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*University of Cambridge*

# 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.

# KTU Health Telematics Science Institute: Team

**1. ICP and glaucoma project:** non-invasive ICP measurments 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)

# Non-invasive ICP in glaucoma

**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

Hindawi Publishing Corporation
Journal of Ophthalmology
Volume 2014, Article ID 937360, 5 pages
http://dx.doi.org/10.1155/2014/937360

Hindawi

*Clinical Study*

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

**Lina Siaudvytyte,[1] Ingrida Januleviciene,[1] Arminas Ragauskas,[2] Laimonas Bartusis,[1,2] Indre Meiliuniene,[1] Brent Siesky,[3] and Alon Harris[1,3]**

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[2] *Telematics Science Laboratory of Kaunas University of Technology, Studentų Street 50, 51368 Kaunas, Lithuania*
[3] *Glaucoma Research and Diagnostic Center, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine, Indianapolis, IN 46202, USA*

Correspondence should be addressed to Ingrida Januleviciene; ingrida.januleviciene@kaunoklinikos.lt

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Clinical science

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

Lina Siaudvytyte[1], Ingrida Januleviciene[1], Akvile Daveckaite[1], Arminas Ragauskas[2], Brent Siesky[3], Alon Harris[3]

Author affiliations +

Acta Ophthalmologica

Acta Ophthalmologica 2015

Review Article

## Update in intracranial pressure evaluation methods and translaminar pressure gradient role in glaucoma

Lina Siaudvytyte,[1] Ingrida Januleviciene,[1] Arminas Ragauskas,[2] Laimonas Bartusis,[1,2] Brent Siesky[3] and Alon Harris[1,3]

[1]Eye Clinic, Lithuanian University of Health Sciences, Kaunas, Lithuania, [2]Health Telematics Science Centre of Kaunas University of Technology, Kaunas, Lithuania, [3]Glaucoma Research and Diagnostic Center, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine, Indianapolis, IN, USA

© Journal for Modeling in Ophthalmology 2016; 1:37-50
*Original article*

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

Lina Siaudvytyte[1], Akvile Daveckaite[1], Ingrida Januleviciene[1], Arminas Ragauskas[2], Brent Siesky[3], Alon Harris[3]

Eye (2015) 29, 1242–1250

www.nature.com/eye

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REVIEW

## Literature review and meta-analysis of translaminar pressure difference in open-angle glaucoma

L Siaudvytyte[1], I Januleviciene[1], A Daveckaite[1], A Ragauskas[2], L Bartusis[1,2], J Kucinoviene[1], B Siesky[3] and A Harris[1,3]

# Non-invasive ICP absolute value measurement projects

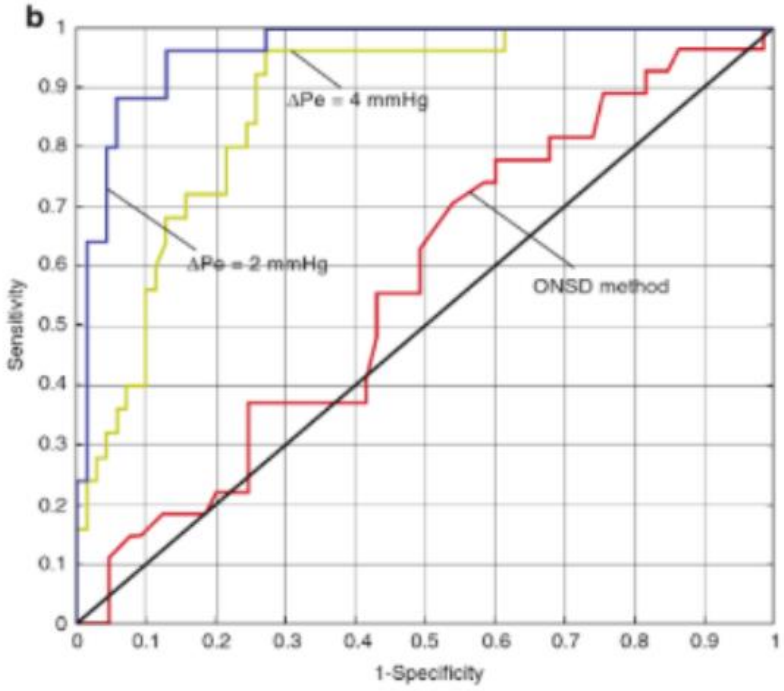
**Objectives:** to perform prospective comparative study of non-invasive ICP meter (simultaneous comparison of invasive and non-invasive ICP measurements) on neurological and neurosurgical patients in order to estimate precision, sensitivity, specificity of non-invasive ICP measurements.

**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).

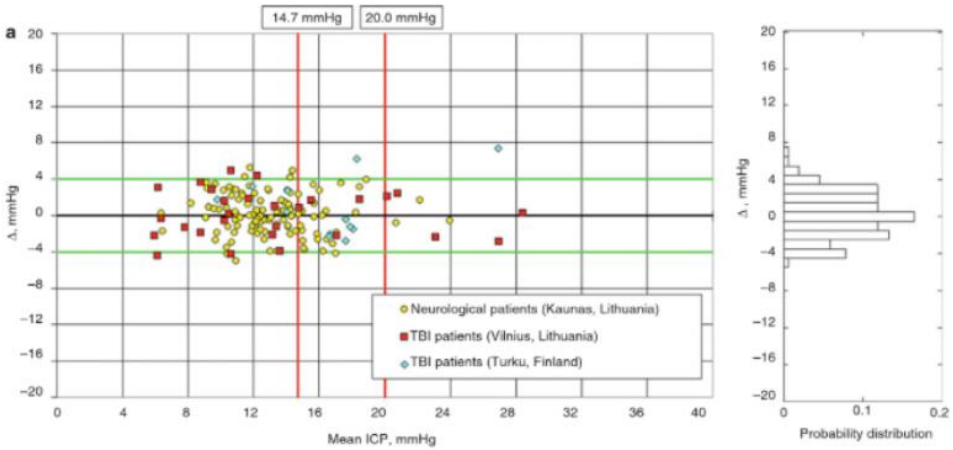
**Conclusions:** non-invasive ICP measurement method is an only method without a need of patient-specific calibration. It has a wide area of clinical applications outside a neurosurgical ICU.

