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Near Infrared Spectroscopy of the diabetic foot

K. Y. Yong, J. E. Cobb and D. J. Claremont
kyyong@bournemouth.ac.uk
School of Design, Engineering and Computing, Bournemouth University

Abstract

Foot amputation due to plantar ulceration increases the burden to diabetic patients. A few risk factors have been identified for the development of ulceration. One of them is the impaired capillary exchange mechanism. However, the mechanism leading to the tissue becoming pre-disposed to damage is still not well understood. Assessment of this risk factor requires the study of blood flow during static and dynamic tissue loading, which has always been excluded in previous clinical studies. Our research team has identified a near infrared spectroscopy technique that may provide some information of cellular respiratory and metabolic activity during the static and dynamic tissue loading. This in turn may provide further understanding of the impaired capillary exchange mechanism leading to plantar ulceration.

1. Introduction

Complications due to diabetic foot ulcers are the main factor leading to foot amputation of diabetic patients. To reduce the trauma suffered by patients due to the loss of limb, early identification of risk factors is important to avoid the possibility of amputation. The factors that contribute to the foot ulceration include increased plantar pressure, loss of sensory perception due to somatic neuropathy [1] and the impaired capillary exchange mechanism due to microvascular disease [2]. This paper focuses on an impaired capillary exchange mechanism in the diabetic foot and a safe novel diagnostic tool is developed to perform the evaluation of tissue metabolism on the foot non-invasively. The diagnostic tool is based on the Near Infrared Spectroscopy (NIRS) technique that has found acceptance in other studies, such as, cerebral oxygenation [3-4] and characterisation of breast tumours [5-6].

1.1 Theory

NIRS is a technique that utilises spectra between 700nm to 1000nm where absorption by chromophores in tissue such as oxyhaemoglobin, deoxyhaemoglobin and cytochrome oxidase are low [7]. This spectral region is often known as the 'optical window'. NIRS technique is possible due to the fact that light can be propagated through biological tissue (see Figure 1) and its attenuation in relation to the biological tissue can be described simply by a modified Beer-Lambert's Law given by;

$$I_e = I_o \exp^{-(\mu a + \mu s)d}$$

where,

I_e is the emergent light intensity from tissue
I_o is the original light intensity before entering tissue
μ_a is the absorption coefficient
μ_s is the scattering coefficient
d is the actual photon pathlength between source and detector

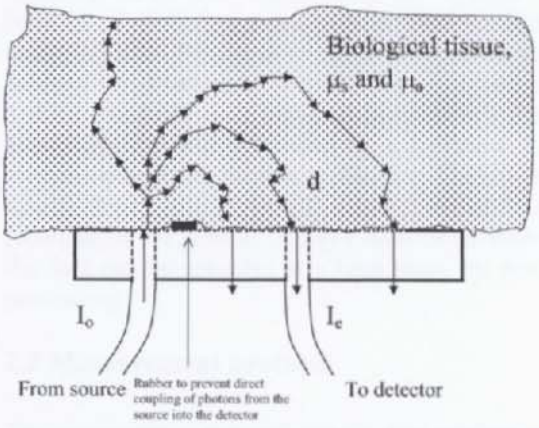

Figure 1. Light propagation in biological tissue.

When considering a single type of chromophore in tissue, any changes of measured intensity, ΔI_e, can be attributed to changes in chromophore

concentration. This is valid provided that μs does not change over the measurement period and the average photon pathlength, d, is a constant when the source and detector separation is fixed. The actual value of d is not known but can be estimated with Monte Carlo simulation [8] even though this information is not a necessity because of the relative measurements considered here.

In monitoring the impaired capillary exchange mechanism in the diabetic foot, the tissue metabolic status can be observed by measuring the concentration change of oxyhaemoglobin, deoxyhaemoglobin and the redox state of cytochrome oxidase. The specific extinction coefficient for these chromophores over the near-infrared region is given in Figure 2. Thus, three different wavelengths from this spectrum can be deployed to obtain individual changes of these chromophores. However, the concentration of cytochrome oxidase is much (at least an order of magnitude) lower than the concentration of oxyhaemoglobin and deoxyhaemoglobin [7] and as a result the signal of cytochrome oxidase is masked by the signal of oxyhaemoglobin and deoxyhaemoglobin. It is the aim of this project to evaluate the possibility of measuring the changing state of cytochrome oxidase which is indicative of cellular respiratory and metabolic activity in the diabetic foot.

