Comparison of Near-Infrared Spectroscopy and Somatosensory Evoked Potentials for the Detection of Cerebral Ischemia During Carotid Endarterectomy

Ulrich Beese, MD; Harald Langer, MD; Werner Lang, MD; Michael Dinkel, MD

Background and Purpose—We sought to assess the clinical value of regional cerebral saturation (rS\textsubscript{O}_2) obtained by means of the cerebral oximeter INVOS 3100A (Somanetics) in comparison to monitoring of somatosensory evoked potentials (SEP) for the reliable detection of severe cerebral ischemia requiring shunt placement in the individual patient undergoing carotid surgery under general anesthesia.

Methods—In 317 patients undergoing reconstructive surgery on the internal carotid artery, simultaneous recordings of SEP and rS\textsubscript{O}_2 were obtained throughout the operation.

Results—All 287 patients with preserved cortical SEP remained neurologically intact. Shunt placement was performed in 27 patients (9%) after flattening of cortical SEP during cross-clamping of the internal carotid artery. A stable rS\textsubscript{O}_2 value just before cross-clamping and the lowest value after cross-clamping were registered, and the decrease was calculated. A statistically significant (P<0.01) decrease of rS\textsubscript{O}_2 after cross-clamping could be found in patients without (64.9±8.3% to 60.9±9.9%) as well as in patients with consecutive loss of cortical SEP (65.8±9.1% to 56.1±13.4%). The difference of the decrease of rS\textsubscript{O}_2 in both groups was highly significant (6.9±9.0% versus 15.6±14.0%; P<0.001). However, substantial interindividual variability of rS\textsubscript{O}_2 and derived change of rS\textsubscript{O}_2 did not allow the definition of a threshold value indicating need of shunt placement.

Conclusions—The reliability of SEP for the detection of clamp-related hypoperfusion has been reaffirmed. As long as rS\textsubscript{O}_2 threshold values indicating critical cerebral ischemia are not defined, therapeutic interventions based on monitoring with the cerebral oximeter INVOS 3100A are not justified. (Stroke. 1998;29:2032-2037.)

Key Words: carotid stenosis ■ cerebral ischemia ■ evoked potentials, somatosensory ■ intraoperative monitoring ■ oximetry ■ surgery

The efficiency of surgical therapy for prevention of stroke in patients with >70% carotid stenosis has recently been clarified.1 The inherent risk of surgery is perioperative stroke. A major cause of cerebrovascular accidents is hypoperfusion during cross-clamping of the internal carotid artery (ICA).2–4 The prompt and reliable recognition of insufficient collateralization is crucial for a good neurological outcome of patients. General use of an intraluminal shunt bears the risk of embolization and undetected shunt malfunction.4 Therefore, proper neuromonitoring needs to identify patients who will benefit from shunt placement not only with a high sensitivity but with a high specificity as well.

The use of electroencephalography, somatosensory evoked potentials (SEP), and transcranial Doppler sonography are established forms of neuromonitoring in patients undergoing carotid surgery.4 However, technical expertise and experience in interpreting the results of these monitors are necessary.

Cerebral oximetry appears to be an attractive alternative because it relies on a continuous, noninvasive measurement principle and is easy to use. Previous studies provided evidence that changes in cerebral oxygenation caused by cross-clamping of the ICA can be monitored by means of near-infrared spectroscopy (NIRS).7–10 Since no “gold standard” with which to test the sensitivity and specificity of cerebral oximetry exists, the results of NIRS need to be compared with other validated forms of neuromonitoring.11 A loss of cortical SEP is a good indicator of cerebral hypoperfusion and is able to identify patients at risk for intraoperative stroke.12–14 However, given the relatively low incidence of clamp-related ischemia in carotid surgery, it is obvious that a large number of patients must be studied to obtain sufficient data from patients developing severe cerebral ischemia.15 This could not be accomplished by previously published studies.

