Quantitative pupillometry, a new technology: normative data and preliminary observations in patients with acute head injury

Technical note


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The authors prospectively used a new hand-held point-and-shoot pupillometer to assess pupillary function quantitatively. Repetitive measurements were initially made in more than 300 healthy volunteers ranging in age from 1 to 87 years, providing a total of 2432 paired (alternative right eye, left eye) measurements under varying light conditions. The authors studied 17 patients undergoing a variety of nonintracranial, nonophthalmological, endoscopic, or surgical procedures and 20 seniors in a cardiology clinic to learn more about the effects of a variety of drugs. Additionally, the authors carried out detailed studies in 26 adults with acute severe head injury in whom intracranial pressure (ICP) was continuously monitored. Finally, five patients suffering from subarachnoid hemorrhage were also studied.

Quantitative pupillary measurements could be reliably replicated in the study participants. In healthy volunteers the resting pupillary aperture averaged 4.1 mm and the minimal aperture after stimulation was 2.7 mm, resulting in a 34% change in pupil size. Constriction velocity averaged 1.48 ± 0.33 mm/second. Pupillary symmetry was striking in both healthy volunteers and patients without intracranial or uncorrected visual acuity disorders. In the 2432 paired measurements in healthy volunteers, constriction velocity was noted to fall below 0.85 mm/second on only 33 occasions and below 0.6 mm/second on eight occasions (< one in 310 observations).

In outpatients, the reduction in constriction velocity was observed when either oral or intravenous narcotic agents and diazepam analogs were administered. These effects were transient and always symmetrical.

Among the 26 patients with head injuries, eight were found to have elevations of ICP above 20 mm Hg and pupillary dynamics in each of these patients remained normal. In 13 patients with a midline shift greater than 3 mm, elevations of ICP above 20 mm Hg, when present for 15 minutes, were frequently associated with a reduction in constriction velocity on the side of the mass effect to below 0.6 mm/second (51% of 156 paired observations). In five patients with diffuse brain swelling but no midline shift, a reduction in constriction velocities did not generally occur until the ICP exceeded 30 mm Hg. Changes in the percentage of reduction from the resting state following stimulation were always greater than 10%, even in patients receiving large doses of morphine and propofol in whom the ICP was lower than 20 mm Hg. Asymmetry of pupillary size greater than 0.5 mm was observed infrequently (< 1%) in healthy volunteers and was rarely seen in head-injured patients unless the ICP exceeded 20 mm Hg. Pupillometry is a reliable technology capable of providing repetitive data on quantitative pupillary function in states of health and disease.

Key Words • intracranial pressure • head injury • constriction velocity • pupillary reactivity • quantitative pupillometry

Abbreviations used in this paper: ICP = intracranial pressure; ICU = intensive care unit; IDN = identification number; LCD = liquid crystal display; SAH = subarachnoid hemorrhage.

were described almost 100 years ago by Wilson, when he coined the term “pupillary correctopia.” In a landmark paper, Fisher described intracranial catastrophes associated with the oval or football-shaped pupil. In a detailed study associating changes in pupil shape and ICP, Marshall, et al., described changes in the shape of the pupil in a number of patients with very low ICPs. Furthermore, the abnormalities in pupil shape associated with posterior frontal and temporal lesions described by Marshall, et al., suggest that changes in other pupillary functions might be detectable...
even when the ICP is lower than 20 mm Hg, particularly in association with lesions adjacent to the brainstem. Measurements of pupillary sphincter function are also possible, and may reveal earlier and more subtle changes associated with elevated ICP. Analyses of such, however, are beyond the scope of this preliminary report. The application of pupillometry has been severely limited by the lack of a uniform standard for assessment of the pupils coupled with the unavailability of easily obtained quantitative measures of pupillary function. This has clearly limited our ability to assess one of the most vital elements of the neurological examination in a systematic and reliable fashion. Reports in critically ill patients have focused primarily on descriptions of dramatic and late changes in pupillary responsiveness and their relationship to outcome.

