25. Alternative indices of vascular reactivity
Non-invasive autoregulation monitoring?

Thanks to Dr.K. Brady
Cerebral Oximetry Index (COx)

Normotensive vs Hypotensive

Thanks to Dr. K. Brady
Cerebral Oximetry Index (COx)

- NIRS as a surrogate measure of CBF
- NIRS-ABP correlation is low above the LLA
- NIRS-ABP correlation is high below the LLA

25 piglet experiments
- Naïve intracranial compartment
- ABP lowered to zero over 3-4 hours
- LLA determined with L-Doppler
- COx curves compared against LLA

COx: Finding a Threshold

- COx > 0.5:
  - 89% Sensitive
  - 81% Specific for ABP below the LLA

... and in patients undergoing coronary bypass surgery, with Somanetics rSO2 used in this case instead of Hamamatsu TOI as in previous cases.

NIRS Can Also Trend CBV

- ICP slow waves replicated with NIRS-based measurements of blood volume
- Coherence between blood volume and ICP is high at “slow wave” frequency

Thanks to Dr. K. Brady

Hemoglobin Volume Index (HVx)

- Substituting cerebral blood volume for ICP in the Cambridge equation re-creates the PRx

Thanks to Dr. K. Brady

HVx and PRx ROC

Thanks to Dr. K. Brady.
Where is the Pediatric LLA during CPB?

- COx is significantly ABP-dependent
- Time below LLA is overrepresented in CPB recordings

Thanks to Dr.K.Brady

**COx: Individual Monitoring During CPB**

A. 6-day-old: IAA (LLA 20 mmHg)

B. 7-month-old: VSD (LLA 40 mmHg)

C. 2-year-old: VSD (LLA at 50 mmHg)

D. 7-year-old: anomalous coronary artery, (LLA at 45 mmHg)

Brady K, et al: *Stroke* 2010
Clinical NIRS measurements

NIRS is can be easily used *longtime* and is *non-invasive*

Sepsis - Basel

Similar presentation of slow waves in FV and NIRS Tissue Oxygenation Index

Significant correlation between Mx and TOx across all patients
Results: Correlation between Mx and Tox

40 years old Lady with ICH

Thanks to Mr.Ch.Zweifel
Results: Correlation between PRx and Thxa

56 years old Lady with TBI

Thanks to Mr. Ch. Zweifel
Subarachnoid haemorrhage - Cambridge

Thanks to Mr. Ch. Zweifel
Slow waves of ICP and blood volume, represented by the total hemoglobin index (THI) measured with near-infrared spectroscopy (NIRS). Both signals were subjected to a moving-average filter with time window of 10 s. The bottom graph shows a high coherence between ICP and THI waves in the 0.055–3 cycles/min frequency band.

Baseline characteristics of patient cohort (n=40)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.5 [23.5; 52.75]</td>
</tr>
<tr>
<td>Female (%)</td>
<td>9 (22.5%)</td>
</tr>
<tr>
<td>GCS on admission</td>
<td>7[4.5; 9]</td>
</tr>
<tr>
<td>Pupils abnormality</td>
<td>12 (30%)</td>
</tr>
<tr>
<td>Intensive Care stay</td>
<td>16 [8; 22]</td>
</tr>
<tr>
<td>CT Marshall Score</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2a</td>
<td>1</td>
</tr>
<tr>
<td>2b</td>
<td>6</td>
</tr>
<tr>
<td>2c</td>
<td>3</td>
</tr>
<tr>
<td>2d</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>6a</td>
<td>1</td>
</tr>
<tr>
<td>6c</td>
<td>5</td>
</tr>
<tr>
<td>6d</td>
<td>1</td>
</tr>
<tr>
<td>In hospital mortality</td>
<td>12 (30%)</td>
</tr>
<tr>
<td>GOS (available in 45% of patients)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
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<td>3</td>
<td>4</td>
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<td>4</td>
<td>3</td>
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<tr>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Values are presented as median [lower quartile; upper quartile], mean (±standard deviation) or counts GCS= Glasgow Coma Scale; GOS=Glasgow Outcome Scale

Baseline characteristics of physiological measurements (n=120)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total recording time</td>
<td>1760h</td>
</tr>
<tr>
<td>Averaged recording time per session</td>
<td>14.6h</td>
</tr>
<tr>
<td>ABP (mmHg)</td>
<td>92.7 (±8.3)</td>
</tr>
<tr>
<td>ICP (mmHg)</td>
<td>18.0 (±5.6)</td>
</tr>
<tr>
<td>CPP (mmHg)</td>
<td>74.7 (±6.9)</td>
</tr>
<tr>
<td>HR (min⁻¹)</td>
<td>73.2 (±14.1)</td>
</tr>
<tr>
<td>RR (min⁻¹)</td>
<td>14.8 (±2.3)</td>
</tr>
</tbody>
</table>

Mean (±standard deviation) or counts (%)
Results

In this example of a 56 year old patient with traumatic brain injury, THx showed a good agreement with PRx during a recording interval of 2 hours ($r=0.77$).

