Optoacoustic angiography of peripheral vasculature

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ABSTRACT

We developed a new optoacoustic microangiography system (OmAS) intended for in-vivo vascular imaging of a human finger. The system employs an arc-shaped acoustic array that is rotated 360 degrees around the finger providing optoacoustic data necessary for tomographic reconstruction of the three-dimensional images of a finger. A near-infrared Q-switched laser is used to generate optoacoustic signals with increased contrast of blood vessels. The laser is coupled through two randomized fiberoptic bundles oriented in orthogonal optoacoustic mode. To demonstrate OmAS capabilities, we present a time-series of optoacoustic images of a human finger taken after the hypothermia stress test. The images show a detailed vascular anatomy of a finger down to the capillary level. A series of quick 30s scans allowed us to visualize the thermoregulatory response within the studied finger as it was manifested via vasomotor activity during the hypothermia recovery. We propose that the developed system can be used for diagnostics of various medical conditions that are manifested in change of the peripheral (finger) blood flow. Examples of the medical conditions that could be diagnosed and staged using the OmAS include the peripheral arterial disease (PAD), thrombosis, frostbite, and traumas.

Keywords: Photoacoustic tomography, peripheral arterial disease, stenosis, thrombosis, embolism, frostbite, ischemia, Raynaud's phenomenon.

1. INTRODUCTION

The visualization of peripheral vasculature can be useful in diagnostics and monitoring of various medical conditions, like vascular disorders, anatomical abnormalities, and obstructed blood flow.[1-3] The examples include stenosis, thrombosis, embolism, frostbite, traumas, peripheral artery occlusive disease, Raynaud's syndrome, etc. The imaging of microcirculation and capillary networks is useful for the diagnosis of ischemia.[4] Another application of the vascular imaging could be related to the physiological stress tests, aimed to study local vasomotor response. The stress tests involve changing environmental conditions (local occlusion, change of temperature, etc.) in order to bring certain physiological parameters, in this case the peripheral blood flow, close to extreme. Then, the environmental conditions are restored to normal, and the recovery of the individual's peripheral blood flow is monitored.[5]

Optoacoustic (OA) imaging is one of the best modalities for visualization of vasculature in live organisms.[6-9] It is based on the acoustic signals generated by a short laser pulse absorbed within biological tissues.[10] The OA imaging of blood vessels using near infrared (NIR) lasers can be effectively performed at depths up to several centimeters.[11] At those laser wavelengths (700-800 nm) blood is 50 to 100 times more absorbing than the surrounding tissues,[12] which eliminates the need for use of external optical contrast agents.

In these studies, we modified a three dimensional OA tomography (3D-OAT) system, which was previously designed and used for experiments on small animals,[6,13] in order to perform microangiography of a human finger. The finger is a good candidate for such type of imaging for multiple reasons. First of all, the microangiography of a finger is currently used to diagnose peripheral vascular diseases.[4] Also, its geometry and size resemble those of a mouse, and it can be fixed within the 3D-OAT system at an optimal location near the focus of the detector.

The mechanical structure of a finger is quite heterogeneous being comprised of blood vessels, soft tissue, bone, and

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nail. This complicates OA imaging, creating additional acoustic artifacts due to the mismatch in acoustic impedances. Three phalanx bones traverse the finger, separated by joints which permit flexion and extension (Fig. 1a). The expanses of the joints are seen as areas of weak optoacoustic response given the high content of loose areolar tissue.[14,15] The nail bed is highly vascularized, and is thus expected to produce a strong aggregate optoacoustic response despite the small diameter of its individual vessels. Blood is supplied to a finger by two major arteries, the radialis indicis and proper digital (Fig. 1b). The radialis indicis is on the lateral/radial side of the index finger and forms several anastomoses with the proper digital artery. The communicating branches distribute around the joints, supplying blood to the structures involved in articulation and to the surrounding cutaneous tissue. The terminal anastomosis found in the nail bed produces a superficial, sheath-like structure and is an important site for regulation of sensory input and thermoregulatory response. The latter is the reaction of the organism to the thermal stimuli, manifested in vasomotor controls constricting or increasing local microcirculation.[16] The venous network in fingers arises from several anastomoses that converge into proper digital veins that further drain via the cephalic vein (Fig. 1c).

