Perioperative Uses of Transcranial Perfusion Monitoring

Martin Smith, MBBS, FRCA

The most important goals of neuroanesthesia are to maintain cerebral perfusion to meet the tissue demands of oxygen and glucose and, under circumstances of reduced perfusion, to protect the brain. Perioperative transcranial perfusion monitoring provides early warning of impending brain ischemia to steer the neurosurgeon and guide the neuroanesthesiologist to optimize cerebral perfusion and oxygenation. The monitoring options include measurement of cerebral blood flow (CBF), intracranial pressure (ICP), and cerebral perfusion pressure (CPP), and assessment of the adequacy of perfusion by measurement of cerebral oxygenation and brain tissue biochemistry. Some monitoring techniques are well established, whereas others are relatively new to the clinical arena and their indications are still being evaluated (Table 1).

There are few widely accepted indications for specific perioperative neuromonitoring techniques. This article reviews currently available monitors and discusses their application in the perioperative period.

INTRACRANIAL PRESSURE MONITORING

ICP is usually monitored by an intraventricular catheter or intraparenchymal microsensor. Other available techniques are rarely used and have a substantially lower accuracy (Table 2). Intraventricular catheters provide the gold standard technique for ICP monitoring. This method measures global ICP and has the additional advantages of allowing in vivo calibration and therapeutic drainage of cerebrospinal fluid. Placement of the ventricular catheter can be difficult, however, in the presence of severe brain swelling or of an intracranial mass lesion. There is also significant risk of catheter-related ventriculitis during prolonged monitoring. Modern microtransducer systems can be placed directly in the brain parenchyma through a cranial access device, or in the subdural space by a burr hole or craniotomy. The complication rates, including infection risk, are minimal.

Measured ICP may not be representative of global pressure, however, because transtentorial and interhemispheric pressure gradients may be present. Microtransducer systems perform well but may drift during long-term monitoring and in vivo recalibration is not possible. ICP monitoring allows measurement of absolute ICP levels, calculation of CPP, and identification and analysis of pathologic ICP waveforms. Cerebrovascular pressure reactivity (CVR) and pressure-volume compensatory reserve may also be calculated.

Indications for perioperative ICP monitoring include patients with traumatic brain injury (TBI), surgery for large brain tumors with mass effect, hydrocephalus, intracranial and subarachnoid hemorrhage (SAH), and the presence of significant cerebral edema from whatever cause. After dural opening the ICP is virtually zero but brain swelling may impair neuromonitoring access and result in regional ischemia. In a prospective...
study of almost 700 patients undergoing craniotomy for supratentorial brain tumor, elevated subdural ICP at the start of surgery was an independent risk factor for intraoperative brain swelling and ICP greater than 13 mm Hg indicated that brain swelling was highly probable. Intraoperative ICP monitoring can also be used to identify, prevent, and treat posture-related intracranial hypertension during surgery. In patients with SAH, 10-degree reverse Trendelenburg position decreased ICP in 25 of 28 patients regardless of anesthetic agent, whereas CPP was unchanged. The effect of preoperative ICP and intraoperative CPP on outcome after TBI has also been examined. Mean ICP was higher in patients with unfavorable compared with favorable outcome (47.4 versus 26.4 mm Hg), although intraoperative CPP was a better overall predictor of outcome.

Neuroendoscopy results in intracranial hypertension in up to 50% of patients and this may be associated with postoperative morbidity, including new neurologic deficits. Postoperative ICP monitoring is indicated in patients in whom there is a risk of intracranial hypertension, particularly if the patient remains sedated. The need for postoperative ICP monitoring should be identified and instituted early. ICP monitoring is commonly used after surgery for TBI to guide postoperative ICP and CPP-directed therapy on the neurocritical care unit and is recommended by expert consensus guidelines.

CEREBRAL BLOOD FLOW

Modern imaging techniques provide sophisticated and detailed hemodynamic and metabolic information.

