NON-INVASIVE ICP AND VRx AS NON-INVASIVE PRx

Arminas Ragauskas
Disclosure

A.R. - inventor and co-inventor of patented non-invasive ICP absolute value measurement technology and non-invasive cerebrovascular autoregulation monitoring technology,

- co-founder and shareholder and CTO of Boston Neuroscience Corp. (Boston, USA),

- received financial support from Boston Neuroscience Corporation, the US Army and the US Dept. of Defense, the US National Space Biomedical Research Institute, NASA, EU Structural Funds, European Commission, Research Council of Lithuania, etc.
1. **ICP and glaucoma project**: non-invasive ICP measurements on glaucoma patients and healthy volunteers.
   Prof. I. Janulevičienė (MD), L. Šiaudvytytė (MD), A. Daveckaitė (MD), J. Kučinovienė (MD), Prof. B. Siesky (PhD), Prof. A. Harris (PhD), L. Bartusis (PhD), R. Žakelis (PhD)

2. **Non-invasive ICP absolute value measurement projects**: neurological and neurosurgical patients.
   Prof. S. Ročka (MD), Prof. S. Vosylius (MD), A. Preikšaitis (MD), Prof. D. Rastenytė (MD), Prof. K. Petrikonis (MD), V. Matijošaitis (MD), J. Kienzler (MD), S. Bäbler (MD), E. Remonda (MD), Prof. J. Fandino (MD), L. Bartusis (PhD), R. Žakelis (PhD), V. Petkus (PhD), R. Chomskis (MSc)

3. **Cerebrovascular autoregulation projects**: neurosurgical, TBI, cardiac surgery and hemodialysis patients.
   Prof. S. Ročka (MD), Prof. S. Vosylius (MD), A. Preikšaitis (MD), Prof. D. Rastenytė (MD), Prof. R. Benetis (MD), Prof. E. Širvinskas (MD), M. Švagždienė (MD), B. Kumpaitienė (MD), V. Petkus (PhD), R. Chomskis (MSc)
Objective: to test hypothesis on decreased ICP in normal tension glaucoma (NTG) and in high tension glaucoma (HTG) patients.

Methods: ICP measured on 340 (NTG, HTG) patients and healthy controls by using non-invasive aICP meter (Vittamed).

Results: statistically significant differences were found between mean aICP values on NTG,HTG patients and healthy volunteers in supine positions:

- NTG (100 patients): mean ICP=8.52 mmHg (SD=2.4 mmHg)
- HTG (140 patients): mean ICP=8.01 mmHg (SD=2.18 mmHg)
- Control (100 volunteers): mean ICP=9.93 mmHg (SD=2.5 mmHg)

Conclusions: glaucoma is a two pressure (IOP and ICP) disease. ICP is abnormally low in NTG and HTG (p<0.001). Repeated diagnosis after 6 months shows that decrease in translaminar pressure difference IOP-ICP above 1.9 mmHg reduced progression of NTG by 2-folds and decrease above 7.1 mmHg reduced progression of HTG by 4-folds.
Non-invasive ICP in glaucoma

Clinical Study
The Difference in Translaminar Pressure Gradient and Neuroretinal Rim Area in Glaucoma and Healthy Subjects

Lina Siaudvytyte, Ingrida Janulevicienė, Arminas Raguaskas, Laimonas Bartusis, Indre Meilūniene, Brent Siesky, and Alon Harris

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Review Article
Update in intracranial pressure evaluation methods and translaminar pressure gradient role in glaucoma

Lina Siaudvytyte, Ingrida Janulevicienė, Arminas Raguaskas, Laimonas Bartusis, Brent Siesky, and Alon Harris

Intracranial, intraocular and ocular perfusion pressures: differences between morning and afternoon measurements

Lina Siaudvytyte, Akvile Daveckaite, Ingrida Janulevicienė, Arminas Raguaskas, Brent Siesky, Alon Harris

Clinical science
Neuroretinal rim area and ocular haemodynamic parameters in patients with normal-tension glaucoma with differing intracranial pressures

Author affiliations +
Objectives: to perform prospective comparative study of non-invasive ICP meter (simultaneous comparison of invasive and non-invasive ICP measurements) on neurological and neurosurgical patients in order to estimate precision, sensitivity, specificity of non-invasive ICP measurements.

Methods: simultaneous invasive and non-invasive ICP measurements by using non-invasive ICP meter (Vittamed) and invasive ICP meters (“gold standard” ventricular ICP sensors and CSF pressure measurements during lumbar puncture). Study included 121 severe TBI and neurological patients.