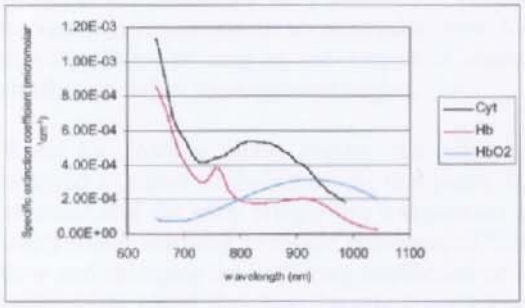

Figure 2. Absorption spectra of oxyhaemoglobin (HbO2), deoxyhaemoglobin (Hb) and cytochrome oxidase (Cyt). Note that the Cyt shown here is the difference between the oxidised and the reduced form. [7].

2. Methods

2.1 System Configuration

The instrument that has been developed so far utilises two light sources, i.e. wavelengths at 670nm and 850nm. A third wavelength at 805nm will be added to the system once it is established that the system is capable of obtaining useful physiological measurement at the sole of the foot. Thus, the results presented in this paper are based on two light sources. The system configuration is shown in Figure 3.

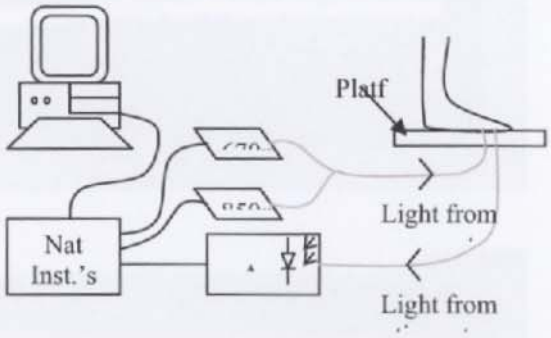

Figure 3. System configuration.

The light sources used are from laser diodes that have maximum optical power of 5mW (class 1). Each laser diode is used in conjunction with a laser diode controller (LasIRvis iC-WJZ) for protection against power surge. Both lasers are alternately switched-on and switched-off at 500Hz with a duty cycle of 50%. Thus, the combined average optical power emitted from the fibers of both lasers is 5mW, which is within the safety level. In reality, the actual power delivered to the tissue is less than 5mW due to the coupling loss between lasers and fibers and fiber bending loss. The light detector used is an avalanche photodiode (APD) manufactured by EG&G C30916E. The APD is reverse-biased to 200V and a transimpedance amplifier (OPA111) is used to convert the APD's current source into voltage signals. The use of a sensitive APD will ensure that the system is capable of detecting heavily backscattered light emerging from the tissue at 10mm away from the source fiber. The two laser sources are switched-on and switched-off via a National Instrument's data acquisition module controlled by a LabView 7.1 program developed for this application. During the measurement, the detected voltage signals are recorded in the control laptop's hard drive where the data can be reloaded at a later stage for post-processing.

2.2 Measurement protocol

The measurement protocol used in this application is to arrange patients sitting on a chair while resting both feet on a purpose-built platform with the sole's region of interest aligned upon the source-detector probe, which is built onto the platform surface. The measurement will begin with

little or no load on the foot. Blood flow into the probed tissue volume is expected to be normal and system's plethysmographic signal. The no load period is to be observed for 1 minute but there are no specific requirements to determine how long this should be as long as the subject is under a steady state when measurement begins.

When the loading phase begins, the subject is required to stand on their feet. At this point, it is assumed that the body weight has compressed the sole's tissue, resulting in higher resistance of blood flow and changing the scattering coefficient of the tissue. If the blood flow into the sole is sufficiently occluded by the body weight, the pulsatile signal will become small in the system's plethysmographic signal and the cellular respiratory and metabolic activity will become prominent. The loading period is expected to last for 5 minutes until the tissue's metabolic status has stabilised. The subject will then be instructed to sit on the chair again and data will be recorded for another 2 minutes to observe the re-perfusion of blood supply into the sole (a hyperaemic type response).