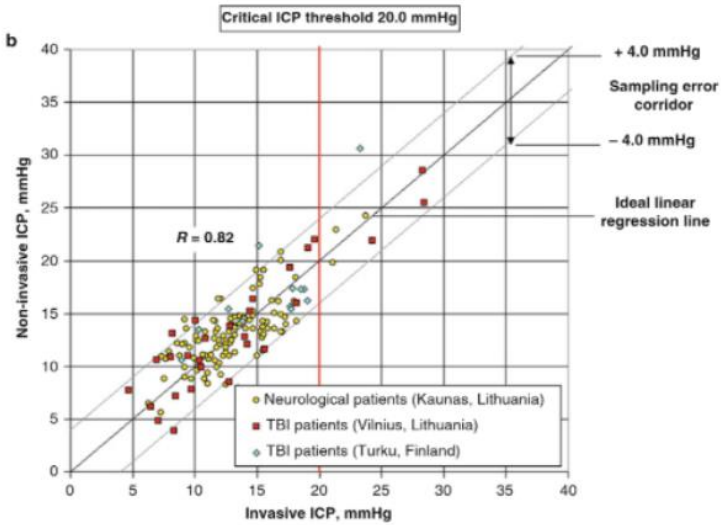
# Non-invasive ICP absolute value measurement projects




ROC analysis of noninvasive ICP measurement with ΔPe = 4 mmHg:

- Sensitivity 73.97 %
- Specificity 81.9%
- AUC 0.91



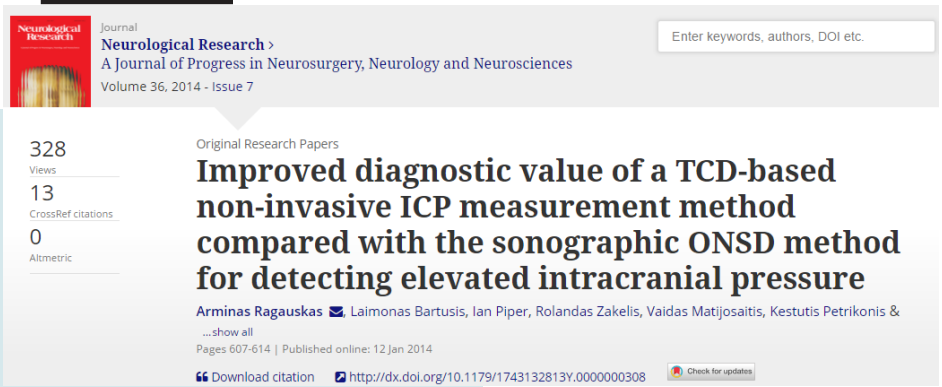




Accuracy: bias less than 1.0 mmHg

Precision: SD=2.44 mmHg (CL =0.96)

Correlation: r=0.82

# Non-invasive ICP absolute value measurement projects



Journal
Neurological Research ›
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Volume 36, 2014 - Issue 7

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Original Research Papers

**Improved diagnostic value of a TCD-based non-invasive ICP measurement method compared with the sonographic ONSD method for detecting elevated intracranial pressure**

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**Clinical assessment of noninvasive intracranial pressure absolute value measurement method**

A. Ragauskas, DSc, V. Matijosaitis, MD, R. Zakelis, MSc, K. Petrikonis, MD, DSc, D. Rastenyte, MD, DHabil, I. Piper, PhD and G. Daubaris, DSc

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Published online before print May 9, 2012, doi: http://dx.doi.org/10.1212/WNL.0b013e3182574f50

*Neurology* May 22, 2012 vol. 78 no. 21 1684-1691

J Clin Monit Comput (2017) 31:459–467
DOI 10.1007/s10877-016-9862-4

ORIGINAL RESEARCH

**Can intracranial pressure be measured non-invasively bedside using a two-depth Doppler-technique?**

Lars-Owe D. Koskinen[1] · Jan Malm[1] · Rolandas Zakelis[2] · Laimonas Bartusis[2] · Arminas Ragauskas[2] · Anders Eklund[3]

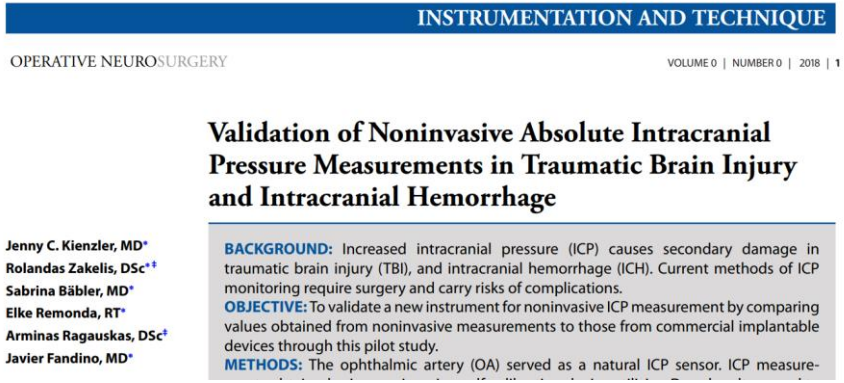


J Neurol Surg A Cent Eur Neurosurg 2015; 76 - P065
DOI: 10.1055/s-0035-1564557

**Validation of Noninvasive Absolute Intracranial Pressure Measurements in Traumatic Brain Injury and Intracranial Hemorrhage: Preliminary Results**

J. C. Kienzler [1], S. Bäbler [1], R. Zakelis [1, 2], E. Remonda [1], A. Ragauskas [2], J. Fandino [1]

[1]Department of Neurosurgery, Kantonsspital Aarau, Aarau, Switzerland
[2]Kaunas University of Technology, Health Telematics Science Institute, Kaunas, Lithuania



INSTRUMENTATION AND TECHNIQUE

OPERATIVE NEUROSURGERY VOLUME 0 | NUMBER 0 | 2018 | 1

**Validation of Noninvasive Absolute Intracranial Pressure Measurements in Traumatic Brain Injury and Intracranial Hemorrhage**

Jenny C. Kienzler, MD*
Rolandas Zakelis, DSc*‡
Sabrina Bäbler, MD*
Elke Remonda, RT*
Arminas Ragauskas, DSc‡
Javier Fandino, MD*

**BACKGROUND:** Increased intracranial pressure (ICP) causes secondary damage in traumatic brain injury (TBI), and intracranial hemorrhage (ICH). Current methods of ICP monitoring require surgery and carry risks of complications.
**OBJECTIVE:** To validate a new instrument for noninvasive ICP measurement by comparing values obtained from noninvasive measurements to those from commercial implantable devices through this pilot study.
**METHODS:** The ophthalmic artery (OA) served as a natural ICP sensor. ICP measure-

