Published in final edited form as:

J Biophotonics. 2013 June ; 6(6-7): 475–484. doi:10.1002/jbio.201200163.

Co-registered pulse-echo/photoacoustic transvaginal probe for real time imaging of ovarian tissue

Patrick D. Kumavor¹, Umar Alqasemi¹, Behnoosh Tavakoli¹, Hai Li¹, Yi Yang¹, Xiaoguang Sun², Edward Warych², and Quing Zhu^{*,1}

¹ Biomedical Engineering program and Electrical and Computer Engineering Department, University of Connecticut, 371 Fairfield Rd. U2157, Storrs CT 06269, USA

² OFS Fitel, LLC, 55 Darling Drive, Avon, CT 06001, USA

Abstract

We present the design and construction of a prototype imaging probe capable of co-registered pulse-echo ultrasound and photoacoustic (optoacoustic) imaging in real time. The probe consists of 36 fibers of 200 micron core diameter each that are distributed around a commercial transvaginal ultrasound transducer, and housed in a protective shield. Its performance was demonstrated by two sets of experiments. The first set involved imaging of blood flowing through a tube mimicking a blood vessel, the second set involved imaging of human ovaries *ex vivo*. The results suggest that the system along with the probe has great potential for imaging and characterizing of ovarian tissue *in vivo*.

Photoacoustic images of the polyethylene tubing filled with blood.

Keywords

co-registered ultrasound and photoacoustic imaging; optoacoustic imaging; ovarian tissue characterization; fiber assembly for high energy delivery; photoacoustic probe and system

* Corresponding author: zhu@engr.uconn.edu.

Author Biographies Please see Supporting Information online.

1. Introduction

Ovarian cancer accounts for more deaths than any other cancer involving the female reproductive system; it is the ninth most common cancer among women and ranks fifth in cancer deaths [1, 2]. This dismal outlook is in part due to the lack of efficacious screening techniques at the disposal of patients. The other reason is that ovarian cancer symptoms are rather vague and usually show up when the cancer has already metastasized to other parts of the body [1]. Statistics indicate that if ovarian cancer is found and treated before the cancer has spread outside the ovary, the chances of survival past 5 years is quite high. For example the epithelial ovarian cancer, the most common type of cancer, has a 5-year relative survival rate of 89% for stage 1 (least advanced stage), compared to 18% only for stage IV (most advanced stage). Unfortunately, only 15% of all ovarian cancers are found at this early stage [1, 2]. Detecting the early onset of ovarian cancer could therefore extend the life of patients by allowing for more effective treatment options [2, 3].

Photoacoustic tomography (PAT), also known as optoacoustic tomography (OAT), [4, 5] is an emerging imaging modality with a great potential to assist ultrasound in detecting ovarian cancer noninvasively via transvaginal approach [6, 7]. It is a hybrid modality that offers excellent optical contrast and good ultrasound resolution. In photoacoustic or optoacoustic imaging, a short-pulsed laser beam irradiates the target region and is absorbed by the chromophores present. This causes a small transient temperature rise with subsequent thermoelastic expansion that generates acoustic waves. These waves can be detected and measured with wideband ultrasound transducers. The acquired waves are then used to reconstruct, at ultrasound resolution, the optical absorption distribution of the chromophores. Optical absorption in the near-infrared region (NIR) is directly related to hemoglobin content. The abnormal growth of cancerous cells requires elevated supply of blood vessel network and oxygen than normal tissue, which triggers rapid growth of complex blood vessel networks or tumor angiogenesis. This makes PAT a potentially excellent tool to image tumor angiogenesis development and detect early stage ovarian cancer.

