Photoacoustic Generation Mechanisms and Measurement Systems for Biomedical Applications

Siridech Boonsang, Member

ABSTRACT

Pulsed photoacoustic techniques for measurements in non-destructive evaluation (NDE) and for non-invasive characterization of tissues have been an increasingly attractive research area for over a decade. The physical principle underlying these techniques is based on the opto-thermal response of an absorbing media from pulsed laser sources. Resulting acoustic waves are generated by the thermal expansion of absorbing volume within the irradiated material. Such waveforms contain valuable information about the optical properties of media, which can be utilized for diagnostic information such as the level of oxygenation in tissue or structure information within tissue. Several research groups have proposed medical diagnostic systems based on pulsed photoacoustic methods. These include intra-arterial imaging and therapy, the monitoring of glucose level, the monitoring of cerebral blood oxygenation, the functional and structural imaging of brain, the monitoring the interface tissue layer within eye, and a diagnostic system for breast cancer. This review paper presents the extensive review of the pulsed photoacoustic techniques for biomedical applications.

Keywords: photoacoustic; photoacoustic generation; photoacoustic wave

1. INTRODUCTION

Photoacoustic techniques have become more attractive for many applications in non-destructive testing and evaluation (NDT&E) and there is now a growing trend to be investigated for several potential biomedical applications. The first quantitative analysis of laser ultrasonic measurements was taken about twenty year ago (Scruby et al. 1980; Dewhurst et al. 1982). Theoretical treatment of laser-generated ultrasound has been published sometime afterwards [1]. Up until now, there are several commercial laser ultrasonic systems developed and applied for industrial NDE applications. In terms of biomedical applications, the first demonstration of photoacoustic techniques was an integral photoacoustic probe for a potential application of laser angioplasty proposed by Chen et al. in 1993 [2][3][4]. Since then, several researchers have been extensively investigated this phenomenon and have already proposed photoacoustic systems that may be valuable for many medical treatments and diagnostics. This paper provides the short reviews of the photoacoustic generation mechanisms. The applications of photoacoustic wave generation for medical treatments such as photoacoustic ablation or transdermal drug transfer are also discussed. Toward the end of the paper, the review details the recent development in biomedical photoacoustic systems.

2. BACKGROUND THEORY

Acoustic generation in liquids or gases by the interaction of laser irradiation can be based on various mechanisms. These include dielectric breakdown, vaporization or material ablation, thermoelastic process, electrostriction and the irradiation pressure [5]. Dielectric breakdown is the most efficient mechanisms among those five processes in term of the energy conversion from laser energy to acoustic energy. There is the report that the conversion efficiency could be up to 30% in liquid [6]. This mechanism requires extremely high laser intensities above 10^{10} W.cm^{-2}. For the absorption of laser intensities below breakdown, vaporization process can be responsible for the generation of acoustic wave. If the absorbed energy (from laser irradiation) exceeds the boiling threshold (2,600 J.cm^{-3} for the case of water), vapour is ejected from the surface. This vaporization process also produces so-called recoil stresses that pass on a momentum to the absorbing medium. Measurements of recoil stresses produced from the irradiation of a nanosecond pulsed laser on to the sample surface have been made by direct pressure measurement using piezoelectric transducers [7][8][9][10]. For example, the average peak pressure for skin vaporization at the radiant exposure of 20 J.cm^{-2} was about 0.3 MPa [11]. The energy conversion efficiency for vaporization process can be up to 1% in liquid [6].

Thermoelastic process is caused by the transient heating (by the absorption of laser irradiation) of a constrained volume within an absorbing medium [1]. The resulting temperature gradient produces the thermal expansion, which consecutively radiate acoustic wave propagating away from the heated

Manuscript received on June 15, 2009 ; revised on July 15, 2009.

S. Boonsang is with the Faculty of Engineering, King Mongkut's Institute of Technology LadkrabangLad, krabang, Bangkok, 10520

E-mail address: siridecb@gmail.com

zone. The energy conversion efficiency of this process is relatively low: for example, the conversion efficiency of laser to stress wave is only 1.3×10^{-6} for thermoelastic pressure amplitude of one bar generated in water [12]. However, this process is more attractive for non-destructive evaluation of tissues because it has relatively less thermal effect on the medium (no phase change within the medium).

