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REVIEW PAPER

Non-invasive intracranial pressure assessment

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Abstract Assessing intracranial pressure (ICP) remains a cornerstone in neurosurgical care. Invasive techniques for monitoring ICP remain the gold standard. The need for a reliable, safe and reproducible technique to non-invasively assess ICP in the context of early screening and in the neurocritical care environment is obvious. Numerous techniques have been described with several novel advances. While none of the currently available techniques appear independently accurate enough to quantify raised ICP, there is some promising work being undertaken.

Keywords Intracranial pressure · Non-invasive monitoring techniques · Traumatic brain injury

Introduction

Early work done by Guillaume and Janny in 1951 [1], followed by Lundberg's magnum opus in 1960 [2] laid the foundation for subsequent developments in intracranial pressure (ICP) monitoring [3–6]. The association between raised ICP and poor neurological outcome has been widely reported, with distinct clinical and therapeutic implications [7–10]. Though some reports have questioned the merits of monitoring ICP [11, 12], the diagnostic and therapeutic role of invasive monitoring techniques, especially in traumatic brain injury (TBI), has been well supported [3, 13–17].

The benefits of reliably and non-invasively assessing ICP, however, have also been described, and while invasive ICP monitoring remains the gold standard, the development of accurate, non-invasive alternatives is ongoing [2, 18, 19]. Perhaps the most benefit of a reliable non-invasive technique lies in early detection, especially where the clinical presentation of raised ICP may be subtle.

In children, determining the threshold for raised ICP is complex because of physiological and morphological heterogeneity. Lower ICP treatment thresholds for younger children are often considered appropriate, but there is still a lack of data to support this. The current recommendation in the guidelines for acute medical care of severe traumatic brain injury in neonates, children and adolescents suggests an ICP treatment threshold of 20 mmHg for children, but there are no age-specific recommendations [20, 21], while age-related ICP thresholds of 2 to 6 years—6 mmHg, 7 to 10 years—9 mmHg and 11 to 15 years—13 mmHg have been described [22]. An ICP threshold of 20 mmHg demonstrated significant correlation with outcome in children with traumatic brain injury [23]. It therefore remains specifically relevant to interpret any recommended ICP threshold in the context of clinical presentation, underlying aetiology, monitoring of physiological variables (where appropriate) and imaging findings in an individual patient.

Monitoring of ICP

There is still no ideal method for evaluating ICP. While the benefit of continuous, real-time monitoring provided by invasive ICP monitoring is clear, it also comes with distinct limitations. The appeal of non-invasive ICP monitoring lies in

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obviating the need for placement of an intracranial device and avoidance of the risks associated with these procedures. Current non-invasive ICP monitoring techniques are, however, limited by inadequate diagnostic accuracy as most non-invasive techniques provide qualitative estimates of ICP but lack quantitative value [19, 24].

The use of invasive ICP monitoring is suboptimal in clinical practice. Patients being ventilated in a neurocritical care environment are good candidates for invasive monitoring, but ambulant patients are less suitable, and as a result, ICP monitoring may not be performed in many patients in whom it is indicated.

Invasive ICP monitoring remains the standard against which all non-invasive methods of assessing ICP are compared [13, 25]. The gold standard for invasive ICP monitoring remains measurement via a transduced intraventricular catheter [14]. The risks and limitations associated with invasive ICP monitoring have inspired considerable efforts towards the development of non-invasive techniques that are reliable, easy to use, cost-effective and reproducible [18, 19, 24, 26]. A variety of non-invasive techniques have been described for assessing ICP; their widespread use, however, remains quite limited. The shortcomings of these non-invasive techniques include the range of cut-off values for detecting raised ICP, inter-rater variability and qualitative rather than quantitative measurement of ICP [18, 19, 26]. For a non-invasive technique to be considered reliable, it would have to correlate well with invasively measured ICP, predict ICP within 2 mmHg in the 0–20 mmHg range, with a maximum error of 10 % for ICP >20 mmHg, which are the specifications supported by the Brain Trauma Foundation [27].

