Measurement of Vascular Response within the Foot Using Dynamic Diffuse Optical Tomography

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Abstract: We present case studies using dynamic diffuse optical tomographic imaging to view the vascular perfusion of patients with Peripheral Arterial Disease with and without calcifications as well as a healthy control group.

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1. Introduction

Peripheral Arterial Disease (PAD) is the narrowing of arteries due to plaque accumulation and in the vascular walls. PAD affects approximately 12 million individuals in the United States and is associated with significant morbidity and mortality [1]. Every year, PAD is responsible for over 2,750,000 office visits, 10% of which result in hospital admissions. Approximately 45,000 PAD patients die from this disease annually [2]. Furthermore, patients with PAD have an increased risk of stroke and myocardial infarction, and show a two-fold increase in the risk of death from cardiovascular disease [3]. Therefore, accurate and timely diagnosis of PAD is crucial in prevention of further health consequences.

In patients with compressible (non-calcified) vessels, PAD is typically diagnosed through calculating the ankle-brachial index (ABI). The ABI is determined by dividing the systolic blood pressure at the ankle by that at the arm. A patient with an ABI reading below 0.9 is considered to have PAD. However, it is well known that the ABI is unreliable in patients with diabetes because they have calcified arteries [4]. This leads to an elevated ABI index and causes false negative readings. Additional noninvasive methods include: duplex ultrasound (DU), computed tomography angiography (CTA), digital subtraction angiography (DSA), and magnetic resonance angiography (MRA). Even when these modalities are used in combination, there are considerable gaps in the diagnostic capabilities, due to the fact that all of the above modalities are surrogate measurements of distal perfusion. As it is the lack of distal perfusion that leads to ulcers and amputations, a direct measure of this perfusion is necessary.

Dynamic diffuse optical tomography (DDOT) promises to overcome the limitations of current diagnostic techniques and could become a platform technology for assessing various vascular diseases. DDOT has the capability to image the response of the vasculature to an external provocation and use this response as a diagnostic marker. In addition, optical imaging systems use less expensive parts than most other imaging instrumentation and can be scaled down to portable systems. Therefore, optical imaging systems could be used at point of care as readily available screening devices and has the potential to be a safe and accurate method to diagnose PAD and allow for monitoring of treatment response.

2. Methods

Optical transmission measurements on the foot were performed with a digital, dynamic near-infrared optical tomography imager [5]. A combined optical beam consisting of two laser diodes (wavelength $\lambda = 765$ nm and $830$ nm) acts as an illuminating source. This source is sequentially coupled into different 1 mm multimode fiber bundles that distribute light to multiple areas along the measurement probe (Fig. 1). The current of each laser diode is modulated to a distinct amplitude and frequency. In this way, multiple wavelengths may be illuminated simultaneously, and their respective amplitude and phase contribution on the attenuated detected signal can be extracted using synchronous detection techniques. Once the light is attenuated and scattered as it propagates through the foot, then is collected by the various fiber bundles positioned around the target.
To generate the two-dimensional reconstructions of the optical properties in the foot, we employ a diffusion-theory-based PDE-constrained multispectral image reconstruction scheme [6]. The method solves the forward problem (boundary radianc at each wavelength) and the inverse problem (spatial distribution of chromophores concentrations) simultaneously using a reduced Hessian sequential quadratic programming method. This scheme directly reconstructs the spatial distributions of hemoglobin concentration in the foot. Note that the differences in \([\text{HbO}_2]\) and \([\text{Hb}]\) obtained through reconstruction is relative to baseline which is assumed to be given by \([\text{HbO}_2] = 23.4306 \text{ [µM]}\) and \([\text{Hb}] = 14.6874 \text{ [µM]}\), throughout the foot. A radial basis function (RBF)-type regularization scheme is employed to obtain quality images by reducing noise and artifacts near the foot surface.

