THE PAST DECADE has seen the emergence of cerebral oximetry, a noninvasive technology based on near-infrared spectroscopic (NIRS) measurement of regional tissue oxygen saturation (rSO2). Like pulse oximetry (SpO2), rSO2 monitoring uses NIRS to measure oxygen saturation. Because the hemoglobin content in blood vessels >1 mm in diameter generally is sufficient to absorb all incident infrared photons, both devices examine primarily small vessels (ie, capillaries, arterioles, and venules). Pulse oximetry uses the pulsatile component of the NIRS signal to assess systemic arterial oxygen saturation (SaO2). In contrast, the nearly nonpulsatile rSO2 signal offers a highly localized and predominantly venous measure of tissue oxygen saturation because the cerebral venule fraction of total small vessel volume ranges from 2/3 to 4/5.1

During this decade, there has been an explosive knowledge growth in the clinical utility of NIRS. In fact, at least 1 new peer-reviewed report on the in vivo applications of NIRS appears daily.2 The associated exponential increase in NIRS clinical experience is the basis for the current debate on the routine application of NIRS-based cerebral oximetry during cardiac surgery. This debate is reminiscent of one that occurred 20 some years ago on the routine application of pulse oximetry for general surgical cases.2

In a landmark multicenter study, Roach et al3 showed a compelling need for improved cerebral surveillance during cardiac surgery. As a result of this, and more recent investigations, it is now widely recognized that overt brain injury3 and postoperative cognitive decline (POCD)4 are disturbingly common complications of cerebral surgery. The etiology of both complications appear to be multifactorial, involving embolism,5 cerebral hypoxia,6 and a systemic inflammatory response.6 Ultimate injury expression depends on the concerted action of these distinct pathophysiologic processes and the extent of underlying cerebrovascular disease.7 Thus, optimal brain protection during cardiac surgery involves attention to changes in local oxygen balance.

Traditionally, cerebral oxygenation could only be assessed indirectly through measurement of SaO2 and mixed venous (SvO2) oxygen saturation. Due to the fact that cerebral oxygen demand is higher than the systemic average, developing brain hypoxia may be invisible to systemic oxygenation measures. As a consequence of diminished blood flow to the brain, the cerebral contribution to the systemic average venous and arterial oxygen saturation will decrease. Although SaO2 and SvO2 provide information on systemic oxygen supply and demand, respectively, rSO2 is a measure of local microcirculatory O2 supply-demand balance. This important systemic versus local distinction has been shown by Hadolt and Litscher,8 who observed a decline in the rSO2/SpO2 ratio during high-altitude ascent. The authors concluded that critical cerebral O2 balance was only partially influenced by systemic supply. Clinical relevance of this study lies in the appearance of acute mountain sickness in some climbers as the ratio approached 0.5 at an altitude of 5,600 m. Similarly, Yeh et al9 found only a weak correlation between SvO2 and rSO2 during cardiopulmonary bypass.

Additional clinical evidence for the limitations of systemic oxygen measurement as an indicator of cerebral oxygen balance arises from a multicenter POCD study in elderly noncardiac surgical patients.10 Despite minimal influence from embolization and inflammation in this surgical population, systemic hypoxemia was not predictive of cognitive decline. Consequently, the authors were unable to define a “brain-safe” SpO2 threshold.

The first attempt to directly monitor cerebral oxygen balance involved invasive jugular bulb oxygen saturation (SjvO2) monitoring. In contrast to systemic oxygen measures, low SjvO2 was shown to be predictive of postoperative cognitive decline.5 Although this device directly monitors global cranial oxygen balance, it has 2 important characteristics that have impeded its general acceptance. First, positioning of the oximeter catheter tip in the jugular bulb poses both a technical challenge and a risk of serious injury. Second, measurement requires the continuous flow of blood past the sensor. This requirement precludes reliable SjvO2 monitoring during critical reduction in
cerebral venous outflow. It should also be appreciated that SjvO₂ samples unspecified venous sinus and large vein drainage that may contain both intracranial and extracranial blood. In contrast, rSO₂ measures primarily venule saturation at the gas exchange site in a small sample of frontal cortical tissue. Because of their fundamentally different sampling character, an expectation of close agreement between these measures is unjustified, particularly during nonpulsatile cardiopulmonary bypass.

