Detection of cerebral ischemia in neurovascular surgery using quantitative frequency-domain near-infrared spectroscopy

MATEO CALDERON-ARNULPHI, M.D.,1 ALI ALARAJ, M.D.,1 SEPIDEH AMIN-HANJANI, M.D.,1 WILLIAM W. MANTULIN, PH.D.,2 CHIARA M. POLZONETTI, M.S.,2 ENRICO GRATTON, PH.D.,2 AND FADY T. CHARBEL, M.D.1

1Department of Neurosurgery, University of Illinois at Chicago Medical Center, Chicago; and 2Laboratory for Fluorescence Dynamics, Department of Physics, University of Illinois at Urbana-Champaign, Urbana, Illinois

Object. There is great value in monitoring for signs of ischemia during neurovascular procedures. Current intraoperative monitoring techniques provide real-time feedback with limited accuracy. Quantitative frequency-domain near-infrared spectroscopy (Q-NIRS) allows measurement of tissue oxyhemoglobin (HbO₂), deoxyhemoglobin (HHb), and total hemoglobin (tHb) concentrations and brain tissue oxygen saturation (SO₂), which could be useful when monitoring for evidence of intraoperative ischemia.

Methods. Using Q-NIRS, the authors monitored 25 neurovascular procedures including aneurysm clip placement, arteriovenous malformation resection, carotid endarterectomy, superficial temporal artery-middle cerebral artery (MCA) bypass surgery, external carotid artery-MCA bypass surgery, encephaloduromyosynangiosis, and balloon occlusion testing. The Q-NIRS technology provides measurable cerebral oxygenation values independent from those of the scalp tissue. Thus, alterations in the variables measured with Q-NIRS quantitatively reflect cerebral tissue perfusion. Bilateral monitoring was performed in all cases.

Five of the patients exhibited evidence of clinical ischemic events during the procedures. One patient suffered blood loss with systemic hypotension and developed diffuse brain edema intraoperatively, one patient suffered an ischemic event intraoperatively and developed an occipital stroke postoperatively, and one patient showed slowing on electroencephalography intraoperatively during carotid clamping; in two patients balloon occlusion testing failed. In all cases of ischemic events occurring during the procedure, Q-NIRS monitoring showed a decrease in HbO₂, tHb, and SO₂, and an increase in HHb.

Conclusions. Quantitative frequency-domain near-infrared spectroscopy provides quantifiable and continuous real-time information about brain oxygenation and hemodynamics in a noninvasive manner. This continuous intraoperative oxygenation monitoring is a promising method for detecting ischemic events during neurovascular procedures.

Key Words • ischemia • near-infrared spectroscopy • brain tissue oxygen monitoring • hemoglobin • bypass surgery

Despite advances in surgical techniques, the risk of perioperative stroke during neurovascular procedures remains a significant potential source of morbidity and death. Intraoperative cerebral ischemia can occur because of prolonged temporary occlusion of intracranial cerebral arteries during aneurysm clip placement, from inadvertent or planned permanent occlusion of a cerebral artery, from sustained elevation of intracranial pressure, or from a severe drop in blood pressure. Several procedures are used to reduce intraoperative cerebral ischemic insults, including deep hypothermic circulatory arrest and EEG burst suppression to reduce cerebral oxygen consumption.

Current intraoperative monitoring techniques such as electroencephalography, transcranial Doppler ultrasonography, SSEP, and CW-NIRS provide only indirect evidence of ischemic insult, and have other technique-specific limitations. Quantitative frequency-domain NIRS, however, is able to provide a continuous measurement of absolute cerebral oxygenation. For this reason, we investigated the use of Q-NIRS for the detection of ischemia during neurovascular procedures.