Several quantitative pupillometer devices have been developed and used primarily in research settings, either because the devices have been relatively cumbersome or because they have not been easily adaptable to the clinical environment of the critically ill patient. Grünberger and colleagues in a number of publications, and Pickworth, et al. have described the application of quantitative pupillometry to assess the effects of opiates in humans and to study pupillary responsiveness in patients with a number of psychiatric disorders and the influence of psychopharmacological therapies. The Pupilscan device was used by Pickworth, et al., to measure pupillary diameter and a number of light reflex parameters in patients receiving opiates. These authors were able to obtain measurements of pupil size as well as pupillary constriction and velocity redilation.

The availability of a new, sophisticated quantitative pupillometer (ForSite; NeurOptics, Irvine, CA), which provides a point-and-shoot methodology readily applicable to the emergency and critical care environment, gave us a unique opportunity to develop normative data in a large number of study participants and to begin to study responses of pupils in the critical care environment. The goal of improving the quantitative assessment of pupils was driven primarily by the long-standing clinical observation that very poor overall prognosis is associated with qualitative changes in pupillary function detected at the bedside of the patient, and the more specific recent observation from a number of clinical trials demonstrating that neurological worsening, as described by Morris, et al., is usually detected because of changes in pupillary symmetry or pupillary reactivity. Table 1 illustrates the profound implications of changes in pupillary responsiveness in a consecutive series of severely head injured patients in a recently completed clinical trial. As noted in this table, 23% of patients had an episode of neurological deterioration and in 73% of these cases the deterioration was declared on the basis of pupillary changes. The mortality rate in those patients with pupillary abnormalities was 62%, whereas only five (20%) of 25 patients had fatal outcomes when neurological deterioration was not accompanied by changes in pupils. It is possible, of course, that earlier detection of such pupillary changes may not alter a patient’s course, given the present methods used to treat such patients; however, an alternative possibility is that much earlier changes in pupillary function, not detectable to the naked eye, may predict deterioration or improvement in brain volume, and that patient outcomes could potentially be improved by modifications in patient care if an earlier warning of pending deterioration could be obtained. To determine the preliminary utility of such a quantitative device, we began to assess pupillary function prospectively in the following study participants:

1. a large number of healthy volunteers under a variety of ambient light conditions; 2) patients with normal brain and pupillary function, who were receiving drugs commonly used in the critical care environment; 3) a series of 26 patients with acute severe head injury, who were managed in the critical-care environment with continuous recording of ICP; and 4) five patients suffering from SAH, who were receiving calcium-channel blocking agents.

**Description of the Device**

The pupillometer is a stand-alone, hand-held, battery-operated instrument, which is illustrated in Fig. 1. The system comes with a charger stand and a thermal printer, which can be activated using wireless infrared technology. The pupillometer is a sophisticated computer with a color LCD, a self-contained digital camera, and an integral illumination source. The pupillometer illuminates the eye of a patient with an infrared light set at a level (850 nm) that is beyond the normal response of the human eye. Images are acquired with the digital camera, which uses an infrared-sensitive sensor array. The device analyzes 124 images in each

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**TABLE 1**

*Neurological deterioration in a recent clinical trial of severely head injured patients*

<table>
<thead>
<tr>
<th>Patient Classification*</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients enrolled</td>
<td>404 (100)</td>
</tr>
<tr>
<td>patients w/ ND</td>
<td>94 (23)</td>
</tr>
<tr>
<td>ND detected because</td>
<td>69 of 94 (75)</td>
</tr>
<tr>
<td>of new pupil abnormalities</td>
<td></td>
</tr>
<tr>
<td>ND detected w/o pupil</td>
<td>25 of 94 (27)</td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
</tr>
<tr>
<td>patients w/ new pupil abnormalities who died</td>
<td>43 of 69 (62)</td>
</tr>
<tr>
<td>patients w/o pupil abnormalities who died</td>
<td>5 of 25 (20)</td>
</tr>
</tbody>
</table>

* Pupil abnormalities include changes in size and/or reactivity. These data have not been published previously. Abbreviation: ND = neurological deterioration.