Results: ROC analysis of non-invasive ICP measurement data showed the area under ROC curve AUC = 0.913 with sensitivity 73.97 % and specificity 91.89 % when ΔPe = 4.0 mmHg. Correlation coefficient between invasive and non-invasive ICP measurements r=0.82, standard deviation of difference between invasive and non-invasive ICP measurements is SD=2.44 mmHg (precision). Accuracy expressed by confidence interval of systematic error is 0.08 – 0.64 mmHg (p=0.023).

Conclusions: non-invasive ICP measurement method is an only method without a need of patient-specific calibration. It has a wide area of clinical applications outside a neurosurgical ICU.
ROC analysis of noninvasive ICP measurement with \( \Delta P_e = 4 \text{ mmHg} \):
- Sensitivity 73.97 %
- Specificity 81.9%
- AUC 0.91

Accuracy: bias less than 1.0 mmHg
Precision: SD=2.44 mmHg (CL =0.96)
Correlation: \( r=0.82 \)
Comparison of continuous non-invasive and invasive ICP monitoring (pilot study)

Non-invasive two depths TCD-based non-invasive ICP monitoring method was proposed for continuous ICP value monitoring.

Non-invasive ICP(t) monitoring data derived from blood flow velocity (BFV) of intracranial (IOA) and extracranial (EOA) segments of ophthalmic artery were collected simultaneously with invasively measured ICP data (Codman).

7 severe TBI patients with intraventricular ICP sensors were included into the pilot study. The patients were subjected to 1 hour simultaneous invasive and non-invasive ICP(t) monitoring sessions.
Red curve – invasively recorded ICP(t) during 1 hour monitoring session, green curve – processed non-invasively recorded OA blood flow velocity data during the same 1 hour monitoring session.

Bland-Altman plot of simultaneous non-invasive and invasive ICP real-time monitoring data (218 data points).
Background: Post-operative cognitive dysfunction (POCD) occurs in approximately 33-83% of patients after cardiac surgery with cardiopulmonary bypass (CPB). Objectives of the study were to detect the episodes of impaired CA during cardiac bypass surgery and to investigate the association between CA impairments and POCD.

Methods: 59 patients undergoing elective coronary artery graft surgery with CPB. All patients underwent series of neuropsychological tests the day before and ten days after the surgery in order to evaluate cognitive function. VRx(t) and COx(t) was monitored in real-time.

Results: 22 patients (37%) experienced POCD, 37 patients (63%) showed no cognitive deterioration. The duration of the single longest CA impairment event was found reliably associated with occurrence of POCD ($p < 0.05$). The critical duration of the single longest CA impairment event was 5.03 minutes (odds ratio 14.5; CI 3.9-51.8) for studied population.

Conclusions: Prospective clinical study showed that single longest CA impairment may result in post-operative deterioration of mental abilities. The duration of the single longest CA impairment event is the risk factor that is associated with POCD.
Non-invasive CA monitoring: cardiac surgery

Non-invasive automatic VRx(t), CO2(t) monitoring sub-system:
- Invos Cerebral & Somatic monitor
- Ultrasonic CA monitor
- TOF(t) data / 50Hz
- ABP(t) data / 50Hz
- Data acquisition module (Data translator DT9803)
- ABP(t) signal (0-5V)

CA monitoring:
- Cardiac surgery

Diagnosis machine “Primus”
- ABP(t)
- IBV(t) ~ 1/TOF(t)
- rSO2(t)

Draeger “Infinity Delta XL” monitor
- Draeger docking station
- Draeger surgical display controller

Heart-lung machine “Stockert S5” (Sorin Group)
- Blood flow modulation equipment in order to induce slow blood pressure waves according to Prof. K. Brady patented method (T=60 sec, modulation ±5 %)

Invasive ABP sensor SP844 (MEMSACAP Inc.)
- Arterial Cannula with BD Flowswitch (20G x 45mm), inserted in radial or brachial artery
- BD Medical, Becton Dickinson Pty Ltd.
• Non-invasive CA monitoring: cardiac surgery
The case of CA monitoring during the patient’s cardiac surgery. The drop of MAP below the lowest patient-specific CA critical threshold causes the impairment of CA (VRx>0) and risk of “secondary brain injury”.

