Volumetric optoacoustic monitoring of endovenous laser treatments

Thomas Felix Fehm[1,2], Xosé Luís Deán-Ben[1], Peter Schaur[3], Ronald Sroka[3,‡], and Daniel Razansky[1,2,‡,]*

[1]*Institute for Biological and Medical Imaging (IBMI), Helmholtz Center Munich, Neuherberg, Germany*
[2]*Faculty of Medicine, Technische Universität München, Munich, Germany*
[3]*Laser Research Laboratory/LIFE Center, Ludwig-Maximilians-Universität, Munich, Germany*

‡ Equal contribution
** Corresponding Author: E-mail: dr@tum.de*

ABSTRACT

Chronic venous insufficiency (CVI) is one of the most common medical conditions with reported prevalence estimates as high as 30% in the adult population. Although conservative management with compression therapy may improve the symptoms associated with CVI, healing often demands invasive procedures. Besides established surgical methods like vein stripping or bypassing, endovenous laser therapy (ELT) emerged as a promising novel treatment option during the last 15 years offering multiple advantages such as less pain and faster recovery. Much of the treatment success hereby depends on monitoring of the treatment progression using clinical imaging modalities such as Doppler ultrasound. The latter however do not provide sufficient contrast, spatial resolution and three-dimensional imaging capacity which is necessary for accurate online lesion assessment during treatment. As a consequence, incidence of recanalization, lack of vessel occlusion and collateral damage remains highly variable among patients. In this study, we examined the capacity of volumetric optoacoustic tomography (VOT) for real-time monitoring of ELT using an ex-vivo ox foot model. ELT was performed on subcutaneous veins while optoacoustic signals were acquired and reconstructed in real-time and at a spatial resolution in the order of 200µm. VOT images showed spatio-temporal maps of the lesion progression, characteristics of the vessel wall, and position of the ablation fiber's tip during the pull back. It was also possible to correlate the images with the temperature elevation measured in the area adjacent to the ablation spot. We conclude that VOT is a promising tool for providing online feedback during endovenous laser therapy.

Keywords: optoacoustic, photoacoustic, chronic venous insufficiency, endovenous laser therapy

1. INTRODUCTION

Endovenous laser therapy (ELT) is the hemodynamic elimination of incompetent truncal via laser coagulation. The endothermal damage of the vessel wall results in occlusion of the treated vein, similarly to other varicose vein treatments employing radiofrequency ablation[1] and foam sclerotherapy procedures[2]. In ELT, laser light is delivered into the vein through a flexible optical fiber via a sheath system. The light energy is absorbed by chromophores in the tissue depending on the optical wavelength used and converted into heat, which further results in cell destruction and collagen shrinkage. Usually, laser emitting light in the near infrared wavelength range are used in the clinical treatment[3,4]. The vein is then punctured in the area of the distal insufficiency point and the sheath is inserted. Sonographic monitoring is employed to position the fiber in the desired area and an anesthetic solution is applied locally before the treatment is initiated. The fluid protects the perivenous tissue from thermal damage and reduces the lumen of the truncal vein by compression and spasm. During the treatment, the fiber is continuously pulled back (velocity 3-5 mm/s) while the laser energy is being delivered into the vessel. The resulting temperature rise induces thermal shrinkage of the collagen and thermal denaturation of the proteins within the vessel wall. The pullback is equally performed under ultrasound control.

Photons Plus Ultrasound: Imaging and Sensing 2016, edited by Alexander A. Oraevsky, Lihong V. Wang
Proc. of SPIE Vol. 9708, 97080F · © 2016 SPIE · CCC code: 1605-7422/16/$18 · doi: 10.1117/12.2209075

