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A Guide to Pupillometry and Neurologic Disorders

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Abstract

Pupillometry, the quantitative measurement of pupil size and reactivity, offers a non-invasive window into the autonomic nervous system (ANS) and its connection to neurological function. While often overlooked, it provides invaluable data for diagnosing and monitoring a range of neurologic disorders. This white paper aims to equip optometrists and ophthalmologists with a thorough understanding of pupillometry, its clinical applications, and its integration with advanced diagnostic tools, including virtual visual field testing.

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Part I: The Basics of the Pupillometry Exam

What is Pupillometry?

Pupillometry involves measuring pupil size, constriction, dilation, and latency in response to various stimuli, most commonly light. Modern pupillometers utilize infrared technology to capture precise measurements, eliminating subjective assessments. It provides clinicians with objective data about the ANS, assessing parasympathetic and sympathetic branches and offering insights into neurological and ocular health. Such data is critical for prognosis assessment and distinguishing optical from neurological causes of vision loss.

How to Conduct a Manual Pupillometry Exam

Efferent pupillary defects are due to problems in the motor pathway that controls pupil response to incoming light or trauma to the iris anatomy. This causation must be assessed and accounted for before identification of any afferent defect indicative of optic nerve or retinal dysfunction.

Anisocoria is absent in purely afferent defects assessed with the swinging flashlight test. Therefore, before the swinging flashlight exam, observe both pupils in ambient room light to ascertain whether they are equal in size. If not, measure the size of each pupil and then dim the room light, again observing the inter-pupillary size disparity.

If the anisocoria is larger in bright light, the larger pupil is abnormal (parasympathetic defect).
If the anisometropia is greater in dim light, the smaller pupil is abnormal (sympathetic defect).

Sorting out causes, including physiologic (benign) anisocoria, pharmacologic mydriasis, Adie's tonic pupil, Horner's syndrome, cranial nerve palsy, iris trauma, and more, is further pursued with pharmacologic testing and rarely also requires imaging studies beyond the scope of this paper.

In the presence of an efferent defect, the anisocoria and abnormal sphincter function must be taken into account when trying to assess for an afferent (optic nerve and retinal defect) with the swinging flashlight test.

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Swinging Flashlight Test to Find Afferent Defects

Conduct the exam in a dimly lit room to minimize ambient light influences and allow for baseline pupil dilation. Use a focused beam such as a muscle light or penlight. The patient is asked to fixate on a distant object to exclude accommodation and its effect on pupil size (evaluation of dissociation of miosis and accommodation is a rarely required nuance of pupillometry).

Shine the light into one eye, observing both the direct pupillary response (the illuminated pupil movement) and the fellow eye's consensual pupillary response. Quickly move the light to the other eye, again observing the pupillary responses in both eyes. Repeat this process multiple times, swinging the light back and forth between the eyes as much as needed to confidently observe and confirm findings. In a normal visual system, both pupils should constrict when light is shone into either eye, and dilate bilaterally when the light is moved away.

If the pupils dilate when the light is shone into one of the eyes but both constrict when the light is shone into the fellow eye, a relative afferent pupillary defect (RAPD) (also known as a Marcus Gunn pupil) is confirmed in the eye that allows the bilateral dilation when illuminated.

In the presence of an efferent defect, only the normal pupil must be observed. Never judge afferent function using the pupil with the efferent defect, as that pupil doesn't move well regardless of the eye stimulated with the light, making it seem like there is an afferent defect in the opposite eye, or "a false RAPD."

Therefore, only observe consensual responses in the eye with the normal functioning pupil. To do so, swing the light between the normal eye (observe direct response in that eye) and the efferent-defect eye (still observing the normal pupil for consensual response). This allows assessment of RAPD based on the good pupil only. If there is a true RAPD, you will still see relative dilation of the normal pupil when the light swings to the efferent pupil eye.

The RAPD can be quantified in log units, thereby tracking severity and progression over time. Neutral density filters of increasing log units are held over the normally performing eye without the RAPD until the swinging flashlight test no longer shows a disparity (the two pupils constrict equally and the RAPD is neutralized), thus determining the magnitude of RAPD.

RAPD Grade (log units)	Clinical Significance
0.3	Mild RAPD
0.6	Moderate RAPD
0.9 - 1.2	Moderate to severe RAPD
>1.2	Severe optic nerve or retinal dysfunction

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How to Conduct an Automated Pupillometry Exam

Automated pupillometry allows practitioners to quickly and objectively detect pupil abnormalities. Since it uses technology, the data gathered does not require subjective observations and highly trained technicians. It does not preclude dilation before the physician exam, with the potential to lose critical physical findings.

