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ORIGINAL RESEARCH

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

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Abstract Measurement of intracranial pressure (ICP) is necessary in many neurological and neurosurgical diseases. To avoid lumbar puncture or intracranial ICP probes, non-invasive ICP techniques are becoming popular. A recently developed technology uses two-depth Doppler to compare arterial pulsations in the intra- and extra-cranial segments of the ophthalmic artery for non-invasive estimation of ICP. The aim of this study was to investigate how well non-invasively-measured ICP and invasively-measured cerebrospinal fluid (CSF) pressure correlate. We performed multiple measurements over a wide ICP span in eighteen elderly patients with communicating hydrocephalus. As a reference, an automatic CSF infusion apparatus was connected to the lumbar space. Ringer's solution was used to create elevation to pre-defined ICP levels. Bench tests of the infusion apparatus showed a random error (95 % CI) of less than ±0.9 mmHg and a systematic error of less than ±0.5 mmHg. Reliable Doppler signals were obtained in 13 (72 %) patients. An infusion test could not be performed in one patient. Thus, twelve patients and a total of 61 paired data points were studied. The correlation between invasive and non-invasive ICP measurements was good (R = 0.74), and the 95 % limits of agreements were −1.4 ± 8.8 mmHg. The within-patient correlation varied between 0.47 and 1.00. This non-invasive technique is promising, and these results encourage further development and evaluation before the method can be recommended for use in clinical practice.

Keywords Non-invasive ICP · Transcranial-Doppler · Intracranial pressure · Ophthalmic artery · Infusion test

1 Introduction

Multimodal measurement of physiological data is a cornerstone in neuro-intensive care. The most-used neuro-specific parameter is intracranial pressure (ICP) [1], most often measured through intra-parenchymal pressure sensors, ventriculostomy or lumbar pressure. A drawback of these methods is that they are invasive. An easy-to-use non-invasive technique that provides high accuracy and precision for ICP assessment would be of great value in medical care outside the intensive care unit. Traumatic brain injury, subarachnoid haemorrhage, intra-cerebral haemorrhage, combat-related injuries, brain tumours, hydrocephalus, pseudotumor cerebri and meningitis are conditions where non-invasive ICP could be used for diagnosis, monitoring and selection of patients for invasive ICP registrations.

Many bed-side methods for correlation-based non-invasive approaches to ICP measurement have been tested. Among them are intraocular pressure assessment [2], tympanic membrane displacement [3], ultrasonography [4, 5] and measurement of intracranial blood flow [6–9]. In the individual, these methods have shown a fairly high correlation between non-invasive and invasive ICP assessments (Table 1). However, the limits of agreement in the patient groups are usually very wide, making the non-invasive methods impossible for clinical use. For instance, the Gosling pulsatility index measured in the middle cerebral

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Table 1 A summary of studies that evaluated non-invasive against invasive techniques for obtaining ICP values

Authors	Method	n	R	Pred interval (mmHg)	Reference
Bellner et al.	TCD	81	0.94	±4.2	[10]
Brandi et al.	TCD	45	NR	±7.9	[34]
Kashif et al.	TCD	37	0.76	±11.8	[9]
Behrens et al.	TCD	8	0.47	±23.8	[6]
Zweifel et al.	TCD	290	0.31	>± 15	[14]
Wakerley et al.	TCD	78	0.65	NR	[35]
Schmidt	TCD/ABP	145	0.78	±12.8	[21]
Kim et al.	TCD/ABP	57	NR	±7.6[a]	[23]
Cardim	TCD/ABP	40	0.47	>± 9.2	[25]
Shimbels et al.	TMD	220	NR	>± 20	[15]
Bershad et al.	DPOAE	18	NR	NR	[17]
Geeraerts et al.	ONSD	37	0.71	NR	[36]
Kimberly et al.	ONSD	15	0.59	NR	[37]
Soldatos et al.	ONSD	32	0.68	NR	[38]
Rajajee et al.	ONSD	65	0.73	NR	[39]
Sekhon et al.	ONSD	57	0.74	±12	[19]
Geeraerts et al.	ONSD MR	38	0.71	NR	[40]
Alperin et al.	MR-ICP	5	0.98	NR	[41]
Yavin et al.	IOP	546 Meta	0.47	NR	[42]
Ragauskas et al.	Ophthalmica	62	0.80	±4.3	[8]

Pred interval is the 95 % prediction interval

R correlation coefficient, *NR* not reported

[a] 75 % prediction interval

artery by transcranial Doppler sonography (TCD) reportedly has a high correlation with ICP [10]. However, some have reported a poor and clinically unusable relationship between pulsatility index and ICP [6], indicating the need for calibration of non-invasive techniques. However, patient-specific non-invasive calibration is impossible.