Non-invasive ICP monitoring

The ideal non-invasive technique should be relatively inexpensive, repeatable, portable and radiation-free and allow continuous monitoring. It could facilitate screening and triage in the acute care setting, allow easier long-term monitoring in a neurocritical care environment and augment follow-up assessment in patients with chronic conditions presenting with raised ICP, e.g. hydrocephalus. The benefits of such a technique are certainly not limited to a neurosurgical environment but include medical emergencies, ophthalmology assessment, anesthesiology and aeronautical health assessment.

Current methods of non-invasive ICP assessment usually involve evaluating physiological or anatomical characteristics influenced by increases in ICP. There are a variety of techniques which include both clinical and technological assessment with varying degrees of diagnostic accuracy [18, 19, 26]. These techniques include the following:

i. Clinical assessment
ii. Methods utilising natural bony windows in the skull
iii. Methods assessing cerebral fluid dynamics properties
iv. Electrophysiological methods
v. Imaging methods
vi. Novel methods

Clinical assessment

Clinical neurological assessment remains an important initial diagnostic and monitoring tool. Careful history taking can be an invaluable tool in making the diagnosis of raised ICP, where symptoms suggestive of raised ICP include headache, impaired level of consciousness, visual disturbance, nausea and vomiting, developmental delay and failure to thrive (in younger children).

The nuances of clinical evaluation differ in the paediatric and adult population. In children with an open anterior fontanelle (AF), where the skull sutures have not yet fused, an abnormal increase in the head circumference and bulging of the fontanelle are good indicators of raised ICP [28, 29]. In severely raised ICP, the sutures may often be separated and palpable. Distended scalp veins may be visible.

After the cranial sutures have fused, assessment of ICP becomes more difficult. Finding papilledema on fundoscopy is a useful but inconsistent finding in raised ICP [30, 31]. Papilledema is usually bilateral and generally develops within 5 days of an abnormal increase in ICP [32, 33]. Fundoscopic examination can provide significant additional evidence of underlying raised ICP, which includes papilledema, haemorrhage, loss of spontaneous venous pulsation and optic atrophy. Spontaneous venous pulsation (SVP) is a sensitive marker for normal ICP but should be interpreted in the context of the patient's clinical presentation [34–36].

Cranial nerve palsies, usually the third and sixth cranial nerves and abnormalities of gaze (usually upward gaze palsy), are ominous signs that raised ICP may be present. Bradycardia and hypertension with abnormal respiration (Cushing's response) may accompany cerebral herniation syndromes, usually signalling critically raised ICP requiring emergent treatment. The benefit of a thorough history and clinical examination can therefore not overemphasised.

Methods utilising the natural bony windows of the skull

The most accessible anatomical windows in the bony skull used to assess ICP are transorbital, auditory canal and AF in infants (Table 1).

Transorbital methods

i. Pupillometry

Infrared pupillometry has been used to quantitatively measure subtle changes in pupil size in response to light stimulus.

Table 1 Methods using natural bony windows in the skull—transorbital and auditory canal

Route	Technique	Level of operator skill required	Quantitative or qualitative assessment of ICP	Continuous monitoring	Main advantage	Main disadvantage
Transorbital	Pupillometry	Medium	Qualitative	No	Requires minimal additional training	Limited data available
	IOP	Medium	Qualitative	No	Relatively inexpensive Minimal discomfort to patients Can be performed in awake patients	Appears to be useful only where ICP is very high
	OCT	High	Qualitative	No	Very sensitive for measuring retinal fibre thickness New techniques described for improving accuracy	Currently limited to use by ophthalmologists
	SLT	High	Qualitative	No	Diagnostic for a wide spectrum of ocular disease	Limited data available
	Venous ophthalmodynamometry	High	Qualitative	No	Can be combined with other techniques to improve accuracy	Cumbersome technique Potential to induce oculo-cardiac reflex
	ONSD	Medium	Qualitative	No	Requires minimal additional training Relatively inexpensive	Poor specificity Wide range of described cut-off values to detect raised ICP
Auditory canal	TMD	Medium	Qualitative	Potentially	Simple, cost-effective	Limited by anatomical variation
	OAEs	Medium	Qualitative	Potentially	Excludes the brainstem pathway	Difficult in older patients