There are two sub-categories of automated pupillometry: infrared videography and computerized pupillometry. Infrared videography is especially useful in patients with dark irises. The exam is administered in the dark, and the melanin, which makes the irises dark, reflects the infrared light. As a result, the pigmented irises appear light on the screen, making the black pupils stand out.

In contrast to infrared videography, technicians can perform computerized pupillometry in dark and light environments. Doing so provides immediate results, enabling providers to make quick, informed assessments.

In the presence of anisocoria, after determining efferent laterality, both direct and consensual responses are observed while looking at the unaffected pupil only to evaluate afferent defect.

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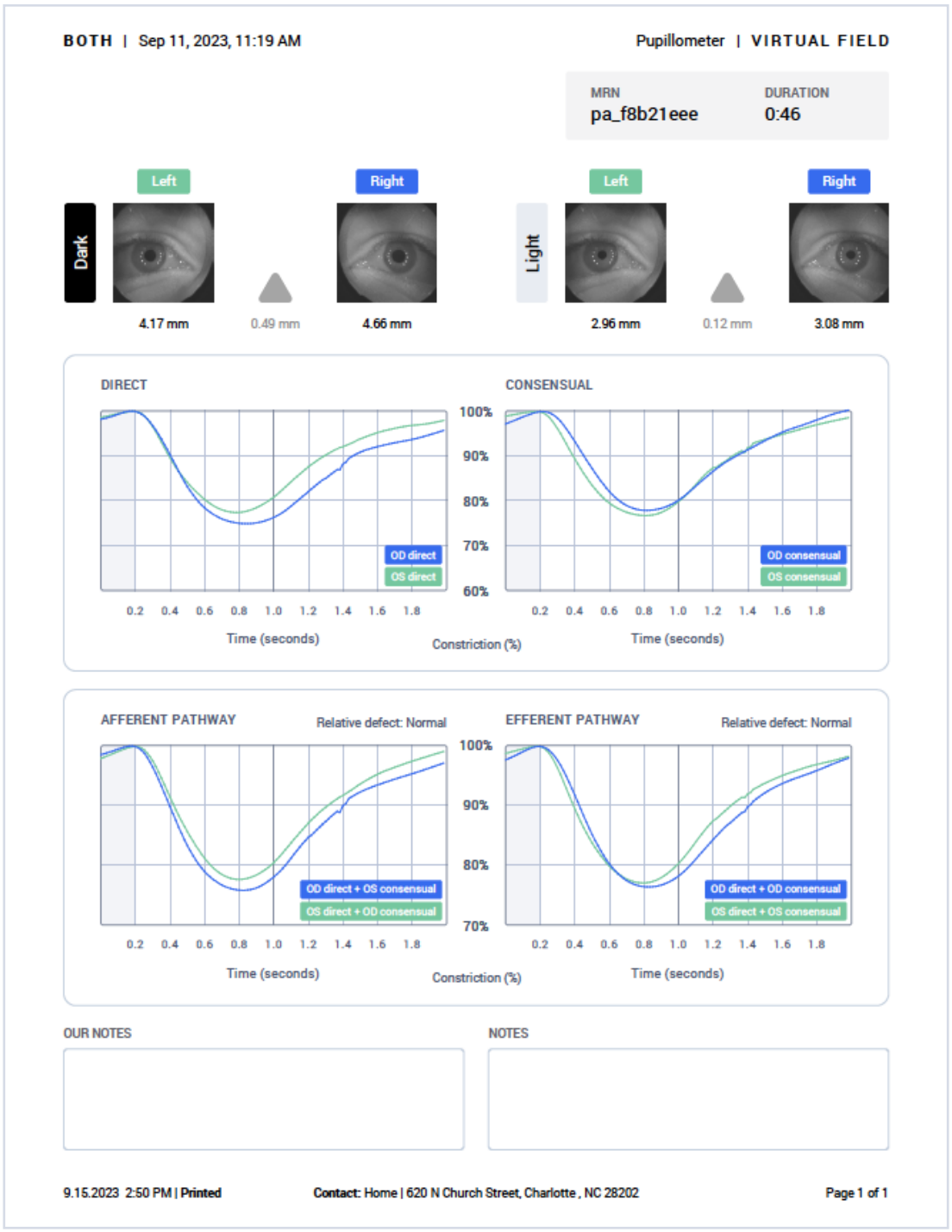
Interpreting Patient Results