Non-invasive CA monitoring: cardiac surgery
The longest CA impairment (LCAI) event was significantly longer ($p<0.05$) for the patient group with deteriorated mental abilities comparing to the group without mental disorders.

The critical threshold of duration of LCAI events showing association with the deteriorated mental ability was 302 sec (odds ratio 14.5 and CI 3.9-51.8)
Non-invasive CA monitoring: cardiac surgery

ROC analysis of non-invasively monitored characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AUC</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>Duration of LCAI (VRx&gt;0)</td>
<td>0.81</td>
<td>0.76</td>
<td>0.82</td>
</tr>
<tr>
<td>Dose of LCAI (VRx&gt;0)</td>
<td>0.76</td>
<td>0.76</td>
<td>0.76</td>
</tr>
<tr>
<td>Total time of CA impairment (VRx)</td>
<td>0.74</td>
<td>0.90</td>
<td>0.50</td>
</tr>
<tr>
<td>Total dose of CA impairments (VRx)</td>
<td>0.74</td>
<td>0.90</td>
<td>0.61</td>
</tr>
<tr>
<td>Duration of LCAI (COx&gt;0.6)</td>
<td>0.59</td>
<td>0.76</td>
<td>0.54</td>
</tr>
<tr>
<td>Dose of LCAI (COx)</td>
<td>0.64</td>
<td>0.43</td>
<td>0.87</td>
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<tr>
<td>rSO2</td>
<td>0.65</td>
<td>0.62</td>
<td>0.71</td>
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</tbody>
</table>
CA monitoring studies

Benefit on optimal cerebral perfusion pressure targeted treatment for traumatic brain injury patients

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Association of Severe Traumatic Brain Injury Patient Outcomes With Duration of Cerebrovascular Autoregulation Impairment Events

Aidas Preiksaitis, MD, Solventa Krauksaite, MSc, Vytautos Petkus, DSc, Saulius Rocka, MD, PhD, Romanas Chomsikis, MSc, FH, Teodoro Forcht Dagi, MD, MPH, DMSc, MBA, Arminas Raguaskas, DSc, FBC, FLSHD

Original Research Article
Association between the outcome of traumatic brain injury patients and cerebrovascular autoregulation, cerebral perfusion pressure, age, and injury grades

Vytautos Petkus 4, Aidas Preiksaitis 4, Solventa Kraukaite 4, Erika Zubaviciute e, Saulius Rocka 1, Raimondas Bendenys 1, Arminas Raguaskas 4

Non-invasive Cerebrovascular Autoregulation Assessment Using the Volumetric Reactivity Index: Prospective Study

Vytautos Petkus 4, Aidas Preiksaitis 2,3,4, Solventa Krauksaite 1, Laimonas Bartusis 1, Romanas Chomsikis 1, Yasin Hamarat 1, Erika Zubaviciute 3,4, Saulius Vosylis 3,4, Saulius Rocka 3,4 and Arminas Raguaskas 4
**Background:** In this study, we aimed to determine the clinical applicability of a non-invasive CA monitoring method by performing a prospective comparative clinical study of simultaneous invasive and non-invasive CA monitoring on intensive care patients.

**Methods:** CA was monitored in 61 patients with severe TBI invasively by recording PRx(t) and by simultaneously non-invasively recording volumetric reactivity index (VRx(t)).

**Results:** A linear regression between VRx and PRx averaged per patients' monitoring session showed a significant correlation ($r = 0.843$, $p < 0.001; 95\%$ confidence interval $0.751 - 0.903$). The SD of the difference between VRx and PRx was 0.192; bias was -0.065.

**Conclusions:** The ultrasonic time-of-flight method reflects blood volume changes inside the acoustic path which crosses both hemispheres of the brain. VRx can be used as a non-invasive cerebrovascular autoregulation index in the same way as PRx and VRx can provide diagnostic information about the CA status.
Non-invasive CA monitoring: clinical study

Example of ICP(t), ABP(t), and IBV(t) raw data monitoring, filtered slow waves (solid black curves) and cerebrovascular autoregulation indexes (PRx(t), VRx(t)) recording over a 20-minute time interval. The IBV(t) slow waves are expressed as changes in the time-of-flight signal (∆TOF(t)).
Non-invasive CA monitoring: clinical study

Examples of 2 hour simultaneous PRx and VRx monitoring on TBI patients in coma.
Non-invasive CA monitoring: clinical study

Examples of 2 hour simultaneous PRx and VRx monitoring on TBI patients in coma.
THANK YOU!