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Morphological characterization of cardiac induced intracranial pressure (ICP) waves in patients with overdrainage of cerebrospinal fluid and negative ICP

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ABSTRACT

Symptomatic overdrainage of cerebrospinal fluid (CSF) can be seen in shunted hydrocephalus patients and in non-shunted patients with spontaneous intracranial hypotension (SIH). In these patients, intracranial pressure (ICP) monitoring often reveals negative static ICP, while it is less understood how the pulsatile ICP (cardiac induced ICP waves) is affected. This latter aspect is addressed in the present study. A set of 40 ICP recordings from paediatric and adult hydrocephalus patients were randomly selected. Each cardiac induced ICP wave was automatically identified and manually verified by the beginning and ending diastolic minimum pressures and the systolic maximum pressure. The ICP wave parameters (static pressure, amplitude, rise time, rise time coefficient, downward coefficient, wave duration, and area-under-curve) were then automatically computed. The material of 40 ICP recordings provided a total of 3,192,166 cardiac induced ICP waves (1,292,522 in paediatric patients and 1,899,644 in adult patients). No apparent changes in ICP wave parameters were seen when mean ICP became negative, except that the parameters amplitude, rise time coefficient, downward coefficient and area under curve somewhat increased when mean ICP was below −15 mmHg.

1. Introduction

The main components of the intracranial volume are the brain tissue (85%), cerebrospinal fluid (CSF; 10%) and blood (5%). The CSF has a vital role in the physical protection of the brain as well as being crucial for brain metabolism [1]. Normally the production and absorption of CSF is balanced; disruption of this balance may cause hydrocephalus with excess of CSF within the brain ventricles [2]. Hydrocephalus is often treated with surgical implantation of a shunt for drainage of CSF from the cerebral ventricles to the abdominal cavity or the heart. Overdrainage of CSF is a frequent complication to shunt treatment [3–5], as well as a complication to other types of neurosurgery and even lumbar puncture (LP) [6,7]. When the cause of CSF overdrainage is unknown, it is denoted spontaneous intracranial hypotension (SIH) [6,7]. Independent of the cause, the symptoms can be severe, including headache, unsteadiness, vertigo, lethargy, and cranial nerve dysfunction.

Cerebrospinal fluid overdrainage often represents a major challenge to the physician. It may cause severe morbidity to the patient, and be hard to diagnose [7]. It is usually difficult and often impossible to differentiate CSF overdrainage from underdrainage solely based on symptoms and imaging the cerebral ventricles [8]. In order to diagnose intracranial hypotension (low intracranial pressure – ICP), usually the fluid pressure is measured through a LP [6,7]. Some previous reports indicate a useful role of continuous ICP monitoring in shunted hydrocephalus patients with possible over- or underdrainage [9–12]. We found continuous ICP monitoring to be useful in shunted patients with severe and lasting symptoms not responsive to management [8].

We have observed that the ICP usually becomes negative during symptomatic CSF overdrainage [8]. However, one obstacle when referring to the ICP is that a negative ICP may also be caused by erroneous baseline pressure [13,14]. For this reason we have incorporated assessment of the cardiac induced ICP waves since they are independent of the baseline pressure [13]. If the morphology of ICP waves relates to the degree of CSF overdrainage, it might be possible to improve diagnostics.

The aim of the present study was to characterize the morphology of cardiac induced ICP waves in patients with CSF overdrainage, either caused by shunt treatment or SIH. As reference, we also characterized the morphology of cardiac induced

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ICP waves in other hydrocephalus patients, both children and adults.

2. Methods

2.1. Patient material

The material consists of 40 patient recordings (11 paediatric patients and 29 adults) that were randomly selected from the Pressure Database of Department of Neurosurgery, Oslo University Hospital – Rikshospitalet. The ICP recordings had been done during the period 2002–2007, as part of diagnostic work-up.

This study was approved by the hospital authority of Oslo University Hospital – Rikshospitalet (10/16550). The Regional Committee for Research Ethics was informed about the study in writing, and had no objections to the study.