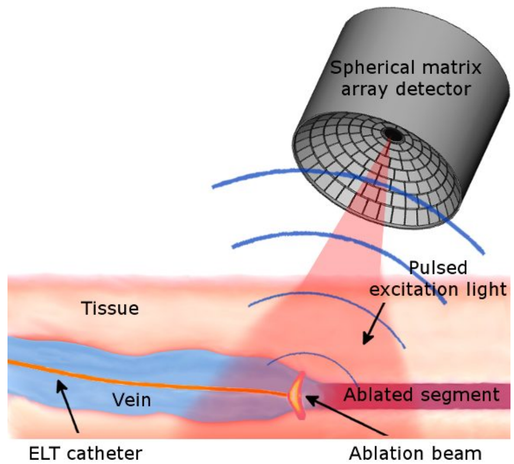

Figure 1. Sketch of the experimental setup. An ELT catheter is inserted into a subcutaneous vein of an ox leg. Thermal coagulation is initiated during catheter pull-back. The procedure is monitored in real-time by illuminating the treated area with nanosecond duration laser pulses in the near-infrared. The induced optoacoustic responses are recoded using a spherical transducer array that is placed above the ablation area.

Great variability of the clinical outcomes still exists among different ELT patients[2]. Further developments of efficient real-time monitoring approaches that are capable of delivering reliable information on lesion formation, ideally including the temperature profiles across the entire treated region are required. Treatment monitoring through conventional or duplex ultrasound[5,6], can reveal in-situ information about position of the fiber tip, the application of tumescence anesthesia and localization of the vessel. Endoluminal experiments using optical coherence tomography (OCT) have been able to visualize contrast changes in backscattering of light from the tissue due to heat-induced denaturation but have not been transitioned into the clinic due to the limited penetration depth of this technique[7]. A non-invasive imaging technique with high spatial resolution and high intrinsic contrast for heat-related alterations therefore is needed to reliably monitor ELT procedures.

Optoacoustic imaging delivers contrast mainly from the distribution of blood and thus is an ideal candidate to match these requirements as it has recently demonstrated through multispectral imaging with high spatial resolution in deep scattering tissues[8,9] by illuminating the imaged object with nanosecond-duration laser pulses and simultaneously collecting the generated optoacoustic signals around the object using a matrix transducer array. Optoacoustic is safe for animal and human use as it uses near-infrared light with typical intensities and per-pulse energy levels below internationally established safety standards[10]. It is also sensitive to temperature variations that lead to consequent changes in the Grüneisen parameter[11]. In the presented work, we demonstrate the feasibility of volumetric monitoring of lesion development during endovenous laser treatments of subcutaneous veins in an ex vivo ox foot model. A more detailed description of the topic can be found elsewhere[12].

2. METHODS

An outline of the experimental setup is shown in Figure 1. The ex-vivo model consists of an ox foot from freshly slaughtered animals (18-24 months of age, right hind leg)[13,14]. The subcutaneous veins (V. saphena lateralis and V. digitalis dorsalis communis III, 20.0-25.0 cm in length, 5-8 mm in diameter) are suited for ex vivo experiments due to their large diameter allowing introduction of the endoluminal application system. The veins were surgically prepared and subsequently treated by means of endoluminal laser irradiation with light guided from the central end (joint) to the peripheral end (hoof). Laser irradiation was performed using a diode laser (CERALAS D15, CeramOptec GnbH, Bonn, Germnay) with a wavelengths of 1470 nm, which was guided through a 600 µm core fibre. The 360° radial fibre tip (Biolitec GmbH, Bonn, Germany) or the 2-Ring-fiber (Biolitec GmbH, BONN, Germany) were used to deliver the light to the vessel walls. For tissue experiments, the 360° radial fibre was inserted into the vein via an introduction sheath. The vein was then irrigated using heparinised blood. The pullback velocity was manually adjusted to about 3-5 mm/s. During the experiments, we used a sheath and a catheter system to perfuse the vein with fluids (e.g. blood, saline). The therapeutic laser allows adjusting the output power in the range of 3-15 W with the corresponding LEED varying between 30-150 J/cm respectively.

