19. Monitoring of CA using TCD- Mx and Sx
Drawing the autoregulatory curve: in clinical practice such dramatic changes in CPP are not permissible.


Monitoring cerebral autoregulation - certainly not a new concept
CEREBRAL AUTOREGULATION

Testing
* Clear stimulation:
  - drug to rise ABP
  - leg cuff release
  - head down tilt
  - lower body pressure
  - slow respiration
  - transient compression

• Better accuracy
• One-off measurement

Monitoring
* No stimulation; spontaneous waves of ABP or CPP

• Worse accuracy (SNR worse)
• Information continuous in time – may be time-averaged
Mx is ‘noisy’; it requires time-averaging. However it may explain changes in cerebral autoregulation which happen in time.
Monitoring of transient phenomena: Positive Mx indicates loss of cerebral autoregulation at the top of plateau waves.

CONTINUOUS MONITORING OF CA: TIME-RELATED CHANGES
Validation of Mx: Positive correlation with static rate of autoregulation (SROR) in 17 head injured patients

Validation: Transient Hyperaemic Response Test (Short [6-8 sec] compression of the CCA)

THRT Positive
Intact Autoregulation

THRR = 1.45

THRT Negative
Impaired autoregulation

THRR = 0.95

THRT agrees with Mx in HI (N=47 patients)

Clinical Article
Pressure-autoregulation, CO₂ reactivity and asymmetry of haemodynamic parameters in patients with carotid artery stenotic disease. A clinical appraisal

I. Gooskens¹, E. A. Schmidt¹, M. Czosnyka¹, St. K. Piechnik¹, P. Smielewski², P. J. Kirkpatrick¹, and J. D. Pickard¹,²

\[ FV = a \times EtCO₂ + b \times ABP \]

Fig. 1. Example of CO₂ reactivity test. \( ABP_m \): mean arterial blood pressure, \( FVm \): mean flow velocity, \( EtCO₂ \): end tidal CO₂

Fig. 3. Relationship between ABP-corrected CR and autoregulation \( (Mx) \). Patients with poor reactivity are more likely to have defective pressure autoregulatory responses
Relatively good correlation between phase shift, CO2 reactivity, and correlation index in patients with carotid stenosis.

Reinhard M, Roth M, Muller T, Czosnyka M, Timmer J, Hetzel A. Cerebral autoregulation in carotid artery occlusive disease assessed from spontaneous blood pressure fluctuations by the correlation coefficient index. Stroke. 2003 Sep;34(9):2138-44
The Relationship Between Cerebral Blood Flow Autoregulation and Cerebrovascular Pressure Reactivity After Traumatic Brain Injury

**BACKGROUND:** Cerebrovascular pressure reactivity is the principal mechanism of cerebral autoregulation. Assessment of cerebral autoregulation can be performed by using the mean flow index (Mx) based on transcranial Doppler ultrasonography. Cerebrovascular pressure reactivity can be monitored by using the pressure reactivity index (PRx), which is based on intracranial pressure monitoring. From a practical point of view, PRx can be monitored continuously, whereas Mx can only be monitored in short periods when transcranial Doppler probes can be applied.

**OBJECTIVE:** To assess to what degree impairment in pressure reactivity (PRx) is associated with impairment in cerebral autoregulation (Mx).
Autoregulation and arterial CO$_2$

Mx responds to PaCO$_2$ during routine CO$_2$-reactivity testing.
Indices of autoregulation should be always CO2-corrected $M_x$:

- $0.2$ per $1\text{kPa}$ of EtCO2
- $\text{RoR: } -0.13$ per $1\text{kPa}$ of EtCO2

--

Study in volunteers:

Mx well agreed with static rate of autoregulation (leg-cuff test, Aaslid et al, 1983) $R^2=0.66$; N=14, 3 PaCO2 levels

MxA: calculated with MAP or Mx: calculated with CPP?