### Table 1
**Applications of neuromonitoring techniques**

<table>
<thead>
<tr>
<th>Neuromonitoring Technique</th>
<th>Established Neuro ICU Applications</th>
<th>Established Perioperative Applications</th>
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<tr>
<td>Intracranial pressure</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Quantitative cerebral blood flow</td>
<td>Yes</td>
<td>Research</td>
</tr>
<tr>
<td>Transcranial Doppler</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Cerebrovascular reactivity</td>
<td>Yes</td>
<td>Research</td>
</tr>
<tr>
<td>Jugular venous oximetry</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Brain tissue oxygenation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Near infrared spectroscopy</td>
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<td>Cerebral microdialysis</td>
<td>Yes</td>
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### Table 2
**Comparison of intracranial pressure monitoring devices**

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
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| Intraventricular catheter | • Gold standard  
• Measures global pressure  
• Allows therapeutic drainage of CSF  
• In vivo calibration possible | • Insertion may be difficult  
• Most invasive method  
• Risk of hematoma  
• Risk of ventriculitis |
| Microtransducer sensor  | • Robust technology  
• Intraparenchymal or subdural placement  
• Low procedure complication rate  
• Low infection risk | • Small zero drift over time  
• No in vivo calibration  
• Measures local pressure |
| Epidural catheter       | • Easy to insert  
• No penetration of dura  
• Low infection rate | • Limited accuracy  
• Rarely used |
| Lumbar CSF pressure     | • Extracranial procedure | • Does not reflect ICP  
• Dangerous if ICP elevated |

*Abbreviations: CSF, cerebrospinal fluid; ICP, intracranial pressure.*
information over multiple regions of interest in the brain. They are only able, however, to provide snapshot images, require transfer of patients to specialized imaging facilities, and have limited availability. Their use in the perioperative period is generally limited to research applications. Positron emission tomography (PET) is widely used as a diagnostic and clinical research tool and is increasing the understanding of cerebral pathophysiology. It also allows data from bedside monitors of perfusion and oxygenation to be compared with actual measures of CBF and oxygen consumption.\textsuperscript{13,14}

**Kety-Schmidt Method**

The first practical method of measuring CBF was described by Kety and Schmidt\textsuperscript{15} in 1945. The methodology has been described in detail\textsuperscript{15} but, in brief, it uses nitrous oxide (N\textsubscript{2}O) as an inert tracer gas and calculates CBF from the arteriovenous difference of N\textsubscript{2}O concentration based on application of the Fick principle. It measures global CBF and is unable to discriminate between gray and white matter flow. The technique as originally described has many disadvantages, including the requirement for timely and repeated arterial and venous blood sampling. The Kety-Schmidt method forms the basis of many CBF measurement techniques in use today, however, and remains the gold standard against which new methods of measurement are validated.

**Radioactive Tracer Techniques**

A modification of the Kety-Schmidt technique using inhalation or injection of \textsuperscript{133}xenon (\textsuperscript{133}Xe) is the most widely used bedside technique for measuring absolute regional and global CBF.\textsuperscript{16} CBF is calculated by analysis of the exponential clearance of the radioisotope from the brain, measured by scintillation counters placed over the scalp and producing two-dimensional maps of cortical blood flow. \textsuperscript{133}Xe is rapidly cleared so repeat studies can be undertaken within 30 minutes. The accuracy and specificity of the method depends on the number of detectors, but it is possible to achieve high spatial resolution. Although this method can be relatively easily applied at the bedside, it has limited clinical applications in the perioperative period, although it is a useful research tool.

**Continuous Quantitative Cerebral Blood Flow Monitoring**

Laser Doppler flowmetry and thermal diffusion flowmetry offer the potential for continuous CBF monitoring. Laser Doppler flowmetry provides reliable measurement of local cortical blood flow based on assessment of the Doppler shift of laser light by moving red blood cells.\textsuperscript{17} The technique requires the cortex to be exposed by a burr hole, so it cannot be used to follow changes during induction of anesthesia or in the early stages of surgery. Laser Doppler flowmetry has been used postoperatively to detect ischemia after SAH,\textsuperscript{18} although arbitrary units and the extremely localized measurement of CBF limit the usefulness of the technique. Thermal diffusion flowmetry differs from laser Doppler flowmetry in offering a quantitative assessment of regional tissue perfusion in terms of absolute flow values. The thermal diffusion flowmetry catheter consists of a thermistor heated to a few degrees above tissue temperature and a second, more proximal, temperature probe. The temperature difference between thermistor and temperature probe is a reflection of heat transfer and can be translated into a measurement of CBF. Thermal diffusion flowmetry provides a sensitive, real-time assessment of local CBF\textsuperscript{19} and, although questions remain about accuracy and reliability, it represents a promising method for the intraoperative and bedside monitoring of regional CBF, including the detection of clinically relevant vasospasm in patients with SAH.\textsuperscript{20} A regional CBF monitor based on thermal diffusion techniques has recently become commercially available (Bowman Perfusion Monitor, Hemedex, Cambridge, Massachusetts).

