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Monitoring of mechano-elastic parameters of brain using Transcranial Doppler Ultrasonography

Monitorowanie parametrów mechano-elastycznych mózgu z zastosowaniem przezczaszkowej ultrasonografii dopplerowskiej

Introduction

The three major compensatory compartments of the brain: arterial blood, venous blood and cerebrospinal fluid (CSF) are responsible for global cerebrospinal pressure-volume compensation. The new techniques based on Transcranial Doppler ultrasound have been recently proposed, based on the model of continuous, non-pulsatile venous blood outflow. The model of cerebrovascular impedance has been used for example to determined the critical closing pressure or to describe the relationship between Pulsatility Index (PI) and CrCP [1].

Hypothesis

The **hypothesis** is that the new and improved models can be utilized, which taking into account pulsatile venous blood outflow using either arterial blood and jointly: arterial blood and intracranial pressure pulsations. Such a scenario will give better reflection of physiological phenomena associated with gradual rise in ICP, recorded during infusion study.

Within a course of my PhD project the proposed models will be studied in patents suffering from hydrocephalus. The parameters, like compartmental compliance of arterial bed (Ca), compliance of CSF and venous space (Ci), along with critical closing pressure (CrCP) and cerebrovascular time constant will be analysed.

Parameters:

1. Pulsatile cerebral arterial blood volume

According to changes in cerebral blood volume (ΔCBV) during a cardiac cycle can be calculated as an integral of the difference between pulsatile arterial inflow (CBFa) and venous outflow (CBFv) of cerebral blood, Originally constant flow forward was used (CFF):

$$\Delta CBV_{cff} = \int (CBFV_a(t) - meanCBFV_a(t))dt$$

Proposed modification of pulsatile flow forward (PPF; forward to resistive arterioles, capillaries, veins etc.):

$$\Delta CBV_{pff} = \int (CBFV(t) - \frac{ABP(t) - ICP(t)}{\frac{\overline{ABP(t) - ICP(t)}}{\overline{CBFV}}})dt$$

2. Compartmental compliances of brain

Knowing amplitude of ΔCBV (CBV_{AMP}) amplitude of arterial blood pressure and ICP, compartmental compliances can be calculated:

$$C_a = \frac{CBV_{AMP}}{ABP_{AMP}}$$

$$C_i = \frac{CBV_{AMP}}{ICP_{AMP}}$$

3. Cerebrovascular time constant.

This is a product of arterial compliance and cerebrovascular resistance. It is theoretically proportional to time needed for arterial blood from the aspect of MCA insonation to a hypothetical border of cerebral arterioles and capillaries.

$$\tau = C_a \cdot CVR = \frac{CBV_{AMP}}{ABP_{AMP}} \cdot \frac{meanABP}{meanCBFV}$$

4. Critical closing pressure (CrCP)

CrCP is the arterial blood pressure (ABP) threshold, below which small arterial vessels collapse and blood flow ceases. It was first described by Burton [2]. Theoretically, cerebral CrCP is the sum of intracranial pressure (ICP) and vascular wall tension (WT) [3]. With the introduction of transcranial Doppler ultrasonography it became possible to assess CrCP noninvasively by comparing the waveforms of cerebral blood flow velocity (CBFV) and ABP [4, 5, 6]. One of the methods, proposed by Aaslid [7, 8] is based on linear regression analysis between single pulse of CBFV and ABP as an intercept point of the regression line with the X axis (ABP) [9].These methods, however, may provide an inaccurate estimation of CrCP as they can produce negative values of CrCP that cannot be interpreted physiologically [10]. Recently Varsos et al. [11] proposed a new methodology for CrCP estimation based on a cerebrovascular impedance model [12] as a function of cerebral perfusion pressure (CPP), ABP, cerebrovascular resistance (CVR), arterial compliance (Ca), and heart rate (HR), assuming constant blood flow forward. Important added value of this method of CrCP calculation is the fact that it is not providing the nonphysiological negative values of pressure, as was in the case of Aaslid's method. However, the originally used **constant flow model** assumes that the a low pulsatility venous outflow (CBFv) may be approximated by constant flow equal to averaged arterial inflow (meanCBFa).