Abbreviations used in this paper: CEA = carotid endarterectomy; CSF = cerebrospinal fluid; CW-NIRS = continuous-wave near-infrared spectroscopy; EEG = electroencephalographic; HbO₂ = oxyhemoglobin; HHb = deoxyhemoglobin; ICA = internal carotid artery; Q-NIRS = quantitative frequency-domain NIRS; SO₂ = oxygen saturation; SSEP = somatosensory evoked potential; tHb = total hemoglobin.
Clinical Material and Methods

Patient Population

Patients with neurovascular procedures performed between May 2004 and February 2006 at the Department of Neurosurgery at the University of Illinois at Chicago were included in the study. Institutional review board approval for the study was obtained from the University of Illinois at Chicago and the University of Illinois at Urbana-Champaign. Patients signed informed consent forms and Health Insurance Portability and Accountability Act documents before surgery. No intraoperative decisions were made based on the results of Q-NIRS monitoring. We monitored 25 neurovascular procedures using the Q-NIRS tissue oximeter (Oxiplex TS, ISS Inc.).

Patient demographic data, diagnoses, treatments, and outcomes are summarized in Table 1. Cases were chosen based on the potential for ischemic insults. During temporary vessel occlusion at the time of surgery, EEG burst suppression was induced in all patients who underwent operations for aneurysms or bypass procedures using up to 2% isoflurane inhalational anesthesia. End-tidal carbon dioxide was monitored continuously and maintained at 30 mm Hg to avoid changes in cerebral blood volume. The clinical outcomes of the surgical interventions were recorded postoperatively (Table 1).

Quantitative Frequency-Domain NIRS Methods

The Q-NIRS tissue oximeter was brought to the operating room and was turned on 30 minutes before surgery to reach room temperature. Prior to the Q-NIRS measurements, the optical probes were calibrated using a silicone phantom with optical properties comparable to those of brain tissue. After patients were placed in a state of anesthesia, they were positioned on the operating table, their scalps were shaved, and monitoring probes were attached bilaterally (one each on the affected and the contralateral side). The NIRS and the frequency-domain multidistance method quantitatively separate absorption and scattering contributions. By determining the light absorption coefficients at two wavelengths, this method uses the differences in the absorption spectra of HbO$_2$ and HHb in tissue to calculate the absolute levels of hemoglobin saturation and total blood volume ($\mu$mol/L). The four source-detector distances of the probe ranged from 1.98 to 3.50 cm with a mean distance of approximately 2.74 cm. A minimum depth of 0.3 cm of the superficial cortex covering a 1 cm$^2$ area was monitored. Using a two-layer model described elsewhere, the HbO$_2$ and HHb concentration and SO$_2$ of the adult brain can be calculated with good accuracy independent of the scalp and skull contributions. Absorption was recorded at two wavelengths (690 and 830 nm), corresponding to the maximum absorp-

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs., Sex</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>68, F</td>
<td>rt ICA ophthalmic aneurysm</td>
<td>aneurysm clipping</td>
<td>good</td>
</tr>
<tr>
<td>2</td>
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<td>aneurysm clipping</td>
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<td>3</td>
<td>48, F</td>
<td>parietal AVM</td>
<td>resection</td>
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</tr>
<tr>
<td>4</td>
<td>69, F</td>
<td>rt ICA stenosis</td>
<td>CEA</td>
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</tr>
<tr>
<td>5</td>
<td>68, M</td>
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<td>CEA</td>
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<td>good</td>
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<tr>
<td>7</td>
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</tr>
<tr>
<td>8</td>
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<td>rt MCA stenosis</td>
<td>rt STA–MCA bypass</td>
<td>good</td>
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<td>9</td>
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<td>lt ECA–lt VA bypass</td>
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</tr>
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<td>10</td>
<td>63, M</td>
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<td>lt STA–MCA bypass</td>
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<tr>
<td>11</td>
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<td>good</td>
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<tr>
<td>12</td>
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</tr>
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<td>brain edema, death after 1 wk</td>
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<td>14</td>
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<tr>
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<td>rt STA–MCA bypass</td>
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<td>rt ECA–ICA bypass</td>
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<tr>
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<td>18</td>
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<td>21</td>
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<td>BOT</td>
<td>passed</td>
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<tr>
<td>22</td>
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<td>hypoperfusion on SPECT</td>
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<td>rt skull base tumor</td>
<td>BOT</td>
<td>passed</td>
</tr>
<tr>
<td>25</td>
<td>81, F</td>
<td>1t ICA cavernous aneurysm</td>
<td>BOT</td>
<td>failed clinically</td>
</tr>
</tbody>
</table>

