

## Elevated intracranial pressure and reversible eye-tracking changes detected while viewing a film clip

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**OBJECTIVE** The precise threshold differentiating normal and elevated intracranial pressure (ICP) is variable among individuals. In the context of several pathophysiological conditions, elevated ICP leads to abnormalities in global cerebral functioning and impacts the function of cranial nerves (CNs), either or both of which may contribute to ocular dysmotility. The purpose of this study was to assess the impact of elevated ICP on eye-tracking performed while patients were watching a short film clip.

**METHODS** Awake patients requiring placement of an ICP monitor for clinical purposes underwent eye tracking while watching a 220-second continuously playing video moving around the perimeter of a viewing monitor. Pupil position was recorded at 500 Hz and metrics associated with each eye individually and both eyes together were calculated. Linear regression with generalized estimating equations was performed to test the association of eye-tracking metrics with changes in ICP.

**RESULTS** Eye tracking was performed at ICP levels ranging from  $-3$  to 30 mm Hg in 23 patients (12 women, 11 men, mean age 46.8 years) on 55 separate occasions. Eye-tracking measures correlating with CN function linearly decreased with increasing ICP ( $p < 0.001$ ). Measures for CN VI were most prominently affected. The area under the curve (AUC) for eye-tracking metrics to discriminate between ICP  $< 12$  and  $\geq 12$  mm Hg was 0.798. To discriminate an ICP  $< 15$  from  $\geq 15$  mm Hg the AUC was 0.833, and to discriminate ICP  $< 20$  from  $\geq 20$  mm Hg the AUC was 0.889.

**CONCLUSIONS** Increasingly elevated ICP was associated with increasingly abnormal eye tracking detected while patients were watching a short film clip. These results suggest that eye tracking may be used as a noninvasive, automatable means to quantitate the physiological impact of elevated ICP, which has clinical application for assessment of shunt malfunction, pseudotumor cerebri, concussion, and prevention of second-impact syndrome.

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**KEY WORDS** cranial nerves; neurocritical care; intracranial pressure; eye movement; diagnostic technique

ELEVATED intracranial pressure (ICP) is associated with multiple neurological conditions including hydrocephalus, trauma, stroke, pseudotumor cerebri, and intracranial mass lesions,<sup>6</sup> as well as with prolonged microgravity associated with space travel.<sup>13,31,32</sup> Acute or uncontrollable elevations in ICP, often seen in the setting of trauma, have an increased association with morbid-

ity and mortality.<sup>3,12,18</sup> Chronic ICP elevations from other causes such as untreated hydrocephalus and idiopathic intracranial hypertension can lead to cognitive difficulties<sup>33</sup> and blindness.<sup>23,25</sup> Even subischemic elevation of ICP has been linked to increased morbidity and neuronal damage<sup>19</sup> and is thought to be at least a partial component of the mechanism for ocular disturbance and cognitive dif-

**ABBREVIATIONS** AUC = area under the curve; CN = cranial nerve; EVD = external ventricular drain; GEE = generalized estimating equation; ICP = intracranial pressure; ROC = receiver operating characteristic; SAH = subarachnoid hemorrhage.

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difficulties experienced in astronauts after prolonged space travel.<sup>13,30,32</sup>

To complicate matters, whereas there are some values of ICP that are accepted as pathological, the precise threshold differentiating normal and elevated ICP varies among individuals and pathologies.<sup>21</sup> Studies of telemetrically monitored individuals demonstrate normal values of  $-10$  to  $+8$  mm Hg depending on subject position.<sup>2,3</sup> The most commonly used treatment thresholds in acute trauma are between 20 and 25 mm Hg,<sup>7,17,20</sup> despite primarily Level III evidence supporting these values. Three recent successive prospective randomized clinical trials with ICP treatment thresholds in the 20- to 25-mm Hg range have failed to demonstrate improved patient outcome.<sup>4,9,10</sup> The Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST:TRIP) trial followed 324 patients with trauma who were randomized to either an ICP-monitored group or medical management. In this study investigators were unable to detect any significant improvement in outcome in monitored patients treated for ICP  $> 20$  mm Hg compared with patients who were not monitored and only treated clinically. Other studies have demonstrated lower mortality rates in trauma patients undergoing ICP monitoring.<sup>24,34</sup> This raises the possibility that the threshold of 20 mm Hg defining elevated ICP may be inappropriately high, or that there may be other factors such as tissue compliance that also impact outcomes.<sup>8,9</sup>