Mxa is well correlated with Mx but discrepancies are possible. Generally Mxa > Mx.
Mx correlates with outcome better than Mxa

F statistics values for different autoregulation indices

Many thanks to Mr. K. Budohoski
Myth: Patients in different clinical conditions can be compared

1- head injury- survivors
2- head injury- died
3- carotid artery stenosis- unilateral
4- carotid artery stenosis- bilateral
5- volunteers (young)- normocapnia
6- volunteers (young)- hypercapnia
7- SAH patients- no spasm
8- SAH patients- spasm
APPLICATIONS: TBI

Relationship between Mx and CPP replicates Lassen’s curve in head injury - review of 188 cases

HEAD INJURY:
AUTOREGULATION IS SIGNIFICANTLY WORSE IN PATIENTS WITH UNFAVOURABLE OUTCOME

Autoregulation is worse first two days following trauma but only in patients who died (red line)
Critical Thresholds for Transcranial Doppler Indices of Cerebral Autoregulation in Traumatic Brain Injury

Enrico Sorrentino · Karol P. Budohoski · Magdalena Kasprowicz · Peter Smielewski · Basil Matta · John D. Pickard · Marek Czosnyka
Example (rare!) of impaired autoregulation on right side and preserved on left side.

SIDE-TO-SIDE DIFFERENCE IN AUTOREGULATION:

VOLUNTEERS:

HEAD INJURY:

SIDE-TO-SIDE DIFFERENCE IS GREATER IN PATIENTS WITH MIDLINE SHIFT AND IN THOSE WHO DIED:

Figure 3 a

**Left side expansion**

\[ M_{xl} - M_{xr} > 0 \]

i.e. \( M_{xl} > M_{xr} \)

**Shift from the Left to the Right**

Worse autoregulation on the Left

Figure 3 b

**Right side expansion**

\[ M_{xl} - M_{xr} < 0 \]

i.e. \( M_{xr} > M_{xl} \)

**Shift from the Right to the Left**

Worse autoregulation on the Right

Thanks to Dr. E.Schmidt
Figure 3 a

Thanks to Dr. E. Schmidt
Continuous Assessment of Cerebral Autoregulation in Subarachnoid Hemorrhage

Martin Soehle, MD‡, Marek Czosnyka, PhD‡, John D. Pickard, MCh, FRCS‡, and Peter J. Kirkpatrick, FRCS(BN)

*Department of Anaesthesiology and Intensive Care Medicine, University of Bonn, Bonn, Germany; and ‡Academic Neurosurgery Unit, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom

Cerebral vasospasm remains a leading cause of morbidity and mortality after subarachnoid hemorrhage (SAH). Cerebral ischemia may occur when autoregulation fails to compensate for spasm. We examined how autoregulation is affected by vasospasm by using transcranial Doppler. The moving correlation coefficient between slow changes of arterial blood pressure and mean or mean flow velocity (if), termed "Mx" and "Sx," respectively, was used to characterize cerebral autoregulation. Vasospasm was declared when the mean FV increased to more than 120 cm/s and the Lindgren ratio was more than 1.5. This occurred in 15 of 52 SAH patients. On the basis of the bilateral transcranial Doppler recordings of the middle cerebral artery in vasospastic patients, Mx and Sx were calculated for baseline and vasospasm. Mx increased during vasospasm (0.46 ± 0.32 vs. 0.21 ± 0.31) and was significantly higher (P = 0.02) than at baseline (0.21 ± 0.31). Sx was also increased (0.22 ± 0.2 vs. 0.05 ± 0.2 at baseline, P = 0.03). Mx correlated with mean FV (r = 0.537; P = 0.025) and the Lindgren ratio (r = 0.672; P < 0.01). Mx (P = 0.056) and Sx (P = 0.044) were higher on the vasospastic side (Mx, 0.44 ± 0.27; Sx, 0.24 ± 0.23) than on the contralateral side (Mx, 0.34 ± 0.29; Sx, 0.16 ± 0.28). The increased Mx and Sx during cerebral vasospasm demonstrated impaired cerebral autoregulation. Mx and Sx provide additional information on changes in autoregulation in SAH patients.