Before the ICP recordings were retrieved from the database, the patients were characterized by one of the authors (TES) according to their history, symptoms, findings, radiological examination, and results of management. Eleven paediatric patients were characterized as either having overdrainage ($n = 7$) or underdrainage ($n = 4$). Fourteen adult patients were characterized as either having spontaneous overdrainage (SIH; $n = 4$), shunt overdrainage ($n = 3$) or underdrainage ($n = 7$). Another 15 adult patients, in whom diagnostic ICP monitoring had been done prior to shunt surgery for idiopathic normal pressure hydrocephalus (iNPH), were characterized as either shunt responders ($n = 8$) or non-responders ($n = 7$), depending on clinical shunt response 12 months after surgery. The characterization of iNPH patients, including outcome assessment, has been described in detail previously [15].

2.2. ICP recordings

The diagnostic ICP recordings were done using a Codman ICP MicroSensor (Codman, Johnson & Johnson, Raynham, MA, USA), as previously described [13,15,16]. In short, in local anaesthesia a small burr hole was made in the frontal scull. The ICP sensor was tunnelled below the skin to the site of skin incision, zeroed against atmospheric pressure, and then placed 1–2 cm into the brain parenchyma via a minimal opening made in the dura. Hence, the ICP signals were retrieved from the parenchyma 1–2 cm below the cortical surface. The continuous ICP waveforms were sampled at 100–200 Hz, and stored on a hospital server (Pressure Database). For digital sampling and analysis of the ICP waveforms the Sensometrics® Software, dPCom A/S, Oslo, was used, as previously described [16].

2.3. Manual identification of cardiac-induced ICP waves, and ICP analysis

For manual identification of single ICP waves, the ICP raw data waveforms were imported to the Sensometrics® Software, Advanced Research Edition (dPCom A/S, Oslo, Norway; see Supplemental file 1). Using this software the ICP waveform was displayed, enabling the user to verify and change detection of each cardiac induced ICP wave. This was done for every single ICP wave of the patients included in this study. Each ICP wave was characterized by the beginning diastolic minimum pressure, systolic maximum pressure, and ending diastolic minimum pressure (Fig. 1a). This was done for every cardiac-induced ICP wave in the pressure recording by two of the authors (MS and AW). The ICP wave identification and verification output were automatically stored in software.

After the identification and verification of the single ICP waves, the output files were imported in the Sensometrics® Software (dPCom A/S, Oslo, Norway) for automatic computation of the single ICP wave parameters (see Supplemental file 2). For every ICP wave the following ICP wave parameters were computed (Fig. 1b): amplitude (SW.dP), rise time (SW.RT), rise time coefficient (SW.RTC), downward coefficient (SW.DWC), wave duration (SW.WD), and area under curve (SW.AUC).

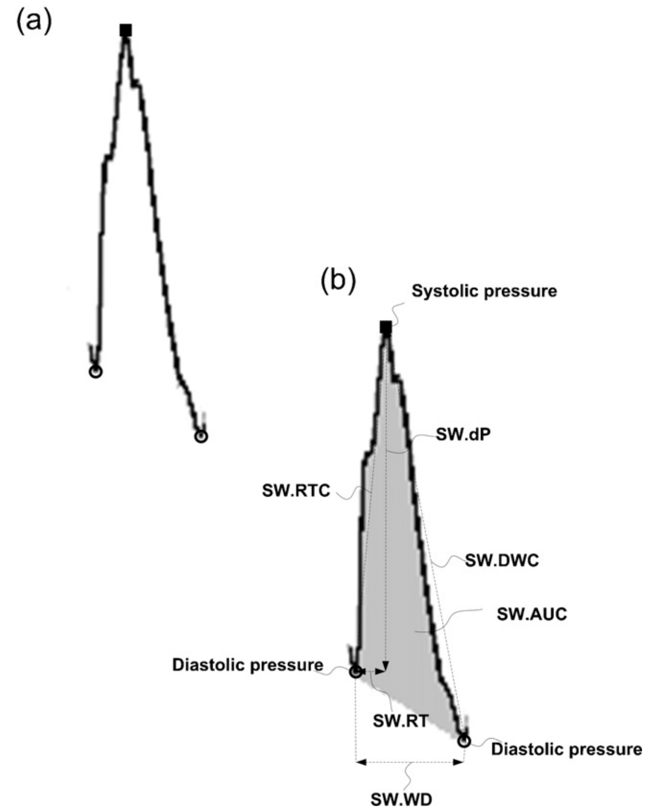

Fig. 1. (a) Each cardiac-induced ICP wave was manually identified by the beginning diastolic pressure, maximum systolic pressure and ending diastolic minimum pressure. (b) From each identified ICP wave the following single wave (SW) pressure parameters were automatically computed: rise time (SW.RT), amplitude (SW.dP), rise time coefficient (SW.RTC), downward coefficient (SW.DWC), wave duration (SW.WD), area under curve (SW.AUC). The total material includes 3,192,166 single waves.

