Imaging of vascular dynamics within the foot using dynamic diffuse optical tomography to diagnose peripheral arterial disease

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ABSTRACT

Peripheral Arterial Disease (PAD) is the narrowing of the functional area of the artery generally due to atherosclerosis. It affects between 8-12 million people in the United States and if untreated this can lead to ulceration, gangrene and ultimately amputation. The current diagnostic method for PAD is the ankle-brachial index (ABI). The ABI is a ratio of the patient’s systolic blood pressure in the foot to that of the brachial artery in the arm, a ratio below 0.9 is indicative of affected vasculature. However, this method is ineffective in patients with calcified arteries (diabetic and end-stage renal failure patients), which falsely elevates the ABI recording resulting in a false negative reading. In this paper we present our results in a pilot study to deduce optical tomography’s ability to detect poor blood perfusion in the foot. We performed an IRB approved 30 patient study, where we imaged the feet of the enrolled patients during a five stage dynamic imaging sequence. The patients were split up into three groups: 10 healthy subjects, 10 PAD patients and 10 PAD patients with diabetes and they were imaged while applying a pressure cuff to their thigh. Differences in the magnitude of blood pooling in the foot and rate at which the blood pools in the foot are all indicative of arterial disease.

Keywords: Peripheral arterial disease, dynamic imaging, diffuse optical tomography, vascular dynamics.

1. INTRODUCTION

1.1 Prevalence

Peripheral Arterial Disease (PAD) is the narrowing of the functional area of the artery generally due to atherosclerosis. It affects between 8-12 million people in the United States and is associated with risk factors including, smoking, hypertension, hyperlipidemia, hypercholesterolemia and diabetes. Symptoms of the disease vary depending on the degree of occlusion, initially the patient will experience pain while walking known as claudication. In more severe cases, this pain can occur during rest and if left untreated can lead to ulceration, gangrene and ultimately amputation. Early diagnosis is essential as lifestyle changes as well as cholesterol reducing drugs (statins) and blood thinners can be used to help control the disease [1, 2].

1.2 Current Diagnostic Techniques

The current diagnostic method for PAD is the ankle-brachial index (ABI). The ABI is a ratio of the patient’s systolic blood pressure in the foot to that of the brachial artery in the arm, a ratio below 0.9 is indicative of affected vasculature. However, this method is ineffective in patients with calcified arteries, which falsely elevates the ABI recording resulting in a false negative reading. The next diagnostic testing the duplex ultrasound scan, which is a combination of B-mode imaging and Doppler ultrasound. The technician will look for occlusions and listen for bruits (“wooshing” sounds) resulting from blood flow through narrowed arteries. Duplex is used to identify lesions within the leg, however the infra-popliteal arteries (below the knee) are small and the results become heavily user dependent. Furthermore, indentifying lesions does not provide direct information on the perfusion of the foot. More invasive imaging techniques such as x-ray computed tomography angiograms (CTA) and magnetic resonance angiography (MRA) are also used pre-surgically to determine the locations of lesions. However, these techniques require the use of contrast agents that are nephrotoxic which renders them dangerous to use for diabetic patients and patients with renal insufficiency [3-5]. Furthermore, these anatomical imaging methods do not provide information on the perfusion response within the foot. We believe dynamic diffuse optical tomography (DDOT) will provide effective way to view foot perfusion and aid in filling the gaps left by the traditional diagnostic techniques [6].
1.3 Dynamic Diffuse Optical Tomography

Diffuse Optical tomography (DOT) is a novel imaging technique in which red and near infrared (NIR) light (650-900 nm) is shone at different projections encompassing some tissue of interest in order to probe its optical properties. This wavelength range is unique because that absorption by the tissue is relatively low allowing it to penetrate deep within tissue and the NIR light is non-ionizing enabling it to be used frequently for monitoring. In addition, the major chromophores that absorb the light are oxy and deoxy hemoglobin enabling DOT to image the blood content within tissue without the use of a contrast agent. Furthermore, it can be geared for fast acquisitions speeds allowing for dynamic imaging studies that can provide functional information on tissue hemodynamics. This technology has been used in medical applications such as rheumatoid arthritis, breast cancer, brain imaging and small animal imaging and has shown great promise to be used within a clinical imaging modality [7-12].

