The Clinical Utility of Cerebral Oximetry Monitoring

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Overview

- General concepts: Near-Infrared Spectroscopy (NIRS) and regional cerebral oxygenation (rSO$_2$)
- Validation work
- Clinical studies
- NIRS and the STS Database
- Expanded clinical use of rSO$_2$
General Concepts
Cerebral oximetry involves the use near infra-red light to assess regional cerebral oxygenation (rSO$_2$) in exchange vessels (i.e. < 100 microns). In practice it assesses only a thimble sized volume of frontal lobe brain tissue but may serve as an index organ reflecting adequacy of tissue oxygenation throughout the body.
Of special note, rSO₂ represents a venous weighted measurement of blood oxygen saturation circulating through both venous and arterial exchange vessels (i.e. vessels < 100 microns in diameter). The sample is venous weighted because there is more venous blood in the measured tissue. Although it is manufacturer dependent, one device’s processing algorithm (Somanetics – INVOS) assumes a ratio of 75:25 of venous to arterial blood ratio in the measured sample, while others use 70:30 (Nonin – Equanox & CASMED – ForeSight).
Thus, rSO$_2$ values represent the regional oxygen balance in the frontal lobes, or stated differently, rSO$_2$ primarily represents the cerebral venous reserve capacity following tissue oxygen extraction.

70-75% venous blood

2010 Avery EG, White paper
General Concepts – \( rSO_2 \) vs \( SaO_2 \)

\( rSO_2 \)  \arrow{Regional oxygen balance, or the venous reserve capacity following tissue oxygen extraction}

\( SaO_2 \)  \arrow{Systemic arterial oxygen availability}

70-75\% venous blood

2010 Avery EG, White paper

(Courtesy of Covidien)
General Concepts — Available devices

There are currently four FDA cleared devices‡ that are marketed to assess cerebral oxygenation which include:

- Somanetics – INVOS
- CASMED – Fore-sight
- Ornim – Cerox
- Nonin - Equanox

‡Devices listed in order of FDA clearance
2010 Avery EG, White paper
Because each device uses a unique processing algorithm one cannot necessarily assume that the outcomes associated with clinical studies of one device are directly transferrable to the others. Indeed, the preponderance of peer reviewed literature (> 600 publications) relate only to the INVOS device.
Near-infrared spectroscopy (NIRS) is used to assess cerebral tissues and involves the use of light ($\lambda = 690-880$ nm)† to detect chromophores (specifically, quantities of both oxygenated and deoxygenated hemoglobin).

†Appl Optics 1989; 28:2245
Of interest regarding NIRS is the fact that other chromophores are known to reflect near infra-red light, notably the orange chromophore found in *Cucurbita styrian*, more commonly known as the pumpkin.
Near infra-red light between these wavelengths ($\lambda = 690-880$ nm) has the ability to pass through the cranial bone and penetrate several centimeters† into the deeper tissues - two wavelengths in this range correspond to oxy- and deoxy-Hb.
Near infra-red light penetrates the scalp, cranium, dura, and subarachnoid space to ultimately reach the cerebral tissues. The reflected signal then returns to one of two photoreceptors.
Emitted light follows a predictable path that resembles a "banana like" arc. Placing a second, more distal sensor allows for a deeper signal penetration.
The devices rapidly alternate activation of the proximal and distal sensors. The more superficial pathway’s signal (proximal detector) represents potential signal contaminants and are thus subtracted from the final signal. Finally, any portion of the deep signal that resembles data from the superficial signal is also subtracted from the final signal using a proprietary algorithm that is manufacturer dependent.
One device (Nonin – Equanox) uses dual photoreceptors and dual light sources (3 or 4 λs) in order to more accurately determine the cerebral saturation. The manufacturer claims that doubling of the LED light sources allows the device to compare rSO₂ measurements in adjacent tissues to confirm accuracy of a measurement.
**General Concepts — Clinical Use**

- Bi-frontal adhesive pads applied to hairless skin
- Room air baseline established (recommended)

**2 Strategies:**

- Maintain bilateral rSO₂ values **within 75% of established room air baseline**
- Maintain bilateral rSO₂ values **above 50% for patients with a baseline value of ≤ 50%**
Validation

Courtesy of Covidien
Laboratory and clinical validation studies are required to demonstrate the utility of any monitoring modality. Cerebral oximetry is not exempt to this form of validation testing. Despite what may be an obvious advantage to either a non-invasive or invasive monitor previous attempts to validate the utility of monitors in widespread clinical use have not reproducibly produced supportive results.

