Role of Automated Pupillometry in Critical Care
Learning Outcomes

• Verbalize the importance of pupillary assessment and limitations of manual assessment methods

• Understand the science speaking to the clinical value of pupillometry

• Discuss clinical benefits of the pupillometer for improved assessment and management of critically ill patients
Overview of Neuroanatomy

• Why do we do a pupil exam?
• What are we testing?
• What does it tell us about the brain and central nervous system?
Why do we test pupils?

- Window into the brain
- Easy, non-invasive, quick
- Can be done on conscious or unconscious patients
- No patient participation needed
What are we testing?

• Part of cranial nerve testing but more specifically testing the brainstem
• Cranial nerve II (optic) and III (oculomotor)
Ciliary Ganglion

Oculomotor Nerve

Optic Tract

Edinger-Westphal Nucleus
(of III nucleus complex)

Constrictor Muscle of Iris

Optic Chiasm

Optic Nerve

Preganglionic Parasympathetic part of Oculomotor III

Pretectal Nucleus

Aqueduct
What do pupils tell us about the brain?

- Any interruption in the CN II & III pathways (compression, swelling, bleeding, ischemia/infarction, obstructed flow, etc) can alter the pupillary light reflex slowing conduction resulting in a sluggish or nonreactive pupil.

- Loss of cranial nerve reflexes or changes in pupillary reactivity signify increased intracranial pressure and/or impending central herniation.
“While consciousness is the earliest and the most sensitive indicator of neurological changes in the conscious patient, pupillary signs are the earliest and the most sensitive indicator of neurological changes in the unconscious patient.”

- Hickey pg. 165
Limitations to Current Pupil Assessment
Current Limitations

- Small pupils (pontine damage, medications)
- Darkly pigmented iris
- Poor/inconsistent lighting
- Examiner’s visual acuity
- Strength of flashlight/penlight
- Distance and orientation to patient’s eye
- Subjective terminology
  - brisk, sluggish, non-reactive
Why do we need a pupillometer?

• Traditional assessment methods are subjective in nature
• High inter-examiner variability (up to 39%) and a severe lack of reliability (Litvan et al., 2000; Du et al., 2005)
• Recent studies show that we aren’t getting any better at it...
Interrater Reliability of Pupillary Assessments

DaiWai M. Olson¹ · Sonja Stutzman¹ · Ciji Saju¹ · Margaret Wilson¹ · Weidan Zhao¹ · Venkatesh Aiyagari¹,²

• 2,329 paired subjective pupillary assessments by practitioners on 127 consented patients, followed by assessment with the pupillometer
• Interrater reliability between 2 practitioners and practitioners and the pupillometer
• Agreement for overall pupil assessment (size, shape, and reactivity) was LOW: k=0.26
• There was only moderate interrater reliability in size (k=0.54), shape (k=0.62), & reactivity (k=0.40)
• Practitioner agreement with pupillometer was fair to moderate in all three parameters (k=0.40-0.52)
Olson 2015 – Results: Reactivity

- OF 189 PRACTITIONER OBSERVATIONS OF A FIXED PUPIL:
  - 49.7% were scored as fixed by both practitioners
  - Only 33.3% were scored as fixed by pupillometry

- Of 83 observations of non-reactive pupil by pupillometer:
- 62.65% of practitioners on average also reported non-reactive

Results  From 2329 paired assessments, the interrater reliability between practitioners was only moderate for pupil size ($k = 0.54$), shape ($k = 0.62$), and reactivity ($k = 0.40$). Only 33.3% of pupils scored as non-reactive by practitioners were scored as non-reactive by pupillometry.

Conclusions  Despite the strong emphasis placed on the traditional pupil examination, especially for patients with a neurological illness, there is limited interrater reliability for subjective scoring of pupillary assessments. Thus, the use
There is low interrater reliability among practitioners performing a manual pupil exam.

There is a need to standardize the assessment of pupillary function in order to provide higher reliability.