After validating the results of SEP with the individual neurological outcome of the patients, we compared the changes of cortical SEP and regional cerebral saturation (rS\textsubscript{O}_2), obtained by the cerebral oximeter INVOS 3100A,
Subjects and Methods

After approval by the local ethics committee of the medical faculty of the University of Erlangen-Nuremberg and after we obtained informed and written consent, 317 patients (215 men, 102 women) aged 42 to 89 years were included. Preoperative neurological classification and angiographic findings are summarized in Table 1.

Patients with known arterial hypertension or coronary artery disease were instructed to take their usual antihypertensive or antianginal medications until the day of the operation. A standard balanced anesthetic technique was used in all patients. Anesthesia was induced with midazolam (0.03 to 0.05 mg/kg IV), fentanyl (2 to 3 μg/kg IV), etomidate (0.2 mg/kg IV), vecuronium (0.1 mg/kg IV), or rocuronium (0.6 mg/kg IV) and maintained by administration of repeated boluses of fentanyl (1 to 2 μg/kg IV), vecuronium/rocuronium, and 0.4% to 1.0% inspired isoflurane. All patients were artificially ventilated with 40% oxygen in nitrous oxide. Analysis of intermittent drawn arterial blood gas samples ensured normoventilation (4.7 to 5.2 kPa). Routine monitoring during anesthesia included standard ECG (lead II, V5), intra-arterial catheter for direct arterial blood pressure measurement, pulse oximetry, and capnography. Blood pressure was kept stable in a range of ±20% of the preoperative level throughout the procedure by adjusting the depth of anesthesia or, if needed, by intravenous administration of a vasodilative (nitroglycerin) or a vasoconstrictive (theophylline) agent.

SEP were recorded from induction to reversal of anesthesia by means of the Nicolet Pathfinder I electrodiagnostic system (Nicolet Biomedical Co). Detailed stimulation and recording parameters are listed in Table 2. Evoked potentials were recorded above the postcentral region of the side that was operated on and above the cervical spine for artifact control. The peak-to-peak amplitudes of the cervical potential N14-P18 and the primary cortical response N20-P25 were measured online. Because of the results of a previous study, a critical cerebral ischemia after cross-clamping was assumed if the peaks of the N20-P25 complex were not readily identifiable, while the cervical control potential N14-P18 remained intact. Such a constellation was the sole index for the insertion of a temporary intraluminal shunt.

The cerebral oximeter INVOS 3100A (Somanetics) was used to measure rSO2 throughout the procedure. After the patient’s skin was thoroughly cleaned, the sensor was placed according to the manufacturer’s instructions over the ipsilateral forehead. The light transmitters were ~3 cm away from midline to avoid distortion from the sagittal sinus. After a stable rSO2 reading was achieved, the margins of the sensor were tightened with an opaque tape. The rSO2 readings were recorded at 30-second intervals and stored for later analysis. In a study protocol the mean value in the last 2 minutes before clamping (rSO2-1) was noted. When the carotid complex was exposed, the common carotid artery was cross-clamped first, followed in rapid succession by the internal and external carotid arteries. After cross-clamping of the ICA, the lowest value was documented (rSO2-2) when this value persisted for ≥2 minutes. The change of rSO2 (ΔrSO2) in the individual patient was calculated on the basis of these data (ΔrSO2 = rSO2-1 − rSO2-2).

All patients were extubated in the operation theater. At this point patients were tested for the development of any new neurological deficit. Patients were followed until the time of discharge from the hospital.

Mean ± SD values are expressed. The Wilcoxon test was used to compare rSO2 values before and after cross-clamping of the ICA. Comparisons of rSO2 values before and after cross-clamping as well as the calculated change of rSO2 between patients with preserved cortical SEP and SEP loss were performed with the Mann-Whitney U test. All P values were 2-sided, and significance was assessed at the 0.05 level. A commercially available statistical package, SPSS for Windows, version 6.1 (SPSS Inc) was used for performing the statistical analysis.