Example Pupillometry Report from Virtual Field



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Interpreting a pupillometry report requires an understanding of normal pupil responses, as well as the deviations that may indicate underlying neurological or systemic disorders. When reviewing patient data, one should evaluate several key parameters:

Baseline Pupil Size (Resting Diameter)

Measures the initial pupil size in normal lighting conditions

Normal Range:	Typically between 2-4 mm in bright light and 4-8 mm in dim light.
Deviations:	• **Anisocoria (unequal pupil sizes):** This may indicate Horner's syndrome*, third nerve palsy, or pharmacologic effects. Sometimes, after thorough evaluation, anisocoria is simply confirmed as physiologic or congenital. • **Miosis (excessive constriction):** Could suggest opioid use, Horner's syndrome, or age-related changes. • **Mydriasis (excessive dilation):** This may be due to trauma, Adie's tonic pupil, or third nerve palsy.

* Note that Horner's syndrome must be further evaluated as first, second, or third order, as, if not congenital, the etiology can be life-threatening. Neck trauma, for example, in sports as well as stroke, cavernous sinus, and tumors, must be ruled out.

Pupil Reaction to Light (Direct and Consensual Response)

Assesses how each pupil constricts in response to light in the tested eye (direct) and in the fellow eye (consensual)

Normal Response:	Quick, equal constriction in both pupils.
Deviations:	• **Sluggish or absent constriction:** This could indicate optic nerve dysfunction (e.g., optic neuropathy, multiple sclerosis). • **Relative Afferent Pupillary Defect (RAPD):** An asymmetry in the pupillary light reflex, often suggesting optic nerve or retinal disease.

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Latency (Time to Constriction) Measures how long it takes for the pupil to begin constricting after light exposure	
Normal Response:	Almost immediate reaction, typically within 200-500 ms.
Deviations:	• **Delayed Reaction:** This may indicate neurodegenerative diseases, autonomic dysfunction, or increased intracranial pressure.

Constriction Velocity Measures how quickly the pupil constricts after light stimulation	
Normal Response:	Rapid constriction within a fraction of a second.
Deviations:	• **Slow constriction:** May be associated with autonomic neuropathies (e.g., diabetic autonomic neuropathy) or midbrain dysfunction. • **Exaggerated constriction:** Can indicate pharmacologic effects or certain neurogenic disorders (e.g., Horner's Syndrome).

Dilation Velocity Measures the speed of pupil re-dilation after the light is removed	
Normal Response:	Gradual dilation, returning to baseline within a few seconds.
Deviations:	• **Slow dilation:** This may indicate sympathetic nervous system dysfunction, such as in Horner's syndrome. • **Rapid dilation:** This can occur in some autonomic disorders or pharmacologic influences.

Pupil Cycling Time Assesses the ability of the pupil to constrict and dilate repeatedly in response to alternating light exposure	
Deviations:	• **Prolonged cycling time:** This could suggest neurodegenerative conditions such as Parkinson's disease or Alzheimer's disease.

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Patient Selection and Testing Frequency

Establishing baseline pupillary parameters is essential for all patients, especially those at risk for neurological disorders or ocular anomalies (anisocoria, pupillary asymmetry). However, in addition, several patient types warrant routine pupillometry testing. Consider the following scenarios:

- **Neurological Symptoms:** Any patient presenting with unexplained anisocoria, abnormal pupillary reflexes, neurological symptoms (headaches, dizziness, vision disturbances), or symptoms suggestive of autonomic dysfunction (e.g., fatigue, syncope) warrants pupillometry.
- **Known Neurological Disorders:** Patients with known neurological conditions (e.g., multiple sclerosis, Parkinson's disease, traumatic brain injury, Alzheimer's disease) should undergo regular pupillometry.
- **At-Risk Patients:** Individuals with a history of trauma, concussions, risk factors for neurodegenerative diseases, glaucoma, optic neuropathies, or systemic conditions affecting neural function (e.g., diabetes) should be considered.

Routine pupillometry should be conducted at baseline eye exams for new patients, annual comprehensive eye exams, and follow-up visits for neurological or systemic conditions.

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Part II: Neurological Disorders and Pupillometry

Pupillometry plays a crucial role in the evaluation of several neurological disorders.