Optical fiber-based photoacoustic or optoacoustic imaging probes usually involve one or two fibers, or fiber bundles that are conveniently integrated with the ultrasound transducer to deliver light to the imaged tissue [8–24]. Single fibers, with small core diameters of several hundreds of microns [8–13] offer a more compact probe design, and hence are ideal for endoscopic and intravascular applications. The drawback to the small core size is the limitation imposed on the available laser energy densities that may be incident at their endfaces during coupling. As a result, single-fiber based probes are most suitable for imaging shallow lesions where only low level of laser light is needed. Besides, single fibers get more and more rigid with increasing core diameters. This situation does not make them amenable to easy bending for endoscopic or intravascular applications. Fiber bundles on the other hand have the advantages of relatively larger optically active areas and mechanical flexibility. The large areas allow them to be able to withstand much higher laser energy densities than their single fiber counterparts. Probes based on these bundles [14–24] are therefore suitable for imaging deeply seated targets in scattering media; their large areas allow high laser energy levels to be coupled into them without damage to the endface to obtain acceptable signal-to-noise ratios. The disadvantage with fiber bundles is that they

make the imaging probes bigger because of their large diameters. Moreover, they are generally more lossy in transmitting light compared to single fibers. This loss is the result of the interstitial spaces in the bundle, and the fiber cladding, both of which do not transmit the light.

In this paper, we present an experimental implementation of a co-registered pulse-echo/photoacoustic (PE/PAT) imaging probe for real-time non-invasive imaging of ovarian tissue *in vivo*. The probe consists of a commercial transvaginal ultrasound array integrated with 36, 200-micron core fibers from a pair of high-power fiber-optic beamsplitter assembly. Both transducer and fibers are housed in a homemade frame that protects the fragile fibers, as well as keep them from getting too close to the tissue and causing injury during imaging. The rest of the paper is organized as follows: Section 2 presents the Monte Carlo simulations of light fluence inside tissue at different imaging depths, design and implementation of the PE/PAT imaging probe, and the experimental setup used in acquiring all the images. The simulation and experimental results are presented in Section 3, followed by the discussion and summary in Section 4.

2. Materials and methods

2.1. Monte Carlo simulations

Figure 1 shows some light-source fiber configurations that may be realized for photoacoustic or optoacoustic imaging using 2, 6, 18, and 36 fibers distributed around a cylindrical-shaped transducer of 2 cm diameter, such as the one shown in Figure 3. Monte Carlo simulations [25] were performed for these configurations to evaluate their fluence distributions at different depths inside tissue. In the simulation, briefly, each photon with unity weight (w) is launched into the medium from a source position at an angle determined by the numerical aperture of the fiber. After that the photon propagates into the medium gradually with the random step size and scattering angle following the exponential probability distribution and Henyey-Greenstein phase function respectively. For each of these steps or scattering events, a fraction of the photon weight, $w \times (\mu_a / (\mu_s + \mu_a))$, is deposited in where μ_a and μ_s denote absorption and scattering coefficients respectively. The residual photon continues to propagate until it gets either transmitted from the boundaries, or its weight becomes smaller than a predefined threshold. This procedure is repeated for millions of photons, with the accumulated photon weights at each grid element corresponding to the absorbed energy. Finally, the fluence is obtained by dividing the absorbed energy with the local absorption coefficient.

Transvaginal imaging of ovaries requires light to first penetrate through approximately 1 cm vaginal muscle wall before reaching the ovary. Consequently, a semi-infinite two-layer scattering medium with a planar boundary was considered for the simulation. The first layer was modeled as the vaginal muscle wall of 1 cm thickness with muscle tissue absorption coefficient of $\mu_a = 0.03 \text{ cm}^{-1}$ and reduced scattering coefficient of $\mu_s' = 4 \text{ cm}^{-1}$. Soft tissue optical properties of $\mu_a = 0.02 \text{ cm}^{-1}$ and $\mu_s' = 8 \text{ cm}^{-1}$ was considered for the second layer. In the experimental setup, the face of the ultrasound (US) probe is painted white in order to provide higher light reflection and transfer the maximum fluence into the medium [26]. To

model this boundary condition, we assumed an effective reflection coefficient of 0.7 for the transducer face [20]. In the prototype PAT probe, the distal ends of the source fibers were located 10 mm above the US transducer face. This resulted in extended light sources due to each of the source fibers at the tissue surface, with a Gaussian beam profile of 1.6 mm beam radius. In order to model this extended source at the tissue surface in the MC simulation, it was discretized by generating 13 point sources that were distributed in a circular area of radius 1.6 mm. Figure 2 shows the profile of this discretized extended source. The intensity of the point sources varied according to the Gaussian beam profile. The results of the simulation are presented in Section 3.