The use of automated pupillometry could be considered as a means to standardize practice when there is a need for accurate assessment of the pupil size and reactivity.
The Message to Clinicians

- Neuro exam is complex, multiple parts, difficult to complete
- Pupil exam is only one portion though is very subjective, inconclusive (sluggish pupils)
- We test pupils on every patient, every shift, often more frequently than once a shift
- Why not use an easy, hand-held tool that will give you accurate, reliable data to tell you how reactive your patient’s pupils are?
Clinical Use & Benefits of the NPi-200 Pupillometer
NPI®-200 Pupillometer System

• Hand held optical scanner
• Stimulates eye with a consistent flash of light
• Captures and analyzes a rapid sequence of digital images (90 images over 3 sec)
• Evaluates entire pupil light reflex
• Optional barcode scanner for pt ID
• Optional SmartGuard® Reader for upload to EMR
SmartGuard®

- Single patient use for duration of admission
- Patient data stored on memory chip (168 paired readings)
- Facilitates patient data upload into EMR system
- Patient data can be destroyed in compliance with HIPAA guidelines and facility policy
Performing a Scan

ID: 123456789 (0/168)

Ready to scan
Displaying Data

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPI</td>
<td>4.1</td>
<td>4.3</td>
<td>L &gt; R 0.2</td>
</tr>
<tr>
<td>Size</td>
<td>3.63 mm</td>
<td>3.09 mm</td>
<td>R &gt; L 0.54</td>
</tr>
</tbody>
</table>

Graph showing data over time.
What is NPi®?
(Neurological Pupil index™)

- NPi determined by Size, MIN, % change in size, Constriction Velocity/Max CV, Latency, and Dilation Velocity
- NPi based on an algorithm comparing patient pupil data to a normative model (>half a million pupil measurements)
- NPi rates strength of pupillary response (sluggish to brisk) on a numeric scale ranging from 0-5
NPi = Reactivity

The Neurological Pupil index™ (NPi®) Pupil Reactivity Assessment Scale

<table>
<thead>
<tr>
<th>Measured Value*</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0 – 4.9</td>
<td>Normal/“Brisk”</td>
</tr>
<tr>
<td>&lt; 3.0</td>
<td>Abnormal/“Sluggish”</td>
</tr>
<tr>
<td>0</td>
<td>Non-Reactive or Atypical Response</td>
</tr>
</tbody>
</table>

*A difference in NPi between right and left pupils of ≥ 0.7 can also be considered an abnormal pupil reading

*Per the Neurological Pupil index (NPi) algorithm

![Eye monitor image](https://via.placeholder.com/150)
Key Benefits of the Pupillometer

• Completely accurate, reliable and objective pupil size and reactivity data … *independent of examiner.*

• Pupil size and reactivity are expressed *numerically and graphically* so that now, *for the first time*, potential changes are *trended over time*, just like other vital signs.
• If pupils are being tested, the pupillometer should be used with each and every assessment.
• The whole point of the frequent neuro check is to detect for changes since we know the neurological exam can deteriorate precipitously.
• The value in pupillometry is a trendable measurement to detect early neurological changes.
Case Study

- 52 year old, history of hypertension, developed sudden onset headache
- BP 212/105, lethargic
- Initial CT L parietal intra-parenchymal hemorrhage with mild surrounding edema
- First exam without sedation: not following commands, purposeful movement and localizing with left side
- 2330: R 3.41 mm NPi 4.6 L 3.05 mm NPi 4.4
Case Study

- 0100: \textbf{R} 3.02 mm NPi 3.4 \textbf{L} 4.49mm \textbf{NPi 0.9}
- No longer purposeful on L, weak localization
- Repeat CT - rapid worsening of edema, increased midline shift
- Intervention: Mannitol & hypertonic saline
- Taken to OR emergently for surgical decompression
- Post-op: \textbf{R} 2.45mm NPi 3.8 \textbf{L} 2.73 mm, NPi 4.3
Clinical Indications for Pupillometry
What can cause changes in the pupillary light reflex?