* AVM = arteriovenous malformation; BOT = balloon occlusion testing; ECA = external carotid artery; EDMS = encephalo-duromyosynangiosis; IJV = internal jugular vein; MCA = middle cerebral artery; SPECT = single photon emission computed tomography; STA = superficial temporal artery; VA = vertebral artery.
tion of HbO$_2$ and HHb, respectively. Continuous arterial blood pressure, heart rate, and peripheral SO$_2$ were also recorded at the same time. This approach allowed us to measure cerebral tissue SO$_2$, quantitative tissue hemoglobin (HbO$_2$ and HHb) concentrations, and tHb concentrations in both hemispheres of the brain. Intraoperative peripheral hemoglobin measurements were also obtained during the monitoring procedure.

For surgery involving the anterior cerebral artery, we placed the probes on the medial frontal region of the head. For other surgeries, the probes were placed on the parietal region of the head. The probes were firmly attached by means of a medical adhesive. The duration of brain oxygenation and hemodynamic changes were recorded during the entire procedure.

**Results**

*Intraoperative Monitoring*

Continuous recordings of quantitative HbO$_2$, HHb, tHb, and SO$_2$ were obtained from both cerebral hemispheres during the 25 procedures. The HbO$_2$ concentration level obtained before skin incision was used as the baseline point. Any acute event with a decrease in HbO$_2$ concentration below the baseline point was recorded and noted. These events were manifested by a decrease in HbO$_2$ and tHb with a concomitant rise in HHb, which represents a decrease in cerebral blood volume (indirectly measured by a decrease in tHb) and an increase in oxygen consumption (indirectly measured by an increase in HHb).

Of all patients monitored, five showed evidence of clinical ischemic events during the procedures: one patient suffered blood loss with systemic hypotension and developed diffuse brain edema intraoperatively; one patient suffered an intraoperative ischemic event and developed an occipital stroke postoperatively; one patient showed a slowing of brain activity on electroencephalography intraoperatively during carotid clamping; and in two patients balloon occlusion testing failed. In all recorded clinical ischemic events, Q-NIRS monitoring showed a decrease in HbO$_2$, tHb, and SO$_2$, with an increase in HHb.

In the five patients with ischemic events, the HbO$_2$, decreases ranged from 3.3 to 11.5 μmol/L (20.5–82.5% from baseline); tHb decreases ranges from 1 to 9.7 μmol/L (1.8–35.6% from baseline); and SO$_2$ decreases ranged from 3 to 26.2% (4.4–90% from baseline). An increase in HHb from 2.8 to 4 μmol/L (8–38.3% from baseline) was detected. For the 20 patients who did not suffer ischemic events, HbO$_2$ decreases ranged from 0.5 to 11 μmol/L (2–24% from baseline); tHb decreases on the ipsilateral side ranged from 0 to 10 μmol/L (0.7–25% from baseline); and SO$_2$ decreases ranged from 1 to 16% (1.5–36.3% from baseline). An increase in HHb from 2.2 to 9.5 μmol/L (2.4–35.8% from baseline) was detected in these 20 patients. Based on these data, HbO$_2$ was the parameter that best discriminated between patients with and without ischemic events (p = 0.03, two-tailed t-test; Fig. 1).

![Graph showing a comparison of the average percentage increase or decrease for HbO$_2$, HHb, tHb, and SO$_2$ using Q-NIRS monitoring in patients who were ischemic or nonischemic.](image-url)
In addition to vessels that are compromised intraoperatively, acute events can be precipitated by the following: an acute drop in blood pressure, especially in the setting of impaired autoregulation (in patients undergoing bypass surgery for cerebral hypoperfusion); an acute drop in systemic hematocrit (in patients with bleeding); or systemic hypoxemia (in patients with compromised respiratory systems). No patient experienced instances of respiratory compromise during surgery. An acute decrease in hematocrit was recorded in one patient (Case 13) with severe intraoperative bleeding.

