

Clinical Assessment of the Accuracy of ICP Non-invasive Measurement

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Introduction

Brain injury is one of the main reasons of young patients death in European Union and other countries of the world. The pathophysiological processes in the injured brain proceed quickly and, therefore are very risky for human life. The intracranial pressure (ICP) is a fundamental physiological parameter with the same importance as the arterial blood pressure (ABP), which is a fundamental parameter of the blood circulation in the body. Raised intracranial pressure must be recognized and managed properly, because there is a considerable risk in traumatic brain injury (TBI) patients of secondary brain damage with long term severe disability [1].

Changes of intracranial pressure in cases of many neurological diseases have a big impact to the pathogenesis and progression of these diseases. Only invasive technologies for diagnostics of ICP are available today. Such procedures require either the placement of a catheter-tip strain gauge device into the brain tissue directly or a fluid filled catheter placed into the cerebral spinal fluid space within the brain. This exposes the patients to the risk of infection (5%), bleeding, and leak of fluids or loss of other body tissue, pain, and hyperthermia as well as risks related to anaesthetics. Moreover uncertainties of the best solid state invasive absolute ICP (aICP) sensors are within the limits from 4.2 mmHg up to 19.2 mmHg [2, 3, 7]. Uncertainties of invasive devices vary in range wide enough. Physicians using these devices are not aware of the exact accuracy of ICP monitoring data. Uncertainties of ICP monitoring can create situations when the treatment decisions based on uncertain ICP data would be wrong or even dangerous for patients. To avoid these problems, non-invasive ICP monitoring technology with high accuracy is expected.

The ideas for non-invasive ICP measurement have been appearing since 1980. A lot of methods and technologies for finding the objects or physiological characteristics of cerebrospinal system that would be related to the ICP and monitor them non-invasively have been patented by

many authors. Most of the proposed monitoring technologies are based on ultrasound and are capable of monitoring physiological properties, such as blood flow in intracranial or intraocular vessels, pulsations of the cerebral ventricles, cranium diameter or acoustic properties of the cranium. However, all these methods have the same problem - calibration procedure is needed for the system "individual patient – non-invasive ICP meter.

New innovative method for a non-invasive absolute ICP value measurement

An innovative method [3, 8-10] for a non-invasive absolute ICP (aICP) value measurement without the individual calibration problem has been created in Telematics Scientific Laboratory of Kaunas University of Technology. New non-invasive aICP meter has the same ultrasonic transmission parameters as existing transcranial Doppler (TCD) diagnostic devices, correspond safety standards and is secure for patients. It is expected, that this system reach the market in the near future. But further validation and identification of clinical situations in which it could be used instead of invasive monitoring is required.

Method [3, 8-10] is based on two-depth TCD technique for aICP and external absolute pressure (aPe) comparison. The intracranial segment of the ophthalmic artery (OA) is compressed by aICP. The extracranial segment of OA is compressed by the controlled external pressure applied to the tissues surrounding the eye ball. The pressure balance is achieved when the absolute value of external pressure aPe is equal to the aICP (Fig. 1).

The blood flow parameters in both OA segments are almost equal independently of the absolute value of arterial blood pressure, hydrodynamic resistance of the eye vessels, the pressure inside the eye ball and the initial absolute values of the blood flow parameters in the case $aPe=aICP$. The specially designed two depth pulse wave transcranial Doppler device is applied to identify simultaneously the blood flow velocities in the intracranial segment and ex-

tracranial segment of the eye artery. The difference between those velocities ΔV is used to control the pressure in pneumatic camera which is in a sealing engagement with a perimeter around the eye. When external pressure P_{EXT} in the pneumatic camera causes ΔV to approach close to zero value, in that case P_{EXT} becomes an indicator of the intracranial pressure absolute value, i. e. $aICP = aPe = P_{EXT}$ (Fig. 1) [3, 4, 8-10].

