PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Use of near–infrared spectroscopy in the adult

Peter J. Kirkpatrick

Phil. Trans. R. Soc. Lond. B 1997 **352**, 701-705
doi: 10.1098/rstb.1997.0052

Use of near-infrared spectroscopy in the adult

PETER J. KIRKPATRICK

Department of Neurosurgery, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK

SUMMARY

Adult near-infrared spectroscopy is a potential method for observing changes in cerebral oxygenation non-invasively. Access of light to the adult brain requires penetration through extracranial tissues; hence the detection of changes in cerebral chromophore concentration can only be achieved by using near-infrared spectroscopy in the reflectance-mode thereby adding variables which are difficult to control. These include the effects of variable anatomy, different intra-optode distances and the presence of an extra- to intracranial collateral blood supply. Although movements of oxygenated haemoglobin concentration following specific cerebral stimuli can be demonstrated, the challenge of separating changes which occur within the extracranial compartment from those occurring in the intracranial compartments remains. Our experience with near-infrared spectroscopy in the three adult clinical scenarios of carotid endarterectomy, head injury and carbon dioxide stress testing will be presented. The influence of extracranial contamination is demonstrated, as are the methods we have developed to help control for extracranial contamination. Provisional experience with spatially resolved spectroscopy technology will also be presented.

1. INTRODUCTION

I would like to develop a case for the use of NIRS in monitoring the adult brain following injury. The pathophysiological events occurring after severe brain trauma are highly complex. However, a number of detrimental processes are understood. In a brain which is injured and swollen, a fall in the net cerebral perfusion pressure (CPP) is common, and the relative fall in cerebral blood flow (CBF) that results leads to a decreased oxygen availability and tissue hypoxia. Secondary consequences include the release of endogenous toxins such as excessive amounts of excitatory amino acids, processes that, together with progressive energy failure, lead to abnormal ionic gradients, and eventually the integrity of the cell membranes is disrupted leading to cell death.

Within an injured brain, a common feature is the heterogeneity of the processes of injury—as seen even at the macroscopic level, where there are areas of swollen parenchyma interlaced with haemorrhagic regions. It is this heterogeneity which makes prognostication and targeting of therapy difficult. However, combinations of certain clinical features are predictive of outcome. We now know that in a patient presenting to casualty with a severe head injury, the presence of both hypoxia and hypotension indicates a uniformly poor outcome and usual death. We also know that in patients who are observed in the intensive care setting, a low cerebral blood flow within the first four hours of injury is detrimental. Further, the presence of very high intracranial pressure, or very low cerebral perfusion pressure, is associated with a poor outcome, as are several episodes of profound cerebral desaturation. Thus basic physiological parameters, although difficult to monitor in the clinical setting, are extremely important in the brain-injured individual.

What is emerging is a common factor—tissue hypoxia, often transient, and which can occur following trauma, stroke or encephalopathy. A requirement for a continuous estimation of tissue oxygenation is therefore of considerable clinical importance. The limitations of conventional brain imaging are well known. These methods can only be carried out intermittently providing poor temporal resolution. They are thereby likely to miss many adverse events lasting for just a few minutes. There is also an issue of X-ray and isotope dosimetry, and a real concern that the transfer of highly unstable patients to imaging facilities is dangerous.

Adult near-infrared spectroscopy is a potential method for assessing changes in cerebral oxygenation non-invasively. However, access of light to the adult brain requires penetration through thick extracranial tissues, and hence detection of changes in cerebral chromophore concentration are contaminated. This adds variables which are difficult to control. They include the effects of a different intra-optode distance, intersubject anatomical variation and the influence of a variable extra- to intracranial collateral blood supply. By incorporating NIRS into a multimodal monitoring system, we have attempted to control these variables in head-injured patients, during carbon dioxide (CO_2) reactivity testing, and during carotid endarterectomy.

Our system has evolved over the past four years to encompass the modalities of: (i) intracranial pressure (ICP); (ii) arterial blood pressure (ABP); (iii) systemic arterial oxygen saturation (SaO_2) using standard pulse

oximetry; (iv) middle cerebral artery flow velocity (FV) using transcranial Doppler; (v) cortical or cutaneous microcirculatory red cell flux using laser Doppler flowmetry (LDF); (vi) jugular bulb oximetry to measure cerebral venous oxygen saturation (SjO_2); and (vii) the measurement of relative changes in frontal oxy- (HbO_2) and deoxy- (Hb) haemoglobin with a Hamamatsu NIRS system (NIR1000 and NIR500). When combining LDF with NIRS, overlap in the light wavelength adopted by the two machines requires consideration. In our system, the Moor's Laser Doppler Flowmeter (MBF3D monitor and modified P3 probe, UK) was fitted with a compatible laser diode using light in the visible spectrum.