(Aanhst Analg 2004;98:1133-9)
<table>
<thead>
<tr>
<th>Variable</th>
<th>DCI group (n=32)</th>
<th>Non-DCI group (n=66)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (±SD)</td>
<td>56±10</td>
<td>57±12</td>
<td>0.17 §</td>
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<td>Sex female/male*</td>
<td>22/10</td>
<td>47/19</td>
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<td>WFNS grade, median</td>
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<td>2</td>
<td>0.04 §</td>
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<tr>
<td>1, n</td>
<td>11</td>
<td>23</td>
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<tr>
<td>2, n</td>
<td>7</td>
<td>22</td>
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<tr>
<td>3, n</td>
<td>1</td>
<td>5</td>
<td>0.38</td>
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<tr>
<td>4, n</td>
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<td>11</td>
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<td>5, n</td>
<td>3</td>
<td>5</td>
<td>0.76</td>
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<td>Modified Fisher grade, median</td>
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<td>4</td>
<td>0.005 §</td>
</tr>
<tr>
<td>1, n</td>
<td>4</td>
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<td>0.10</td>
</tr>
<tr>
<td>2, n</td>
<td>4</td>
<td>5</td>
<td>0.43</td>
</tr>
<tr>
<td>3, n</td>
<td>19</td>
<td>26</td>
<td>0.06</td>
</tr>
<tr>
<td>4, n</td>
<td>5</td>
<td>17</td>
<td>0.26</td>
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<tr>
<td>Aneurysm location</td>
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<td></td>
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<tr>
<td>AComA, n</td>
<td>6</td>
<td>21</td>
<td>0.17</td>
</tr>
<tr>
<td>ACA, n</td>
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<td>0.04</td>
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<tr>
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<td>16</td>
<td>0.50</td>
</tr>
<tr>
<td>ICA, n</td>
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<td>2</td>
<td>0.18</td>
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<tr>
<td>AChA, n</td>
<td>2</td>
<td>1</td>
<td>0.20</td>
</tr>
<tr>
<td>PComA, n</td>
<td>12</td>
<td>17</td>
<td>0.23</td>
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<tr>
<td>PCA, n</td>
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<td>1</td>
<td>0.48</td>
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<tr>
<td>PICA, n</td>
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<tr>
<td>BA, n</td>
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<tr>
<td>VB, n</td>
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<td>0.32</td>
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<td>Clipping/coiling, n *</td>
<td>23/11</td>
<td>44/23</td>
<td>0.60</td>
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<tr>
<td>Re-bleeding, n</td>
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<td>7</td>
<td>0.06</td>
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<tr>
<td>Hydrocephalus, n</td>
<td>18</td>
<td>31</td>
<td>0.39</td>
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<tr>
<td>EVD, n</td>
<td>12</td>
<td>19</td>
<td>0.38</td>
</tr>
<tr>
<td>Vasospasm, n</td>
<td>28</td>
<td>24</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Non-invasive ABP</td>
<td>18</td>
<td>51</td>
<td>0.03 §</td>
</tr>
<tr>
<td>Total monitoring time per patient per session, min±SD</td>
<td>86±65</td>
<td>82±63</td>
<td>0.14 §</td>
</tr>
<tr>
<td>Total sessions per patient, median (range)</td>
<td>4 (2-11)</td>
<td>4 (2-7)</td>
<td></td>
</tr>
</tbody>
</table>
Yellow: Early disturbed autoregulation, Blue: normal autoregulation

Dashed line indicates median onset time of macrovascular spasm
## DCI Multivariate analysis

<table>
<thead>
<tr>
<th></th>
<th>B (SE)</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt;55 y</td>
<td>-0.68 (0.68)</td>
<td>0.98</td>
<td>0.32</td>
<td>0.51</td>
<td>0.13-1.94</td>
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<tr>
<td>Male sex</td>
<td>-0.05 (0.74)</td>
<td>0.004</td>
<td>0.95</td>
<td>0.95</td>
<td>0.22-4.04</td>
</tr>
<tr>
<td>WFNS</td>
<td>-0.12 (0.27)</td>
<td>0.19</td>
<td>0.66</td>
<td>1.12</td>
<td>0.67-1.9</td>
</tr>
<tr>
<td>Mod Fisher 3</td>
<td>1.83 (0.74)</td>
<td>6.04</td>
<td><strong>0.014</strong></td>
<td><strong>6.21</strong></td>
<td><strong>1.45-26.68</strong></td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>0.11 (0.85)</td>
<td>0.02</td>
<td>0.9</td>
<td>1.11</td>
<td>0.21-5.82</td>
</tr>
<tr>
<td>EVD</td>
<td>0.21 (1.05)</td>
<td>0.04</td>
<td>0.84</td>
<td>1.23</td>
<td>0.16-9.61</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1.49 (0.9)</td>
<td>2.79</td>
<td>0.095</td>
<td>4.42</td>
<td>0.077-25.24</td>
</tr>
<tr>
<td>Metabolic derangements</td>
<td>-1.13 (1.02)</td>
<td>1.23</td>
<td>0.27</td>
<td>0.32</td>
<td>0.04-2.39</td>
</tr>
<tr>
<td>FV &gt; 120 [cm/s]; LR &gt; 3.0</td>
<td>-0.92 (0.79)</td>
<td>1.38</td>
<td>0.24</td>
<td>0.4</td>
<td>0.09-1.85</td>
</tr>
<tr>
<td>Sxa</td>
<td>2.54 (0.74)</td>
<td>11.75</td>
<td><strong>0.001</strong></td>
<td><strong>12.66</strong></td>
<td><strong>2.97-54.07</strong></td>
</tr>
<tr>
<td>TOxa</td>
<td>1.68 (0.74)</td>
<td>5.11</td>
<td><strong>0.024</strong></td>
<td><strong>5.34</strong></td>
<td><strong>1.25-22.84</strong></td>
</tr>
</tbody>
</table>
Asymmetry of CA- DCI & Outcome