- Interruption of CN pathways and/or brainstem compression due to increased intracranial pressure, cerebral edema, infarction, etc.
- Mechanism of secondary brain injury:
  - delayed, physiologic response to primary injury, activation of biochemical, metabolic, and inflammatory cascades which worsens ischemia, leads cell death, and thus neurological deficit.
Anoxic Brain Injury after cardiac arrest

Hemorrhagic stroke/Intracerebral hemorrhage

Traumatic Brain Injury

Ischemic stroke

Hemorrhagic stroke

Anoxic Brain Injury after cardiac arrest
Multimodal Neuro Monitoring

Copyright © McGraw-Hill Education. All rights reserved.
Pupillometry provides a numerical value for reactivity which we know is an indicator for early signs of brainstem compression and can be a helpful “vital sign” in managing the patient with or at risk for neurological injury.
2011: Multicenter Trial in 134 TBI, SAH, & ICH Patients
Purpose of this study was to introduce the NPi
Results showed a correlation between NPi and ICP
- Normal NPi group ($\geq 3.0$) = Average ICP 19.6
- Abnormal NPi group ($<3.0$) = Average ICP 30.5
- Non-reactive NPi group (0) = Average ICP 33.8
In patients with abnormal pupillary reactivity, first evidence of pupil abnormality occurred, on average, 15.9 hours prior to the time of the peak of ICP
Pupillary reactivity as an early indicator of increased intracranial pressure: The introduction of the Neurological Pupil index

Jeff W. Chen¹, Zoe J. Gombart², Shana Rogers³, Stuart K. Gardiner⁴, Sandy Cecil⁵, Ross M. Bullock⁶

- 2011: Multicenter Trial in 134 TBI, SAH, & ICH Patients
- Purpose of this study was to introduce the NPi
- Results showed a correlation between NPi and ICP
  - Normal NPi group (≥3.0) = Average ICP 19.6
  - Abnormal NPi group (<3.0) = Average ICP 30.5
  - Non-reactive NPi group (0)= Average ICP 33.8
- In patients with abnormal pupillary reactivity, first evidence of pupil abnormality occurred, on average, 15.9 hours prior to the time of the peak of ICP
ICP peaked around hour 40

L Eye NPi started to decline around hour 25 (15 hours prior to peak ICP)

L NPi reached lowest value of 1.5 just after the peak of ICP

Chen, et al. (2011)
54 patients studied, single center, with cohort of severe TBI (GSC <9)

Study Purpose:
- To examine the relationship between non-invasive NPi and invasive ICP in patients with severe TBI at risk of intracranial hypertension (ICHT)
- Analyzed NPi trends over time prior to sustained elevated ICP and cumulative abnormal NPi burden during ICP monitoring
Jahns F, et al - Results

• Results showed:
  – Sustained elevations of ICP (> 20 mmHg) are associated with a concomitant and clinically relevant decrease of NPi
  – Treatment of elevated ICP with hyperosmolar agents was in turn associated with a normalization of NPi
  – Cumulative burden of abnormal NPi was a marker of increased severity of intracranial hypertension, a more complicated ICP course requiring decompressive craniectomy, and a worse 6-month outcome
  – Failure of NPi to recover to normal values was associated with very poor prognosis

• Conclusion: Elevated ICP episodes correlated with decrease of NPi and worse outcome at 6 months
Study:
• 72 neuro patients (403 paired assessments)
• 403 paired pupil measurements within 2 hours of either 23.4% HTS or 20% mannitol

Conclusions:
• Significant quantifiable improvement in pupillary reactivity (NPI) after the administration of osmotic therapy in a critical ill population.
• Osmotic medication administration was significantly associated with improved pupil reactivity (NPI) within 2 hours of delivery.
The aim of this study: To investigate the role of automated pupillometry in the setting of SAH as a potential adjunct to transcranial doppler.
Aoun S, et al Conclusions