JAMA 1996; 276: 889

Anes 1993; 78: 445
The validation of rSO$_2$ monitoring is challenged by the fact that there is no gold standard, or index test, invasive or non-invasive of cerebral oxygenation.
Initial validation work established that the rSO$_2$ value reflected blood oxygenation in cerebral tissue by a series of experiments involving indocyanine green dye injection.†

Indocyanine green dye injected into the *external carotid artery* revealed that the arterial blood supply to the scalp is indeed distinct from the cerebral tissue’s blood supply. The green dye has similar absorbance characteristics to hemoglobin allowing its measurement with NIRS.

†Neurol Res 1995; 17: 89
Validation — brain vs scalp blood supply

- Signal processing algorithms in the cerebral oximeter minimize interference from the scalp and cranium but it is not clear that they completely eliminate the potential noise from this tissue.

- Indocyanine green dye injected into the internal carotid artery confirmed that the arterial blood supply to the brain is indeed distinct from the scalp’s blood supply\(^\dagger\).

- Venous congestion in the scalp appears to have a measurable effect on rSO\(_2\) values as evidenced by a tourniquet experiment\(^\ddagger\).

- Selective interruption of external arterial flow does not appear to greatly affect rSO\(_2\) values\(^\‡\).

\(^\dagger\)Neurol Res 1995; 17: 89
\(^\ddagger\)J Neurol Neurosurg 1995; 58: 477
\(^\‡\)Anaesthesia 1997; 52: 116
Validation — interrupting brain blood supply

One experiment employing balloon occlusion of a single internal carotid artery demonstrated that rSO$_2$ values are acutely sensitive to blood flow interruption$^\dagger$.

In the same experiment, single photon emission computed tomographic (SPECT) blood flow imaging demonstrated ipsilateral signal loss (absence of yellow/red color) which accompanied rSO$_2$ decrease during balloon occlusion.

Validation — relevant comparators

Relevant monitoring modalities to validate the rSO₂ parameter:
- \( S_{\text{jvO}_2} \) — jugular venous oxygen saturation
- \( t\text{iPO}_2 \) — regional tissue oxygen pressure (17 mm³)
- \( S_{\text{aO}_2} \) — systemic arterial oxygen saturation
- \( S_{\text{pO}_2} \) — systemic arterial oxygen saturation of pulsatile blood flow
Among the most widely quoted validation studies on rSO₂ is the well conducted study by Kim et al from Univ. of Rochester. They looked at unilateral rSO₂ values obtained with the INVOS while simultaneously collecting data from an ipsilateral jugular venous bulb catheter (SjvO₂) and a radial A-line (SaO₂) while their healthy subjects breathed from a high flow gas mixing chamber that permitted controlled hypoxia as well as controlled normocapnia and hypercapnia.

N = 42 subjects (healthy volunteers)
The study revealed that SjvO$_2$ and rSO$_2$ both increased with hypercapnia in the setting of 5 different levels of systemic oxygenation that included hypoxia, indicating that increased CO$_2$ resulted in higher cerebral blood flow. The SjvO2 increased to a greater extent than the measured rSO$_2$ values. Cerebral metabolic rate was presumably constant throughout the experiment.
Note that $S_jvO_2$ increased slightly more (3-8%) than $rSO_2$ (2-6%) with hypercapnia. Hypercapnia is expected to increase CBF.

