Near-Infrared Spectroscopy (NIRS) in the Neonatal Intensive Care Unit: Tissue Oxygenation Physiology and Monitoring Approaches

Jonathan P. Mintzer, MD, FAAP
Assistant Professor of Pediatrics
Stony Brook Children’s Hospital, Division of Neonatal-Perinatal Medicine, Stony Brook, NY

The speaker has signed a disclosure statement indicating that he has no significant financial interest or relationship with the companies or the manufacturer(s) of any commercial product and/or service that will be discussed as part of this presentation.

Session Summary
This session will provide.

Session Objectives
Upon completion of this presentation, the participant will

▪ understand tissue oxygenation;
▪ be able to explain how NIRS is used to provide information on the balance of oxygen delivery and consumption at the bedside;
▪ be able to identify approaches to NIRS monitoring, to include baseline monitoring and disease-specific approaches.

References


Mintzer J.P., et al. Effects of progressive anemia on regional oxygen extraction in very low birth weight neonates. Submitted for publication.

Additional references noted throughout presentation.
Near-Infrared Spectroscopy in the Neonatal Intensive Care Unit

“NIRS in the NICU” Introduction & Overview

Florida Association for Neonatal Nurse Practitioners
Clinical Update and Review

MONITORING

- Vital signs
  - HR, BP, RR, SpO₂
- Laboratory measures
  - Blood gases, CBC, chemistries
- Oxygen delivery (supply) vs. oxygen consumption (demand)

MONITORING

- Proactive
  - Before clinical sequelae
  - Minimization of tissue injury
- Reactive
  - After clinical sequelae
  - Tissue injury underway

MONITORING

- Noninvasive
  - Cardiopulmonary monitoring
- Invasive
  - Arterial BP monitoring
  - Laboratory measures

PERFUSION CHANGES

Seconds/Minutes
- Pulses
- Color change
- Capillary refill
- Cold extremities
- Lactate ↑

Minutes/Hours
- Metabolic acidosis
- Oliguria
- Renal injury
- Hypotension
- Shock
- Cardiac arrest

CRITICAL O₂ POINT

Oxygen Extraction

Oxygen Utilization (consumption)

Tissue metabolic failure (shock)

Measurable?

Normal metabolism

Critical O₂ Point

Oxygen Delivery
CLINICAL QUESTION

Can we demonstrate impairment to the balance of oxygen delivery and consumption before clinical sequelae occur?

NIRS DEFINITION

Near-Infrared Spectroscopy (NIRS)

A noninvasive technique for assessing and trending the balance of oxygen delivery and consumption in regional tissues.

SPECTROSCOPY

• Lambert-Beer Law
• Passage of light through solution
  - Characteristics of light
  - Length of travel through solution
  - Concentration of solution
  - Content / properties of light absorbing components of solution

SPECTROSCOPY

• Light-based oxygenation measure

\[
\text{Pulse Oximetry} = \frac{\text{Oxyhemoglobin}}{\text{Oxyhemoglobin} + \text{Deoxyhemoglobin}} \times 100
\]

- Elimination of non-pulsatile flow
- Pre-capillary saturation estimate
- “Anticipated tissue oxygenation”
**NEAR-INFRARED SPECTROSCOPY**

- Light-based oxygenation measure
- No elimination of non-pulsatile flow
- Assessment of all blood flow beneath a given sensor
  - Venous (~75%), arterial, capillary
  - “Predominantly post-capillary”

**NEAR-INFRARED SPECTROSCOPY**

- "Regional oxygen saturation"
  \[
  \text{Regional O}_2 \text{Sat} = \frac{\text{Oxyhemoglobin}}{\text{Oxyhemoglobin} + \text{Deoxyhemoglobin}} \times 100
  \]
- Cerebral (CrSO2): ~ 80-90’s, stable
- Renal (RrSO2): ~ 50-90’s, more variable
- Splanchnic (SrSO2): ~ 30-80’s, VARIABLE
- Real-time trending

**FRACTIONAL TISSUE OXYGEN EXTRACTION (FTOE)**

- Pulse oximetry (SpO2) = arterial inflow
- NIRS (rSO2) = mostly post-capillary
  \[
  \text{FTOE} = \frac{\text{SpO}_2 - \text{rSO}_2 \text{ (local)}}{\text{SpO}_2}
  \]
- Cerebral: least extraction (0.1-0.2)
- Renal: moderate extraction (0.2-0.3)
- Splanchnic: most extraction (0.3-0.4+)