2.2 Co-registered PE/PAT probe design and implementation

For deep tissue imaging, higher laser energy is required to generate sufficient initial pressure high enough to provide acceptable signal-to-noise ratio. Unfortunately, the maximum incident light intensity that may be used in vivo is limited by the maximum permissible exposure (MPE) level [27]. Consequently, during the construction of our imaging probe, we employed a fiber-optic light splitter that divided the incoming laser light among 36 fibers as a way to reduce the fluence. These fibers surrounded the ultra-sound transducer and together were housed inside a plastic cover, as would be shown later. The entire assembly of ultrasound transducer, fibers and the cover is referred as probe in the manuscript. Additionally, the fibers were positioned so that their distal ends were approximately 1 cm away from the tissue surface during imaging; by so doing, the beam was expanded at the tissue surface and further decreased the fluence. The 1 cm distance also ensured that the light propagated from the fiber, with a numerical aperture of 0.2, to the tissue surface without reflecting off the surfaces of the plastic cover and transducer. Multiple reflections from these surfaces would decrease the total light throughput of the probe, unless the cover size is increased. Doing so would in turn increase the size of the imaging probe, which is undesirable. Alternatively, coating the surfaces with a highly reflective material such as silver would minimize the light loss, but would come at the expense of additional complexity.

The picture of the co-registered PE/PAT imaging probe is shown in Figure 3. It comprises of 36 fibers of 200-micron core diameter mounted around a commercial transvaginal ultrasound transducer array of 6 MHz center frequency and 80% bandwidth, similar to the configuration in Figure 1(d). A light-weight protective frame, made of acrylonitrile butadiene styrene (ABS) material and constructed by 3-D printing, encloses the array of fibers around the transducer. This frame protects the fragile fibers from getting broken and also getting close to the tissue and causing injury during imaging. The protective frame is securely affixed to the ultrasound transducer by means of a pair of fixtures that go around it and the transducer handle, and screwed together to provide a firm grip. The frame measures 2.5 cm in diameter and is 8 cm long. The design allows for easy and quick assembly of the probe, as well as disassembly for cleaning and sterilization when required. The light fluence delivered by the probe on the tissue surface is about 17 mJ/cm^2 , and is below the MPE of 24 mJ/cm^2 at the 750 nm wavelength used for imaging. The array of 36 fibers is the output arms of a pair of custom-made high-energy fiber-optic beam-splitter assembly (OFS, Inc). Each splitter is made up of a 1 mm-core input fiber that is fused to 19 smaller 200-micron

core output fibers using a proprietary technology. The insertion loss of the fiber assembly is about 1.2 dB. 18 fibers from each splitter, making 36 in all, were used for illumination during the photoacoustic imaging. The remaining two were used as intensity monitors for observing the laser energy levels during imaging. To verify that the output of the laser-intensity fiber monitor correlates well with the intensity directly from the laser, a curve of “laser output intensity” vs. “fiber monitor output” is measured from experiments and shown in Result section.

2.3 Experimental imaging setup

The entire experimental setup of the real-time imaging system is shown in Figure 4. Light from a laser was first coupled into the input ends of the two splitters using a convex lens and 50/50 beamsplitter arrangement as shown in the figure. The laser used was a tunable-wavelength Ti : Sapphire (Symphotics TII, LS-2211) optically pumped by a Q-switched Nd : YAG (Symphotics TII, LS-2134). It delivered 20 ns pulses at 15 Hz repetition rate with 20 mJ/pulse at the imaging wavelength of 750 nm. By using two of such splitters instead of one, we further decreased the energy density on the fiber end-face by half. The light from the 36 output fibers propagate diffusely to the imaged target, which is immersed in intralipid solution. The intralipid has a reduced scattering coefficient of 4 cm^{-1} and absorption coefficient 0.02 cm^{-1} . Transient acoustic signals picked up by the ultrasound transducer is received by the real-time image acquisition system for image processing and display. The real-time system, reported in Refs. [29, 30], consists of four 16-channel customized modules combined to form a 64-channel system. Each module is controlled by a separate Field Programmable Gate Array (FPGA) processor and has all the necessary analog and digital circuitry for ultrasound transmission and reception. The FPGA controls the ultrasound pulse-echo transmission and detection, the photoacoustic data acquisition process, the parallel processing and storage of the beam, and the real-time switching between the two modalities. The beam-formed data storage of each module is made available for a digital signal processor (DSP) to access using an external memory interface (EMIF). Image reconstruction is done using the delay-and-sum beamforming algorithm. Ultrafast reconfiguration of the FPGA allows it to quickly switch between the two imaging modes, perform transmission control, laser synchronization, internal memory structuring, beamforming, and adjusting the EMIF size and structure. The result is a seamless co-registered photoacoustic imaging that is interlaced with ultrasound pulse-echo imaging.