# Comparison of contineous 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.

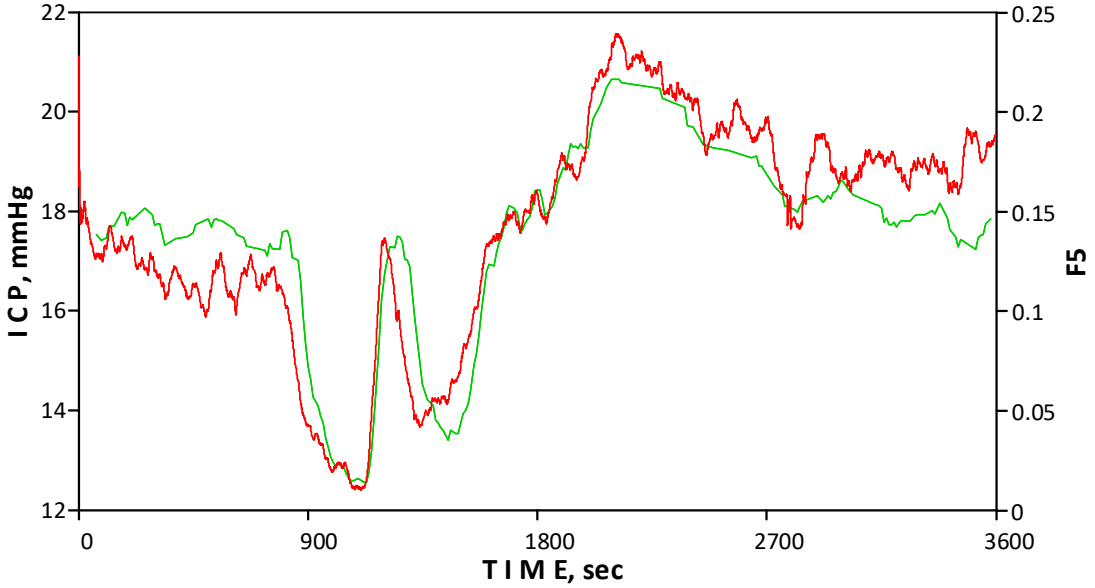
Non-invasive ICP(t) monitoring data derived from blood flow velocity (BFV) of intracranial (IOA) and extracranial (EOA) segments of ophthalmic artery were collected simultaneously with invasively measured ICP data (Codman).

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.

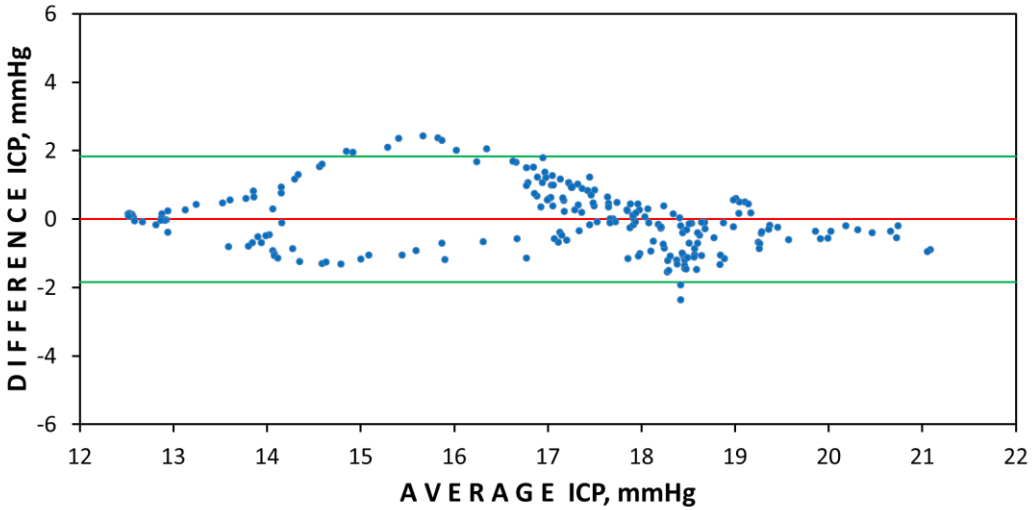
**Invasive and non-invasive ICP(t) monitoring session in neurosurgical intensive care unit.**

# Comparison of contineous non-invasive and invasive ICP monitoring (pilot study)

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).