Online monitoring of the ELT procedure was enabled by a previously developed hand-held volumetric optoacoustic tomography probe[15] that was placed on top of the ox foot above the target area (Figure 1). The custom-made probe consists of 256 piezoelectric detection elements distributed over a spherical surface. With a central frequency of 4 MHz and >80% detection bandwidth, this probe was previously shown to deliver a nearly isotropic spatial resolution of about 200 µm[16]. Acoustic coupling to the surface of the ox foot was facilitated by an acoustically-and optically-transparent foil while the cavity between the foil and

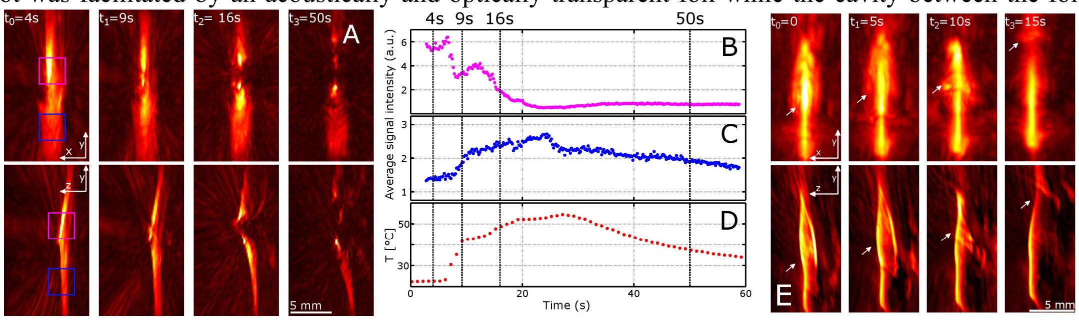

Figure 2. Real-time optoacoustic monitoring of vein coagulation. (A): Axial (top) and lateral (bottom) MIPs of reconstructed optoacoustic signals at consecutive time instances during the procedure. Catheter had been inserted from the top and was positioned in the middle of the vessel. (B) and (C): Time traces of the pink and blue VOI, as depicted in (A); (D) Temperature profile measured by the thermocouple probe placed on the surface in the proximity of the ablated area. (E) Axial (top) and lateral (bottom) MIPs of reconstructed optoacoustic volumes at different time instances during catheter pull-back. The position of the tip of the ELT catheter can be clearly tracked by inspecting alterations in the vessel morphology along the lateral direction (white arrows).

the surface of the array was filled with water. A pulsed laser source delivering pulses in the nanosecond range was used to excite the optoacoustic signals. The laser wavelength can be tuned in the wavelength range 690-950 nm with peak per-pulse energy of 30 mJ and pulse repetition frequency (PRF) of up to 100 Hz. The laser light was delivered onto the sample via a custom-made fibre bundle (CeramOptec GmbH, Bonn, Germany) inserted into a cylindrical cavity in the center of the array probe to provide coaxial optical illumination of the imaged sample. The illumination had a Gaussian profile at the tissue surface with a full-width at half maximum (FWHM) of approximately 10 mm. The 256 optoacoustic signals detected by the spherical array probe for each laser pulse were simultaneously time sampled at 40 mega-samples per second (MSPS) by a custom-made high-speed data acquisition system triggered by the Q-switch output of the laser.

For optoacoustic image reconstruction, the acquired signals were deconvolved with the frequency response function of the transducer elements before a band-bass filter (0.8 and 6 MHz) was applied to remove high-frequency noise and low frequency drifts. A three-dimensional back-projection algorithm[17] was employed to reconstruct image volumes with voxel size of 100 x 100 x 100 corresponding to 1 cubic centimeter. Image reconstruction was implemented in CUDA and executed on a GeForce GTX Titan X card. This implementation allowed for real-time reconstruction and preview of the volumetric images during the experiments, thus enabling proper positioning of the laser tip before the treatment, a useful capability during clinical procedures.