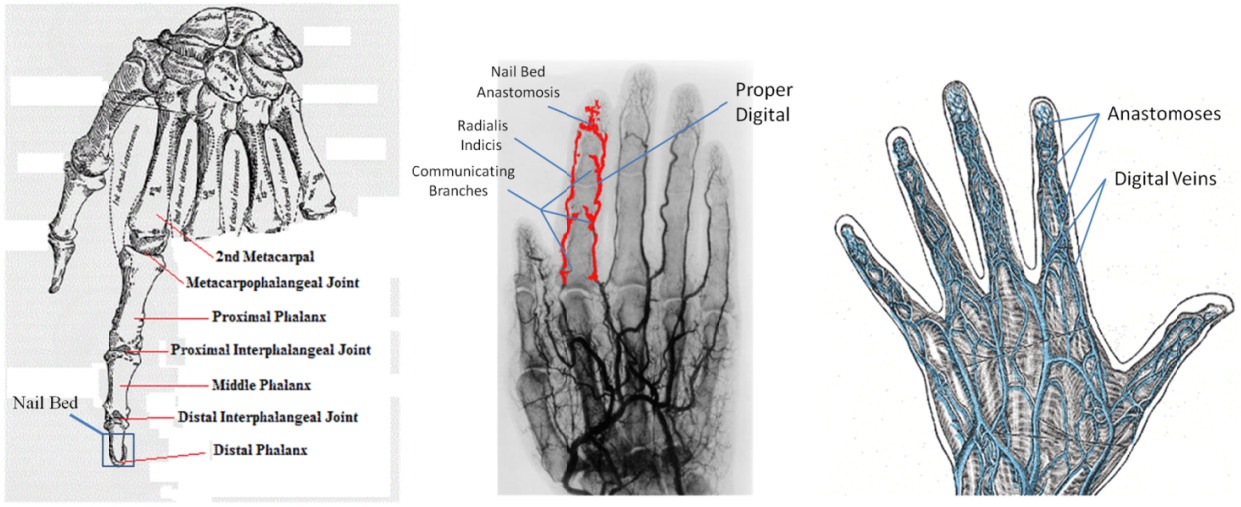

Figure 1: Anatomy of a human finger. (a) Bones and joints; (b) Arterial supply; (c) Venous network.

Currently, microangiography is performed by either MRI or CT.[2,4] While these methods have been extensively explored, they have several drawbacks. CT angiography requires contrast agents to distinguish the vasculature. MRI scans are costly, and time required for MRI image acquisition is not optimal for dynamic monitoring of blood flow on short time scales. For comparison, Wang et. al. (2008) reports a 3min 30s acquisition time.

Here we propose that the thermoregulatory response may be assessed by observing changes on optoacoustic images of the index finger caused by the physiological recovery after the thermal stress test. Three dimensional optoacoustic microangiography of a finger is used to perform the assessment. We present the proof of principle by analyzing the optoacoustic images acquired immediately and seven minutes after the induced local hypothermia.

2. MATERIALS AND METHODS

Optoacoustic Imaging

A custom-made bowl system consisting of optical illumination, acoustic array probe, and rotational motor was used for these studies (Fig. 2). An acoustically dampening chamber (bowl) had a spherical inside with a curvature matching that of the array probe. The array and optical fiber bundles were fixed within the bowl. Acoustic signals were detected by an arc array of 128 piezo-composite elements having a central frequency of 5MHz. The array aperture was spanning a 152° arc with a radius of 65mm (Imasonic SAS, Voray sur l'Ognon, France). The array was tilted such that there were transducers passed the south pole (lowest portion of the probe). Illumination was set to be in orthogonal optoacoustic mode coming from a bifurcated, randomized fiber bundle with a rectangular output

profile of 1mm x 50mm. The bowl was mounted and centered on the rotational stage operated by a stepper motor (DG200, Oriental Motor, Tokyo, Japan) which would rotate around the finger for a complete 360° scan. The remaining components like the digital acquisition hardware, time gain control, and laser were similar to those of the previously described 3D-OAT mouse imaging system that utilized a water tank as an experimental chamber.[6,13]