Pupillometers have been found to be more sensitive than manual scoring for noting small changes in pupil size [37, 38]. In normal individuals, the pupil decreases by 34–36 % in size, in response to a standard light stimulus. This response is reduced to 20 % in head-injured patients, with a reduction of less than 10 % associated with an ICP >20 mmHg [39, 40]. While promising, the clinical applicability of this technique requires further investigation.

ii. Intraocular pressure (IOP)

The appeal of this technique lies in the anatomical proximity and direct communication between the eye and the intracranial space [41]. The indirect transmission of ICP to the orbit via intervening venous anatomy has long been recognised [42]. The use of handheld tonometers by clinicians without any specialised training has increased the interest in IOP as a rapid screening tool for raised ICP [41, 43, 44]. Lehman et al. demonstrated in their study on rhesus monkeys that a relationship between IOP and ICP did exist, albeit at rather high mean values of ICP (46.8 mmHg) [45]. Later studies evaluating the relationship between IOP and ICP provide mixed results [42, 43]. A meta-analysis by Yavin et al. concluded that the pooled diagnostic accuracy suggested IOP may be a useful clinical adjunct in the detection of raised ICP, but felt the benefit of the technique would be best assessed in future studies where clinical equipoise exists regarding the use of invasive ICP monitoring [46]. While there appears to be a relationship between an increase in IOP and raised ICP, IOP does not appear sufficiently accurate for predicting individual patient ICP measurement [47].

iii. Optical coherence tomography (OCT)

OCT is a technique using broadband near infrared light. This technology can be used to quantitatively measure and monitor the thickness of the retinal nerve fibre layer (RNFL) and the optic nerve head morphology [48], making it a useful, objective method for distinguishing nerves with papilledema from normal nerves, and optic atrophy. This application has been found useful in adults and children with raised ICP and papilledema [49, 50]. A recent study has also demonstrated structural changes of the optic nerve head on OCT in a small group of patients before and after lumbar puncture [51].

iv. Scanning laser tomography (SLT)

SLT uses a laser to produce a 3D scan of the retinal surface. It can be used as an alternative to OCT when measuring the RFNL. The technique has been described as being highly reproducible [52, 53]. Though SLT measurements of the optic nerve volume and height have been found reliable in quantifying papilledema [54] and have been correlated with CSF

pressure measured via LP [55], its value in reliably estimating ICP has yet to be established.

v. Venous ophthalmodynamometry (vODM)

This method was originally described by Baurmann in 1925 and involves measurement of the retinal venous outflow pressure (VOP) while observing the retinal vessels with an ophthalmoscope [56]. The technique usually involves applying a suction cup to the globe in order to increase the IOP until the central retinal vein (CRV) collapses and begins to pulsate, which usually happens at the point when the applied external pressure nears the VOP, which is an approximate of ICP. The venous outflow pressure which has a close linear relationship with ICP [57] is calculated by adding the pressure from the ophthalmodynamometer to the IOP. The technique requires the pupils to be dilated and should be performed by an experienced ophthalmologist. The application of external ocular pressure could also trigger the oculo-cardiac reflex, leading to hypotension, which is undesirable, especially if ICP is increased.

vi. Optic nerve sheath diameter (ONSD)