During the imaging protocol the subjects were asked to place their foot on a stable holding platform (Fig. 1) while sitting upright on a chair. A total of 34 fibers were brought in contact with the foot (14 source and 20 detection fibers). Subsequently, the instrument ran a self-calibration test to determine and store the ideal gain settings for each channel at every source position. To illicit a controlled vascular response a pressure cuff was applied to the upper thigh. First a baseline measurement was taken for approximately 1 minute (~ 400 frames). Then, the pressure cuff was inflated to 60 mmHg to induce venous occlusion and trap the blood in the foot. The pressure was maintained for another minute at which point the pressure was rapidly released. Data was acquired for another minute during the rest period before an increased pressure of 120 mmHg was applied.

3. Results

Three cases, a patient with PAD (ABI = 0.66), a patient with diabetes and PAD (ABI = 1.07) and a healthy control (ABI = 1.00) are presented. Using the ABI measurements it is easy to discern between the healthy control and the PAD patient. However the diabetic PAD patient is indistinguishable from the healthy individual. Diabetics tend to have incompressible arteries elevating their ABI readings and resulting in false negatives.

In Fig. 2 a-c the representative optical time traces are shown for a healthy, PAD, and diabetic PAD subjects respectively. The detector readings were first normalized to the initial baseline rest period. It can clearly be observed that during both 60 mmHg and 120 mmHg occlusions the healthy volunteer had a significantly higher drop in intensity (20% and 45%) than the PAD Patient (10% and 15%) and the diabetic PAD Patient (20% and 20%). The signal attenuation is directly proportional to the total hemoglobin concentration; this implies that more blood reaches the foot in the healthy patient than the PAD affected blood vasculatures. Furthermore, the occlusion and recovery rates of the detector intensities vary greatly between the three cases. The healthy volunteer exhibits an exponential decay and occlusion rate with a distinct plateau phase while the PAD patients exhibit a more linear trend, and the diabetic PAD patient has a diminished exponential recovery rate. It is suspected that the PAD exhibits a more linear trend due to diseased arteries having more resistance due to plaque build up and lack of arterial wall capacitance due to arterial wall calcifications. Despite the similarity in the ABI measurements of the diabetic PAD patient and the healthy volunteer, DDOT detector readings were capable of distinguishing between the two subjects.

The detector readings from multiple source positions were then used to reconstruct a 2D cross-section image of the foot shown in Fig. 3. The reconstructed images show changes in total hemoglobin concentration 1 minute after the pressure cuff is initiated. It is evident that there is a substantial change in HbT within the foot of the healthy volunteer, demonstrating an expected response of a healthy vasculature to the cuff stimulus. In both PAD patients various sections of the foot do not seem to respond to the provocation suggesting a poor perfusion in these areas, caused by a compromised vascular network.

![Fig. 2. Normalized detector readings for a single source illumination over time for a healthy volunteer, PAD patient, and a diabetic PAD patient.](BTu2A.4.pdf)
Taking the weighted average total hemoglobin concentration in each reconstructed image over time, it was possible to quantify the overall hemodynamic changes within the foot (Fig. 4). In these time traces we could observe that the percent change in the amount of blood within the foot increased when the thigh cuff was applied to the foot. As observed in the detector readings, the percent change in the concentration of hemoglobin in the foot during thigh occlusions is greatest within the healthy volunteer. Furthermore, the patients with diseased vasculature had a more linear response to the thigh cuff while the healthy volunteer had an exponential occlusion and recovery rates.

4. Conclusion

Examining a non-diabetic patient with PAD, a diabetic patient with PAD and a healthy volunteer, we observed that DDOT has the potential to greatly aid in the diagnosis and monitoring of PAD within the diabetic population. There appear to be multiple features that can be extracted from the dynamic imaging protocol that can be applied and used as contrast mechanisms between healthy and diseased vasculature. Here we have that PAD in diabetic patients can be detected by differences in detector intensity during thigh cuff occlusion, the weighted average total hemoglobin signal from the whole foot, as well as tomographic images of cross-sections through the foot. We are in the process of enrolling additional patients are currently, and as the sample size increases more quantitative conclusions can be made about the sensitivity and specificity of DDOT in vascular diagnostics. This work is supported in part by a grant from the Wallace H. Coulter Foundation.

5. References