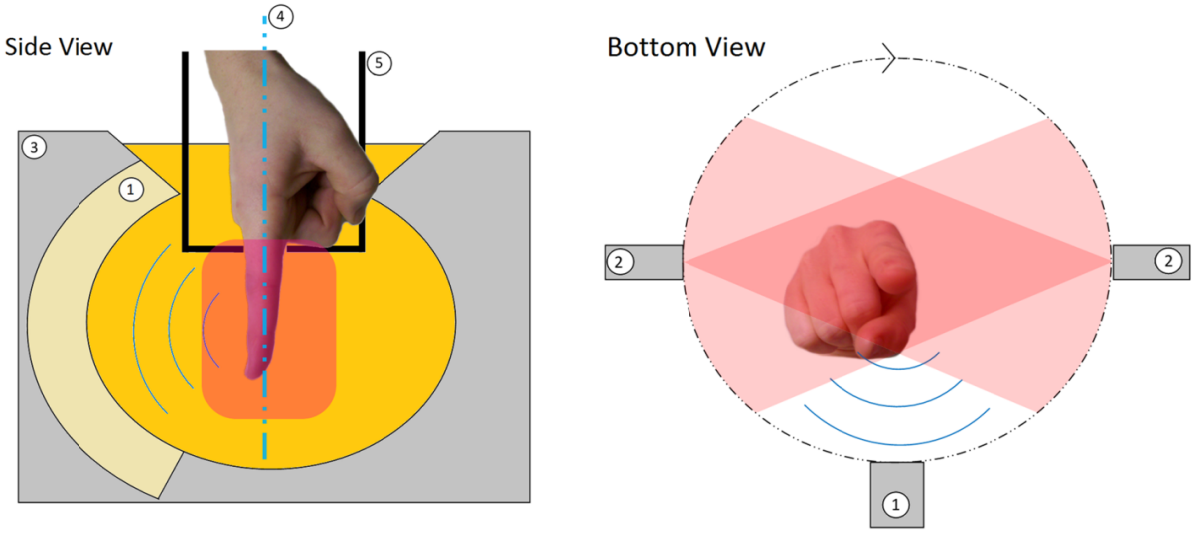

Figure 2: Schematic of the three-dimensional optoacoustic microangiography system. 1- acoustic array probe; 2 – laser fiberbundles; 3 – scanning chamber (bowl); 4 – hand of a human subject; 5 – hand bracket.

Imaging was performed in vegetable oil, which provided acoustic coupling and also reduced the noise picked up by piezoelements of the acoustic array. Temperature of the coupling oil was recorded before and after the imaging procedure and was all the time between 26°C and 27°C. A full scan consisted of 150 acquisitions with 2.4° steps made without averaging on every other laser pulse. The total scan time was less than 30 seconds. 1536 samples were recorded per acquisition with a sampling frequency of 20MHz. The amplifier gain was set to 60dB. During a scan, the index finger of a volunteer was positioned co-linear and in the proximity to the axis of rotation of the bowl. The motion of the finger was restricted at the most proximal (Metacarpophalangeal) joint using a custom-made hand bracket.

Hypothermia Stress Test

To demonstrate the ability of the system in evaluation of thermoregulatory response of the peripheral vascular system, we designed a simple hypothermia stress test and employed a healthy volunteer. A hypothermia stress test consisted of placing the targeted index finger in the ice-cold water for five minutes. Immediately afterwards, the finger was positioned inside the bowl of 3D-OAT system and a series of optoacoustic scans were performed approximately 1, 3, 5, and 7 min after the end of the hypothermia stress test. During the last scan, the volunteer reported return of the normal sensory feelings in the finger under study. Each optoacoustic scan continued for about 30 seconds, providing information about thermoregulatory recovery of the peripheral blood flow averaged over that time frame.

Data Processing and Visualization

Signal conditioning, image processing, and visualization parameters were frozen with respect to the initial scan in order to observe temporal changes. Signal conditioning involved application of a high-pass filter based on a one-scaled wavelet[17] designed to highlight fine optoacoustic features, like small blood vessels and capillaries. Unfortunately, this type of processing also produced speckled imaging noise commonly found in high frequency reconstructions. It was alleviated using a three dimensional Gaussian filter with a standard deviation of 1.5 voxels. 3D optoacoustic images were reconstructed using filtered radial backprojection[6] and visualized using VolView 2.0 (Kitware, Clifton Park, NY). Using the image intensity histogram, we made all the values of less than 0.8 transparent to get rid of the noise. A linear opacity ramp terminating at the opacity level of 0.05 was applied to voxels with intensities up to 3.2. Then a stepwise increase in opacity to the level of 0.3 was used for the remaining

data. Color palette was set to a 12-bit grayscale linearly distributed between the intensity values of 0.8 (black) and 3.2 (white). Gradient opacity mapping was handled by the heuristics of the Strong Edge Detection of VolView with the exception of the zero-opacity point, which was set to the mode of the gradient histogram.

3. RESULTS

Figure 3a-c shows the three-dimensional optoacoustic images reconstructed from the scans, which were performed 1, 3, and 7 minutes after the hypothermia stress test. Here, we do not display the results from the scan, which was performed 5 minutes after the test, since it failed due to accidental movement of the finger. The images clearly show the recovery of peripheral blood circulation under the normal (ambient temperature) conditions. Analyzing the panels (a) and (b) we can say that the capillary blood flow remained restricted for the first 3 minutes, particularly in the areas of the joints. The capillary and venous blood flow significantly increased 7 minutes after the removal of hypothermia, as seen from the Fig. 3c.

