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Efficacy of High Temporal Frequency Photoacoustic Guidance of Laser Ablation Procedures

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Abstract

Inaccurate placement of the ablation catheter and the inability to monitor the real-time temperature within the tissue of interest such as veins curbs the treatment efficacy of laser ablation procedures during thermal therapies. Our previous studies have validated the efficacy of photoacoustic (PA) imaging during endovenous laser ablation (EVLA) procedures. However, the PA-guided therapies suffer from low temporal resolution, due to the low pulse repetition rates of pulsed lasers, which could cause a problem during fast catheter motion and rapid temperature changes. Herein, to enhance the accuracy and sensitivity for tracking the ablation catheter tip and temperature monitoring, we proposed to develop a high frame rate (500 Hz), combined ultrasound (US), and PA-guided ablation system. The proposed PA-guided ablation system was evaluated in a set of ex vivo tissue studies. The developed system provides a 2 ms temporal resolution for tracking and monitoring the ablation catheter tip's location and temperature, which is 50 times higher temporal resolution compared to the previously proposed 10 Hz system. The proposed system also provided more accurate feedback about the temperature variations during rapid temperature increments of 10°C per 250 ms. The co-registered US and PA images have an imaging resolution of about 200 μm and a field of view of $45 \times 40\,mm^2$. Tracking the ablation catheter tip in an excised tissue layer shows higher accuracy during a relatively fast catheter motion (0.5–3 mm/s). The fast US/PA-guided ablation system will potentially enhance the outcome of ablation procedures by providing location and temperature feedback.

Keywords

photoacoustic imaging, repetition rate, ultrasound, laser ablation, temperature monitoring, catheter tracking

Background

Minimally invasive treatment procedures such as laser-equipped locoregional ablation procedures have been used for treating several maladies in the breast,[1] soft tissues,[2] liver,[3] prostate,[4] veins,[5] and pulmonary vessels.[6] Significant advantages of laser ablation treatments including minimal side-effects, rapid recovery, being repeatable and no need for general anesthesia or radiation, made it a preferred choice for various applications. The effectiveness of thermal therapies depends on accurate tracking of ablation applicators, real-time temperature monitoring, and minimizing damage to surrounding healthy tissues. Laser ablation procedures such as endovenous laser ablation (EVLA), utilize an ultrasound (US) imaging to guide the ablation catheter carrying high power continuous wave (CW) laser energy. The poor contrast of US images of the ablation catheter, difficulty to locate the tip of the catheter, are often limiting factors, affecting the surgeon's precision in placement of the ablation catheter at the desired site.[7,8] Additionally, the lack of a real-time temperature feedback system results in a blind, unregulated deposition of thermal dose within the tissue and causes peri or post complications, such as deep vein thrombosis and skin burns.[9,10]

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Photoacoustic (PA) imaging is a novel modality that has shown tremendous potential for diagnostic and image-guided applications.[11–15] In PA imaging, the acoustic waves are generated by photoabsorbers (i.e., tissue chromophores) as a response to short (typically nanosecond) laser pulses.[16,17] The subsequent thermoelastic expansion of the absorbers releases broadband acoustic waves omnidirectionally, which can be probed by a US transducer. In contrast to US imaging that visualizes tissue's structure, PA imaging contrast is based on the optical absorption and thus it is able to detects molecular composition and functional properties of the tissue.[16,18,19] Superior features, including the ability to detect tissue's molecular composition,[20] small molecules and nano-sized contrast agents,[21] as well as providing high-contrast images of external objects such as stents,[22] needles,[23] and catheters,[8,11,13,24] has enabled PA imaging to be used in preclinical and clinical applications.[8,11,14,15,25–29] These unique features of PA imaging were used for accurate ablation catheter tracking and real-time temperature monitoring. Our previous studies[8,11] have validated the capability of PA imaging for ablation catheter positioning and temperature monitoring during ablation procedures. It was demonstrated that PA tracking method is accurate and insensitive to the ablation catheter orientation since the PA signals are only generated at the ablation catheter tip and propagate omnidirectionally. PA thermometry has high accuracy and can provide real-time feedback on the ablation catheter tip's temperature within the tissue. However, one major limitation of existing PA-guided methods, is the limited imaging frame rate, inherited from typical low repetition rate of excitation lasers. The low temporal resolution of PA-guided procedures can negatively affect the accuracy in tracking the catheter's fast motion and monitoring rapid temperature variations. These inaccuracies may hinder the surgeon's ability to accurately visualize the position of the ablation catheter within the tissue. Besides, the low repetition rate method yields limited ability to analyze rapid temporal changes in temperature, which may lead to incomplete ablation and potential damage to the surrounding tissue such as skin burns, ecchymosis, and perivenous damage. These limitations call for integrating a high repetition rate pulsed laser for improving the PA guidance in ablation procedures. Therefore, this study aims to demonstrate the feasibility and utility of a high frame-rate PA-guided system in ablation procedures. It is known that increasing the pulse repetition rate comes as a price of lower pulse energy. However, PA-guided ablation procedures using internal illumination as we proposed, does not require a high energy pulses and thus a fast repetition rate laser will fit well within this application. This research work demonstrates the feasibility of utilizing a high repetition rate, low energy pulsed laser for fast PA-guided laser ablation applications. The proposed fast US/PA-guided ablation system will offer a significant advantage over a low repetition rate pulsed laser for more accurate and effective laser-guided thermal therapies.