2. METHODS

2.1 Instrumentation

To perform the imaging studies we used a digital dynamic diffuse optical tomography system described in [13]. This system is comprised of two wavelengths (760 and 830nm), which are modulated with a low frequency (5-7kHz) and combined into a single beam. This beam is de-multiplexed among 16 source fibers placed at different locations encompassing the foot. This light shone around the foot and upon exiting the tissue detector fibers collect the light and the wavelengths are separated using synchronous detection techniques [14].

![Imaging system set-up with measuring probe.](image)

The measuring probe was designed to accommodate the various shapes and sizes of feet seen in a clinical setting. Utilizing a sandal-shaped design, optical fibers are guided towards the foot via spring-loaded shoulder screws. This design gives each fiber the ability to translate different lengths to make contact with the non-uniform curvature of the foot. To obtain the mesh for the image reconstruction a photograph is taken of the patient’s foot such as shown in Figure 1, using two references a coordinate system can be made to identify the locations the sources and detectors and segment the foot boundary.
2.2 Image Reconstruction

To generate the two-dimensional reconstructions of the optical properties in the foot, a diffusion-theory-based PDE-constrained multispectral image reconstruction scheme was employed [10]. This method solves the forward problem (boundary radiance at each wavelength) and the inverse problem (spatial distribution of chromophores concentrations) simultaneously using a reduced Hessian sequential quadratic programming (rSQP) method [10, 15]. This scheme directly reconstructs the spatial distributions of the oxy and deoxy-hemoglobin concentrations in the foot. Note that the differences in [HbO₂] and [Hb] obtained through reconstruction is relative to baseline which is assumed to be given by [HbO₂] = 23.43 μM and [Hb] = 14.69 μM, throughout the foot. A radial basis function (RBF)-type regularization scheme is employed to obtain quality images by reducing image noise such as artifacts near the foot surface. More details about this code can be found in [15].

2.3 Measurement Protocol

The data presented were a result of a pilot study performed at the New York-Presbyterian Hospital–Columbia (NYP). The institutional review board (IRB) of the NYP approved the human subject protocol and written consents were obtained from all patients. During the imaging protocol the subjects were asked to place their foot on the patient interface (Figure 1) while sitting upright in a chair. A total of 34 fibers (14 source and 20 detection fibers) encompassed the foot, forming a coronal cross-section at the mid-metatarsal level. This location was chosen because it contains the major arteries of the foot the dorsalis pedis and the major branches of the posterior tibial artery. Physicians can probe these arteries when measuring a patient’s ABI. Furthermore, it is a common location for diabetic foot ulcers to occur and the vasculature in that region is too small to diagnose even with the high resolution anatomical imaging modalities such as CTA and MRA.

After positioning the probe around the patient’s foot, the instrument automatically determined and stored 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. Patients are familiar with leg cuffs from ABI measurements, making this dynamic protocol a natural extension of the existing diagnostic procedures. The protocol consists of five stages. First a baseline measurement was taken while the patient is seated at rest for approximately one minute. Second, the pressure cuff is inflated to 60mmHg around the thigh. This induces venous occlusion, allowing arteries to supply blood the foot but preventing the veins from returning it to the heart, causing the blood to pool in the foot. The pressure was maintained for one minute after which it was rapidly released. During the third stage of the sequence, the foot was left to recover for one minute. In the fourth portion of this protocol a 120mmHg was applied to the thigh inducing greater venous occlusion for one minute. Then the pressure was released enabling the foot was left to recover. This five-stage protocol was applied three times for each subject to show repeatability.

3. RESULTS

3.1 Time Traces

We present three select cases, one patient with PAD (ABI = 0.66), one patient with diabetes and PAD (ABI = 1.07) and one healthy subject (ABI = 1.00). Using the traditional ABI measurement it is possible to discern between the healthy control and the PAD patient, however the diabetic PAD patient is not distinguishable. Diabetic patients often have incompressible arteries due to calcifications which result in elevated ABI readings and leads to false negative diagnoses.

