

Use of near infrared spectroscopy to estimate cerebral blood flow in conscious and anaesthetized adult subjects

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Summary

Near infrared spectroscopy (NIRS) can be used to quantify cerebral haemodynamic states non-invasively and to estimate cerebral blood flow (CBF). In the first part of this study we have compared CBF measurements in conscious and anaesthetized subjects. In the second part we have compared paired measurements made during anaesthesia, first on the scalp and then the dura after craniotomy. Mean CBF was 17 (SD 7) ml 100 g⁻¹ min⁻¹ in the conscious subjects compared with 21 (8) ml 100 g⁻¹ min⁻¹ on the scalp during anaesthesia ($P > 0.1$). Mean CBF on the dura was 68 (21) ml 100 g⁻¹ min⁻¹ ($P < 0.0001$). Computer modelling suggests that the difference in magnitude between scalp and dura measurements of CBF is likely to be caused by the optical effect of extracerebral tissue which powerfully scatters light passing through it but does not contribute significantly to the measured CBF because it has only a small blood content itself. The results lend support to this method of estimating CBF although formal validation by comparison with an established technique is needed. (*Br. J. Anaesth.* 1996; 76: 43–48)

Key words

Brain, blood flow. Measurement techniques, near infrared spectroscopy.

Although the assessment of cerebral perfusion is of great clinical importance, the measurement techniques that are currently available have notable drawbacks. Some use ionizing radiation and others require cannulation of the large cerebral vessels. Doppler velocimetry is non-invasive but measures cerebral blood flow velocity and not cerebral blood flow (CBF) directly; furthermore, it is affected by changes in the diameter of the insonated vessel and the angle of insonation.

Near infrared spectroscopy (NIRS) is a non-invasive technique which is capable of measuring changes in the concentration of tissue oxy- and deoxyhaemoglobin (HbO₂ and Hb) [1, 2]. If optical fibre bundles are applied to the scalp, measurements can be obtained from the intact head. Several variables may be measured, including cerebral blood volume (CBV) [3], cerebral blood flow (CBF) [4] and

the response of the cerebral circulation to alterations in Pa_{CO₂} [5]. The technique for measuring CBF was described initially using a bolus of HbO₂ generated in the lungs as a marker of brain-blood inflow but a modification using indocyanine green has been developed recently [6]. The HbO₂ method has been validated in newborn infants [7, 8]. The method has also been used to measure CBF [9] and forearm muscle blood flow in adults [10].

The aim of the first part of the study was to apply this technique using optical fibres placed on the scalp as described previously [9] in order to compare measurements of CBF in conscious adult volunteers with those made in patients undergoing general anaesthesia. The second part of the study, in patients undergoing craniotomy, compared measurements of CBF obtained when the optical fibres were placed on the scalp with measurements obtained using fibres placed directly on the dura.

Methods and materials

SUBJECTS

Conscious subjects

Eleven healthy volunteers with a mean age of 30 (range 21 to 44) yr gave informed consent. The subjects lay supine with eyes closed, breathing a gas mixture of oxygen and nitrogen from a modified anaesthetic machine using a mouthpiece and nose occluder. Fractional inspired oxygen concentration (F_IO₂) (model 5550, Hudson, CA, USA), end-tidal carbon dioxide concentration (Datex Cardiocap, Datex Inc., Helsinki, Finland) or transcutaneous carbon dioxide concentration (Novametrix 850, Novametrix Inc., Wallingford, CT, USA), were monitored. Arterial oxygen saturation (Sp_{O₂}) was measured on the earlobe with a pulse oximeter

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modified to update the value with every heartbeat (Nellcor N200E, Nellcor, Hayward, CA, USA). Heart rate was recorded from the pulse oximeter. The subject's haemoglobin concentration was estimated from a sample of blood.

