First monitoring case
Modern intensive care monitoring
Multimodal monitoring - patterns recognition needed
MultiScale Entropy (MSE) algorithm

1. Coarse-grain the time series
2. Calculate SampEn for each coarse-grained series
3. Plot it as a function of scale factor
4. Analyze the MSE curve profiles
Coarse-graining procedure

Coarse-graining schematic

Original time series

Scale 3

Scale 6
CALCULATING SAMPLE ENTROPY (M, R, N)

\[ \ln(\text{patterns of length } m) - \ln(\text{patterns of length } m+1) \]

\( m = 2 \)

\( r = \text{tolerance} = 0.1 \sim 0.2\text{SD} \)
Complexity Index (CI)
defined as the area under the MSE curve

\[ CI = \sum_{i=1}^{sn} SampEn(i) \]

where sn is presented scale numbers.

If the CI value is greater, the complexity is higher.
Complexity of intracranial pressure correlates with outcome after traumatic brain injury

Cheng-Wei Lu,¹,²,³ Marek Czosnyka,¹ Jiann-Shing Shieh,³ Anna Smielewska,⁴ John D. Pickard¹ and Peter Smielewski¹

Table 2 Variables calculated by ICM+ and Multiscale Entropy algorithm

<table>
<thead>
<tr>
<th></th>
<th>GOS 1</th>
<th>GOS 2</th>
<th>GOS 3</th>
<th>GOS 5</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>49</td>
<td>77</td>
<td>93</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>ICP (mmHg)</td>
<td>15.9 ± 4.2</td>
<td>16.1 ± 4.0</td>
<td>16.2 ± 4.4</td>
<td>20.1 ± 8.5*</td>
<td>0.0000006</td>
</tr>
<tr>
<td>ABP (mmHg)</td>
<td>94.8 ± 6.9</td>
<td>94.8 ± 6.5</td>
<td>94.9 ± 6.5</td>
<td>96.6 ± 9.9</td>
<td>0.37</td>
</tr>
<tr>
<td>CPP (mmHg)</td>
<td>78.9 ± 6.9</td>
<td>78.7 ± 5.6</td>
<td>78.6 ± 6.5</td>
<td>76.5 ± 8.4</td>
<td>0.14</td>
</tr>
<tr>
<td>AMP (mmHg)</td>
<td>1.68 ± 0.83</td>
<td>1.54 ± 0.85</td>
<td>1.51 ± 0.88</td>
<td>1.98 ± 1.81</td>
<td>0.05</td>
</tr>
<tr>
<td>PRx</td>
<td>0.04 ± 0.14</td>
<td>0.05 ± 0.14</td>
<td>0.08 ± 0.15</td>
<td>0.14 ± 0.17†</td>
<td>0.001</td>
</tr>
<tr>
<td>ICP-CI</td>
<td>11.9 ± 4.4*</td>
<td>9.5 ± 4.5</td>
<td>9.4 ± 4.4</td>
<td>6.8 ± 4.1*</td>
<td>0.00000002</td>
</tr>
<tr>
<td>AMP-CI</td>
<td>9.0 ± 5.2</td>
<td>7.3 ± 5.3</td>
<td>7.0 ± 5.0</td>
<td>5.0 ± 4.5†</td>
<td>0.00004</td>
</tr>
</tbody>
</table>
Heart rate variability
Heart rate variability (ECG or ABP)

Thanks to Dr. P. Smielewski
Heart rate variability
(Power spectral density – FFT method)

Thanks to Dr. P. Smielewski
Heart rate variability
(ECG or ABP – similar but not the same)
Baroreflex – Sensitivity

Early Phase II of Valsalva-Manoeuvre
\( \Delta RR \)-Intervals/\( \Delta ABP \)

Slope of the linear regression between RR intervals and systolic blood pressure changes
Baroreflex sensitivity (Sequence method)
Baroreflex Monitoring
Spectral analysis

- BRS < 3 ms/mmHg, increased risk of infections after stroke (Sykora Stroke 2009)
- Baroreflex-failure determines outcome in heart failure (Mortara Circulation 1997)
- Renal failure: Correlation between GFR and BRS (Bavanandan 2005)

(Adapted from Parati G. J Hypertens 2000;18:7-19).
Baroreflex sensitivity (Spectral method)
Real time monitoring
( Neuro Critical Care Unit )

Real-time monitoring
- Autonomic system
- Cerebral autoregulation
Cerebrovascular reactivity and autonomic drive following traumatic brain injury

Andrea Lavinio · Bogdan Ene-Iordache · Ilaria Nodari · Alan Girardini · Elena Cagnazzi · Frank Rasulo · Piotr Smielewski · Marek Czosnyka · Nicola Latronico

Low logHF associates with mortality

HRV (frequency domain analysis)
Prognostic value in TBI patients
Baroreflex and Cerebral Autoregulation Are Inversely Correlated