# Non-invasive CA monitoring: cardiac surgery

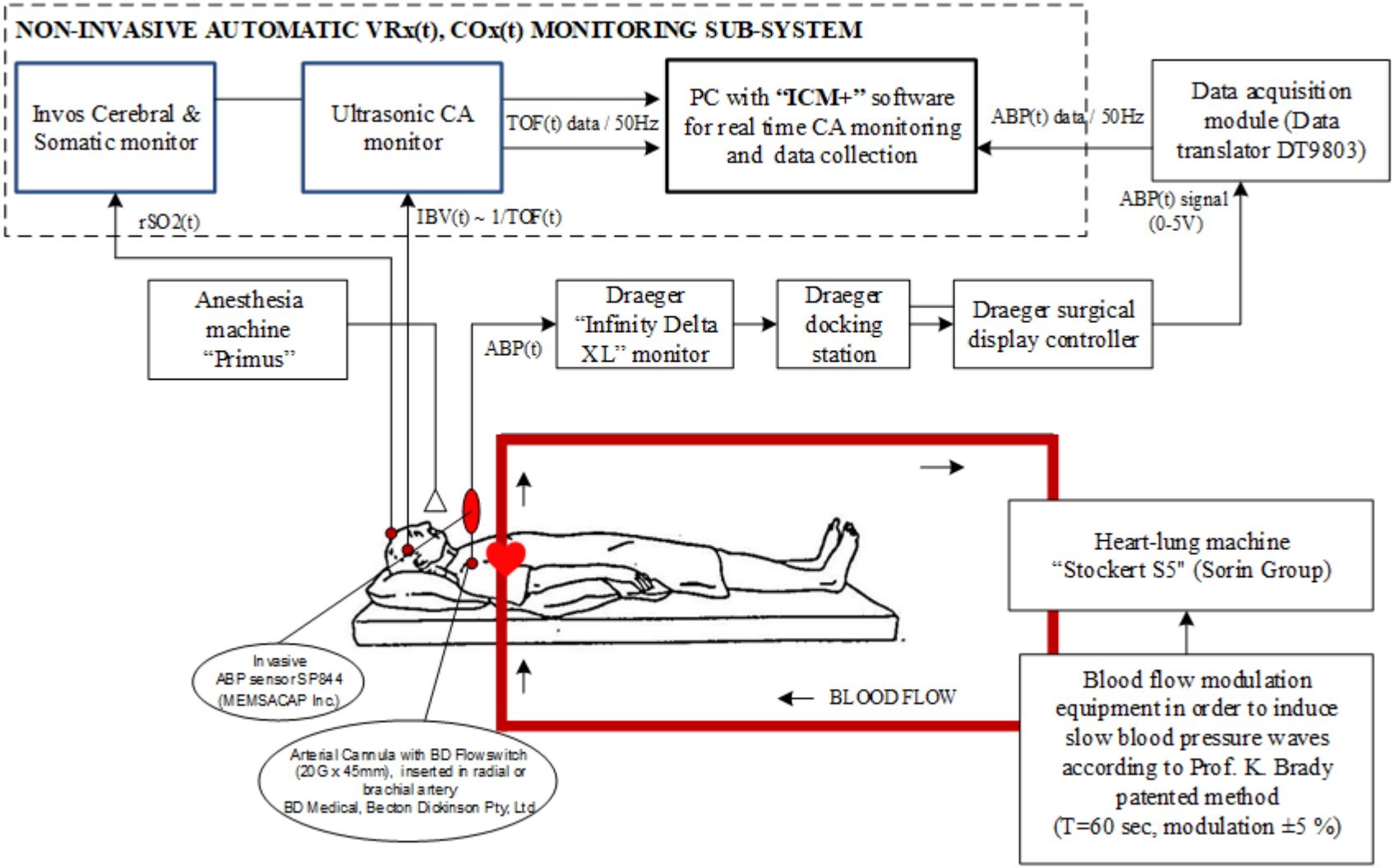
**Background:** Post-operative cognitive dysfunction (POCD) occurs in approximately 33-83% of patients after cardiac surgery with cardiopulmonary bypass (CPB). Objectives of the study were to detect the episodes of impaired CA during cardiac bypass surgery and to investigate the association between CA 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.

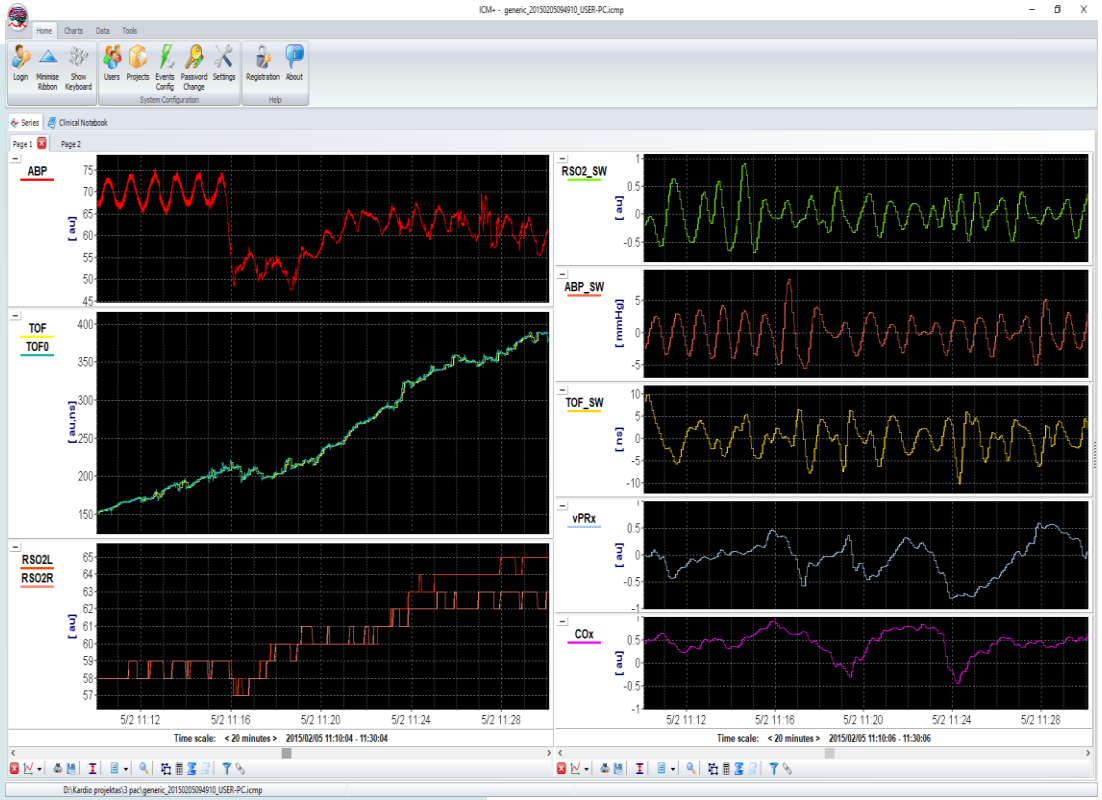
**Results:** 22 patients (37%) experienced POCD, 37 patients (63%) showed no cognitive deterioration. The duration of the single longest CA impairment event was found reliably associated with occurrence of POCD ($p < 0.05$). The critical duration of the single longest CA impairment event was 5.03 minutes (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.