The optic nerve originates from the central nervous system. It is surrounded by a CSF-filled, perineural, subarachnoid space and encased by a dural sheath. Direct communication with the intracranial subarachnoid space means that an increase in ICP displaces CSF along this pathway, leading to an increase in CSF within the ONS and subsequent expansion of this sheath. Changes in the ONSD can be visualised on ultrasound, magnetic resonance imaging (MRI) and CT scan [58–64]. Several studies have demonstrated a strong association between distension of the ONSD and an increase in ICP [60, 65–69]. The suggested cut-off value in adult studies ranges between 4.1 and 5.9 mm and the definition of increased ICP varies between 14.7 and 30 mmHg [24, 60, 65, 67, 68]. In children, there are age-related differences in ONSD cut-off values [63, 70, 71]. Recent work suggests that using patency of the anterior fontanelle is a more useful marker for describing ONSD cut-off values [72]. ONSD measurements using higher frequency, smaller footprint ultrasound probes to better define the borders of the ONS have been larger than historic values [72, 73]. Comparison to invasive ICP measurements has allowed the relationship between ONSD and ICP to be evaluated at different ICP thresholds [72]. The main limitations of ultrasound-based ONSD measurements are hyperechoic artefacts, inter-rater variability, submillimetric measurements, variation in optic nerve sheath cut-off values and heterogeneity of the patient population [63, 65, 70, 71, 74–81]. Despite these limitations, ONSD measurement remains a very promising method for detecting raised ICP [63, 82–84].

Methods utilising the auditory canal The cochlea of the ear is in direct communication with the intracranial subarachnoid space via the cochlear aqueduct. Methods investigating displacement of the tympanic membrane and measurement of sound generated by movement of the ossicles have been described as markers of ICP.

i. Tympanic membrane displacement (TMD)

Tympanic membrane vibration is usually transmitted through the ossicles in the middle ear to the cochlea. Contraction of the stapedius and tensor tympani muscles is accompanied by a small, measurable displacement of the tympanic membrane from its resting position. As the perilymph and CSF communicate through the cochlear aqueduct, an increase in ICP is directly transmitted to the footplate of the stapes leading to a change in the direction and magnitude of TMD.

Movement of the tympanic membrane caused by stimulation of the stapedial reflex can be quantitatively assessed. This movement is altered by increased ICP, where inward displacement is suggestive of high ICP, and outward displacement is suggestive of normal or low ICP [85]. While it appears to have a utility in detecting raised ICP, limited accuracy confines it to providing qualitative ICP data [86–88]. In the study by Shimbles et al., no valid measurement of TMD could be made in about 60 % of patients, casting doubt on the clinical value of the technique [89]. Patency of the cochlear aqueduct, integrity of the tympanic membrane and strength of the acoustic reflex influence the TMD, which is further limited by poor inter-subject reproducibility [90].

ii. Otoacoustic emissions (OAEs)

OAEs are sounds originating from movement of the sensory hair cells within the cochlea in response to auditory stimulation. These sounds can be recorded by a probe placed in the ear canal. OAE is often used in clinical practice to test for hearing deficits in young children where cooperation is poor.

Auditory measurements of OAEs that depend on middle ear function are theoretically influenced by changes in ICP [91]. This method has been used as an alternative to TMD; specifically, a technique called distortion product otoacoustic emissions (DPOAEs) has been shown to change with ICP [91, 92]. It has the advantage over TMD of not requiring the middle ear reflex arc, which involves brainstem pathways. Poor inter-subject variability limits its use in measuring ICP, but it could be useful for monitoring patients once baseline ICP has already been measured [24, 93].

Assessment of the anterior fontanelle Palpation of the AF, measurement of head circumference, shape and palpation of suture ridges during clinical examination are basic but

extremely valuable assessments which can be performed by health-care workers at all levels. Raised ICP in infants almost always causes a bulging or tense AF, and this should prompt further investigation. ICP assessment via the AF includes measuring pulsation of the AF [94–96] and the use of an applanation transducer, modified Shiotz tonometer [29] and the Rotterdam Teletransducer (RTT) [97]. None of these have been widely used in routine practice and are largely of historic significance. Recently, transfontanelle ICP monitoring using an existing ICP probe secured against the AF was described as an accurate technique for detecting raised ICP in infants [98]. Where the AF is closed or not reliably patent, other non-invasive techniques are required to assess ICP.

Methods assessing cerebral fluid dynamic properties

Studying dynamic changes in ICP, cerebral blood flow (CBF) and cerebral compliance can be quite challenging. Reliable non-invasive techniques for assessing these parameters are therefore rather limited. Ultrasound, MRI and infrared spectroscopy have been used to examine some of these dynamic alterations (Table 2).

