List of Published Papers Using the NeurOptics® Pupillometer in Ophthalmology

1. Brown SM, Bradley JC. Comparison of 2 monocular pupillometers and an autorefractor for measurement of the dark-adapted pupil diameter. J Cataract Refract Surg. 2011 Apr;37(4):660-4.

Abstract PURPOSE: To compare the performance of the Marco Nidek ARK-530A autorefractor pupillometer function and the Keeler PupilScan II pupillometer (study pupillometer) against the clinical standard NeurOptics PLR-200 pupillometer (standard pupillometer) for measurement of the dark-adapted pupil diameter. SETTING: Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, USA. DESIGN: Evaluation of diagnostic test or technology. METHODS: Subjects aged 20 to 60 years were dark-adapted for 2 minutes at 1 lux ambient illumination. Accommodation was controlled through distance fixation. The dark-adapted pupil diameter was measured with the standard pupillometer, then the study pupillometer, then the autorefractor. Results were compared using Bland-Altman graphs. RESULTS: The autorefractor underestimated the dark-adapted pupil diameter by a mean of 1.03 mm (range 0.0 to 2.3 mm). Thirty-four (85%) measurements were at least 0.5 mm smaller than the corresponding standard pupillometer values, and 16 (40%) were more than 1.0 mm smaller. Observer experience did not improve accuracy. The study pupillometer underestimated the dark-adapted pupil diameter by a mean of 0.31 mm (range 0.0 to 0.9 mm). Ten (25%) measurements were at least 0.5 mm smaller than the standard pupillometer values. Accuracy improved in the final 10 subjects (study pupillometer smaller; mean difference 0.16 mm; range 0.0 to 0.4 mm). CONCLUSIONS: The autorefractor pupillometry function had an unpredictable negative bias (variable underestimation of dark-adapted pupil diameter). The study pupillometer had a slight negative bias but required significant examiner skill and knowledge of normal pupil movement to obtain a valid result. Neither device was sufficiently accurate for confident surgical planning or clinical diagnosis. FINANCIAL DISCLOSURE: Neither author has a financial or proprietary interest in any material or method mentioned.

2. Bradley JC, Cohn CD, Wu PW, Brown SM. Comparison of a monocular pupillometer and the pupillometry function of a binocular free-viewing autorefractor. J Cataract Refract Surg. 2011 Jul;37(7):1257-62. Epub 2011 May 20.

Abstract PURPOSE: To compare a binocular free-viewing autorefractor pupillometer (WAM 5500 Binocular Accommodation Instrument) and a monocular occlusion pupillometer (Neuroptics pupillometer). SETTING: Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, USA. DESIGN: Evaluation of diagnostic test or technology. METHODS: Normal subjects were tested under 1 lux and 7 lux ambient illumination with controlled distance fixation. The monocular occlusion pupillometer and free-viewing autorefractor pupillometer test order and eye test order were randomized. Devices were compared using Bland-Altman plots. Effects of eye test order and device test order were analyzed. The number of outliers (ie, difference ≥0.5 mm between devices) was tabulated. RESULTS: The mean device difference (monocular pupillometer minus binocular pupillometer) was +0.51 mm ± 0.36 (SD) (range -0.20 to +1.50 mm) in right eyes and +0.27 ± 0.31 mm (SD) (range -0.30 to +1.00 mm) in left eyes at 1 lux and +0.26 ± 0.28 mm (range -0.30 to +0.90 mm) and +0.21 ± 0.24 mm (range -0.80 to +0.40 mm), respectively, at 7 lux. The outlier frequency (N = 49) at 1 lux was 23 (47%) in right eyes and 7 (14%) in left eyes and at 7 lux, 11 (22%) and 10 (20%), respectively. At all age decades, the free-viewing autorefractor underestimated dark-adapted pupil diameter. Eye test order and device order did not cause unidirectional bias. CONCLUSIONS: The free-viewing pupillometer frequently disagreed with the monocular occlusion pupillometer by more than 0.5 mm. Testing the first eye with the monocular pupillometer did not induce sustained pupillary constriction that might bias results in the second eye.