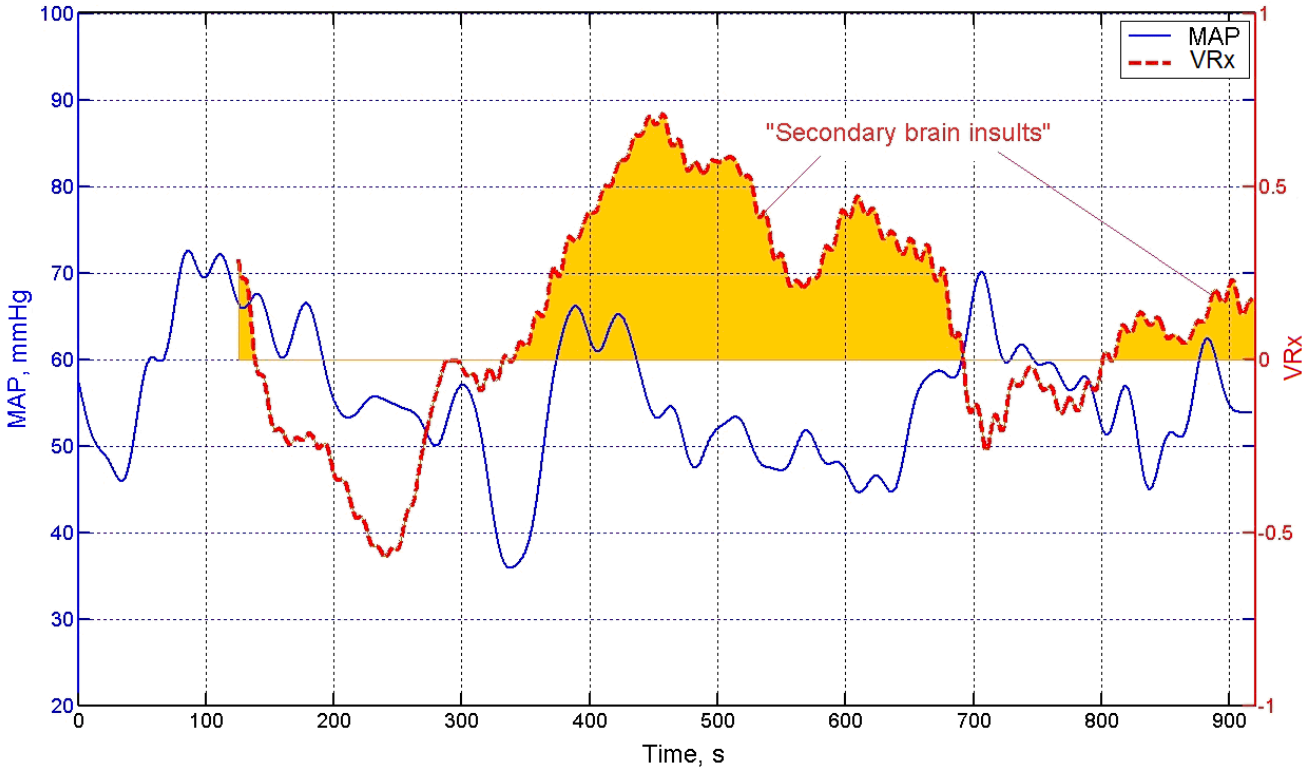
# Non-invasive CA monitoring: cardiac surgery



- **Non-invasive CA monitoring: cardiac surgery**

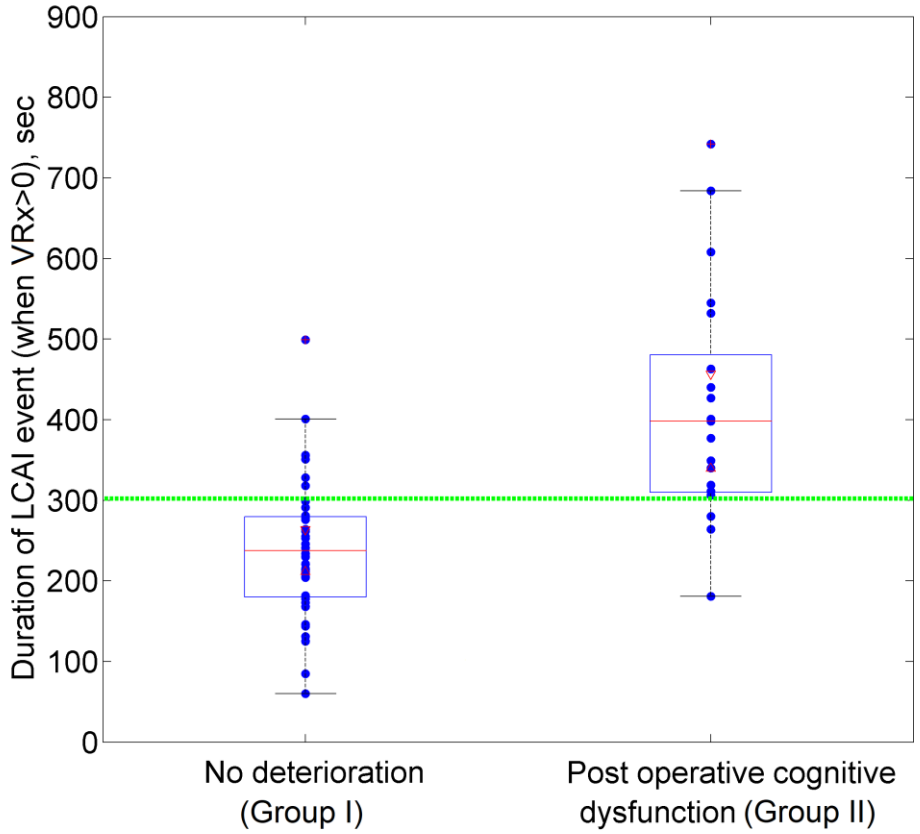



# Non-invasive CA monitoring: cardiac surgery




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".

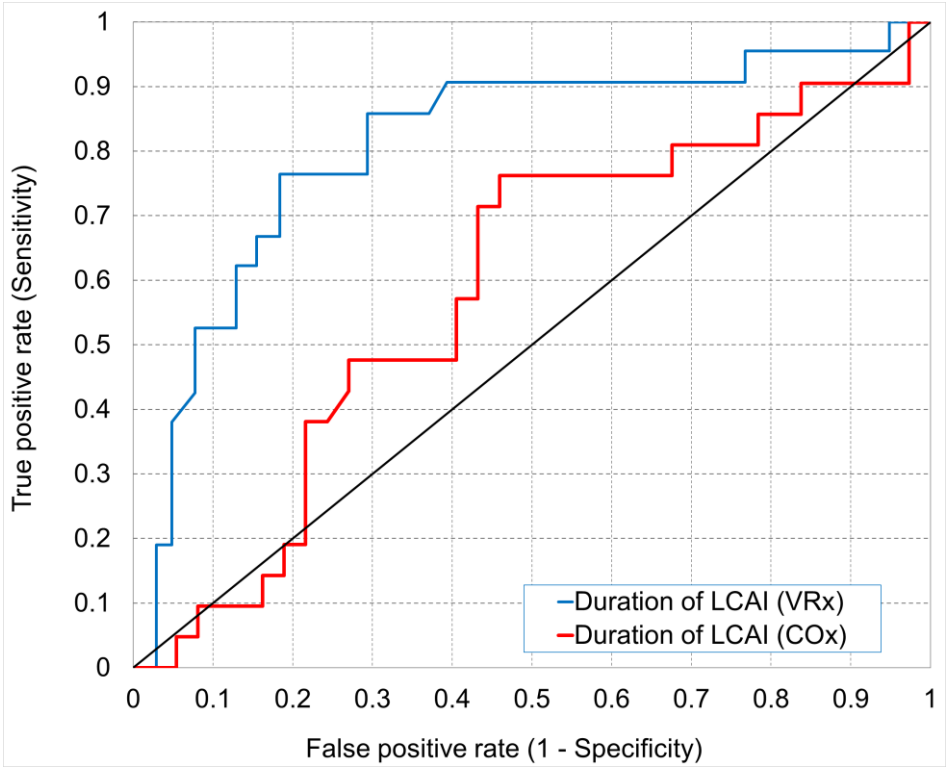
# Non-invasive CA monitoring: cardiac surgery