Materials and Methods

High Repetition Rate Pulsed Laser for Fast PA Imaging

A PA-guided catheter tracking system was developed using a low pulse energy (~1 mJ), high repetition rate enabled frequency-doubled diode-pumped solid-state (DPSS) laser (Repetition rate: 500 Hz, pulse duration ~10 ns, $\lambda = 532$ nm, NL 204-1K-SH, EKSPLA, Vilnius, Lithuania). Our previous characterization study[30] revealed that the pulse energy for tracking the ablation catheter tip in deep tissue could be as low as 50 µJ/pulse because the internal illumination strategy generates PA signals and is not affected by fluence variations and acoustic attenuation. In other words, the tracking method is independent of the pulsed laser energy. During EVLA procedures, the ablation catheter pullback speed varies (0.5–3 mm/s). Due to this fast-motion, the proposed low frame rate (10 Hz) US/PA-guided ablation imaging system may cause inaccuracies in the ablation catheter tip positioning and tracking. Therefore, with a high repetition rate laser, US/PA imaging performed at a frame rate of 500 frames per second (FPS) will potentially enhance the accuracy in tracking the location of the catheter tip and monitoring the real-time temperature variations.

Design and Development of a High Repetition Rate US/PA-Guided Ablation System

The fast US/PA-guided ablation system is an improvised version of our previous study.[8,11,24] The enhanced system has three main parts (Figure 1): (a) Integrated ablation and imaging system, which couples a high-power CW laser (LuOcean Mini 4, Lumics GmbH, Berlin, Germany) ablation beam ($\lambda = 1470$ nm, 10 W, continuous wave) and a high repetition pulsed laser beam ($\lambda = 532$ nm) into one ablation catheter (FP1000ERT, Thorlabs, Newton, NJ, USA) by using low-cost optical components including a dichroic mirror (CMR 45, Newport, Irvine, CA, USA). (b) The timing control unit that triggers the CW laser and synchronizes the imaging sequence with the temperature measurements. (c) Acquisition system, which probes and reconstructs the acquired US and PA signals. A clinical linear US probe (L11-4v, Philips Inc., Andover, Massachusetts, USA) was used for the US and PA data acquisition with a transmitted center frequency of 10 MHz and acquisition bandwidth of 4 to 11 MHz. The timing control unit generates the imaging sequence for fast PA imaging (500 FPS) and the control signal for triggering and terminating the ablation laser system.

Evaluating the Feasibility of the Fast US/PA-Guided Ablation System for Catheter Tip Tracking

A series of ex vivo experiments were performed to evaluate the performance of the fast US/PA-guided ablation system.