In order to investigate the feasibility of optoacoustic monitoring varicose vein ablation, the ELT catheter was positioned in the focal area of the spherical detector and the laser light was delivered into the vein for 20 seconds, where the output power was adjusted to 6W. Optoacoustic signals were acquired using excitation laser wavelength of λ=700 nm and a pulse repetition frequency of 5 Hz. During the experiment, blood was flushed manually through the vein using a syringe and the temperature at the tissue surface was digitally monitored using a thermocouple probe (Physiotemp, New Jersey, USA) placed in the vicinity of the ablated vein. The ELT monitoring experiment was repeated with the fiber pulled back slowly at a speed of about 3-5 mm/s while blood was flushed manually through the vein using a syringe. Optoacoustic images of the treated volume were simultaneously acquired.

3. RESULTS

In Figure 2a, a time series of the reconstructed volumetric optoacoustic images taken during the stationary ELT procedure is given. The maximum intensity projections (MIPs) along the axial (top row) and lateral (bottom row) direction at different time points show that the shape of the vein can be clearly identified before the thermal treatment is initiated (Figure 2a, t_0=4s). Contrast along the depth direction is limited in this case due to the strong light absorption by the blood inside the vessel. During the treatment, the vessel is progressively destroyed, with all vessel structures diminishing around the coagulation spot after ca. 50 seconds after starting the procedure. Changes in optoacoustic contrast were quantified by plotting the average voxel intensity within two volumes of interest (VOIs) for the entire duration of the procedure. The VOI corresponding to the pink label box in Figure 2a contains the ablated volume so that its corresponding time trace is affected by the structural alterations as well as changes in the chemical composition (and the related changes in optical absorption) due to denaturation of the vein (Figure 2b). As the vein and blood inside it are being ablated, the optoacoustic signal intensity in this region drops by almost 50% within several seconds after the outset of coagulation, further reducing to below 10% from the baseline intensity within the next 20 seconds. The VOI corresponding to the blue box in Figure 2a contains another part of the vein, which is located outside the ablated region. No coagulation occurs here, thus the variation in optoacoustic contrast is mainly attributed to a local variation in temperature. The corresponding time trace (Figure 2c) shows over two-fold increase in the average optoacoustic signal intensity in the blue VOI within the first 20 seconds of heating. This time trace correlates well with the measured temperature from the thermocouple (Figure 2d), which was placed in the proximity of the coagulated area on the surface of the tissue. This result is well expected due to the (nearly) linear dependence of the optoacoustic signal on temperature[11]. Finally, optoacoustic imaging was performed in a realistic clinical ELT scenario including catheter pullback. Figure 2e shows MIPs along the axial and lateral directions of the reconstructed 3D volumes at different time instances during catheter pullback. Even though the glass fiber tip is not expected to generate significant optoacoustic contrast, its position can be indirectly identified and followed by observing morphological changes of the surrounding vein (see arrows in Figure 2e). As the catheter is pulled back, the freed space inside the lumen is filled with blood, which makes the deeper part of the vein invisible due to strong light absorption by the blood.

4. DISCUSSION

The lack of real-time feed-back on the delivered thermal damage during endovenous laser therapy makes it challenging to guarantee optimal outcome of ELT procedures. Although various ultrasound-based clinical imaging tools are widely available for ELT monitoring, interpretation of thermally-induced volumetric tissue alterations is often limited by insufficient contrast, spatial resolution and lack of real-time 3D imaging capacity.

In this work we demonstrated the applicability of volumetric optoacoustic tomography for real-time monitoring of ELT procedures. Experiments performed in subcutaneous veins of an ox foot greatly delivered accurate spatio-temporal maps of the lesion progression and further showed good correlation with the temperature elevation measured in an intact area in the proximity to the coagulated spot. Our promising in-situ findings indicate that the suggested imaging approach can be used to regulate the delivered thermal dose to achieve efficient and uniform occlusion of the vein around its entire circumference. In addition, the technique holds promise for real-time non-invasive thermometry to prevent overheating of the perivascular tissue. However, with the current setup the position of the fiber tip cannot be tracked directly since it does not create optoacoustic signals. Combining the optoacoustic imaging approach with ultrasonography may only help to overcome this limitation and also will help physicians to better integrate optoacoustic images in the treatment routine. Finally, multi-spectral illumination and spectral unmixing of the reconstructed images can render spectroscopically-enriched information about individual tissue chromophores[9], which may facilitate more accurate differentiation of tissue types and levels of thermal damage. However, further studies are essential in order to evaluate the monitoring performance in real in-vivo clinical setting to quantify the advantages of the suggested imaging technique in terms of minimizing the incidence of re-canalization, undesirable sensations and other side effects.