**Double-Indicator Dilution Technique**

An intriguing bedside method of assessing CBF, the transcerebral double-indicator dilution technique, has been described by Wietasch and colleagues.\textsuperscript{21} Bolus injections of ice-cold indocyanine green are administered via a central venous line and the resulting thermo-dye curves are recorded simultaneously in the aorta and jugular venous bulb using combined fiberoptic thermistor catheters. CBF is calculated from the mean transit times of the indicators through the brain. The authors claim that transcerebral double-indicator dilution technique is less time consuming and less cumbersome than alternative methods.

**Transcranial Doppler Ultrasonography**

Transcranial Doppler (TCD) was introduced in 1982 and has become established as a noninvasive, real-time technique for the examination of cerebral hemodynamics.\textsuperscript{22} It is the only method that can be used with relative ease in the operating room.\textsuperscript{23} TCD uses ultrasound waves to measure
the velocity of blood flow through large cerebral vessels from the Doppler shift caused by red blood cells moving through the field of view. TCD does not determine actual blood flow but is a technique for measuring relative changes in CBF.

A low frequency (2 MHz) pulsed wave probe is used to insonate a basal cerebral vessel through an acoustic cranial window, an area of the skull with sparse or no cancellous bone that causes little attenuation and scattering of the signal. The TCD flow velocity waveform resembles an arterial pulse wave and may be quantified into peak systolic, end diastolic, and mean flow velocities, and pulsatility index. If the angle of insonation and the diameter of the insonated vessel remain constant, changes in measured blood flow velocity reflect changes in CBF. Pulsatility index reflects distal cerebrovascular resistance and, because it is dimensionless, is not affected by angle of insonation. Providing the limitations are recognized, it is possible to use TCD to monitor the cerebral circulation and guide the perioperative care of patients with TBI, SAH, and others at risk of cerebral ischemia. The probe can be fixed in place to ensure a constant angle of insonation and artifact-free recordings during and after surgery (Fig. 1).

TCD is widely used during carotid endarterectomy and can quantify the risk of cerebral ischemia during carotid cross clamping. TCD indices during carotid endarterectomy correlate well with subsequent EEG changes and have been used as an indication for shunt placement. Emboli can be detected as characteristic short-duration, high-intensity “chirps,” and waveform analysis allows differentiation between air and particulate emboli.

TCD also has a role in the diagnosis and management of cerebral vasospasm after SAH and has become routine in the perioperative care of patients during surgical or neuroradiologic treatment of intracranial aneurysms. Because changes in CBF itself affect flow velocity, the assessment of vasospasm from measurement of flow velocity alone may be insufficient. Lindegaard and coworkers described the use of a hemispheric index, comparing flow velocity in the middle cerebral artery and internal carotid artery on the same side, that is unaffected by changes in CBF. An index of greater than 3 is indicative of vasospasm and values greater than 6 suggest severe spasm. The sensitivity and specificity of TCD for the diagnosis of vasospasm is generally high, although there is considerable interindividual variation. High flow velocities may be tolerated in some patients, whereas in others vasospasm may be present despite normal flow velocity. Treatment decisions are not usually based on TCD findings alone. Mascia and colleagues assessed the accuracy of TCD using receiver-operator characteristic analysis and found that mean flow velocity thresholds of 100 and 160 cm/s were most accurate for the detection of angiographic and clinical vasospasm, respectively, in the middle cerebral artery. Consecutive TCD examinations should be performed after SAH and flow velocity greater than 140 cm/s, or flow velocity increases greater than 50 cm/s/d from baseline, are generally accepted to be indicative of developing or established vasospasm.