The clinical introduction of new technology inevitably generates skepticism among those responsible for patient care. Such skepticism is certainly appropriate to limit widespread application of devices or procedures that are ineffective or potentially harmful. With regard to cerebral oximetry, skepticism thus far has been based on 2 broad topics. The first focuses on the technical reliability of the measure, whereas the second concentrates on evidence of clinical benefit. Thus, a convincing advocacy of routine cerebral oximetric monitoring should address both legitimate concerns. Although there are several distinctly different technologic approaches to cerebral oximetry, until very recently, only 1 had received US Food and Drug Administration clearance. Because the extant literature revolves primarily around this 1 product, the discussion centers on the continuous wave dual-wavelength spatially resolved reflectance spectrometer, the INVOS 5100 (Somanetics Corp, Troy, MI).

CEREBRAL OXIMETRY: TECHNICAL CONSIDERATIONS

The adult human skull does not totally block the passage of infrared photons. Clinical studies have shown beyond reasonable doubt that exclusive perturbation of regional intracranial cerebral perfusion is detectable by forehead-located oximeter sensors. Congenital, traumatic or surgically created skull defects may reduce signal attenuation and alter the calculated saturation estimate. In extreme cases, ultra–high-intensity reflected signals may totally preclude measurement because of amplifier saturation. As with bone, normal skin pigments seem to have minimal impact on rSO₂ measurement.

Of more concern is signal contamination by extravascular hemoglobin or other chromophores. Pools of stagnant hemorrhagic blood represent giant photon sinks that may interfere with accurate measurement of cerebrocortical oxygen saturation. The influence of extracerebral signal contamination is reduced by the process of spatial resolution. This approach is based on the demonstration that the mean photon reflection path from a forehead-mounted infrared source through adult skull and brain is banana shaped, with the depth of photon penetration proportional to source-detector separation. Assuming an optimal separation of 4 cm, signals from detectors located closer to the source contain proportionally more photons originating from extracerebral reflections. Thus, the differential signal eliminates features common to both paths, representing photon reflections predominantly from the outer layers of the cerebral cortex. Of course, the differential rSO₂ signal may be affected by atypical extracranial or cranial chromophore contributions or photon scattering, such as may be produced by hair, hemangioma, scalp tourniquet, tumor, edema, frontal sinus mucosal hyperemia, or purulence.

Determination of absolute oxy- and deoxyhemoglobin concentrations via the Beer-Lambert law requires direct knowledge of the photon path length between the infrared source and sensor. Because the biologic tissues underlying the oximeter sensors produce marked and highly variable photon scattering, it is currently not possible to accurately measure path length. Fortunately, the clinically valuable measurement of oxygen saturation does not use path length; it requires only the relative signal strengths of oxy- and total hemoglobin.

Because the infrared absorption spectra of oxy- and deoxyhemoglobin differ, dual-wavelength spectrometers can distinguish between them in the absence of competing chromophores. However, SpO₂ and rSO₂ may be confounded by heme (eg, methemoglobin, carboxymethemoglobin, and fetal hemoglobin) and nonheme (eg, bilirubin and biliverdin) biologic chromophores, as well as infrared-absorbing dyes. Interference from competing chromophores may lead to a spurious positive or negative offset in the apparent rSO₂ value. Nevertheless, the performance of the oximeter as a trend monitor is not compromised. Sudden marked rSO₂ decreases from a baseline reference still signify new cerebral oxygen imbalance.