Aim of the dissertation

The main goal of my research is to analyse the changes of mechano-elastic parameters in scenario of a controlled increase in intracranial pressure (ICP) induced by infusion tests, performed in patients with suspected normal pressure hydrocephalus (NPH). The subject of proposed research are two main mechanisms determining components of intracranial compliance evaluated based on pulsatile changes of cerebral blood flow velocity:
a) vascular component incorporated in critical closing pressure (CrCP),
b) component related to cerebrospinal fluid circulation: intracranial compliance (Ci).
c) cerebrovascular time constant τ
The particular hypotheses to be verified are the following:
a) During infusion and plateau phase, simultaneously with controlled increase of intracranial pressure, changes of intracranial compliance and critical closing pressure appear in opposite directions (increase of CrCP, decrease of Ci).
b) CrCP and Ci variations may reflects changes in cerebrospinal compensatory reserve.
c) Both CrCP and Ci may be monitored continuously. Methods utilizing these parameters would have essential clinically relevant influence on understanding brain dynamics in hydrocephalus.
d) Introduction of PFF model, decreases previously estimated value of τ from average 0.2 second to 0.1 second. Changes in τ during controlled rise in ICP should be re-evaluated.

Completed work

Assessment of current progress is 60%. The concept of doctoral thesis is a consequence of my studies performed during the internship completed at Cambridge University. Using ICM+ software (Intensive Care Monitor – Cambridge Enterprise, Cambridge, UK, http://www.neurosurg.cam.ac.uk/icmplus/) I designed calculation profile comprising an algorithm determining such hemodynamic brain parameters as: arterial compliance, cerebrovascular resistance, intracranial compliance, time constant of cerebral arterial bed and critical closing pressure.

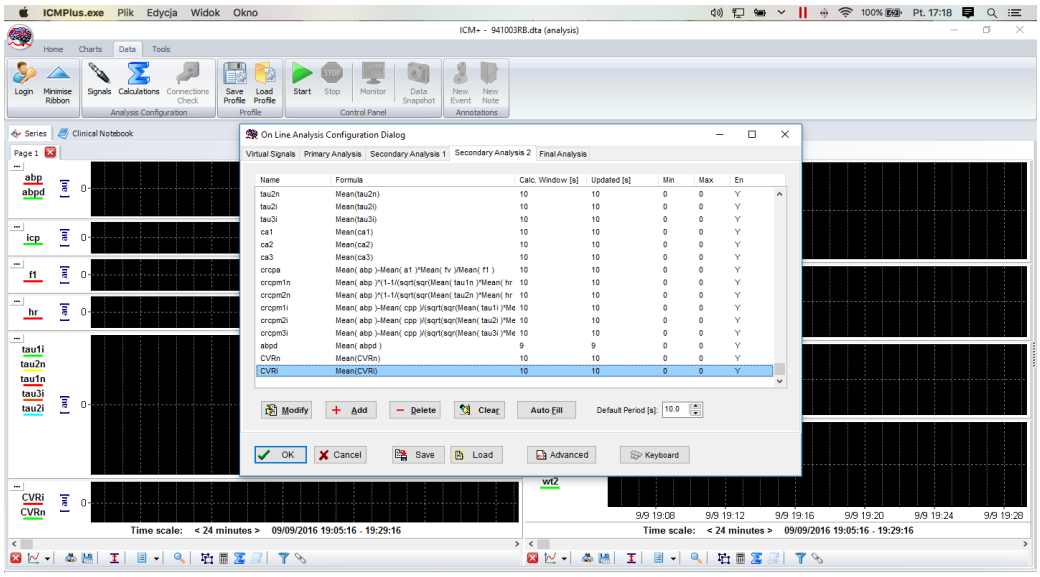

Figure 1 – the view of the ICM+ dialog window with the calculation profile.

The parameters were determined on the basis of such registered signals as: intracranial pressure (ICP), arterial blood pressure (ABP) and cerebral blood flow velocity (CBFV) evaluated from the middle cerebral artery (MCA) by Transcranial Doppler ultrasonography (TCD).