3. Results

3.1. Patient material

Demographic data of the patient material are summarized in Table 1. A total of 40 patient recordings were included in the study; the recordings of these patients incorporated a total of 3,192,166 manually identified cardiac induced ICP waves (1,292,522 in paediatric patients, and 1,899,644 in adult patients). Among the 40 patients the median number of single waves was 71,103; the median number of single waves among patients in each group is presented in Table 1.

3.2. ICP wave morphology – paediatric and adult patient categories

Table 2 summarizes the ICP wave parameters of the different patient categories. The main observations were as follows: The ICP wave amplitudes (SW.dP) were high (above 4 mmHg) in paediatric and adult patients with shunt underdrainage. The same was observed in shunt responders prior to shunt implantation. On the contrary, the ICP wave amplitudes were low (about 3 mmHg) in paediatric and adult patients with overdrainage, adult patients with

Table 1
Demographic data of patient material.

	Paediatric		Adult				
	Shunt failure over-drainage	Shunt failure under-drainage	Spontaneous over drainage	Shunt failure over-drainage	Shunt failure under-drainage	Response to shunting	No response to shunting
Patients (n)	7	4	4	3	7	8	7
Years of age (median, ranges)	9 (7–11)	11 (3–12)	47 (42–51)	64 (38–72)	29 (23–36)	72 (67–79)	69 (51–77)
Sex (F/M)	2/5	2/2	3/1	2/1	5/2	4/4	5/2
Patients with shunt (n)	7	4	–	3	7	–	–
N single waves per patient (median, ranges)	79,120 (57,805–107,176)	148,853 (74,271–350,120)	57,593 (35,430–73,482)	75,076 (51,968–83,949)	47,450 (662–176,016)	63,506 (14,514–84,683)	64,898 (45,314–159,054)

Table 2
Quantitative morphological characteristics of ICP waves.

	Paediatric		Adult				
	Shunt failure over-drainage	Shunt failure under-drainage	Spontaneous over drainage	Shunt failure over-drainage	Shunt failure under-drainage	Shunt response	Shunt non-response
ICP waves (n)	570,426	722,096	224,098	210,993	453,764	468,610	542,179
SW.dP	3.1 ± 1.1	4.8 ± 2.4	3.4 ± 1.4	2.9 ± 1.3	6.1 ± 3.5	6.1 ± 2.1	3.3 ± 1.5
SW.dRT	0.14 ± 0.08	0.12 ± 0.05	0.21 ± 0.08	0.23 ± 0.08	0.21 ± 0.07	0.25 ± 0.05	0.25 ± 0.06
SW.RTC	25.9 ± 11.5	43.1 ± 20.3	18.8 ± 9.7	13.6 ± 10.2	31.2 ± 19.5	25.2 ± 8.6	13.8 ± 6.1
SW.WD	69.0 ± 17.4	66.3 ± 15.9	92.7 ± 14.8	91.0 ± 29.3	81.1 ± 19.1	81.6 ± 14.7	91.3 ± 29.2
SW.DWC	6.0 ± 3.8	9.8 ± 6.6	4.9 ± 2.7	5.1 ± 5.3	10.8 ± 6.6	11.2 ± 5.1	5.5 ± 3.9
SW.AUC	7.6 ± 5.5	11.2 ± 16.2	7.5 ± 2.9	8.1 ± 8.3	12.9 ± 7.3	13.9 ± 3.9	8.8 ± 5.6
SW.MeanICP	2.5 ± 8.6	11.2 ± 6.7	−1.2 ± 7.3	−1.6 ± 7.2	10.4 ± 9.0	7.4 ± 4.9	4.1 ± 5.0

spontaneous overdrainage (SIH), and shunt non-responders. The profiles of both ICP wave area under curve (SW.AUC) and ICP wave downward coefficient (SW.DWC) were comparable to that seen for ICP wave amplitude (SW.dP). Both ICP wave rise time (SW.RT) and wave duration (SW.WD) differed between paediatric and adult recordings, while differences between patient categories were less evident.