TCD may be used to monitor the integrity of pressure autoregulation and CO2 reactivity in the perioperative period to guide management of CBF and minimize the risk of ischemia. TCD has also been used to estimate ICP noninvasively with an absolute accuracy of ±10 to 15 mm Hg.

MEASUREMENT OF CEREBROVASCULAR REACTIVITY

The loss of CVR renders the brain more susceptible to ischemic insults. Because CVR may be disturbed or abolished by intracranial pathology and some anesthetic agents, the ability to monitor CVR in the perioperative period is an attractive proposition.

Methods of testing static and dynamic autoregulation are well established but most are interventional, intermittent, and are not practical options in the perioperative period. More recently, methods for the continuous assessment of CVR that require no intervention have been described. The ICP response to changes in arterial blood pressure depends on the pressure-reactivity of

Fig. 1. PC-based transcranial Doppler system (Doppler-Box, Compumedics Germany GmbH, Hamburg, Germany) and probe fixation device suitable for perioperative use.
cerebral vessels. This is a key component of pressure autoregulation and disturbed pressure reactivity implies disturbed pressure autoregulation. A pressure-reactivity index can be derived from continuous monitoring and analysis of slow waves in arterial blood pressure and ICP. Under normal circumstances, an increase in arterial blood pressure leads to cerebral vasoconstriction within 5 to 15 seconds and a secondary reduction of cerebral blood volume and ICP. When CVR is impaired, cerebral blood volume and ICP increase passively with arterial blood pressure. Opposite effects occur when arterial blood pressure is reduced. Pressure-reactivity index is determined by calculating the correlation coefficient between arterial blood pressure and ICP, indicates a normal CVR, and a positive value indicates a nonreactive cerebrovascular circulation. Pressure-reactivity index correlates with standard measures of cerebral autoregulation and abnormal values are predictive of poor outcome after TBI. Oxygen reactivity, measured using brain tissue oxygen monitoring (intraparenchymal brain tissue oxygenation [Ptico2]), provides additional information about cerebrovascular autoregulation, and has been correlated with pressure-reactivity index. CVR can also be assessed continuously using TCD. The moving correlation coefficient between arterial blood pressure and mean and systolic flow velocities during spontaneous fluctuations in arterial blood pressure is calculated over 3-minute epochs, yielding a mean and systolic index of autoregulation.

The potential value of CVR assessment in the perioperative period was demonstrated in a recent study when pressure-reactivity index was used to monitor changes in CVR in patients undergoing decompressive craniectomy. Dynamic pressure autoregulation has also been measured during acute aneurysm surgery and can be used to optimize intraoperative blood pressure management.

**MEASUREMENT OF CEREBRAL OXYGENATION**

**Jugular Venous Oximetry**

Jugular venous oxygen saturation (Sjvo2) provides information about the balance between global cerebral oxygen delivery and metabolic demand and can be used as a nonquantitative assessment of the adequacy of CBF. The normal Sjvo2 is 55% to 75%, which is lower than mixed venous saturation reflecting the high oxygen requirement of the normal brain. Derived variables, such as the arterial to jugular venous oxygen concentration difference (Ajvdo2), have also been extensively used in the study of cerebral metabolism. Normal Ajvdo2 is 4 to 8 mL O2/100 mL blood.

The technique of jugular venous oximetry is relatively straightforward. A catheter is inserted into an internal jugular vein and advanced to the jugular bulb. The position of the catheter is crucial to minimize the risk of extracranial contamination, which is around 3% if the catheter is correctly placed. Typically, around two thirds of the sampled blood is drained from the ipsilateral hemisphere, although there is large interindividual variability and it is impossible to predict in an individual patient which side gives more relevant information.

Sjvo2 monitoring accurately reflects global cerebral oxygenation only if the dominant jugular bulb is cannulated. The right side is often chosen because it is usually dominant. The correct side can be identified more accurately, however, by ultrasound examination of the internal jugular vein, by identifying the largest ICP rise caused by manual compression of each internal jugular vein, or by identification of the larger jugular foramen on CT scan. Once the catheter position has been checked on a lateral cervical spine radiograph, measurement of Sjvo2 can be made continuously using a fiberoptic catheter or directly by aspirating blood samples. Blood should be withdrawn at a rate of less than 2 mL/min to minimize the risk of falsely elevated values caused by aspiration of extracranial blood.