Figure 2 shows the detector intensity measurements for a single source position for the healthy, PAD patient and Diabetic PAD patient respectively. We can view the five stages of the imaging procedure within the raw detector readings. Initially there is a baseline period then upon application of the 60mmHg pressure cuff venous occlusion is induced. The blood pumps from the heart into the foot but since the veins are occluded it does not return but pools within the foot. This causes greater attenuation within the foot as the hemoglobin absorbs the light. This causes a dip in the detected intensity. The pressure cuff is then released and the blood returns to the heart and the light intensity returns to initial value during rest. Then when the pressure cuff is reapplied with greater magnitude of 120mmHg there was more blood that pooled in the legs causing a greater magnitude drop in detector intensity. Upon release the signal returned to its baseline rest state.
We observe a greater amplitude drops within the healthy subject (20% and 45%) than the PAD patient (10% and 15%) and the diabetic PAD patient (20% and 20%), before the release of the 60mmHg and the 120mmHg thigh cuffs (between phases 2-3 and 4-5). Furthermore, there appears to be a slower rate of decay and recovery of the detector readings within the affected vasculature patients during application and release of the thigh cuff. We suspect this is due to blood flow impedance caused by plaque within the vascular lumen as well as calcifications within the arterial wall decreasing arterial compliance. DDOT was capable of discerning between these three case studies even though the diabetic PAD patient suffered from calcified arteries, the traditional ABI measurement however resulted in a false-negative reading.

![Figure 2](image.jpg)

Figure 2. Normalized Detector Readings (different detector positions shown as colored lines) for a Single Source Illumination over time for (A) a Healthy volunteer, (B) PAD patient, and (C) a Diabetic PAD patient. The individual traces were filtered with a 50-point moving average filter. A dip in intensity is observed at approximately 1 minute when the 60mmHg cuff is applied to thigh. This impedes blood from returning to the heart and causes it to pool in the leg increasing light absorption. Upon release of the cuff the signal returns to baseline the same behavior can be seen with the 120mmHg cuff. There are clear differences in the magnitude drop during thigh occlusions as well as the recovery rates from release of the thigh cuff.

3.2 Image Reconstructions

Using models of light propagation in tissue [10, 15] we were able to obtain two-dimensional reconstructions of the change in total hemoglobin within the foot for each time point during the imaging protocol. Looking at the blood volume dynamics during the imaging sequence we see that the two time points prior to release of the thigh cuffs show the most significant differences between the three cases. Figure 3 shows reconstruction results before the release of the 60mmHg pressure, and before the release of the 120mmHg pressure. These images show clear differences between the healthy patient and the two PAD patients. The changes in [HbT] are much less pronounced in the feet of the PAD patients than the healthy volunteer. This suggests that there is significantly less blood pooling in PAD patients’ feet during a minute of venous occlusion. Physiologically we suspect that the differential is due to the blood flow impedance caused by plaque in the affected vasculature as well as arterial stiffening due to calcifications within the arterial wall lowering the vascular compliance.
To further quantify the hemodynamic change within the feet we calculated the sum of the [HbT] in each frame of the dynamic imaging sequence and obtained a area weighted average signal (Figure 4). These time traces show that the amount of blood within the foot increased when the thigh cuff was applied to the foot (phases 2 and 4). The increase in total hemoglobin in the foot during thigh occlusions is greatest within the healthy volunteer (Figure 4(A)), in concordance with the time-dependent detector readings. Furthermore, the patients with diseased vasculature (Figures 4(B), 4(C)) show slower occlusion and recovery rates than the healthy volunteer. This correlates with our previous assertion that plaque in the arterial walls is causing blood flow impedance caused less blood to pool in the foot and that arterial stiffening due to calcifications within the arterial wall is lowering the vascular compliance.

![Figure 3](image1.png)

**Figure 3.** 2D Reconstructions of the Total Hemoglobin Concentration [HbT] for Healthy volunteer, PAD patient and a Diabetic PAD patient. There is more hemoglobin present within the healthy volunteer than the two patient cross sections shown below it.

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![Figure 4](image2.png)

**Figure 4.** Area weighted Average Total Hemoglobin Signal Healthy for (A) Healthy Volunteer, (B) a PAD patient, and (C) a Diabetic PAD patient. We recover the five phases seen in the raw detector time traces and observe more blood pooling within the healthy volunteer than the patients with affected vasculature.

### 4. CONCLUSION

We reported on dynamic diffuse optical imaging (DDOT) results obtained for one healthy volunteer, one PAD patient and a patient with both PAD and diabetes. DDOT was used to show the hemodynamic responses observed within the foot while providing cross-sectional images that correspond to the foot vasculature. We found differences between all...
three cases in the magnitude of the detector intensity drop during thigh cuff occlusion and the weighted average change in [HbT] signal obtained from the image reconstructions. In addition, DDOT was capable of discerning between the diabetic patient’s vasculature, despite their arterial calcifications, which render the traditional diagnostic methods inapt. These preliminary results show that DDOT has the potential to aid in the diagnosis and monitoring of PAD. Furthermore it has the potential to fill the diagnostic gap that currently exists within the diabetic patient population.

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REFERENCES