So far, no non-invasive technique has proven accurate and precise enough to replace invasive procedures (Table 1). Besides agreement between techniques, a general ICP method must fulfil specifications such as age and disease independence, operator independence and informative without patient-specific calibration.

A new non-invasive ultrasonic device (Vittamed 205®) for ICP measurement has been developed [8]. Without the need for patient-specific calibration, it measures ICP in absolute values (mmHg) using the equilibrium between blood flow pulsations in the intracranial (IOA) and extracranial (EOA) segments of the ophthalmic artery (OA). Such equilibrium is automatically identified by two-depth trans-orbital Doppler technology. A recent study [8] of a young group of neurological patients showed that the method provides clinically acceptable accuracy (systematic error of less than 1.0 mmHg) and precision (random error SD of 2.3 mmHg). The study was conducted in the limited

interval of ICP values between 5.0 and 24 mmHg, and only one patient had an ICP above the critical threshold of 20 mmHg.

Measures of ICP via a lumbar puncture corresponds well with the intra-parenchymal pressure if the cerebrospinal fluid (CSF) system is communicating [11]. The objective of this study was to assess ICP measurements obtained using a Vittamed 205® and compare them with those obtained via an invasive Celda® technique, which accurately and precisely measures ICP via the lumbar route and automatically increases ICP to a pre-determined level through infusion of Ringer's solution [12].

2 Materials and methods

2.1 Non-invasive ICP measurements

The non-invasive ICP absolute value measurement (ICP-$_{Non-Inv}$) was based on two-depth Doppler ultrasound monitoring of pulsations in the blood flow velocity in the IOA and EOA. The rationale is that the OA is a natural ICP sensor wherein the ICP compresses the IOA, and the blood flow velocity waveform in the IOA depends on the ICP.

The waveform in the EOA depends on the surrounding intra-orbital pressure. This non-invasive ICP measurement procedure was automatic after manually adjusting the position of the ultrasonic transducer on the closed eyelid. The non-compressible tissues surrounding an eyeball were subjected to an externally applied pressure, P_{ext}, which was automatically increased in six steps of 4 mmHg and held on each level for 40 s (Fig. 1). The ICP meter's software determined at which P_{ext} level the best match between IOA and EOA waveforms was achieved. Therefore, $ICP_{Non-Inv}$ was identified when $ICP = P_{ext}$ for that level. A direct comparison between ICP and P_{ext} eliminated the need for patient-specific calibration in this proposed method. The six steps in P_{ext} were used to minimize the time needed to produce the measurement. To achieve greater precision, P_{ext} can be increased in steps of 3.0, 2.0 or 1.0 mmHg pressure, but this extends the duration of "snapshot" measurements. Together with a torus-shaped pressure chamber, the scanning ultrasonic TCD transducer attached to the eyelid was mounted into a mechanical head frame. Mechanical and electronic scanning modes of the ultrasonic transducer were used during the search for OA segments.

Insonation of the OA through the orbit is a standard and safe procedure in Doppler examination of the blood flow in orbital vessels. The special two-depth TCD device meets all international safety standards for intra-orbital ultrasonic measurements. The acoustic output parameters of the device are: spatial peak temporal average intensity = 49.48 mW/cm^2, spatial peak pulse average intensity = 1.335 W/cm^2, maximal pressure of pulse intensity integral = 0.2147 MPa, output ultrasonic pulse duration = 3.705 μs and mechanical index = 0.1518.