Fiberoptic catheters require regular recalibration and, even under stable conditions, less than half of total monitoring time produces high-quality data. Notwithstanding these practical difficulties, Sjvo2 is widely used for perioperative oxygenation monitoring.

Sjvo2 levels less than 55% suggest cerebral hypoperfusion with oxygen demand exceeding supply, whereas levels greater than 80% indicate relative hyperemia, caused either by raised CBF or reduced oxygen demand (Fig. 2). Because Sjvo2 is a global, hemispheric measure it cannot detect regional ischemia. PET evidence suggests that Sjvo2 does not fall below 50% until approximately 13% of the brain becomes ischemic.

Calculation of the Ajvdo2 can serve as an indirect measure of relative changes in CBF: CBF = CMRO2/Ajvdo2, where CMRO2 is the cerebral metabolic rate for oxygen. If CMRO2 remains constant, changes in Ajvdo2 reflect changes in CBF, but such estimates of CBF are often inaccurate because of the anatomic limitations of the technique. Jugular bulb catheters are most commonly used to measure trends in oxygenation indices.

In 1994, Matta and colleagues reported the intraoperative use of Sjvo2 monitoring in 100
consecutive patients undergoing craniotomy. They found that the jugular catheter could be placed quickly and detected frequent episodes of jugular venous desaturation that would otherwise have been undiagnosed and untreated. The benefits of SjvO₂ monitoring to assess cerebral hypoperfusion and guide intraoperative blood pressure management have been confirmed in a study of patients undergoing intracranial aneurysm surgery.⁵⁰ SjvO₂ monitoring has also been extensively investigated in patients undergoing cardiopulmonary bypass when episodes of jugular desaturation occur frequently, particularly during rewarming, and are correlated with higher incidence of severe postoperative cognitive dysfunction and higher mortality.⁵¹

Most of the literature regarding SjvO₂ monitoring has focused on the monitoring and management of TBI.⁵² There is a significant association between jugular venous desaturation and poor neurologic outcome, with poor outcome occurring in 55% of patients with no episodes of desaturation, 74% of those with one episode, and 90% of those with multiple episodes.⁵³ There is some evidence that SjvO₂ monitoring can be used to guide hyperventilation after TBI and that treatment of desaturation may improve outcome.⁴⁷ This is controversial, however, because of the lack of sensitivity of this technique to regional ischemia.

**Brain Tissue Oxygen Tension**

PtiO₂ is increasingly being measured whenever ICP monitoring is indicated and is becoming established as the gold standard bedside monitor of cerebral oxygenation.⁵⁴ Currently, only one PtiO₂ monitor is commercially available for use in humans (Licox, GMS, Kiel-Mielkendorf, Germany) (Fig. 3). This sensor uses a closed polarographic (Clark-type) cell with reversible electrochemical electrodes. Oxygen diffuses from the brain tissue across a semipermeable membrane and is reduced by a gold polarographic cathode. This produces a flow of electrical current proportional to the oxygen concentration in a temperature-
dependent manner. A sensor-specific smart card allows straightforward and rapid calibration. A run-in time of around 1 hour is required following insertion of a brain PtiO2 probe and this has implications for intraoperative monitoring. PtiO2 provides a highly focal measurement of cerebral oxygenation and, although this offers the potential of selective monitoring of critically perfused tissue, accurate placement of the probe is crucial and global changes may be missed.

Brain PtiO2 is related to other physiologic variables and these relationships have been examined to understand the physiologic basis for critical oxygenation thresholds. PET studies have shown correlation between PtiO2 and regional CBF and also between changes in PtiO2 and changes in regional venous oxygen saturation. Brain PtiO2 is increased by an increase in fraction of inspired oxygen (and in PaO2), red cell transfusion, and increases in MAP and CPP and is most likely to represent a balance between CBF, oxygen extraction fraction, and PaO2. Normal brain PtiO2 values are in the region of 35 to 50 mm Hg. Under normoxic conditions, a high brain PtiO2 reflects increased tissue perfusion, whereas low PtiO2 reflects low or inadequate perfusion. Low PtiO2 does not always represent ischemia, however, because it may occur as a result of cerebral hypometabolism (eg, related to sedative agents or hypothermia) in the presence of stable oxygen extraction and coupled hypoperfusion.