3.3. *ICP wave parameters for different categories of ICP*

The ICP wave parameters for different categories of ICP (SW.MeanICP) are shown in Table 3 (paediatric patients) and 4 (adults).

With increasing ICP above 0 mmHg, there was a clear tendency towards increasing ICP wave amplitudes (SW.dP), rise time coefficient (SW.RTC), down-ward coefficient (SW.DWC), and area under curve (SW.AUC), which was comparable in children and adults. Such a clear profile was not evident when ICP was falling below 0 mmHg. When ICP was in the range 0 to −15 mmHg, no apparent change in ICP wave parameters was seen. However, with very low ICP below −15 mmHg in adults, the amplitudes somewhat increased, giving a U-shaped curve (Fig. 2). Intracranial pressure below −15 mmHg is rare, and constituted only 0.8% of the ICP waves of this material. In adults a comparable U-shape was seen for the

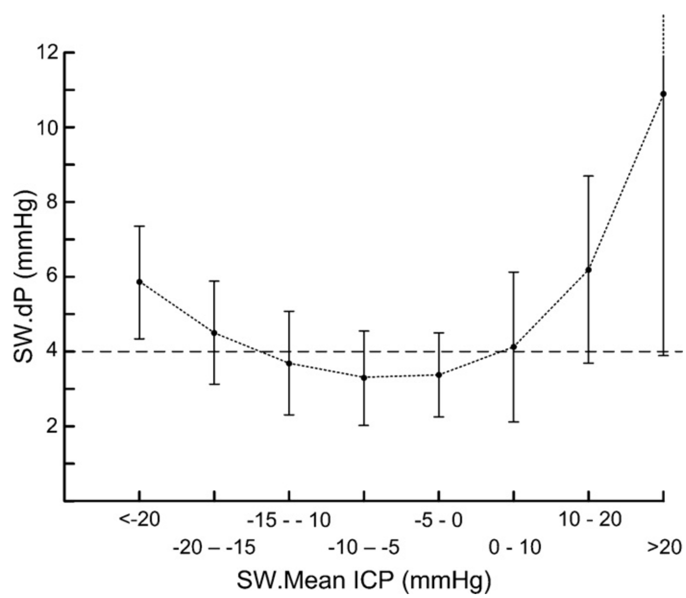

Fig. 2. The ICP wave amplitude (SW.dP) levels were plotted for different categories of ICP wave mean pressure (SW.MeanICP) in adults.

Table 3
ICP wave parameters for different categories of ICP (SW.meanICP) in adults.

	SW.Mean ICP (mmHg)							
	<−20 mmHg	−20 to −15 mmHg	−15 to −10 mmHg	−10 to −5 mmHg	−5–0 mmHg	0 to 10 mmHg	10 to 20 mmHg	>20 mmHg
ICP waves (n)	229	15,125	60,292	70,739	234,423	1,095,714	369,605	53,517
SW.dP	5.9 ± 1.5	4.5 ± 1.4	3.7 ± 1.3	3.3 ± 1.2	3.4 ± 1.2	4.2 ± 2.0	6.2 ± 2.5	10.8 ± 7.0
SW.RT	0.15 ± 0.07	0.23 ± 0.09	0.20 ± 0.08	0.23 ± 0.08	0.22 ± 0.08	0.24 ± 0.07	0.24 ± 0.07	0.23 ± 0.06
SW.RTC	47.2 ± 19.3	23.6 ± 12.8	21.3 ± 17.2	16.3 ± 8.5	16.6 ± 7.8	19.1 ± 9.8	27.2 ± 13.1	52.3 ± 39.5
SW.WD	78.5 ± 14.7	86.2 ± 33.8	84.0 ± 27.8	85.7 ± 26.7	87.6 ± 22.0	86.9 ± 23.9	86.4 ± 18.6	81.8 ± 20.1
SW.DWC	9.8 ± 3.8	8.2 ± 8.9	6.4 ± 5.5	5.8 ± 3.6	5.6 ± 3.3	7.4 ± 4.7	10.7 ± 5.7	18.8 ± 12.8
SW.AUC	13.1 ± 2.9	11.3 ± 4.7	8.9 ± 4.5	8.1 ± 3.8	7.8 ± 3.1	10.0 ± 4.4	14.1 ± 6.4	23.5 ± 19.2

Table 4
ICP wave parameters for different categories of ICP (SW.meanICP) in paediatric patients.