**CRITICAL O2 POINT**

- Oxygen Delivery
- Oxygen Utilization (consumption)
- Measurable?
- Normal metabolism
- Critical O2 Point
- Tissue metabolic failure (shock)

**NEAR-INFRARED SPECTROSCOPY**

- Birth
- Transition
- Anemia
- pRBC transfusion
- Patent ductus arteriosus
- Indomethacin
- Ibuprofen
- Ligation
- Procedures
  - Routine care
  - UAC/UVC blood draws

**NICU NIRS STUDIES...**

- Resuscitation
- RDS
- Intubation
- Surfactant
- Congenital heart disease
- Metabolic / Lactic acidosis
- NaHCO3 correction
- Necrotizing enterocolitis
- Prediction?
- Outcomes?
- “Normative”
- “Variability”

**NEAR-INFRARED SPECTROSCOPY**

- "Predominantly post-capillary"
**CLINICAL APPROACHES**

**“Responsive Monitoring”**

**“Routine Monitoring”**

**SYMPTOMATIC ANEMIA**

<table>
<thead>
<tr>
<th>Subject</th>
<th>GA</th>
<th>BW</th>
<th>CGA (pRBC)</th>
<th>Wt (pRBC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailey</td>
<td>28wk</td>
<td>1115g</td>
<td>33wk</td>
<td>1415g</td>
</tr>
<tr>
<td>Dani</td>
<td>27wk</td>
<td>904g</td>
<td>1530g</td>
<td></td>
</tr>
<tr>
<td>van Hoften</td>
<td>27wk</td>
<td>1010g</td>
<td>30wk</td>
<td></td>
</tr>
</tbody>
</table>

- Increased cerebral & splanchnic regional O₂ saturation
- Increased cerebral, renal, and splanchnic regional O₂ saturation; decreased FTOE in all sites
- Increased cerebral regional O₂ saturation; decreased FTOE
- FTOE decrease most pronounced with lower pre-pRBC hematocrit

**BOOSTER TRANSFUSION**

- VLBW neonates; first postnatal week
- 10mL/kg “blood out”
- 15mL/kg booster transfusion
  - Transfusion given over 3-4h
- Replenish red cell mass
  - Restore O₂-carrying capacity
  - Not based on clinical signs / labs

**CLINICAL QUESTION**

Do booster transfusions cause changes in regional tissue oxygenation and calculated oxygen extraction?
**DEMOGRAPHICS**

n = 10 patients; Total 14 booster transfusions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk*)</td>
<td>26 ± 0 (26; 24-28wk)</td>
</tr>
<tr>
<td>Birth weight (g*)</td>
<td>879 ± 49 (880; 610-1210g)</td>
</tr>
<tr>
<td>Maternal age (y*)</td>
<td>28 ± 2 (28; 22-44y)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>6/10</td>
</tr>
<tr>
<td>5min Apgar &lt; 7</td>
<td>2/10</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>9/10</td>
</tr>
</tbody>
</table>

*Mean ± SEM (median; range)

---

**CARDIOVASCULAR STATUS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate and Blood Pressure Pre- and Post-RBC Transfusion</td>
<td></td>
</tr>
</tbody>
</table>

**REGIONAL OXYGEN SATURATION**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Blood pH</td>
<td></td>
</tr>
<tr>
<td>Base Deficit</td>
<td></td>
</tr>
<tr>
<td>Lactate</td>
<td></td>
</tr>
</tbody>
</table>

**BOOSTER TRANSFUSION**

- Increases hematocrit
- Increases regional saturations
- Decreases oxygen extraction
  - Improved oxygen delivery?
- Asymptomatic patients…
CRITICAL O₂ POINT

Oxygen Delivery

Oxygen Utilization (consumption)

Oxygen Extraction

Tissue metabolic failure (shock)

Normal metabolism

Critical O₂ Point

Measurable?

CONTROVERSY

• “Basically Useless Therapy”
• Is this treatment needed?
• Risk / benefit ratio
  o Hypernatremia, hyperosmolality, metabolic alkalosis, intracellular acidosis

“NaHCO₃ CORRECTION”

• Base deficit > 5
  o pH < 7.20 all treated
  o pH 7.20-7.25: MD discretion
• Correction Type (MD discretion)
  o “½ correction” = 0.3 x BD x Wt.
  o 0.2 mEq / kg
  o Repeat gas after 30min

CLINICAL QUESTION

Do sodium bicarbonate corrections cause changes in regional tissue oxygenation and calculated oxygen extraction?