Elevated ICP may be associated with brain injury, which causes ocular dysmotility by several mechanisms.<sup>14</sup> These can range from palsies of individual cranial nerves (CNs) to more global deficiencies such as dorsal midbrain syndrome, due in part to elevated ICP.<sup>1,5,11</sup> Pure CN palsies due to traumatic brain injury and elevated ICP most commonly involve the abducent nerve (CN VI),<sup>1,5,11</sup> followed by the trochlear (CN IV) and the oculomotor (CN III) nerves. The abducent and trochlear nerves are often injured due to their long intracranial course and relatively small size compared with other nerves, whereas the oculomotor nerve is impacted via direct compression by the temporal lobe. Global changes can affect both supranuclear circuitry in cortical command centers for eye movements as well as the vertical and horizontal gaze centers they control in the midbrain and pons, respectively. Due to the proximity of these centers to the ventricular system, elevations in ICP from hydrocephalus cause stretching of the pathways, ultimately leading to gaze abnormalities. Putative mechanisms include increased CSF volume leading to stretching of neural pathways, to compression of the tectum or shearing injuries of long tracts as they ascend and descend to their target nuclei.<sup>11,15,28</sup> Interestingly, when a patient's hydrocephalus is treated, his or her ocular motility dysfunction often resolves.<sup>5</sup>

Recently we described a novel technique to detect subclinical eye movement abnormalities while patients watch a short film clip<sup>26,27</sup> and have demonstrated that this methodology enables direct assessment of the physiological function of CN III and CN VI, which impact eye movement in the vertical and horizontal planes, respectively. The hypothesis that elevated ICP would cause alterations consistent with CN palsies detectable with eye tracking while watching a 220-second film clip was tested by per-

forming eye tracking in 23 patients with ventriculostomy catheters for ICP monitoring after trauma. By obtaining an objective measure, we aim to better describe the physiological changes associated with changing ICP, even in ranges previously believed to be "normal."

## Methods

Institutional review board approval was obtained for this study, and consent was obtained from all participants.

### Patient Population

The inclusion criteria included patients ages 18–70 years who were admitted to the Bellevue Hospital neurosurgical intensive care unit with vision correctable to within 20/500 bilaterally, denied a history of ocular dysmotility, and were conscious and able to communicate and provide an ophthalmological, medical, and neurological history as well as medications, drugs, and/or alcohol consumed within the 24 hours prior to eye tracking. Patients required external ventriculostomy drainage catheters for clinical indications. At the time when eye tracking was performed, all patients were awake with spontaneous eye opening. None of the patients reported a prior history of CN palsy. Patients were positioned with the head of the bed at  $30^{\circ}$ – $45^{\circ}$ , and external ventricular drain (EVD) height relative to the tragus was maintained. To capture the most accurate pressure value, the EVD was clamped and the sensor was zeroed. The ICP was measured continuously during tracking, and recorded during the middle of the 220-second tracking session.

### Exclusion Criteria

Patients were excluded if they were noted to have a prior history of strabismus; diplopia; palsy of CN III, CN IV, or CN VI; papilledema; optic neuropathy; macular edema; retinal degeneration; dementia or cognitive impairment; sarcoidosis; myasthenia gravis; multiple sclerosis; or other demyelinating disease. Comatose and sedated individuals were excluded. Pregnant individuals and prisoners were excluded from the study, as were patients who were missing eyes, not opening eyes, or wearing excessive mascara and/or false eyelashes. Eye-tracking trials capturing  $< 30\%$  of eye movement over the course of the stimulus were also excluded for providing insufficient data for statistical analysis.

### Eye-Tracking Technique

A 220-second music video was played continuously within a square aperture moving around the perimeter of a 19-in viewing monitor fixed 55 cm away from the patient. The video aperture size was approximately one-ninth the area of the display monitor. Eye movement position was obtained at 500 Hz by using the SR Research Eyelink 1000 with a stabilized chin rest to minimize head movement during the eye-tracking session. The first and last 10 seconds of each data set were discarded to yield 200 seconds of data and 100,000 data points. The afferent stimulus was presented binocularly and eye tracking was performed binocularly. The ICP values were recorded

during stimulus presentation, and patients underwent serial eye-tracking sessions on different days and times.