	SW.MeanICP (mmHg)							
	<−20 mmHg	−20 to 15 mmHg	−15 to 10 mmHg	−10 to 5 mmHg	−5 to 0 mmHg	0 to 10 mmHg	10 to 20 mmHg	>20 mmHg
ICP waves (*n*)	21,802	5,245	11,692	61,659	105,299	595,167	425,061	66,597
SW.dP	2.9 ± 0.9	3.5 ± 1.3	3.1 ± 1.0	3.3 ± 0.9	3.3 ± 1.1	3.4 ± 1.3	4.6 ± 2.2	8.9 ± 3.1
SWRT	0.16 ± 0.08	0.18 ± 0.09	0.14 ± 0.08	0.15 ± 0.09	0.13 ± 0.08	0.13 ± 0.07	0.12 ± 0.05	0.12 ± 0.05
SW.RTC	21.6 ± 8.8	23.1 ± 9.5	27.4 ± 10.8	29.3 ± 13.1	28.3 ± 11.6	30.4 ± 13.8	39.7 ± 15.1	79.1 ± 31.0
SW.WD	67.8 ± 12.9	69.8 ± 16.8	74.2 ± 19.1	68.7 ± 22.0	63.7 ± 18.5	67.8 ± 15.5	68.9 ± 16.2	58.7 ± 17.3
SW.DWC	6.0 ± 3.6	7.4 ± 5.4	5.8 ± 4.3	6.8 ± 3.5	6.9 ± 3.7	6.7 ± 3.8	8.8 ± 5.9	20.1 ± 9.6
SW.AUC	7.1 ± 2.6	8.8 ± 4.1	8.1 ± 3.4	8.7 ± 3.8	8.3 ± 4.3	8.1 ± 3.9	10.6 ± 5.5	19.9 ± 11.1

ICP wave parameters SW.RTC, SW.DWC and SW.AUC (Table 3). The same profile was not seen in children (Table 4).

To further explore how ICP wave parameters change when ICP is declining below 0 mmHg, we also determined the Pearson correlations between ICP (SW.MeanICP) and the ICP wave parameters (Table 5). When ICP becomes lower below zero, there is a tendency towards increasing SW.dP, SW.RTC, SW.DWC and SW.AUC in adults, but not in children.

4. Discussion

In this observational study we describe how ICP wave morphology is changed during CSF overdrainage when ICP becomes negative. The ICP wave parameters in patients with shunt overdrainage compared best with the ICP wave morphology seen in patients with spontaneous overdrainage (or SIH), and with the preoperative ICP wave morphology in shunt non-responders. During CSF overdrainage when ICP is in the range 0 to −15 mmHg, no apparent change in ICP wave parameters was seen, while in adult the ICP wave parameters amplitude, rise time coefficient, downward coefficient and area under curve tended to increase when ICP fell below −15 mmHg.

The patient material consists of well characterized patients. The determination of over- or underdrainage was thus based on their history, symptoms, clinical and radiological findings, and results of management. They were characterized to different patient groups before the ICP analysis to avoid bias. It should be noted, however, that the reason for ICP monitoring was to better understand the underlying cause of their symptoms and radiological findings.

In these patients we were able to identify 570,426 ICP waves in paediatric patients with shunt-failure CSF overdrainage, 210,993 ICP waves in adult patients with shunt-failure overdrainage, and 224,098 ICP waves in adult patients with spontaneous CSF overdrainage (SIH). All these patients had verified CSF overdrainage, based on the clinical and radiological information, and results of clinical management.

We also explored the ICP wave characteristics of other patient categories in order to best characterize the morphology of ICP waves during CSF overdrainage. Hence, we retrieved clinically and radiologically well characterized paediatric and adult patients with shunt underdrainage, which represents the opposite situation of CSF over-drainage. In addition, we identified the ICP waves of patients undergoing pre-operative diagnostic monitoring before shunt implantation [15]; they were dichotomized as either being shunt responders or non-responders [15].