Anaesthetized subjects

Ten anaesthetized patients were studied during neurosurgery for medically intractable epilepsy. Their mean age was 32 (range 19 to 48) yr. The neuropathological diagnosis in nine was hippocampal sclerosis. The remaining subject had a dysembryoplastic neuroepithelial tumour. The patients were otherwise healthy. Anaesthesia was induced with fentanyl 100 µg and thiopentone 3–6 mg kg⁻¹ i.v. and maintained with isoflurane up to 1.1 % in 30–35 % oxygen with nitrous oxide. Vecuronium 0.1 mg kg⁻¹ was used to provide neuromuscular block for tracheal intubation and paralysis was subsequently maintained with an infusion of the same drug. In addition to routine clinical monitoring end-tidal carbon dioxide and end-tidal isoflurane concentration (Datex Capnomac) were measured throughout the procedure. End-tidal isoflurane concentration was kept constant during CBF measurements. The lungs were ventilated to normocapnia. Mean arterial pressure (MAP) was measured either oscillometrically or by transduction from a radial arterial cannula. Incremental doses of fentanyl and labetalol were given to keep MAP as constant as possible throughout the studies. Sp_O₂ was measured on the earlobe. Body temperature was not measured as all measurements were made close to the start of anaesthesia and normal warming techniques were employed. Near infrared spectroscopy measurements were obtained from the scalp in all 10 subjects and from the dura in seven subjects.

NEAR INFRARED SPECTROSCOPY (NIRS)

A portable NIRS apparatus (NIRO 500 or 1000, Hamamatsu Photonics KK, Hamamatsu, Japan) was used. Near infrared light at four (NIRO 500) or six (NIRO 1000) wavelengths between 700 and 910 nm was conveyed by a fiberoptic cable to the subject's head. A similar fibre bundle conveyed light transmitted through the head back to the apparatus. The end of the fibre (optode) was positioned on the left frontal region of the scalp avoiding the temporalis muscle. The median distance between the optodes was 4.2 (range 3.4–5.3) cm on the scalp. The optodes were covered with an opaque cloth to prevent interference from background illumination.

When measurements were made on the dura the optical fibres were sealed in sterile plastic film ('Steridrape', 3M) and held gently in position on the temporal dura using a Yasargil clamp (Down's Aesculap, London, UK). The interoptode distance was 2.5 cm.

Changes in light absorption were detected and converted into changes in the intracranial concentrations of HbO₂ and Hb using a previously established algorithm [11, 12]. This makes use of the

Lambert-Beer relationship modified to take account of the increase in optical pathlength because of intense light scattering by biological tissue. A pathlength factor of 5.9 times the distance between the optical fibres was assumed [13]. Changes in total cerebral haemoglobin concentration (Hbsum) were calculated from the sum of the changes in HbO₂ and Hb concentrations. The details of these calculations have been described elsewhere [14].

Measurements were made continuously with a sampling interval of 0.5 s and displayed on a computer screen during the study. The NIRS, Sp_O₂ and end-tidal carbon dioxide data were recorded simultaneously onto a computer disk for analysis later. All measurements were made under steady-state conditions.

The studies were approved both by the Joint Committee on the Ethics of Medical Investigation of University College London Hospitals and by the Joint Medical Ethics Committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology. Informed written consent was obtained before each study.

CBF MEASUREMENTS

CBF was estimated using a modification of the Fick principle according to a previously established technique [4, 9]. A transient increase $F_{I_{O_2}}$ in produced a bolus of HbO₂ which acted as an intravascular tracer; it was measured in the arterial system by pulse oximetry and its entry into the brain was detected by NIRS.