PtiO2 monitoring allows rapid detection of intraoperative cerebral ischemia and the possibility that therapy may be initiated before irreversible neuronal damage occurs. It has been recommended during aneurysm surgery and may identify patients at risk for procedure-related ischemia. Using a threshold of 15 mm Hg, brain PtiO2 is more effective than somatosensory evoked potential monitoring at predicting ischemia. Hoffman and colleagues compared PtiO2 of cortex adjacent to arteriovenous malformations with control (nonischemic) areas of brain in patients undergoing elective aneurysm surgery. Brain PtiO2 in control patients did not change during surgery. In the arteriovenous malformations patients, PtiO2 was low before arteriovenous malformation resection, suggesting reduced perfusion and chronic hypoxia, and increased markedly postresection suggesting hyperperfusion. The effect of dural opening and tumor resection on PtiO2 has also been investigated. In patients with intraoperative brain swelling, low peritumoral PtiO2 increased dramatically on dural opening and following tumor resection, suggesting the presence of significant hypoxia in peritumoral edema. This emphasizes the importance of maintaining CPP during brain tumor surgery and suggests that PtiO2 monitoring might be used to guide intraoperative blood pressure management. Reduced brain PtiO2 has also been shown to improve in association with reductions in ICP and increases in CPP following decompressive craniectomy. Furthermore, patients with severe brain hypoxia before surgery were more likely to have poorer outcome, raising the possibility that PtiO2 monitoring may be used to select patients who might benefit from surgical decompression.

Most clinical data on PtiO2 monitoring come from studies after TBI. Reduced PtiO2 is associated with poor outcome, but a threshold for cerebral hypoxia has not been clearly identified. It is likely, however, that such a threshold would relate to both duration and depth of hypoxia. In a recent PET study of TBI, brain regions with PtiO2 values less than 10 mm Hg had significantly lower hyperventilation-induced increases in mean oxygen extraction fraction. The ceiling of PtiO2 during augmentation of CPP is highest in areas of focal ischemia, suggesting that beneficial effects are occurring in at-risk tissue. What is less clear is whether manipulation of PtiO2 is able to affect outcome. In a recent study of 28 patients, however, standard ICP- and CPP-guided therapy combined with interventions to maintain PtiO2 greater than 25 mm Hg resulted in lower mortality than that in a group of 25 historical controls receiving ICP- and CPP-guided therapy alone.

Regional and global oxygenation monitoring techniques are not competitive or mutually exclusive. Neither SjvO2 nor PtiO2 monitoring alone identifies all episodes of ischemia and they should be considered complementary with monitoring strategies taking advantage of the unique features of each technique.

NEAR INFRARED SPECTROSCOPY

Near infrared spectroscopy (NIRS) is a noninvasive technique based on the transmission and absorption of near infrared light (700–1000 nm) as it passes through tissue. Oxygenated and deoxygenated hemoglobin have different absorption spectra and cerebral oxygenation and hemodynamic status can be determined by their relative absorption of near infrared light. Earlier NIRS methodology was limited to measuring changes in tissue chromophore concentration, but recent
advances have allowed measurement of absolute hemoglobin oxygen saturation\textsuperscript{69} and absolute concentrations of oxyhemoglobin and deoxyhemoglobin.\textsuperscript{70} NIRS interrogates arterial, venous, and capillary blood within the field of view and the derived saturation represents a tissue oxygen saturation measured from these three compartments. In addition to monitoring oxygenation variables, NIRS has been used to measure regional CBF\textsuperscript{71} and cerebral blood volume,\textsuperscript{72} but these techniques have not been validated. More recently, it has become possible to measure changes in the concentration of the terminal complex of the electron transfer chain, cytochrome-c oxidase, in adults.\textsuperscript{73} This measurement has been validated in animal studies as a measure of changes in cellular energy status\textsuperscript{74} and offers the potential to assess intramitochondrial redox state after human brain injury. Two types of NIRS instrumentation are available for clinical use: the INVOS series (Somanetics Corporation, Troy, Michigan) and the NIRO series (Hamamatsu Photonics, Hamamatsu City, Japan) (Fig. 4). The INVOS presents a single numerical value for regional cerebral saturation ($r$SO$_2$), whereas the NIRO provides an absolute tissue oxygenation index in percentage terms and changes in oxyhemoglobin and deoxyhemoglobin variables and oxidized cytochrome-c oxidase.