3. Bradley JC, Bentley KC, Mughal AI, Bodhireddy H, Brown SM. Dark-Adapted Pupil Diameter as a Function of Age Measured with the NeurOptics Pupillometer. J Refract Surg. 2011 Mar;27(3):202-7. doi: 10.3928/1081597X-20100511-01. Epub 2010 May 17.

Abstract PURPOSE: To measure the dark-adapted pupil diameter of normal research participants in their second through ninth decades of life using the NeurOptics pupillometer (Neuroptics Inc). METHODS: Individuals aged 18 to 80 years with no history of eye disease or injury, intraocular surgery, or use of systemic antihistamines or opiates were recruited. After 2 minutes of adaptation at 1 lux illumination, the right dark-adapted pupil diameter was measured using the NeurOptics pupillometer, with accommodation controlled by distance fixation. The NeurOptics pupillometer reported a mean dark-adapted pupil diameter and a standard deviation of the mean, which were analyzed as a function

of age-decade. RESULTS: Two-hundred sixty-three individuals participated. For participants aged 18 to 19 years (n=6), the mean dark-adapted pupil diameter was 6.85 mm (range: 5.6 to 7.5 mm); 20 to 29 years (n=66), 7.33 mm (range: 5.7 to 8.8 mm); 30 to 39 years (n=50), 6.64 mm (range: 5.3 to 8.7 mm); 40 to 49 years (n=51), 6.15 mm (range: 4.5 to 8.2 mm); 50 to 59 years (n=50), 5.77 mm (range: 4.4 to 7.2 mm); 60 to 69 years (n=30), 5.58 mm (range: 3.5 to 7.5 mm); 70 to 79 years (n=6), 5.17 mm (range: 4.6 to 6.0 mm); and 80 years (n=4), 4.85 mm (range: 4.1 to 5.3 mm). These values were consistent with studies using infrared photography. The standard deviation was >0.1 mm in 10 (3.8%) participants, all of whom were younger than 55 years. CONCLUSIONS: The dark-adapted pupil diameter is an important clinical variable when planning refractive surgery. Surgeons can compare a patient's dark-adapted pupil diameter with the results of this population study to identify outlier measurements, which may be erroneous, and repeat testing prior to surgery.

Excerpt: Although geometric optics supports the psychovisual importance of the emmetropic optical zone diameter relative to the dark-adapted pupil diameter, for a period of time the refractive surgery literature held that the dark-adapted pupil diameter was an unimportant clinical variable. Despite this idea, which was well received as it increased the number of patients considered suitable refractive surgery candidates, ophthalmologists continued to measure the dark-adapted pupil diameter and new devices for this purpose were developed, marketed, and compared. Opinion on the importance of the dark-adapted pupil diameter is currently polarized, but some excimer laser manufacturers now warn patients in their product labeling about vision quality loss with large low-light pupils; the US Food and Drug Administration also warns the public of this possibility. In our opinion, if ophthalmologists measure the dark-adapted pupil diameter they should do so accurately. This requires a correct testing protocol and an accurate pupillometer. From the quality-of-practice and medicolegal perspectives, a cursory dark-adapted pupil diameter measurement is more dangerous than no measurement at all.

4. Brown SM, Bradley JC. Comparison of 2 monocular pupillometers and an autorefractor for measurement of the dark-adapted pupil diameter. J Cataract Refract Surg. 2011 Apr;37(4):660-4.

Abstract PURPOSE: To compare the performance of the Marco Nidek ARK-530A autorefractor pupillometer function and the Keeler PupilScan II pupillometer (study pupillometer) against the clinical standard NeurOptics PLR-200 pupillometer (standard pupillometer) for measurement of the dark-adapted pupil diameter. SETTING: Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, USA.
DESIGN: Evaluation of diagnostic test or technology. METHODS: Subjects aged 20 to 60 years were dark-adapted for 2 minutes at 1 lux ambient illumination. Accommodation was controlled through distance fixation. The dark-adapted pupil diameter was measured with the standard pupillometer, then the study pupillometer, then the autorefractor. Results were compared using Bland-Altman graphs. RESULTS: The autorefractor underestimated the dark-adapted pupil diameter by a mean of 1.03 mm (range 0.0 to 2.3 mm). Thirty-four (85%) measurements were at least 0.5 mm smaller than the corresponding standard pupillometer values, and 16 (40%) were more than 1.0 mm smaller. Observer experience did not improve accuracy. The study pupillometer underestimated the dark-adapted pupil diameter by a mean of 0.31 mm (range 0.0 to 0.9 mm). Ten (25%) measurements were at least 0.5 mm smaller than the standard pupillometer values. Accuracy improved in the final 10 subjects (study pupillometer smaller; mean difference 0.16 mm; range 0.0 to 0.4 mm). CONCLUSIONS: The autorefractor pupillometry function had an unpredictable negative bias (variable underestimation of dark-adapted pupil diameter). The study pupillometer had a slight negative bias but required significant examiner skill and knowledge of normal pupil movement to obtain a valid result. Neither device was sufficiently accurate for confident surgical planning or clinical diagnosis.