DEMOGRAPHICS

n = 12 patients; Total 17 NaHCO₃ corrections

<table>
<thead>
<tr>
<th></th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk*)</td>
<td>27 ± 1 (26; 24-30)</td>
</tr>
<tr>
<td>Birth weight (g*)</td>
<td>868 ± 42 (912; 810-1080)</td>
</tr>
<tr>
<td>Maternal age (y*)</td>
<td>29 ± 2 (30; 19-44)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>5/10</td>
</tr>
<tr>
<td>Smin Apgar &lt; 7</td>
<td>2/10</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>7/10</td>
</tr>
</tbody>
</table>

*Mean ± SEM (median; range)

Aschner JL & Poland RL. Pediatrics, 2008
CARDIOVASCULAR STATUS

<table>
<thead>
<tr>
<th></th>
<th>Pre-NaHCO₃</th>
<th>Post-NaHCO₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>163 ± 3</td>
<td>163 ± 3</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>48 ± 8</td>
<td>49 ± 9</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>27 ± 5</td>
<td>27 ± 6</td>
</tr>
<tr>
<td>SpO₂</td>
<td>92 ± 2</td>
<td>93 ± 1</td>
</tr>
</tbody>
</table>

Mean ± SD; all pre-post comparisons NS

LABORATORY

<table>
<thead>
<tr>
<th></th>
<th>p &lt; 0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

REGIONAL OXYGEN SATURATION

* p < 0.05 between sites
All within-site pre-post comparisons NS

FRACTIONAL TISSUE OXYGEN EXTRACTION (FTOE)

* p < 0.05 between sites
All within-site pre-post comparisons NS

“NaHCO₃ CORRECTION”

- Increases pH
- Decreases base deficit
- No effect on cardiopulmonary, tissue oxygenation, or fractional tissue oxygen extraction measures
- Useful therapy?
UA BLOOD SAMPLING

• Common procedure
• Smallest, sickest neonates
• “Well-tolerated”
  o Implied safety
• Effects on cerebral tissue oxygenation?
  o Near-infrared spectroscopy

Roll, et al. (2000)¹
  o 20 VLBW UAC draws studied
  o ↓ cerebral oxygenation
  o Short interval, single draw per patient

Schulz, et al. (2003)²
  o n=20; 25-35wk GA, 650-2540g BW
  o Slower draw (40sec) may prevent effect
  o Generalizability?


UA BLOOD SAMPLING

• Roll, et al. (2006)
  o n=48 VLBW, single draws
  o 45/48 intubated; antenatal steroids?
  o Smaller volume, not draw velocity, may prevent change in cerebral oxygenation
  o Generalizability?


CLINICAL QUESTIONS

1) What are the characteristics of cerebral oxygenation changes associated with umbilical arterial blood sampling?
2) What is the natural history of these changes?

NIRS ANALYSIS

• Cerebral regional oxygen saturation:
  o Baseline
  o 2 min intervals
  o Recovery either to baseline or “new plateau” lasting 10 min
• Comparisons
  o Baseline versus nadir and recovery
  o Coefficient of Variability (sd / mean)

DEMOGRAPHICS

<table>
<thead>
<tr>
<th></th>
<th>n = 15 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk*)</td>
<td>28 ± 1 (26; 24-29)</td>
</tr>
<tr>
<td>Birth weight (g*)</td>
<td>877 ± 172 (910; 540-1210)</td>
</tr>
<tr>
<td>Maternal age (y*)</td>
<td>29 ± 4 (29; 22-34)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>60% (9/15)</td>
</tr>
<tr>
<td>Smin Apgar &lt; 7</td>
<td>27% (4/15)</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>93% (14/15)</td>
</tr>
</tbody>
</table>

*Mean ± SEM (median; range)
CEREBRAL NIRS

(n = 15 patients; 201 UABS procedures)

<table>
<thead>
<tr>
<th>Cerebral rSO2 (%)</th>
<th>Baseline</th>
<th>Nadir</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70 ± 1 (71; 38-95)</td>
<td>63 ± 1 (65; 26-93)</td>
<td>70 ± 1 (71; 37-95)</td>
</tr>
</tbody>
</table>