**TABLE 2**

*Representative example of pupillary data obtained in a healthy volunteer and shown on the LCD*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>patient IDN</td>
<td>123456</td>
</tr>
<tr>
<td>resting aperture*</td>
<td>3.0 mm</td>
</tr>
<tr>
<td>min aperture†</td>
<td>2.1 mm (30%)</td>
</tr>
<tr>
<td>latency period‡</td>
<td>0.200 secs</td>
</tr>
<tr>
<td>constriction velocity</td>
<td>2.33 mm/sec</td>
</tr>
<tr>
<td>ICP</td>
<td>0</td>
</tr>
<tr>
<td>eye specified</td>
<td>left</td>
</tr>
<tr>
<td>date</td>
<td>04-07-02</td>
</tr>
<tr>
<td>time</td>
<td>2:32:21 pm</td>
</tr>
</tbody>
</table>

* Resting aperture before stimulation.† Aperture after stimulation; the percentage of change in the size of the pupil is shown in parentheses.‡ Time from the initial presentation of light stimulus to the beginning of pupil constriction.
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measurement sequence, and provides detailed information regarding a number of pupillary functions within 3 to 4 seconds.

The system contains a menu-driven graphic user interface consisting of a color LCD screen for readout and keypad for input. These features allow the user to enter specific information about the patient manually such as the patient’s IDN and ICP. The device is powered by a 4.2-V rechargeable battery.

The device is designed to produce minimal risk to the user and patient. The only designated mechanical contact point with the patient is the headrest, a disposable item designed to protect the patient. All levels of radiation fall below threshold values recommended by the International Commission on Non-Ionizing Radiation Protection. The worst-case scenario limits the infrared exposure to a factor of 30 below the maximum permissible exposure, and visible radiation is also well below the safety limit.

Table 2 illustrates data typically displayed by the device after use on a patient and illustrates normal values for a healthy volunteer. The device is designed so that there is a prompt display of results on the LCD monitor. The device has the capacity to store more than 150 consecutive measurements. The data are sent directly to a printer through an infrared port for ease in charting. Data can also be sent through an infrared port to a multiparameter monitor, automatically updating the patient’s medical record, or the data can be directly downloaded to a computer from the pupillometer. Each time the device is used, a patient’s IDN is entered, the eye under study is noted (right compared with left), and, if appropriate, the ICP is entered by the nurse. The data are time stamped, documenting compliance with the medical protocol. Such electronic documentation is designed to eliminate entry errors that can occur when data are entered by hand.

Clinical Material and Methods

Approval was obtained from the institutional review board of each participating institution before initiation of the study. The quantitative pupillometer was initially used to study 310 healthy volunteers under a wide variety of ambient light conditions. These preliminary studies were necessary because the resting pupillary size and reactivity are influenced by ambient light, a number of genetic factors, and various classes of drugs. Furthermore, the speed of constriction, herein called the constriction velocity, is directly related to the size of the pupil, that is, the larger the initial pupil size the faster it will constrict (Fig. 2). There is also a constant and direct relationship in healthy individuals between the initial pupil diameter and the poststimulus diameter. We, therefore, determined the relationship between the initial diameter and the poststimulus diameter under a variety of ambient light conditions simulating those of the outpatient setting and the critical care environment with changes in light intensity, between 300 and 1400 lx (Fig. 3).

Seventeen patients undergoing nonintracranial surgical procedures or endoscopic procedures, who had no history of intracranial or ophthalmological disease and who were receiving intravenous morphine (2–6 mg), midazolam (2–5 mg), or both were studied to provide some preliminary information regarding the response of pupils to these agents.

Finally, in a series of 40 patients, the capability of the device to measure the size of the pupil was compared with the nurse’s estimation of pupil size and a separate observer’s measurement based on the use of a ruler.

Results

All quantitative pupillometry measurements could be re-
peatedly replicated under the same ambient light conditions (300–1400 lux) in healthy volunteers and in patients in the ICU and in other patient care environments including outpatient settings and the emergency department.