Waveforms were processed using specific software. Data was stored on an IBM 386 portable PC. A minute-by-minute graphical display of mean CPP, ICP, LDF, FV, SjO_2, HbO_2 and Hb was provided to assist in the clinical management of the individual patients.

2. OBSERVATIONS USING NIRS DURING CAROTID ENDARTERECTOMY

The first 40 patients were monitored whilst undergoing a standard carotid endarterectomy (CE) with clamping of the internal carotid artery (ICA) before the external carotid artery (ECA). On ICA clamping, approximately 50% of patients demonstrate a significant fall in both the HbO_2 and FV signal which is accompanied by a reciprocal rise in Hb (figure 1).

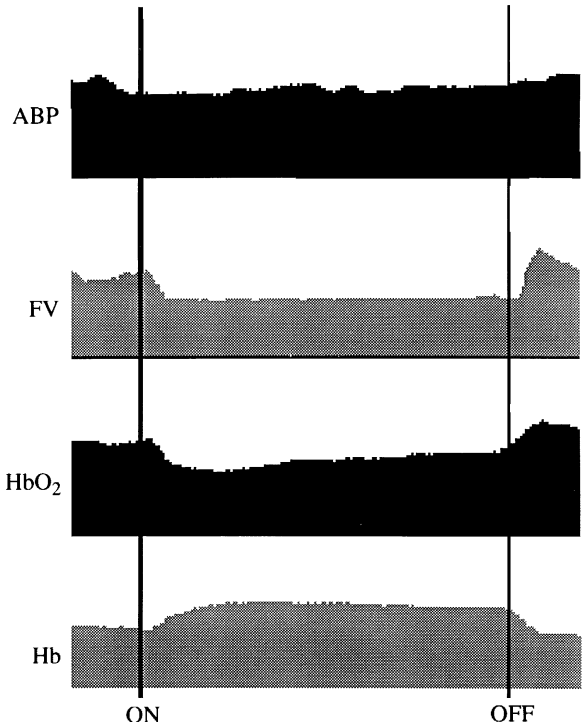

Figure 1. Intraoperative recording during carotid endarterectomy showing changes occurring when the ICA cross clamp was applied (ON) and subsequently removed (OFF) after the endarterectomy. A clear fall in HbO_2 and reciprocal rise in Hb is seen during clamping which reverses when the clamp is removed. A mild hyperoxyaemia is seen after clamp removal.

Application of the ECA did not appear to result in any further change in these variables. At the end of the CE, reperfusion of the extracranial territory shows only minor increases in HbO_2. On release of the ICA a marked increase in HbO_2 is typical, and is accompanied by hyperaemia as registered by high FV (figure 1).

The pooled data from the first 14 consecutive patients indicated that the reciprocal changes in HbO_2 and Hb were approximately equal and opposite during the clamping stage of surgery suggesting that on average the total Hb concentration (tHb), and hence the whole blood volume assuming a constant haematocrit, remains constant at these times. If this is the case, we would expect the HbO_2 signal to vary directly with cerebral saturation according to the equation:

$$\text{oxygen saturation of Hb (\%)} = HbO_2/\text{tHb}.$$

However, when SjO_2 measurements were carried out in 29 consecutive patients undergoing CE with NIRS monitoring, the correlation was poor ($r = 0.26$) when compared to the correlation between SjO_2 and cerebral blood flow estimated by the measurement of FV ($r = 0.73$). Either the assumptions regarding constant tHb during CE were incorrect, or other variables (such as extracranial contamination) were influential. It is also possible that the cortical area interrogated by NIRS does not drain exclusively into the internal jugular vein.

We now know that the blood volume does not remain constant during CE. Thus two patient groups can be identified (figure 2): those that have increases tHb during carotid clamping indicating compensatory vasodilation, and those that demonstrate a gradual fall in tHb indicating depleted cerebrovascular reserve.

