Three-dimensional optical-tomographic dynamic imaging of small tissue volumes

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Abstract: We have developed a system for acquiring three-dimensional dynamic images of small tissue volumes. As a first example we explored the real-time response of changes in optical properties inside a human finger caused by partial occlusion of distal veins.

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1. Introduction

Optical imaging of large physiological structures has already been studied and well documented. [e.g. 1-4]. There is however an immediate and practical need for imaging objects of small geometry. For example, there is currently considerable interest in small animal imaging systems that allow for in vivo monitoring of cancer growth or drug-tissue interactions. Small animals can be infected with assorted diseases and bacteria while researchers try to mark their progress in response to various chemical and antibiotic injections. Another application is diagnosis and disease-progression monitoring rheumatoid arthritis (RA) in finger joints. RA is one of the most common and severe diseases of human joints and is most prevalent in the hands and feet. Current diagnostic techniques are only reliable once the disease has advanced to a later more aggressive stage but detection at its onset is not easily assessed. In early stages, rheumatoid arthritis causes the inner membrane (synovium) to thicken and change its permeability, which in turn changes the optical properties of the synovium and its surrounding fluid. By capitalizing on this phenomenon, optical tomography has great potential of detecting the early characteristics of the disease [5]. Establishing a systematic method for making qualitative measurements on the finger is an essential criterion for making this an effective diagnostic tool.

We have developed the hardware and software necessary for generating three-dimensional images of small tissue volume. As a first application we show in this study changes in the optical properties around a finger joint that are caused by an occlusion of the veins in the upper arm. By gathering full tomographic measurement sets within a fraction of a second we can follow the spatial-temporal development of these changes.

2. Methods

2.1 Instrumentation and Measurement Probe

The instrument used for collecting data was a dynamic near-infrared optical tomographic imager. This instrument encompasses a continuous wave multichannel parallel-detection scheme with dual wavelength capabilities. The light sources used in this experiment were 785nm and 810nm. Image acquisition and source switching were performed at a rate of 2.4 Hz for 12 source positions. Further details concerning the hardware design can be found elsewhere [6].

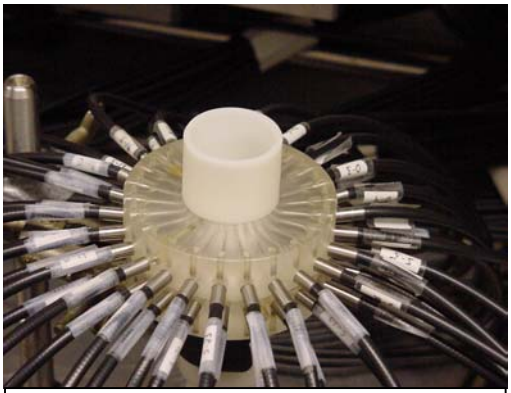

Fig. 1) Hardware setup for delivering and detecting light around the circumference of the finger.

Of special interest for small tissue volumes is the design of the optical measuring probe. This probe is comprised of a 1.25" diameter low-scattering Delrin® tube of variable length to accommodate a wide range of finger or animal sizes. The optical fibers are held in place by two rings secured to the outer surface of the measuring head, each supporting a maximum of 24 fibers (Fig. 1). For our experiment, we used 12 source and detector fibers per ring arranged in an alternating pattern. The rings were aligned

parallel to the center joint of the index finger. A diluted intralipid solution with optical properties similar to that of the finger was added to the measuring head to fill the voids between its walls and the finger. A holder on the tip of the finger and a custom fit cover at its base stabilizes the finger to avoid motion artifact.

2.2. Image Reconstruction

For the volumetric image reconstruction of the changes of the optical properties during various stimuli we employed a model-based iterative image reconstruction scheme that was recently introduced by Bluestone et al [1]. Using the GiD software package (GiD http:\\gatxan.cimne.upc.es), a cylindrical mesh was generated that mimicked the geometries of our delrin measurement head. This mesh was used for the finite-element based image reconstruction scheme. The exact source-detector coordinates were added to the mesh. The computational technique used to generate the image was a gradient-based iterative reconstruction algorithm, which uses adjoint differentiation techniques to calculate the gradient [7]. The resulting image was a mapping of the absorption coefficient changes over the volumetric mesh.

2.3 Data Collection Protocol

To test the performance of the device and algorithm, we studied perturbations induced by a pressure cuff. A sphygmomanometer cuff was wrapped around the upper arm just above the elbow. The experiment consisted of a five-phase protocol yielding 1000 images. The measurement data for one image was recorded in 400 ms. An initial rest period of 80 sec was followed by the rapid inflation of the cuff to 80mmHg, which was held for 60 seconds. The cuff was rapidly deflated and another rest period of 80 seconds followed. Another re-inflation and rest-period of the same length concluded the experiment.

3. Results

A typical normalized time trend showing the transmitted intensity changes in response to inflation and deflation of the cuff is shown in Fig. 2. This is the intensity plot seen at detector 6 from source 2 where the fibers were arranged as in the following manner: Source 1 was positioned perpendicular to the top of the finger joint, and subsequent source positions were 30 degrees apart in a clockwise rotation. Detector 1 was 15 degrees from source 1 and subsequent detector positions were 30 degrees apart in a clockwise rotation.