Table 3 illustrates 2432 paired data measurements in 310 healthy volunteers. The mean maximum resting aperture was 4.1 ± 0.34 mm and the mean minimum aperture after stimulation was 2.7 mm. The mean constriction velocity in healthy volunteers was 1.48 ± 0.33 mm/second. Of the 2432 paired measurements, constriction velocity was noted to fall below 0.85 mm/second in 33 measurements and below 0.6 mm/second in only eight measurements. The mean percentage of reduction in pupil size after stimulation was 34% and, in only one of 2432 measurements was the percentage of reduction below 10%. The latency period varied from 120 to 360 msec and was more strongly and directly related to age than to other variables.

In nonneurosurgical patients, bolus doses of morphine (2–5 mg) had a transient albeit clear bilateral effect on pupil size and constriction velocity, but never reduced the percentage of reduction in pupil size to below 10%. In fewer than 10% of observations of patients without head injuries the constriction velocity of the pupil was reduced to below 0.8 mm/second. Not surprisingly, morphine had no effect on pupillary symmetry, even within the highly accurate quantitative data obtained with the pupillometer. A combination of a diazepam compound and morphine, when given as a bolus (usually 2–5 mg of midazolam and 2–4 mg of morphine), can transiently (<5 minutes) reduce the constriction velocity of the pupil in the occasional patient below 0.8 mm/second. In general, midazolam is not used in the ICU environment as a bolus, but rather as a continuous infusion, which is equivalent, in an hourly dose, to the 5 mg given as a bolus in patients studied here.

The effects of oral psychotropic medications and oral calcium-channel blocking drugs received by patients in the absence of narcotics had no effect on pupillary dynamics; however, the combination of oral narcotics and calcium-channel blocking agents appeared to reduce the constriction velocity of the pupil by approximately 0.25 mm/second, from 1.8 mm/second to a mean of 1.23 mm/second. This however, did not produce a substantial change in the percentage of reduction in the pupil’s aperture. The device was much more accurate than the nurse’s estimate of the size of the pupil as shown in Table 4. In patients in whom the mean pupillary size was larger than 4 mm, the pupillometer and the ruler were significantly more accurate than the nurse’s judgment.

Head-Injured Patients

The data from patients with acute severe head injury were studied in considerable detail in an attempt to determine thresholds of abnormality that one could rely on to be highly associated with increases or decreases in brain volume. Particular attention was paid to the influence of sedative medications such as propofol, morphine, and barbiturates in potentially confounding quantitative pupillary assessments. All patients received continuous infusions of morphine sulfate in doses varying from 2 to 14 mg/hr. Thirteen of the 26 patients also received continuous infusions of propofol during the period of quantitative pupillary assessment.

Of 168 paired measurements obtained in 26 head-injured patients while the ICP was lower than 20 mm Hg (Table 3), the mean aperture of the pupil was 2.1 ± 0.16 mm compared with 4.1 mm in healthy volunteers (p < 0.001), and the mean constriction velocity was 1.18 ± 0.18 mm/second compared with 1.48 ± 0.33 mm/second (p < 0.05). Although these patients were receiving morphine and, in many instances, propofol, a constriction velocity lower than 0.8 mm/second was rarely observed. The mean percentage of reduction in pupil size in head-injured patients was 19 ± 3% when ICP was lower than 20 mm Hg. In eight of 26 patients the ICP remained lower than 15 mm Hg through-
out the period of assessment and no significant changes in pupillary dynamics were observed.

In 13 of the patients a midline shift greater than 3 mm was noted. One hundred fifty-six paired observations made in these patients when the ICP was greater than 20 mm Hg were analyzed. The mean constriction velocity fell to $0.81 \pm 0.31$ mm/second and values of less than 0.6 mm/second were seen in 84 paired measurements when the ICP was in excess of 20 mm Hg. In all but five of these measurements the reduction in constriction velocity was greater on the side of the mass. The percentage of reduction in the size of the pupil decreased to lower than 10% in six patients when the ICP exceeded 30 mm Hg, and in four patients when the ICP was higher than 20 mm Hg. Interestingly, in these four patients the mesencephalic cisterns were unilaterally absent. Pupillary latency was preserved in most instances and in only one of these 13 patients did the latency period exceed 360 msec, even when the ICP was sustained above 30 mm Hg.