During surgery of the latest 43 patients, a different protocol was adopted in which the ECA was clamped for a full two minutes before ICA clamping. Under these surgical conditions, 34 (79%) patients showed a fall in HbO_2 on clamping the ECA which was accompanied by a fall in cutaneous blood flow measured with a LDF probe placed between the NIRS optodes. On subsequently clamping of the ICA, a bi-exponential fall in HbO_2 was resolved in the majority. Of those that showed no change in NIRS during ECA clamping, none of these had a drop in skin blood flow during the operation. Thus in patients submitted to CE, there is frequently an extracranial component contributing to the signal changes during clamping which can be monitored with cutaneous LDF. Twenty-three of the 43 patients had a drop in HbO_2 during ICA clamping, all of whom showed a drop in FV without skin blood flow changes. The degree to which HbO_2 fell in these patients corresponds closely to the presence of patent anterior circulation collateral flow in the Circle of Willis as assessed on the preoperative digital subtraction angiograms. If the anterior communicating artery is patent, HbO_2 falls to a lesser degree than in patients without cross flow from the opposite anterior cerebral artery.

By simply subtracting the extracranial contribution to the NIRS changes seen during CE, we have found that NIRS parameters give an accurate indication of

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

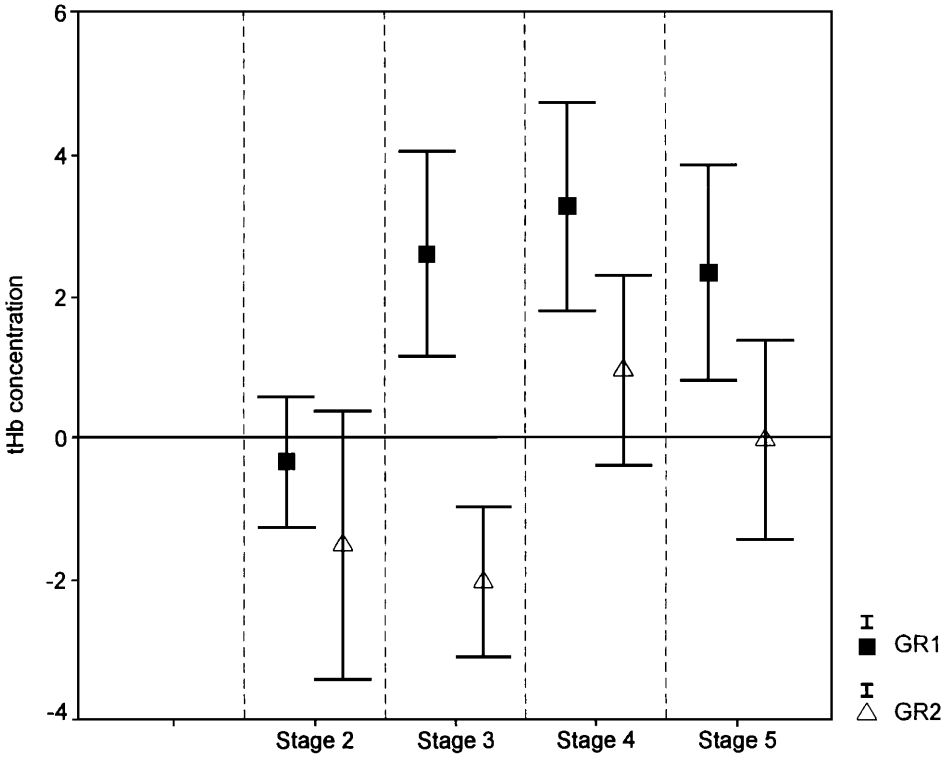

Figure 2. Changes in total haemoglobin (tHb) in two groups of patients submitted to carotid endarterectomy. In group 1, tHb increases during ICA clamping, whilst in group 2 patients tHb falls. Stage 2 is 5 minutes after ICA clamping; stage 3 is 15 minutes after ICA clamping; stage 4 is 5 minutes after ICA release; stage 5 is 15 minutes after ICA release.