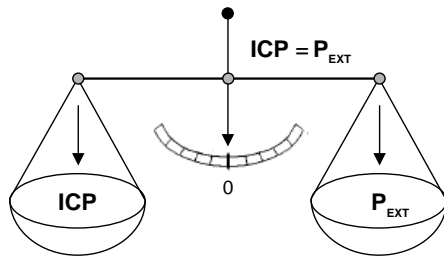


Fig. 1. The principle of absolute ICP non-invasive measurement method. The difference between OA intracranial segment and extracranial segment blood flow velocities must be minimized up to zero for obtaining a balance between aICP and external pressure $P_{EXT} = aPe$ applied to the tissues surrounding the eye ball

The structure of non-invasive ICP value meter is showed in Fig. 2

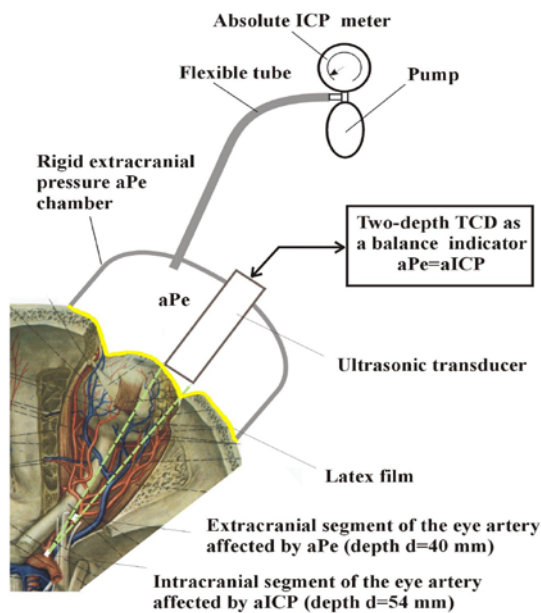


Fig. 2. Structure of non-invasive absolute ICP value meter

This device will be the first measurement device of its kind, being able to obtain aICP values by a fast and easy non-invasive way, since current methods are based on invasive methods. Such device does not need individual calibration.

The principle of the accuracy evaluation of new non-invasive method

In order to evaluate the accuracy of new non-invasive absolute ICP value meter a clinical study will be held. In this study it will be seeking to compare this new non-invasive method with invasive „golden standard“ ICP

measurement method. Neurological patients appointed to standard lumbar puncture procedure will be selected to this research. Patients with symptoms of absolute ICP value above 25 mmHg will be excluded from the study because lumbar puncture is not applicable then $ICP > 25$ mmHg.

Non-invasive ultrasound Doppler device for measurement of the ophthalmic artery blood flow parameters

Blood flow signals in internal and external ophthalmic artery segments will be measured with non-invasive orbital Doppler device. Both blood flow segments will be measured at the same time with modified ultrasound transducer. Doppler signals are different in their parameters (pulsation index, mean velocity, etc), because internal ophthalmic artery segment is compressed by ICP. If external ophthalmic artery segment is compressed by external pressure which is equal to ICP, blood flow parameters in both OA segments would be approximately the same. Thus, ICP would be equal to the external pressure. Mechanical head frame with fixed ultrasonic TCD transducer will be added to close eye lid of a patient. Special acoustic conductive gel will be used for a better ultrasonic contact. Elastic pillow, which is around transducer, will be pumped up step by step increasing pressure until 28 mmHg. Such pressure has no damage for patient health. Transducer and external pressure device are connected to computer with software dedicated to measure blood flow parameters in both ophthalmic artery segments. The value of external pressure, when ophthalmic artery blood flow parameters in both segments are the same, will be fixed and expressed automatically in absolute units (mmHg) [3, 4, 8-10].

Lumbar puncture and cerebrospinal fluid pressure measurement

Non-invasive ICP measurements will be performed simultaneously with “golden standard” invasive ICP measurements. CSF column height measurement method is a “golden standard” invasive ICP measurement method ($SD < 0,21$ mmHg).