Before each measurement of CBF the $F_{I_{O_2}}$ was reduced to allow Sp_O₂ to equilibrate at 91–93 % for 10–20 s. Three to four breaths of 100 % oxygen were then given, causing Sp_O₂ to increase rapidly to 97–98 % in less than 10 s. The change in cerebral HbO₂ concentration was determined by the NIRS apparatus. The first 4 s of tracer wash-in were taken for each estimation of CBF, on the basis of evidence that mean cerebral transit time is between 6 and 10 s [15]. After re-establishment of a stable baseline a mean of 4 usable measurements were obtained in each subject. The mean value for CBF was then calculated for each subject using the formula:

$$CBF = K \frac{\Delta HbO_2}{\int_0^t \Delta f Sp_{O_2} dt}$$

where ΔHbO_2 is the change in haemoglobin concentration measured by NIRS in time t , $\Delta f Sp_{O_2}$ is the change in fractional arterial oxygen saturation and K is a constant incorporating blood haemoglobin concentration, molecular mass of haemoglobin and cerebral tissue density. This converts the units for CBF from $\mu\text{mol litre}^{-1} \text{s}^{-1}$ to $\text{ml } 100 \text{ g}^{-1} \text{min}^{-1}$. As part of the CBF calculation procedure approximately 30 % of measurements are typically rejected on the basis of an excessively varying baseline Hbsum, end-tidal carbon dioxide or MAP. These aspects and others comprising the theoretical basis of the technique in adults have been discussed previously in detail [15].

STATISTICAL ANALYSIS

The values for CBF in conscious and anaesthetized subjects were compared using an unpaired *t* test. The values for CBF measured on the scalp and on the dura were compared with a paired *t* test.

Results

With the optical fibres positioned on the scalp, the mean CBF in the conscious subjects was 17 (SD 7) ml 100 g⁻¹ min⁻¹ compared with 21 (8) ml 100 g⁻¹ min⁻¹

in the anaesthetized subjects (*P* > 0.1). In the seven patients in whom CBF was measured on the dura, mean CBF with the fibres on the dura was 68 (21) ml 100 g⁻¹ min⁻¹ *P* < 0.0001 compared with the scalp. The values for CBF, heart rate and end-tidal carbon dioxide in the conscious volunteers are given in table 1. The values for mean end-tidal carbon dioxide and MAP in each anaesthetized subject are shown in table 2 together with the mean value for CBF in each subject. Table 3 shows the paired values for CBF measured on the scalp and dura during anaesthesia with the corresponding values for end-tidal carbon dioxide and MAP. Data collected during a typical

Table 1 Age and mean values for cerebral blood flow (CBF), heart rate and end-tidal (ET) or transcutaneous pCO₂ (TCCO₂) in conscious subjects. n = number of CBF measurements

Subject	Age	CBF (ml 100 g ⁻¹ min ⁻¹) Mean (SD)	n	Heart rate (beat min ⁻¹) Mean (SD)	ET/TCCO ₂ (*) (kPa) Mean (SD)
1	21	23 (12)	7	67 (1)	4.2 (0.3)
2	29	9 (4)	6	63 (1)	4.7 (0.3)
3	44	17 (9)	5	60 (3)	4.5 (0.3)
4	29	16 (7)	5	55 (1)	3.0 (0)
5	27	10 (4)	5	61 (5)	4.1 (0.4)
6	28	12 (3)	3	65 (10)	4.5 (0.5)
7	26	10 (3)	6	67 (2)	4.3 (0.1)*
8	36	15 (10)	4	68 (3)	5.5 (0.1)*
9	36	23 (11)	4	69 (3)	4.3 (0.1)*
10	22	19 (9)	4	56 (4)	7.2 (0.3)*
11	29	30 (10)	6	84 (2)	5.7 (0.1)*
Mean (SD)	30 (6)	17 (7)	5	65 (8)	4.7 (1.1)

Table 2 Age diagnosis and mean values for cerebral blood flow (CBF), mean arterial pressure (MAP) and end-tidal CO₂ (ETCO₂) in anaesthetized subjects. (HS = Hippocampal sclerosis; DNET = dysembroplastic neuroepithelial tumour)