Mean ± SEM (median; range)
*p < 0.001 Baseline versus Nadir
*p < 0.001 Nadir versus Recovery

VARIABILITY

(n = 15 patients; 201 UABS procedures)

<table>
<thead>
<tr>
<th>Coefficient of Variation (sd/mean)</th>
<th>Baseline</th>
<th>Nadir</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.02 ± 0.001 (0.01; 0.00-0.14)</td>
<td>0.05 ± 0.004 (0.03; 0.01-0.43)</td>
<td>0.03 ± 0.003 (0.02; 0.00-0.37)</td>
</tr>
</tbody>
</table>

Mean ± SEM (median; range)
*p < 0.001 all comparisons

NORMALIZED UABS EFFECT

Effects of Individual Umbilical Arterial Blood Draws on Cerebral Regional Oxygen Saturation

Mean (± SD) recovery to baseline (median; range) = 10 ± 4 min (10; 4-30)

UA BLOOD SAMPLING

- Decreased cerebral regional oxygen saturation
- Increased variability
- Highly variable “recovery” time
- Safety?
- Outcomes?
- Subpopulation at risk?
Changes in Cerebral Oxygenation during Umbilical Arterial Blood Sampling in Very Low Birth Weight Neonates

OBJECTIVE

To determine patient- and procedure-related factors contributing to CrSO₂ decrements occurring during UABS procedures in premature neonates.

HYPOTHESES

Patients
The smallest, most premature neonates will be most likely to demonstrate CrSO₂ decrements during UABS procedures.

Procedures
Large volume and/or long duration blood draws will be most likely to be associated with CrSO₂ decrements.

METHODS

Prospective observational cohort
A priori design for UABS blood draws
IRB approved (2014), informed consent
Inclusion: ≤1500 g BW, thoracic UA catheter
Exclusion: <500 g BW, congenital/chromosomal anomalies, severely immature skin, unexpected survival >48 postnatal hours
NIRS monitoring during UABS procedures

POWER / SAMPLE SIZE

NIRS CrSO₂ decrement
- 5% relative change from baseline
- 5-minute interval: 2% baseline variability
Assumed >90% CrSO₂ decrement rate
Assumed 3-4 blood draws per subject
Thirty subjects required (80% power)
- Differences based on patient factors
- Adequate for procedural analyses

UABS PROCEDURE

1) “Waste” blood draw
2) Sample blood draw
3) Waste reinfusion
4) Normal saline flush

RESULTS

- 30 subjects analyzed
  - 27 ± 2 wk GA
  - 1058 ± 279 g BW
  - 84 UABS procedures (5-183 hours of life)

- CrSO2 decrements: 6/30 subjects (20%)
  - Subjects demonstrating at least one relative 5% CrSO2 decrement in context of UABS
  - Less than in previous reports

RESULTS - DEMOGRAPHIC

- Gestational Age
  - Decrement: 26 ± 2 (24-29)
  - No Decrement: 28 ± 2 (23-32)
  - P-value: 0.16

- Birth Weight
  - Decrement: 937 ± 297 (610-1300)
  - No Decrement: 1089 ± 272 (625-1480)
  - P-value: 0.24

Antenatal steroids, Apgars, PDA, IVH all NS

RESULTS - CEREBRAL NIRS

- CrSO2 Decrement (n=6) No Decrement (n=24) P-value
  - Pre-UABS (%)
    - (-15 to 0min)
      - 67 ± 9 (48-83)
      - 73 ± 11 (46-93)
      - P-value: 0.01
  - During UABS (%)
    - (variable)
      - 64 ± 10 (45-78)
      - 73 ± 10 (52-93)
      - P-value: <0.001
  - Post-UABS-1 (%)
    - (To 15min)
      - 62 ± 8 (45-78)
      - 74 ± 10 (51-93)
      - P-value: <0.001
  - Post-UABS-2 (%)
    - (15-30min)
      - 65 ± 9 (47-85)
      - 74 ± 11 (42-93)
      - P-value: <0.001

Mean ± SD (range)