Lumbar puncture will be performed by a standard method. Patient will lie on side in horizontal position with knees pulled up toward the chest, and chin tucked downward. After the back is clean, local numbing medicine (lidocaine 2ml 2%) will be injected into the lower spine. Then a spinal needle (22 GA) will be inserted into the lower back area. Once the needle is properly positioned, CSF is collected from subarachnoid space. Trident distributed tube with stopped spigot is connected to the needle. 2 pressure-gauge parts, calibrated from 0 to 40 cmH₂O, are connected to the upper tube part and CSF pressure is measured (Fig. 3).

Patients only with free circulation of CSF between intracranial media and spinal canal will be included into our study. CSF pressure is equal to ICP in such cases. Patients with $ICP \geq 25$ mmHg will be excluded from the study because it is dangerous for patients to perform the lumbar puncture in such cases.

When invasive/non-invasive aICP measurements will be finished, it would be possible to compare values of

aICP and invasive “golden standard” ICP and to assess the accuracy of non-invasive aICP meter.

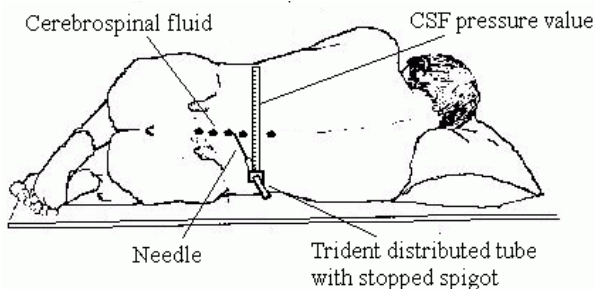


Fig. 3. Lumbar puncture procedure. Cerebrospinal fluid pressure measurement

The algorithm of simultaneous non-invasive and invasive „golden standard” ICP measurements

Clinical study of simultaneous invasive and non-invasive aICP measurements will be performed on neurological patients at Neurological clinics, Kaunas University of Medicine. The proposed algorithm of invasive/non-invasive aICP measurements is showed in Fig. 4

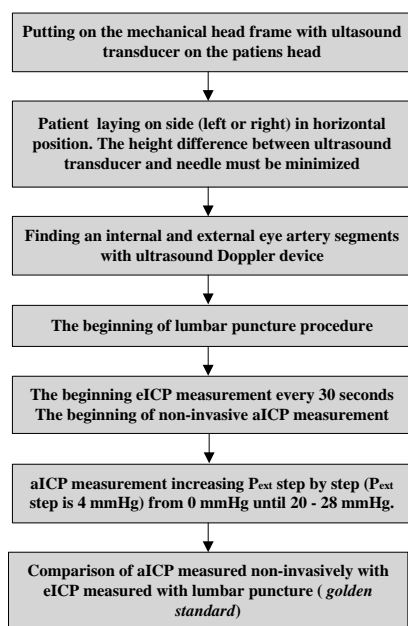


Fig. 4. The algorithm of simultaneous non-invasive and invasive „golden standard” ICP measurements on neurological patients

This ongoing study will be completed when the number N_p of simultaneous non-invasive and “golden standard” invasive measurements will be sufficient for statistically significant evidence about the accuracy of non-invasive aICP meter under study with $CI \geq 95\%$ ($N_p > 40$).

Ethical issues

During the development of this clinical study proposal and research approach it will be done with consideration of the ethical requirements according to the law of Lithuania on biomedical research involving human subjects [5] and according to World Medical Association Declaration

of Helsinki “Ethical Principles for Medical Research Involving Human Subjects” [6].

According to the Declaration of Helsinki B. Principles for all medical research p. 14, the clinical research protocol will be included with the information regarding funding, institutional affiliations, other potential conflicts of interest. The clinical research protocol will be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins taking in consideration the laws and regulations of the countries in which the research is to be performed.

All neurological patients will be thoroughly informed on procedure and expected outcome. An informed written consent form will be issued to all volunteers for signing which is a prerequisite for participating in the clinical testing. Clinical testing on humans inevitably means that there will be a requirement to record data. All personal data will be kept strictly confidential.

Benefit of research

Non-invasive aICP measurement method would be very useful in diagnosing raised ICP in cases of such diseases as idiopathic hypertonic headache, malignant medium brain artery stroke, bleeding to brain, brain tumours, meningitis, liver transplantation hemodialysis, etc, when invasive ICP measurement is not available.