5. Bradley JC, Bentley KC, Mughal AI, Bodhireddy H, Brown SM. Dark-Adapted Pupil Diameter as a Function of Age Measured with the NeurOptics Pupillometer. J Refract Surg. 2010 May 27:1-6. doi: 10.3928/1081597X-20100511-01.

Abstract PURPOSE:To measure the dark-adapted pupil diameter of normal research participants in their second through ninth decades of life, using the NeurOptics pupillometer (Neuroptics Inc). METHODS:Individuals aged 18 to 80 years with no history of eye disease or injury, intraocular surgery, or use of systemic antihistamines or opiates were recruited. After 2 minutes of adaptation at 1 lux illumination, the right dark-adapted pupil diameter was measured using the NeurOptics pupillometer, with accommodation controlled by distance fixation. The NeurOptics pupillometer reported a mean dark-adapted pupil diameter and a standard deviation of the mean, which were

analyzed as a function of age-decade. RESULTS:Two-hundred sixty-three individuals participated. For participants aged 18 to 19 years (n=6), the mean dark-adapted pupil diameter was 6.85 mm (range: 5.6 to 7.5 mm); 20 to 29 years (n=66), 7.33 mm (range: 5.7 to 8.8 mm); 30 to 39 years (n=50), 6.64 mm (range: 5.3 to 8.7 mm); 40 to 49 years (n=51), 6.15 mm (range: 4.5 to 8.2 mm); 50 to 59 years (n=50), 5.77 mm (range: 4.4 to 7.2 mm); 60 to 69 years (n=30), 5.58 mm (range: 3.5 to 7.5 mm); 70 to 79 years (n=6), 5.17 mm (range: 4.6 to 6.0 mm); and 80 years (n=4), 4.85 mm (range: 4.1 to 5.3 mm). These values were consistent with studies using infrared photography. The standard deviation was >0.1 mm in 10 (3.8%) participants, all of whom were younger than 55 years. CONCLUSIONS:The dark-adapted pupil diameter is an important clinical variable when planning refractive surgery. Surgeons can compare a patient's dark-adapted pupil diameter with the results of this population study to identify outlier measurements, which may be erroneous, and repeat testing prior to surgery. Copyright 2010, SLACK Incorporated.

6. Bradley JC, Bentley KC, Mughal AI, Brown SM., Clinical performance of a handheld digital infrared monocular pupillometer for measurement of the dark-adapted pupil diameter, J Cataract Refract Surg. 2010 Feb;36(2):277-281.

PURPOSE: To compare the accuracy of a handheld infrared digital pupillometer and digital infrared photography for measurement of the dark-adapted pupil diameter. SETTING: Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, USA. METHODS: The right horizontal pupil diameter in healthy volunteers was measured using a NeurOptics PLR-200 pupillometer and then videographed using the infrared function of a CyberShot video camera after 2 minutes and 5 minutes dark adaptation at 1 lux ambient illumination. The best still image was extracted from the video file, and the horizontal pupil diameter was determined by comparison against an internal photographic length standard using digital image software. Accommodation and alertness were controlled during testing. RESULTS: The mean horizontal pupil diameter by infrared photography after 2 minutes of dark adaptation by subject age was 7.71 mm for ages 20 to 29 years, 6.80 mm for ages 30 to 39 years, 6.53 mm for ages 40 to 49 years, 5.94 mm for ages 50 to 59 years, and 6.01 mm for ages 60 to 69 years. The mean difference (infrared photography minus pupillometer) was +0.09 mm (range +0.30 to -0.14 mm) at 2 minutes of adaptation and +0.07 mm (range +0.25 to -0.13 mm) at 5 minutes. CONCLUSIONS: The pupillometer accurately measured the horizontal pupil diameter at 1 lux, with no measurement more than 0.3 mm different from infrared photography measurements. The pupillometer had a slight negative bias that is unlikely to introduce an error greater than 0.5 mm in clinical measurements.