2.2 The reference system

The infusion investigations were performed using an invasive device for measuring and controlling ICP via lumbar pressure (Celda®; Likvor AB, Umeå, Sweden). Two 18-G lumbar needles were inserted into the CSF space at the L3–L4 interspace. The needles were connected to the device via a disposable tubing set that included two pressure transducers (Celda® Tools) and separate Ringer's solution in a bag. One needle was used for ICP registration and the other for infusion and withdrawal of Ringer's solution with a built in peristaltic tubing pump that was set to automatically adjust and stabilize the patient's ICP. Measures of ICP using the Celda® have previously been compared with those taken by a probe placed in the brain parenchyma, showing good agreement [11].

A specially-designed bed with a rectangular hole at the lumbar level allowed for placement of two needles while the patient maintained a sitting position and subsequent investigation with the patient in the supine position. The set-up was mounted on an electrically maneuvered pillar to set a zero pressure level. A built-in horizontal laser line was used for zero level alignment.
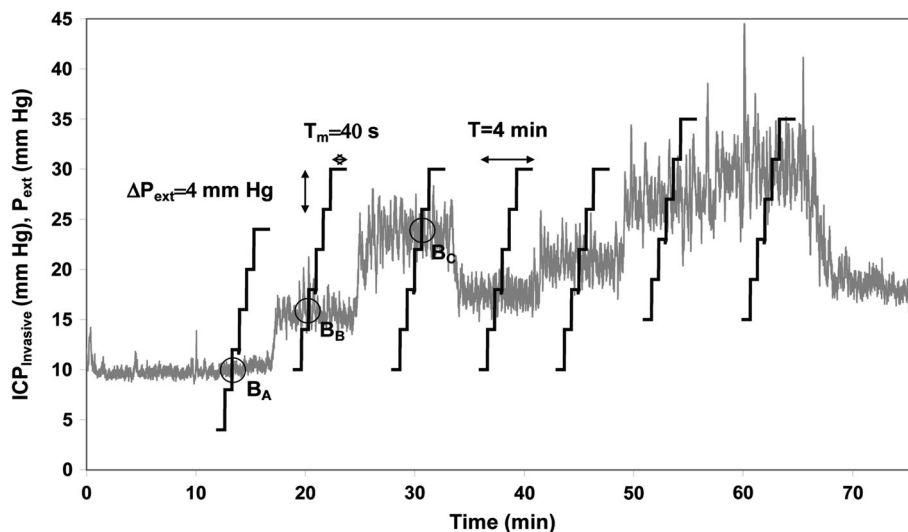

Fig. 1 Time diagrams of the infusion test caused step-by-step mean ICP (t) changes (*gray line*), and externally applied pressure P_{ext} (t) caused step-by-step changes (*black lines*): *A. B. C* initial steps of P_{ext} (t) in three repeatable non-invasive absolute value ICP measurements. B_A. B_B. B_C balance points, where $ICP_{A.B.C.} = (P_{ext})^{A.B.C}$. Δt is the duration of the transient infusion processes. ΔP_{ext} is the sampling step of P_{ext} (t) and was equal to 4.0 mmHg (six steps in each snapshot of $ICP_{Non-Inv}$ measurement cycle, A, B or C). T is the duration of each snapshot $ICP_{Non-Inv}$ measurement cycle. T_M is the duration of $ICP_{Non-Inv}$ value averaging during snapshot measurement in cycle C, equal to 40 s

The CSF dynamic investigations began with a baseline registration of ICP followed by infusion to predetermined pressure levels (Fig. 1).

2.3 Bench test evaluation of reference system

Pressure measurements obtained by the Celda® system were evaluated using a bench test and a hydrostatic column open to the air in a 50-mL syringe. The syringe was movably mounted on a stable stand and placed at seven different levels to produce hydrostatic columns between -0.1 m and 0.5 m. Eleven Celda® tubing sets were tested, and measures were taken six times at each level for each set.

2.4 The investigation protocol

On the day prior to the planned infusion test, the accessibility and normality of both the IOA and EOA Doppler signals was confirmed using the TCD of the non-invasive ICP device. If a reliable signal could not be detected, no further non-invasive measurements were performed on that patient.