The non-destructive and reversible features of photoacoustic generation in thermoelastic regime have made it attractive for many applications in medical diagnostic. Several medical applications i.e. breast cancer detection [13] based on this regime have been reported.

3. BIOLOGICAL EFFECTS OF PHOTOACOUSTIC WAVES

Biological effects of laser irradiation have been extensively studied since the commencement of the application of laser in medical researches [14]. The stress wave or pressure wave as a result from laser irradiation can be generated from either ablation or rapid heating in thermoelastic regime. Characteristics and effects of the pressure wave in ablation regime is thoroughly discussed in the paper [15]. In thermoelastic regime, however, the characteristic of pressure wave is more complex than that in ablation regime [15]. The interaction of biological tissue and photoacoustic wave in this regime involves complicated processes [15][12]. The exact nature of interaction of thermoelastic photoacoustic wave with biological tissues is comprehensively under investigated. The studies of biological effects of photoacoustic wave can be categorised in two main themes. Firstly, combined effects of laser irradiation, heating effects, cavitation and pressure waves have been considered with the laser pulse energies below the complete vaporized ablation threshold [12][16][17][18]. In this theme, their research emphasised on the pressure wave mechanic and its physical effects in tissue level. The term so-called “photomechanical ablation” is usually employed to describe this effect. In the other hand, the second theme involved the investigation of solely pressure wave effect on biological tissues [15]. Their approaches were to generate the pressure wave outside cell cultures by using a highly absorbing material (polyimide or polystyrene) as a laser target. The resulting high-amplitude (several hundred bar) pressure wave propagates into the medium containing cells under investigation [19][20]. By this arrangement setup, the effects of laser irradiation, heat and cavitation were minimized.

Ablation techniques based on laser irradiation are mainly based on three processes namely: photothermal, phochemical and photomechanical decompositions [21]. Photothermal decomposition refers to tissue ablation by vaporization of irradiated tissues to relatively high temperatures (normally more than boiling threshold). Photochemical decomposition is principally caused by the chemically interaction of tissue molecules with photon energies, resulting in the fracture of chemical bonds [21]. These two processes require relatively high laser intensity in order to achieve the effective ablation. In contrast, photomechanical ablation process in thermoelastic regime firstly reported by Dingus and Scammon requires the laser energy density 10 times less than that for the complete vaporization [22]. This process has the implication of providing a controlled ablation method with the minimum damage to remaining tissues. The mechanism of photomechanical process has been extensively studied [12][18][22][23]. Good description of the mechanism of photomechanical ablation presented by Paltauf et al.[12] is shown in Figure 1.

A short laser pulse (short enough to create pressure waves under thermal and stress confinements) is used to generate thermoelastic stress in a tissue (Figure 1(a)). The initial pressure distribution within the tissue is determined by the optical absorption coefficient, which is assumed constant. This initial pressure distribution is entirely positive or compressive stress acting in the perpendicular direction to the surface. Thermoelastic pressure wave propagates in the right hand side direction with the speed of sound in tissue. Due to acoustic mismatch at the tissue-air interface, the negative pressure (tensile stress) is created (Figure 1(b)). Since most of tissue materials are weaker in tension rather than compression, the material will fail whenever the imposed tensile stress exceeds its threshold σ^*. If the negative pressure (tensile stress) is about the threshold (Figure 1(c)), it may cause the tissue fracture or cavitation at a certain depth[18] (Figure 1(d)) and followed by the ejection of the tissue fragment at the front surface (Figure 1e)). The term “photospallation” has been used to describe this effect [24][12]. It is worth noting here that not only the tensile stress but also the heating contributes to the material ablation [12].

The photomechanical ablation threshold (normally described in term of energy density as the product of I0) for biological tissue is similar to that of water. Oraevsky et al. [25] reported the ablation thresholds for the aqueous solution, collagen gel, and liver were 20, 38, and 55 J.cm^{-3}, respectively, which correspond to temperature increment of 5, 10, and 15 °C. Paltauf et al. [18] reported that the thresholds of both water and gelatine are linearly proportional to the absorption coefficient of a sample. The value of the threshold is in the range of several hundred J.cm^{-3}, which is greatly lower than the vaporization threshold of water (2,600 J.cm^{-3} for the case of water). The difference between these two reports may be caused by the different methods of measurements.