We expect that ICP measured non-invasively and the “golden standard” ICP measured simultaneously according to the algorithm of Fig.4 will be analysed using Bland and Altman plot and other methods of medical statistics. We expect to obtain the clinical statistically significant evidence about the high accuracy of proposed non-invasive absolute ICP measurement method.

Conclusions

- Uncertainties of the best solid state invasive absolute ICP (aICP) sensors are within the limits from 4.2 mmHg up to 19.2 mmHg. Such sensors can not be calibrated in situ.
- A non-invasive absolute ICP (aICP) measurement method was proposed which at first time does not need calibration of the system “individual patient non-invasive aICP meter”.
- In order to evaluate the accuracy of new non-invasive absolute ICP value meter clinical study of simultaneous invasive and non-invasive aICP measurements will be performed on neurological patients comparing aICP measured non-invasively with eICP measured using invasive “golden standard” ICP meter.
- In order to achieve a statistically significant value of non-invasive aICP measurement accuracy ($CI=95\%$), at least 40 invasive/non-invasive aICP measurements will be collected.

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According to the invasive ICP monitoring technologies disadvantages and that uncertainties of the best solid state invasive absolute ICP (aICP) sensors are within the limits from 4.2 mmHg up to 19.2 mmHg, a new innovative method for a non-invasive absolute ICP value measurement without the individual calibration problem has been created in Telematics Scientific Laboratory of Kaunas University of Technology. In order to evaluate the accuracy of new non-invasive absolute ICP value meter clinical study of simultaneous invasive and non-invasive aICP measurements will be performed on neurological patients comparing aICP measured non-invasively with eICP measured with lumbar puncture, which is considered „golden standard“ and every new method must be compared with it. Ill. 4, bibl. 10 (in English; abstracts in English, Russian and Lithuanian).

A. Рагаускас, Р. Шунокас, Р. Жакалис, В. Матиошайтис. Оценка точности измерения неинвазивного внутричерепного давления (ИСП) // Электроника и электротехника. – Каунас: Технология, 2010. - № 8(104). – С. 31–34.

Учитывая недостатки инвазивных приборов наблюдения внутричерепного давления и тот факт, что диапазон неопределенности составляет от 4,2 мм рт.ст. до 19,2 мм рт.ст., в лаборатории телематики КТУ был разработан измеритель неинвазивного абсолютного внутричерепного давления. Принцип данного прибора, в отличие от других неинвазивных методов, не требует процедуры калибровки. Для оценки точности этого прибора будут проводиться клинические испытания с неврологическими пациентами, сравнивая значения ИСП, полученные новым патентованным прибором неинвазивного метода с eИСП, полученными путем спинномозговой пункцией, которая рассматривается как "золотой стандарт" и все новые методы должны сравниваться с ним. Илл. 4, библи. 10 (на английском языке; рефераты на английском, русском и литовском яз.).

A. Ragauskas, R. Šunokas, R. Žakelis, V. Matijošaitis. Neinvazinio intrakranijinio spaudimo (ICP) matavimo tikslumo įvertinimas // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2010. – No. 8(104). – P. 31–34.

Atsižvelgiant į invazinių intrakranijinio spaudimo stebėsenos įrenginių trūkumus ir tai, kad jų neapibrėžtys yra gana didelės 4,2 mmHg – 19,2 mmHg, KТУ Telematikos laboratorijoje buvo sukurtas neinvazinis absoliutinio intrakranijinio slėgio matuoklis. Šio prietaiso veikimo principas yra toks, kad, priešingai nei kitų, nereikia kalibruoti. Siekiant įvertinti šio prietaiso tikslumą, bus atliekami klinikiniai tyrimai su neurologiniais pacientais lyginant ICP vertes, gautas neinvaziniu būdu su nauju patentuotu įrenginiu, ir eICP, gautas juosmeninės punkcijos būdu, kuri yra laikoma „auksiniu standartu“ ir visi nauji metodai turi būti lyginami su juo. Il. 4, bibl. 10 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).