**Illustrative Cases**

**Case 4**

This 69-year-old woman presented with recent onset of recurrent transient ischemic attacks over a 3-week period. She was evaluated using cerebral angiography, which showed a 70% stenosis in the right ICA. Quantitative frequency-domain NIRS detected lower oxygenation (HbO$_2$) at baseline on the affected side (3 μmol/L) compared with the nonaffected side (11 μmol/L). During a right CEA, the right ICA was clamped temporarily; electroencephalography showed slowing after 2 minutes, which necessitated arterial shunt placement. Quantitative frequency-domain NIRS monitoring revealed immediate cerebral ischemia after the ICA was clamped: HbO$_2$ decreased from 4 to 0.7 μmol/L (82.5% from baseline); tHb dropped from 18.5 to 16.2 μmol/L (12.4% from baseline); SO$_2$ dropped from 20 to 2% (90% from baseline); and HHb increased from 15 to 19 μmol/L (21% from baseline). This ischemic state improved after an intraluminal shunt was placed; however, it did not reestablish oxygenation to the baseline level. A second ischemic event was noted when the ICA was clamped again briefly to extract the arterial shunt (Fig. 2). The changes detected by Q-NIRS monitoring preceded the intraoperative slowing of brain activity on electroencephalography. The patient had no neurological complications after surgery.

**Case 13**

This 58-year-old man presented with severe intracranial hypertension secondary to bilateral occlusion of both internal jugular veins after radical neck dissection and past radiation therapy. Right transverse sinus–subclavian vein bypass surgery was performed using a Gore-Tex venous graft. During anastomosis, severe bleeding from the sinus was encountered, along with hypotension and massive intraoperative brain swelling. Continuous Q-NIRS monitoring showed acute ischemia in both hemispheres, but more severely on the ipsilateral side: HbO$_2$, decreased from 18.2 to 6.7 μmol/L (63.1% from baseline); tHb decreased from 25.5 to 16.4 μmol/L (35.6% from baseline); SO$_2$, decreased from 81.5 to 55.5% (32% from baseline); and HHb increased from 4.5 to 7.3 μmol/L (38.3% from baseline) (Fig. 3). These changes corresponded to a decrease in the mean systemic arterial pressure to 40 mm Hg, a drop in the hematocrit, brain edema, and an increase in intracranial pressure with brain herniation outside the calvarial defect.

**Case 25**

This 81-year-old woman presented with a 1-week history of worsening left eye palsy and ptosis. She was evaluated using cerebral angiography, which demonstrated a 2.5-cm left cavernous ICA aneurysm. The patient underwent endovascular balloon occlusion testing. The balloon was placed in the ICA; 3 minutes after inflation of the balloon, aphasia developed and the patient experienced a right facial droop and right upper- and lower-extremity weakness.
These symptoms were associated with a concomitant and immediate decrease in cerebral oxygenation as demonstrated by Q-NIRS monitoring on the ipsilateral side: HbO$_2$ decreased from 15.5 to 11.5 μmol/L (25.8% from baseline); tHb decreased from 30 to 27 μmol/L (10% from baseline); SO$_2$ dropped from 50 to 44% (12% from baseline); and HHb increased from 13.5 to 15.2 μmol/L (11.1% from baseline). The contralateral hemisphere showed a compensatory increase in brain oxygenation. The balloon was deflated with subsequent complete resolution of the symptoms and restoration of brain oxygenation as shown by Q-NIRS. The continuous EEG monitoring showed no changes, demonstrating greater sensitivity of Q-NIRS monitoring to the clinical ischemic event (Fig. 4).

