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Preliminary evaluation of a new fibre-optic cerebral oximetry system

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Abstract

A new system for measuring the oxygen saturation of blood within tissue has been developed, for a variety of patient monitoring applications. A particular unmet need is in the central nervous system, and this project aims to devise a means for measuring blood oxygen saturation in the brain tissue of patients recovering from neurosurgery or head injury. Coupling light sources and a photodetector to optical fibres results in a probe small enough to pass through a cranial bolt of the type already in use for intra-cranial pressure monitoring. The development and evaluation of a two-wavelength fibre-optic reflectance photoplethysmography (PPG) system are described. It was found that good quality red and near-infrared PPG signals could be obtained from the finger using a fibre-optic probe. Experiments were conducted to find the inter-fibre spacings that yield signals most suitable for calculating oxygen saturation. Reliable signals could be obtained for inter-fibre spacings between 2 mm and 5 mm, the latter being the size of the maximum aperture in the cranial bolt. A preliminary measurement from human brain tissue is also presented.

Keywords: cerebral, brain, oximetry, photoplethysmography, fibre-optic, cranial bolt

1. Introduction

Neurological damage following traumatic head injury or brain surgery does not all occur at the time of the impact or operation (primary injury), but can develop afterwards sometimes many hours or days later (Hinds and Watson 1996). The commonest causes of such secondary injury are intracranial bleeding and swelling of the brain, causing increased intracranial pressure (ICP), which in turn impedes cerebral blood perfusion leading to ischaemia and a lack of oxygen in the brain (Ghajar 2000). Several modalities have been developed to monitor the

causes and prevent such ischaemic injury including tissue oxygen sensors, jugular venous bulb oximeters and near-infrared spectroscopy (NIRS) (Mortara 1982).

The partial pressure of oxygen dissolved in the extracellular fluid of the cerebral tissue ($PbtO_2$) may be measured by introducing a Clark-type electrochemical sensor into the tissue; the sensor is inserted via a cranial bolt screwed into the skull. This technique provides a highly localized measurement reflecting the availability of oxygen at the tissue level (Haitsma and Maas 2007). Clinical experience with these sensors has shown, however, that a run-in time of up to 2 h is required before stable measurements are obtained (van den Brink *et al* 2000). Furthermore, the measurement is potentially sensitive to small haemorrhages occurring in the region of the probe (van den Brink *et al* 1998).

Jugular bulb venous oximeters measure the oxygen saturation $(SjvO_2)$ of the venous blood draining from the brain by inserting a catheter into the internal jugular vein, giving an indirect assessment of global cerebral oxygen use (White and Baker 2002). Although jugular bulb oximetry is used routinely in many head trauma units, there are numerous technical limitations associated with the technique. Incorrect positioning of the catheter, for example if the catheter tip is resting on the vessel wall, can lead to measurement errors. Approximately 3% of the blood in the jugular bulb is contaminated with extra-cerebral blood (i.e. from the scalp, skull and meninges), and the percentage increases with lower cerebral blood flows. In addition, the cerebral venous blood may not be representative of all regions of the brain, especially if the patient has asymmetric venous drainage (Schell and Cole 2000).

Near-infrared spectroscopy (NIRS) is a noninvasive optical technique and is a modality that can be used for monitoring brain tissue oxygen saturation, changes in blood volume and, indirectly, brain blood flow and oxygen consumption (Ferrari *et al* 2004). With NIRS however, there is a high degree of uncertainty in the exact brain volume being assessed. Computer models have shown that the volume of tissue interrogated by NIRS typically consists of 30% brain and 70% non-cerebral tissues (i.e. scalp and skull) (Hiraoka *et al* 1993). Absorption of light by these tissues, particularly the blood within the scalp vasculature complicates algorithms used in NIRS systems and can lead to inaccuracies in these systems' calculation of oxygen saturation (Germon *et al* 1994, 1995). The varying thickness of the skull and the cerebro-spinal fluid (CSF) layer affects the optical path length and can cause variation in measurements from one patient to another (Okada and Delpy 2003a, 2003b). Finally, NIRS does not work with certain patients, especially those who have an abnormally large sinus cavity, thus preventing the light reaching the cerebral tissue (Sehic and Thomas 2000).