In five patients with diffuse brain swelling, changes in quantitative pupillary parameters occurred only when the ICP exceeded 24 mm Hg (mean 29 mm Hg) and were less dramatic until the ICP exceeded 35 mm Hg. Constriction velocity decreased to below 0.8 mm/second when the ICP exceeded 30 mm Hg in eight of 34 paired observations. Constriction velocity fell below 0.6 mm/second and the percentage of reduction in pupil size fell below 10% only when the ICP exceeded 35 mm Hg.

**Pupillary Asymmetry**

Pupillary asymmetry measuring less than 0.5 mm is difficult to detect with the naked eye. In the present study pupillary asymmetry of up to 0.5 mm was frequently observed in healthy volunteers and patients without head injury, indicating that asymmetry less than 0.5 mm is within the normal range. In contrast, in head-injured patients with a mass effect, pupillary asymmetry (> 0.5 mm) was common when the ICP rose above 30 mm Hg. In nine patients, 64 paired observations were made when the ICP exceeded 30 mm Hg. Pupillary asymmetry greater than 0.5 mm was detected in 81% of the paired observations, but was detected by nurses only 22% of the time.

**Subarachnoid Hemorrhage**

In five patients who suffered Hunt and Hess Grade III or worse SAHs, there appeared to be little or no effect of calcium-channel blocking agents when they were administered in the absence of a concurrent regimen of narcotic agents. The combination in this very small sample appeared to reduce constriction velocity to approximately 0.2 mm/second when compared with severely head injured patients.

### TABLE 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>healthy volunteers (310 persons, 2432 paired measurements)</td>
<td></td>
</tr>
<tr>
<td>mean maximum resting aperture (mm)</td>
<td>$4.1 \pm 0.34$</td>
</tr>
<tr>
<td>mean minimum aperture (mm)</td>
<td>$2.7 \pm 0.21$</td>
</tr>
<tr>
<td>mean reduction in size (%)</td>
<td>34</td>
</tr>
<tr>
<td>mean constriction velocity (mm/sec)</td>
<td>$1.48 \pm 0.33$</td>
</tr>
<tr>
<td>mean latency duration (secs)</td>
<td>$0.24 \pm 0.4$</td>
</tr>
<tr>
<td>head-injured patients w/ ICP &lt; 20 mm Hg (26 persons, 168 paired measurements)</td>
<td></td>
</tr>
<tr>
<td>mean maximum resting aperture (mm)</td>
<td>$2.10 \pm 0.16$</td>
</tr>
<tr>
<td>mean minimum aperture (mm)</td>
<td>$1.7 \pm 0.1$</td>
</tr>
<tr>
<td>mean reduction in size (%)</td>
<td>19</td>
</tr>
<tr>
<td>mean constriction velocity (mm/sec)</td>
<td>$1.18 \pm 0.18$</td>
</tr>
<tr>
<td>mean latency duration (secs)</td>
<td>$0.26 \pm 0.6$</td>
</tr>
</tbody>
</table>
in whom ICP was less than 20 mm Hg but not below 0.6 mm/second. No significant effect on the percentage of reduction in pupil size was noted.

**Barbiturate Medications**

The use of high doses of barbiturates is known to affect pupillary responsiveness. When burst suppression was reached, the constriction velocities usually fell below 0.6 mm/second and the percentage of reduction in the size of the pupil fell below 10%, under circumstances in which the ICP was well controlled. This demonstrates the confounding effect of these drugs on pupillary responsiveness.

To illustrate the potential clinical use of quantitative pupillometry more clearly, two cases are described in the following section.