At 8.30 a.m. after 12 h of bed rest, the needles were placed while the patient was in the sitting position. A minimum leakage of CSF was strived for. The patient was then placed in the supine position, and the zero-pressure reference level of the infusion apparatus was placed at the centre of the auditory meatus using the horizontal laser line.

The Celda® investigation protocol started with a 15-min recording of baseline pressure. This was followed by pressure-regulated infusion performed using a pressure-controlled pump. Six ICP levels were strived for in each patient. The pressure levels were approximately 5–20 mmHg above baseline pressure (Fig. 1) with 3-mmHg intervals. Each level was stabilized as much as possible and held for at least 7 min. The expert operator (1 person) chose the order of the elevated pressure levels, which differed between patients and was blind to the operator. In the non-invasive method, two expert operators with extensive experience with Doppler investigations were informed of the expected ICP interval (excluding the resting ICP), which was either 4–24, 10–30 or 15–35 mmHg. This was done only to minimize the time needed for the non-invasive measurement; it was deemed unacceptable to sustain a high ICP for a long duration. A manual command, "Start non-invasive ICP measurement," was given by the Celda® operator to the Vittamed 205® operator at the beginning of each new ICP pressure level.

When it was difficult to withdraw fluid from the CSF space, a modified protocol in which pressure control with "only inflow" infusion or a constant flow infusion was used. When the "only inflow" infusion was used, the protocol was limited to four elevated pressure levels, but when the constant flow protocol was used, the number of elevated ICP levels was limited to one or two.

The investigation was performed in a private room that was kept as silent as possible. Experienced investigators performed all measurements.

2.5 Patients

The internal review board at Umeå University approved the study (2011-256-31M). Written informed consent was obtained from all participants. Eighteen patients (seven female) evaluated at the neurological ward for the suspicion of normal pressure hydrocephalus (i.e., ventriculomegaly, gait disturbance and/or cognitive decline) were included. They were aged 73 ± 8 years (mean $\pm$ SD), and their mini-mental state estimation was 25 ± 4 points. One patient had simplex glaucoma, and three had cataracts.

2.6 Analysis and blinding procedure

The mean $ICP_{Invasive}$ was automatically calculated for each of the 7-min pressure levels by the Celda® apparatus. The $ICP_{Non-Inv}$ was assessed in the same time interval. For baseline pressures and in a few special measurements (e.g., constant infusion or pump stop), $ICP_{Invasive}$ was manually calculated as the mean pressure over the same 7-min time period during which $ICP_{Non-Inv}$ was measured. Depending on the infusion protocol and success of ICP measurement, two to seven independent pairs of ICP measurements were produced for each patient. After each patient, the operators of the non-invasive technique, still blinded to the reference ICP, made a post hoc analysis of the waveform data and calculated the $ICP_{Non-Inv}$ estimates. Hydrostatic errors caused by the vertical distance between the point of invasive ICP measurement, defined by the auditory meatus, and the point of the IOA segment were eliminated. The standard Celda® investigation report from the infusion investigation, which included the $ICP_{Invasive}$ values, was placed in a sealed envelope together with a written report from the non-invasive operator, which included the $ICP_{Non-Inv}$ estimates. The envelopes were opened after patient enrolment was completed at a meeting in which the authors were present. The crew groups were thus blinded to each other's results throughout patient enrolment. The calculated values in the envelopes are the primary ICP data presented in this paper. The Introduction and Methods sections of this manuscript were agreed upon by all authors before envelopes were opened, thus un-blinding the study.

2.7 Statistics and validation criteria

We hypothesized that values of $ICP_{Non-Inv}$ will reflect values of $ICP_{Invasive}$, allowing a general linear model with $ICP_{Non-Inv}$ as the dependent variable of the two. Pearson's method was used for correlation analysis.

Differences ($ICP_{Invasive} - ICP_{Non-Inv}$) were compared to means ($ICP_{Invasive} + ICP_{Non-Inv}$)/2 in a Bland–Altman plot [13]. This plot reveals ICP-dependent differences and exposes systematic and random errors and thus the agreement between the two methods. The criteria for acceptable accuracy in $ICP_{Non-Inv}$ measurement was that the paired ICP data points in the plot should be within ± 5 mmHg (the error corridor) with a confidence level of 95 %.