To avoid the problems associated with the absorption of light by the superficial tissues, it has been proposed that pulse oximetry measurements be made directly from the brain tissue (Phillips *et al* 2006). A new system for directly monitoring brain tissue haemoglobin oxygen saturation using photoplethysmography (PPG) has been developed. The proposed fibre-optic system will be in direct contact with the brain tissue via a cranial bolt of the type used for the measurement of ICP, thereby eliminating tissues such as the scalp, skull and dura from the optical path. The aim is to produce a rapidly responding indicator of cerebral hypoxemia, which may be used for patients in whom the use of a cranial bolt is indicated for measurement of ICP.

Optical fibres enable monitoring within small cavities or biological areas where the placement of conventional optoelectronic probes is impossible due to size limitations. Additionally, optical fibres have the advantage that the tissue is electrically and thermally isolated from the light sources. The conduction of heat from the electrical components to the tissue is thus minimized, but heating is still possible due to the radiation transmitted to the tissue by the fibres. Experiments to estimate the thermal effect on brain tissue of the radiation from the new optical fibre PPG system are described.

Before any measurements were conducted on the brain, investigations of the fibre-optic system were carried out using the fingers of volunteers to find the optimum conditions for obtaining good quality PPG signals. In particular, the effect of changing the inter-fibre separation on the characteristics of the detected PPG signal was determined. The results of preliminary clinical PPG measurements on brain tissue using the system are also presented.

2. Methods

2.1. Measurement system

The measurement system for this study has been developed and evaluated in our laboratory and is based around a fibre optic reflectance PPG probe comprising two optical fibres, one of which is used to transmit light to the tissue and the other to return a fraction of the backscattered light to a photodetector. A signal-processing system consisting of a circuit interfaced with a notebook computer has been implemented for the calculation of clinical variables from the measured light intensities. The details of the design and development of the instrumentation and software are described below.

2.2. Instrumentation and software

2.2.1. Optical fibre probe. This consists of two silica optical fibres (a transmitting fibre and a receiving fibre) each with a core diameter of 400 μ m, an outer cladding diameter of 730 μ m and a numerical aperture (NA) of 0.39 (Ocean Optics Inc., Dunedin, FL, USA). The distal end of each fibre is cut and polished flat and the proximal end terminated with a male SMA connector. The fibres are coated in a protective PVC jacket, which is stripped away over a length of 16 cm from the distal end. The probe materials are biomedically compatible and allow steam sterilization at 136 °C.

2.2.2. Optical components. The light sources used are red and infrared light emitting diodes (LEDs), with peak emission wavelengths at 660 nm and 850 nm, respectively, mounted in SMA packages (the Optoelectronic Manufacturing Corporation Ltd, Redruth, UK). Both LEDs are connected to the single transmitting optical fibre using a Y-coupler, i.e. a bifurcated optical fibre assembly (Ocean Optics Inc., Dunedin, FL, USA). The photodetector is an SMA-packaged PIN photodiode of active surface area 0.8 mm² (the Optoelectronic Manufacturing Corporation Ltd). The photodetector is coupled directly to the receiving optical fibre (see figure 1).

2.2.3. Light source control and signal acquisition hardware. Figure 1 shows a block diagram of the instrumentation used for the control of the light sources and acquisition of signals from the tissue. The hardware is interfaced to a 16 bit DAQCard-AI-16XE-50 data acquisition card (National Instruments Inc., Austin, TX, USA) installed into a notebook computer. The LEDs are driven by a pair of switchable regulated current sources, one for each wavelength, supplying 25 mA and 14 mA to the red and infrared LEDs, respectively. Timing signals are provided by a programmable counter timer built into the data acquisition card, driving a down-counter. The output from the down-counter is connected to a multiplexing logic circuit, the output of which is used for switching the red and infrared LEDs. The duty cycle for each LED is 25%. The infrared LED is on for the first quarter cycle, then both LEDs are off to allow measurement of the ambient light intensity, the red LED is on for the third quarter cycle



Figure 1. Block diagram of the measurement system.

and, finally, both LEDs are off again for the last quarter cycle. Hence, the LEDs are switched on alternately and the frequency of the full cycle is 100 Hz.