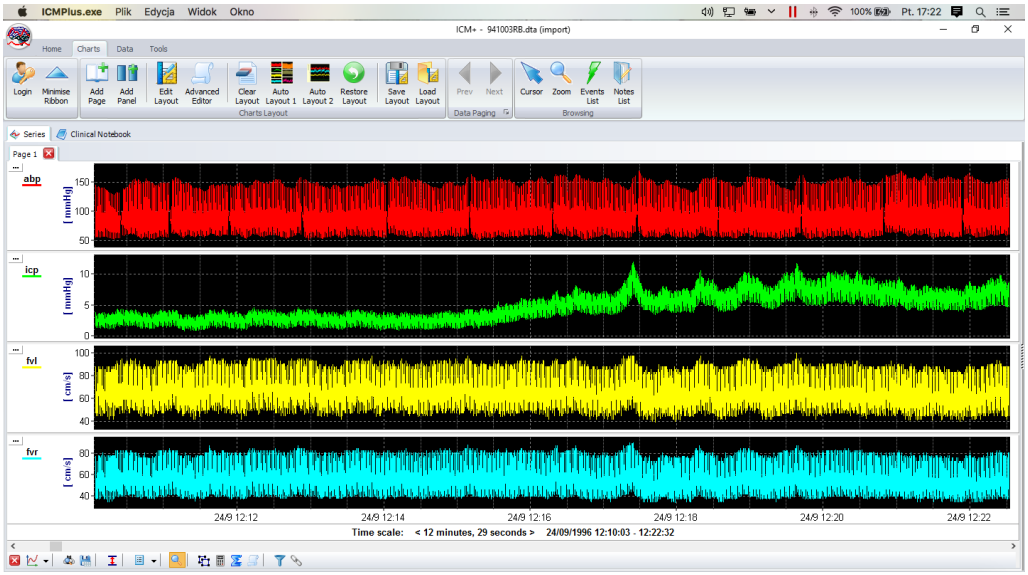

Figure 2 – Example of time trends of basic signals: arterial blood pressure, intracranial pressure and both sides' cerebral blood flow velocity.

Although, the initial studies were made on the basis of retrospective analysis of ICP, ABP and CBFV, I learned how to perform signals recordings and apply it in patients studied in Mossakowski Medical Research Centre in Warsaw.

The Bland–Altman plots obtained for pooled data from both phases of the test (baseline and infusion) demonstrate a moderately good agreement between the Aaslid's method and both model–based methods (invasive and non–invasive ones) for CrCP calculation. The biggest discrepancies were seen when the $CrCP_A$ demonstrated negative values. On the other hand, a very good agreement was found between invasive and non–invasive model–based methods.

According to Burton's idea [1, 2] vascular wall tension can be expressed as the difference between CrCP and intracranial pressure and represent active vasomotor tone. WT was calculated using two methods, the Aaslid's CrCP conception ($WT_A = CrCP_A - ICP$) and cerebrovascular impedance methodology ($WT_{inv} = CrCP_{inv} - ICP$). Having available CrCP and WT, the ratio of these parameters was determined. WT shows a tendency to decrease due to compensating vasodilatation. The values of WT_Awere lower than impedance–model based estimator ($p<0.0001$). Changes in in cerebrovascular resistance (ΔCVR) was strongly correlated with changes in wall tension calculated by invasive model–based method ΔWT_{inv} $R=0.7564$, $p<0.0001$.

There is a significant correlation between the analyzed methods of CrCP determining. All three indices are in agreement, although the best agreement between impedance model–based methods (invasive and non–invasive) is observed. The strongest correlation between ICP and CrCP occurs in case of application invasive impedance model–based method, which can be explained due to

the use of ICP in the $CrCP_{inv}$ calculation formula. Rising ICP lead to increases in all three estimators of CrCP with vascular wall tension (WT) decreasing, signifying vasodilatation. Correlation between CrCP and ICP may be disturbed by decrease in WT during infusion.