This validation criteria for $ICP_{Non-Inv}$ agrees with the results of a prospective clinical assessment using a young group of neurological patients [8]. In that study, the Vittamed 205® had the following specifications: ICP ranged from 0 to 50 mmHg, an SD for random error was ± 2.3 mmHg (95 % CI) and a systematic error was less than 1.0 mmHg (95 % CI). This gives an uncertainty (2SD) close to 5.0 mmHg. Each patient's ICP agreement is presented by plotting $ICP_{Non-Inv}$ against $ICP_{Invasive}$ along with the line of equality.

3 Results

Comparisons between the Celda® ICP measurement and the hydrostatic water column yielded a random error (95 % CI) of less than ± 0.9 mmHg; the systematic error was less than ± 0.5 mmHg.

Eighteen patients were screened, and reliable Doppler signals for estimation of $ICP_{Non-Inv}$ were obtained in 13 (72 %). For one patient, the infusion test was aborted because the patient fainted at the lumbar puncture. Thus, the study population consisted of twelve patients. From each of these, we obtained 2–8 simultaneous assessments of ICP using both methods, giving 61 data points. For three ICP measurements, the scanning interval of P_{ext} did not include, or were at the limits of, the mean $ICP_{Invasive}$. For these measurements, the $ICP_{Non-Inv}$ assessment was questionable, and they were excluded from the statistical calculations.

The concordance between the two ICP measures is shown in Fig. 2, and the correlation was R = 0.74 ($p < 0.001$, n = 58). A Bland–Altman plot (Fig. 3) shows that the 95 % limits of agreements were -1.4 ± 8.8 mmHg, and regression analysis showed that there was a trend (R = −0.32; $p = 0.016$, n = 56), indicating a larger underestimation of $ICP_{Non-Inv}$ at higher ICPs.

Within any individual, the two methods yielded correlation coefficients between 0.47 and 1.00. The slopes of the correlations were between 0.34 and 0.87 (Table 2).

To investigate possible biases from the 20 mmHg limitation in the P_{ext} range, we performed a simulation in which the pressure within the given range of each interval was randomised and compared with $ICP_{Invasive}$. Thirty simulations with new randomised pressures yielded an average correlation of 0.38 ± 0.09 and limits of agreement of ± 15 mmHg. This shows an expected bias from interval selection, but it was significantly ($p < 0.001$) lower than the correlation found in the study and had much larger limits of agreement. Post hoc analysis revealed that if we used only the measurements taken when the P_{ext} interval was 10–30 mmHg (n = 32), the correlation was 0.44 ($p = 0.013$), and the limits of agreement was 2.1 ± 8.4 mmHg.

4 Discussion

This study is important because most patients prefer ICP measurement without the use of needles. There is a growing commercial market for this type of device, and it is important that new products are tested before they are incorporated into clinical practice.

We compared a bedside non-invasive absolute ICP measurement method using an invasive method by taking multiple measurements in an elderly group of patients over a wide ICP span. When compared to previously suggested non-invasive methods, this method appears promising. Unlike other techniques, it offers the advantage of an estimation of the absolute value of ICP, rather than an indirect index that changes with ICP. Additionally, it does not need patient-specific calibration.

Other bedside methods have previously failed to show reliable results. Using TCD for assessing flow velocity pulsatility index in the middle cerebral artery has been suggested as a correlation-based non-invasive technique, and while Bellner et al. [10] found very promising results, they have not been reproduced by others (Table 1). A recent large study by Zweifel et al. [14] showed that the TCD pulsatility index for non-invasive assessments of ICP is very limited. Tympanic membrane displacement (TMD) from the stapedius reflex was shown to correlate with ICP but with a wide ICP prediction interval [15]. Another audiological approach was based on the evoked distorsion product otoacoustic emissions, which correlates with ICP [16, 17], but it has not been thoroughly evaluated against invasive measurements. Optic nerve sheath diameter increases with ICP [18]. Most studies evaluated correlation (Table 1) and/or the ability to detect ICPs exceeding 20 mmHg. Sekhon et al. [19] showed that the optic nerve