### Experiment 1 (normocapnia) +2 mmHg above resting ETCO$_2$

<table>
<thead>
<tr>
<th>Test stage</th>
<th>$P_{ET}CO_2$ (mmHg)</th>
<th>Sa$_O_2$ (%)</th>
<th>Sj$_vO_2$ (%)</th>
<th>rSO$_2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$39.1 \pm 3.4$</td>
<td>$97.5 \pm 1.3$</td>
<td>$64.3 \pm 6.2$</td>
<td>$70.7 \pm 6.1$</td>
</tr>
<tr>
<td>2</td>
<td>$39.1 \pm 3.1$</td>
<td>$81.3 \pm 3.0$</td>
<td>$53.9 \pm 6.0$</td>
<td>$58.5 \pm 6.1$</td>
</tr>
<tr>
<td>3</td>
<td>$39.4 \pm 3.2$</td>
<td>$91.5 \pm 1.9$</td>
<td>$60.7 \pm 6.0$</td>
<td>$65.7 \pm 6.5$</td>
</tr>
<tr>
<td>4</td>
<td>$39.0 \pm 3.1$</td>
<td>$74.5 \pm 3.8$</td>
<td>$50.4 \pm 5.6$</td>
<td>$53.1 \pm 6.2$</td>
</tr>
<tr>
<td>5</td>
<td>$39.3 \pm 3.2$</td>
<td>$99.7 \pm 2.5$</td>
<td>$69.0 \pm 6.3$</td>
<td>$74.6 \pm 6.7$</td>
</tr>
</tbody>
</table>

### Experiment 2 (hypercapnia) +7 mmHg above resting ETCO$_2$

<table>
<thead>
<tr>
<th>Test stage</th>
<th>$P_{ET}CO_2$ (mmHg)</th>
<th>Sa$_O_2$ (%)</th>
<th>Sj$_vO_2$ (%)</th>
<th>rSO$_2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$44.3 \pm 3.0$</td>
<td>$97.3 \pm 0.6$</td>
<td>$70.3 \pm 5.2$</td>
<td>$73.9 \pm 5.5$</td>
</tr>
<tr>
<td>2</td>
<td>$44.2 \pm 3.0$</td>
<td>$79.8 \pm 4.0$</td>
<td>$58.4 \pm 5.2$</td>
<td>$60.7 \pm 6.1$</td>
</tr>
<tr>
<td>3</td>
<td>$44.2 \pm 3.1$</td>
<td>$91.8 \pm 1.5$</td>
<td>$67.0 \pm 5.3$</td>
<td>$70.8 \pm 6.0$</td>
</tr>
<tr>
<td>4</td>
<td>$44.1 \pm 3.0$</td>
<td>$73.3 \pm 3.5$</td>
<td>$54.2 \pm 5.4$</td>
<td>$55.4 \pm 5.9$</td>
</tr>
<tr>
<td>5</td>
<td>$44.2 \pm 3.1$</td>
<td>$100 \pm 0.4$</td>
<td>$77.1 \pm 5.6$</td>
<td>$81.0 \pm 7.3$</td>
</tr>
</tbody>
</table>

$P_{ET}O_2 = 80 \text{ mmHg}$

$P_{ET}O_2 = 45 \text{ mmHg}$

$P_{ET}O_2 = 60 \text{ mmHg}$

$P_{ET}O_2 = 41 \text{ mmHg}$

$F_iO_2 = 50\%$
Validation — Kim et al, rSO$_2$ & SjvO$_2$

Under these testing conditions rSO$_2$ correlated well with SjvO$_2$ during changes in inspired oxygen concentration. In fact rSO$_2$ tracked SjvO$_2$ better than SaO$_2$ (esp weak at higher saturations) did as evidenced by the scatter plots and correlations coefficients (r).

![Scatter plots showing correlation between measured SjvO$_2$ and SaO$_2$, r = 0.77, and measured SjvO$_2$ and rSO$_2$, r = 0.90.](image-url)
The Bland-Altman plots also demonstrated less bias, or error, between the rSO₂ value and the SjvO₂ values compared to the bias observed between the SaO₂ and the SjvO₂.

**J Clin Monit 2000; 16; 191**
tiPO₂, or regional tissue oxygen pressure, is used to assess the partial pressure of oxygen in cerebral tissue. It is clear that tiPO₂ is not the same parameter as rSO₂ and thus no direct correlations may be expected to exist between these two parameters. Three clinical studies assessed the relationship between rSO₂ and tiPO₂; good correlations were noted across these studies.
In an early analysis involving the study of significant desaturation events 10 neurosurgical ICU subjects were monitored with both a tiPO\textsubscript{2}, or regional tissue oxygen pressure system and INVOS rSO\textsubscript{2}; a range of correlations from poor to very good were observed; the mean correlation observed was fair.

\[( r ) = 1.0 \text{ is a perfect correlation} \]

Correlation range \(( r )\) range\(\dagger\): 0.15 to 0.86

Mean Correlation \(( r ) = 0.73\)