Transcranial Doppler sonography (TCD) TCD measures the velocity of blood flow through major intracranial vessels by emitting a high-frequency (>2 MHz) wave and detecting the frequency shift between the incident and reflected wave. This difference directly correlates with the speed of blood flow (the Doppler effect) [99]. TCD as a technique for evaluating cerebral haemodynamics was described by Aaslid et al. in 1982 [100]. It has since been used to measure the CBF velocity in the circle of Willis and the vertebrobasilar system, both diagnostically and to adjust treatment strategies in a variety of neurovascular disorders [101–104]. Insonation of one of the arteries, usually the middle cerebral artery, produces a reproducible arterial waveform. The most commonly assessed parameters using this arterial waveform are the peak systolic and diastolic velocity, mean velocity, resistance index (RI) and pulsatility index (PI). The criteria for adequate vessel insonation include the cranial window used, transducer position, angle of insonation, depth of sample volume, direction of blood flow, relative flow velocity and experience of the investigator [99, 105].

The measurement is taken over regions of the skull with the thinnest bony windows (temporal region, transorbital or at the back of the head). TCD is most suited to providing a qualitative estimate (low, normal or high) of ICP [101, 106].

In an adult study, the PI (difference between systolic and diastolic flow velocity divided by the mean flow velocity) correlated well with ICP (correlation coefficient of 0.938, $p < 0.001$) [101]. A study in children with severe TBI found the PI to be a less reliable indicator of absolute ICP values [107], while a subsequent study also in children found TCD to be an excellent first-line examination for identifying patients likely to need invasive ICP monitoring [108].

TCD remains an attractive alternative to invasive ICP because of its ability to detect cerebral ischemia, relative cost effectiveness and widespread availability. The main disadvantages are the requirement of a trained and skilled operator to perform and interpret the measurements and the limited accuracy for estimating absolute ICP [107].

Magnetic resonance imaging-based elastance index MRI-based cine phase-contrast pulse sequences are used to determine the blood and CSF volumetric flow rates within the brain. A novel method using the arterial inflow, venous outflow and CSF flow between the cranium and spinal compartment to calculate changes in intracranial volume; these measurements are then used to derive ICP using an elastance index [109, 110]. Prediction of ICP using this dynamic MRI technique has demonstrated strong correlation with invasive ICP measurement. In children with hydrocephalus, dynamic MRI correlated well with shunt valve opening pressure and symptom resolution [111, 112].

Near infrared spectroscopy (NIRS) Transcranial NIRS is a method for assessing regional changes in cerebral blood oxygen saturation (rSO_2) and cerebral blood volume (CBV) and CBF [113]. NIRS works in the infrared spectrum (700–1000 nm) of light, where low absorption allows it to easily pass through the skin and bone resulting in deep-tissue penetration. This light is both scattered and absorbed as it passes

Table 2 Methods based on cerebral fluid dynamic assessment

Technique	Level of operator skill required	Quantitative or qualitative assessment of ICP	Continuous monitoring	Main advantage	Main disadvantage
TCD	High	Qualitative	No	Versatile technique with a wide array of indications	Technical expertise limit its widespread use
MRI-based elastance index	Medium	Qualitative	No	Exquisite detail, with potential for describing new indices	High cost with extensive infrastructure required
NIRS	Medium	Qualitative	Yes	Allows long-term monitoring	Readings are influenced by a number of variables

through brain tissue. Variations in the absorption of infrared light by different substances allow the detection of changes in deoxyhaemoglobin and oxyhaemoglobin concentration. A significant difference in rSO_2 values was demonstrated in a study of severe TBI patients with normal and raised ICP [114]. Changes in cerebral oxygenation correlated well with vasogenic ICP slow waves in CSF infusion studies and TBI [115]. NIRS allows for the calculation of certain indices which have been correlated with cerebrovascular pressure reactivity in TBI patients [116]. At present, NIRS does not provide an estimation of absolute ICP nor does it facilitate the detection of changes in ICP [19]. The technique is also limited by the requirement for specialised equipment and the extended period required to obtain the required indices [116].