Fig. 2 ICP$_{Non-Inv}$ versus ICP$_{Invasive}$. Square markers indicate that ICP$_{Non-Inv}$ was on the limit or below the ICP, according to ICP$_{Invasive}$. *Solid line* represents line of equality
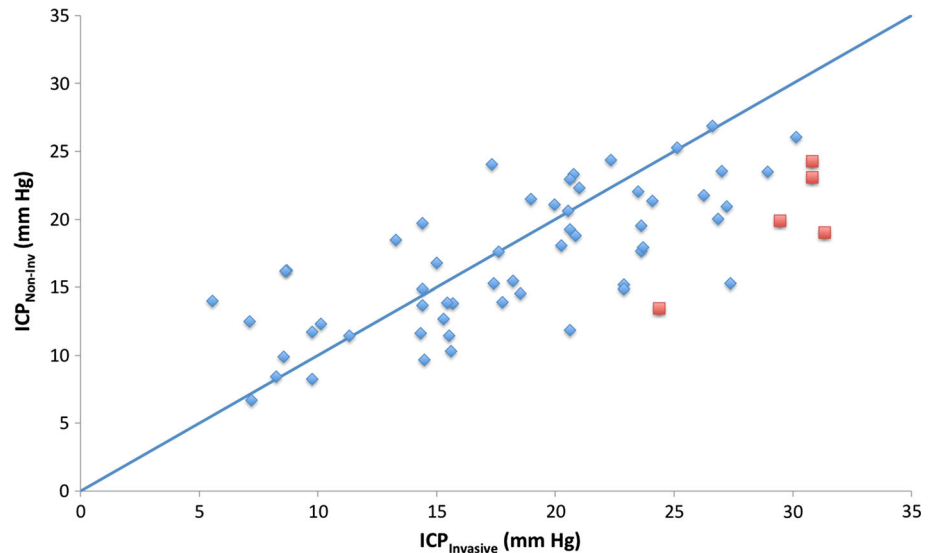

Fig. 3 Bland–Altman plot showing the difference (ICP$_{Invasive}$ − ICP$_{Non-Inv}$) plotted against the mean measured ICP value (ICP$_{Invasive}$ + ICP$_{Non-Inv}$)/2. The solid line shows the systematic difference between the two, and dotted lines represent the 95 % CI of agreement. *Square* markers same as in Fig. 2. The limits of agreement between ICP$_{Invasive}$ and ICP$_{Non-Inv}$ including all data was −1.8 ± 9.4 mmHg
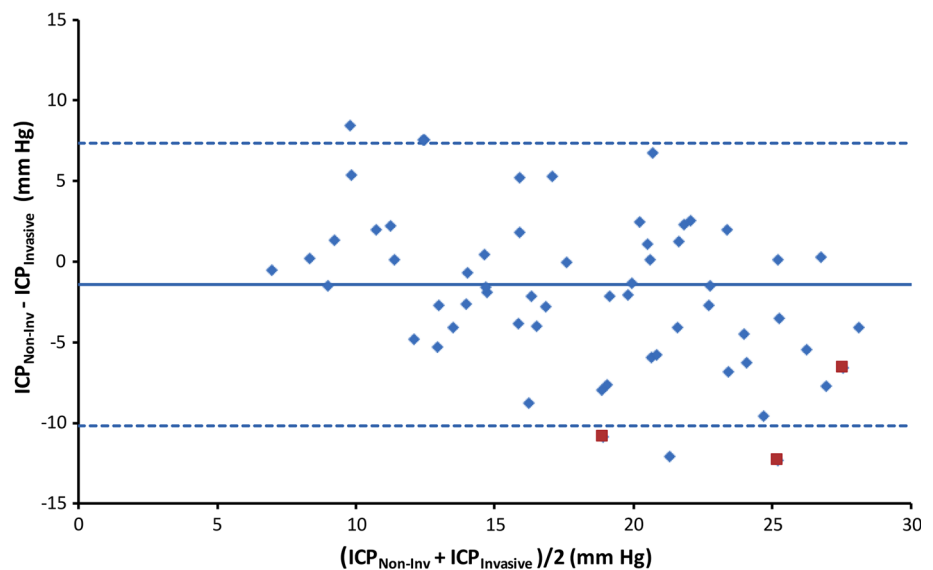
sheath diameter had a prediction interval against invasive ICP of ±12 mmHg. Correlation between intraocular pressure and ICP has been studied, and a meta-analysis from 12 studies revealed a significant but low correlation (Table 1). A number of suggested and evaluated methods for predicting ICP use blood flow velocity from TCD and arterial blood pressure curves as inputs to mathematical models. Schmidt et al. [20] suggested a black box system that was evaluated on a group of hydrocephalus patients during infusion and showed promising results [21]. It was also evaluated on 145 severely head-injured patients, and they concluded that the method could be used to provide a noninvasive and continuous assessment of the state of cerebral autoregulation [22]. Kim et al. [23] used similar inputs and an assessment using a nonlinear mapping

