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2020

Sharma, A., Srishti, S., Periyasamy, V., & Pramanik, M. (2020). Monte Carlo simulations and photoacoustic experiments to compare imaging depth at 532 nm, 800 nm, and 1064 nm. Proceedings of SPIE - Photons Plus Ultrasound: Imaging and Sensing 2020, 11240, 145-. doi:10.1117/12.2544568

<https://hdl.handle.net/10356/146649>

<https://doi.org/10.1117/12.2544568>

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Monte Carlo simulations and photoacoustic experiments to compare imaging depth at 532 nm, 800 nm, and 1064 nm

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ABSTRACT

Photoacoustic imaging (PAI) is a rapidly growing imaging modality which offers the advantages of good optical contrast and high ultrasound resolution. Although PAI provides imaging depth beyond the optical diffusion limit, penetration depth in biological samples is limited due to absorption and scattering of light in tissues. Improvement in imaging depth has been achieved by irradiating the sample with laser pulses of near infrared-I (NIR-I) region (700 nm–900 nm) due to decreased scattering of light in tissues within this optical window. Recently, further improvement in imaging depth has been reported by irradiating the sample in near infrared-II (NIR-II) region (900 nm–1700 nm). In this work, imaging depth in breast tissues when samples were irradiated by wavelengths in different optical windows has been compared. Initially, Monte Carlo simulation for light propagation in biological tissues was performed to compute imaging depth for excitation wavelengths of 532 nm, 800 nm, and 1064 nm. Further, photoacoustic tomography at 532 nm, 740 nm, and 1064 nm and acoustic resolution photoacoustic microscopy at 570 nm and 1064 nm were conducted to validate the results. We have shown that maximum imaging depth is achieved by NIR-I (740 nm/ 800 nm) when surface energy for all wavelengths is kept constant. However, when the energy density is proportional to maximum permissible exposure (MPE) at corresponding wavelength, maximum imaging depth is achieved by 1064 nm (NIR-II window). Therefore, we conclude that increased MPE in NIR-II window is responsible for the improved penetration depth in breast tissue in this region.

Keywords: Photoacoustic imaging, imaging depth, near-infrared window, photoacoustic tomography, acoustic resolution photoacoustic microscopy, Monte Carlo simulation with embedded object

1. INTRODUCTION

Photoacoustic imaging (PAI) is a non-invasive imaging modality which is based on the principle of photoacoustic effect [1-4]. In this effect, absorption of light pulses by a sample results in generation of ultrasound waves. In photoacoustic imaging of biological tissues, the target tissue is irradiated with nanosecond pulsed laser. Absorption of laser pulses by chromophores present in tissue results in rise and fall in temperature leading to generation of ultrasound (photoacoustic) waves which can be detected using an ultrasound transducer (UST). Being a hybrid imaging modality, PAI provides the advantages of good optical contrast and high ultrasound resolution making it a promising tool for pre-clinical and clinical applications [5-7]. This imaging modality has therefore been employed for various applications such as sentinel lymph node (SLN) imaging [8], small animal whole body imaging [9], breast imaging [10, 11], brain imaging [12, 13], monitoring of hemoglobin concentration [14] etc.

PAI can be broadly classified as photoacoustic microscopy (PAM) and photoacoustic tomography/photoacoustic computed tomography (PAT/PACT) [15, 16]. PAM uses focused beam to illuminate the target and/or a focused ultrasound detector with high central frequency to acquire the generated PA waves. Raster scanning of the confocally aligned optical illumination and acoustic detection gives 3-dimensional volumetric image of the target sample [17]. On the other hand, in PAT the sample is homogeneously illuminated by laser pulses and single or multiple USTs are used to

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acquire photoacoustic (PA) waves from different angles around the sample [18, 19]. Reconstruction algorithms are used to process the collected PA waves and form cross-sectional images of the target. PAM configuration is generally employed for high resolution imaging while PAT finds more advantages during deep tissue imaging [20, 21].

Although PAI can provide higher imaging depth compared to purely optical imaging modalities, its imaging depth is limited by the wavelength of light used, optical properties of target sample, and optical properties of the background tissue. Increased imaging depth can be achieved by using illumination wavelength which has low scattering and low absorption in the background medium and high absorption in the target sample. Due to high absorption coefficient of blood in visible region (400 to 600 nm), imaging of vasculature is generally performed by irradiating the sample using light wavelengths in this window [22]. But the imaging depth during such illumination is quite low due to high absorption of visible light by surrounding biological tissue. Increase in imaging depth was obtained by illuminating samples using wavelengths in near-infrared I (NIR-I) region (700 to 900 nm) which have comparatively lower scattering in biological tissues [23, 24]. However, this increase in imaging depth also increased the cost of the system and made the system bulky as two stage lasers (Ti:sapphire, dye, or optical parametric oscillator (OPO)) were needed for generation of this wavelength. Last few years have seen a rise in use of near-infrared II (NIR-II) window (900 to 1700 nm) for sample illumination in PAI [10, 25]. In this range, there is a decrease in scattering of light, an increase in maximum permissible exposure of light illumination according to American National Standards Institute (ANSI) safety limit, and an increase in absorption of light by surrounding tissues and water [26]. Although the first two changes help in improving the imaging depth, the final one leads to a decrease in the same. To understand the effects of change in wavelength on imaging depth, a systematic study of all the variables is required.