pulsatile signals should be discernible in the

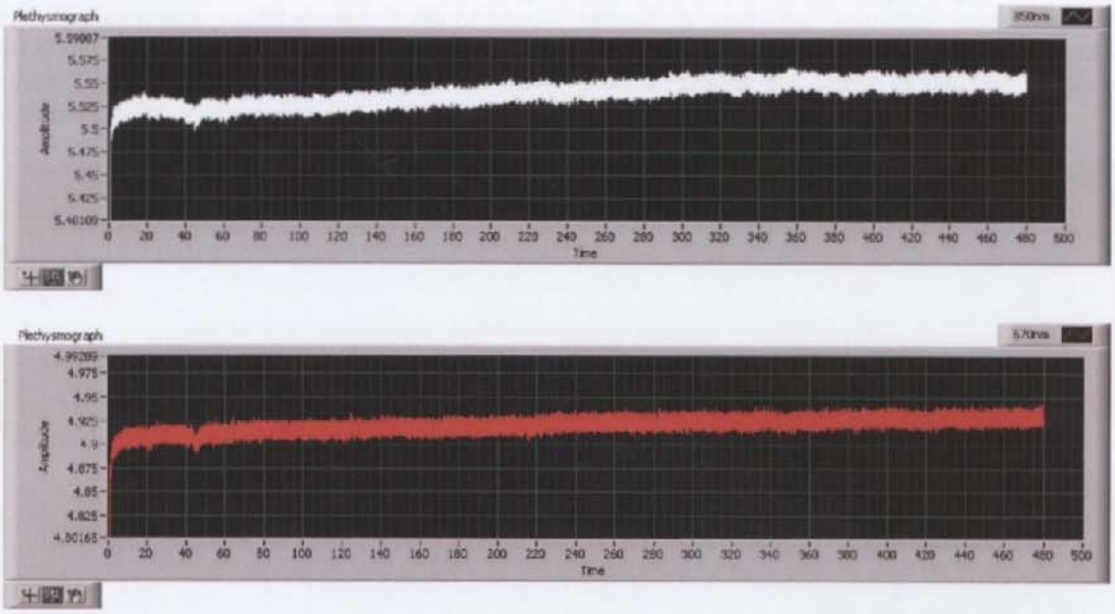

Figure 4. System stability test. The drift is 25mV over 8 minutes duration and the Vpeak-peak noise is around 20-25mV at 25°C room temperature.

3. Results

To measure any physiological changes of biological tissue, it is necessary that the system is stable over the measurement period. The laser diode noise and the detector noise are crucial in determining overall system sensitivity and measurement resolution. An important factor that affects the system stability is the ambient temperature. Figure 4 demonstrates the stability of our present system and the optical power drift is around 25mV over a period of 8 minutes, which is reasonably stable at 25°C room temperature. It is noticeable that the optical power drifts between the two lasers are similar. This is because both laser diodes are placed close to each other and share a common temperature change. Thus, it demonstrates that the instrument can be used as a differential measurement system with self-referencing, which means the system does not need calibration. This will be useful in isolating signals that are due to movement artefacts and thermal drifts. Even though this is not to state that thermal drift is insignificant, it can be reduced with the use of Peltier temperature controls. This will be incorporated into the laser diode controller in the future.

Figure 5 demonstrates a typical plethysmograph obtained with the protocol described in the previous section. In this case the overall measurement duration is 8 minutes. The loading phase begins at time, t = 60 second. It can be seen that at this point in time, both signals increase to a higher level. There are two possible factors that contribute to this increase. The first is that blood is squeezed out of the sole and blood supply into the sole is met with a higher flow resistance due to the body weight, thus it results in less light absorption and detection of higher light signal level. The second is that the scattering coefficient has increased and more light is being backscattered as a result. During the course of the loading phase,

