Near Infrared Spectroscopy in Medical Diagnostics

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The following relationships with commercial interest related to this presentation existed during the past 12 months:

- Full time employee of Somanetics Corporation.
- Shareholder of stock and options Somanetics Corporation.
- NIRS patent pending.

The following FDA disclosures related to this presentation exist:

- All NIRS equipment referenced is FDA approved for use on all patients including neonates.
- Animal studies presented are investigational.
Near Infrared Spectroscopy

NIR Spectroscopy
- What is it?
- What does it measure?
- How accurate is it?
- What are the limitations?

Tissue Monitoring - Animal studies

Clinical Evidence
Beer’s Law

Spectrophotometric Analysis

\[
\log \frac{I_0}{I} = \text{Absorbance}
\]

Beer’s Law
Absorbance = \( \varepsilon \times \text{conc} \times l \)
Near Infrared Spectroscopy - NIRS

- 700 to 1000 nm wavelength light
- Bond specific
- Few molecules absorb at this wavelength
- Iron containing heme ring
- H2O at >900 nm
Near Infrared

Diagram showing the wavelength spectrum from visible light to infrared, highlighting the near infrared range between 400 to 700 nm.
Specific – Hb/HbO2

Accurate – validation data in human subjects

Sensitive – extreme sensitivity to change in human subjects and animal model - $R^2 0.96$
What does it measure?

- rSO$_2$ - regional hemoglobin oxygen saturation in tissue under the sensor -
- % saturation - Does NOT measure Hb concentration
- 25% arterial / 75% venous
- rSO$_2$ – venous weighted, no standard value
- SvO2 – no standard value – flow / metabolism coupled
- Tissue Hb saturation– delivery / consumption
- Reflects perfusion distribution
Specific

Overtone bands with extremely low molar absorptivity
Hemoglobin Molar Absorptivity
Analyte Specificity

Lipids show minimal absorption by hydrocarbons at 700-880 nm.
Light Emitting Diode

Inside a Light Emitting Diode

- Emitted Light Beams
- Diode
- Transparent Plastic Case
- Terminal Pins
Laser Diodes with Fiber Optics
Photodiode
Cerebral Oximetry

Diffuse Reflectance Spectroscopy

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Spatially Resolved NIRS

- Multiple detectors spatially “localize” the measurement of brain oxygenation
- deep-shallow detector compensation isolates brain signals from scalp and surface matter

Average age 4.5 years (n=30)
Abdul-Kaliq H et al. Biomed Tech (Berl); 2000; 45; 328-32
$y = 1.0372x - 0.0062$

$R^2 = 0.9609$

Bias = -0.02

Std Dev = 1.63

$fSO_2 = \text{field saturation (25% arterial:75% venous)}$
Measuring Oxygen

Hb = hemoglobin (Hb) concentration in grams per 100 ml blood
PO$_2$ = partial pressure of oxygen (mm Hg) in air or liquid
PaO$_2$ = Arterial partial pressure of dissolved oxygen in plasma (mm Hg)
SO$_2$ = % saturation of Hb with oxygen
SpO$_2$ = % saturation of Hb in arterial blood measured by pulse oximetry
SaO$_2$ = % saturation of Hb in arterial blood
SvO$_2$ = % saturation of Hb in mixed venous blood
SjvO$_2$ = % saturation of Hb in jugular vein blood
FiO$_2$ = fraction of oxygen in inspired air at sea level
CaO2 = total Oxygen content of arterial blood
DO$_2$ = Delivered oxygen
rSO$_2$ = amount of hemoglobin bound oxygen in tissue
Arterial vs Tissue HbO$_2$

- Related but different issues - supply vs demand
- Clinical emphasis on O$_2$ supply – blood gas, pulse ox
- Defined interventions for supply side
- SpO$_2$ – fix the number and you fix the problem
- rSO$_2$ – perfusion balance / AV difference
- Arterial O$_2$ doesn’t guarantee tissue O$_2$
While there is an absolute number or target saturation for arterial blood (SpO2 = 98%) there is no absolute number for venous saturation.

SvO₂ depends on flow, pH, 2,3 DPG, Hb form, Hb concentration, vascular abnormalities, capillary exchange, tissue O₂ demand, autoregulation, etc.

Arterial Hb saturation does not guarantee sufficient O₂ delivery.
Baselines

<table>
<thead>
<tr>
<th>Normal Cerebral rSO₂</th>
<th>Dark Skin</th>
<th>Light Skin</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=76</td>
<td>n=138</td>
<td>n=50</td>
<td>n=175</td>
<td>n=225</td>
<td></td>
</tr>
<tr>
<td>rSO₂ ± SE</td>
<td>70.0</td>
<td>80.0</td>
<td>90.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Normal, ambulatory adults (n=225)
Following are the most recognized values published in the pediatric arena – most often on congenital heart patients.