In this work, we have compared the imaging depth of PAI in breast tissue due to illumination at 532 nm, 800 nm, and 1064 nm wavelengths. Initially, Monte Carlo simulations for light propagation in biological tissues were performed to simulate the propagation of light of different wavelength in breast tissue [27]. These simulations were further extended to study absorbance of light in a blood vessel and an absorbing sphere kept at different depths in breast tissue. Following these simulations, photoacoustic experiments were conducted to compare the imaging depths at 570 nm and 1064 nm in acoustic resolution photoacoustic microscopy (ARPAM) system and at 532 nm, 740 nm, and 800 nm in PAT system.

2. MATERIALS AND METHODS

2.1 Monte Carlo simulations

Monte Carlo simulations for light propagation in multilayered tissues (MCML) with embedded objects (MCEO) were altered to simulate fluence in breast tissues at different depth [28, 29]. Following this, a blood vessel or a spherical absorber (a sphere having absorption coefficient of 1.00 at all wavelengths) was placed in the breast tissue, and simulations were performed to compute absorbance in the embedded object. Cross-sectional views of simulation geometries at $Y = 0$ plane are shown in Figs. 1(a-c). Table 1 shows the optical properties of breast tissue, blood vessel, and spherical absorber which were used for computing the fluence and absorbance for different wavelengths.

Figure 1(a) shows the simulation geometry used for calculating fluence at various depths in breast tissue. 10^8 photons were launched in the form of an infinitely narrow collimated beam along the z-axis, inside a 30 cm thick breast tissue. Properties of tissue were manipulated to simulate wavelengths of 532 nm, 800 nm, and 1064 nm. The second geometry used for simulation was made by placing an infinitely long cylinder of 1 mm thickness inside the breast tissue. Optical properties of cylinder were similar to those of blood vessels at the three wavelengths. Vertical position of cylinder was varied from 1 to 6 cm in steps of 1 cm, to calculate absorbance in blood vessels at different depths.

Figure 1(c) shows the last simulation geometry wherein the blood vessel was replaced with a sphere of 1 cm diameter which had a constant absorption coefficient across all wavelengths and scattering coefficient equal to that of surrounding breast tissue. Depth of sphere was changed in manner similar to that of cylinder, and absorbance in sphere was calculated for all three wavelengths.

Table 1. Optical properties of tissue and objects used during Monte Carlo simulations: μ_a : absorption coefficient, μ_s : scattering coefficient, g : scattering anisotropy

Properties	μ_a (cm ⁻¹)			μ_s (cm ⁻¹)			g		
	532	800	1064	532	800	1064	532	800	1064
Breast tissue [30]	0.45	0.011	0.033	120	116	77	0.9	0.9	0.9
Cylinder [31]	224.8	3.8	4.5	727.8	767.3	592.6	0.9687	0.9833	0.9799
Sphere	1	1	1	120	116	77	0.9	0.9	0.9

Figure 1. (a-c) Cross-sectional view of simulation geometry at $y = 0$ during MC simulation for (a) only breast tissue, (b) tissue with blood vessel, and (c) tissue with spherical absorber. (d-i) Results of MC simulation showing (d, g) fluence in tissue, (e, h) absorbance in blood vessel, and (f, i) absorbance in sphere at different depths when surface energy at all wavelengths was (d-f) same (g-i) proportional to MPE

2.2 Acoustic resolution photoacoustic microscopy system

Laser pulses of 1064 nm wavelength were generated by a nanosecond diode-pumped solid-state laser (INNOSLAB, Edgewave, Wurselen, Germany) and of 570 nm were generated by using this laser in combination with the dye laser (Credo-DYE-N, Sirah dye laser, Spectra Physics, Santa Clara, California). Respective laser beams having a pulse repetition rate of 5000 Hz, were focused on multimode optical fiber followed by a conical lens and an optical condenser to enable loosely focused dark field illumination of the target sample. The PA signal generated after illumination from 570 nm and 1064 nm beams was acquired using a focused UST with central frequency of 50 MHz and 30 MHz, respectively. Confocal alignment of optical and acoustic beams was done in both the systems. The scanning head was connected to a three-axis motorized stage which was raster scanned over the sample to produce volumetric images of the same. The scanning head was immersed in a water tank having an imaging window sealed with polyethylene membrane, under which the sample was placed during imaging. Detailed system description has been reported earlier [32, 33].