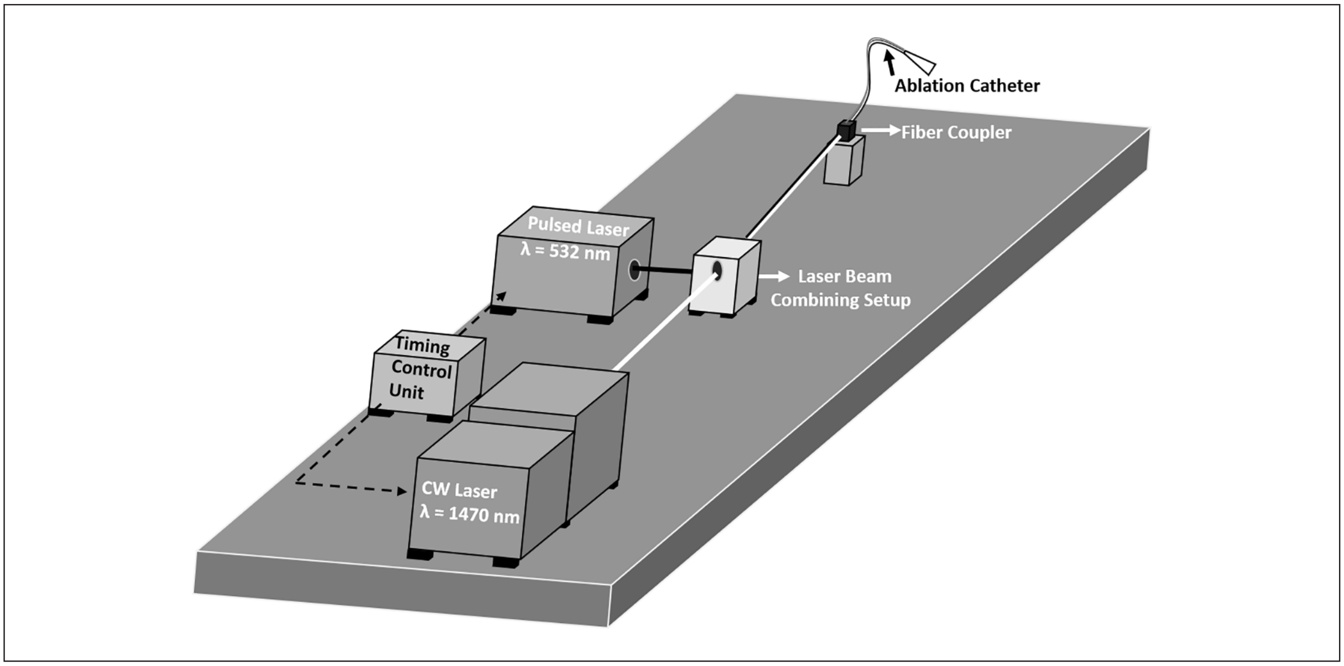

Figure 1. Schematic of the block diagram of the fast US/PA-guided ablation system. The US imaging platform, power source for the laser, and US transducer were not shown in the figure. The dashed black arrows indicate that the timing control unit generates the imaging sequence for fast PA imaging and the control signal for triggering and terminating the ablation laser system. The CW laser beam is indicated in solid white color, the pulsed laser beam is indicated in solid black color. The merged black and white solid line, at the output of the laser beam combining setup, indicates the combined beam.

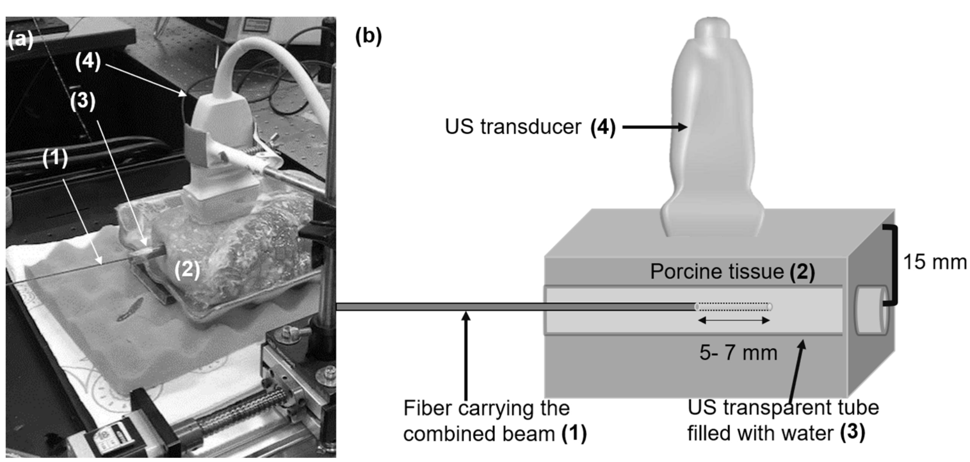

Figure 2. (a) Photograph of the experimental setup. (b) Schematic diagram illustrating the ablation catheter insertion and pullback procedure during the EVLA procedure. The speed of the ablation catheter motion varies from 0.5 to 3 mm/s. (Number's markings made in (a) correspond to the labels in (b)).