7. Schallenberg M, Bangre V, Steuhl KP, Kremmer S, Selbach JM., Comparison of the colvard, procyon, and neuroptics pupillometers for measuring pupil diameter under low ambient illumination., J Refract Surg. 2010 Feb;26(2):134-43. doi: 10.3928/1081597X-20100121-09. Epub 2010 Feb 12.

PURPOSE:To compare three different pupillometers (Colvard, Procyon, and Neuroptics) for determining pupil diameter at 0.04 and 0.4 lux ambient illumination. METHODS:In 92 eyes of 46 healthy volunteers, pupil diameter was measured at 0.04 and 0.4 lux. After dark adaptation for 2 minutes, measurements were performed with each device by two examiners. Interobserver agreement, instrument agreement, and repeatability were analyzed. RESULTS:Mean pupil diameter was 6.63+/-0.68 mm, 6.24+/-1.01 mm, and 6.99+/-0.67 mm at 0.04 lux and 6.22+/-0.74, 4.64+/-1.04, and 6.73+/-0.72 mm at 0.4 lux with the Colvard, Procyon, and Neuroptics pupillometers, respectively. The interobserver disagreement ranged within narrower limits for the Colvard (0.04 lux: -1.0 to 0.5 mm; 0.4 lux: -0.75 to 1.0 mm) and Neuroptics (0.04 lux: -1.0 to 0.5 mm; 0.4 lux: -1.7 to 0.7 mm) than for the Procyon (0.04 lux: -0.74 to 1.14 mm; 0.4 lux - 1.82 to 2.4 mm) under both light conditions. Instrument agreement ranged within narrower limits for the Colvard versus Neuroptics (0.04 lux: -1.3 to 0.75 mm; 0.4 lux: -1.55 to 1.40 mm) than for the Neuroptics versus Procyon (0.04 lux: - 1.06 to 2.69 mm; 0.4 lux: 0.18 to 3.69 mm) or Colvard versus Procyon (0.04 lux: -0.63 to 2.60 mm; 0.4 lux: -0.32 to 3.13 mm) at both light levels. At 0.04 lux, repeatability showed no measurement difference outside +/-0.5 mm for the Colvard and Neuroptics; for the Procyon, 25% of consecutive measurements showed a difference >+/-0.5 mm. At 0.4 lux, 2.5% of consecutive measurements for the Colvard and 5% for the Neuroptics differed by >+/-0.5 mm; for the Procyon, 13% of measurements differed by more than this amount. CONCLUSIONS:Pupil diameters under both light conditions were largest with the Neuroptics pupillometer and smallest with the Procyon. The most "examiner independent" Procyon pupillometer performed poorly. The underestimation of the pupil diameter might have severe

consequences for refractive surgery patients. The Neuroptics pupillometer showed a high interobserver agreement and repeatability and therefore high safety.

8. Privitera CM, Stark LW., **A Binocular Pupil Model for Simulation of Relative Afferent Pupil Defects and the Swinging Flashlight** Test., Biol Cybern. 2006 Jan 10;:1-10.

Many important intracranial neural pathways are involved in the control of the two muscles of the human pupil and the observation and analysis of pupil responses to light or other stimuli is of great interest in many clinical procedures. The binocular pupil model presented in this document has a topology encompassing much of the complexity of the pupil system neurophysiology. The dynamic parameters of the model were matched against pupil experiments under multiple conditions. It is employed here to simulate responses to the swinging flashlight test, a procedure which is routinely practiced in ophthalmology to diagnose different degrees of relative afferent pupil defects often a consequence of severe optic nerve diseases or retinal dysfunctions. Other, not light-dependent, pupil stimuli are briefly discussed.