Traumatic Brain Injury (TBI) and Concussions

In the United States, TBI is a significant public health problem. Millions of people sustain TBIs each year. However, precise figures are difficult to obtain due to underreporting of milder cases, especially concussions. In Canada, similarly, TBI is a significant cause of disability. There are estimated to be many new cases of Acquired Brain Injury (ABI) annually, with a high percentage of those being TBI. Older adults (75 and older) experience the highest rates of TBI-related hospitalization and death, primarily due to falls, while children and adolescents are particularly vulnerable to sports-related concussions.

Pupillary abnormalities, such as anisocoria and sluggish reflexes, are common in TBI. Pupillometry can help assess the severity of injury and monitor recovery. Irregular pupillary reactions can reflect intracranial pressure changes or damage to the midbrain.

Multiple Sclerosis (MS)

MS affects hundreds of thousands of people in the U.S. and Canada. It is estimated that nearly one million people live with MS in the United States. Women are two to three times more likely to develop MS than men. Onset typically occurs between 20 and 50 years of age.

Pupillary light reflex abnormalities can occur in MS due to optic nerve or brainstem involvement. Pupillometry can help detect subclinical optic neuritis. Abnormal PLR results may indicate demyelination in the optic pathway.

Parkinson's Disease

It is estimated that roughly one million people live with Parkinson's disease in the United States. While the risk increases with age, most cases develop after age 60. Men are slightly more likely to develop Parkinson's disease than women.

Pupillary abnormalities, including reduced pupil size and delayed responses, are common in Parkinson's disease. Pupillometry can help monitor disease progression and can be an early marker for disease progression. Reduced pupillary light response is often observed, linked to dopaminergic neuron dysfunction.

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Horner's Syndrome

Horner's syndrome is relatively rare. It is not a disease but a set of symptoms resulting from an underlying neurological problem. It can affect people of any age. Risk depends on the underlying cause (e.g., stroke, tumor, injury).

Pupillometry is essential for confirming the diagnosis of Horner's syndrome, characterized by miosis, ptosis, and anhidrosis. Pupillometry confirms sympathetic nervous system dysfunction.

Third Nerve Palsy

Like Horner's syndrome, Third Nerve Palsy is relatively rare. It is a symptom of an underlying condition and can occur at any age. Risk factors include stroke, diabetes, hypertension, and head trauma. Pupillometry helps differentiate between complete and partial third nerve palsies, aiding in lesion localization.

Brainstem Lesions

Stroke, tumors, and other traumas can cause brainstem lesions. Risk factors include age, vascular disease, and genetic predisposition.

Pupillary abnormalities can indicate brainstem involvement, providing valuable information for localization.

Alzheimer's Disease

Alzheimer's is a major public health crisis, affecting millions in the U.S. and Canada. It is the most common form of dementia. Risk increases significantly with age, particularly after 65. Those with a family history of Alzheimer's Disease are at the greatest risk.

Abnormal pupil responses to cognitive tasks provide insights into early cognitive decline.

Autonomic Neuropathy

Diabetes is a major contributor to autonomic neuropathy. Since diabetes is so prevalent in the U.S. and Canada, autonomic neuropathy is also fairly common. Other susceptible demographics include older adults and people with autoimmune diseases.

As seen in conditions like diabetes, pupillometry can reveal impaired autonomic control of the pupil. Conditions like dysautonomia can cause abnormal pupil responses. Pupillometry provides objective metrics for autonomic dysfunction assessment.

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Glaucoma and Optic Neuropathy

Glaucoma affects millions worldwide, with significant numbers in the U.S. and Canada. Optic neuropathy also affects a large number of people, but the cause and, therefore, prevalence vary. Those at the highest risk include older adults, people with a family history of glaucoma, certain ethnic groups (including African Americans), and those who have diabetes.

Afferent pupillary defects (APD) are significant indicators of optic nerve damage. Early detection through pupillometry allows for timely intervention.

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Part III: The Importance of Baselining Patients

Establishing baseline pupillary parameters during every patient visit, regardless of age, ethnicity, or risk factors, is essential for several reasons. Baseline data enables the early detection of subtle changes in pupil response, which may indicate underlying neurological disorders. This baseline information helps monitor disease progression and evaluate treatment responses in patients with known neurological conditions. It also considers individual variations in pupil size and reactivity, enhancing the accuracy of future assessments.

Tracking changes in pupil dynamics over time can reveal early signs of neurological deterioration. In cases of head trauma, having baseline data provides a valuable point of reference for assessing potential neurological damage.

Early identification of anomalies allows clinicians to personalize treatment plans effectively. Data obtained from routine pupillometry exams aids in making more informed decisions, especially in complex cases. Additionally, routine pupillometry testing may be necessary to provide objective data for insurance purposes and documentation. Standardized baseline results support insurance claims and assist in clinical decision-making.