RESULTS - VITALS

<table>
<thead>
<tr>
<th></th>
<th>Decrement (n=6)</th>
<th>No Decrement (n=24)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-HR (bpm)</td>
<td>154 ± 9 (133-167)</td>
<td>156 ± 18 (123-157)</td>
<td>0.45</td>
</tr>
<tr>
<td>Pre-dSBP (mmHg)</td>
<td>46 ± 11 (29-70)</td>
<td>47 ± 9 (29-68)</td>
<td>0.68</td>
</tr>
<tr>
<td>Pre-dDBP (mmHg)</td>
<td>24 ± 7 (14-42)</td>
<td>25 ± 6 (13-39)</td>
<td>0.33</td>
</tr>
<tr>
<td>Pre-SpO2 (%)</td>
<td>92 ± 3 (65-98)</td>
<td>94 ± 4 (80-100)</td>
<td>0.004</td>
</tr>
<tr>
<td>Pre-TcCO2 (mmHg)</td>
<td>53 ± 13 (27-75)</td>
<td>48 ± 16 (18-87)</td>
<td>0.24</td>
</tr>
<tr>
<td>Post-HR (bpm)</td>
<td>151 ± 14 (136-170)</td>
<td>155 ± 16 (121-190)</td>
<td>0.34</td>
</tr>
<tr>
<td>Post-dSBP (mmHg)</td>
<td>47 ± 12 (32-77)</td>
<td>50 ± 8 (33-67)</td>
<td>0.07</td>
</tr>
<tr>
<td>Post-dDBP (mmHg)</td>
<td>23 ± 6 (14-38)</td>
<td>26 ± 7 (14-44)</td>
<td>0.052</td>
</tr>
<tr>
<td>Post-SpO2 (%)</td>
<td>91 ± 4 (84-97)</td>
<td>95 ± 5 (76-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-TcCO2 (mmHg)</td>
<td>54 ± 12 (27-75)</td>
<td>48 ± 16 (18-84)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Mean ± SD (range)

RESULTS - LABS

<table>
<thead>
<tr>
<th></th>
<th>Decrement (n=6)</th>
<th>No Decrement (n=24)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>14.4 ± 1.3 (12.2-17.0)</td>
<td>14.9 ± 1.9 (11.2-19.4)</td>
<td>0.25</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>41.6 ± 4.1 (35.9-50.2)</td>
<td>43.4 ± 5.1 (33.0-56.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>pCO2 (mmHg)</td>
<td>49 ± 11 (38-75)</td>
<td>63 ± 19 (37-127)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pO2 (mmHg)</td>
<td>22 ± 3 (18-29)</td>
<td>21 ± 3 (15-29)</td>
<td>0.72</td>
</tr>
<tr>
<td>Base excess (mEq/L)</td>
<td>-4.7 (-9.4 to +3.6)</td>
<td>-5.3 (-10.9 to +3.5)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Mean ± SD (range)
### RESULTS – UABS

<table>
<thead>
<tr>
<th>Decrement (n=6)</th>
<th>No Decrement (n=24)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Waste&quot; (mL)</td>
<td>1.3 ± 0.5 (0.5-2.0)</td>
<td>1.4 ± 0.6 (0.5-3.0)</td>
</tr>
<tr>
<td>Sample (mL)</td>
<td>0.9 ± 0.7 (0.2-2.3)</td>
<td>1.0 ± 0.5 (0.2-2.0)</td>
</tr>
<tr>
<td>Saline (mL)</td>
<td>1.0 ± 0.5 (0.5-2.0)</td>
<td>1.3 ± 0.6 (0.5-3.0)</td>
</tr>
<tr>
<td>&quot;Waste&quot; draw (sec)</td>
<td>15 ± 6 (5-30)</td>
<td>17 ± 9 (4-36)</td>
</tr>
<tr>
<td>Sample draw (sec)</td>
<td>26 ± 28</td>
<td>26 ± 16</td>
</tr>
<tr>
<td>&quot;Waste&quot; infuse (sec)</td>
<td>13 ± 6 (6-33)</td>
<td>19 ± 11 (4-58)</td>
</tr>
<tr>
<td>Saline infuse (sec)</td>
<td>8 ± 5 (1-24)</td>
<td>11 ± 7 (3-29)</td>
</tr>
<tr>
<td>Total UABS (sec)</td>
<td>114 ± 47 (42-241)</td>
<td>124 ± 46 (52-341)</td>
</tr>
</tbody>
</table>