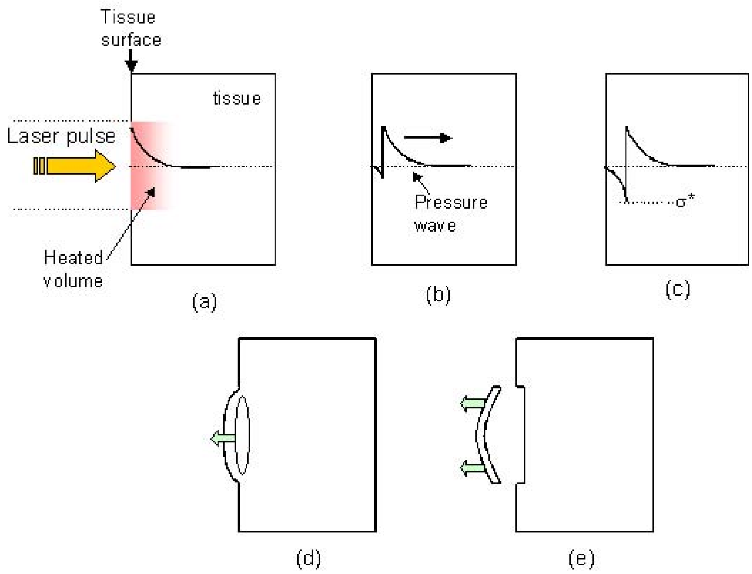

Fig.1: *Mechanism of photomechanical ablation. Tissues front surface is "spalled" by thermoelastic pressure generated by a short laser pulse. Adapted from Paltauf et al.[12].*

4. PHOTOACOUSTIC MEASUREMENT SYSTEMS AND APPLICATIONS

The first published description of photoacoustic system developed at DIAS, UMIST was in 1993 [2]. The probe consisted of a 600 m diameter fibre-optic laser beam delivery system combined with a polymer (PVDF) transducer mounted at the tip of the probe for ultrasonic reception. Such an integral probe was designed to optically transmit and receive near on-axis ultrasonic transients.

Figure 2 illustrates the schematic diagram of the probe. The inner diameter of an annular PVDF film was slightly larger than the diameter of an optical fibre, in order to allow the delivery of laser pulses from the fibre tip. The thickness of annular PVDF film was 9 μm. Silver loaded epoxy was used for both backing material and electrically conducting material to a signal wire. Insulating Perspex shell was employed as the housing of the probe. Photoacoustic signals from the probe were amplified by an external broadband amplifier.

Characteristics of received signals were extensively studied [26][27][28]. A parameter model was used to predict photoacoustic signals at the output of an ultrasonic receiver in both forward and backward mode. A classical damped oscillation model was employed to explain the pressure-to-voltage response of an ultrasonic receiver. Pressure waves at a receiver were calculated by solving the one-dimensional opto-thermal expression. A system identification approach was used to determine the key parameters of transducer behaviour. The response function predicted voltage signal using three constants to define transducer response characteristics. Good agreement with experimental waveforms was demonstrated. Potential applications of the probe are for laser angioplasty, ophthalmology have been demonstrated [2][29][30][31]. In addition, this probe was also used to construct 2D image using synthetic aperture techniques [32]. The resolution of the resulting image of 400 μm was achieved.

Photoacoustic measurement systems in both backward detection [33] and forward detection modes [34] have been proposed by Oraevsky et al. In backward detection mode (Figure 3(a)), the probe consists of an optical fibre (1) was used to deliver laser pulses. The laser beam was focused by lens (2) onto the rear surface of quartz prism (3). The prism acted as the transmission of laser light on to a sample (4). The angle of incident was about 16^o. Photoacoustic pressures generated from the laser pulses propagate backward within the prism. Piezoelectric transducer (5) (bandwidth about 100 MHz [33]) was used to detect photoacoustic pressures at the normal direction to the sample surface. Preamplifier (6) was directly connected to the transducer and it transforms the output impedance of transducer to match the 50 Ω of a data acquisition system. The characteristics of photoacoustic pressures detected in the backward mode are systematically described in the paper [33].