• In this sample of 56 patients, an NPi decrease in patients with SAH was associated with DCI.
• NPi changes are strongly associated with the advent of DCI and could be an early herald of clinical deterioration.
• “Pupillometer changes may occur hours prior to the clinical neurological decline. This may provide the treatment team with enough warning to initiate pre-emptive therapeutic measures before the development of irreversible neurological damage, especially in the context of elevated TCD readings and in patients who have significant clinical and radiological risk factors for DCI.”
Automated Pupillometry for the Non-Neuro Patient
Why every patient is neuro patient

• There are ~5.7 million patients admitted to US hospital ICU’s each year
• 1.4 million of these are admitted with primary neurological diagnosis
• The remaining 4.3 million patients are admitted to other ICU’s (cardiac, medical, surgical etc) with other diagnoses
• As standard of care, all of these patients receive a neurological exam, including *pupil assessments*
Because every patient admitted to a high acuity area has the potential for neurologic sequela related to

- Secondary effects of their primary diagnosis
  - Stroke after cardiac arrest
  - Metabolic or hepatic encephalopathy
- Effects of therapeutic measures/treatment
  - Sedation
  - ECMO
  - Therapeutic hypothermia
Mechanical Ventilation, Sedation & Neuromuscular Blockade

- Affects patients in nearly every type of ICU/PACU/ED
- Many indications for ventilation and sedation
- Reduces our ability to do an effective neurological assessment.
  - Limited to pupils and other cranial nerves
- May not be able to lighten sedation to get a better neuro exam
• Pt may be on chemical paralytics for multiple reasons
  • Ventilator synchrony for severe Acute Respiratory Distress Syndrome (ARDS)
  • ICP management
  • Complicated abdominal surgeries
• While on paralytics the patient does not have a neurological exam except for pupils
• Thus any patient on paralytics prompts the usage of pupillometry as a means to monitor their neurological function
Post Cardiac Arrest Syndrome

- Post-cardiac arrest syndrome (PCAS)
  - anoxic brain injury
  - myocardial dysfunction
  - systemic ischemia/reperfusion response
- Optimal CPR can restore initial cardiac output to 25-40% of pre-arrest values, but the brain receives only 20% of this
- Delayed neurologic deficit can occur up to 3 weeks post ROSC
- Bedside neurological examination plays a pivotal part in predicting poor outcome.

Bottom line: Every cardiac patient is a neuro patient!

Uchino et al (2016); AHA (2017)
Therapeutic Hypothermia

- Goal: to slow the cellular reactions (secondary injury) that can cause brain and other organ damage after cardiac arrest

---

Scirica (2013)
Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double-blinded study

Mauro Oddo1*, Claudio Sandroni2, Giuseppe Citerio3,4, John-Paul Miroz1, Janneke Horn5, Malin Rundgren6, Alain Cariou7,8, Jean-François Payen9, Christian Storm10, Pascal Stammet11 and Fabio Silvio Taccone12
Background

This large, multicenter study is the first of its kind to assess the prognostic value of pupillary reactivity using Neurological Pupil index (NPI) in the acute phase of post-anoxic coma in patients following cardiac arrest (CA).

*Intensive Care Medicine* is the official journal of the European Society of *Intensive Care Medicine* (ESICM) and the European Society of Paediatric and Neonatal Intensive Care; it is a highly respected medical journal.
Aim of the Study

• The study had two primary objectives:

1. to assess the ability of quantitative pupillometry [using the Neurological Pupil index (NPi)] to predict an unfavorable neurological outcome 3 months after cardiac arrest (CA).

2. to evaluate whether NPi can help discriminate between good outcome (full recovery or moderate disability) vs. unfavorable outcome (severe disability, vegetative state or death).