REFERENCES

1 Almeida, J. I. & Raines, J. K. Radiofrequency ablation and laser ablation in the treatment of varicose veins. *Annals of vascular surgery* **20**, 547-552 (2006).

2 Jia, X. *et al.* Systematic review of foam sclerotherapy for varicose veins. *British journal of surgery* **94**, 925-936 (2007).

3 Van den Bos, R., Kockaert, M., Neumann, H. & Nijsten, T. Technical review of endovenous laser therapy for varicose veins. *European Journal of Vascular and Endovascular Surgery* **35**, 88-95 (2008).

4 Doganci, S. & Demirkilic, U. Comparison of 980 nm laser and bare-tip fibre with 1470 nm laser and radial fibre in the treatment of great saphenous vein varicosities: a prospective randomised clinical trial. *European Journal of Vascular and Endovascular Surgery* **40**, 254-259 (2010).

5 Kim, H. S., Nwankwo, I. J., Hong, K. & McElgunn, P. S. Lower energy endovenous laser ablation of the great saphenous vein with 980 nm diode laser in continuous mode. *Cardiovascular and interventional radiology* **29**, 64-69 (2006).

6 Kabnick, L. S. Outcome of different endovenous laser wavelengths for great saphenous vein ablation. *Journal of vascular surgery* **43**, 88-88. e87 (2006).

7 Schmedt, C.-G. *et al.* Evaluation of endovenous radiofrequency ablation and laser therapy with endoluminal optical coherence tomography in an ex vivo model. *Journal of vascular surgery* **45**, 1047-1058 (2007).

8 Deán-Ben, X. L., Ford, S. J. & Razansky, D. High-frame rate four dimensional optoacoustic tomography enables visualization of cardiovascular dynamics and mouse heart perfusion. *Scientific reports* **5** (2015).

9 Deán-Ben, X. L. & Razansky, D. Adding fifth dimension to optoacoustic imaging: volumetric time-resolved spectrally enriched tomography. *Light: Science & Applications* **3**, e137 (2014).

10 American National Standards Institute, Safe Use of Lasers, ANSI Z136.1-2000, (Laser Institute of America, 2000).

11 Pramanik, M. & Wang, L. V. Thermoacoustic and photoacoustic sensing of temperature. *Journal of biomedical optics* **14**, 054024-054024-054027 (2009).

12 Fehm, T. F., Deán-Ben, X. L., Schaur, P., Sroka, R. & Razansky, D. Volumetric optoacoustic imaging feedback during endovenous laser therapy–an ex vivo investigation. *Journal of biophotonics* (2015).

13 Schmedt, C.-G. *et al.* Investigation on radiofrequency and laser (980nm) effects after endoluminal treatment of saphenous vein insufficiency in an ex-vivo model. *European journal of vascular and endovascular surgery* **32**, 318-325 (2006).

14 Sroka, R. *et al.* Ex-vivo investigation of endoluminal vein treatment by means of radiofrequency and laser irradiation. *Medical Laser Application* **21**, 15-22 (2006).

15 Deán-Ben, X., Fehm, T. F. & Razansky, D. Universal hand-held three-dimensional optoacoustic imaging probe for deep tissue human angiography and functional preclinical studies in real time. *JoVE (Journal of Visualized Experiments)*, e51864-e51864 (2014).

16 Deán-Ben, X. L. & Razansky, D. Portable spherical array probe for volumetric real-time optoacoustic imaging at centimeter-scale depths. *Optics Express* **21**, 28062-28071 (2013).

17 Xu, M. & Wang, L. Universal back-projection algorithm for photoacoustic computed tomography. *Physical Review E* **71** (2005).