**Discussion**

**Neuromonitoring Methods**

There is an inherent risk of perioperative stroke during neurovascular operations. The primary cause of perioperative stroke is hypoperfusion due to temporary or permanent occlusion of a vessel, intraoperative retraction, or systemic hypotension.$^{1,46}$ Inadvertent permanent occlusion of a feeding or perforating artery occurs in 3.1% of patients undergoing aneurysm surgery and is a primary cause of intraoperative complications.$^{18}$ In these patients, the prompt and accurate recognition of insufficient collateral circulation is crucial to a good neurological outcome. Transcranial Doppler ultrasonographic, EEG, and SSEP monitoring are established methods of neuromonitoring during neurovascular procedures.$^4$ The role of intraoperative EEG monitoring can be limited during aneurysm surgery if burst suppression is used. Electrophysiological monitoring, particularly with SSEPs, is an accepted method of detecting procedure-related cerebral ischemia.$^{16,24,25,30,36}$ There is a considerable time delay after potential ischemic events,$^{3,24}$ however, with limited predictability of these events on an individual basis.$^{14,36}$ Additionally, anesthesia can alter SSEPs through several other mechanisms.$^{21,23}$

In this study we examined the role of Q-NIRS monitoring of ischemic events during neurovascular procedures. Twenty-five patients were monitored throughout the neurosurgery. In all cases with evidence of ischemic events (brain edema, slowing of electroencephalography, postoperative stroke, and failure of balloon occlusion testing), there was a decrease in HbO$_2$, tHb, and SO$_2$, with an increase in HHb concentrations.

**Role of NIRS**

Continuous-wave NIRS has been available since 1977 as a tool to measure changes in the hemoglobin oxygenation state in the human brain.$^{17}$ Use of CW-NIRS allowed observation of dynamic changes in regional blood flow in real time by measuring concentration changes in hemoglobin, but failed to provide absolute values of hemoglobin concentrations. Thus, CW-NIRS measurements could not be compared between individuals, or between regions within the same individual.

The use of semiquantitative NIRS (INVOS 3100A, Somanetics Corp.)—a form of CW-NIRS—for neuromonitoring in carotid artery surgery has been assessed,$^{17}$ but studies in which semiquantitative NIRS was used, failed to demonstrate clinical usefulness in this setting.$^{19,42}$ Moreover, Beese et al.$^2$ used semiquantitative NIRS to study patients with restricted cerebral circulation, as indicated by the loss of cortical SSEPs; their results showed that severe cerebral ischemia, as indicated by cortical potential loss, occurred in some patients with minimal or even no change of the regional cerebral oxygenation displayed using semiquantitative NIRS. Data from previous studies demonstrated that absolute numbers of regional SO$_2$ are of little value in interpreting results obtained by semiquantitative NIRS.$^{4,8,26,28}$ Recently, Q-NIRS measurements were introduced, which enabled accurate quantification of brain tissue oxygenation.$^{5,9,15,39,43}$

FIG. 3. Case 13. Graphs showing Q-NIRS values of HbO$_2$, tHb, SO$_2$, and HHb during a right transverse sinus–subclavian vein bypass. Arrows denote the following stages of the operation: 1, acute bleeding with drop in mean arterial pressure and an associated decrease in HbO$_2$, tHb, and SO$_2$ and an increase in HHb in both hemispheres; 2, blood transfusion and subsequent slow improvement of mean arterial pressure; and 3, recurrence of bleeding and moderate hypotension.
Quantitative frequency-domain NIRS has two major advantages compared with CW-NIRS: it provides quantitative values of hemoglobin concentrations (HbO₂, HHb, tHb), and it directly monitors brain tissue oxygenation independently from oxygenation of the skin and scalp. Unlike CW-NIRS, Q-NIRS readings of cerebral oxygen concentration are not affected by extracranial layers of the scalp, skull, and CSF. When brain tissue is measured by NIRS, photons travel across layers of the cranium displaying different optical properties as the light’s path to the brain is intersected by the scalp, skull, and CSF. Unless the layered structure is accounted for, measurements could be inaccurate. There are results from many studies demonstrating the ability of Q-NIRS to isolate brain tissue oxygenation from skin and scalp oxygenation. Franceschini et al. demonstrated in multilayered silicone phantoms that Q-NIRS successfully recovered the optical properties of the lowest layer at approximately 1 cm from the surface. This phantom was next used to model the multilayer architecture of the head (skin, scalp, CSF, and brain). Furthermore, Choi et al. used Q-NIRS to demonstrate that the adult human head can be reasonably described by a two-layer model, and by using this model, the hemoglobin concentration and SO₂ of the brain can be calculated with good accuracy. Other studies have used concomitant Q-NIRS and functional magnetic resonance imaging of brain hemodynamics to generate functional maps during task-related brain activation. A high temporal correlation between the blood oxygenation level-dependent signal (using functional magnetic resonance imaging) and the HHb concentration (using Q-NIRS) was demonstrated. This correlation can only be explained by the simultaneous detection of brain activation by both methods.