The ICP wave analysis was done after the characterization of the patients. In this study the cardiac-induced ICP waves were manually verified after automatic identification, which represents an advantage, as compared to sole automatic identification. This manual verification ensures >99.9% identification of cardiac beat induced single ICP waves compared to sole automatic identification which has a hit range of >96%. This was done to ensure proper identification of the cardiac-induced ICP waves. As previously described [16], the cardiac induced ICP waves were identified by the key features starting diastolic minimum pressures, systolic maximum pressures, and ending diastolic minimum pressures (Fig. 1a). Other features are the three peaks P1, P2 and P3, which were not manually identified in this particular study. Other algorithms for peak identification in continuous ICP signals have recently been described [17].

When comparing the different patient categories, the findings of low ICP (SW.meanICP) in those with shunt failure or spontaneous CSF overdrainage are as expected. The literature is scarce regarding changes in ICP during overdrainage, and only refers to changes in ICP [8,9]. The ICP thresholds that can be regarded as abnormal depend on the patient's body position. It should be noted that the scope of the present study was not to examine how ICP depends on varying body position, but how ICP wave parameters vary for different levels of ICP, including negative ICP.

Regarding ICP wave parameters in hydrocephalus, we have so far most focused on the ICP wave amplitude, and have given evidence that the amplitude on average should stay below 4 mmHg [15]. On this background, it is of interest that the ICP wave amplitude (SW.dP) was low (about 3 mmHg) in paediatric and adult patients with shunt overdrainage, spontaneous overdrainage (SIH), and in those not responding to shunt, while ICP wave amplitude was high (above 4 mmHg) in shunt underdrainage and preoperatively in shunt responders. The present data extend previous observations by showing similar profiles for ICP wave area under curve (SW.AUC) and downward coefficient (SW.DWC) as for ICP wave amplitude. Moreover, this study also showed that the ICP wave rise time (SW.RT) and wave duration (SW.WD) differentiated children from adults, while not differentiating the various patient categories. Obviously, these observation are related to the fact that heart rate is higher in the children.

When ICP was in the range 0 to −15 mmHg, there were no apparent changes in the ICP wave parameters of children or adults, though there was a tendency towards increasing ICP wave amplitude (SW.dP), rise time coefficient (SW.RTC), downward coefficient (SW.DWC), and area under curve (SW.AUC) when ICP became

Table 5
Correlations between ICP wave parameters and negative ICP (SW.meanICP) in paediatric and adult patients.

		SW.dP	SW.RT	SW.RTC	SW.WD	SW.DWC	SW.AUC
Paediatric (*n* = 205,697)	SW.MeanICP <0 mmHg	*R* = 0.07[a]	*R* = −0.1[a]	*R* = 0.16[a]	*R* = −0.1[a]	*R* = 0.07[a]	*R* = 0.07[a]
Adult (*n* = 380,808)	SW.MeanICP <0 mmHg	*R* = −0.14[a]	*R* = 0.06[a]	*R* = −0.18[a]	*R* = 0.05[a]	*R* = −0.11[a]	*R* = −0.18[a]

n = number of ICP waves included in correlation analysis.

[a] Significance of Pearson correlation < 0.001.

increasingly more negative. This latter was quite evident when ICP fell below −15 mmHg. This is an interesting observation though an ICP below −15 mmHg is rare, and constituted only 0.8% of ICP wave observations in this material. It is of interest to note that symptoms in severe CSF overdrainage may be comparable to those seen in CSF under-drainage [8].

It is essential, but difficult to define the "normal" range of ICP wave parameters. Since ICP monitoring is an invasive procedure, it is unethical to monitor ICP in healthy people. Though none of the present patient recordings can be considered as "normal", the ICP wave parameters seen for the ICP categories −15 to 0 mmHg (and even up to 10 mmHg) were in ranges that we tentatively consider as "normal" values. Therefore, according to our experience, it seems as the ICP wave parameters for the ICP categories 0 to −15 mmHg represent "normal" values.

In conclusion, during CSF overdrainage when ICP is in the range 0 to −15 mmHg, the ICP wave morphology appears not to change. However, in adults (not children) the ICP wave parameters amplitude, rise time coefficient, downward coefficient and area under curve increase when ICP falls below −15.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.medengphy.2011.11.011.

Conflict of interest statement

PKE has financial interest in the software company (dPCom AS) that manufactures the software (Sensometrics® Research Software and Sensometrics® Software) in this study. MS, AW, and TES report no conflicts of interest.

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