Electrophysiological methods

Electroencephalography (EEG) EEG represents spontaneous electrical activity of the cerebral cortex recorded through electrodes placed on the scalp. These electrical signals are then amplified, filtered and displayed according to the number of channels required (generally 8 or 16 channels).

The use of a novel technique called EEG power spectrum analysis has recently been reported by Chen et al. [117]. Power spectral analysis allows a graphical representation of the EEG readings over time. An index called the intracranial pressure index (IPI) was derived using the EEG power spectrum analysis, and this was then correlated with ICP measurements. The authors concluded that there was a correlation between the IPI and ICP. Its clinical utility depends on validation in further studies. Recent development of both wireless, portable and field deployable EEG systems has improved the application of this technique [117].

Visual evoked potentials (VEPs) VEPs are recorded from electrodes positioned in the occipital scalp and accurately reflect disturbances of the visual pathways [118, 119]. Rosenfeld and Owen described a method using flashing light into the eye and estimating ICP through recordings obtained from a few occipital EEG electrodes, using the latency of the second negative-going wave (N2) [119]. A linear relationship between ICP and the latency of the third positive-going wave (P3) has also been reported using high-density electrode arrays and independent component analysis extraction [120]. The N2 wave appears to be stable and easily identifiable using flash-evoked VEPs in healthy control patients. Earlier studies demonstrated a strong correlation between the N2 latency of the VEP and ICP in children with hydrocephalus and young adults with head trauma [121, 122]. The relationship between a prolonged N2 latency period and raised ICP has subsequently also been reported in children [123, 124]. A recent study has, however, demonstrated a high inter-subject variability, suggesting a limited ability to reliably predict ICP [125].

Ocular vestibular evoked myogenic potentials (oVEMPs) This technique employs vestibular stimulation of the extraocular muscles to generate electromyographic activity. These evoked potentials can be recorded from the contralateral eye using surface electrodes. A recent study has suggested that this technique may have a role in non-invasive ICP assessment [88] (Table 3).

Imaging methods

Radiological imaging has historically been a fundamental tool in making the diagnosis of raised ICP. Skull X-rays were used to assess whether chronically raised ICP was present by detecting separation of the skull sutures, 'copper beaten' appearance of the skull and erosion of the clinoid [126–128]. This modality is perhaps less useful in the modern era [129]. Imaging features on CT and MRI consistent with clinical findings of raised ICP have been well described [64, 126, 130–133].

CT scan CT scan still remains the most widely used diagnostic imaging modality when assessing patients with acutely raised ICP. A variety of findings on CT have been associated with raised ICP, depending on the underlying aetiology. These findings include the following:

- Absence/compression of the basal cisterns and/or ventricles
- Midline shift
- Enlarged ventricles (hydrocephalus)
- Transependymal fluid shift
- Presence of haematoma/space occupying lesion
- Blood in the subarachnoid space
- Size of sulci
- Grey/white differentiation

The benefit of the initial CT scan has been investigated widely in the context of traumatic brain injury [64, 126, 131, 134]. CT scan still forms the cornerstone of acute imaging in hydrocephalus, where features depend on the aetiology and relate to the level of obstruction, presence of transependymal fluid shift, volume of CSF in the subarachnoid space and shape of the third ventricle [135–137].

The discussion regarding which of these CT findings and which correlate best with raised ICP is still ongoing [19, 24, 64, 134]. While CT scans remain a valuable diagnostic adjunct in the acute diagnosis of raised ICP, it must be remembered that a 'normal' CT scan does not rule out raised ICP. In children, additional radiation exposure to the susceptible, developing brain and the compound effect over the lifetime of the

Table 3 Electrophysiological methods

Technique	Level of operator skill required	Quantitative or qualitative assessment of ICP	Continuous monitoring	Main advantage	Main disadvantage
EEG	High	Qualitative	Yes	Allows high-quality data that can provide information about other conditions as well, i.e. seizures, ischemia	Requires trained personnel to set up and interpret
VEP	High	Qualitative	Potentially	Ability to provide data on a spectrum of visual abnormalities	Lack of clear evidence to support correlation with ICP
oVEMP	Medium	Qualitative	No	Still unclear	Paucity of data

child should always be considered [135, 138–142]. To this effect, the 'image gently' recommendations for children should always be kept in mind (www.imagegently.org).