As with the invasive SjvO₂ measurement of cerebral saturation, generally accepted normative absolute rSO₂ values and alarm criteria have not been established. Nevertheless, sufficient data have been published to reasonably identify noteworthy abnormality. A group mean rSO₂ of 67 ± 10 has been reported in both conscious adult healthy volunteers (n = 94) and cardiac surgery patients (n = 1,000). In the cardiac patients, right versus left differences of >10% occurred in <5% of the individuals. Thus, from a statistical perspective, awake cardiac patients with rSO₂ values <50 or right-left difference of >10% comprise <5% of the population and may be considered abnormal.

There are 2 distinct bases for this statistical abnormality. The first is technical. The enormous variation in adult cranial anatomy compromises the capacity of any single computational algorithm to uniformly remove extracranial contamination from the intracranial NIRS signal. As a result, a tiny fraction of abnormal baseline rSO₂ values represent a functionally normal brain inside a spectroscopically abnormal cranium. In these few individuals, apparently low rSO₂ values determined during wakefulness do not represent an underlying clinical abnormality.

The more common cause for a low rSO₂ baseline is an actual cerebral oxygen imbalance that is not necessarily predictable from patient history. A low or asymmetric rSO₂ baseline usually represents the consequences of cerebral vascular disease, chronic obstructive pulmonary disease, congestive heart failure, chronic hypertension, diabetes mellitus, or sickle cell disease. For example, Goto et al used preoperative magnetic resonance imaging to identify preexisting cerebral infarcts in patients scheduled for myocardial revascularization. Radiographic evidence of infarct was seen in half of the patients as was a 30% incidence of clinically silent infarcts. Furthermore, infarct presence significantly increased the risk of POCD.

Fortuitously, distinction between the technical and clinical causes of a low baseline rSO₂ is straightforward. Preoxygenation will substantially increase a low rSO₂ baseline only in the case of a genuine cerebral oxygen imbalance.
Because the cerebral oximeter has been cleared for use as a trend monitor, the preferred approach is to rely primarily on a relative measure of oxygen imbalance. The concept of a 20% \(rSO_2\) decline as indicative of clinically significant imbalance has been established in a wide range of studies involving cardiac occlusion,\(^{13,23}\) implantable cardioverter-defibrillator testing,\(^{11}\) tilt-table testing,\(^{24}\) negative gravitational force testing,\(^{33}\) and cardiac surgery.\(^{19}\)

The proprietary algorithm used in the INVOS cerebral oximeter incorporates a fixed arterial:venous ratio of 25:75. Nevertheless, marked shifts in this ratio have minimal effect on the accuracy of the measure.\(^{19}\) Even reversal of the normal ratio to 75:25 during transcranial Doppler ultrasound–confirmed retrograde cerebral perfusion typically has only a slight impact on \(rSO_2.\)^{19}

The relationship between \(rSO_2\) and hemoglobin concentration is complex and somewhat unpredictable. Hemoglobin fluctuations within the normative range seem to have little effect on \(rSO_2\), whereas sub- or supernormal concentrations may alter cerebral oxygen balance.\(^{26}\) Han et al\(^{27}\) showed that, with the onset of cardiopulmonary bypass, the magnitude of transient \(rSO_2\) decrease was directly related to the volume of crystalloid prime. Presumably, the prime reduced the hemoglobin concentration in the cerebral microcirculation. The resultant change in venular oxy-/deoxyhemoglobin balance reflected the combined effects of a temporary decrease in local oxygen supply and increased oxygen extraction.

The potential influence of hemoglobin concentration on \(rSO_2\) has been proposed as the basis for a transfusion trigger.\(^{28}\) However, it should be appreciated that hemoglobin is both an indirect and imperfect measure of oxygen delivery. It is well established that blood processing may reduce hemoglobin oxygen–carrying capacity by up to 90%.\(^{29}\) This phenomenon helps explain the observation of occasional \(rSO_2\) decrease after blood transfusion.\(^{21}\) Certainly, potential users of cerebral oximetry should not expect a predictable mathematical relationship to uniformly exist between hemoglobin concentration and \(rSO_2.\)

Unambiguous determination of the exclusive effect of shifts in the oxyhemoglobin dissociation association curve on \(rSO_2\) has not been achieved. The difficulty arises from the fact that factors that affect dissociation (eg, acid-base balance, temperature, and oxygen tension) simultaneously alter other relevant physiologic processes such as cerebral blood flow, blood viscosity, cerebral metabolic demand, and oxygen extraction.