### Eye-Movement Plotting

For each tracking session, we created scatterplots of the entire time series by plotting the 100,000 (x,y) pairs representing the 2 orthogonal components of the instant angle of pupil reflection over time to create “box” trajectories that reflected the temporal nature of the pupillary movement. In control volunteers these figures look like boxes, reflecting the timing of the aperture as it moved around the screen. We then calculated metrics for eye movements reflecting function of both CN III and CN VI.<sup>26</sup> Specifically, CN III function was assessed by measuring the vertical distance moved by the pupil over time, because CN III controls superior and inferior recti. The CN VI function was assessed by measuring the horizontal distance moved by the pupil over time, because CN VI controls the lateral rectus. Area was defined as height of the box plot times its width, and thus reflects function of both CN III and CN VI. In addition, we used metrics assessing conjugacy and velocity of eye movement.<sup>27</sup> Conjugacy was defined as the difference between the positions of the right and left eyes measured horizontally and vertically and then summed. Velocity is the distance moved by the pupil between given time points. These eye-tracking metrics were correlated with ICP as described below. The scatterplot analysis was performed algorithmically such that the total testing time (running the eye tracker for 220 seconds plus plotting the result) required approximately 4 minutes per patient tested.

### Statistical Analysis

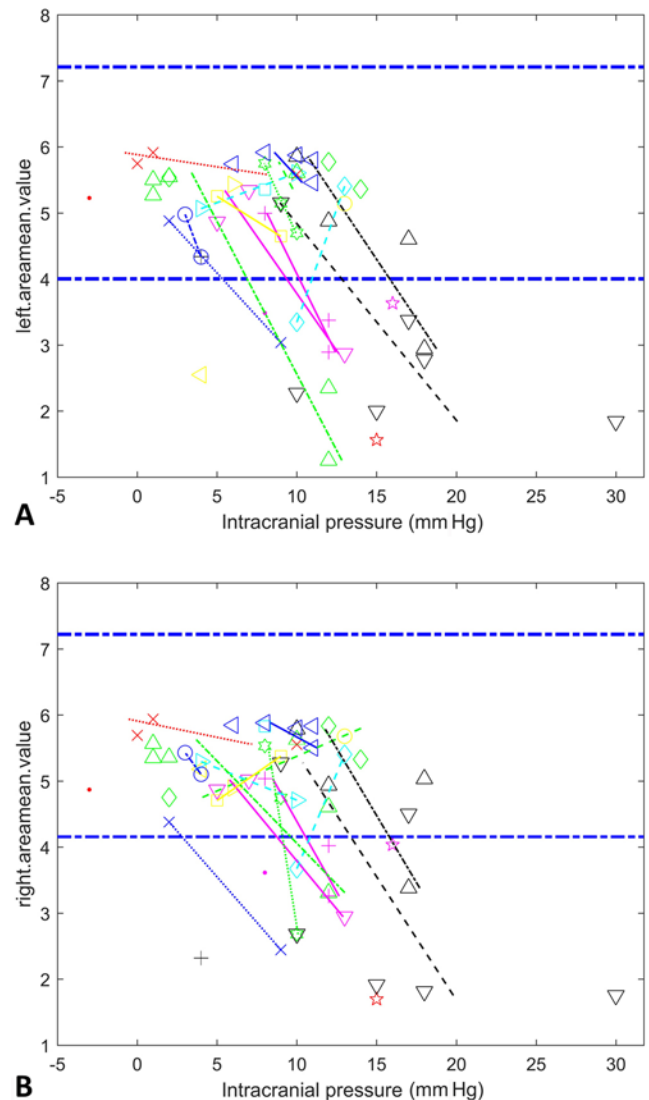
Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS Statistics, version 19; IBM Corp.). The figures were created using Matlab r2015b (Mathworks, Inc.).

Linear regression with generalized estimating equations (GEEs), to account for multiple observations per patient, were used to model ICP (as a numeric variable), using intercept and eye-tracking metrics as predictors. To appraise the ability of eye-tracking trials to discriminate between elevated and normal ICP as a binary variable, we treated ICP values  $\leq 12$  mm Hg as normal and ICP values  $> 12$  mm Hg as elevated. This was followed by binary logistic GEE modeling and a receiver operating characteristic (ROC) curve analysis. The best predictor was further tested with additional ICP thresholds of ICP  $\geq 15$  mm Hg and ICP  $\geq 20$  mm Hg as elevated. The area under the ROC curve was calculated for these elevated thresholds as well.