Results

Reconstruction of the ICA was successfully completed in all 317 patients. The most commonly performed procedures were thromboendarterectomy with patch closure (n=208, 65.6%) and evasion endarterectomy (n=79, 24.9%). No deaths occurred during the observation period. The range of fluctuations for mean arterial pressure between the points at which preclamp and postclamp rSO2 was determined was +18% to −14% for the studied population. The mean duration of carotid cross-clamping was 35 ± 11 minutes, with a range of 7 to 106 minutes.

Continuous recording of SEP and rSO2 was possible in all patients. All 287 patients (90.5%) with preserved cortical function were followed until discharge from the hospital.}

### Table 1. Preoperative Neurological Status and Angiographic Findings (n=317)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Neurological classification</th>
<th>Ipsilateral ICA</th>
<th>Contralateral ICA</th>
<th>Vertebral arteries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asymptomatic lesion</td>
<td>33.4%</td>
<td>9.1%</td>
<td>No occlusion</td>
</tr>
<tr>
<td></td>
<td>Transient ischemic attack</td>
<td>44.5%</td>
<td>52.7%</td>
<td>Occlusion</td>
</tr>
<tr>
<td></td>
<td>Completed stroke</td>
<td>23.1%</td>
<td>38.2%</td>
<td>Occlusion (1 or both)</td>
</tr>
<tr>
<td></td>
<td>Preoperative angiographic findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ipsilateral ICA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stenosis ≤70%</td>
<td>77.3%</td>
<td>7.3%</td>
<td>No occlusion</td>
</tr>
<tr>
<td></td>
<td>Stenosis 70–90%</td>
<td>9.8%</td>
<td>9.8%</td>
<td>Occlusion</td>
</tr>
<tr>
<td></td>
<td>Stenosis &gt;90%</td>
<td>12.9%</td>
<td>12.9%</td>
<td>Occlusion (1 or both)</td>
</tr>
<tr>
<td></td>
<td>Occlusion 70–99%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vertebral arteries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No occlusion</td>
<td>75.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Occlusion (1 or both)</td>
<td>21.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not determined</td>
<td>2.6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Stimulation and Recording Parameters for SEP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Stimulus</th>
<th>Site</th>
<th>Electrodes</th>
<th>Rate</th>
<th>Duration</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impedance</td>
<td>rSO2</td>
<td></td>
<td>ECG electrodes (Ag-AgCl)</td>
<td>5.3 Hz</td>
<td>200 ms</td>
<td>20 mA, constant electric current</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 3. Comparison of rSO₂ Before (rSO₂-1) and After Carotid Cross-clamping (rSO₂-2) and the Calculated Decrease of rSO₂ (ΔrSO₂=rSO₂-1−rSO₂-2) in Patients With and Without SEP Loss During Cross-clamping of the ICA

<table>
<thead>
<tr>
<th>SEP Preserved</th>
<th>SEP Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=287)</td>
<td>(n=30)</td>
</tr>
<tr>
<td>rSO₂-1</td>
<td>64.9±8.3 (39–87)</td>
</tr>
<tr>
<td>rSO₂-2</td>
<td>60.9±9.9 (30–87)*</td>
</tr>
<tr>
<td>ΔrSO₂</td>
<td>4.1±4.8 (−9–34)†</td>
</tr>
</tbody>
</table>

Values are median±SD (range), expressed as percentages. Patients with SEP loss had lower rSO₂ values after carotid cross-clamping (*P<0.05, Mann-Whitney U test) and a higher decrease from the preclamp value (†P<0.001, Mann-Whitney U test).

SEP remained neurologically intact after surgery. In 30 patients (9.5%), an SEP loss with unaffected cervical components occurred during the clamping phase. In 27 of these patients shunt placement was performed. Cortical SEP recovered after shunt placement in all patients. Three patients were not shunted despite a loss of SEP. The reasons were hypoplastic vessel (1 case) or SEP loss in the late clamping phase and impairment of arteriotomy closure (2 cases). In 1 of these patients cortical SEP was restored by carotid declamping within 6 minutes; the patient remained neurologically intact. The other 2 patients and 4 patients who received an intraluminal shunt during cross-clamping of the ICA awoke with a new neurological deficit on the side of the endarterectomy. That deficit resolved completely within 12 hours in all patients.