Many of the negative reports on cerebral oximeter performance appear to have been based on a fundamental misunderstanding about the expected relationship between \(rSO_2\) and neuronal function. Because a dual-wavelength spectrophotometer (eg, pulse and cerebral oximeter) measures only oxy- and deoxyhemoglobin, no direct information is provided regarding tissue viability (eg, the oxidation state of cytochrome moieties). Thus, the expectation that oxygen saturation measurement should permit discrimination between live and dead or animal and plant tissue is unfounded.\(^{30}\) This essential point is shown by a study from Maeda et al\(^{13}\) who measured cerebral venous oxygen saturation during 214 autopsies. They found values ranging from 0.3% to 95%. The variation was dependent on the total hemoglobin content, cause of death, and cadaver-storage conditions.

CEREBRAL OXIMETRY: EVIDENCE OF CLINICAL BENEFIT

The precepts of evidence-based medicine include a requirement for outcome studies based on a prospective randomized control design. Preliminary evidence of such a benefit for cerebral oximetric monitoring during cardiac surgery recently has been presented by Murkin et al.\(^{32}\) These authors examined perioperative major organ morbidity in 200 myocardial revascularization patients, 101 of whom had been randomly assigned to receive cerebral oximeter monitoring. A significant morbidity reduction was observed in the group managed with cerebral oximetry by using a standardized intervention protocol.

A randomized trial with elderly noncardiac surgical patients also noted benefit with cerebral oximetry.\(^{33}\) Intraoperative \(rSO_2\) was recorded in all 122 subjects, but in the control group (\(n = 66\)), no effort was made to correct cerebral oxygen desaturation of \(>25\)% below baseline. Noteworthy desaturation occurred in 23% of the control group and 20% of the intervention group. In this patient subset with cerebral oxygen imbalance, control subjects had significantly longer time to PACU discharge and hospital stay as well as larger decline in cognitive function as measured by the Mini-Mental Status Exam.

Although randomized clinical trials are currently viewed as the most reliable basis for determination of diagnostic or therapeutic efficacy, they have an important limitation. Because the information is obtained from selected patients by using formal management and data-collection protocols, the results are not necessarily applicable to the vagaries of customary clinical practice. Alternatively, effectiveness determined by outcomes research describes what actually works in the uncontrolled world of traditional health care.\(^{34}\) Conclusions regarding practical effectiveness are typically derived from observational studies during routine clinical practice. Full appreciation of the opportunities for optimal patient care is best achieved by consideration of information on both efficacy and effectiveness.

In fact, there is close agreement between the findings of the prospective and retrospective studies examining the clinical benefit of cerebral oximetry for cardiac surgery. The available 11 retrospective cardiac surgery studies that incorporated a standardized intervention protocol comprise an aggregate study population exceeding 7,000.\(^{35-45}\) All these studies found that intraoperative \(rSO_2\) monitoring was associated with significant reductions in neurologic injury, duration of hospital stay, or both. In addition, a growing number of case reports show likely prevention of catastrophic brain injury with cerebral oximetric monitoring\(^{46-55}\).

In summary, the technical considerations discussed previously should be viewed as an aid to the thoughtful use of the cerebral oximeter. None of these limitations is sufficient excuse to avoid using the technology. The evidence for clinical benefit during cardiac surgery is consistent and compelling. In addition, the availability of published normative values and alarm criteria, a modest operational expense, and the lack of use-associated risk of injury further support the routine use of cerebral oximetry monitoring for cardiac surgery.
REFERENCES