2.3 Photoacoustic tomography system

Laser pulses of wavelengths 532 nm and 1064 nm were generated at a PRR of 10 Hz using a Q-switched Nd:YAG laser and of 740 nm were generated using this laser with a tunable dye OPO laser. Individual beams were guided through a series of mirrors and lenses to fall homogeneously on the imaging sample from the top. Circular scanning geometry in orthogonal mode was used to get cross sectional images of the sample. The generated PA signal was collected using a single element UST rotating continuously around the sample [34]. Placing both the UST and the sample in water helped in achieving better acoustic coupling of the sample.

2.4 Sample preparation

Two low density polyethylene tubes filled with blood and black ink, respectively, were used to compare the imaging depth of different wavelengths. Vasculature imaging is a commonly used application of PAI and therefore comparing the imaging depth of blood seemed important. Black ink has high absorption coefficient for all wavelengths and therefore was used to compare the imaging depth on using external contrast agent for respective wavelengths. Slices of different thickness of commercially available chicken breast tissue were stacked in the LDPE tubes to illustrate imaging at different depths.

2.5 Laser Power

Another method of improving the imaging depth is to increase the laser power illuminating the sample. However, the allowed surface fluence on biological tissues is governed by ANSI safety limit and depends on the wavelength of light and duration of exposure on the sample. For same time duration, permissible energy for NIR-II region is higher than that of NIR-I and visible region, relatively increasing the imaging depth of NIR-II. Simulations and experiments were first conducted using the same surface fluence for all wavelengths. Later, surface fluence for different wavelengths was made proportional to their respective MPE and imaging depths were again compared. Table 2 provides the MPE values for different wavelengths for exposure of greater than 10 seconds using a laser with PRR of 10 Hz.

Table 2: Per pulse MPE for different wavelengths for exposure of greater than 10 sec using laser with PRR of 10 Hz

Wavelength	532 nm	740 nm	800 nm	1064 nm
MPE/pulse [26]	20 mJ/cm ²	24 mJ/cm ²	32 mJ/cm ²	100 mJ/cm ²

3. RESULTS AND DISCUSSION

3.1 Monte Carlo simulations

Simulation results showing fluence in breast tissue, absorbance in blood vessel, and absorbance in spherical absorber are shown in Figs. 1(d, g), Figs. 1(e, h), and Figs. 1(f, i), respectively. Results obtained when same energy was used for all wavelengths are shown in Figs. 1(d-f) and when the energy for each wavelength was proportional to the MPE of that wavelength are shown in Figs. 1(g-i). Simulation results show a decrease in fluence and absorbance for all three wavelengths with an increase in depth. However, it can be observed that the decrease in fluence of 532 nm beam is steeper as compared to the other wavelengths, resulting in a corresponding rapid decrease in absorbance in blood vessel and spherical absorber. This may be attributed to high scattering of light in biological tissues at this wavelength. Further, a relatively low MPE restricts increase in imaging depth by increasing the laser power.

Further analysis of the results shows that when same laser power is used, fluence at higher depths is higher for 800 nm wavelength compared to 1064 nm wavelength. As can be shown in Table 1, although scattering in breast tissue at 1064 nm is less than that at 800 nm, absorbance in breast tissue is more at 1064 nm. The decreased absorption at 800 nm compensates for the increased scattering at that wavelength, resulting in overall higher laser fluence at this wavelength at deeper depths. However, making the surface fluence proportional to MPE, results in higher fluence for 1064 nm wavelength till an approximate depth of 4.5 cm. After this depth, the fluence in breast tissue becomes higher for 800 nm than for 1064 nm. Similar trend was observed for absorption in blood vessel and sphere. Absorption was higher for 800

nm wavelength when all wavelengths had the same fluence. However, when fluence was made proportional to MPE, absorption in the embedded objects was higher for 1064 nm till a depth of approximately 6 cm.

3.2 Photoacoustic experiments

ARPAM and PAT experiments were conducted to validate the results of MC simulations. Maximum amplitude projection (MAP) images obtained from ARPAM experiments and cross-sectional images obtained from PAT experiments are shown in Fig. 2 and Fig. 3, respectively. Same surface fluence was maintained for laser illumination at 570 nm and 1064 nm to obtain images shown in Figs. 2(a-g). Surface fluence of 1064 nm beam was then increased and made proportional to its MPE to obtain images shown Figs. 2(h-j). From the ARPAM images it was observed that an imaging depth of 3 mm could be achieved for 570 nm while the same laser fluence gave an imaging depth of 4 mm for 1064 nm illumination. However, increase in laser fluence of 1064 nm led to an increase in imaging depth for this wavelength. Thus, when surface fluence for both the wavelengths was proportional to their respective MPE, the achievable imaging depth for 1064 nm was more than double the imaging depth for 570 nm. It is however important to note that the tube containing blood was discernible in images obtained using 570 nm system and not in images by 1064 nm system. This is due to low absorption of blood at 1064 nm. Although the blood tube was visible when high laser power was used with less than 2 mm of tissue layer, those results led to overheating of black ink tube and therefore have not been included here.