• The study involved 456 comatose patients with a GCS of ≤ 6 resuscitated post-cardiac arrest (CA) and treated with Targeted Temperature Management (TTM).
Oddo et al: Results

• The predictive value for an unfavorable outcome of NPi was superior to sPLR at every time-point in the test.

• The most striking results were:
  
  – NPi had 100% PPV, meaning 100% of patients that had even one NPi reading of $< 2$ had an unfavorable outcome.

  – NPi had 100% specificity, meaning all patients (100%) with a good outcome had ZERO NPi readings of $< 2$. 
Conclusions

1. Measuring NPi in coma patients following resuscitation post-CA predicted an unfavorable neurological outcome at 3 months more accurately than a standard pupil exam using a manual device.

3. The predictive value for an unfavorable outcome of NPi was superior to that of sPLR at each time-point tested. An NPI ≤ 2 between day 1 and day 3 following hospital admission was 100% specific to predict (able to predict 100% of the time) an unfavorable 3-month neurological outcome and provided greater prognostic performance than standard manual pupillary light reactivity.

4. The data further suggest that using a prognostic approach that combines NPi with somatosensory evoked potentials (SSEP) improved the sensitivity to predict an unfavorable outcome in patients post-CA, while providing equal 100% specificity.
Neurologic complications are second only to heart failure as a cause of morbidity and mortality following cardiac surgery.

Complications include:
- Ischemic/hemorrhagic stroke
- Encephalopathies
- Seizure
- Coma

The presence of neurologic sequelae significantly increases the likelihood of requiring long-term care.

McGarvey et al (2017)
CPBypass/ECMO/IABP/LVAD
ECMO (ExtraCorporeal Membrane Oxygenation) provides cardiopulmonary support for patients (neonates, peds, adult) with severe refractory cardiac or pulmonary failure

- Drastic increase in numbers of patients receiving ECMO: 2001-2011
  - 40% increase in pediatric patients
  - 650% increase in adult patients receiving ECMO

- Neurologic complications: ischemic and hemorrhagic stroke, seizure, encephalopathy, coma and brain death

- Reports vary from 11% to nearly 50% of patients treated with ECMO having one of these neurologic complications.

- Patients suffering neurologic complications while on ECMO have higher rates of long-term disability, morbidity and mortality

- Increasing age associated with higher risk of death and disability

Nasr & Rabinstein (2015)
Hepatic Encephalopathy

- Common neurologic complication associated with liver disease, liver failure, liver transplantation
- Caused by metabolic dysfunction and build-up of toxins (ammonia and neurotransmitters) leading to astrocyte swelling and oxidative stress in the brain
- Characterized by personality and cognitive changes; may progress to decreased LOC, cerebral edema and brain stem herniation
Use the Pupillometer for Baseline Assessment & Trending

- Stroke
- Head Trauma
- Metabolic Disorders
- Cardiac Arrest
- Seizures
- Any Critical Illness
- Evaluation of Therapy
Incorporating Pupillometry into Clinical Practice

- Establish a **baseline** pupil data set as soon as the patient is admitted into the unit.
- Continue to use for **routine pupil exams** for accurate and trendable data.
- Establish **clinical protocols & order sets** to ensure standardization in monitoring.
  - Sample protocols available.
Summary

• The pupillometer can **reliably detect smaller changes than the human eye** and allows **trending** of gradual changes.

• The value of NPi can quantify rates of change giving **more discrimination** than simply “Brisk”, “Sluggish” or “Non-reactive”.

• The pupillometer **removes subjectivity** from pupillary examination and is an important tool in the assessment and management of critically ill patients.
18th Annual
Neurotrauma Symposium

Monday, December 2, 2019

Byers Auditorium, Genentech Hall
UCSF Mission Bay Campus, San Francisco

Register online after September 1, 2019 at:
www.brainandspinalinjury.org

For information contact:
Julia Thompson Gallego, NP
(415) 206-3226
julia.gallego@ucsf.edu

www.brainandspinalinjury.org