Table 1. *Relationship between CFM, TCD and NIRS monitoring*

	ΔHb_{diff} median (range)/μmol	ΔHbO_2 median (range)/μmol	Drop in MCA FV median (range)/%
Drop in CFM	9.5 (6.1–12.7)[a]	6.0 (3.7–6.6)[a]	67 (66–87)[a]
No drop in CFM	0.0 (0.0–5.1)[a]	0.0 (0.0–3.0)[a]	27 (0–69)[a]

[a] Mann–Whitney *U*-tests: $p < 0.0001$.

impending severe cerebral ischaemia. Thus a fall in Hb_{diff} (differential haemoglobin concentration [HbO_2] minus [Hb]) of 6.0 μmol l^{-1} correlates highly with a fall in cerebral electrical activity, and/or a fall in MCA FV to below 40% of the baseline velocities, know indicators of impending cerebral ischaemia. This is certainly the first evidence to our knowledge that NIRS parameters, under highly controlled operative conditions, have been quantified in terms of clinically relevant endpoints.

3. OBSERVATIONS USING NIRS DURING CO_2 REACTIVITY TESTING

Our experience with the use of NIRS in testing CO_2 reactivity in awake adults has also been encouraging. Thus in both volunteers and patients with extracranial carotid occlusive disease a good relationship between FV reactivity and frontal NIRS changes has been found. This relationship is improved if one controls for changing ABP, and corrects for ABP-induced changes in the extracranial circulation using a similar method described above. By observing the relationship between HbO_2 and cutaneous LDF during temporary compression of the superficial temporal artery, the software can be instructed to subtract cutaneous changes affecting NIRS signals during the test. In 60 successive patients being investigated for carotid artery disease, the average estimated skin contribution to NIRS changes was 15.8%, and correction of calculations for HbO_2 reactivities for cutaneous factors resulted in an improved relationship with FV reactivity (table 2). Other variables affecting HbO_2 signal changes during the CO_2 challenge included ABP ($p = 0.025$). Despite these variables, the reproducibility of HbO_2 reactivity was similar to FV reactivity (a variation of 14.3 and 18.6%, respectively).

Table 2. *Correlation between reactivity expressed using FV and NIRS parameters. For NIRS both uncorrected and corrected for skin flow values are given*

	Spearman *R*	*p* value
HbO_2	0.48	< 0.000001
corrected HbO_2	0.55	< 0.000001
Hb_{diff}	0.49	< 0.000001
corrected Hb_{diff}	0.57	< 0.000001
tHb	0.26	0.008
corrected tHb	0.31	0.001

4. OBSERVATIONS USING NIRS IN HEAD INJURY

I would now like to move on to the subject of NIRS in the intensive care setting. The data I will present concerns 18 patients who were admitted with a coma-producing closed-head injury, who did not require open craniotomies and who did not have excessive scalp trauma for reasons which will become apparent. They were treated in a standard fashion to help provide a comparable baseline in these patients. The pharmacological support was identical in all, and we aimed to keep the important variables within specified limits.

Over 1700 h of data was captured, of which only 50% was entered for final analysis due to the signal failures as listed. The two sources of considerable concern being the jugular catheter (clotting, intimal impaction), and errors in NIRS due to extraneous light and probe displacement. From intact data with no artefact, we looked for specific cerebral events in which changes in multiple parameters were seen. An example is shown in figure 3, whereby a plateau wave is seen