Detection of Ischemic Events

Due to the quantitative nature of Q-NIRS measurements, recordings can be compared over time as well as with recordings obtained in other patients. Factors that could affect absolute cerebral tissue oxygenation intraoperatively include the baseline status of the cerebral tissue perfusion, presence and duration of vessel compromise, increase in intracranial pressure, extent of brain oxygen consumption (including the effects of EEG burst suppression), systemic changes in blood pressure, and systemic oxygen carrying capacity (as reflected by hematocrit). A change in any one of these variables can result in a decrease in brain tissue oxygen content, which can precipitate brain ischemia. In this study, changes in tissue oxygenation during surgery occurred in patients both with and without ischemic events, although the absolute decrease in HbO₂ appeared to be the best discriminating factor between the groups (Fig. 1). A tissue oxygenation threshold that patients have to reach before developing ischemia may not solely depend on the degree of oxygenation decrease. Given that the ischemic insult to the brain depends on both the degree and duration of decreased oxygenation, a future paradigm that combines these two factors may be the most appropriate for predicting ischemic insults, although such a predictive model is beyond the scope of this study.

Our findings support a useful role for Q-NIRS in intraoperative monitoring, although the small number of documented procedure-related ischemic events limits the ability to generalize our results. Based on further data collection, we hope that in the future we will further validate a threshold value that indicates severe cerebral ischemia.

Limitations of Q-NIRS

The main limitation of the Q-NIRS technology is its restriction to cortical brain tissues and the area beneath the probe. Although cortical tissues are primarily at risk of infarction after prolonged arterial occlusion, deeper tissues...
Detecting ischemia with quantitative NIRS

supplied by perforators can be selectively at risk as well, and cannot currently be monitored using Q-NIRS. Furthermore, only relatively small regions of any particular vascular territory can be monitored because the average monitored area is approximately 1 cm². The use of multiple probes may reduce this particular limitation, but does not currently address the lack of monitoring for deep tissues. Although the accuracy of Q-NIRS recordings is independent of the skull and scalp, increased skull thickness reduces the breadth and depth by which the near-infrared light travels into the brain tissues, thus reducing the area of tissue measured by this method. In the future, advances in Q-NIRS technology that allow the ability to monitor deeper tissues over a larger area would be optimal.

Currently, given the limitations of the technology, Q-NIRS may not be optimal for detection of focal territory or ischemia in perforating vessels. For example, during aneurysm or distal bypass surgery, the Q-NIRS probes may not predictably monitor the specific cortical, or deep, region of tissue at risk. The primary clinical applications of Q-NIRS to cerebrovascular surgery would be procedures in which there is potential for large territory ischemia, such as balloon occlusion testing and CEA. In such cases, the hemispheric reduction in blood flow would be easily amenable to Q-NIRS monitoring. Additionally, procedures involving the risk of severe intraoperative bleeding with the potential for global hypoperfusion would be amenable to monitoring with Q-NIRS.

Conclusions

Quantitative frequency-domain NIRS provides quantitative, noninvasive, and continuous real-time information about brain oxygenation and hemodynamics directly related to vascular events. It appears that the use of this technique is feasible and can provide accurate information in the operating room during certain neurovascular procedures. Continuous intraoperative oxygenation monitoring with Q-NIRS to provide real-time feedback on absolute tissue oxygenation may improve the outcome of neurovascular procedures by minimizing ischemia.

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Disclaimer

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