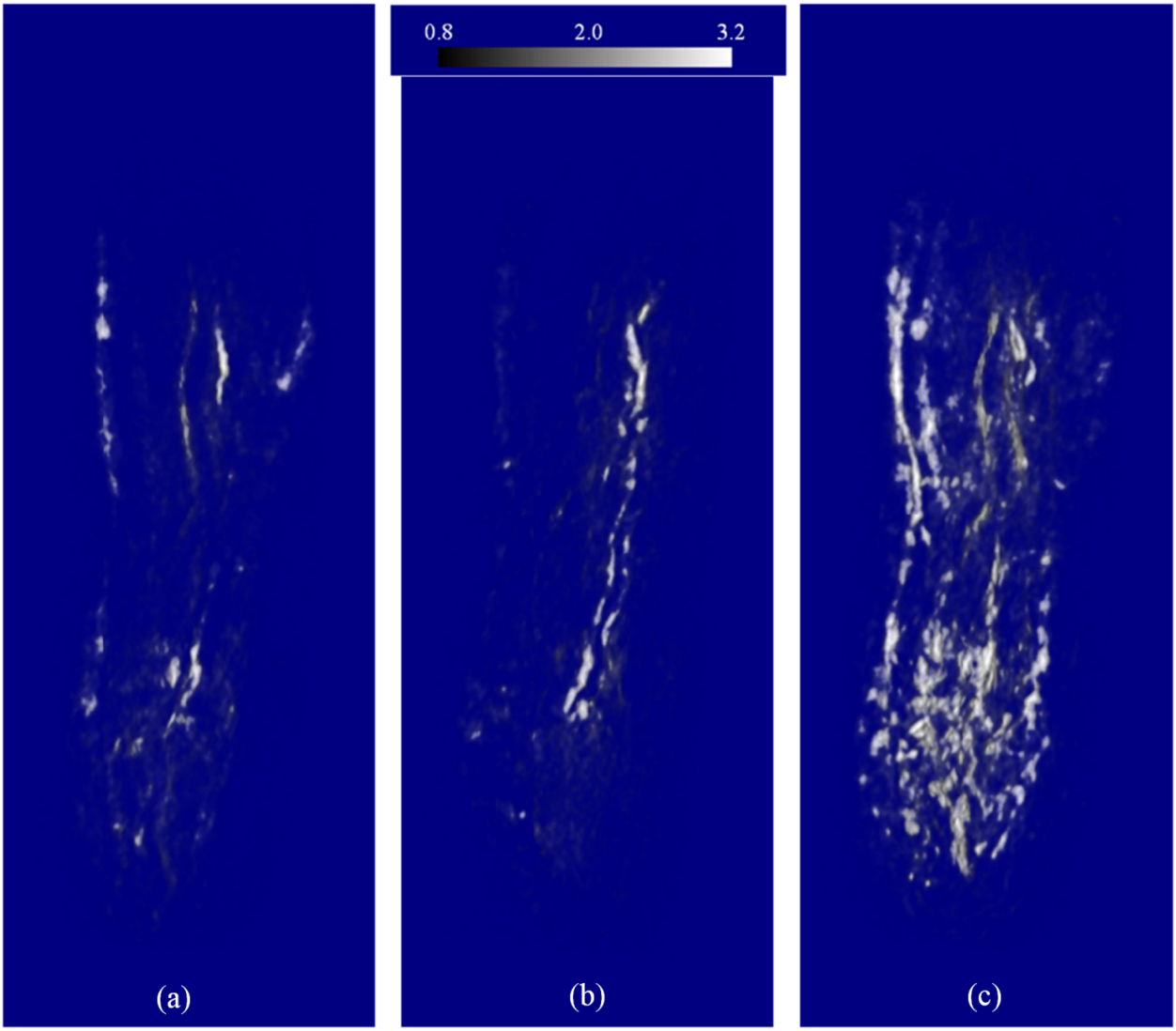

Figure 3: Three-dimensional optoacoustic images of a human finger following the hypothermia stress test. (a) 1 minute, (b) 3 minutes, (c) 7 minutes following the test. The colorbar shows the dynamic range of the implemented linear grayscale palette.

4. CONCLUSIONS

Our work demonstrated that the thermoregulatory response and other physiological effects regulated via vasomotor activity could be studied by repetitive three-dimensional optoacoustic imaging following the stress test that modifies the finger blood flow. Future improvements to the stabilization of the finger during the scans will provide less motion artifacts, better resolution and contrast of individual optoacoustic images, which is essential for quantitative differential image analysis. We also plan to increase the speed of each scan and allow uninterrupted multiple scanning, which will allow studying of the faster processes that happen as a result of vasomotor activity.

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