Corresponding preclamp and postclamp rSO₂ values, as well as the calculated change of rSO₂ (ΔrSO₂) for patients with preserved SEP and SEP loss during cross-clamping of the ICA, are summarized in Table 3. On average the initial absolute values of regional cerebral oxygenation in patients with or without later SEP loss were nearly identical; however, considerable variability was noted. In both groups a statistical significant decrease of rSO₂ (P<0.01 by nonparametric Wilcoxon test) after cross-clamping was found. Patients with restricted cerebral collateralization and consecutive loss of cortical SEP after cross-clamping had significantly lower rSO₂ values than patients with unaffected SEP (P<0.05; nonparametric Mann-Whitney U-test). The difference of the calculated change of rSO₂ in both groups of patients was highly significant (P<0.001; nonparametric Mann-Whitney U test). However, the magnitude of change again showed a high variability (Figure 1).

As the accuracy parameters in Table 4 indicate, no critical threshold value of ΔrSO₂ could be defined that could identify patients with SEP loss who would benefit from shunt placement.

Discussion

Reconstructive surgery at the carotid bifurcation is particularly suitable to evaluate NIRS as a new form of neuromonitoring.18 In addition to the fact that cross-clamping of the ICA offers a well-defined period in which cerebral damage due to hypoperfusion is most likely to occur, the results of cerebral oximetry can be compared with other simultaneously employed monitoring methods and the neurological outcome of the patient immediately after surgery. However, previous studies failed to demonstrate the clinical usefulness of the cerebral oximeter INVOS 3100A in carotid surgery. One reason was the use of reference methods, such as jugular-venous oximetry,10 that are well recognized as unreliable for detection of focal ischemia.17 Furthermore, because of the limited number of patients studied, comparison of the NIRS results with individual neurological outcome did not provide conclusive evidence for the usefulness of this device.18,19 Continuous monitoring of the patient under regional anesthesia is accepted as a sensitive monitor of cerebral function and can reveal clinically significant cerebral ischemia.1 Additionally, the effect of an intervention such as shunt placement can be readily assessed. However, in a study by Samra et al,9 none of the 38 patients in their series who underwent carotid surgery under regional anesthesia developed a new neurological deficit during carotid cross-clamping. Thus, no information about rSO₂ values with regard to critical cerebral ischemia could be obtained.

The purpose of our investigation was to determine whether NIRS by means of the cerebral oximeter INVOS 3100A is capable of identifying patients with restricted cerebral collateralization and resulting severe cerebral ischemia, as indicated by a loss of cortical SEP. A similar study was recently published by Duffy and coworkers.20 In contrast to their study, in which they used an arbitrary threshold value of rSO₂ decrease of >10% for comparison with SEP, it was our intention to determine a threshold value for rSO₂ under which SEP loss occurred and neuronal damage was likely to

TABLE 4. Results of Validating Decrease of rSO₂ (ΔrSO₂) Against SEP Loss During Carotid Cross-clamping

<table>
<thead>
<tr>
<th>ΔrSO₂</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5</td>
<td>76</td>
<td>64</td>
<td>18</td>
<td>96</td>
</tr>
<tr>
<td>&gt;10</td>
<td>40</td>
<td>88</td>
<td>27</td>
<td>93</td>
</tr>
<tr>
<td>&gt;15</td>
<td>17</td>
<td>97</td>
<td>36</td>
<td>92</td>
</tr>
<tr>
<td>&gt;20</td>
<td>7</td>
<td>99</td>
<td>50</td>
<td>91</td>
</tr>
</tbody>
</table>

Different thresholds for ΔrSO₂ were used for calculations.
develop. This should answer the question of whether NIRS can replace SEP, which is more technically demanding.4

The results of our study confirmed that SEP monitoring reliably identifies patients with impending cerebral damage, since all patients with preserved cortical SEP remained neurologically intact. In 30 patients (9.5%), a loss of cortical evoked potentials was found after cross-clamping of the ICA. Six patients (1.8%) awoke with a new neurological deficit, which was transient in all cases.