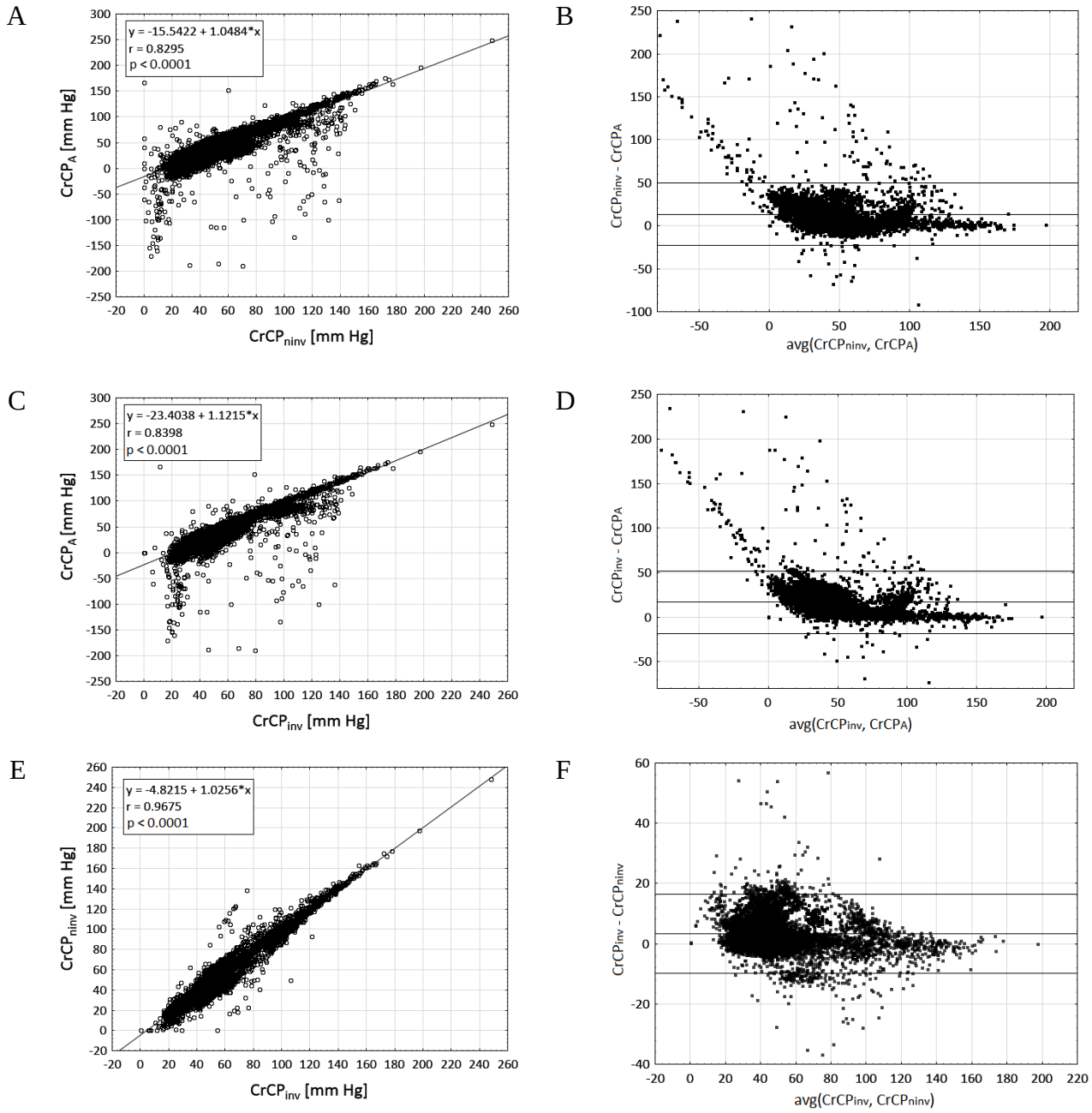

Figure 3 -Scatterplots of relationship between difference method of critical closing pressure calculation A) non–invasive model–based method (CrCPninv) vs. Aaslid's method (CrCPA), B) invasive model–based method (CrCPinv) vs. Aaslid's method (CrCPA) C) invasive vs. non–invasive model–based method (CrCPinv vs. CrCPninv).The Bland–Altman plots for comparing difference between A) CrCPninv and CrCPA B) CrCPinv and CrCPA C) CrCPinv and CrCPninv for all measurement points. Horizontal lines are drawn at the mean difference and ± 2 times standard deviation (SD) of the differences.

Further works

In the next step of my research, I plan to implement to an existing algorithm, a new model for calculating the mechano-elastic parameters of brain, not only the CrCP but compliances of brain, wall tension and time constant too. After calculating all the parameters, I would like to compare constant flow model and new pulsatile flow model including all four parameters aforementioned (Ca, Ci, CrCP and τ). If the results of my research fulfil the assumptions, the thesis will be proven.

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