## Results

### Demographic Data

In total, 23 patients (12 women, 11 men) were admitted to the neurosurgical intensive care unit for ventriculostomy drainage and were enrolled in the study (mean age 46.8 years, range 26–68 years). Eighteen patients presented with hemorrhage (14 aneurysmal subarachnoid hemorrhage [SAH], 3 traumatic SAH, and 1 intraventricular hemorrhage) and 5 presented with obstructive hydroceph-



**FIG. 1.** Charts showing that as the ICP increases, the area of the box plot decreases, suggesting impaired ocular motility at higher ICPs. The area of the eye-tracking scatterplot (box plot) is charted against the ICP in 23 patients undergoing 55 eye-tracking sessions. Each symbol represents an individual patient, with lines connecting the occasions on which each patient was tracked at a different ICP. Patients who were only tracked once do not have lines. Panel **A** represents the mean area in the left eye, and panel **B** is of the mean area in the right eye. Figure is available in color online only.

alus (4 with tumors, 1 with bilateral cerebellar infarcts). Of these 23 patients, 9 were tracked once, whereas the remaining 14 were tracked in 46 different sessions. The mean ICP observed was 9.14 mm Hg (SD 5.67, range –3 to 30 mm Hg). None of the patients experienced significant flux in ICP during the 220 seconds of testing. The value recorded during the middle of the test period fluctuated by at most  $\pm 2$  mm Hg between the beginning and end of the 220-second session.

The box areas (Fig. 1A and B) for the right and left eyes were seen to decrease with increasing ICP in a linear fashion. Linear regression with GEEs was performed to test this association. In ROC curve analysis, right skew top was

the single best predictor for ICP  $\geq 12$  mm Hg (area under the curve [AUC] = 0.775). The model with both left area mean and right skew top yielded an AUC of 0.798. The ROC analysis using right skew top as the predictor for ICP  $\geq 15$  mm Hg as abnormal (with 7 elevated and 48 normal ICP instances) yielded an AUC of 0.833. There was only 1 patient at 1 time point with an ICP of 30 mm Hg. All other ICP values were  $\leq 18$  mm Hg. The ROC analysis performed using the right skew top as the predictor for ICP  $\geq 20$  mm Hg as abnormal yielded an AUC of 0.889. Analysis of individual patient examples showed that as ICP increased, these metrics moved away from normal values, and as it decreased, the values returned toward normal, as illustrated by the following exemplary cases.