**Mean ± SD (range)**

### RESULTS – PRE-POST

<table>
<thead>
<tr>
<th>DECREMENTS</th>
<th>NO DECREMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 6 patients; 21 blood draws</td>
<td>N = 24 patients; 63 blood draws</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>156 ± 16 (123-195)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>47 ± 9 (29-68)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>25 ± 7 (13-39)</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>94 ± 3 (80-100)</td>
</tr>
<tr>
<td>TC*CO2 (mmHg)</td>
<td>53 ± 13 (27-75)</td>
</tr>
</tbody>
</table>

**Mean ± SD (range)**

### SUMMARY

- UABS procedures infrequently associated with CrSO2 decrements
  - Unlike previous studies
- Associations with CrSO2 decrements:
  - Lower baseline SpO2, PaO2, and cerebral rSO2
    - Effects on cerebral autoregulation?
  - Faster "waste" reinfusion and saline flush

### LIMITATIONS

- Limited patient sample
- Preliminary analysis
- Frequency of CrSO2 decrements limited
  - Effects on power analysis for sample size
- NIRS monitor reapplied for each UABS
- Events between blood draws affecting CrSO2 and/or autoregulation?

### FUTURE

Whether CrSO2 decrements occurring with UABS procedures affect long-term outcomes remains to be determined.

NIRS monitoring may help identify neonates particularly sensitive to UABS procedures.

In Conclusion…

Whether CrSO2 decrements occurring with UABS procedures affect long-term outcomes remains to be determined.

NIRS monitoring may help identify neonates particularly sensitive to UABS procedures.
RESPONSIVE MONITORING SUMMARY

• **Proactive** trend monitor
• **Noninvasive** measure of oxygenation adequacy

• “Early warning system”
• Effectiveness of interventions

WHERE TO FROM HERE?

• **Responsive Monitoring**
  - Effectiveness metrics
  - Noninvasive
  - Normative subpopulation data required

• **Clinical Implications**
  - Individualized patient management
  - Translation into clinical practice?

CLINICAL APPROACHES

“Responsive Monitoring”

“Routine Monitoring”

“Routine Monitoring”

- Quiescent variability
- Conventional vital signs
- Hematocrit
- Arterial blood gases
- Oxygenation parameters

Original Research

Quiescent variability of cerebral, renal, and splanchnic regional tissue oxygenation in very low birth weight neonates

J.P. Marrines, B. Purvis, M. Chiodo, G. Alpan, and E.E. LaGarza

JOURNAL OF NEONATAL-PERINATAL MEDICINE

Stable

Variable

Cerebral

Renal

Splanchnic
VARIABILITY

- Expected “signal noise”
- What is a significant change?
  - Cerebral vs. renal vs. splanchnic
  - Statistical vs. clinical
- Quiescent analysis

QUIESCENT ANALYSIS

- No clinical status changes
- No ventilator adjustments
- No feeding regimen changes
- No bedside procedures
- No nursing assessments / cares
- Consistent data collection

QUIESCENT ANALYSIS

- Varied data averaging epochs
  - 5, 15, 30, 60-min
- Coefficients of variation (sd/mean)
- Variability comparisons
  - Between-leads
  - Within-lead; between epochs

DEMOGRAPHICS

n = 21 patients
- Gestational age (mo.; mean ± SD) 27 ± 2
- Birth weight (g; mean ± SD) 967 ± 170
- Maternal age (y; mean ± SD) 28 ± 7
- Maternal steroids (%) 20/21 (95%)
- Cesarean section (%) 11/21 (52%)
- 5-min Apgar < 7 (%) 2/21 (10%)
- Small for gestational age (%) 4/21 (19%)

QUIESCENT VARIABILITY

<table>
<thead>
<tr>
<th>Coefficients of Variation (sd/mean)</th>
<th>5min*</th>
<th>15min*</th>
<th>30min*</th>
<th>60min*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>--</td>
<td>0.04</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cerebral</td>
<td>0.03</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Renal**</td>
<td>0.06</td>
<td>0.08</td>
<td>0.09</td>
<td>0.10</td>
</tr>
<tr>
<td>Splanchnic***</td>
<td>0.16</td>
<td>0.20</td>
<td>0.22</td>
<td>0.24</td>
</tr>
</tbody>
</table>

* P<0.01 for between-lead comparisons (ANOVA)
** P<0.01 for renal within-lead epoch comparisons (ANOVA)
*** P<0.05 for splanchnic within-lead epoch comparisons (ANOVA)
QUIESCENT VARIABILITY

• Between-site
  o Cerebral < Renal < Splanchnic

• Within-site
  o 5 < 15 < 30 < 60 minutes

Signal variability is significantly lead-specific and may correlate to various clinical conditions

A priori determination of data averaging epoch lengths is necessary for NIRS studies!