The photodiode is connected to a differential transimpedance amplifier, which converts the photodiode current into a voltage proportional to the detected light intensity (see figure 1). A differential transimpedance amplifier is chosen as it has good noise rejection properties for common-mode signals in the leads of the photodiode (Webster 1997). The output of the transimpedance amplifier is fed into a demultiplexer consisting of three LF398 sampleand-hold circuits, synchronized with the multiplexer. A 1.25 ms time delay is introduced between switching on the LEDs and the triggering of the sample-and-hold circuits in the demultiplexer, which allows the detection circuits to settle before sampling. The signal is separated into three components by the demultiplexer, representing the infrared (IR), red (R) and ambient (AMB) light intensities. The infrared (IR) and red (R) PPG signals each contain a DC component and also a very much smaller AC component (usually less than 2% of the DC). The AC PPG components are separated from the IR and R signals at the demultiplexer output using second-order Butterworth bandpass filters with frequency responses extending from 0.4 to 16 Hz (at -3 dB). These AC PPGs are amplified with a non-inverting amplifier with a gain of 101 to give the R_{AC} and IR_{AC} signals shown in figure 1. The total intensities of the red R_{AC+DC} and infrared IR_{AC+DC} signals are obtained by filtering to remove high frequency switching noise from the demultiplexer using second-order low-pass Butterworth filters each

with a cut-off frequency of 16 Hz (at -3 dB). The instrumentation is powered by two 12 V 1.2 A h sealed lead-acid batteries (Yuasa Inc.).

2.2.4. Software. The red (R_{AC} and R_{AC+DC}), infrared (IR_{AC} and IR_{AC+DC}) and ambient light (AMB) signals are all fed into the analogue-to-digital converter built into the data acquisition card installed in a Sony VAIO PCG-Z600HEK notebook computer running a LabVIEW (National Instruments) Virtual Instrument (VI). The VI reads each of the five digitized signals at a rate of 100 samples per second, displays the PPG waveforms and records the signals in a spreadsheet file. The DC value may be calculated by subtracting the AC signal from the total signal. The 'ratio of ratios' *R* commonly used in pulse oximetry for the calculation of oxygen saturation (Mendelson 1992) is also calculated from the measurements. A value for *R* is calculated from the ratio of the quotients of the AC and DC amplitudes for the red (660 nm) and infrared (850 nm) wavelengths using the following formula:

$$R = \frac{R_{\rm AC}/R_{\rm DC}}{IR_{\rm AC}/IR_{\rm DC}}.$$
(1)

The ratio R is used to find the arterial oxygen saturation (SpO_2) by substituting in the equation

$$SpO_2 = 110 - 25R,$$
 (2)

which is a linear approximation to an empirically determined calibration curve, obtained from measurements in healthy volunteers (Moyle 2002).

2.3. Thermal safety test

A test was performed using a simulated tissue sample to assess the likely thermal effect of placing the optical fibre probe in contact with tissue. A spherical glass flask containing a water-based agar medium was used to simulate the thermal properties of nervous tissue, which is largely water. A single optical fibre coupled to the red and infrared LEDs by means of the bifurcated fibre assembly was embedded in a 100 g sample of the agar medium. The flask containing the agar sample and the fibre was placed in a temperature regulated water bath, which was maintained at 37 °C throughout the measurement. A K-type thermocouple was placed 1 mm from the end of the fibre within the medium. The thermocouple junction was placed in line with the fibre axis so that the radiation from the fibre was incident directly upon it. A second thermocouple was used to monitor the temperature of the water bath. Prior to the measurements, the agar sample was left in the water bath at 37 °C for 3 h for the agar to reach a steady state. The temperatures of the thermocouples were then recorded for 60 min, after which the circuit was switched on so that both light sources were emitting continuously. The drive currents for the red and infrared LEDs were 25 mA and 14 mA, respectively. The temperatures were recorded for a further 60 min. The light sources were then switched off and the temperatures recorded for another 60 min. The measurements were then repeated with the light sources pulsed as if in the operational state (i.e. a 25% duty cycle for each LED), with the drive currents of the red and infrared LEDs equal to 25 mA and 14 mA, respectively, whilst under the 'ON' condition.

