, 2010.

[10] T. J. Allen, E. Zhang, and P. C. Beard, "Large-field-of-view laser-scanning OR-PAM using a fibre optic sensor," in *Proc. of SPIE, Photons Plus Ultrasound: Imaging and Sensing*, 2015, vol. 9323, p. 93230Z.

[11] E. Z. Zhang and P. C. Beard, "A miniature all-optical photoacoustic imaging probe," in *Proceedings of SPIE*, 2011, vol. 7899, pp. 78991F–1– 78991F–6.

[12] E. Z. Zhang and P. C. Beard, "Characteristics of optimized fibre-optic ultrasound receivers for minimally invasive photoacoustic detection," in *Proc. of SPIE, Photons Plus Ultrasound: Imaging and Sensing*, 2015, vol. 9323, pp. 932311–1–9.