Correlations between Conventional Bedside Vital Signs and Cerebral, Renal, and Splanchnic Oxygen Extraction in Very Low Birth Weight Neonates

<table>
<thead>
<tr>
<th>DEMOGRAPHICS</th>
<th>n = 15 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk)</td>
<td>26 ± 1 (26; 24-29)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>877 ± 172 (910; 540-1210)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>60% (9/15)</td>
</tr>
<tr>
<td>5min Apgar &lt; 7</td>
<td>27% (4/15)</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>93% (14/15)</td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>n = 15 patients: 211 HR &amp; SpO2 hrs; 187 BP hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>159 ± 10 (159, 111-182)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>50 ± 9 (48, 32-75)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>28 ± 8 (27, 12-64)</td>
</tr>
<tr>
<td>Pulse oximetry (%)</td>
<td>92 ± 4 (92, 79-99)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>38 ± 5 (37, 31-53)</td>
</tr>
<tr>
<td>Cerebral rSO2 (%)</td>
<td>70 ± 10 (70; 41-95)</td>
</tr>
<tr>
<td>Renal rSO2 (%)</td>
<td>60 ± 14 (60; 22-91)</td>
</tr>
<tr>
<td>Splanchnic rSO2 (%)</td>
<td>43 ± 21 (43; 15-93)</td>
</tr>
<tr>
<td>Cerebral FTOE</td>
<td>0.24 ± 0.10 (0.24; 0.03-0.54)</td>
</tr>
<tr>
<td>Renal FTOE</td>
<td>0.35 ± 0.14 (0.32; 0.03-0.75)</td>
</tr>
<tr>
<td>Splanchnic FTOE</td>
<td>0.53 ± 0.23 (0.55; 0.04-0.99)</td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)
Correlations between Hematocrit Levels and Cerebral, Renal, and Splanchnic Oxygen Extraction in Very Low Birth Weight Neonates

HEMATOCRIT

- Multi-organ NIRS data analyzed for hours of hematocrit draws
  - 6sec raw data
  - 15min averaging intervals
  - Organ-specific FTOE calculated

- Pearson (r) correlations between changes in hematocrit and FTOE

DEMOnOGRAPHICS

<table>
<thead>
<tr>
<th></th>
<th>n = 27 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk*)</td>
<td>27 ± 2 (27; 24-31)</td>
</tr>
<tr>
<td>Birth weight (g*)</td>
<td>966 ± 181 (945; 540-1220)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>59% (16/27)</td>
</tr>
<tr>
<td>5min Apgar &lt; 7</td>
<td>15% (4/27)</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>56% (15/27)</td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)
CLINICAL

n = 116 Hematocrits (27 patients)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD (median; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit (%)</td>
<td>40 ± 5 (39; 27-53)</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
<td>159 ± 11 (159; 131-182)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>52 ± 9 (50; 37-78)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>28 ± 7 (28; 13-49)</td>
</tr>
<tr>
<td>Pulse Oximetry (%)</td>
<td>93 ± 5 (95; 79-100)</td>
</tr>
</tbody>
</table>

CLINICAL - NIRS

n = 116 Hematocrits (27 patients)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD (median; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral rSO2 (%)</td>
<td>72 ± 10 (72; 46-95)</td>
</tr>
<tr>
<td>Renal rSO2 (%)</td>
<td>65 ± 15 (66; 27-95)</td>
</tr>
<tr>
<td>Splanchnic rSO2 (%)</td>
<td>40 ± 19 (38; 15-91)</td>
</tr>
<tr>
<td>Cerebral FTOE</td>
<td>0.23 ± 0.10 (0.22; 0.04-0.46)</td>
</tr>
<tr>
<td>Renal FTOE</td>
<td>0.31 ± 0.14 (0.30; 0.03-0.68)</td>
</tr>
<tr>
<td>Splanchnic FTOE</td>
<td>0.57 ± 0.21 (0.59; 0.04-0.85)</td>
</tr>
</tbody>
</table>

HEMATOCRIT

Decreased hematocrit:
1) Increased cerebral FTOE
2) Increased renal FTOE
3) No correlation seen for splanchnic FTOE; higher baseline extraction, variability