A

\[ p=0.00001 \]

\[ p=0.0004 \]

non-DCI  DCI

B

\[ p=0.02 \]

\[ p=0.006 \]

Favorable  Unfavorable
Conclusions from prospective study

- Early impairments in cerebral autoregulation can predict DCI

- Similar accuracy of TCD- and NIRS-based autoregulation, but 100% specificity when all indices show impaired autoreg.

- Unilateral autoregulatory failure is related to DCI

- Bilateral autoregulatory failure is related to unfavourable outcome at 3 months.
Unilateral CCA stenosis

Ipsilateral vs contralateral difference in cerebrovascular reactivity are significant and dependant on level of stenosis

Cerebral Autoregulation in Carotid Artery Occlusive Disease Assessed From Spontaneous Blood Pressure Fluctuations by the Correlation Coefficient Index

M. Reinhard, MD; M. Roth, PhD; T. Müller, PhD; M. Czosnyka, PhD; J. Timmer, PhD; A. Hetzel, MD

Background and Purpose—Estimation of dynamic cerebral autoregulation from spontaneous fluctuations of arterial blood pressure (ABP) and cerebral blood flow velocity (CBFV) is an attractive noninvasive option for cerebral hemodynamic impairment. We evaluated the correlation coefficient index method in patients with severe obstructive carotid disease and compared it with transfer function analysis (frequency domain approach to cerebral autoregulation) and CO₂ vasoreactivity.

Methods—In 139 patients with severe unilateral carotid stenosis (≥70%) or occlusion, CBFV (transcranial Doppler) and ABP (Finapres method) were recorded over 10 minutes. Correlations between systolic pressure, diastolic pressure, and mean ABP and CBFV oscillations over 1-minute epochs were averaged over 10 minutes to form the correlation coefficient indexes (Ix, Dx, Mx, respectively). Transfer function parameters (phase shift and gain between ABP and CBFV oscillations) were determined from the entire 10-minute period. CO₂ reactivity was assessed by inhalation of 7% CO₂.

Results—The correlation indexes Dx and Mx were significantly higher (ipsilateral to stenosis and increased with degree of stenosis, indicating increasing dependence of CBFV on ABP and thus impairment of cerebral autoregulation. Dx and Mx correlated moderately but highly significantly with transfer function parameters and CO₂ reactivity and showed a good level of agreement in detecting pathological values. Patients with a small variance of the 1-minute source correlations of Dx and Mx showed clearly better correlation values. Transfer function parameters and CO₂ reactivity but not Dx and Mx were significantly poorer in patients with symptomatic stenosis or occlusion.

Conclusions—The potential of the correlation coefficient indexes Dx and Mx in detecting hemodynamic impairment in patients with carotid stenosis is comparable to that of transfer function analysis and CO₂ reactivity testing. In future, a combination of various hemodynamic tests might help to identify patients at risk for ischemic events. (Stroke. 2003;34:2136-2144.)

Figure 2. Box plots of autoregulation parameters in different groups of ICA stenosis. ○, Denotes exceeding values (>1.5 box

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>A, 70–79% (N=40)</th>
<th>B, 80–89% (n=21)</th>
<th>C, 90–99% (N=56)</th>
<th>D, 100% (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Unilateral</td>
</tr>
</tbody>
</table>
Normal Pressure Hydrocephalus

Relationship between pressure autoregulation and CSF compensatory reserve in hydrocephalus (43 patients with NPH, infusion studies)

In patients with normal CSF circulation there is an association with dysautoregulation that is not found in patients with increased resistance to CSF outflow. Does this indicate underlying cerebrovascular disease?