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

| Parameter | AUC | Sensitivity | Specificity |
|---|---|---|---|
| Duration of LCAI (VRx>0) | 0.81 | 0.76 | 0.82 |
| Dose of LCAI (VRx>0) | 0.76 | 0.76 | 0.76 |
| Total time of CA impairment (VRx) | 0.74 | 0.90 | 0.50 |
| Total dose of CA impairments (VRx) | 0.74 | 0.90 | 0.61 |
| Duration of LCAI (COx>0.6) | 0.59 | 0.76 | 0.54 |
| Dose of LCAI (COx) | 0.64 | 0.43 | 0.87 |
| rSO2 | 0.65 | 0.62 | 0.71 |

# CA monitoring studies

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Novel Method and Device for Fully Non-Invasive Cerebrovascular Autoregulation Monitoring

V. Petkus, A. Preiksaitis, S. Krakauskaite, R. Chomskis, S. Rocka, A. Kalasauskiene, E. Kalvaitis, A. Ragauskas

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Noninvasive Cerebrovascular Autoregulation Monitoring in Hemodialysis Patients: A Pilot Study

Arminas Ragauskas [1], Edita Žiginskienė [2,3], Inga Arunė Bumblytė [2,3,4], Irena Nedzelskienė [5], Justina Kurganaitė [2,3], Romanas Chomskis [1], Saulius Gražulis [3], Vytautas Kuzminskis [2,3], Vytautas Petkus [3]

Journal of Critical Care 41 (2017) 49–55
Contents lists available at ScienceDirect
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journal homepage: www.jccjournal.org

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

Vytautas Petkus, PhD [a], Aidanas Preiksaitis, MD [a,b,c,d], Solventa Krakauskaite, MSc [a,*], Erika Zubaviciute [c], Saulius Rocka, MD [c,d], Daiva Rastenyte, MD [b], Saulius Vosylius, MD [c,d], Arminas Ragauskas, PhD [a]

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[b] Department of Neurology, Academy of Medicine, Lithuanian University of Health Sciences, Lithuania
[c] Clinic of Neurology and Neurosurgery, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[d] Department of Neurosurgery, Republic Vilnius University Hospital, Vilnius, Lithuania

Medicina
Volume 52, Issue 1, 2016, Pages 46–53
Open Access

Original Research Article

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

Vytautas Petkus[a], Solventa Krakauskaitė[a], Aidanas Preikšaitis[b], Saulius Ročka[b], Romanas Chomskis[a], Arminas Ragauskas[a]

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Volume 79, Issue 1
July 2016

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

Aidanas Preiksaitis, MD, Solventa Krakauskaite, MSc, Vytautas Petkus, DSc, Saulius Rocka, MD, PhD, Romanas Chomskis, MSc, FH, Teodoro Forcht Dagi, MD, MPH, DMedSc, MBA, Arminas Ragauskas, DSc, FBC, FLSHD

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Neurocrit Care
https://doi.org/10.1007/s12028-018-0569-x

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ORIGINAL ARTICLE

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

Vytautas Petkus[1*], Aidanas Preiksaitis[1,2,3,4], Solventa Krakauskaite[1], Laimonas Bartusis[1], Romanas Chomskis[1], Yasin Hamarat[1], Erika Zubaviciute[3,4], Saulius Vosylius[3,4], Saulius Rocka[3,4] and Arminas Ragauskas[1]

Minerva Anestesiologica 2018 May 11
DOI: 10.23736/S0375-9393.18.12358-3

language: English

Cerebrovascular autoregulation impairments during cardiac surgery with cardiopulmonary bypass are related to postoperative cognitive deterioration: prospective observational study

Birute KUMPAITIENE [1], Milda SVAGZDIENE [1,2], Edmundas SIRVINSKAS [1,2], Virginija ADOMAITIENE [1], Vytautas PETKUS [3], Rolandas ZAKELIS [3], Solventa KRAKAUSKAITE [3], Romanas CHOMSKIS [3], Arminas RAGAUSKAS [3], Teodoro F. DAGI [4,5], Rimantas BENETIS [1,2]