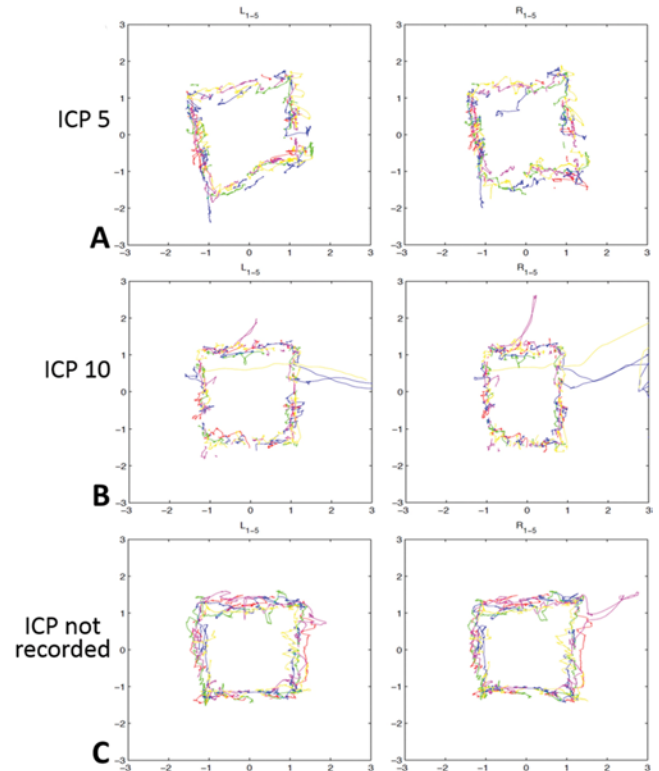
## Illustrative Cases

### Case 1

A 45-year-old woman with acute-onset headache and meningismus presented with lethargy. A noncontrast head CT scan was obtained at a referring hospital, which revealed a Hunt and Hess Grade III SAH of unknown origin, primarily in the basilar cisterns and left sylvian fissure. A right frontal EVD was placed and an opening pressure  $< 20$  mm Hg was obtained. After placement of the EVD, the patient became alert and oriented to person and place. Her first eye-tracking session (Fig. 2A) was performed 24 hours after placement of the EVD, with an ICP of 5 mm Hg. This was done prior to a diagnostic angiogram, which was unrevealing for a cause of hemorrhage. The second eye-tracking session (Fig. 2B) was performed on Day 3, with an ICP of 10 mm Hg with the EVD clamped. Her EVD was discontinued on Day 5 after ICPs were stable at approximately 5 mm Hg. The final eye-tracking trial performed after EVD removal (Fig. 2C) was on Day 6. Although she experienced a headache throughout her stay, she never had clinical evidence of vasospasm, and a repeat angiogram that was performed on Day 8 was negative for an aneurysm. She was discharged from the neurosurgery intensive care unit on Day 9.

### Case 2

A 46-year-old woman with a medical history of hypertension presented after a syncopal episode while at work, followed by a headache, nausea, and vomiting, which began on arrival at the hospital. A noncontrast head CT scan revealed an SAH from a ruptured left supraclinoid internal carotid artery aneurysm. Somnolence improved after placement of a right frontal EVD, which was followed by surgical clipping. Her first eye-tracking session (Fig. 3A) was performed on postoperative Day 2 with an ICP of 3 mm Hg, and no evidence of vasospasm. The patient was alert and oriented to person, place, and time. The second eye-tracking trial (Fig. 3B) was performed on Day 3 with an ICP of 9 mm Hg, and the patient reported a mild headache during this time. The patient's frontal ventriculostomy was converted to a ventriculoperitoneal shunt with a low-pressure valve on Day 8. She was discharged on Day 22 to inpatient occupational therapy after improvement in mental status, and her third eye-tracking session (Fig. 3C) was performed on Day 36.



**FIG. 2.** Case 1. Eye tracking is impaired at elevated ICP and recovers as the patient recovers clinically. Serial eye tracking was performed in a 45-year-old woman who sustained an SAH. **A:** The first eye-tracking session was at an ICP of 5 mm Hg and demonstrated normal metrics. **B:** The second session was at an ICP of 10 mm Hg and tracking was impaired. **C:** The third trial was after clinical and radiographic recovery from hydrocephalus and removal of ventriculostomy. It demonstrated normal metrics. Figure is available in color online only.