**Illustrative Cases**

**Case 1**

This 21-year-old man was injured while riding a bicycle and presented with a right subdural hematoma associated with a 4- to 5-mm midline shift to the left side, and a right occipital contusion. The patient’s ICP was initially stable, but on the 2nd day of his hospitalization his ICP rose to 32 mm Hg. In Fig. 4, the quantitative changes in the right pupil over time in this patient are shown. Note that following administration of mannitol at 1:19 p.m. when the patient’s ICP had risen to 32 mm Hg, the constriction velocity rose from 0.19 to 0.51 mm/second in approximately 20 minutes. It then began to decline, even though the ICP remained the same. Over the course of almost 1 hour the ICP rose slowly to 22 mm Hg and the constriction velocity fell to a level of 0.005 mm/second, which could be detected by the nurse; in fact, by 2:32 p.m. the patient’s right pupil was reported by the nursing staff to be unreactive. At 2:41 p.m., when the ICP had been sustained at or above 20 mm Hg for 10 minutes, the treatment criteria used for the initiation of further therapy, ventricular drainage, was instituted and within 9 minutes the constriction velocity rose to 0.73 mm/second and the ICP fell to 15 mm Hg. The right pupil was reported by the nurse to be reactive at 2:50 p.m. In reviewing the percentage of reduction in pupil size we found that it progressively fell below 10% as the constriction velocity declined, reaching a low of 4% at 2:32 p.m., and that it improved as the ICP fell and the constriction velocity rose. The latency period rose rather dramatically from 120 to 360 msec when the ICP increased to 22 mm Hg and fell as the constriction velocity improved with treatment.

**Case 2**

This 52-year-old man fell backward and presented with diffuse brain swelling, a left frontal contusion, bilateral subdural hematomas, which were quite small, a shift to the right side, and evidence of brainstem hemorrhage. Figure 5 shows that at 11:52 a.m. the patient had a normal constriction velocity of the right pupil of 1.05 mm/second and an ICP of 19 mm Hg. The ICP rose to 23 mm Hg at 12:02 p.m. and the constriction velocity fell to 0.34 mm/second. Mannitol was administered in response to the rise in ICP. Within 9 minutes the constriction velocity had risen to 0.79 mm/second and the ICP had fallen to 18 mm Hg. At 12:25 p.m. the ICP was 17 mm Hg, but the constriction velocity had fallen to 0.31 mm/second and the percentage of reduction in pupil size was 10%. Hyperventilation was instituted at this time because the nurse reported that the right pupil was sluggish. Within 7 minutes the constriction velocity had risen to 0.94 mm/second and the percentage of reduction in the size of the pupil had improved to 27%. No significant relationship between the latency period and changes in ICP was seen.

These two cases suggest a relationship between changes in ICP, constriction velocity, and the percentage of reduction in pupillary aperture even at relatively modest levels of change in ICP.

**Discussion**

The work described here represents the first detailed ap-
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Application of quantitative pupillometry to a large number of healthy volunteers and patients under varying ambient light conditions. The patient group included those patients undergoing endoscopic, nonintraocular, or nonophthalmological procedures who received medications known to affect pupillary function; a small series of severely head injured patients in whom the ICP was continuously monitored; and five patients with aneurysmal SAH.

Quantitative pupillometry can produce reliable, repetitive, pupillary measurements that are clearly superior to those obtained at the patient’s bedside by the nurse or physician. Although this work must clearly be viewed as very preliminary, a number of observations in both healthy volunteers and patients are evidence based. First, the ambient light within the ICU and in other patient-care environments, including physician offices and the emergency department, falls within ranges that permit accurate pupillary measurements. Second, all quantitative pupillary measures could be repeatedly replicated within study participants with almost no instances of device failure.

The normative data obtained in this study indicate that parameters routinely used in patient assessment at the bedside can be quantitatively measured and are potentially quite useful in assessing brain volume. The clinical observation of briskly reactive, sluggish, or nonreactive pupils is likely to be a combination of several factors including latency, constriction, and dilation velocities. The quantitative measurement of constriction velocity is a sole measure of the speed at which the pupil constricts and at which it appears to be quite sensitive to elevations in ICP and, surprisingly, relatively resistant to even large doses of morphine and propofol. The difference in mean constriction velocity between healthy volunteers and patients with severe head injury with ICPs lower than 20 mm Hg is relatively small (∼0.3 mm/second), indicating that constriction velocity is usually preserved, except under circumstances in which the ICP is elevated and/or in which patients receive large doses of barbiturates.