# Non-invasive CA monitoring: TBI patients

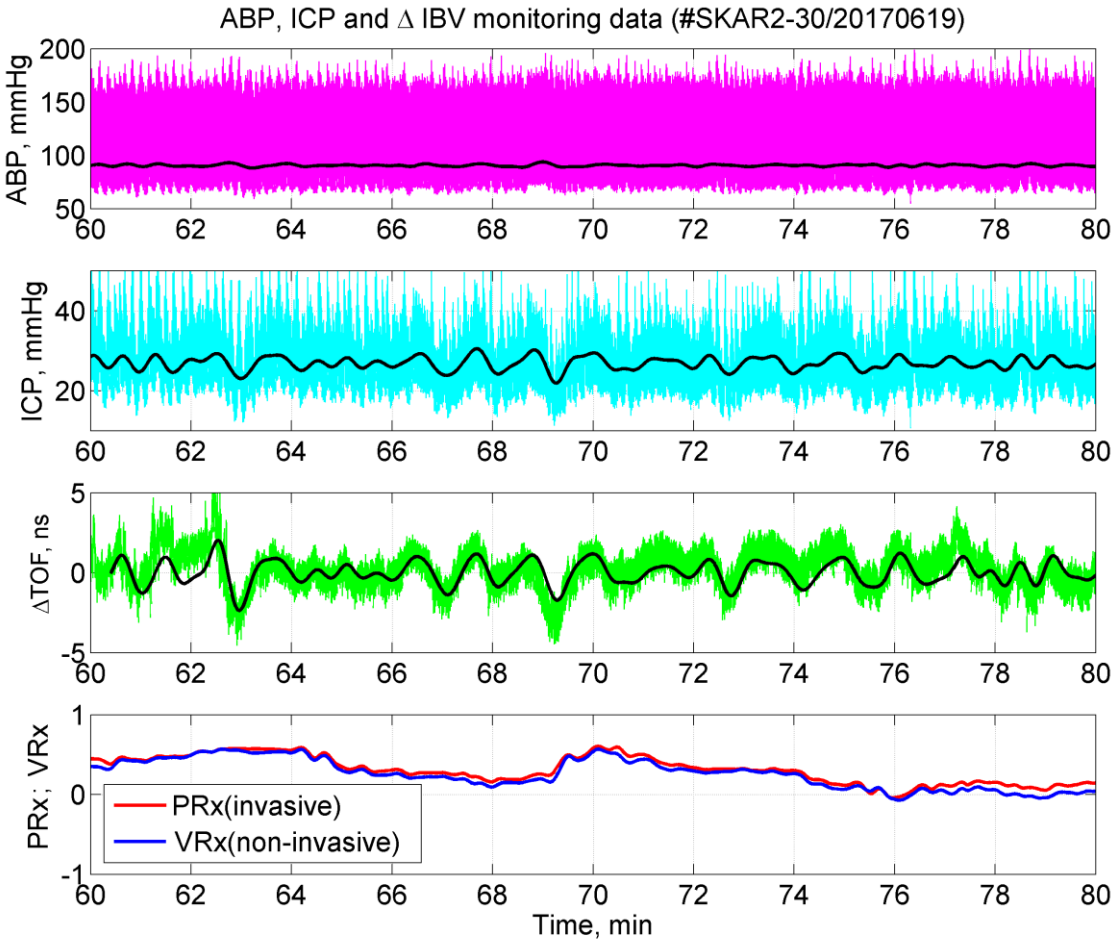
**Background:** In this study, we aimed to determine the clinical applicability of a non-invasive CA monitoring method by performing a prospective comparative clinical study of simultaneous invasive and non-invasive CA monitoring on intensive care patients.

**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.

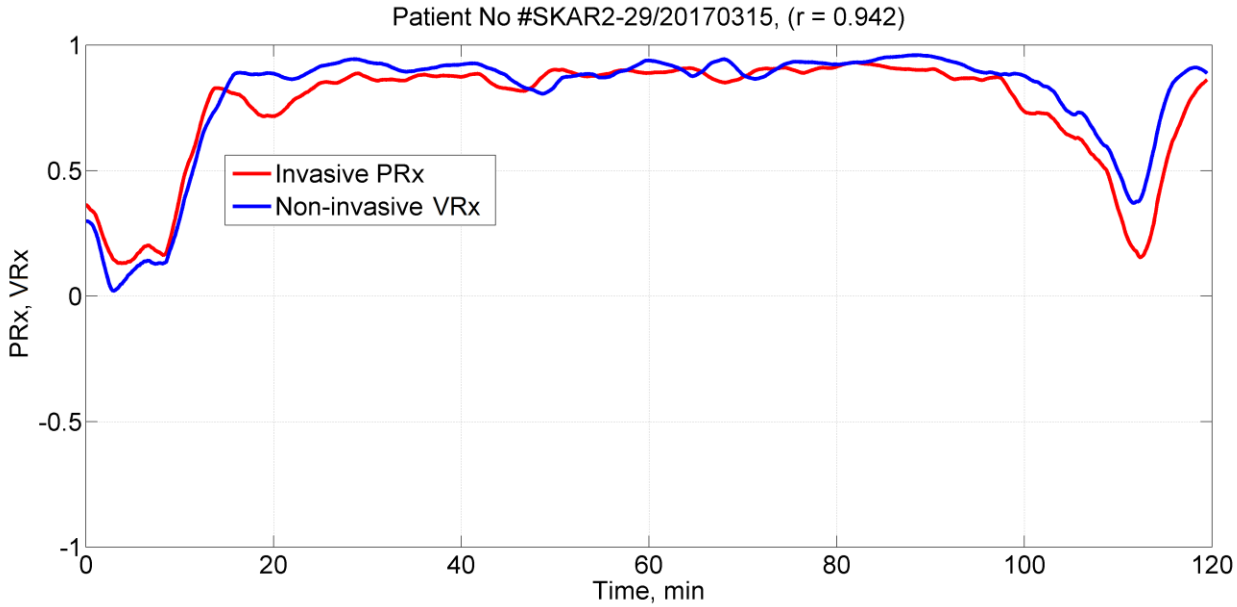
**Conclusions**: The ultrasonic time-of-flight method reflects blood volume changes inside the acoustic path which crosses both hemispheres of the brain. VRx can be used as a non-invasive cerebrovascular autoregulation index in the same way as PRx and VRx can provide diagnostic information about the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

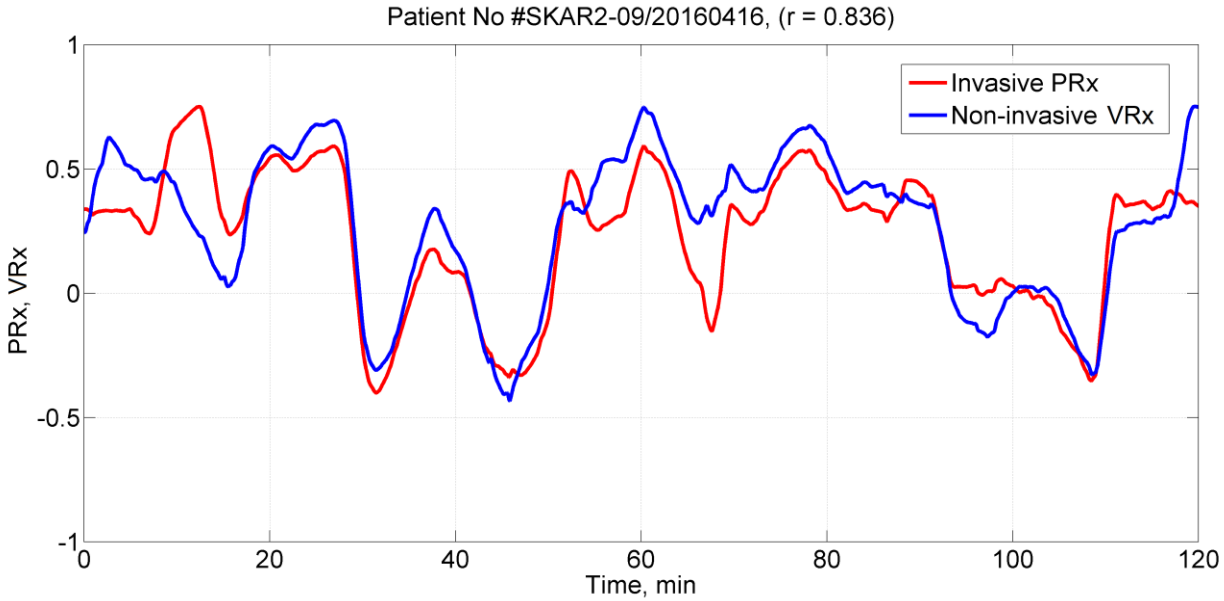
# Non-invasive CA monitoring: clinical study