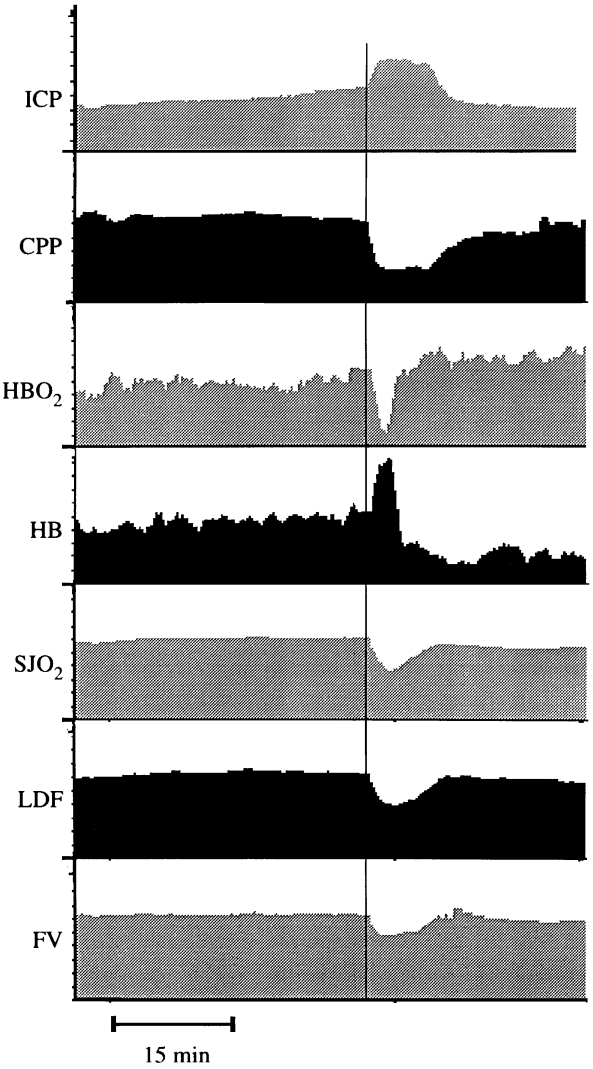

Figure 3. Cerebral event recorded from a head-injured patient. During the plateau wave of raised ICP, blood flow parameters fell with associated cerebral desaturation indicating hypoperfusion.

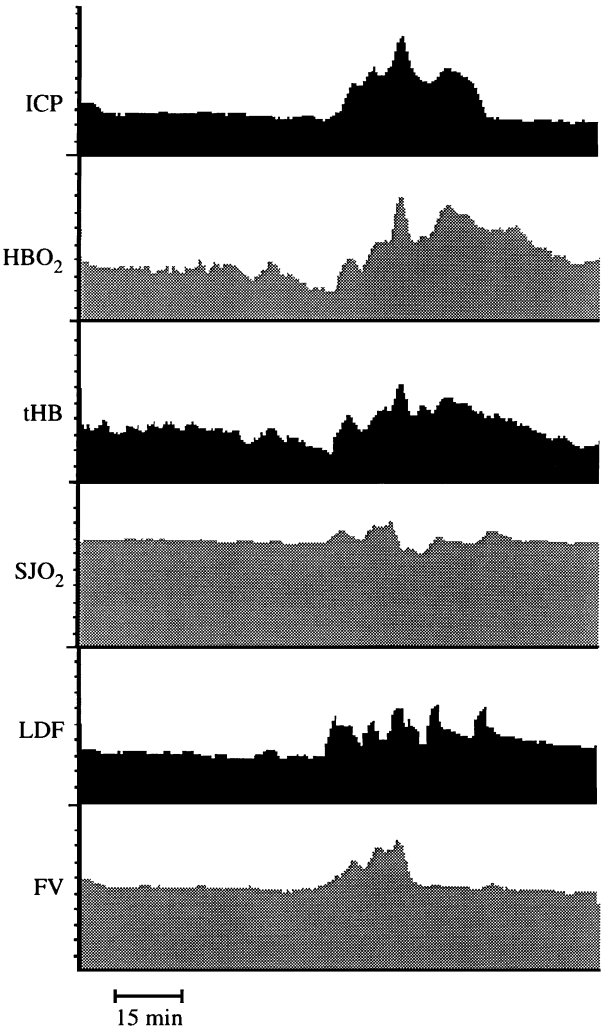

Figure 4. Cerebral event recorded from a head-injured patient. During the episode of raised ICP, all recorded parameters also increased indicating hyperaemia.

demonstrating reciprocal changes in HbO_2 and Hb. The cerebral desaturation is confirmed by recordings from the jugular venous catheter (SjO_2).

In all, 58 cerebral events were found from 16 patients. Most were short-lived, of mean duration 23.8 min, a minority lasting over 1 h. This is an important point, indicating the need for real-time monitoring if such events are to be detected. The majority were associated with hypoperfusion, a fall in relative blood flow and CPP. Approximately one-quarter were associated with hyperperfusion resulting from hyperaemia or hypoxia. An example of hyperaemia is seen in figure 4 with the elevation in ICP closely correlated to increases in HbO_2, tHb and relative CBF parameters. During hypoxic episodes, a fall in peripheral oxygen saturation frequently caused a fall in cerebral oxygenation and reactive hypertension with raised CBF.

This brings me on to an important finding that, of the 58 events identified, 94% were associated with recognizable and understandable changes in NIRS, whereas only 50% were associated with changes in SjO_2, a testimony to the sensitivity of the NIRS technique.