Trends in NIRS variables may detect ischemic events and $r$SO$_2$ has been used to monitor ischemia during interventional radiologic procedures\textsuperscript{75} and carotid cross clamping.\textsuperscript{76,77} NIRS has also been used to detect intraoperative increases in cortical oxygen saturation and blood volume, indicative of a hyperemic state, after arteriovenous malformation resection.\textsuperscript{78} NIRS-measured cerebral oxygenation has been compared with $\text{SjvO}_2$ and brain PtiO$_2$ in patients with TBI\textsuperscript{57} and tentative ischemic thresholds for NIRS variables have recently been described.\textsuperscript{79} Monitoring and treatment of $r$SO$_2$ during cardiopulmonary bypass has been shown to minimize the incidence of cerebral desaturation and is associated with a lower incidence of postoperative systemic organ dysfunction.\textsuperscript{80}

NIRS has the potential to provide continuous, noninvasive measurement of cerebral hemodynamic, oxygenation, and metabolic variables over multiple regions of interest with high temporal resolution. There is lack of standardization of the technology for clinical use, however, and in some cases the algorithms are not published.\textsuperscript{81} It is difficult to translate data between studies using different technologies. Another concern is the potential contamination of the NIRS signal from extracranial sources, although the wider application of spatially resolved spectroscopy, which has high sensitivity and specificity to intracranial changes, helps in resolving this issue.\textsuperscript{77} Modern broadband spectroscopy systems also allow improved temporal and spatial resolution and the

![Fig. 4. Near infrared spectroscopy system. (A) NIRO 300 spectrometer (Hamamatsu Photonics, Hamamatsu City, Japan). (B) Transcranial optodes. (C) Schematic of optodes.](image-url)
opportunity for multisite, real-time measurement. NIRS has many potential advantages over other techniques but further technologic advances are necessary before it can become a reliable clinical monitor.

CEREBRAL MICRODIALYSIS

Cerebral microdialysis (MD) is a well-established laboratory tool that is being increasingly used as a bedside monitor to provide on-line analysis of brain tissue biochemistry during neurointensive care. The principles and clinical applications of cerebral MD have recently been reviewed. The MD catheter consists of a fine double-lumen probe, lined at its tip with a semipermeable dialysis membrane that is placed in brain tissue (Fig. 5). The probe is perfused by an inlet tube with fluid isotonic to the tissue interstitium and the perfusate passes along the membrane before exiting by outlet tubing into a collecting chamber. Diffusion drives the passage of molecules across the membrane along their concentration gradient (Fig. 6). The MD catheter acts as an artificial blood capillary and the concentration of substrate in the collected fluid (the microdialysate) depends in part on the balance between substrate delivery to, and uptake and excretion from, the brain extracellular fluid. A commercially available MD analyzer (CMA, Solna, Sweden) measures microdialysate concentrations of glucose, lactate, pyruvate, glycerol, and glutamate on-line (see Fig. 3). The concentration of these substances in the microdialysate does not correspond to their true extracellular fluid concentration and the proportion of the extracellular fluid concentration in the microdialysate is termed the “relative recovery.” This is dependent on membrane pore size, membrane area, perfusate flow rate, and diffusion speed of the substance. In clinical practice the most commonly used system comprises a catheter that is 10 mm in length with a 20- or 100-kd molecular weight cutoff, perfused with commercially available perfusate solution (Perfusion Fluid CNS, CMA Microdialysis) at a rate of 0.3 µL/min. Samples are usually collected and analyzed at hourly intervals. It is recommended that the MD catheter be placed in at-risk tissue (i.e., adjacent to a mass lesion or, in the case of an aneurysm, in the territory of the parent vessel). This allows biochemical changes to be measured in the area of brain most vulnerable to ischemic insult.