3. Results

3.1 Simulation results

The simulated fluence on the line located in the imaging plane under the transducer elements was calculated for various depths. The elements are shown as the gray stripes in Figure 1. The fluence along those lines of length 4.5 cm, and located at depths of 5 mm to 25 mm under the probe, is shown in Figure 5. The fluence for each point is normalized to the fluence in the imaging area of $4.5 \text{ cm} \times 4.5 \text{ cm}$ on the surface. Note that this fluence is equal for all configurations with different number of sources. The 2-D spatial illumination profiles at different depths inside tissue is also shown in Figure 6. We note that the 2- and 6-fiber configurations provide very inhomogeneous light distribution with high intensity regions at

the shallower depths which becomes more and more uniform as the depth increases. The 18- and 36-fiber configurations on the other hand, provide a more homogeneous light distribution. At 1 cm depth and beyond, the simulation shows that there are no high intensity regions from the fibers that would generate strong acoustic artifacts. It can also be seen from Figures 5 and 6 that the beams are merged after 1 cm depth for 6, 18 and 36 fiber sources. In order to evaluate this effect quantitatively, we defined a Merging factor (M) as following:

$M = \frac{\text{MaxFluence} - \text{CenterFluence}}{\text{MaxFluence}}$. This factor, M is calculated for each depth using different source configurations and the result is shown in Figure 7. It can be seen that M approaches zero when the beam of different sources merged in the center. It is clear that the beams merge faster by increasing the number of sources.

3.2 Experimental results

The fluence delivered to the tissue surface for the source fiber configurations shown in Figure 1 was experimentally measured as follows: It was assumed that the beam from the source fiber was Gaussian shaped and its diameter at the point where its peak intensity drops to 1/e was measured using a variable iris diaphragm and energy meter. This diameter corresponds to about 63.2% of the energy from the source fiber. Therefore, the beam diameter was measured to be the diameter of the iris that allowed 63.2% of the light energy to pass through it, when the beam was centered on the iris. Using this diameter, the beam area and consequently the energy density was calculated at the tissue surface. The fluence was measured for each configuration using this procedure and compared to the MPE, for different laser input energies. The result is shown in Figure 8. For the 20 ns pulse width and 750 nm wavelength laser parameters that were used for imaging, the MPE came out as about 24 mJ/cm². Obviously the fluence for the 2-fiber arrangement has the highest fluence and exceeds the MPE even at 10 mJ/pulse laser energy input. At about 20 mJ/pulse and beyond, the 6-fiber configuration is unsuitable for imaging as the fluence goes over the MPE. The 18- and 36-fiber configurations are good up to 40 mJ/pulse input, at which point they are just at the safety threshold limit. One would expect the 36-fiber configuration to generate less fluence than the 18-fiber, however the figure shows that both are the same. This is because for the particular imaging configuration and transducer size used, the beams from the 36 source fibers overlap and causes an increase in the fluence.

Variations in the mode of the laser beam coupled into the 1 mm core fiber can affect the coupling efficiency into each of the 19 output fibers. This would make the output fiber used to monitor the laser energy ineffective in tracking changes in the laser output. To verify that this was not the case for our setup, we performed a simple experiment that compared the energy exiting the laser with that from the laser intensity fiber monitor as follows: The laser was first allowed to run for about 30 minutes in order for it to reach its stable operation level. After that, the light was coupled into the 1 mm-core input fiber for the highest total coupling efficiency from the 36 fibers used for imaging. The energies from the laser and fiber monitor were then measured with the same energy meter in 5-minute intervals for an hour. The plot of the energies is shown in Figure 9, where it is seen that the beam from the fiber monitor has slightly more fluctuations compared to the direct laser beam. The intensity fluctuation was measured to be within $\pm 5\%$ of the mean intensity level, and hence is fairly acceptable.