Subject	Diagnosis	Age	CBF (ml 100 g ⁻¹ min ⁻¹) Mean (SD)	n	MAP (mm Hg) Mean (SD)	ETCO ₂ (kPa) Mean (SD)
1	HS	48	23 (7)	3	82 (4)	4.5 (0.1)
2	HS	19	30 (3)	4	68 (4)	4.0 (0.1)
3	HS	25	26 (2)	3	63 (1)	4.0 (0.1)
4	DNET	39	30 (18)	3	59 (1)	5.3 (0.1)
5	HS	37	16 (3)	3	79 (5)	5.3 (0.1)
6	HS	34	13 (8)	4	72 (2)	4.5 (0.1)
7	HS	34	9 (3)	5	78 (5)	5.3 (0.1)
8	HS	31	22 (10)	4	57 (3)	5 (-)
9	HS	29	28 (9)	4	74 (9)	3.8 (0.3)
10	HS	21	21 (13)	4	81 (1)	6.7 (1.8)
Mean		32 (9)	21 (8)	4	71 (9)	4.7 (0.8)

Table 3 Mean values for cerebral blood flow (CBF), end-tidal (ETCO₂) and arterial pressure (MAP) in anaesthetized subjects measured both on the scalp and on the dura

Subject	Scalp			Dura		
	CBF (ml 100 g ⁻¹ min ⁻¹) Mean (SD)	ET/TCCO ₂ (kPa) n Mean (SD)	MAP (mm Hg) Mean (SD)	CBF (ml 100 g ⁻¹ min ⁻¹) Mean (SD)	ET/TCCO ₂ (kPa) n Mean (SD)	MAP (mm Hg) Mean (SD)
1	23 (7)	3 4.5 (0.1)	82 (4)	65 (6)	5 4.1 (0.1)	71 (1)
2	30 (3)	4 4.0 (0.1)	68 (4)	67 (13)	4 4.1 (0.4)	93 (2)
3	26 (2)	3 4.0 (0.1)	63 (1)	95 (34)	5 5.4 (0.3)	64 (2)
4	30 (18)	3 5.3 (0.1)	59 (1)	79 (49)	5 5.4 (0.3)	57 (2)
5	16 (3)	3 5.3 (0.1)	79 (5)	27 (4)	4 4.5 (0.3)	72 (3)
6	13 (8)	3 4.5 (0.1)	72 (2)	73 (35)	4 4.1 (0.1)	72 (2)
7	9 (3)	5 5.1 (0.1)	78 (5)	70 (18)	4 4.9 (0.1)	77 (3)
Mean	21 (8)	3 4.6 (0.5)	72 (9)	68 (21)	4 4.6 (0.7)	72 (11)

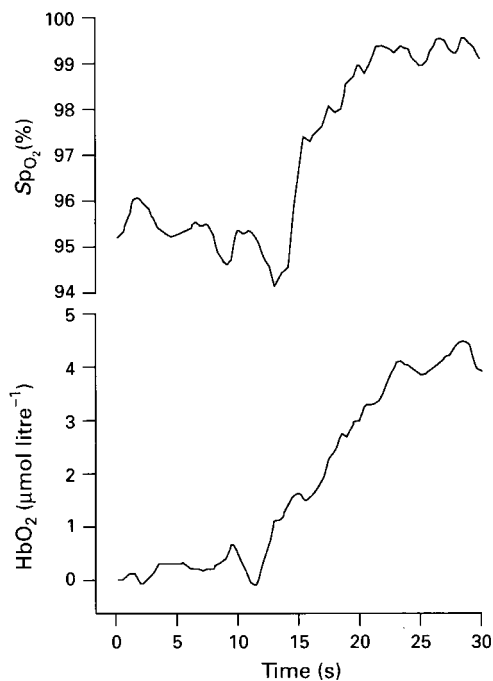


Figure 1 Representative data collected from an anaesthetized subject during a CBF measurement. The temporal offset between the increase in HbO₂ concentration and the increase in SpO₂ is a result of the faster arrival of the tracer in the cerebral circulation than at the earlobe.