Previous studies had demonstrated that absolute numbers of rSO2 are of little value in interpreting results obtained by means of INVOS 3100A.7,9,10,21–30 That is why the definition of "normal values" for rSO2 is highly questionable.

Misra and colleagues28 recently reported wide scattering of rSO2 values obtained by normal subjects. Using the same kind of cerebral oximeter, Samra et al9 found a similar high variability in awake patients undergoing carotid endarterectomy under regional anesthesia. They noted that a wide range of rSO2 values are obviously unrelated to neurological dysfunction. The results of our study confirmed the variability of this parameter. Accordingly, we focused our interest on the individual change of rSO2. For the calculation we used a stable value just before cross-clamping of the ICA and the lowest stable value after cross-clamping. The use of a stable value after cross-clamping should ensure that autoregulative changes were taken into account, increasing the specificity of the derived threshold value. Two minutes were allowed for stabilization because results by Lam and coworkers31 suggest that autoregulation after cross-clamping usually occurs within 1 minute. Since the blood pressure was kept stable throughout the procedure, the displayed rSO2 values could be expected to reflect the changed oxygen balance of cerebral tissue after application of the cross-clamp.

On average, rSO2 values in patients with SEP loss after carotid cross-clamping were lower than in patients with preserved cortical SEP. In turn, the calculated decrease of rSO2 was significantly higher in patients with SEP loss. However, no calculated value would reliably identify patients with SEP loss who will benefit from shunt placement with high sensitivity and acceptable specificity and predictive power. Given a residual error of the displayed readings of ±10%,28 an arbitrary threshold value of >10% decrease of rSO2, as done by Duffy et al29 is not appropriate. Therefore, selective use of an intraluminal shunt based exclusively on the results of NIRS cannot be recommended.

Whether a reduction of interindividual variability can be achieved is uncertain for various reasons. As suggested by Kurth and Uher,32 this variability originates in the continuous-wave NIRS technology, since there is no way to measure optical path length and absorption. Therefore, the algorithm for calculation of rSO2 is based on several assumptions, which may lead to an oversimplification of that very complex issue.11,20,31 Anatomic variations leading to differences of extracranial layers of scalp, skull, and cerebrospinal fluid need to be considered as well as changes resulting from biological variations in cerebral hemoglobin concentration.27,20,30 The estimated proportions of blood in the venous, arterial, and capillary compartments are assumed to be stable. However, the fulfillment of this condition in a clinical situation is difficult to verify.24,30 A sudden decrease of cerebral blood flow during cross-clamping of the ICA under general anesthesia is possibly the closest approximation.16 If variability of rSO2 values unrelated to neurological function occurs under these circumstances, the usefulness of this device in more complex clinical situations such as intensive care patients or patients undergoing cardiac surgery must be questioned.33