Next, the performance of the probe was assessed by imaging a polyethylene tubing filled with the blood of a mouse that mimicked a blood vessel. The tube had inner and outer diameters of 0.86 mm and 1.27 mm respectively. Fresh excised ovaries from a 40-year old premenopausal patient who had a carcinoma were also imaged as well. All the images were taken at a depth of 1 cm below the transducer, in intralipid solution having 4 cm^{-1} scattering coefficient and 0.02 cm^{-1} absorption coefficient. Figure 10 shows in log-scale the photoacoustic images of the blood-filled tube and is displayed using 15 dB dynamic range. The two lines seen are the front and back of the tube. The photoacoustic signal in the time-domain from a cylindrical object like the tube shows up as a characteristic “N-shape” pulse, when picked up with a very wide-band ultrasound transducer [28]. However, because the transducer that we used had a limited bandwidth, only the two positive and negative peaks of the N-shape pulse is observed. These peaks correspond to the two lines that are seen in the photoacoustic image of the tube. The image in Figure 10(a) was taken with only intralipid layer between the tube and the probe. The maximum signal-to-noise ratio (SNR) for this image is 27, whereas the mean is 21. This is compared to the image obtained when a piece of chicken breast layer of about 1 cm thickness was used to cover the entire front face of the probe (Figure 10(b)). It is seen that the tube is clearly visible with the addition of the chicken layer. The maximum SNR dropped to 22, and mean SNR to 14, after placement of the chicken layer. “Maximum SNR” in this context is defined as the highest SNR that was obtained among the 64 acquired RF channel data from the transducer elements, and the “mean SNR” refers to the SNR averaged over all the 64 RF data.

Figure 11(a) shows a sequence of five co-registered PE/PAT image frames of the malignant ovary arranged in time. The grayscale image is the pulse-echo, whereas the color image is the photoacoustic. The arrangement demonstrates the progression of the frames as acquired with the real-time imaging system. The images were obtained by mounting the imaging probe on a translation stage and then scanning across the ovary in the lateral direction. One observes that each successive frame reveals more of the features of clusters of blood vessels inside the ovary: Frame 1 shows virtually no photoacoustic trace, as the probe position is further away from the vessels. As the probe is continuously scanned across the ovary, the subsequent frames begin to show more and more features until at a certain position of the probe, we obtain the best image contrast (frame 5). The image in frame 5 is again showed in Figure 11(b), where one can see more clearly the dimensions of the cluster of vessels; the vessels lie between 2–6 mm from the surface of the ovary. The maximum and mean SNRs obtained for the photoacoustic part of the image were 22.0 dB and 17.7 dB respectively. Figure 11(c) also shows another cluster of vessels at a different location of the ovary. Again, this was obtained by scanning the probe across the ovary to obtain images with the best contrast. The vessels in Figure 11(c) appear to be in a more localized position inside the ovary, and lie between 3–6 mm from the ovary surface. For this image too, the maximum and mean SNRs were 22.4 dB and 19.3 dB respectively. The hematoxylin and eosin stain revealed that this malignant ovary consisted predominantly of small vessels. Note that due to the finite bandwidth of the ultrasound transducer and aperture, it cannot see vessels except if they are aligned to provide good signals toward the face of the transducer with sizes several times larger than the central wavelength of the transducer. Tumor microvessels contribute to the photoacoustic signals seen as clustered small masses with different appearances in 2-D

cross-section images. If a tomography system is used, the blood vessels can be resolved better with a 360 degree receiving aperture [31].

3.3 Discussion

The ultimate goal of this research is to translate the prototype imaging probe from the laboratory to clinical environment. Before this is accomplished however, several issues will need to be addressed in the final design and construction. First, the material for future probe construction will be a more durable and stronger one such as stainless steel, rather than ABS. Furthermore, stainless steel has inert surface and lends itself to easy cleaning and sterilization, making it ideal for medical applications. The other modification to the probe would be the blunting of all the sharp edges and corners to prevent those surfaces from adding discomfort to the patient during imaging. In the present experimental setup, we used two fiber-optic beamsplitters to deliver light to the imaged tissue. The reason for this simply was to reduce the laser energy density at the tip of the fiber and avoid damage to it. As this setup takes more space, a new line of an integrated fiber-optic beamsplitter/coupler unit is currently being developed that would be able to withstand the high energy density of the laser. This would require the use of just one 1×19 splitter and would reduce the size of the imaging setup and make it more compact.