Images obtained using PAT system after 532 nm, 740 nm, and 1064 nm illumination are shown in Figs. 2(a-c), Figs. 2(d-h), and Figs. 2(i-o), respectively. PAT images obtained when experiments were conducted by keeping the surface fluence for all wavelengths constant are shown in Figs. 2(a-m). An imaging depth of 10 mm was observed when sample was irradiated with 532 nm beam and of 25 mm when the sample was irradiated with 740 nm or 1064 nm beam. These results confirm that the imaging depth of 532 nm is less than that of 740 nm or 1064 nm. However, it was again observed that blood signal at lower depths was higher after 532 nm illumination compared to illumination in NIR range. It can be further noted that although the obtained imaging depth was same for both 740 nm and 1064 nm illumination, the signal to noise ratio at this depth was higher for 740 nm beam, implying that fluence at 25 mm depth was higher for this wavelength.

To further compare imaging depth within NIR range when laser fluence was proportional to MPE, experiments were conducted by changing the surface fluence of 1064 nm laser pulses. Surface fluence of 1064 nm beam was increased by approximately 4 folds, to make the fluence of 740 nm and 1064 nm beams proportional to their respective MPE. Increasing the surface fluence led to an increase in imaging depth to 35 mm for 1064 nm beam.

Figure 2: ARPAM images obtained after illumination of tubes containing blood (left tube) and ink (right tube) at (a-d) 570 nm and (e-l) 1064 nm wavelengths. Illumination energy was same in (a-i) and was increased in proportion to increase in MPE for (j-l). Values on top indicate the thickness of tissue placed on tubes during imaging. Scale bar is same as that shown in j.

Figure 3. PAT images obtained after illumination of tubes containing blood (left tube) and black ink (right tube) at (a-c) 532 nm, (d-h) 740 nm, and (i-p) 1064 nm wavelengths. Illumination energy was same in (a-m) and was increased in proportion to increase in MPE for (o, p). Values on top indicate the thickness of tissue placed on tubes during imaging. Scale bar is same as that shown in m.

3.3 Discussion

Both the simulation and experimental results suggest that the imaging depth in breast tissues for wavelength in visible range is lesser than that in NIR range. This is due to high absorption and high scattering in surrounding biological tissues and relatively low MPE. However, experimental results also showed that for lower imaging depth, visible region showed higher PA signal (and therefore higher signal to noise ratio) for blood, suggesting that such wavelengths should be employed for vasculature imaging at low imaging depths.

Similar pattern was observed while comparing imaging depth for the two near infrared windows in both simulations and experimental results. It was observed that for same surface fluence, higher imaging depth in breast tissue can be achieved for NIR-I region (740 nm or 800 nm). However, making the surface fluence proportional to MPE provides a higher imaging depth for 1064 nm wavelength, which is in NIR-II window. Therefore, although 1064 nm pulses show less scattering in biological tissues, high absorption of these pulses in the surrounding tissue leads to a lower imaging depth. Nevertheless, the imaging depth of 1064 nm can be increased by increasing the laser fluence irradiating the sample. This increase is limited for radiations in NIR-I due to lower MPE as per ANSI safety limit.

4. CONCLUSION

In this work, we have compared the imaging depth in breast tissues for three wavelengths in visible, NIR-I, and NIR-II ranges, respectively. Monte Carlo simulations were performed for the comparison and the results were validated through photoacoustic experiments. Both the simulations and the experiments suggested that although pulses in visible range (532 nm, 570 nm) have low imaging depth, they have high absorption of blood and therefore should be used during vasculature imaging at low imaging depths. We have further shown although high absorption of 1064 nm laser pulses in surrounding tissues limit their imaging depth, a higher MPE of this wavelength more than compensates for it. Therefore, 1064 nm wavelength can be a good option for deep tissue imaging.

ACKNOWLEDGEMENT

The authors would like to thank Singapore Ministry of Health's National Medical Research Council (No. NMRC/OFIRG/0005/2016:M4062012) for funding this research. Srishti would also like to thank NTU-India Connect Research program for providing her an opportunity to visit NTU, Singapore. The authors have no relevant financial interest in the manuscript and no other potential conflicts of interest to disclose.

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