Since early concerns were raised by Harris and Bailey34 in 1993, the issue of extracranial contamination of the derived signal has been a matter of considerable debate. Based on experimental studies on artificial models, there is evidence that changing emitter-detector separation will cause differential spatial resolution.35 The fixed interoptode spacing of 3 and 4 cm in the INVOS 3100A sensor is supposed to ensure that by subtracting the signals from superficial layers, extracranial contamination can be effectively reduced.10 This assumption has been challenged by various authors.27,36 Obviously, the fixed interoptode spacing of the sensors will lead to differences in the effectiveness of reducing extracranial contamination due to differences in the anatomy of the patient’s skull.30,31 In contrast to other applications, carotid surgery provides the unique opportunity of selectively clamping the external carotid artery, thereby greatly reducing the influence of extracranial tissue. Studies in which sequential clamping of the external carotid artery before the ICA was performed provided contradictory results. Duncan and colleagues1 found a nonsignificant fall of the displayed rSO2 after clamping of the ECA. Using a different type of cerebral oximeter (NIRO-500, Hamamatsu), Lam and coworkers31 showed that the contribution of extracranial vascular circulation to the results of NIRS was significant. In contrast to the study by Duncan, parallel monitoring of superficial blood flow by means of laser-Doppler flowmetry was used. This offers the advantage of controlling extracranial contamination, making collateral flow from the contralateral side detectable. Furthermore, this monitor will track blood pressure fluctuations that predominantly influence in a pressure-passive fashion the extracranial vascular territory and are a significant source of artifact. We believe that in future investigations efforts should be made to adopt this proceeding and not to rely on spatial resolution claimed for the Somasensor used in the INVOS 3100A. The importance of extracranial contamination was highlighted in a recently published study by Kirckpatrick et al.37 Using the same device as in the study by Lam, the authors were able to identify all patients with severe cerebral ischemia, as indicated by a fall of MCA velocity >60% or sustained fall in cortical electric activity by means of a derived parameter of NIRS. However, this threshold was only apparent when extracranial contamination was reduced by previous clamping of the ECA. In our study we did not try to resolve the extracranial and intracranial vascular territories by sequential clamping of the carotid arteries. Therefore, it is possible that the displayed rSO2 values are heavily influenced by extracranial contamination. However, the results of our study showed that severe cerebral ischemia, as indicated by cortical SEP loss, occurred in some patients with minimal or even no change of the displayed regional cerebral oxygenation. Removal of extracranial con-
tamination will probably increase specificity of derived threshold values, indicating need for intervention. However, most important for the outcome of the patients and the value of the monitoring device is prompt recognition of all patients with impending cerebral ischemia. The discrepancy between cortical SEP loss and no or minimal change of rSO2 after carotid cross-clamping might be attributed to the different monitoring areas. Given the low spatial resolution of the measurement system, 23,26 placement over the parietal middle cerebral artery territory, as advocated by Williams and coworkers, 10,22 might lead to a better agreement between SEP monitoring and NIRS. 19 However, this approach is hampered by the necessity of shaving an area of the patient’s head the size of the sensor pad (3.5 x 1.75 inches), which will probably not be acceptable to many of the patients undergoing the procedure for investigational purposes. The possibility of placing the sensor over other parts of the skull without having to shave them first needs to be addressed by the manufacturers. Interestingly, the threshold values indicating severe cerebral ischemia in the study by Kirczpatrick et al 27 could be defined with sensors placed over the patient’s forehead, the same area as recommended for the Soma-Sensor INVOS system. 38

Further studies are needed to evaluate the importance of probe positioning for the sensitivity and specificity of NIRS. As suggested by previous studies and our own clinical experience, NIRS appears to work extremely well in some cases. 7,8,19 As shown in Figure 2, a dramatic fall of rSO2 occurred immediately after cross-clamping of the ICA in a patient in whom an SEP loss was documented. In addition, rSO2 showed a prompt recovery after shunt insertion and a hyperperfusion phenomenon after definite declamping. The fall of rSO2 occurred much earlier than the loss of the cortical SEP because reduction of cerebral perfusion leads to predominantly venous desaturation, and concomitant fall of rSO2 before cerebral dysfunction occurs. However, the clinical relevance of an early detection of impending cerebral ischemia before cerebral dysfunction remains unclear, since no patient in our series developed sustained neurological deficits when shunt placement was performed after the complete loss of cortical SEP. A possible relationship between changes in cerebral oxygenation and more subtle adverse neurological outcome, such as cognitive deterioration, needs to be addressed in further studies. 39

The advantage of NIRS is that it is easy to use and that it offers a real-time and noninvasive means for the assessment of cerebral oxygenation. Unfortunately, these advantages cannot outweigh the represented methodological problems in the cerebral oximeter INVOS 3100A. Since our study and previous investigations 7 were unable to define a threshold value indicating severe cerebral ischemia in individual patients, we would not advise therapeutic interventions based on obtained rSO2 7,25–27,30 and would suggest not using this instrument for detection of cerebral ischemia in patients undergoing carotid endarterectomy under general anesthesia.

References


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