The data acquisition system used for this study achieved 1.5 frames per second for co-registered photoacoustic and ultrasound imaging. A new improved acquisition system has been built for *in vivo* clinical study and being debugged for much faster acquisition and image display. The new system has 128 channels of parallel acquisition using FPGA-based modular design. The data is collected from the FPGA modules by another advanced FPGA, postprocessed, and transferred to the PC instantly using a 2.5 GT/s PCIe link. The new system is capable of imaging at 15 co-registered frames per second, which is limited by the pulse repetition rate of the used laser [32].

4. Summary

A co-registered PE/PA imaging probe for the real-time imaging of human ovaries has been demonstrated. The probe size, as well as the safe energy levels it emits, makes it suitable for *in vivo* studies. Additionally, the real-time co-registered imaging approach affords one the rapidity, ease, and convenience of locating and characterizing blood vessels in human ovaries. Therefore, this imaging system is a potentially good candidate for *in vivo* diagnosis of ovarian tissue.

Acknowledgements

This research is supported by the National Cancer Institute 1R01CA151570. The authors thank Dr. Molly Brewer for providing the ovaries with results reported in the manuscript.

References

1. <http://www.cancer.org>.
2. <http://www.ovariancancer.org>
3. <http://www.cdc.gov>

4. Xu M, Wang L. Rev Sci Instrum. 2006; 77:041101–1–22.
5. Beard P. Biomedical photoacoustic imaging. Interface Focus. 2011; 1:602–631.
6. Aguirre A, Guo P, Gamelin J, Yan S, Sanders M, Brewer M, Zhu Q. J Biomed Opt. 2009; 14:054014–054022. [PubMed: 19895116]
7. Aguirre A, Ardeshipour Y, Sanders M, Brewer M, Zhu Q. Transl Oncol. 2011; 4:29–37. [PubMed: 21286375]
8. Kolkman RGM, Hondebrink E, Steenbergen W, de Mul FFM. IEEE J Sel Top Quantum Electron. 2003; 9:343–346.
9. Yuan Y, Yang S, Xing D. Opt Lett. 2010; 35:2266–2268. [PubMed: 20596215]
10. Wang B, Su JL, Karpouk AB, Sokolov KV, Smalling RW, Emelianov SY. IEEE J Sel Top Quantum Electron. 2010; 16:588–599.
11. Yang JM, Maslov K, Yang HC, Zhou Q, Shung KK, Wang LV. Opt Lett. 2009; 34:1591–1593. [PubMed: 19448831]
12. Viator JA, Choi B, Ambrose M, Spanier J, Nelson JS. Appl Opt. 2003; 42:3215–3224. [PubMed: 12790472]
13. Song L, Maslov K, Bitton R, Shung KK, Wang LV. J Biomed Opt. 2008; 13:054028. [PubMed: 19021408]
14. Allen TJ, Beard PC. Opt Lett. 2006; 31:3462–3464. [PubMed: 17099750]
15. Erpelding TN, Kim C, Pramanik M, Jankovic L, Maslov K, Guo Z, Margenthaler JA, Pashley MD, Wang LV. Radiology. 2010; 256:102–110. [PubMed: 20574088]
16. Mallidi S, Larson T, Tam J, Joshi PP, Karpouk A, Sokolov K, Emelianov S. Nano Lett. 2009; 9:2825–2831. [PubMed: 19572747]
17. Dean J, Gornstein V, Burcher M, Jankovic L. Proc. SPIE. 2008; 6856:685622–1–11.
18. Kim C, Erpelding TN, Jankovic L, Pashley MD, Wang LV. Biomed. Opt. Express. 2010; 1:278–284. [PubMed: 21258465]
19. Yaseen MA, Brecht HP, Ermilov SA, Gharieb RR, Conjuteau A, Oraevsky A. Proc. SPIE. 2008; 6856:68560T–1–11.
20. Agarwal A, Huang SW, O'Donnell M, Day KC, Day M, Kotov N, Ashkenazi S. J Appl Phys. 2007; 102:074301.
21. Patterson MP, Arsenault MG, Riley C, Kolios M, Whelan WM. Proc. SPIE. 2010; 7564:75641B–1–5.
22. Ermilov SA, Fronheiser MP, Brecht HP, Su R, Conjuteau A, Mehta K, Otto P, Oraevsky AA. Proc. SPIE. 2009; 7177:717703–1–10.
23. Haisch C, Zell K, Sperl JJ, Ketzner S, Vogel MW, Menzenbach P, Niessner R. Proc. SPIE-OSA BioMed Opt. 2007; 6631:663105–1–14.
24. Jaeger M, Preisser S, Kitz M, Ferrara D, Senegas S, Schweizer D, Frenz M. Phys Med Biol. 2011; 56:5889–5901. [PubMed: 21852726]
25. Wang L, Jacques SL, Zheng L. Comput Methods Programs Biomed. 1995; 47:131–146. [PubMed: 7587160]
26. Tavakoli B, Kumavor PD, Aguirre A, Zhu Q. J Biomed Opt. 2010; 15:046003. [PubMed: 20799805]
27. American National Standard for the Safe Use of Lasers ANSI Z136. Laser Institute of America; Orlando, Florida: 2007. p. 1-2007.
28. Diebold GJ, Sun T, Khan MI. Phys Rev Lett. 1991; 67:3384–3387. [PubMed: 10044720]
29. Alqasemi U, Li H, Aguirre A, Zhu Q. Proc. SPIE. 2011; 7899:78993S.
30. Alqasemi U, Li H, Aguirre A, Zhu Q. IEEE Trans Ultrason, Ferroelectr, Freq Control. 2012; 59(7): 1344–1353. [PubMed: 22828830]
31. Gamelin J, Aguirre A, Maurudis A, Huang F, Castillo D, Wang LV, Zhu Q. J Biomed Opt. 2008; 13(2):024007. [PubMed: 18465970]
32. Alqasemi U, Li H, Aguirre A, Zhu Q. Proc. SPIE. 2012; 8223:82232U.