\(\dagger\)The authors hypothesized that the poor correlations may have been related to poor rSO\textsubscript{2} signal quality, perhaps related to the low signal to noise ratio in this earlier version of the INVOS monitor.
In a later analysis involving the study of 12 neurosurgical ICU subjects, coherence of tiPO$_2$ and rSO$_2$‡ monitoring was assessed. Highly complex mathematics were used to find the higher frequency signals between the data collected between the devices to assess coherency. Ultimately the authors concluded that both monitoring modalities contain similar information.

\[ S(f) = \sum_{k=0}^{4} \omega_k (f) S_k (f) \]

\[ S_k(f) = \left| \sum_{m=0}^{n-1} x(t) \frac{v_{t,k} (n, W)}{a_k} e^{-i2\pi f \left( t - \frac{n-1}{2} \right)} \right|^2 \]

\[ F(f) = \frac{4 |\mu (f)|^2 \sum_{k=0}^{4} U_k (n,W;0)^2}{\sum_{k=0}^{4} \left| y_k (f) - \mu (f) U_k (n, W;0) \right|^2} \]

\[ C(f) = \frac{\sum_{k=0}^{4} \hat{A}_k (f) B_k (f)}{\left( \sum_{k=0}^{4} \hat{A}_k \left( f \right) B_k \left( f \right) \sum_{j=0}^{4} \hat{A}_j \left( f \right) B_j \left( f \right) \right)^{1/2}} \]

‡Performed with INVOS 3100

In a later analysis involving the study of 12 neurosurgical ICU subjects, both tiPO\textsubscript{2} and rSO\textsubscript{2} monitoring was assessed. Highly complex mathematics were used to find the higher frequency signals between the data collected between the devices to assess coherency. Ultimately, the authors concluded that both monitoring modalities contain similar information.

Validation — #2: tiPO\textsubscript{2} & rSO\textsubscript{2}

Frequency domain Fourier analysis

In this more straightforward study, rSO₂ (termed Tissue Oxygen Index (or TOI)), SjvO₂ and tiPO₂ were all compared among severely head injured patients (n=8). See mean raw data below. rSO₂ values were obtained with the NIRO 300 monitor, not presently approved for clinical use. The tabular form of the data demonstrates that all 3 modalities were generally tracking similar changes. Note that rSO₂ monitoring appeared to be the most sensitive to changes among the 3 modalities.

**Table 2. Values for Each Measure of Cerebral Oxygenation at Four Different Fraction of Inspired Concentration (FIO₂) Values**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>1.0</th>
<th>0.6</th>
<th>2%–5% less than baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOI (%)</td>
<td>77.6 ± 3.4</td>
<td>83.2 ± 4.8*</td>
<td>80.4 ± 3.9*</td>
<td>76.2 ± 3.0*†</td>
</tr>
<tr>
<td>rSO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PbrO₂ (mm Hg)</td>
<td>29.9 ± 4.9</td>
<td>147.4 ± 36.2*</td>
<td>62.8 ± 6.2*</td>
<td>29.3 ± 4.0</td>
</tr>
<tr>
<td>SjO₂ (%)</td>
<td>79.1 ± 6.9</td>
<td>89.4 ± 5.6*</td>
<td>83.6 ± 8.5</td>
<td>78.5 ± 7.3</td>
</tr>
</tbody>
</table>

TOI = tissue oxygenation index. Values = mean ± standard deviation. †* Significant difference from baseline (P < 0.05).
The three parameters can be seen to grossly track the same changes under these experimental conditions that notably included stepwise changes in FiO₂.

Anesth & Analg 2003; 97: 851
Several published laboratory and clinical validation studies of NIRS rSO₂ have been conducted and all ultimately conclude that although there is no index test to compare rSO₂ values to the data appears to reflect dynamics of regional cerebral oxygen balance.

Of note is the fact that the FDA did not require the same degree of validation testing for the predicate devices that followed FDA clearance of the first monitor. Caution should be taken in comparing the results of validation studies performed with one monitor to the others because their internal processing algorithms are all unique and key to the clinical data that they generate.
Clinical Studies — Cardiac Surgery #1

- Cardiac surgical patients provided many of the early clinical outcome data related to the use of rSO₂ monitoring (INVOS).
- Goldman et al conducted a large retrospective analysis of cardiac surgical patients to determine the impact of rSO₂ monitoring coupled with a standardized interventional protocol† on stroke incidence for patients demonstrating cerebral desaturation events. A well matched historical control was compared to an active treatment cohort.