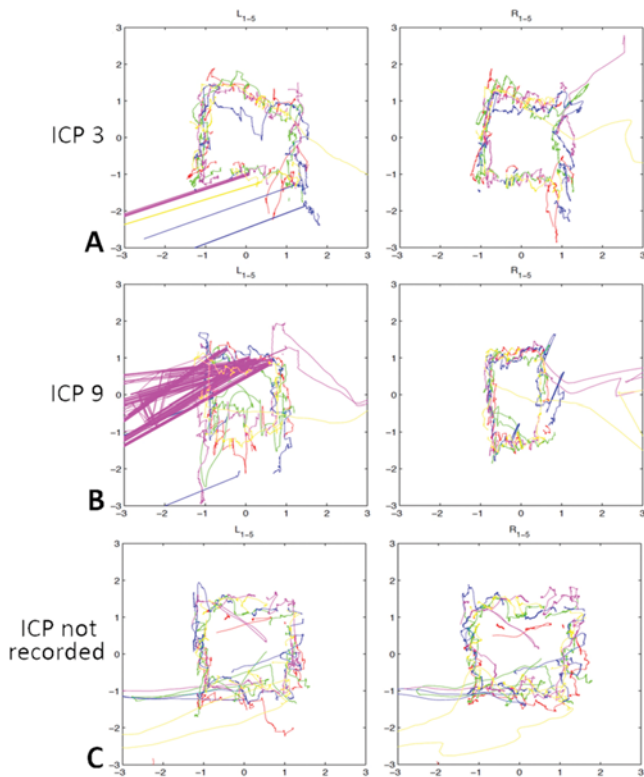
### Case 3

A 55-year-old woman with history of hypertension presented with a sudden onset of the “worst headache of her life,” which persisted for 5 days and was refractory to Excedrin, with no nausea, vomiting, vision changes, weakness, or sensory changes. A noncontrast head CT scan revealed right temporal intraparenchymal hemorrhage and right-sided Hunt and Hess Grade IV SAH from aneurysmal rupture. A CT angiogram revealed a right  $M_1$  aneurysm. She underwent transfusion of platelets for reported aspirin use and ultimately underwent a craniotomy for middle cerebral artery aneurysm clipping and a right frontal EVD placement. The first eye-tracking trial (Fig. 4A) was performed  $< 24$  hours after admission and operation, with an ICP of 8 mm Hg. The second eye-tracking session (Fig. 4B) was on Day 3, with an ICP of 10 mm Hg. The third eye-tracking session was again at an ICP of 8 mm Hg. The fourth eye-tracking trial (Fig. 4C) was on Day 8, after the EVD had been removed and a CT scan demonstrated normal ventricular size.

## Discussion

Neurological examination is the most widely used noninvasive method for monitoring the physiological im-



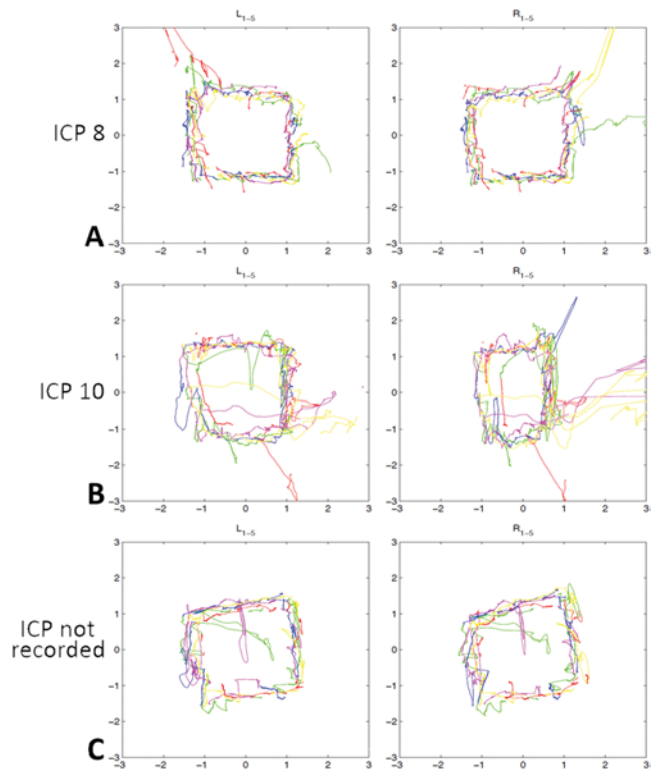


**FIG. 3.** Case 2. Eye tracking is impaired at elevated ICP and recovers as the patient recovers clinically. Serial eye tracking was performed in a 46-year-old woman who sustained an SAH. **A:** The first eye-tracking session was performed at an ICP of 3 mm Hg and demonstrated normal metrics. **B:** The second trial was at an ICP of 9 mm Hg and tracking was impaired. **C:** The third trial was performed after placement of a shunt to treat hydrocephalus and resolution of clinical symptoms. It demonstrated normal metrics. Figure is available in color online only.

pect of elevations in ICP; however, variability in clinical acumen for detection of papilledema or CN palsies may confound assessment. Furthermore, clinically apparent CN palsies are likely to be a relatively late indicator of elevated ICP, even to a highly skilled examiner.<sup>29</sup> In this study, we present data that suggest that eye tracking may be used as an objective measure of the physiological impact of increased ICP.

Our eye-tracking algorithm assesses ratios of horizontal and vertical movements, with horizontal movement, partially mediated by CN VI, impacting the width metric most directly.<sup>26</sup> To evaluate the interdependence of CN III and CN VI inputs, we use the area metric—defined as the product of the width and height of the horizontal and vertical trajectories—for both eyes. Both box width and area were noted to decrease with increasing ICP, as expected if CN VI was being impacted by increasing pressure. In the patients described above, we demonstrate that the ICP and area are inversely correlated; as ICP increases, the area decreases in a linear fashion.