Most clinical experience with cerebral MD relates to monitoring patients with TBI and SAH in the neurocritical care unit. Severe cerebral hypoxia or ischemia is typically associated with marked increases in the lactate-pyruvate ratio and lactate-pyruvate ratio greater than 20 to 25 is associated with poor outcome after TBI. It has traditionally been assumed that increases in

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Fig. 5. Components of clinical microdialysis catheter. (A) Perfusate pump connector. (B) Inlet tube. (C) Microdialysis catheter. (D) Microdialysis membrane. (E) Outlet tube. (F) Collecting vial and holder.

Fig. 6. Schematic of microdialysis catheter located in brain tissue. Isotonic fluid is pumped through the microdialysis catheter at a rate of 0.3 µL min⁻¹. Molecules at high concentration in the brain extracellular fluid equilibrate across the semipermeable microdialysis membrane and can be analyzed in the microdialysate. ECF, extracellular fluid; MD, microdialysis.
lactate-pyruvate ratio are caused only by tissue ischemia and, although increases in lactate-pyruvate ratio correlate with PET-measured oxygen extraction fraction, it has not been possible to establish a hypoxic threshold associated with raised lactate-pyruvate ratio. It is now apparent that anaerobic glycolysis may occur not only because of hypoxia and ischemia but also because of mitochondrial failure and failure of effective use of delivered oxygen. Cerebral MD offers a unique opportunity to monitor such cellular dysfunction. Glycerol is a marker of ischemic cell damage and increased MD glycerol concentrations are associated with poor outcome after TBI. Increased levels of excitatory amino acids and reduced brain extracellular fluid glucose levels may also predict or be associated with metabolic catastrophes occurring after acute brain injury. MD is becoming established as a tool to assist clinical decision making during neurointensive care.

Because cerebral MD measures changes at the cellular level, it has the potential to detect hypoxia and ischemia before changes can be detected by more conventional monitoring techniques or before a change in clinical status. In one study, a rise in lactate-pyruvate ratio and glycerol predicted the occurrence of a delayed ischemic deficit related to cerebral vasospasm 11 to 23 hours before its clinical appearance. In a recent study, MD monitored molecular events triggered by TBI occurred before the onset of intracranial hypertension, suggesting that biochemical impairment can be present before low CPP is detectable. Such predictive value of MD might offer substantial advantages over other monitoring techniques in the perioperative period.

MD is an attractive technique to monitor impending ischemia during neurovascular surgery when early detection may prevent or minimize damage by prompting a change in operative or anesthetic management. In one study, increases in lactate, lactate-pyruvate ratio, and glutamate were associated with reductions in brain PtiO2 during aneurysm surgery, although, unlike PtiO2, were not predictive of subsequent infarction. Changes in glutamate have also been demonstrated to be an excellent marker of neuronal damage and subsequent neurologic deficit after extracranial-intracranial bypass surgery.

The intraoperative applications of cerebral MD are currently limited by technology. The usual hourly sampling rate is unlikely to offer adequate time resolution in the operative setting. Increased perfusate flow rate allows sufficient volume of sample to be retrieved at 15-minute intervals, albeit at the expense of lower relative recovery of measured variables. For clinically useful detection of metabolic changes during surgery, however, more rapid sampling is likely to be required. A continuous cerebral MD technique has been described, although such technology is currently not available commercially. The future success of cerebral MD as a perioperative monitor depends on the choice of biomarkers; their sensitivity, specificity, and predictive value for secondary neurochemical events; and the availability of practical methods for analysis of biomarkers.

SUMMARY

Given the physiologic complexity of the human brain it is not surprising that a single variable or a single device is unable to provide adequate monitoring of cerebral well-being during surgery or of the multiple pathophysiologic processes that occur after brain injury. It is for this reason that multimodality monitoring, including combined measures of cerebral perfusion, oxygenation, and metabolic status, is often recommended. Most neuromonitors have been developed and tested in the neurocritical care unit and, although some translate well into the operating room, others are less suited to this environment because of incompatibility or inadequate temporal resolution. Multiparameter probes that measure ICP, PtiO2 and CBF are likely to be available for clinical use in the near future. It is also likely that technical advances will lead to the development of monitors that deliver noninvasive, continuous, multisite measurement of cerebral hemodynamics, oxygenation, and metabolic status and that will be suited to the perioperative period. Currently, every monitor of cerebral perfusion and oxygenation has its own specific shortcomings and none is a standard of care in the perioperative period.

REFERENCES

Transcranial Perfusion Monitoring