Correlations between Arterial Blood Gases and Cerebral, Renal, and Splanchnic Oxygen Extraction in Very Low Birth Weight Neonates

DEMOGRAPHICS

n = 15 patients: 215 Arterial Blood Gases

<table>
<thead>
<tr>
<th></th>
<th>Cerebral rSO2 (%)</th>
<th>70 ± 10 (70; 41-95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.28 ± 0.07 (7.28; 7.01-7.45)</td>
<td></td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>51 ± 12 (50; 29-98)</td>
<td></td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>57 ± 17 (52; 20-117)</td>
<td></td>
</tr>
<tr>
<td>Pulse oximetry (%)</td>
<td>92 ± 4 (92; 79-99)</td>
<td></td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>38 ± 5 (37; 31-53)</td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)

PH - FTOE

PaCO₂ - FTOE

PaO₂ - FTOE

A3: NIRS IN THE NEONATAL INTENSIVE CARE UNIT: TISSUE OXYGENATION PHYSIOLOGY AND MONITORING APPROACHES
Correlation between Derived Oxygenation Parameters and Cerebral, Renal, and Splanchnic Oxygen Extraction in Very Low Birth Weight Neonates

DEMOCRACIES

\[ n = 15 \text{ patients} \]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk*)</td>
<td>26 ± 1 (26; 24-29)</td>
</tr>
<tr>
<td>Birth weight (g*)</td>
<td>877 ± 172 (910; 540-1210)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>60% (9/15)</td>
</tr>
<tr>
<td>5min Apgar &lt; 7</td>
<td>27% (4/15)</td>
</tr>
<tr>
<td>Intubated in delivery room</td>
<td>93% (14/15)</td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)

CLINICAL

\[ n = 15 \text{ patients: 63 } O_2 \text{ Contents, 213 A-a Gradients, 178 OIs} \]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(O_2) Content (mL O_2/dL)</td>
<td>16 ± 2 (16; 12-23)</td>
</tr>
<tr>
<td>(A-a) Gradient (mmHg)</td>
<td>179 ± 168 (106; 2-629)</td>
</tr>
<tr>
<td>Oxygenation Index</td>
<td>9 ± 8 (6; 1-19)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13 ± 2 (13; 10-19)</td>
</tr>
<tr>
<td>Pulse Oximetry (%)</td>
<td>92 ± 4 (92; 79-99)</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>9 ± 3 (7; 4-14)</td>
</tr>
<tr>
<td>(FiO_2) (%)</td>
<td>42 ± 24 (30; 21-100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral rSO_2 (%)</td>
<td>70 ± 10 (70; 41-95)</td>
</tr>
<tr>
<td>Renal rSO_2 (%)</td>
<td>60 ± 14 (62; 22-91)</td>
</tr>
<tr>
<td>Splanchic rSO_2 (%)</td>
<td>43 ± 21 (42; 15-93)</td>
</tr>
<tr>
<td>Cerebral FTOE</td>
<td>0.24 ± 0.10 (0.24; 0.03-0.54)</td>
</tr>
<tr>
<td>Renal FTOE</td>
<td>0.35 ± 0.14 (0.3; 0.03-0.75)</td>
</tr>
<tr>
<td>Splanchic FTOE</td>
<td>0.53 ± 0.23 (0.5; 0.04-0.99)</td>
</tr>
</tbody>
</table>

*Mean ± SD (median; range)
In Conclusion...

**OXYGENATION INDEX (OI) - FTOE**

- **Cerebral**
- **Renal**
- **Splanchnic**

![Graphs showing correlations between O2 Content, A-a Gradient, Oxygenation Index, and Oxyhemoglobin Saturation](image)

**DERIVED OXYGENATION PARAMETERS CORRELATIONS**

- **O2 Content**
- **A-a Gradient**
- **Oxygenation Index**


**ROUTINE MONITORING SUMMARY**

- **Proactive** trend monitor
- **Noninvasive** measure of oxygenation adequacy
- “Choosing wisely”
- Correlations with invasive measures

**WHERE TO FROM HERE?**

- **Baseline Monitoring**
  - Normative data
  - Values versus variability
  - Normal versus abnormal
- **Clinical Implications**
  - Scaling of utilization
  - Translation into care practices?

**QUESTIONS?**