\[ n = 2,279 = \text{Historical control (1,245)} + \text{study group (1,034)} \]

† Sequence of Interventions Used to Maintain Cerebral Oxygen Saturation at or near Preoperative Baseline*

<table>
<thead>
<tr>
<th>Interventions</th>
<th>On-Pump</th>
<th>Off-Pump</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increase FiO₂ to 100%</td>
<td>Increase FiO₂ to 100%</td>
</tr>
<tr>
<td>2</td>
<td>Adjust head or cannula position</td>
<td>Adjust head or heart position</td>
</tr>
<tr>
<td>3</td>
<td>Increase PaCO₂ by reducing fresh gas flow rate</td>
<td>Increase PaCO₂ by reducing respiration rate</td>
</tr>
<tr>
<td>4</td>
<td>Increase mean arterial pressure</td>
<td>Increase mean arterial pressure</td>
</tr>
<tr>
<td>5</td>
<td>Increase pump flow</td>
<td>Increase cardiac output</td>
</tr>
<tr>
<td>6</td>
<td>Increase anesthetic depth</td>
<td>Increase anesthetic depth</td>
</tr>
<tr>
<td>7</td>
<td>Administer nitroglycerin to dilate cerebral vessels</td>
<td>Administer nitroglycerin to dilate cerebral vessels</td>
</tr>
<tr>
<td>8</td>
<td>Administer packed red cells if hematocrit is &lt;23%</td>
<td></td>
</tr>
</tbody>
</table>

*FiO₂ indicates fraction of inspired oxygen.
Clinical Studies — Cardiac Surgery #1

The study group had fewer permanent strokes, shorter hospital length of stay and lower incidence of prolonged ventilation.

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Historical Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Strokes (0.97%)‡</td>
<td>25 Strokes (2.5%)</td>
</tr>
<tr>
<td><strong>p &lt; .044</strong></td>
<td></td>
</tr>
<tr>
<td>Median Ventilation Time (4 hrs)†</td>
<td>Median Ventilation Time (5 hrs)</td>
</tr>
<tr>
<td><strong>p &lt; .0016</strong></td>
<td></td>
</tr>
<tr>
<td>Prolonged Ventilation (6.8%)§</td>
<td>Prolonged Ventilation (10.6%)</td>
</tr>
<tr>
<td><strong>p &lt; .0014</strong></td>
<td></td>
</tr>
</tbody>
</table>

2004 Heart Surg Forum 7(5); E376
The study group also had fewer permanent strokes when assessed by NYHAC I-III (p < .023).
The study group had a lower incidence of requiring prolonged ventilation ($p < .0014$) when corrected for NYHAC. (Definition of prolonged ventilation not specifically defined)
The study group had a significantly shorter hospital length of stay when assessed by NYHAC, no numerical data was provided.
Clinical Studies — Cardiac Surgery #1

Summary-

A large retrospective study with some methodological problems demonstrated that rSO₂ monitoring can reduce the risk of permanent stroke in cardiac surgical patients that are managed with a standardized interventional protocol for cerebral desaturations. The greatest benefit was noted in the least sick patients studied (NYHAC I).

2004 Heart Surg Forum 7(5); E376
Murkin et al prospectively randomized CABG patients to blinded rSO₂ monitoring (control) vs open rSO₂ monitoring with a standardized interventional protocol for observed desaturation. The authors hypothesized that by using the brain as an index organ, rSO₂ interventions would have measurable and systemic benefits in this patient population.

```
<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100</td>
</tr>
<tr>
<td>Treatment</td>
<td>100</td>
</tr>
</tbody>
</table>
```
The standardized intervention data and observed efficacy is presented below.

**40/56 (71%) required > 3 interventions**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>No. of patients</th>
<th>% Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raise pump flow</td>
<td>39</td>
<td>67</td>
</tr>
<tr>
<td>Raise MAP</td>
<td>42</td>
<td>62</td>
</tr>
<tr>
<td>Normalize Paco₂</td>
<td>34</td>
<td>50</td>
</tr>
<tr>
<td>Deepen anesthesia</td>
<td>27</td>
<td>48</td>
</tr>
<tr>
<td>Increase Fio₂</td>
<td>28</td>
<td>43</td>
</tr>
<tr>
<td>Pulsatile perfusion</td>
<td>6</td>
<td>17</td>
</tr>
</tbody>
</table>

Overall % Efficacy of Interventions 80.4% (45/56)

---

Table 5. Type of Cerebral Regional Oxygen Saturation (rSO₂) Interventions in the Intervention Group

No. of patients indicates those patients in whom a specific intervention was undertaken; % Efficacy indicates those instances in whom the intervention was successful in restoring rSO₂. For some patients multiple interventions were used at various intervals such that No. of patients is larger than the Intervention group total. MAP is mean arterial blood pressure.