2.4. Measurement of the effect of varying the inter-fibre separation on the PPG signal

The effect of changing the inter-fibre separation on the characteristics of the detected PPG signal was investigated by making PPG measurements from the finger. A diagram of the apparatus for measuring PPG signals from the finger is shown in figure 2. The two optical



Figure 2. Measurements of the inter-fibre separation, s.

fibres shown are the probes of the PPG measurement system, and for these experiments it was necessary to mount the fibres so that the lateral separation, *s*, measured between the axes of the fibres, could be adjusted and measured accurately.

The two optical fibres were mounted on to the jaws of a pair of Vernier callipers. The lateral separation, s, was adjusted by varying the distance between the jaws. This adjustment was facilitated by means of a thumbwheel, and the distance between the jaws was indicated by a Vernier scale reading to an accuracy of 0.02 mm. The callipers were mounted on an optical bench platform. An adapted pulse oximeter finger probe casing with an aperture cut into it was also attached to the optical bench. The casing performed the function of holding the finger in the correct position during the measurements. The calliper platform could be moved longitudinally so that the optical fibres were placed so as to just touch the skin surface without exerting any excess pressure.

The inter-fibre separation was set in randomized order to various distances in the range 1.0–8.0 mm and a continuous PPG signal recorded for 1 min at both the red (660 nm) and infrared (850 nm) wavelengths. Measurements were taken from the index finger and the middle finger of three volunteer subjects. During the measurements, drive currents of 25 mA and 14 mA were supplied to the red and infrared LEDs, respectively.

2.5. Preliminary measurements from the brain

These measurements utilize the IM-3 Cranial Access System (Integra Neurosciences Inc., Plainsboro, NJ, USA), which incorporates a triple lumen cranial bolt. This study was to investigate the feasibility of obtaining PPG signals from the brain tissue in neurosurgical patients and was approved by the local Research Ethics Committee. Consenting patients who required cranial bolts as part of their routine neurosurgical care were recruited. The cranial bolt was inserted by the neurosurgeon and the source and detector optical fibres were inserted via two of the lumens of the IM-3, approximately 5 mm into the brain, as shown in figures 3(a) and (b), and PPG signals were recorded for 5 min. The inter-fibre distance was 2 mm (set by the design of the IM-3 system) and 5 mm was chosen as a suitable depth of penetration to ensure that the detected light originated entirely from brain tissue and not from the dura and other surrounding tissues.



Figure 3. IM-3 cranial bolt with optical fibres inserted (a). Cranial bolt and fibres in situ (b).

3. Results

3.1. Thermal safety test

After the LED sources were switched on, the temperature of the agar rose and the sample appeared to reach a steady state after approximately 20 min, as shown in figure 4, where the difference between the temperature of the 37 °C water bath (T_1) and that of the agar sample (T_2) is plotted against time.

When the light sources were switched off, again a steady state temperature was achieved after approximately 20 min. The maximum temperature rise was no greater than 0.4 °C with both light sources emitting continuously. When the light sources were pulsed at a 25% duty cycle, the temperature rise was less than 0.2 °C.

3.2. The effect of varying the inter-fibre separation on the PPG signal

Samples of the AC PPG traces obtained from a finger at the red wavelength of 660 nm are shown in figure 5(a) for a 2 mm fibre separation. To reduce the effect of variations in light source intensity, the PPG trace was normalized by dividing by the total (AC+DC) signal intensity. It can be seen that the time-varying (AC) component of the signal at 2 mm separation



Figure 4. Graph showing changes in temperature induced in simulated tissue by the optical fibre probe, with LEDs operating at 25% and 100% duty cycles.

was very small (<0.5%) compared with the total photodiode output (AC+DC). At the greater 4 mm inter-fibre separation, the PPG amplitude, relative to the total (AC+DC) signal, was larger, as shown in figure 5(b). At the 8 mm inter-fibre separation the PPG amplitude was larger still, approximately 2% of the total (AC+DC) signal as shown in figure 5(c).

The normalized peak-to-peak amplitudes of the PPG traces for each cardiac cycle were averaged over the 1 min duration of each measurement. The mean of these amplitude results was determined for each subject. Figure 6 shows the mean of the average peak-to-peak amplitudes for the subjects plotted against the separation distance, *s*, for measurements at the red and infrared wavelengths. The value of this mean amplitude was found to increase as the inter-fibre separation increased for both wavelengths with the mean of the normalized amplitude for the red PPG being consistently smaller than that for the infrared PPG.