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 (ΔTOF(t)).

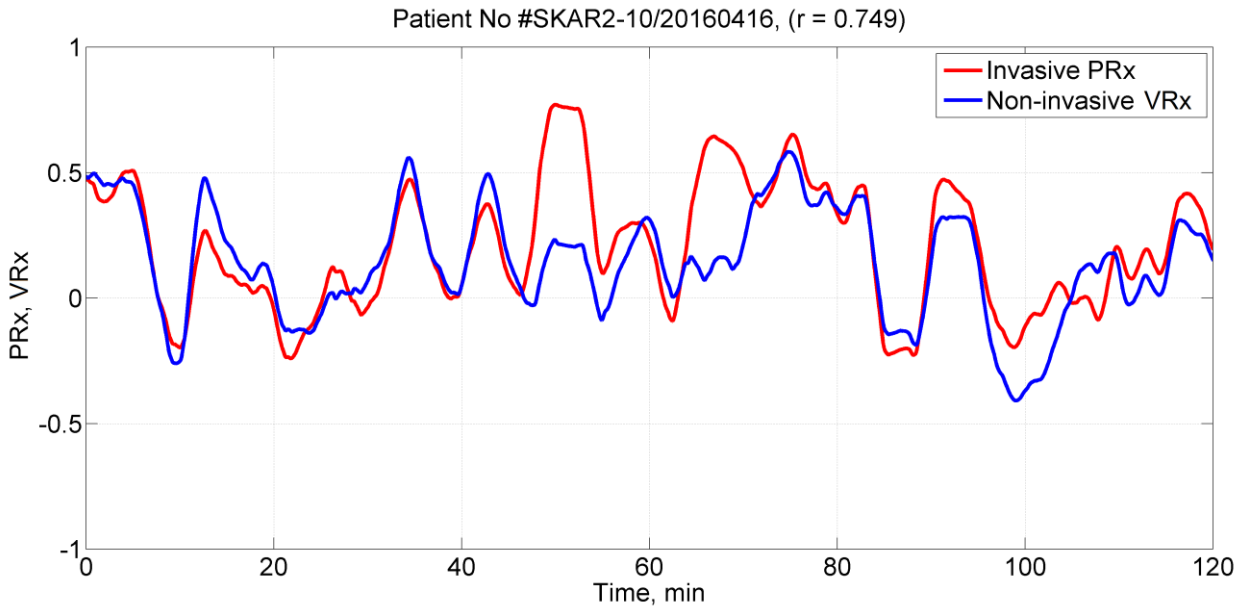
# Non-invasive CA monitoring: clinical study

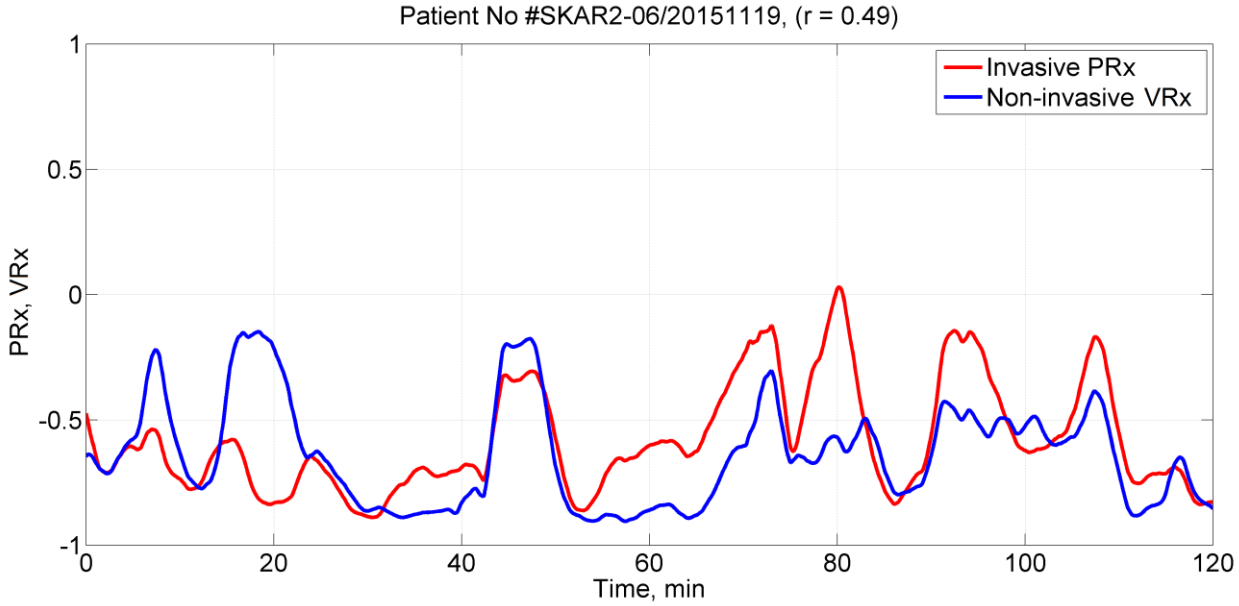



**Examples of 2 hour simultaneous PRx and VRx monitoring on TBI patients in coma.**

# Non-invasive CA monitoring: clinical study




**Examples of 2 hour simultaneous PRx and VRx monitoring on TBI patients in coma.**

# THANK YOU !

Health Telematics Science Institute at KTU Santaka Valley, Kaunas, Lithuania

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