2007 Anesth & Analg 104; 51
The percentage of serious desaturations was significantly greater in the control group.

**Control Group**
- rSO$_2$ AUC $< 70\%$ Baseline
- $> 150 \text{ min} \cdot \%$
- 6 patients

**Study Group**
- rSO$_2$ AUC $< 70\%$ Baseline
- $> 150 \text{ min} \cdot \%$
- none$^\dagger$

$^\dagger$p $< 0.014$
The ICU length of stay (LOS) was significantly longer in the control group.

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU LOS (days)</td>
<td>ICU LOS (days)</td>
</tr>
<tr>
<td>1.87 ± 2.67</td>
<td>1.25 ± 0.84†</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td>(mean ± SD)</td>
</tr>
</tbody>
</table>

Note: CVA x 4

Note: CVA x 1

†p < 0.029

2007 Anesth & Analg 104; 51
The 30-day major organ morbidity and mortality (MOMM)† was significantly lower in the study group ($p < 0.048$)

†MOMM as defined by the STS

2007 Anesth & Analg 104; 51
Summary-
The Murkin study employed solid methodological techniques and produced tangible outcome benefits demonstrating the potential clinical and cost benefits of intraoperative rSO₂ monitoring in cardiac surgical patients when the brain is used as an index organ.

2007 Anesth & Analg 104; 51
Casati et al prospectively studied elderly abdominal surgery patients randomized to either an intervention group (open rSO₂ data + standardized intervention protocol) vs. a control group (blinded rSO₂ + standard anesthetic management). The goal was to determine if rSO₂ monitoring and intervention would mitigate cerebral desaturation and/or effect clinical outcomes.

n = 122

Control
n = 66

Treatment
n = 56
The standardized intervention protocol for ↓rSO₂ is presented below

**Step 1**
- Check ventilator
- Check head position
- Check tubing position
- ↑ FiO₂
- ↑ ETCO₂ if < 35 mmHg
- ↑ BP via IV fluid (250 mL colloid) if SBP ≤ 90 mmHg
- ↑ BP via vasoconstrictors (ethylephrine 2-5 mg) if SBP ≤ 90 mmHg

**Step 2**
- Deepen anesthetic with propofol (0.5 mg/kg)
For the intervention group the goal was to maintain INVOS rSO₂ values above 75% of subject’s established room air baseline. The number of subjects experiencing cerebral desaturation was similar between the control and intervention groups.

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 15 (23%) subjects</td>
<td>n = 11 (20%) subjects</td>
</tr>
<tr>
<td>With rSO₂ Desaturation</td>
<td>With rSO₂ Desaturation</td>
</tr>
</tbody>
</table>

p = 0.82
The magnitude of the rSO\textsubscript{2} desaturations were significantly smaller in the intervention group suggesting efficacy resulted from their 2 step intervention schema.

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean rSO\textsubscript{2} AUC &lt; 75% Baseline</td>
<td>Mean rSO\textsubscript{2} AUC &lt; 75% Baseline</td>
</tr>
<tr>
<td>80 min% [2-144 min%]†</td>
<td>0.4 min% [0.1-0.8 min%]</td>
</tr>
</tbody>
</table>

†p = 0.017
Among the subjects experiencing a $r\text{SO}_2$ desaturation the Mini Mental Status Examination (MMSE) score on POD# 7 was lower in the control group (baseline MMSE scores were similar between these groups).

**Control Group**
Median MMSE Score 26
Subjects with any $r\text{SO}_2 < 75\%$ Baseline

**Study Group**
Median MMSE Score 28
Subjects with any $r\text{SO}_2 < 75\%$ Baseline

†$p = 0.02$

$y = -0.7 - 0.012 \text{AUC}_{r\text{SO}_2<75\%}$ of Baseline 
($r^2 = 0.26; \ P = 0.01$)
Among the subjects experiencing a rSO₂ desaturation, the PACU discharge time and hospital length of stay (LOS) were both significantly longer in the control group.