The experiments were conducted by placing the ablation catheter within a 50 mm thick porcine tissue at about 15 mm (Figure 2(a) and (b)). The fast motion of the ablation catheter during the ablation procedure was simulated by moving the ablation catheter axially and parallelly to the transducer surface. The speed of the ablation catheter pullback motion is about (0.5–3 mm/s).[31–37] Two different frame rates of PA images were acquired. A frame rate of 500 FPS (PA) was used for fast imaging, and a frame rate of 30 FPS (PA) was used for the existing imaging system. The maximum displacement error under those frame rates is calculated as:

$$\varepsilon_{Max_{displacement}} = \frac{V_{motion}}{Frame\,rate} \tag{1}$$

Where, $\varepsilon_{Max_{displacement}}$ presents the maximum displacement error, and V_{motion} is the expected motion speed (m/s).

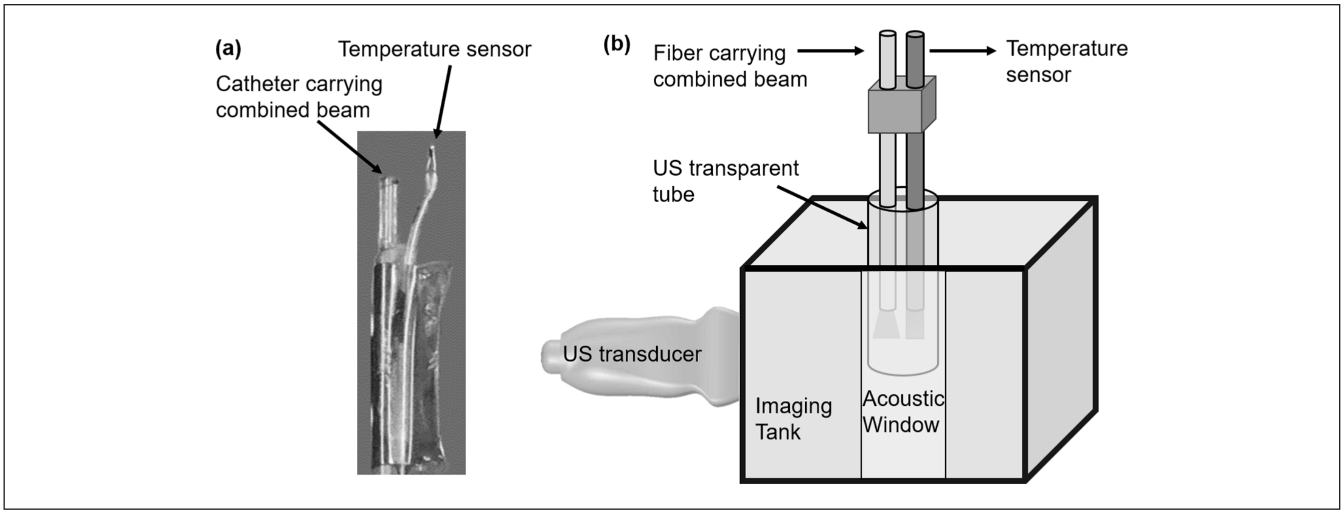

Figure 3. (a) Photograph of the distance between k-type thermocouple and the ablation catheter. (b) Schematic diagram of the experimental setup for evaluating the accuracy of PA thermometry. The power rating of the CW laser beam was varied from 0 W (OFF state) and 4, 8, 10 W. PA images were acquired at 500 FPS.

Accuracy is defined as the capability of the fast-imaging system to track the motion within the limitation of maximum displacement error. The videos containing the ablation catheter tracking using high and low repetition rates are included as Supplemental Videos. The FPS of the supplementary videos were scaled down by a factor of 30 for better visualization.

Evaluating the Accuracy of the Fast US/PA-Guided Ablation System for Rapid Temperature Monitoring

The accuracy of the fast US/PA-guided ablation system to monitor the rapid temperature variations was evaluated using a standard k-type thermocouple (COMINHKPR131287, Perfect Prime, New York, USA) of temperature sensing capability ranging from 0 to 200°C. The temperature sensor and the ablation catheter were placed in close proximity with each other (~1 mm distance) within a US transparent tube filled with water (Figure 3(a) and (b)). The tube was then placed within an imaging tank. The temperature readings of the thermocouple and synchronized PA amplitude values were recorded through the microcontroller enabled data logging system. The k-type thermocouple acquired temperature readings with a sampling rate of 40 Hz. The power rating of the CW laser beam was varied (0, 4, 8, and 10 W). Temperature variations were acquired using the fast PA imaging system (500 Hz). The differences in the PA signal amplitudes were computed and plotted. The initial PA pressure was used to indicate the temperature changes (ΔT).