**Cerebral**

- Typical range: 60-80; assuming SpO₂ is >90
- < 50 rSO₂ or 20% Δ from rSO₂ baseline
- < 45 rSO₂ or 25% Δ from rSO₂ baseline is critical threshold

**Somatic**

- Response to intervention
- Watch for drops 20% below patient baseline

Data on file.
Piglet Model

- Yorkshire- Duroc blend
- Michigan State University
- 1.5 – 10 kg
- 1 to 30 days old
- Accepted model of human infant
- Very similar biology and anatomy
- 1-5 days old - very unstable
- Anesthetized vs unanesthetized
Piglet Model – Fully Instrumented

- Temp
- Invasive BP
- HR
- $\text{SpO}_2$
- $\text{SvO}_2$ co-oximeter
- $\text{SaO}_2$ co-oximeter
- ET-$\text{CO}_2$
- Electrolytes
- Blood gases
- Lactate
- Glucose
Piglet Cerebral rSO₂ Validation

Cumulative CrSO₂ vs SijvO₂

\[ y = 0.9131x + 2.5908 \]

\[ R^2 = 0.9076 \]

piglets
1.1 to 5.4 kg
n = 5
Normal Piglet

Normal Piglet (Avg n=4)

rSO2

0:00 0:20 0:40 1:00 1:20 1:40 2:00 2:20 2:40 3:00 3:20 3:40 4:00

Head  Leg  Kidney  Gut
Cerebral Ischemia

021508 Carotid Occlusion

3.5 kg piglet

Time

rSO2

Head
Liver
Kidney
Gut

bilateral occlusion
unilateral occlusion

Release
Functional and Biochem Ischemic Thresholds

FIG. 5. Logistic regression plot between near-infrared spectros-copy ScO2 and the percent of piglets without minor change in EEG activity or without major change in EEG activity compared with baseline. Data points indicate mean ± SD. Logistic regression equation variables are presented in Table 2.

FIG. 6. Logistic regression plot between near-infrared spectros-copy ScO2 and the percent of piglets with normal brain tissue lactate concentrations and normal brain tissue ATP concentra-tions. Data points indicate mean ± SD. Logistic regression equation variables are presented in Table 2.

Kurth CD, Levy WJ and McCann J. 2002 J Cerebral Blood Flow and Metab 22; 335-341
Structural Ischemic Thresholds

>60% 40-50%

35-40% 30-35%

~2.2 kg piglets

Hou X et al. 2007. Physiol Measures 28; 1251-1265
Renal Ischemia

![Graph showing rSO2 over time with different organ regions and labels for renal artery occlusion and release.](image)

2.7 kg piglet

Graph legend:
- Cerebral
- Gut
- Kidney
- Muscle

- renal artery occluded
- artery released
Hypovolemic shock

Time vs. rSO2 for different organ regions:
- Head
- Liver
- Kidney
- Gut

Key events:
- 60 cc
- 40 cc
- 20 cc
- 10 cc
- 10 cc
- 8 cc
- 10 cc FA

SpO2, HR, MAP values at each time point:
- SpO2 93, HR 181, MAP 66
- SpO2 9, HR 212, MAP 44
- SpO2 95, HR 241, MAP 35
- SpO2 93, HR 254, MAP 24
- SpO2 93, HR 277, MAP 22
- SpO2 92, HR 279, MAP 20
- SpO2 92, HR 279, MAP 20
- SpO2 off, HR 279, MAP 20

Other values:
- SiO2 35, SiaO2 23
- SiO2 30, SiaO2 25
- SiO2 30, SiaO2 25

3.5 kg piglet
Anemia

061808 Anemia

1.4 kg piglet

Infant Sensor

20 cc blood draw
60 cc LRS infused with each blood draw
25 cc blood draw
20 cc blood draw
25 cc blood draw
25 cc blood reinfused
45 cc blood infused
Euthanasia

Hb (gm/dl)

rSO2

0 2 4 6 8 10 12

0 10 20 30 40 50


Head Leg Kidney Gut Hb
Anemia Baseline

091708 Shock Study Baseline

1.6 kg piglet

1/4 NS + D5W

Total Hb 4.8 gm/dl
Using NIRS

- Look at the rSO2 first
  - Cerebral, perirenal and gut
  - Perfusion distribution

- Then decide how the other clinical variables relate

- Decide on interventions based on all clinical data
Diagnostic Use – Rule Out

- Perirenal rSO$_2$ decline with acceptable cerebral rSO$_2$
  - Reduced peripheral perfusion, autoregulation keeping up
  - GA, Day of life, SpO$_2$, CHD (PDA, septal defect, FO) shunt, drugs, sepsis, FiO$_2$

- Perirenal rSO$_2$ decline with cerebral rSO$_2$ decline
  - Reduced global O$_2$ delivery
  - GA, DOL, SpO$_2$, CHD, myocardial failure, drugs, sepsis,