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PACU Discharge time 47 min [13-56]</td>
<td>PACU Discharge time 25 min [15-35]</td>
</tr>
<tr>
<td>Subjects with any ↓rSO2 &lt; 75% Baseline</td>
<td>Subjects with any ↓rSO2 &lt; 75% Baseline</td>
</tr>
</tbody>
</table>

†p = 0.01

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Hospital LOS 24 d [7-53]</td>
<td>Median Hospital LOS 10 d [7-23]</td>
</tr>
<tr>
<td>Subjects with any ↓rSO2 &lt; 75% Baseline</td>
<td>Subjects with any ↓rSO2 &lt; 75% Baseline</td>
</tr>
</tbody>
</table>

‡p = 0.007

2005 Anesth & Analg 101; 740
Among the subjects experiencing a rSO$_2$ desaturation, the hospital length of stay (LOS) correlated with the magnitude of the cerebral desaturations.
Summary-

This early study of elderly general surgery patients established that significant cerebral desaturations are common in this patient population (≥ 20%)

Further, it established that the magnitude of the desaturations can be mitigated by a standardized intervention protocol

Finally, this analysis demonstrated that among these types of patients who experience a desaturation that they are more likely to have a significantly longer PACU and hospital LOS
Clinical Studies — Carotid endarterectomy surgery

The utility of rSO₂ monitoring in carotid endarterectomy surgery (CEA) has been investigated in multiple clinical studies by comparison to the index of EEG monitoring. A review of three studies with this general design demonstrated a similar and somewhat limited utility of rSO₂ monitoring for CEA procedures.
Rigamonti et al investigated the relationship between rSO2 values and EEG (index) proven episodes of cerebral ischemia during carotid cross clamping.

- n = 50
- EEG proven ischemia requiring shunt
  - Mean ↓rSO2 = 17% (± 4)†
  - p = 0.01

- No EEG evidence of ischemia
  - Mean ↓rSO2 = 8% (± 6)

Sensitivity of rSO2 for ischemia 44%
Specificity of rSO2 for ischemia 82%

Negative predictive value = 94%
Botes et al investigated the relationship between rSO$_2$ values and carotid stump pressure to EEG (index) proven episodes of cerebral ischemia during carotid cross clamping.

- EEG proven ischemia requiring shunt (n=6)
  - $\downarrow$rSO$_2$ > 20%

- No EEG evidence of ischemia in n=12 (12%)

Positive predictive value = 33%
Negative predictive value = 100%
Friedel et al examined the accuracy of rSO\textsubscript{2} monitoring’s ability to accurately determine the need for shunting during CEA surgery when EEG and median nerve somatosensory evoked potentials (SSEP) serve as the index.

- **n** = 323
- **n** = 24 (7.4%)
  - rSO\textsubscript{2} discrepancies compared to EEG + SSEP
  - n = 16 with significant ↓rSO\textsubscript{2}
    - With no EEG + SSEP
  - n = 7 with no Δ in rSO\textsubscript{2}
    - With EEG + SSEP ischemia

Sensitivity of rSO\textsubscript{2} for ischemia 68%
Specificity of rSO\textsubscript{2} for ischemia 94%

Positive predictive value = 47%
Negative predictive value = 98%
Clinical Studies — Carotid endarterectomy surgery

Summary-

- In three separate studies with various sample sizes similar conclusions were drawn with relation to the utility of rSO₂ use in CEA when EEG is the index test.

- rSO₂ has a powerful negative predictive value (NPV) for cerebral ischemic events in CEA but its low sensitivity and specificity obviate the option for it to be used as the sole monitor for these procedures.

2005 J Clin Anes 17;426
2008 J Vasc Surg 48; 601
2005 Anesth & Analg 101; 740
Recently published data suggests that the room air baseline and oxygen supplemented rSO₂ values may serve as a simple, noninvasive risk stratification tool for cardiac surgical patients.
Heringlake et al. recently published results of an observational analysis of 1,178 cardiac surgical patients which examined the relationship between preoperative rSO$_2$ values and 30 day/1-yr mortality.

Key findings centered around the relatively high correlation of low preoperative O$_2$ supplemented rSO$_2$ values with 30-d mortality and that rSO$_2$ < 50% are an independent risk factor for 30-d and 1 yr mortality.