function. The same group later added electrocardiogram as an input, developed a method with semi-supervised learning and demonstrated that it was promising for detection of intracranial hypertension [24]. In two recent studies, Cardim et al. compared four methods used for non invasive ICP estimation using both arterial blood pressure and flow velocity as inputs. In a cohort of traumatic brain-injured patients [25] and in a group of patients investigated with infusion tests [26], limits of agreements were larger than ±9 mmHg in all four methods.

This study shows that the method presented here could assess ICP with limits of agreement of ±8 mmHg on the studied patients with only a small systematic underestimation. According to our selected validation criteria, this is not sufficient for recommending its routine clinical use.

Table 2 Linear regression results for the eleven patients from whom we could collect three or more valid data points

Patient no.	Number of ICP points	Slope	R
1	3	0.82	1.00
2	4	0.74	0.96
3	5	0.87	0.93
4	6	0.36	0.80
5	5	0.55	0.58
8	7	0.69	0.90
11	4	0.52	0.63
13	4	0.34	0.56
15	6	0.45	0.47
17	6	0.52	0.68
18	5	0.53	0.48

The mean value of ICP in healthy individuals is 10 mmHg, and the upper normal limit is around 15 mmHg [27]. The definition of idiopathic intracranial hypertension and normal pressure hydrocephalus is above and below 18 mmHg, respectively [28]. A common limit for initiating a therapy to lower ICP in traumatic brain injuries is about 20 mmHg [29]. Consequently, if the clinical purpose is to classify and treat wide age groups of patients according to pre-set thresholds, ICP assessment should have an accuracy that discriminates between these. Therefore, we suggest that to be clinically useful, a non-invasive ICP method should have limits of agreement comparable to that found in invasive ICP (no more than ±5 mmHg). As yet, none of the suggested methods, including the one we investigated, fulfill this criteria. However, when comparing our results to those obtained using other suggested methods (see Table 1), the limits of agreement found here (±8.8 mmHg) is promising.

When using the Bland–Altman plot to determine whether the difference ($ICP_{Invasive} - ICP_{Non-Inv}$) was pressure-dependent, we found that underestimation of $ICP_{Non-Inv}$ was greater at higher pressures. This was indicated both by the significant negative correlation found in the Bland–Altman plot and by the generally flat (less than 1) slopes found by plotting ($ICP_{Non-Inv}$ against $ICP_{Invasive}$) for each individual patient (Fig. 3). A reduction in slope is partly caused by the ordinary least square regression. Random errors in both variables yields an underestimation of the slope [30]. It also indicates a trend in the method, suggesting that lower P_{ext} is needed at higher pressure levels to produce the best concordance. It is possible that the diastolic pressure in the ICP waves, rather than the mean ICP, is detected by non-invasive methods. The underestimation would then be small at normal ICPs because the ICP pulse amplitude is small, but it would be larger at higher ICPs because the ICP amplitudes are greater and the difference

between diastolic ICP and mean ICP then becomes significant [31].

There are sources that contribute to the difference between $ICP_{Non-Inv}$ and $ICP_{Invasive}$. One is the sampling error, which depends on the P_{ext} steps of 4.0 mmHg. Another is the methodological limitation of how well the change in measured IOA and EOA waveforms reflects the concordance between P_{ext} and $ICP_{Invasive}$. A third source is from the amount of time needed; in practical clinical use, six levels of P_{ext} are examined over 7 min to produce a single estimate of $ICP_{Non-Inv}$. Natural variations in ICP during these 7 min can contribute to errors in $ICP_{Non-Inv}$. When using the non-invasive method, it is crucial to get high-quality Doppler signals from the EOA and IOA. This can be technically demanding for non-trained investigators.