Although the decrease in box width and area correlated with increased ICP, attributing this entire effect solely to CN VI, or even to the function of CN III and CN VI, would represent an oversimplification of the impact of elevated ICP on neurological function. Multiple pathways



**FIG. 4.** Case 3. Eye tracking is impaired at elevated ICP and recovers as the patient recovers clinically. Serial eye tracking was performed in a 55-year-old woman who sustained an SAH. **A:** The first eye-tracking session was at an ICP of 8 mm Hg and demonstrated normal metrics. **B:** The second trial was at an ICP of 10 mm Hg. The third trial was at an ICP of 8 mm Hg, and was again normal (not shown). **C:** The last eye-tracking session was performed after clinical and radiographic recovery from hydrocephalus and removal of ventriculostomy. It demonstrated normal metrics. Figure is available in color online only.

impacting motility may be affected by elevated ICP. Additionally, in all of the patients in this study a ventriculostomy catheter was placed for the clinical indication of acute hydrocephalus due to intracranial pathology. This underlying pathology may itself impact ocular motility independently of hydrocephalus. In many patients we were able to track the eyes serially at several different ICPs to reduce the likelihood that the abnormalities seen were due to the underlying pathology. Our own prior work has shown decreased conjugacy of eye movement in patients with concussion and structural brain injury relative to patients without trauma, whereas patients with nonhead trauma were unchanged relative to those without trauma.<sup>27</sup> Interestingly, some of the eye-tracking metrics that are impaired in concussed patients (area, horizontal conjugacy, box width) are also impaired in those with high ICP in this study, and normal in those same patients when their ICP is normal. Such a result suggests that concussion may be associated with high ICP.

With the patient in Case 2, headache symptoms developed with an elevation of the ICP to 9 mm Hg from a previously recorded level of 3 mm Hg, and she was found to have alterations in her eye-tracking metrics. This was seen during a clamp trial for attempted weaning from the ventriculostomy, and although her ICP remained in a range

that is currently accepted as normal, she was symptomatic, and her eye tracking was abnormal. Her symptoms improved and eye-tracking metrics returned to normal after shunt placement (Fig. 3B).

With the patient in Case 3 (Fig. 4B and C), the area is seen to decrease as expected with the increased ICP, which was elevated above the currently accepted normal level. We quantify the relative motion of the left eye to the right eye by using a metric called “total conjugacy.” Total conjugacy is the difference in pupil position between the left and right eye where perfect sustained vergence would result in a value of 0. Total conjugacy also was seen to decrease linearly with increasing ICP, fitting the inverse correlation relation of area and width as described above. As with the other metrics measured, this is seen to normalize when the ICP decreases. These results are consistent with our current understanding of the impact of elevated ICP on CN III and CN VI, as described previously.<sup>1,11</sup>

Current neurocritical care guidelines for management of traumatic brain injury propose that ICP should be maintained at < 20 mm Hg. In this study, we have demonstrated that CN III and CN VI palsy can be seen within the clinically established normal range of ICP. Recently, the Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP (RESCUE-ICP) trial has shown that lowering ICP by performing decompressive craniectomy decreases the mortality rate.<sup>16</sup> The median interquartile range for ICP in the surgical group was 14.5 mm Hg (range 1.7–18.0 mm Hg), compared with 17.1 mm Hg (range 4.2–21.8 mm Hg) in the medical management group. Interestingly, the 75th percentile of ICP even in the medical management group (21.8 mm Hg) is close to the current recommended threshold of 20 mm Hg. The ICP range studied herein coincided with the interquartile range of the ICP in this large clinical trial. The median ICP in the surgical group was 14.5 mm Hg, much lower than the previously supported 20 mm Hg. A median decrease of just 2.6 mm Hg in the surgical group lowered the overall mortality in this group by 22%. This suggests potential utility for noninvasive measurement of ICP in patients deemed to be at risk for developing elevations in ICP, but lacking a clinical indication for invasive ICP monitoring. It additionally supports others’ findings that the definition of normal ICP ranges should be reevaluated. This concept has previously been proposed by Andresen et al., who showed data suggesting that actual resting ICP in the non-pathological state is much lower than the ICP that has been targeted in previous ICP management trials. It is possible that previous clinical trials, such as BEST:TRIP,<sup>9</sup> failed to demonstrate improved outcome with measurement of ICP because the threshold for treatment was higher than the ICP value that is clinically significant.