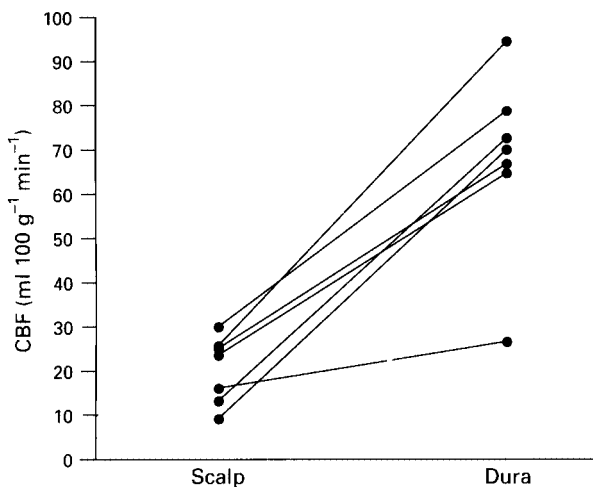


Figure 2 Cerebral blood flow (CBF) measured on the scalp and dura by NIRS in seven subjects.

CBF measurement are shown in figure 1 and the paired data for CBF on the scalp and dura are shown in figure 2.

Discussion

We have obtained non-invasive estimates of CBF using NIRS in adult subjects with the optodes placed on the scalp and directly on the dura. There are several assumptions underlying the use of NIRS to estimate CBF. In particular we have assumed that over the short period of the measurement (4 s) the small quantity of additional oxyhaemoglobin which enters the cerebral circulation acts as an inert tracer,

and causes no significant effect on CMRO₂, CBF or cerebral blood volume (CBV). Previous physiological studies have shown that CBF is virtually constant when arterial oxygen tension varies between 5.7 and 12.3 kPa [16]. Furthermore, during our measurements the total cerebral haemoglobin concentration ([Hbsum]) was seen to remain constant, suggesting that, despite rapid changes in SpO₂, there had been no significant change in CBV. Finally, it is well known that, provided SpO₂ is maintained within the physiological range, and brain metabolic requirements are being met, an increase in cerebral oxygen delivery does not result in an increase in oxygen extraction [17]. In these circumstances the small additional increment in HbO₂ concentration can be justifiably regarded as an inert tracer. This is discussed further elsewhere [9].

The values obtained for CBF when the optical fibres were positioned on the scalp were much lower than those obtained by invasive techniques, such as the i.v. ¹³³Xe washout technique [18], the Kety-Schmidt method [19], or by positron emission tomography (PET) [20]. However, the measured values for CBF when the optodes were positioned directly on the dura are in close agreement with those obtained using other established methods. Kety and Schmidt estimated mean CBF as 54 (12) ml 100 g⁻¹ min⁻¹ [21]. In healthy young men, a typical value by ¹³³Xe washout is 48 (7) ml 100 g⁻¹ min⁻¹ [18] and a typical value for grey matter by PET is 55 ml 100 g⁻¹ min⁻¹ [20].

The underestimation of CBF when the fibres were placed on the scalp is probably caused by the effects of extracerebral tissue on the transmission of light through the cranial cavity. Although it is a fundamental principle of NIRS that biological tissue is translucent to infrared light, nevertheless photons crossing the head travel on a path substantially longer than the linear distance between their points of entry and exit because of the scattering effect mentioned above. The true pathlength has been measured as 5.9 times greater than the linear pathlength (the interoptode spacing) in the adult head.

When this pathlength factor (DPF) is known, the distance that light has travelled through the head can be inserted into the Lambert-Beer equation and changes in haemoglobin concentration can be quantified. Computer modelling of near infrared light propagation in the adult head suggests that extracerebral tissue contributes 60–70% of the total optical pathlength [22] but has very little blood flow (around 5–8 ml 100 g⁻¹ min⁻¹ [23]). When a rapid change in SpO₂ is induced in order to make a measurement of CBF, the change in haemoglobin concentration occurs almost entirely in the cerebral tissue over the 4-s period of the measurement, since the blood flow to extracerebral tissue is so low. As cerebral tissue occupies only 30–40% of the illuminated tissue volume the true CBF is thus underestimated by a factor which is equal to the ratio of the optical pathlength in brain compared with the total optical pathlength. When the optical fibres are placed directly on the dura the extracerebral component of the pathlength is reduced to zero and there is

therefore no underestimation of CBF. Our results suggest that there is an approximately threefold underestimate of CBF with fibres on the scalp.