Nathalie Nasr, MD, PhD; Marek Czosnyka, PhD; Anne Pavy-Le Traon, MD, PhD; Marc-Antoine Custaud, MD, PhD; Xiuyun Liu, BSc; Georgios V. Varsos, BSc; Vincent Larrue, MD

Atherosclerotic carotid stenosis patients (N=45)
Health volunteers (N=10)
BRS – Time domain sequence method
CA - Mx

Carotid stenosis patients
Worse CA and BRS

Better BRS correlates with worse CA
Intracranial Hypertension
Increase BRS and change in LF/HF during
# Autonomic Impairment in Severe Traumatic Brain Injury: A Multimodal Neuromonitoring Study

Marek Sykora, MD, PhD, MSc, Marek Czosnyka, PhD, Xiuyun Liu; Joseph Donnelly, MBChB; Nathalie Nasr, MD, PhD; Jennifer Diedler, MD, MSc; Francois Okoroafor, MD; Peter Hutchinson, BSc (hons), MBBS, PhD, FRCS (Surg Neurol); David Menon, MBBS, MD, PhD, FRCP, FRCA, FmedSci; Peter Smielewski. PhD

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DOI: 10.1097/CCM.0000000000001624

<table>
<thead>
<tr>
<th></th>
<th>Survivors, n=201</th>
<th>Non-survivors, n=61</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, median (range, IQR)</strong></td>
<td>33 (16-76, 23)</td>
<td>44 (18-76, 32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>ICP, mmHg, median (range, IQR)</strong></td>
<td>15.8 (4.5-29.0, 5.6)</td>
<td>17.6 (3.0-50.9, 9.7)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>CPP, mmHg, median (range, IQR)</strong></td>
<td>77.7 (57.7-100.1, 6.6)</td>
<td>74.2 (56.2-102.1, 11.6)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>PRx, median (range, IQR)</strong></td>
<td>0.05 (-0.29-0.70, 0.20)</td>
<td>0.14 (-0.30-0.70, 0.23)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>BRS, ms/mmHg, median (range, IQR)</strong></td>
<td>6.6 (1.6-18.8, 4.2)</td>
<td>5.1 (1.3-18.7, 4.0)</td>
<td>0.026</td>
</tr>
<tr>
<td><strong>HF power, ms², median (range, IQR)</strong></td>
<td>160.0 (9.9-1853.9, 285.4)</td>
<td>115.0 (6.2-1840.3, 212.1)</td>
<td>0.024</td>
</tr>
<tr>
<td><strong>HF relative power, median (range, IQR)</strong></td>
<td>25.8 (5.0-65.4, 17.5)</td>
<td>33.4 (6.6-81.8, 22.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>LF/HF ratio, median (range, IQR)</strong></td>
<td>1.6 (0.2-8.3, 1.3)</td>
<td>1.0 (0.0-8.8, 1.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Age-dependent trend towards higher correlation coefficients between PRx and BRS

Thanks to Prof. Marek Sykora
BRS after SAH – work in progress

BRS – Time domain cross-correlation method

\[ P < 0.001 \]
Mann Whitney U test

N=50

- Bad prognosis (mRS > 2)
- Good prognosis (mRS 0-2)
Correlation approach

- $r \sim 1$
- $r \sim 0$
- $r \sim 1$

Impaired

Intact

Impaired
Pressure reactivity (PRx)

- ABP (mmHg)
- ICP (mmHg)
- PRx = 0.90
- PRx = -0.61
‘Optimal’ Cerebral Perfusion Pressure

Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury.

Lucius A. Steiner, MD; Marek Czerny, PhD, DSc; Stefan K. Fleischhak, PhD; Piotr Smialowski, PhD; Doris Chatfield, BSc; David K. Memn, PhD, FRCP, FRCA, FMedSci; John D. Pickard, MChir, FRCS, FMedSci
‘Optimal’ CPP in individual patients
‘Optimal’ CPP and Outcome

How far mean CPP is from ‘optimal CPP’?

In patients with poor outcome this distance is greater.
Black box approach

ABP → [Black box] → FV
Phase shift

64-yr-old patient with 80% ICA stenosis


AutoRegulation Index

Figure 4. Responses of cerebral autoregulation model to a step change in blood pressure.

Slow waves ARI

ARI function was implemented in ICM+ (Mary Liu)
Which is the best index for CA assessment?

FFT: across the whole period

Wavelet: uses localized waveform to convert a signal into another form which unfolds it in time and scale
Wavelet Phaseshift between ABP and ICP
Wavelet Phase Shift

PRx

Error Bars: ± 1 SE
Results of CPPopt analysis using wPRx- 575 TBI patients
ICP analysis: Morphology (MOCAIP, or equivalent) - coming soon?


Message to take home

- New functions:
  - Entropy (complexity index)
  - HRV, BRS (spectral and time domain)
  - ARI (autopregulation index)
  - Wavelet PRx
  - New arrivals (soon): multiwindow CPPopt, visualisation CPPopt, cardiac output (Michał Placek)
Entropy of Cam River in July?