- Cerebral rSO$_2$ decline with minimal perirenal rSO$_2$ change
  - CO$_2$, cooling, sedation, drugs, brain death

- Cerebral and perirenal rSO$_2$ stable abdominal rSO$_2$ of 15 – 25
  - Ominous sign of gut ischemia if prolonged
  - Swelling, ascites, sepsis, drain, antibiotics, feeds,
MRI Brain Lesions and rSO$_2$

- Preop MRI (n =22) demonstrated ischemic lesions in 23% of patients.
- Postoperative (Norwood) MRI (n =15) demonstrated new or worsened ischemic lesions in 73% of patients
- Periventricular leukomalacia and focal ischemic lesions most common
- Prolonged low postoperative rSO$_2$ (45% for 180 minutes) associated with the development of new or worsened ischemia on postoperative MRI (P = .029)

“Prolonged low postoperative rSO2 was a more predictive indicator of neurologic damage than today’s traditional OR and CICU measures...Post-op cerebral oximetry seems to offer value as a standard of care following the Norwood procedure or other surgical interventions that may impair cardiac output.”

Dent CL et al. 2006  J Thorac Cardiovasc Surg 131; 190-197
Post Norwood Outcome

Adverse outcome was defined as hospital death, need for extracorporeal membrane oxygenation or cardiac intensive care unit length of stay greater than 30 days.

Phelps HM et al. 2009 Ann Thorac Surg 87; 1490-1494
Neonatal Baselines

- Vanderbilt University study – Susannah McNeal et al. 2009
- 12 premature neonates, 29-34 wks GA
- First 21 days of life
- Cerebral, renal and gut mean daily avg rSO2
- Cerebral and renal decline 10 pts over first 2 weeks of life
- 29-30 vs 32-33 wks GA - gut rSO2 p< 0.005
- Gut rSO2 variability decreases over first 2 weeks

CONCLUSIONS: In preterm infants, baseline cerebral, renal, and abdominal rSO2 values change significantly over the first weeks of life. Abdominal and renal baselines vary significantly from older children and abdominal rSO2 demonstrates significant variability. These differences may reflect important maturational changes in regional blood flow and metabolism, particularly within the premature GI tract.

First Author is a Fellow in Training
E-PAS2009:S311.162

Susannah McNeill, Christopher Gatenby, Kelly McLin, Stephen McElroy, Barbara Engelhardt. Neonatology, Vanderbilt University, Nashville, TN; Radiology, Vanderbilt University, Nashville, TN.
Perirenal Tissue Ischemia

Separation from ECMO

Underlying data and case notes on file ISC-10005.
Pleural Effusion Following ASD/VSD Repair

Poor cardiac output indicated by lower than expected somatic trends and desaturations with stress.

rSO2 desats without desaturation of pulse oximetry and SvO2.

Marked desaturation SpO2 88% on 100% FiO2; stat CXR.

Pleural effusion found and treated; immediate cardiac output response noted in improved somatic rSO2.
Neonate with Cardiac Defects - Early Indicator

Tetralogy of Fallot, Pulmonary Atresia and Coarctation of the Aorta.

- **No change in map (37)**
- **Map remains (37-40)**
- **Cardiac arrest**
- **No wave form on art line**
- **Pt. sx and assessed**
- **X ray**
- **Pt sx and assessed**
- **Bilateral grade three-four head bleed**

15 mcg/kg of dopamine, epinephrine and hydrocortisone for blood pressure support.
FIGURE 1.

Cost Distribution by Gestational Age Groups

Graph of distribution of incidence of NICU admissions compared to distribution of costs proportion by gestational age groups. Costs by each group are expressed in average cost/patient ($1000) based on claims data for inpatient stay.

Kirkby S et al. 2007 Advances in Neonatal Care 7; 80-87
Cerebral rSO₂ Drug Response (n=3)

R Nachar Hidalgo, M Wider, E Booth, S Drake, I Seri 2009
Perirenal rSO₂ Drug Response (n=3)

R Nachar Hidalgo, M Wider, E Booth, S Drake, I Seri 2009
Gut rSO$_2$ Drug Response (n=3)

R Nachar Hidalgo, M Wider, E Booth, S Drake, I Seri 2009
Gut $r\text{SO}_2$ Drug Response (n=3)

Muscle $r\text{SO}_2$ Drug Response (n=3)

R Nachar Hidalgo, M Wider, E Booth, S Drake, I Seri 2009
MAP Drug Response (n=3)

Invasive BP Drug Response (n=3)

Dobutamine
Dopamine
Milrinone
Epinephrine
Norepinephrine

TIME
IV Drug Infusion

R Nachar Hidalgo, M Wider, E Booth, S Drake, I Seri 2009