Several potential applications of backward detection probe have been demonstrated. These include imaging of layered structures in biological tissues [35], monitoring of cerebral blood oxygenation [36][37], monitoring optical properties of blood [38]. In the case of monitoring of blood oxygenation, two laser systems of Nd:YAG and Alexandrite were used to provide laser pulses of the wavelength of 1,064 and 750 nm respectively. Blood oxygenation is the measure of oxyhemoglobin saturation, which is determined by the concentration of oxyhemoglobin and

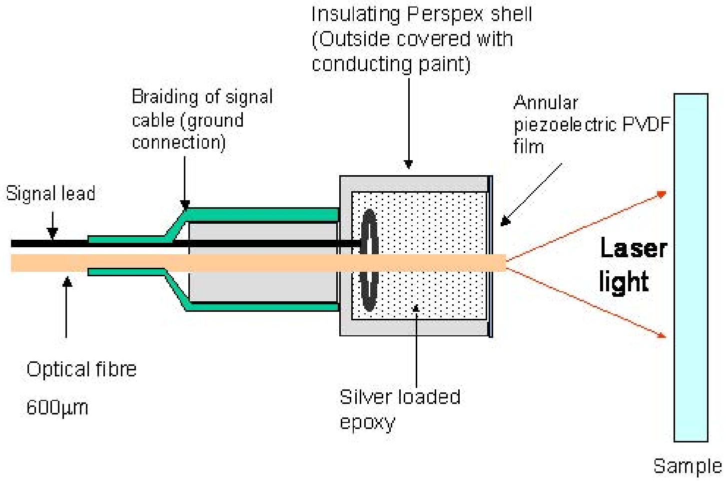

Fig.2: *Schematic diagram of a photoacoustic probe developed at DIAS, UMIST. Adapted from A. Kuhn [26][27]*

deoxyhemoglobin. Since both oxy- and deoxyhemoglobin have different absorption at both laser wavelength, therefore the measured optical absorptions at both two wavelengths could provide the information of blood oxygenation [37][38].

For imaging purpose, Oraevsky et al. also proposed a forward detection array system shown in Figure 3(b). The system comprises of an Nd:YAG laser (Big sky laser) providing laser pulses (1,064 nm wavelength) with repetition rate of 20 Hz. Laser pulses was delivered on to a sample via 1mm optical fibre and expansion lens. The diameter of a circular laser beam was 8 mm. The laser intensities used was about 10-20 mJ.cm^{-2}.

The detection of photoacoustic pulse was achieved by a specially designed arc array of PVDF transducers. The array had 32 rectangular (1.5×1.5 mm) PVDF elements. The thickness of PVDF transducer was 110 μm. They claimed that the sensitivity of PVDF transducer was about 6 V.Pa^{-1} [39]. The minimum detectable pressure of 6 Pa was estimated by using theoretical noise level generated from a capacitor of the PVDF film. However, it is worth noting here that this minimum detectable figure was not considered noises contributed from an amplifier and a power supply, which sometime dominate the actual pressure signal output. The performance of the system was tested using a gelatine phantom containing absorbing spheres. The gelatine phantom optical properties were about the same as breast tissues. To simulate tumours in breast tissues, the 7-mm absorbing spheres were made of the same gelatine colored with bovine haemoglobin. The resulting photoacoustic image is shown in Figure 4(b). The image shows the correct positions of absorbing spheres with relatively larger diameter (about 10 mm) than the real absorbing spheres. This indicates the limitation of the system resolution. However, in their paper [39], they claimed that the best resolution of 1 mm was achieved.

5. CONCLUSION

This paper presents the review of photoacoustic generation and its biological effects. Some applications such as photoacoustic ablation as the implication from the studies of biological effects of photoacoustic waves are also described. The extensive review of recent development in photoacoustic measurement systems and biomedical applications is also given.

References

[1] D. A. Hutchins, "Ultrasonic Generation by Pulsed Lasers," *Physical Acoustics* 18, pp. 21-123, 1988.

[2] Q. X. Chen, A. Davies, R. J. Dewhurst and P. A. Payne), "Photoacoustic Probe for Intraarterial Imaging and Therapy," *Electronics Letters* 29(18), pp. 1632-1633, 1993.

[3] Q. X. Chen, A. Davies, R. J. Dewhurst and P. A. Payne, "Photoacoustic Probe for Intraarterial Imaging and Therapy," *Electronics Letters* 29(18), pp. 1632-1633, 1993.

[4] Q. X. Chen, R. J. Dewhurst, P. A. Payne and B. Wood, "A New Laser-Ultrasound Transducer for Medical Applications," *Ultrasonics* 32(4), pp. 309-313, 1994.