As Fig. 2 indicates, the venous blockage produces vasoengorgement, which results in a rapid decay in intensity. As soon as the pressure cuff is released, venous blood flow returns and the signal gradually returns to baseline. Evidently, the decrease in transmitted light intensity directly corresponds to the volumetric changes resulting from the venous blockage.

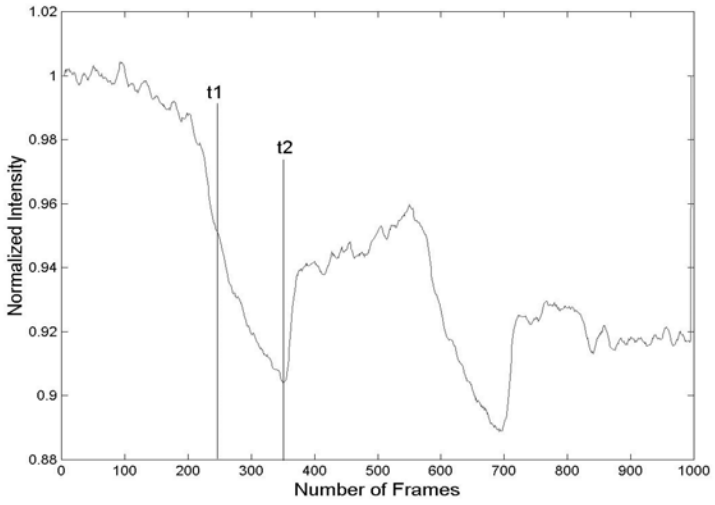

Fig. 2) Normalized transmitted intensities at a wavelength of λ=785nm as function of time for a single source-detector pair. The x-axis is given in frames, where each frame corresponds to a full tomographic data set, which was acquired in 0.4 seconds.

The full tomographic data set obtained at time t = t1 (100 sec) was used to generate a 3-dimensional reconstruction of the distribution of changes in the optical properties. Fig. 3a shows the resulting image. Shown are volumes in which the absorption coefficient increased as compared to time t = 0 by more than 3% (green) and 10%(brown), respectively. It clearly can be seen that these increases take place in tissue areas surrounding the joint, rather than in the joint itself. The increase is highest at the interior base of the finger and moderate around the outer perimeter. This behavior is expected since it reflects the distribution of blood vessels inside the finger. A buildup of venous blood in the finger should lead to an increases the absorption coefficient mainly in areas occupied by blood vessels. Regions occupied by synovial fluid, cartilage and bones show little change during an arm cuff.

A cross-sectional image of the distribution of absorption-coefficient changes based on data taken at time t = t2 (140 sec) is shown in Fig 3b. Again, inspection of the image reveals that optical absorption changes are highest at the interior base of the finger, moderate around the outer perimeter, and low in its center, which is mainly occupied by synovial fluid, and adjacent cartilage and bones. Since more time has past since the inflation of the cuff, the changes in the absorption coefficients have become more pronounced, as expected.

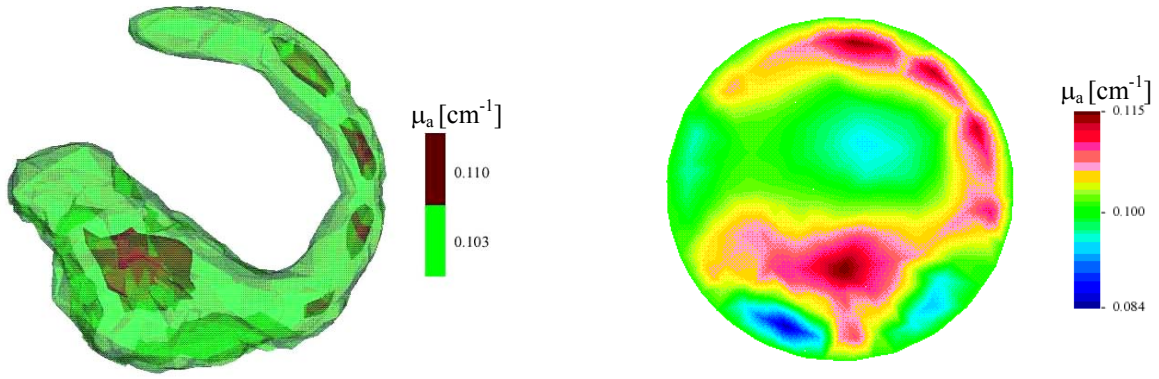

Fig. 3. (a-left) Volumetric image of the distribution of changes in the absorption coefficient at time t1 (see Fig. 1). Shown are volumes inside a finger (diameter d = 2.5 cm) in which the absorption coefficient increased as compared to time t = 0 by more than 3% (green) and 10%(brown), respectively. (b-right) Cross-section of changes in absorption coefficient at time t2 (see Fig. 1). In both images the background absorption is assumed to be μ_a= 0.10 cm^{-1}.

4. Discussion

We have devised a systematic method for acquiring and reconstructing three-dimensional optical tomographic images from small tissue volumes. So far, our experiments focused on collecting and analyzing the dynamic response of the finger vasculature to occlusion of venous return. We have observed a close correlation between known physiological functions and their expected optical response. We expect that joints affected by rheumatoid arthritis (RA) will experience an atypical dynamic response enabling us to identify and characterize features of the disease. Beyond application to the diagnosis of RA the imaging system can easily be employed to study optical changes in small animal models. Being able to reconstruct the image in three dimensions provides us with details and insight into the physiologic response that would otherwise be unobtainable.

5. References:

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