Of great interest was the observation that in high risk patients the O$_2$ supplemented rSO$_2$ value better predicted 30-d mortality than EuroSCORE.
Clinical Studies — Baseline rSO₂ & Risk Stratification

The authors collected a wide range of peri-procedural variables that included two related to rSO₂ monitoring to examine the relationship between these variables.

Preoperative Bilateral room air rSO₂ values

Preoperative Bilateral oxygen supplemented rSO₂ values

\[ \text{ScO}_2\text{min-ox} \]
Clinical Studies — Baseline rSO$_2$ & Risk Stratification

ScO$_{2\text{min-ox}}$ had significant correlations with several collected peri-procedural variables are presented:

- N-terminal pro-B-type natriuretic peptide ($\rho; -0.35$)
- Troponin T: ($\rho; -0.28$)
- Hematocrit: ($\rho; 0.34$)
- Glomerular Filtration Rate: ($\rho; 0.19$)
- EuroSCORE: ($\tau; 0.20$)
- LV ejection fraction class: ($\tau; 0.12$)

All: ($P < 0.0001$)

†$\rho$ (rho) is the Spearman’s Rank Correlation Coefficient and is a non-parametric measure of the statistical dependence between two variables. A value of +/- 1 describes two variables that are perfect monotones of each other.

†$\tau$ (tau) is the Kendall’s Rank Correlation Coefficient and it represents the similarity of the orderings of the data when ranked by each of its quantities. If the there is perfect agreement between the 2 variables then tau = 1, -1 if they are opposite and 0 if no relation.
### Clinical Studies — Baseline rSO₂ & Risk Stratification

ScO$_{2\text{min-ox}}$ 30-d mortality data is also interesting in that the non-survivors had a highly significant difference in their ScO$_{2\text{min-ox}}$ values:

<table>
<thead>
<tr>
<th>ScO$_{2\text{min-ox}}$ 30-d non-survivors</th>
<th>ScO$_{2\text{min-ox}}$ 30-d survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>58% (95% CI, 50.7-62%)</td>
<td>64% (95% CI, 64-65%)†</td>
</tr>
</tbody>
</table>

†p < 0.0001
Clinical Studies — Baseline rSO$_2$ & Risk Stratification

The 30-d mortality ROC curves comparing ScO$_2$min-ox and EuroSCORE are presented below:

- AUC ScO$_2$min-ox 0.71
- AUC ScO$_2$min-ox 0.77

p=0.015

p=0.0044

Total Cohort

EuroSCORE > 10 Cohort
Clinical Studies – Baseline rSO₂ & Risk Stratification

The Kaplan-Meier 1 yr survival curves comparing subjects with ScO₂min-ox > 50% vs. ≤ 50% are presented below:

- **Total Cohort**
- **EuroSCORE > 10 Cohort**
Clinical Studies — Baseline rSO₂ & Risk Stratification

Summary:
- This study demonstrated remarkably strong correlations between baseline O₂ supplemented rSO₂ values and 30-d mortality.
- Further, it established significant relationships between known objective measures of cardiopulmonary function and rSO₂ values.
- Finally, it established the ScO₂_{min-ox} value as nearly as strong a predictor of 30-d mortality as the EuroSCORE in the studied population and even stronger in a sicker, select sub-group analysis.

2011 Anesthesiology 114:58
STS Database was queried for the subjective, dichotomous variable (Y/N?) did rSO\textsubscript{2} monitoring serve as a first indicator of an intraoperative event (i.e. technical problem or physiologic change) lead that could lead to an adverse outcome. DCRI conducted the query that included rSO\textsubscript{2} data from Jan 2008 – Dec 2009. 

n = 36, 548 out of which \textbf{8,406 (23\%)} entries indicated that rSO\textsubscript{2} monitoring served as a “First Alert” indicator of a potential adverse outcome.
The preponderance of supportive literature related to the clinical use of rSO$_2$ monitoring begs the question of whether it is not appropriate to be using this non-invasive, safe, modestly expensive monitoring modality more broadly?

- Thoracic surgery (especially single lung ventilation)
- Vascular surgery procedures
- Surgical procedures involving controlled hypotension
- ICU patients with severe pulmonary infections, septic shock or cardiogenic shock
- Elderly general surgery patients
- Elderly orthopedic surgical patients


The End – Thank You

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