[5] M. W. Sigrist, "Laser Generation of Acoustic-Waves in Liquids and Gases," *Journal of Applied Physics* 60(7), pp. R83-R121, 1986.

[6] L. M. Lyamshev and K. A. Naugolnykh, "Optical-Generation of Sound - Non-Linear Effects," *Soviet Physics Acoustics-Ussr* 27(5), pp. 357-371, 1981.

[7] F. W. Cross, R. K. Aldhahir, P. E. Dyer and

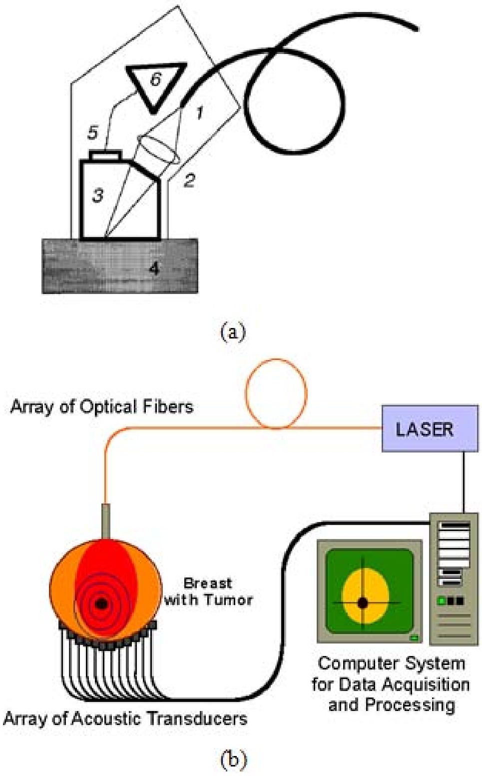

Fig.3: *Schematic diagrams of (a) backward detection probe (b) forward detection array developed by Oraevsky et al. Adapted from Karabutov et al. and Oraevsky et al.[33]; Oraevsky et al. [38]*

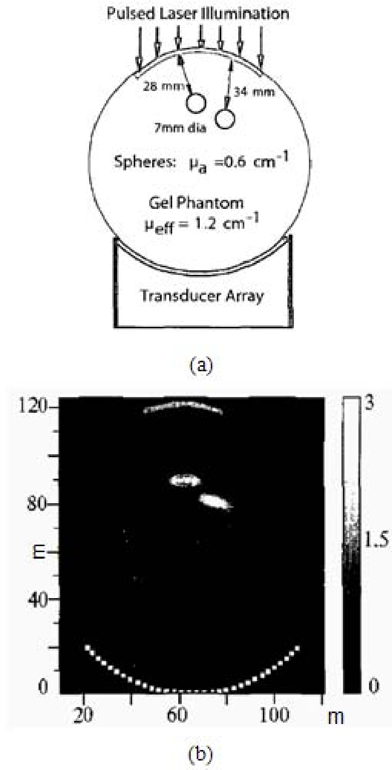

Fig.4: *(a) Experimental geometry and optical properties of a gelatine phantom used in forward detection array measurement. (b) Photoacoustic image of two absorbing spheres in a gelatine phantom detected by an array of 32 transducers is marked by an arc dots. Adapted from V. G. Andreev et al. [39]*

A. J. Macrobert, "Time-Resolved Photoacoustic Studies of Vascular Tissue Ablation at 3 Laser Wavelengths," *Applied Physics Letters* 50(15), pp. 1019-1021, 1987.

[8] F. W. Cross, R. K. Aldhahir and P. E. Dyer, 1988), "Ablative and Acoustic Response of Pulsed Uv Laser-Irradiated Vascular Tissue in a Liquid Environment," *Journal of Applied Physics* 64(4), pp. 2194-2201.

[9] V. Venugopalan, N. S. Nishioka and B. B. Mikic, "The Thermodynamic Response of Soft Biological Tissues to Pulsed Ultraviolet-Laser Irradiation," *Biophysical Journal* 69(4), pp. 1259-1271, 1995.

[10] V. Venugopalan, N. S. Nishioka and B. B. Mikic, "Thermodynamic response of soft biological tissues to pulsed infrared-laser irradiation," *Biophysical Journal* 70(6), pp. 2981-2993, 1996.