Figure 1. Photoacoustic light source configurations showing different number of fibers surrounding the ultrasound transducer; **(a)** 2 fibers, **(b)** 6 fibers, **(c)** 18 fibers, and **(d)** 36 fibers.

Figure 2. Illustration of one discretized extended source at tissue surface consisting of 13 point sources arranged as shown. Gaussian profile was used to model the intensity distribution.

Figure 3.

(a) Photograph of the side-view of the prototype co-registered PE/PAT imaging probe. (b) photograph of the bottom-view of the same probe showing the ultrasound transducer, illumination fibers, and protective cover.

Figure 4. Experimental setup used for acquiring the co-registered PE/PA real-time images.

Figure 5. Normalized fluence at the central line located in the center of the probe at depth of 5 mm–25 mm with 5 mm increments. Using (a) 2 sources, (b) 6 sources (c) 18 sources and (d) 36 sources.

Figure 6. 2-D spatial illumination profiles inside tissue at different depths for (a) 2-source fiber, (b) 6-source fiber, (c) 18-source fiber, and (d) 36-source fiber configurations.

Figure 7.
Calculated Merging factor versus depth.

Figure 8.

Measured fluence distribution delivered on the tissue surface for different laser energies for the 2, 6, 18, and 36 light source configurations. The horizontal dashed line is the MPE level beyond which it is unsafe for imaging.

Figure 9. Comparison of the output beam intensity of the fiber monitor with that directly from the laser. Intensity measurements were recorded for both using the same energy meter at 5 min intervals for one hour.

Figure 10. Photoacoustic images of the polyethylene tubing filled with blood. (a) is the image with only intralipid layer, (b) is the same image but with about 1 cm chicken breast layer covering the front of the probe.

Figure 11.

(a) Progression of co-registered PE/PAT image frames acquired in real time with the imaging system. Each successive frame shows more of the features of clusters of blood vessels in the human ovary as the imaging probe is scanned across the ovary. (b) and (c) Co-registered PE/PAT images of a human ovary taken from two different locations.