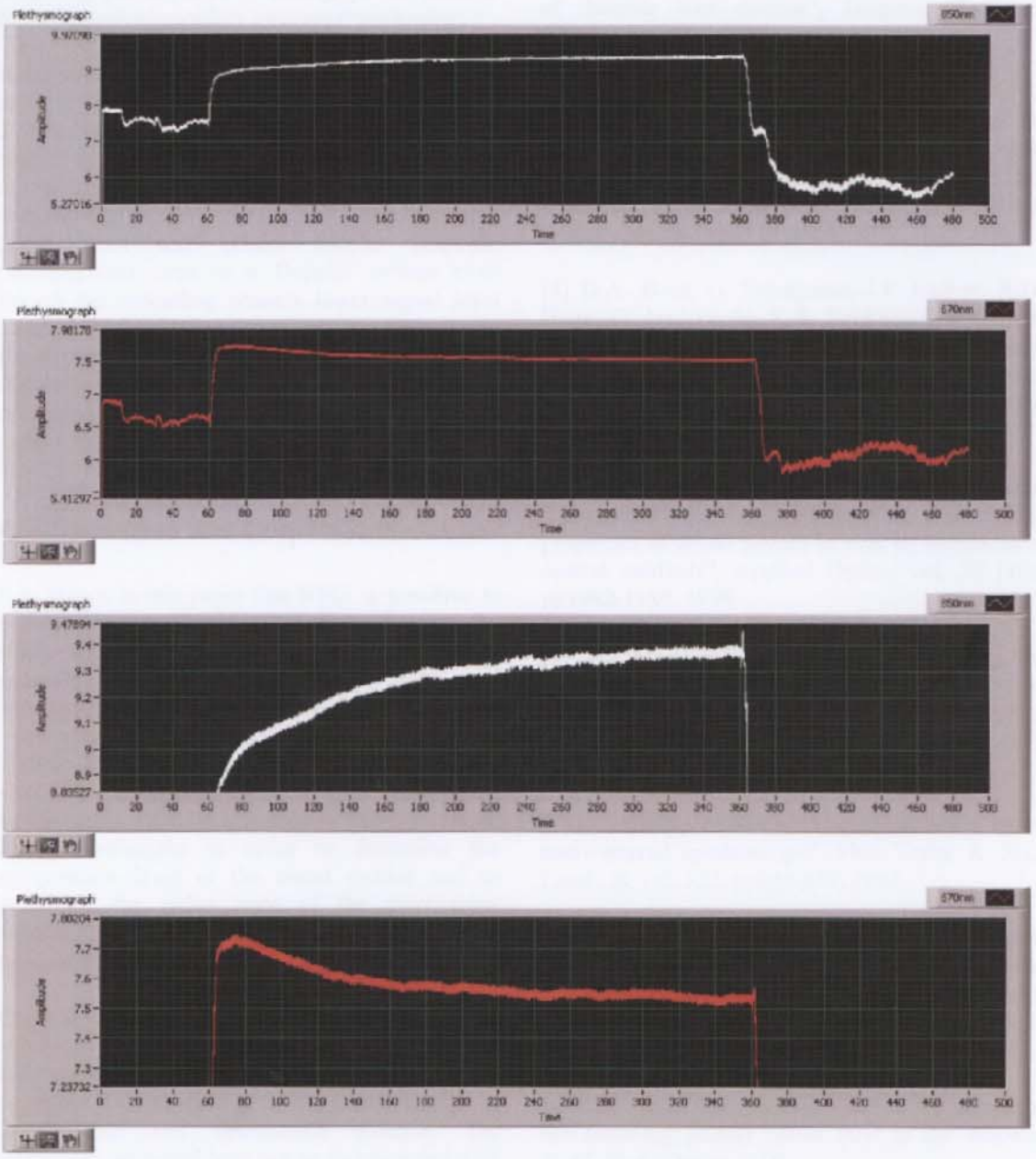

Figure 5. The top two graphs are typical plethysmographs obtained with the measurement protocol described in section 2.2. The bottom two graphs are the close up view of the loading phase.

the system picks up some small signal changes and this maybe due to the cellular respiratory and metabolic activity when blood supply is absent. It is important to note that the two different wavelengths experience a different amount of absorption over the five-minute loading phase

before levelling off towards the end of the phase. The 850nm wavelength indicates an up shift of 480mV from time, t = 80 to 360 second. While at the same time, the 670nm wavelength indicates a downshift of 200mV. Interpretation for these changes will only be possible when a third wavelength is introduced to the system. It is hoped that these signals may indicate early signs of tissue becoming pre-disposed to damage in the diabetic foot of impaired capillary exchange mechanism.

It has been reported by Cobb et al.'s laser Doppler study [9] that after a loading period of longer than 2 minutes, a hyperaemic response on unloading with a slow recovery time indicates microvasculature autonomic dysfunction of the sampled region. However, in NIRS the unloading phase does not exhibit similar response characteristics seen in a Doppler system even though the unloading phase's lower signal level means a higher haemoglobin concentration due to the hyperaemic response. The difference between the two systems is that the laser Doppler is optimised for blood flow speed while NIRS is used mainly for measuring chromophore concentration.

4. Discussion and Conclusions

It is shown in this paper that NIRS is sensitive to cellular respiratory and metabolic activity in the sole's tissue, which is naturally masked by the pulsatile signal. However, with only two wavelengths, it is not possible to make any specific interpretation of the signal changes during the loading phase. This is because there are three unknown quantities of chromophores in the tissue in this study. Thus, it is necessary to have at least three wavelengths in order to determine the oxygenation level of the blood residue and to determine the redox state of the cytochrome oxidase during the absence of blood supply induced by normal tissue loading.

Other than the need for more wavelengths in the system, the next development of the instrumentation is to determine the sensitivity or resolution of the system to the concentration of haemoglobin and cytochrome oxidase. The instrument presented here can be incorporated with a variety of other studies such as pulse oximetry and laser Doppler when appropriate algorithms are implemented. It will further strengthen our understanding of plantar ulceration due to the impaired capillary exchange mechanism and autonomic dysfunction when laser Doppler and NIRS data can be analysed concurrently.

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Acknowledgements

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