Impaired Autoregulation of Cerebral Blood Flow During Rewarming from Hypothermic Cardiopulmonary Bypass and Its Potential Association with Stroke

Brijen Joshi, MD*
Kenneth Brady, MD*
Jennifer Lee, MD*
Blaine Easley, MD*
Rabi Panigrahi, MD*
Peter Smielewski, PhD†
Marek Czosnyka, PhD†
Charles W. Hogue, Jr., MD*†

BACKGROUND: Patient rewarming after hypothermic cardiopulmonary bypass (CPB) has been linked to brain injury after cardiac surgery. In this study, we evaluated whether cooling and then rewarming of body temperature during CPB in adult patients is associated with alterations in cerebral blood flow (CBF)-blood pressure autoregulation.

METHODS: One hundred twenty-seven adult patients undergoing CPB during cardiac surgery had transcranial Doppler monitoring of the right and left middle cerebral artery blood flow velocity. Eleven patients undergoing CPB who had arterial inflow maintained at >35°C served as controls. The mean velocity index (Mx) was calculated as a moving, linear correlation coefficient between slow waves of middle cerebral artery blood flow velocity and mean arterial blood pressure. Intact CBF—blood pressure autoregulation is associated with an Mx that approaches 0. Impaired autoregulation results in an increasing Mx approaching 1.0. Comparisons of time-averaged Mx values were made between the following periods: before CPB (baseline), during the cooling, ANESTHESIA & ANALGESIA and after CPB. The number of patients in each phase of CPB was 12 (Mx > 0.4), indicative of impaired CBF autoregulation, was determined.

RESULTS: During cooling, Mx (left, 0.29 ± 0.18; right, 0.28 ± 0.18 [mean ± SD]) was greater than that at baseline (left, 0.17 ± 0.21; right, 0.17 ± 0.20; P = 0.0001). Mx increased during the rewarming phase of CPB (left, 0.40 ± 0.19; right, 0.39 ± 0.19) compared with baseline (P = 0.001) and the cooling phase (P = 0.0001), indicating impaired CBF autoregulation. After CPB, Mx (left, 0.27 ± 0.20; right, 0.28 ± 0.21) was higher than at baseline (left, P = 0.0004; right, P = 0.0003), no different than during the cooling phase, but lower than during rewarming (left, P = 0.0001; right, P = 0.0005). Forty-three patients (34%) had an Mx > 0.4 during the cooling phase of CPB and 68 (53%) had an average Mx > 0.4 during rewarming. Nine of the 11 warm controls had an average Mx > 0.4 during the entire CPB period. There were 7 strokes and 1 TIA after surgery. All strokes were in patients with Mx ≥ 0.4 during rewarming (P = 0.015). The unadjusted odds ratio for any neurologic event (stroke or transient ischemic attack) for patients with Mx ≥ 0.4 during rewarming was 6.57 (95% confidence interval, 0.79 to 55.0, P < 0.08).

CONCLUSIONS: Hypothermic CPB is associated with abnormal CBF—blood pressure autoregulation that is worsened with rewarming. We found a high rate of strokes in patients with evidence of impaired CBF autoregulation. Whether a pressure-passive CBF state during rewarming is associated with risk for ischemic brain injury requires further investigation.

Monitoring during liver transplant

Figure 8–9  Example of arterial blood pressure (ABP) and transcranial Doppler ultrasonography (TCD) monitoring during liver transplantation. Note worsening of autoregulation (positive mean index [Mx] value) during anhepatic phase, which improves during reperfusion (after 14:30). During reperfusion, noninvasive cerebral perfusion pressure (nCPP) and blood flow velocity (FV) values gradually improve, and critical closing pressure (CCP) decreases (which may indicate either a decrease in intracranial pressure or gradual vasodilation).
A comparison study of cerebral autoregulation assessed with transcranial Doppler and cortical laser Doppler flowmetry

Christian Zweifel, Marek Czosnyka, Andrea Lavinio, Gianluca Castellani, Dong-Joo Kim, Emmanuel Carrera, John D. Pickard, Peter J. Kirkpatrick and Peter Smielewski

Academic Neurosurgical Unit, University of Cambridge Clinical School, Cambridge, UK

Mx < LDx. Is cortex more vulnerable than rest of the brain?
Messages to take home:

• CA can be monitored continuously
• Methods: ARI, phase shift, Mx
• Impaired autoregulation predicts bad outcome in TBI
• In vasospasm autoregulation deteriorates
• In unilateral spasm, carotid artery stenotic disease, TBI with midline shift, unilaterally impaired autoregulation indicates haemodynamically relevant asymmetry