The coefficient of variation (CV) of the normalized peak-to-peak amplitudes of the AC PPG for each of the 1 min measuring periods was calculated. The coefficient of variation is the standard deviation of the amplitudes of the AC PPG divided by the mean amplitude over the 1 min measurement interval. The average value of CV for each subject was calculated. The mean of these CV values for the subjects is shown plotted against the inter-fibre separation, s, in figure 7.

For the red and infrared wavelengths, the CV was fairly constant at about 13% for separations of 2 mm and above but increased rapidly when the fibres were less than 2 mm apart. The two curves in figure 7 are very similar despite the large difference in source wavelength. An inter-fibre separation of 2 mm or greater was therefore sufficient to give a reasonably stable PPG trace. Figures 6 and 7 serve as a quantitative representation of the deterioration in quality observed in the PPG signal, as may be deduced from figure 5(a), when the inter-fibre separation was reduced below 2 mm.

Figure 8 shows a graph of the ratio-of-ratios R against separation derived from the finger data. Values were calculated using (1) and the means of variables obtained from the 60 s measurement periods for all subjects. The mean value of R was found to be fairly constant at about 0.52 over the entire range of separations. However, at separations below 2 mm the fluctuations in the value of R appeared to increase markedly as the fibre separation decreased, suggesting that the corresponding values of SpO_2 are likely to be unreliable. The values of



Figure 5. Samples of normalized AC PPG waveform traces at 660 nm obtained from a finger at an inter-fibre axial separation, s, of 2.0 mm (a), 4.0 mm (b) and 8.0 mm (c).

 SpO_2 , calculated using (2) and the mean values of *R*, are indicated on the right-hand *y*-axis in the figure and are in agreement with expected values for normal arterial blood.

3.3. Results from preliminary measurements from human brain tissue

Figure 9(a) shows a typical segment of the normalized infrared AC PPG waveform obtained from brain tissue and was recorded while the patient was lightly sedated and breathing



Figure 6. Effect of the inter-fibre axial separation, s, on the mean (\pm SD) normalized peak-to-peak amplitude of the AC PPG at 660 nm and 850 nm.



Figure 7. Effect of the inter-fibre separation, *s*, on the mean (\pm SD) of the coefficient of variation of the AC PPG amplitude at 660 nm and 850 nm.

spontaneously. Figure 9(b) shows the corresponding normalized red AC PPG waveform recorded simultaneously. The PPG waveforms appear to be slightly noisier than those in figures 5(b) and (c) obtained from the fingers of normal volunteers, but are reasonably well defined.

A 1 min sample, taken midway through the 5 min monitoring period, of the PPG brain waveforms was analysed and compared with the results from the fingers of volunteer subjects at the same inter-fibre separation. The mean peak-to-peak amplitudes and CV of PPG waveforms obtained from the brain tissue are shown in table 1. These values are compared with the mean normalized amplitude values for waveforms from the finger in the axial separation measurements at the same inter-fibre separation (2 mm), see figures 6 and 7.

It can be seen that the mean peak-to-peak amplitudes of the red and infrared brain waveforms were larger than those obtained from the finger at the same inter-fibre distance. The ratio-of-ratios obtained for the single 1 min sample period was found to have a value of



Figure 8. Effect of the inter-fibre axial separation, *s*, for a finger on the mean (\pm SD) of the 'ratio of ratios' *R* of the PPG signals and the derived *Sp*O₂.



Figure 9. Normalized infrared (a) and red (b) PPG signals recorded from the brain tissue via a cranial bolt, with a pulse rate of 52 beats per minute.

Table 1. Comparison of mean peak-to-peak amplitude and CV (shown in parentheses) for PPG waveforms obtained from the brain of a patient and the fingers of normal volunteers. Inter-fibre separation was 2 mm in each case.

Measurement site	Infrared	Red
Brain tissue	0.0440 (20.0%)	0.0328 (18.6%)
Finger	0.007 40 (14.7%)	0.003 62 (14.9%)

 0.74 ± 0.10 , which equates to an oxygen saturation value of $91 \pm 12\%$. The arterial oxygen saturation measured simultaneously from a finger pulse oximeter was 99%.