As the effects of extracerebral tissues are likely to be relatively consistent between different subjects, reliable comparisons of measurements between and within patients may be possible. In future it may be possible to determine directly the contribution of extracerebral tissue to the total optical pathlength in each subject, thus enabling CBF measurements obtained by NIRS from the scalp to be compared directly with measurements obtained by other techniques.

We did not observe a significant change in CBF as a result of anaesthesia in our study whereas there was a significant (approximately threefold) increase in CBF values measured on the dura in all except one patient. Mean arterial pressure was assumed to be in the normal range in the conscious objects and was not measured; the values for heart rate are normal supporting this assumption. The difference between end-tidal carbon dioxide, and P_{aCO_2} is unlikely to have introduced a significant error. The mean end-tidal carbon dioxide of the anaesthetized group was the same as that of the conscious subjects (4.7 kPa). There was no significant difference in mean end-tidal carbon dioxide between measurements on the scalp and on the dura but it is notable that the patient with the smallest difference between scalp and dura CBF (patient 5) exhibited a decrease in end-tidal carbon dioxide and the patient with the greatest change (patient 3) exhibited an increase in end-tidal carbon dioxide. Two patients had arterial pressures which were close to the lower end of the autoregulatory range but in both cases the values for MAP on the scalp and dura were almost identical. The neuropathological diagnoses in the anaesthetized group were unlikely to have influenced CBF.

The drugs used during anaesthesia are thought to have minimal effects on CBF. In human studies to date, fentanyl [24] has not been observed to cause a significant increase in CBF, although in one study, when given at a dose of $10 \mu\text{g kg}^{-1}$ it caused a decrease [25]. Similarly, the administration of isoflurane is not associated with an increase in CBF when administered in nitrous oxide to a combined MAC of 1.5 [26, 27]. No patient in our study received an inspired isoflurane concentration greater than 1.1% in 60% nitrous oxide (i.e. a combined MAC of 1.7) and most received less. In each patient the end-tidal isoflurane concentration was maintained at a constant value for both sets of measurements.

The evidence on the effect of nitrous oxide on CBF is less clear although there is a tendency for CBF to increase during anaesthesia. In one recent study, CBF was measured by ^{133}Xe washout in volunteers during the inhalation of 30% and 50% nitrous oxide. CBF was said to be significantly greater breathing nitrous oxide than air although absolute values were not given [28]. In another study also using ^{133}Xe washout, patients receiving 35% oxygen in air or nitrous oxide, supplemented with isoflurane, nitrous oxide caused an increase in CBF

from 40 to 57 ml $100 \text{ g}^{-1} \text{ min}^{-1}$ [29], a 43% rise. Our study showed an increase of 24% from 17 to 21 ml $100 \text{ g}^{-1} \text{ min}^{-1}$ but this was not statistically significant. In summary, we are not able to demonstrate a significant effect of general anaesthesia on CBF with the present technique.

We conclude that NIRS has the potential to provide non-invasive bedside assessment of CBF in adult subjects when the contribution of surface tissues to the differential pathlength factor in each individual studied is quantified. Although the values obtained from the scalp appear to underestimate the true CBF because of the optical effect of the extracerebral tissues, the technique allows comparison of measurements between and within subjects. In neurosurgical procedures involving craniotomy NIRS allows intraoperative measurement of CBF with the optical fibres positioned on the dura. The values thus obtained are in close agreement with those obtained by other means. Although further validation studies are required this technique appears to have potential for the non-invasive, bedside assessment of cerebral perfusion.

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