Results

Fast PA Imaging for Ablation Catheter Tip Tracking

Figure 4 shows the displacement of the PA guided ablation catheter tip position during the insertion and the pullback procedure. Figure 4(a) shows the path traveled by the ablation catheter tip at an imaging frame rate of 500 FPS (PA). Figure 4(b) indicates the path traveled by the ablation catheter tip at an imaging frame rate of 30 FPS (PA). Compared to

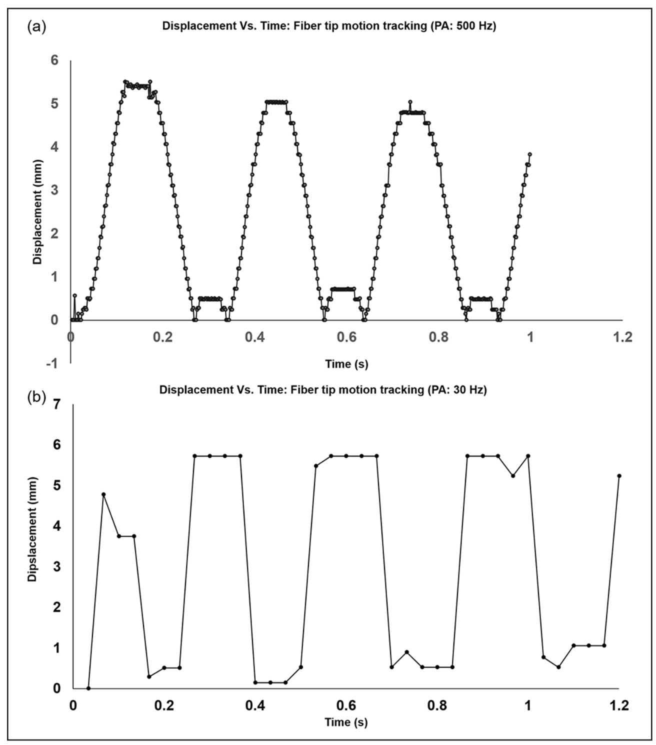

Figure 4. Fast PA-guided ablation system for accurate tracking of the ablation catheter tip motion. Displacement (mm) of the ablation catheter tip position w.r.t time (s). (a) Fast imaging system. (b) Existing or slow imaging system. Fast PA imaging accurately tracks the intermediate positions of the ablation catheter tip within the porcine tissue.