Finally I would like to present our provisional experience using spatially resolved spectroscopy (SRS) in which back-scattered light is detected by a new design of detector consisting of three closely placed photodiodes arranged in parallel strips. The light detected by each photodiode is used to generate a plot of log of attenuation against distance from source, giving a value for the rate of increase of attenuation with respect to the source–detector spacing. We have initially assessed this instrument in the relatively controlled clinical setting of cardiac bypass. Results showed that the correlation between SjO_2 measurements and SRS varied from patient to patient ($r =$ 0.08–0.97), and a significant correlation was seen in only 12 out of 24 patients. Overall, the SRS measurements tended to indicate a cerebral saturation that was 10–15 % lower than those indicated by SjO_2 measurements during the bypass period.

That SRS provided good correlation with SjO_2 values in some patients is encouraging, since peripheral (i.e. scalp) haemoglobin saturation remained at 98–100 % in all patients. However, we conclude that the variables discussed above, which are of equal importance in the application of SRS, have contributed to the variety of results obtained. A method to reliably exclude extracranial factors is clearly necessary before this technology can progress.

In conclusion, adult NIRS has shown promise when applied in a highly controlled environment. However, our experience indicates that extracranial contributions to NIRS do occur and are significant. If we are to progress with his technology, novel methods to subtract the extracranial changes are required. Anatomical resolution may not be the answer and our single most important observation has given some indication that physiological segregation is possible.

I am grateful to the organizers for the opportunity to present work concerning near-infrared spectroscopy (NIRS) which has accumulated in Cambridge over the past four years. It would be remiss of me not to mention the immense support I have enjoyed from our Polish physicists, Marek Czosnyka and Piotr Smielewki, who were central to helping in the development of the necessary computer support and analysis of data, and also to Joseph Lam, a visiting clinical fellow from Hong Kong, who has made a major contribution to NIRS research in our unit.

REFERENCES

Al-Rawi, P., Smielewski, P., Gosh, S. & Kirkpatrick, P. J. 1996 Calibration of spatially resolved spectroscopy during cardiopulmonary bypass. *J. Neurol. Neurosurg. Psychiat.* **61**, 554.

Czosnyka, M., Whitehouse, H., Smielewski, P. *et al.* 1994 Computer supported multimodality bedside monitoring in neurointensive care. *J. clin. Monitor. Comput.* **11**, 223–232.

Kirkpatrick, P. J., Czosnyka, M. & Pickard, J. 1996*a* Multimodality monitoring in neurointensive care (editorial). *J. Neurol. Neurosurg. Psychiat.* **60**, 131–139.

Kirkpatrick, P. J., Lam, J., Al-Rawi, P., Smielewski, P. & Czosnyka, M. 1997 Determination of near-infrared spectroscopy (NIRS) thresholds for severe cerebral ischaemia during carotid surgery. *J. Cereb. Blood Flow Metab.* (In the press.)

Kirkpatrick, P. J., Smielewski, P., Lam, J. & Al-Rawi, P. 1996*b* Near infrared spectroscopy in adults (editorial). *J. Biomed. Opt.* **1**, 363–372.

Kirkpatrick, P. J., Smielewski, P., Czosnyka, M., Menon, D. A. & Pickard, J. D. 1995*a* Near infrared spectroscopy in head injured patients. *J. Neurosurg.* **83**, 963–970.

Kirkpatrick, P. J., Smielewski, P., Whitfield, P. W., Menon, D. A. & Pickard, J. D. 1995*b* An observational study of near infrared spectroscopy during carotid endarterectomy. *J. Neurosurg.* **82**, 756–763.

Lam, J., Smielewski, P., Al-Rawi, P., Griffiths, P. & Kirkpatrick, P. J. 1997 Internal and external carotid contributions to near infrared spectroscopy during carotid endarterectomy. *Stroke.* (In the press.)

Matcher, S., Kirkpatrick, P. J., Nahid, P. & Delpy, D. T. 1997 Absolute quantification methods in tissue near infrared spectroscopy. *Proc. SPIE.* (In the press.)

Smielewski, P., Kirkpatrick, P. J., Czosnyka, M. & Pickard, J. D. 1997 Reliability of near infrared spectroscopy (NIRS) in the assessment of CO_2 reactivity in patients with cerebrovascular disease. *Stroke.* (In the press.)

Smielewski, P., Kirkpatrick, P. J., Minhas, P., Pickard, J. D. & Czosnyka, M. 1995 Can cerebrovascular reactivity be measured using near infrared spectroscopy? *Stroke* **26**, 2285–2292.