These preliminary observations suggest that a reduction in constriction velocity to below 0.8 mm/second is suggestive of increases in brain volume and that when the constriction velocity falls below 0.6 mm/second, there is a real likelihood that the ICP, if not already elevated, will become elevated, within 15 to 30 minutes in patients with a significant mass effect.

The percentage of reduction in the size of the pupil from the resting state following stimulation is approximately 20% in head-injured patients when compared with healthy volunteers in whom the percentage of reduction in size averages a bit more than 30%. Based on these preliminary observations, one can conclude that a percentage of reduction in pupillary aperture below 10% is very rare in healthy volunteers, indicating that with quantitative pupillometry the standard at which pupillary asymmetry indicates the possibility of third nerve palsy or brainstem compression is incapable of quantifying asymmetry that is less than 0.4 mm.

ICP was elevated and/or brainstem compression occurs only at much higher ICPs than in patients in whom there is a midline shift. This observation obviously requires further corroboration.

The length of the latency period appeared to be quite robust and its use alone is probably not going to be helpful in the ICU setting.

The relative preservation of quantitative pupillary function in patients with diffuse brain swelling until ICP generally rose to greater than 30 mm Hg is in keeping with previous observations14 that, in such patients, third nerve palsy and/or brainstem compression occurs only at much higher ICPs than in patients in whom there is a midline shift. This may suggest that in such patients therapy for elevated ICP
could be safely instituted when their ICP is higher (25–35 mm Hg) than in patients with a midline shift.

The device has been used in approximately 40 children, both in the outpatient environment and in the critical care setting. In the outpatient environment a skilled pediatric nurse practitioner was able to obtain measurements on a repetitive basis in 18 of 20 children ranging in age from 1 month to 5 years. In the critical care environment, the ease of use was similar to that in adults. There is a special forehead rest for children of different ages, which facilitates its use in that population.

The observations reported here in both healthy volunteers and patients are based primarily on traditional parameters that have been used in outpatient and critical care settings, that is, the size of the pupil and the speed at which the pupil reacts. Quantitative pupillometry, however, is capable of providing much more detailed information than the parameters shown here, such as the first and second dilation velocity and measurements of subtle changes in the shape of the pupil not detectable by the human eye. Such variables may be extremely important in providing more sensitive information than the results reported here. It is likely that, just as in measurements of traditional vital signs such as blood pressure and heart rate, in which wide variations fall within a normal range, relative changes within patients rather than absolute changes may be more important in detecting early changes in intracranial volume. A combination of measurements, perhaps constructed in an algorithm, might be much more powerful in reliably predicting changes in brain volume that precede or are concurrent with changes in ICP. For example, because of the length tension curve of the pupillary muscles, it is theoretically possible that a unilaterally dilating pupil may transiently demonstrate an increasing constriction velocity. Nevertheless, an algorithm could potentially be constructed that would indicate that pupillary asymmetry would take precedence in clinical management.

The symmetry of pupillary responses for all parameters, as demonstrated in more than 2000 observations to date in healthy volunteers, further increases our confidence that subtle differences in pupil size and reactivity detected using a variety of measures in patients could be more sensitive in detecting potentially dangerous changes in ICP, particularly when there is a midline shift.

The high mortality rate associated with changes in the pupils, using traditional methods of measurements, indicates that if it were possible to detect changes in brain volume earlier by using much more sophisticated measures of pupillary function, the mortality rate for a variety of disorders might be reduced.

**Conclusions**

Quantitative pupillometry is a reliable and safe method that provides detailed and accurate information regarding patterns of pupillary responsiveness. There is a robust relationship, particularly in patients with a mass effect, an ICP higher than 20 mm Hg, and a reduction in constriction velocity. A percentage of reduction in pupil size of less than 10% following stimulation in this limited sample of patients appears to be strongly associated with increases in brain volume, which are potentially unsafe. Further investigation of this technology in a much larger number of patients is warranted.

**Disclosure**

Drs. Taylor and Marshall are investors in NeuroOptics, the manufacturer of the device investigated in this study.

**References**

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