4. Discussion

The aim of this study was to demonstrate the feasibility of obtaining PPG signals of suitable quality for the calculation of SpO_2 using optical fibres to conduct light to and from the tissue. For the thermal safety measurements, it was supposed that the agar medium accurately simulated the thermal conductivity and specific thermal capacity of tissue, as both consist mainly of water. In tissue, however, the vascular perfusion has the effect of transporting heat away from regions of local heating. A 'worst case scenario' was thus represented in the measurements so we might expect a smaller temperature rise in tissue than in agar with the same power input. The maximum temperature rise noted was 0.4 °C, which was deemed to be too small to cause damage to the tissue at the monitoring site. Moreover, at the operational duty cycle and drive currents, a temperature rise of less than 0.2 °C was recorded. It can therefore be concluded that optical measurements from nervous tissue using this system should present a negligible risk of thermal injury.

It was found that good quality red and near-infrared PPG signals could be obtained from the finger using the fibre-optic probe. The PPG signals obtained with different inter-fibre separations were analysed and it was concluded that the signal amplitude and beat-to-beat variability were strongly dependent on the separation; the PPG amplitude increased and the variability decreased as the inter-fibre separation was increased. However, good signals could still be obtained at small separations down to 2 mm. The maximum lateral separation of the optical fibres may be limited by the diameter of a probe, whose size may be dictated by the intended application. For measurements in the brain, the cranial bolts currently available do not permit an inter-fibre axial separation greater than 2 mm. However, these results suggest that a separation of 2 mm is just sufficient to obtain PPG signals suitable for clinical measurements, see figures 6 and 7.

The exact behaviour of light when entering an inhomogeneous scattering/absorbing material is not clearly understood (Webster 1997). As tissue is a highly scattering medium, photons arriving at the detector (the distal end of the 'return' fibre) could have taken any one of many paths through the scattering medium. In a reflectance oximetry system, the light path increases significantly as the separation between the light source and an adjacent sensor is increased (Mendelson and Ochs 1988). In the finger the arterioles and capillaries do not extend up to the skin surface. At larger inter-fibre separations the light path traverses a greater volume of pulsatile tissue than at smaller separations. The light incident on the detector is therefore modulated to a greater degree by the pulsation of the tissue bed. This may explain the increase in the AC PPG amplitudes with increasing inter-fibre separation at both wavelengths shown in figure 6.

These preliminary measurements on the brain have demonstrated that satisfactory photoplethysmographic signals can be obtained from brain tissue using a fibre-optic probe inserted via a cranial bolt. The normalized peak-to-peak amplitudes of the brain PPG signals appear to be larger than those obtained from the fingers of normal volunteers using a similar probe. However, the arterial oxygen saturation value calculated using the brain PPGs slightly underestimates the value obtained from the patient's finger using a conventional pulse oximeter, although there is considerable variability in the estimated value for the brain. An optical-fibre-based system for determination of cerebral oxygen saturation in rats has been described previously (Rampil *et al* 1992), but our study appears to be the first report of PPG measurements from the human brain. The animal system used a bundle of fibres of diameter 3.0 mm,

and utilized a mercury-arc lamp in conjunction with filters to produce a two-wavelength oximeter.

Although the fact that NIRS is noninvasive seems advantageous, a large proportion of patients with severe head injury currently receive cranial bolts for the measurement of intracranial pressure (Murray *et al* 1999). The addition of a fibre-optic probe into an already present bolt would therefore incur minimal extra invasiveness and would be justifiable as it could provide valuable information regarding oxygenation, free of extracerebral contamination. Direct comparison of this technique with NIRS may be difficult because the fibre-optic measurements are highly localized, whereas NIRS produces a global measurement of oxygen saturation. Careful placement of the bolt, guided by CT/MRI images however might allow monitoring of localized injury which could not be resolved using NIRS.

Further evaluation of this technique in a larger number of patients is required to establish its value for monitoring. The aim would be to improve signal quality and to see if signals could be recorded for a clinically relevant period to allow effective monitoring. Oxygen saturation values obtained using this method would also be compared with those from other observations, preferably those relying on 'gold standard' CO oximetry.

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