MRI scan MRI provides superb quality images of the brain but can be time consuming and costly as a first-line diagnostic modality in the acute care setting. MRI techniques for evaluating ICP are based on the relationship between intracranial compliance and pressure [109, 143]. Using a motion-sensitive technique to measure the arterial, venous and CSF flow into and out of the cranial cavity during the cardiac cycle, Alperin et al. demonstrated a strong correlation between the MRI-derived elastance index and invasively measured ICP [109]. These results, however, were found to have poor repeatability in a subsequent study, due to technical errors in measurement and intra-individual variation, with the authors suggesting caution when interpreting individual measurements [144]. Despite these shortcomings, specific MRI sequences appear promising, both for screening in acutely raised ICP and for assessment of ICP in other conditions, like hydrocephalus [145]. MRI has also been used to evaluate the optic nerve sheath diameter as a marker for raised ICP [146], and appears to be more accurate than ultrasound in assessing the CSF-filled subarachnoid space surrounding the optic nerve [78]. The current role of MRI as a diagnostic and monitoring tool in neurosurgery far outweighs its function as a purely non-invasive technique for assessing ICP.

Novel methods

Ultrasonic time of flight (*TOF*) for non-invasive assessment of ICP is based on measurement of the acoustic properties of intracranial structures, i.e. dura, brain, blood and CSF. Using the propagation speed and attenuation of ultrasound and the respective change within the intracranial components in the acoustic pathway, an estimation of ICP was described [147, 148]. *Two-depth transorbital Doppler* (*TDTD*) is an innovative technique using the principle of externally applied pressure to the eyeball as a means of equilibrating the blood flow pulsation parameters between the intracranial and extracranial segments of the ophthalmic artery. This technique is based on the assertion that the external applied pressure is equal to ICP at this balance point [149, 150]. While initial work described very high correlation between this method and CSF pressure measurement on lumbar puncture, subsequent external validation has demonstrated much lower accuracy [150, 151]. A method using dynamic imaging of the ONS to evaluate the stiffness of the sheath in cases of raised and normal ICP described a novel parameter, the *deformability index* (DI), to define the motion of the ONS as a marker of its stiffness. The DI demonstrated a significant difference in raised ICP, and the authors described coupling DI with ONSD to improve our understanding of the ONS response in raised ICP to further refine the diagnostic accuracy of this method [152].

Despite a relatively long history of innovative thinking regarding suitable techniques for non-invasively assessing ICP, most developments remain in an exploratory phase. The main limitations are inadequate diagnostic accuracy for detecting raised ICP, poor quantitative estimation of ICP and lack of continuous monitoring capability. Most methods appear suitable to identify subjects with low to normal ICP or very high ICP, but are poor at detecting moderately raised ICP, which arguably is the most important group. The idea of combining selected non-invasive techniques to improve accuracy in a 'non-invasive multi-modality model' is certainly appealing in principle.

Non-invasive ICP assessment is still most suitable as a screening tool for patients with suspected raised ICP. Future development of non-invasive techniques will likely depend on substantial improvements in the accuracy, ease of use and potential for continuous monitoring. This need is perhaps most distinct in the children, where early detection of increasing ICP has the potential to spare the developing nervous system unnecessary exposure to radiation from repeated CT scans or limit the need for invasive monitoring in certain cases making this quest worthwhile. Promising developments aimed at improving diagnostic accuracy and possibly even simplifying the acquisition technique may contribute significantly towards improving the performance of these methods [149, 150, 152].

Compliance with ethical standards

Conflict of interest There is no conflict of interest to declare.

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