However, in special circumstances, when the clinical purpose is to non-invasively verify that ICP is significantly elevated, the method could be useful.

The method is also promising for following an individual in situations where invasive methods are not available, such as investigating visual impairment intracranial pressure syndrome in astronauts in space [32]. However, the within-patient variation was similar to the total variation (Table 2); therefore, precision greater than ± 8 mmHg can not be expected in elderly patients. A recent report using our non-invasive method showed promising results in a younger population, but only a few patients had ICPs above 20 mmHg [33].

Clinical studies using this non-invasive ICP measurement method have not demonstrated relevant patient risk. The applied P_{ext} is limited to 50 mmHg, corresponding to 0.68 m under water. When the pressure applied to the tissues surrounding the eyeball is this low, it guarantees safety. The two-depth TCD device used in this study conforms to all international safety standards for ultrasonic Doppler devices.

Though the Vittamed 205® was used by experts, 28 % of the patients could not be investigated because reliable Doppler signals were impossible to trace. A previous study [8] that used younger patients indicated a higher success rate, suggesting age-related effects. The method's age-related usefulness must be investigated. When using expert investigators, inter-operator studies are needed. To develop into a useful clinical tool, a universal ICP assessment method should be easy to use, age independent and functional irrespective of what caused ICP to increase. Parts of the deviations between methods seen in this study depend on patient-specific errors, such as poor cooperation, moving, speaking or other unacceptable interruptions during Doppler measurements. Also, an actual clinical situation is likely to be noisier and more stressful.

The bench test of the Celda® showed that invasive pressure measurement was reliable both within a tubing set

and between tubing sets, supporting its use in invasive methods for obtaining accurate ICP assessment. It also offers the advantage of monitoring the dynamic ICP variation rather than taking a snapshot of the ICP. While ICP is not a fixed value, it is described by a curve that is continuously moving as a result of physiological variations such as arterial pulsations, vasomotion, cerebrovascular autoregulatory activity and respiratory waves. A limitation in using the Vittamed 205® is that these variations will not be captured because at least 7 min are needed to produce each ICP reading.

The limitation of 7 min restricted total infusion time, produced a required reduction in the P_{ext} sweep interval to 20 mmHg (Fig. 1). Although the study was blinded in its design, the maximum interval that could be scanned in each 7-min interval was 20 mmHg. Therefore, the Vittamed operators had to have a limited amount of knowledge of the expected ICP interval, and this was found to yield a bias. Using only those measurements taken over a P_{ext} interval of 10–30 mmHg, we found a correlation of 0.44 and no change in the range for limits of agreement. As seen in three ICP assessments, there was a risk that the P_{ext} interval did not cover the invasively-obtained ICP, resulting in questionable $ICP_{Non-Inv}$ estimates. Because all such estimates were at high pressures and deviated substantially (Fig. 2), the validity of the non-invasive method at high pressures should be further investigated so that outliers are avoided when the correct P_{ext} interval is used.

We have shown that a non-invasive method for obtaining ICP as an absolute value measurement using this technology is likely in the near future. This is important in situations where a snapshot and rapid screening of ICP is necessary, such as in the emergency room. In addition, ICP can be followed at intervals in patients with different neurological and neurosurgical diseases when a continuous measurement is not possible or needed. However, the prototype Vittamed 205® non-invasive ICP device, or any other non-invasive ICP method, can not yet be recommended for routine use in the assessment of ICP in a neurological or neurosurgical setting.

In conclusion, non-invasive attempts to measure ICP seem to be rising in popularity. This is not surprising because patients want comfort and a minimal risk of complications. We explored the relationship between noninvasively and invasively measured ICP. The results are promising for the non-invasive two-depth Doppler technique, and continuing with additional development and evaluation is encouraged and necessary before the method can be recommended for use in clinical practice.

Compliance with ethical standards

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