[11] J. P. Cummings and J. T. Walsh, "Tissue Tearing Caused by Pulsed Laser-Induced Ablation Pressure," *Applied Optics* 32(4), pp. 494-503, 1993.

[12] G. Paltauf and P. E. Dyer, "Photomechanical processes and effects in ablation," *Chemical Reviews* 103(2), pp. 487-518, 2003.

[13] A. A. Oraevsky, V. A. Andreev, A. A. Karabutov, D. R. Fleming, Z. Gatalica, H. Singh and R. O. Esenaliev Laser opto-acoustic imaging of the breast, pp. *Detection of cancer angiogenesis. Optical Tomography and Spectroscopy of Tissue III,* Proceedings Of. 3597, pp. 352-363, 1999.

[14] L. R. Solon, R. Aronson and G. Gould, "Physiological Implications of Laser Beams - Very High Radiation Flux Densities of Optical Masers Point to Important Biomedical Applications," *Science* 134(348), pp. 1506-&, 1961.

[15] A. G. Doukas and T. J. Flotte, "Physical characteristics and biological effects of laser- induced stress waves," *Ultrasound in Medicine and Biology* 22(2), pp. 151-164, 1996.

[16] D. Albagli, M. Dark, L. T. Perelman, C. Vonrosenberg, I. Itzkan and M. S. Feld, "Photomechanical Basis of Laser-Ablation of Biological Tissue," *Optics Letters* 19(21), pp. 1684-1686, 1994.

[17] D. Albagli, M. Dark, C. Vonrosenberg, L. Perelman, I. Itzkan and M. S. Feld, "Laser-Induced Thermoelastic Deformation - a 3-Dimensional Solution and Its Application to the Ablation of Biological Tissue," *Medical Physics* 21(8), pp. 1323-1331, 1994.

[18] G. Paltauf and H. SchmidtKloiber, "Microcavity dynamics during laser-induced spallation of liquids and gels," *Applied Physics a-Materials Science & Processing* 62(4), pp. 303-311, 1996.

[19] A. G. Doukas, D. J. McAuliffe and T. J. Flotte, "Biological Effects of Laser-Induced Shock-Waves - Structural and Functional Cell-Damage Invitro," *Ultrasound in Medicine and Biology* 19(2), pp. 137-146, 1993.

[20] A. G. Doukas, D. J. McAuliffe, S. Lee, V. Venugopalan and T. J. Flotte, "Physical Factors Involved in Stress-Wave-Induced Cell Injury - the Effect of Stress Gradient," *Ultrasound in Medicine and Biology* 21(7), pp. 961-967, 1995.

[21] R. S. Dingus and R. J. Scammon. Gruneisen-Stress Induced Ablation of Biological Tissue. Proceedings of Laser-Tissue Interaction Ii. Bellingham, *SPIE - Int. Soc. Optical Engineering.* 1427, pp. 45-54, 1991.

[22] I. Itzkan, D. Albagli, M. L. Dark, L. T. Perelman, C. Vonrosenberg and M. S. Feld, "The Thermoelastic Basis of Short Pulsed-Laser Ablation of Biological Tissue," *Proceedings of the National Academy of Sciences of the United States of America* 92(6), pp. 1960-1964, 1995.

[23] G. Paltauf and H. Schmidtkloiber, "Model Study to Investigate the Contribution of Spallation to Pulsed-Laser Ablation of Tissue," *Lasers in Surgery and Medicine* 16(3), pp. 277-287, 1995.

[24] H. J. Hoffman and W. B. Telfair, "Photospallation, pp. A new theory and mechanism for mid-infrared corneal ablations," *Journal of Refractive Surgery* 16(1), pp. 90-94, 2000.

[25] A. A. Oraevsky, S. L. Jacques, R. O. Esenaliev and F. K. Tittel, "Pulsed laser ablation of soft tissues, gels, and aqueous solutions at temperatures below 100 degrees C," *Lasers in Surgery and Medicine* 18(3), pp. 231-240, 1996.

[26] Q. Shan, A. Kuhn and R. J. Dewhurst, "Characterization of polymer ultrasonic receivers by a photoacoustic method," *Sensors and Actuators a-Physical* 57(3), pp. 187-195, 1996.