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Part IV: Pupillometry Testing Using a Virtual Reality Headset

Traditional automated pupilometry modalities can present challenges for accurate pupillometry, particularly in patients with physical restrictions that render travel to a clinic challenging. Traditional perimetry usually requires a dedicated spacious room with dimmable lighting. Optical refractive lenses are sometimes required to be loaded. Pupillometry testing using a virtual reality device offers several advantages:

- **Improved Patient Engagement:** Virtual environments provide a more engaging and immersive experience, enhancing patient compliance and reducing fatigue.
- **Precise Pupillometry Integration:** Virtual systems can seamlessly integrate pupillometry, measuring visual fields and pupillary responses in one sitting and testing sequence.
- **Reduced Artifacts:** Virtual environments minimize external light influences, improving the accuracy of pupillometry measurements.
- **Enhanced Data Visualization:** Virtual platforms offer advanced data visualization tools, facilitating the analysis of pupillary parameters and their correlation with visual field defects.
- **Enhanced Accuracy:** Virtual systems provide immersive environments that minimize distractions, yielding more reliable pupil response data.
- **Dynamic Stimulus Presentation:** Virtual systems allow for more diverse and controlled light stimuli, enabling nuanced assessments of pupil dynamics.
- **Accessibility and Mobility:** Portable virtual devices open avenues for diagnostic testing in non-traditional settings such as home care or outreach programs.
- **Comprehensive Testing in One Device:** Virtual-based technology integrates visual field testing with automated pupillometry in a single device, reducing the need for multiple diagnostic equipment investments.
- **Improved Compliance for Neurological Patients:** Many patients with neurological disorders struggle with traditional testing setups, whereas virtual testing makes the experience easier and more engaging.

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Billing and Coding for Pupillometry

In the United States, the updated CPT code for pupillometry is 95919. This code is used specifically for automated quantitative pupillometry exams, and you must interpret both unilateral and bilateral results.

The Medicare Physician Fee Schedule (MPFS) indicates reimbursement between $6 and $20, depending on your location, setting, modifiers, and other practice factors.

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Conclusion

Pupillometry is a valuable tool for optometrists and ophthalmologists. The common (yet inadequate) “pupils equal round and reactive to light (PERRL)” designation will miss significant findings. Routine patients, particularly those being evaluated for optical problems with surgical solutions, deserve pupillometry for accurate prognosis in weighing the risks against the benefits of intervention. For diagnosing and managing neurological disorders, pupillometry is indispensable, as life-threatening conditions can be missed without it.

Integrating routine pupillometry exams and utilizing virtual reality devices when appropriate ensures more accurate, efficient, and patient-friendly diagnostic experiences. With virtual testing, optometrists and ophthalmologists can seamlessly conduct pupillometry exams and visual field tests, providing a higher standard of care while streamlining their workflow.

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Dr. Lisa Brothers Arbisser, MD, a recognized leader in cataract and anterior segment Surgery, co-founded Eye Surgeons Associates, PC., an eight-office/22-doctor/ 180-employee integrated Iowa and Illinois practice. Graduating with honors from Princeton University, she received her MD (AOA) from the University of Texas Health Science Center at Houston and NIH fellowship in neurobiology and retina before completing ophthalmology residency and associate fellowship in anterior segment surgery at the University of Iowa.

She's an adjunct professor at the University of Utah Moran Eye Center, a frequent visiting professor and invited speaker, an author of textbook chapters, and a former writer/editor of Focal Points. She surgical coaches privately since retiring from direct patient care after 30 years in practice. She has earned numerous awards, including two AAO Secretariat awards and two ASCRS peer-voted Golden Apple Awards for surgical teaching. She has performed satellite surgery in the U.S. and abroad. She served on the AAO online news and education network (ONE) for over a decade, as well as on numerous editorial boards.

Dr. Lisa is a former president of the American College of Eye Surgeons and served as education director on the board of Women in Ophthalmology. She was voted among the top 50 opinion leaders by Cataract and Refractive Surgery Today and was one of the earliest female KOLs for the industry in cataract surgery. The American Women's Medical Association recognized her as an Iowa Living Legend, and she's been honored as a lifetime member of the Iowa Volunteer Hall of Fame. She is a third-generation professional woman, wife, and mother of four and grandmother of five.

She is a co-founder and co-owner of Minute Suites, private rooms to rent inside security at U.S. airports.