When every single recording interval for PRx and THx get averaged for each patient (avoiding the effect of multiple sampling), PRx and THx correlate even better ($n=40$).

When PRx and THx get averaged for a single recording interval, PRx and THx shows a significant correlation in 120 recordings.
Results II

With PRx, determination of an individual of CPP\textsubscript{OPT} was possible in 72 recordings (60%) and with THx, in 59 recordings (49.1%) (Figure 4). A direct comparison of CPP\textsubscript{OPT}(PRx) and CPP\textsubscript{OPT}(THx) was possible in 50 measurements (41.7%). Differences CPP\textsubscript{OPT}(PRx) and CPP\textsubscript{OPT}(THx) are shown below. There was a significant correlation between PRx- and THx assessed CPP\textsubscript{OPT} in this 50 recordings (r=0.74, p<0.0001). There was no statistically significant difference in a paired comparison (p<0.0001).

Determination of ABP\textsubscript{OPT} was possible in 76 (63.3%) recordings using PRx and in 60 (50%) using THx (Figure 4). In 53 recordings (44.1%), a direct paired comparison was possible (see below). Correlation of PRx- and THx assessed ABP\textsubscript{OPT} was 0.82 (p<0.00001). No differences of PRx- and THx assessed ABP\textsubscript{OPT} was found in the direct paired comparison (p<0.00001).

Examples of pressure reactivity index (PRx, THx) vs. cerebral perfusion pressure plots that allow determination of CPP\textsubscript{OPT} and ABP\textsubscript{OPT} in an individual patient recorded over a time span of 10 hours. CPP\textsubscript{OPT} assessed with both PRx and THx was 80mmHg, ABP\textsubscript{OPT} was assessed to 100mmHg with both methodologies.
Transient hyperaemic response test with NIROS
PAX. Why new index? At low ICP, where pressure-volume curve is flat, changes in ABP do not provoke changes in ICP. Therefore PRx is zero.

Thanks to Dr. D. Radolovich
Theory: PRx and Pax with intact cerebrovascular reactivity

Mechanism of PRx:

ABP ➔ Vasodilatation or Vasoconstriction ➔ CBV ➔ ICP

Mechanism of Pax:

ABP ➔ Vasodilatation or Vasoconstriction ➔ CBV ➔ ICP ➔ AMP

Thanks to Dr. D. Radolovich
Relatively good agreement between Poax and PRx (between Pax and Mx is worse, although still significant (R=0.41))

Thanks to Dr. D. Radolovich
PAx and age

All patients

\[ R=0.18; p<0.0001 \]

Good recovery only

\[ R=0.31; p<0.001 \]

Thanks to Dr. D. Radolovich
Relationship of Pax versus ICP and CPP

Thanks to Dr. M. Aries
Thanks to Dr. M. Aries
Does PArx anticipate brain-stem herniation in refractory intracranial hypertension?
Fix - correlation between mean FV and mean ICP

Thanks to Mr. P. Lewis
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Monitoring of Cerebrovascular Reactivity for Determination of Optimal Blood Pressure in Preterm Infants

Cristine Sortica da Costa, MD\(^1\), Marek Czosnyka, PhD\(^{2,3}\), Peter Smielewski, PhD\(^2\), Subhbrata Mitra, MRCPCH\(^4\), Gordon N. Stevenson, PhD\(^1\), and Topun Austin, PhD\(^1\)

TOI – was measured using NIRO 200NX
MABP and HR were simultaneously recorded using ICM+ software\(^1\)

We previously demonstrated that clinical score is correlated with TOIHRx. We presumed that with TOIHRx we can find optimal ABP like in PRx in adults after TBI.

Thanks to Dr. Cristine Sortica da Costa.
Optimal ABP- ABP at which TOIHRx reaches minimum. This point can be found in 49/60 patients

Thanks to Dr.Cristine Sortica da Costa
2.1+/−1.63 mm Hg
4.2+/−2.7 mm Hg

Greater distance between ABPopt and ‘real’ averaged ABP associated with increased mortality

Thanks to Dr. Cristine Sortica da Costa
Means and 95.0 Percent LSD Intervals

P=0.049

IVH>1

Thanks to Dr.Cristine Sortica da Costa
Direction of deviation had its own clinical consequence: ABP reasonably greater than ABPopt correlated with IVH (IVH score greater than 1)

Thanks to Dr.Cristine Sortica da Costa
P=0.0061; Kruskall-Wallis P= 0.0053 t-test

Thanks to Dr.Cristine Sortica da Costa
Messages to take home

• Tox (Cox), THx (HVx) - indices of autoregulation/reactivity based on NIRS
• They all correlate with Mx and PRx
• Correlation with outcome - to be established
• Useful for ‘optimal’ CPP and ABP?
• Fix – correlation between ICP and FV: high coherence in slow waves bandwidth
• Fix deteriorates with impaired reactivity
• Fix correlates with outcome!
• TOIHRx - for ‘optimal’ ABP in newborns