This study demonstrates that alterations in ocular motility, as represented by a decrease in total conjugacy, trajectory area, and width may be accurately assessed with eye-tracking technology. The eye-tracking metrics described here correlate closely with changes in ICP obtained through more invasive means. The clinical implication of these findings is that eye-tracking technology may potentially allow for accurate, noninvasive monitoring of the physiological impact of elevated ICP in alert patients with significant

intracranial pathology. Further findings demonstrate that deviations from normal eye movements, as established through analyzing eye movements in healthy control volunteers, associated with oculomotor (CN III) and abducent (CN VI) palsies can begin at ICP values below 15 mm Hg, and possibly as low as 8 mm Hg. This eye-tracking method has potential to be used as a physiological monitor for conditions impacting ICP. Such conditions include prolonged microgravity associated with space travel. Six astronauts developed ocular dysfunction after space travel, possibly due to impaired venous drainage leading to elevated ICP.<sup>22</sup>

Eye tracking can be performed easily without a skilled examiner, and the data can then be reviewed remotely by a trained clinician. Potential applications of remote monitoring of ICP are numerous, and include the monitoring of astronauts in microgravity environments associated with space travel. Cranial and ocular complications of microgravity are one of the factors limiting long-duration space travel. Assessing physiological changes that occur in space and that impact astronauts on their return to earth will enable further understanding of what factors provoke ICP changes during space travel.

### Limitations of the Study

The major limitation of our current study is the lack of continuous data in patients with higher ICP recordings. Relatively few patients with elevated ICP open their eyes for long enough periods to perform eye tracking, and thus additional studies with noninvasive measures of elevated ICP for use in less severely impaired patients might be beneficial.

An additional limitation of this study is that all of the patients had neuropathological conditions leading to not only elevated ICP or hydrocephalus, but also to other pathophysiological changes that could potentially impact eye movements. In several patients we were able to record both increases and decreases in ICP over time, so it is clear that the changes we are seeing in eye tracking are not solely representing recovery over time. Additional studies are currently underway to investigate the impact of brain tissue oxygenation and other physiological impacts on eye tracking.

Future research will be required to determine how rapidly cranial nerves and the neurological pathways impacting their function are impaired by elevated ICP and how quickly these changes normalize with the restoration of physiological ICP.

### Conclusions

Eye tracking provides a noninvasive means for assessing the physiological impact of elevated ICP. It has the advantage of not requiring a trained examiner, pupil dilation, imaging studies, or an invasive procedure such as a lumbar or ventricular puncture. The data we present suggest that elevated ICP may have an impact at levels lower than those currently considered pathological. With these data, we are presenting a new application for eye-tracking technology, as well as a new mechanism for assessment of elevated ICP that is noninvasive, automatable, and could potentially

be performed and analyzed remotely. Such a technology has clinical applications for assessment of shunt malfunction, pseudotumor cerebri, concussion, and prevention of second-impact syndrome.

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## Disclosures

Dr. Samadani has been issued a patent describing the technology used in this paper. The ICP patent which has been issued is jointly owned by New York University (NYU) and the Veterans Administration (VA). Other patents related to this work are owned by NYU, the VA, and the Hennepin County Medical Center (HCMC) and are licensed to Oculogica Inc., a company in which Dr. Samadani, NYU, the VA, and HCMC have an equity interest. She also discloses support from Abbott Diagnostic Labs and Integra, Inc., for a non–study-related clinical or research effort that she oversees. Dr. Kondziolka discloses support from Brainlab for a non–study-related clinical or research effort that he oversees.

## Author Contributions

Conception and design: Samadani, Kolecki. Acquisition of data: Kolecki, Dammavalam, Reyes, Han, Wang, Papas, North. Analysis and interpretation of data: Samadani, Kolecki, Dammavalam, Bin Zahid, Hubbard, Gilbertson, Kondziolka, JH Huang, PP

Huang. Drafting the article: Samadani, Kolecki, Bin Zahid, Hubbard, Choudhry, Reyes, Han, Kondziolka, JH Huang, PP Huang. Critically revising the article: Samadani, Kolecki, Dammavalam, Hubbard, Choudhry, Gilbertson, Kondziolka, JH Huang, PP Huang. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Samadani. Statistical analysis: Bin Zahid, Hubbard, Gilbertson. Administrative/technical/material support: Samadani, Kolecki, Dammavalam, Reyes. Study supervision: Samadani, Kolecki, Dammavalam, Reyes, Kondziolka, PP Huang.

## Supplemental Information

### Previous Presentations

Portions of this work were presented in abstract form at the Congress of Neurological Surgeons Meeting in New Orleans, September 2015.

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