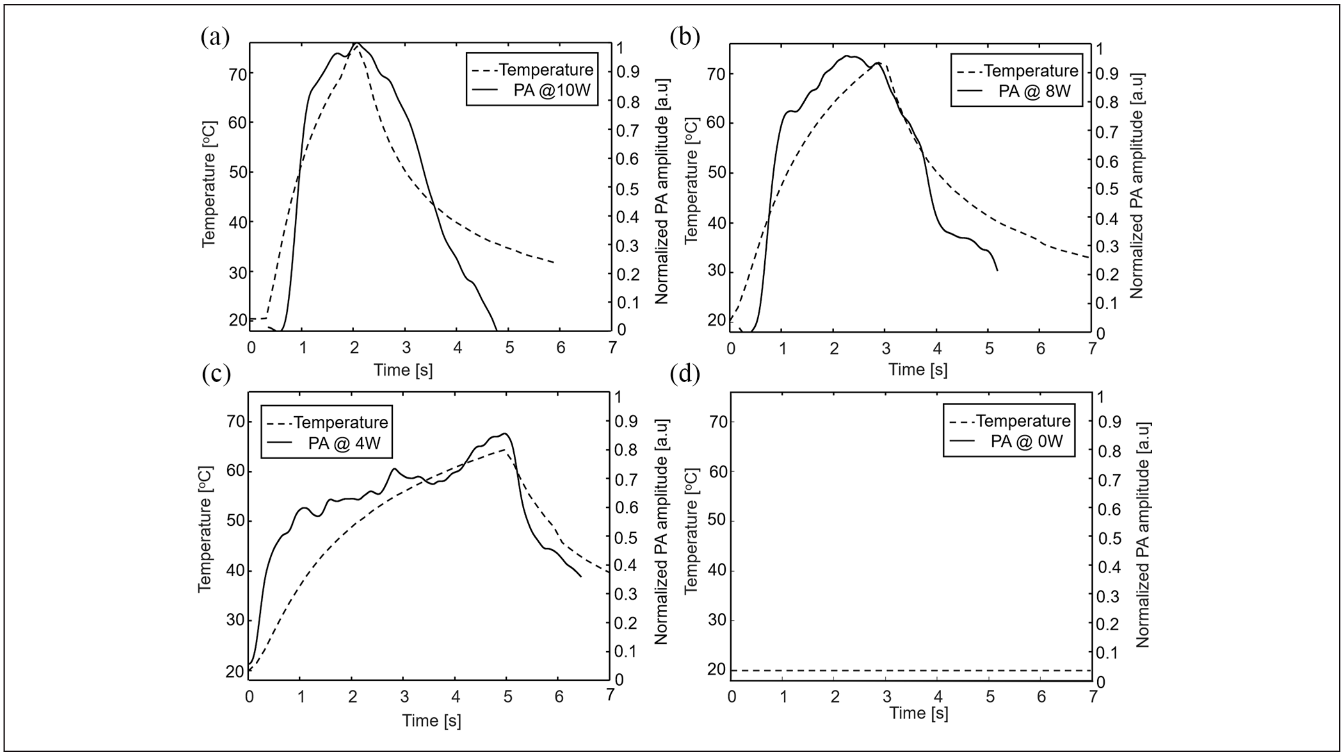

Figure 5. Fast PA imaging for monitoring rapid temperature changes induced by laser ablation. (a-d) portrays the measurements of temperature with fast (500 Hz) PA imaging followed the k-type thermocouple readings. The solid lines indicate the normalized PA amplitude due to temperature variations (indicated by dashed lines) caused by a CW laser at different power ratings.

slow frame rate enabled PA imaging (Figure 4(b)), the use of a higher repetition rate pulsed laser (Figure 4(a)) improves the temporal resolution and visualizes more intermediate positions of the ablation catheter tip, providing a more precise ablation catheter tip tracking. The ablation catheter pullback speed in existing EVLA procedures varies from 0.5 to 3 mm/s. The maximum displacement error for a speed of 3 mm/s using fast PA (500 Hz) is 0.006 mm, slow PA (30 Hz) is 0.1 mm. High repetition rate PA imaging provides a smooth ablation catheter tip motion. Precise ablation catheter tip tracking will enable surgeons to produce a uniform ablation pattern, achieving optimal damage to the tissues, and perform successful ablation procedures in patients.

Fast US/PA-Guided Ablation Imaging System for Monitoring Rapid Temperature Variations

Figure 5 shows the ability of fast PA imaging for monitoring rapid temperature changes. The results indicated that fast PA imaging performed at a frame rate of 500 Hz is capable of monitoring the rapid temperature changes induced by the ablation laser. The ablation catheter tip temperature rose to 75°C within 1 second of the laser power at 10 W. The PA signal closely followed the temperature changes (caused by the CW laser at different power ratings 4, 8, 10 W) recorded by the k-type thermocouple. When the CW laser was turned off, the amplitude of the PA signal decreased as expected. Besides, the measurements illustrated the non-linear changes of the PA signal when the temperature of the water was higher than 65°C. The non-linear changes of the PA signal are due to the change in the optical absorption properties of water at higher temperatures.