[27] Q. Shan, A. Kuhn, P. A. Payne and R. J. Dewhurst, "Characterisation of laser-ultrasound signals from an optical absorption layer within a transparent fluid," *Ultrasonics* 34(6), pp. 629-639, 1996.

[28] K. A. Roome, P. A. Payne and R. J. Dewhurst, "Towards a sideways looking intravascular laser-ultrasound probe," *Sensors and Actuators, A:Physical* 76, pp. 197-202, 1999.

[29] A. Sadr, P. A. Payne, E. S. Rosen and R. J. Dewhurst. *Laser-generated ultrasound in the eye. Nondestructive Characterization of Materials* Ix. Woodbury, AIP PRESS. 497, pp. 142-148, 1999.

[30] P. A. Payne, A. Sadr, E. S. Rosen and R. J. Dewhurst. Ophthalmic applications of laser-generated ultrasound. Ophthalmic Technologies X. Bellingham, *Spie-int society optical engineering.* 1, pp. 13-22, 2000.

[31] A. Sadr, P. A. Payne, E. S. Rosen and R. J. Dewhurst. Laser-ultrasound for interface monitoring within the eye. *Acoustical Imaging,* Vol 25. New York, Kluwer academic / PLENUM PUBL. 25, pp. 549-554, 2000.

[32] S. Boonsang, J. Zainal and R. J. Dewhurst, "Synthetic aperture focusing techniques in time and frequency domains for photoacoustic imaging," *Insight* 46(4), pp. 196-199, 2004.

[33] A. A. Karabutov, E. V. Savateeva, N. B. Podymova and A. A. Oraevsky, "Backward mode detection of laser-induced wide-band ultrasonic transients with optoacoustic transducer," *Journal of Applied Physics* 87(4), pp. 2003-2014, 2000.

[34] A. A. Oraevsky, A. A. Karabutov, S. V. Solomatin, E. V. Savateeva, V. G. Andreev, Z. Gatalica, H. Singh and R. D. Fleming. Laser optoacoustic imaging of breast cancer in vivo. Biomedical Optoacoustics Ii. Bellingham, *Spie-int society optical engineering.* 2, pp. 6-15, 2001.

[35] A. A. Karabutov, E. V. Savateeva and A. A. Oraevsky. Imaging of layered structures in biological tissues with opto- acoustic front surface transducer. *Laser-Tissue Interaction X, pp. Photochemical, Photothermal, and Photomechanical,* Proceedings Of. 3601, pp. 284-295, 1999.

[36] R. O. Esenaliev, Y. Y. Petrov, M. Klasing, D. S. Prough, D. J. Deyo and M. Motamedi. Optoacoustic technique for noninvasive, real-time monitoring of cerebral blood oxygenation. Leos 2001, pp. *14th Annual Meeting of the IEEE Lasers & Electro- Optics Society,* Vols 1 and 2, Proceedings, pp. 192-193, 2001.

[37] R. O. Esenaliev, I. V. Larina, K. V. Larin, D. J. Deyo, M. Motamedi and D. S. Prough, "Optoacoustic technique for noninvasive monitoring of blood oxygenation, pp. a feasibility study," *Applied Optics* 41(22), pp. 4722-4731, 2002.

[38] E. V. Savateeva, A. A. Karabutov, S. V. Solomatin and A. A. Oraevsky. Optical properties of blood at various levels of oxygenation studied by time resolved detection of laser-induced pressure profiles. *Biomedical Optoacoustics III.* 3, pp. 63-75, 2002.

[39] V. G. Andreev, A. A. Karabutov and A. A. Oraevsky, "Detection of ultrawide-band ultrasound pulses in optoacoustic tomography," *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control* 50(10), pp. 1383-1390, 2003.

S. Boonsang received his bachelor degree (Honours) in electrical engineering from King Mongkut's Institute of Technology Ladkrabang (KMITL), Bangkok, Thailand, in 1995, MSc in electrical engineering (electronic instrumentation system) from University of Manchester Institute Science and Technology (UMIST), UK, in 2000 and PhD in instrumentation from the same university in 2004. He had been working in Engineering Department, Siam Cement Public Company for 5 years before he became a lecturer in the Electronics Department, Faculty of Engineering, KMITL, in 2005. His research area is in photonic and ultrasonic instrumentations for biomedical and NDE applications. Now he is also the associate director of College of Data Storage Technology and Applications at KMITL.