Discussion

This paper describes the development of a fast (up to 500 Hz) PA-guided ablation system using a high repetition rate pulsed laser at $\lambda = 532$ nm combined with an ablation laser at $\lambda = 1470$ nm. Although a lower repetition rate laser (10 Hz) can provide accurate slow-motion catheter tip tracking and monitor the slow temperature variations, it lacks the ability to provide fast motion catheter tip tracking and monitor the rapid temperature variations. Unexpected variations in PA amplitude changes with temperature can be explained by considering the variations in the optical absorption properties of blood and water at higher temperatures, as reported in literature.[38] The changes in the optical absorption properties of blood and water at higher temperatures have been studied and compensated in our previous study.[30] Yes, it is worth to mention that this PA-guided ablation monitoring system is not affected by parameters including varying fluence and acoustic attenuation of the tissue medium between the transducer and the ablation catheter within the vein, given the PA signals are generated using an internal illumination. Hence, our proposed thermometry system can be calibrated by measuring the temperature-dependent optical properties of the medium (blood and water) and establishing a direct relationship between the change in the PA signal and variations of the Grüneisen parameter to perform accurate quantitative thermometry. The enhanced PA-guided ablation system can provide higher temporal resolution enabled catheter tip tracking and real-time temperature monitoring. The high repetition rate laser-guided ex vivo experimental results have validated its ability to provide more accurate, precise, and smooth catheter motion tracking. Moreover, fast (500 Hz) PA imaging exhibits much lower displacement error compared to the slow (10 Hz) PA tracking method. Tracking the microscale displacements in the path traveled by the catheter will help in maintaining a uniform ablation pattern within the tissues, which can lead to quick and effective treatments. Moreover, the uniform ablation pattern will help in minimizing repetitive ablation procedures and reduce complications in patients. The high repetition rate of the pulsed laser provides a more precise estimation of the temperature at the catheter tip during rapid temperature variations (20°C–75°C, within 1 second) caused by a CW laser. In general, high repetition laser pulses carry low energy.[39] Hence, in our PA-guided ablation system, since the PA signals were generated locally and internally, the energy per pulse can be as low as about 50 μJ, which makes the power of the pulsed laser operating at a repetition rate of 500 Hz to be 0.25 W. The enhanced PA-guided ablation system was easily integrated with the current ablation system. The safety of the patient will not be compromised since the magnitude of the pulsed laser energy is a hundred times lesser than the CW laser. Integration of a low energy pulsed laser and dichroic optics will offer a cost-effective solution for minimizing errors caused due to catheter tracking and temperature monitoring in existing ablation procedures. The pathway for clinical translation from laboratory settings will be relatively simple due to the cost-effectiveness, added abilities of the proposed system, and minimal modifications in the existing ablation systems. Moreover, the high repetition rate pulsed laser imaging can be adopted into other key clinical applications, including needle biopsy and cancer ablation procedures, because PA imaging depends on the endogenous contrast agents to provide label-free functional images. In light of the internal PA signal generation, the proposed method is not affected by imaging depth and can also be used for deep ablation procedures for treating deep vein thrombosis and specific heart-related maladies. However, the proposed fast PA-guided ablation system acquires PA images at 500 FPS, far beyond the refresh rate of any current computer displays. Hence the acquired US/PA images can only be displayed at 240 Hz, which corresponds to the maximum refresh rate of existing computer displays.

Though the human eye cannot detect changes beyond the repetition rate of 48 to 50 Hz,[40] monitoring the temperature variations caused by the CW laser during ablation procedures at a faster rate will enable more accurate control of the heat deposition into the tissues by providing feedback to control the CW laser power and ablation duration. Most ablation procedures, including EVLA procedures, utilize high-power laser within a short period of time for providing effective therapies. The time duration for laser ablation during EVLA therapies is reported as 1.6 minutes for a vein which measures 20 cm in length.[32] However, lack of temperature monitoring in these therapies can lead to complications, such as collateral damage to surrounding tissues. Hence, high repetition rate imaging can potentially reduce these complications by monitoring the small-scale temperature variations caused during ablation. This temperature information can be used as a feedback for automated or robotic-guided ablation systems for regulating the energy or power settings of the CW laser. This feedback can also aid vascular surgeons (or any other operator of an ablation device) to provide an optimal thermal dose for providing an effective therapy.

In addition, having a higher repetition rate, catheter tip tracking can potentially be used to provide location-related feedback to an automated catheter maneuvering or pullback system. In such automated cases, having a higher repetition rate PA imaging will provide a more accurate guidance to the catheter manipulating system.

Conclusion

A fast US/PA-guided ablation system was successfully developed and tested. The system integrated a high repetition rate laser into a standard ablation system to enhance the tracking and temperature monitoring during ablation procedures. The temporal resolution of the imaging system was significantly improved. High frame rate enabled PA imaging provides more accurate ablation catheter tracking. Additionally, the ability of the fast-imaging system to monitor the rapid temperatures caused by the CW laser was validated. The development of the fast US/PA-guided ablation system paves the way for easy translation of the developed technology into other ablation therapies (such as cancer and venous insufficiencies), where temperature monitoring is critical.

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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