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ARTICLE

Automated Functional Color Field Tester (FCFTester) Trends and Reproducibility – A Multicenter Pilot Study

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ABSTRACT

Background

The present study was designed to assess a protocol for investigating normative trends of kinetic color visual field sizes and reproducibility of such utilizing the Automated Functional Color Field Tester (FCFTester).

Methods

The participants were recruited at three clinical sites. The participants were screened for the study based on a questionnaire designed by the authors to help assess the inclusion and exclusion criteria. There were 116 adult-only participants, however, only those reporting White race (n = 106) were used for statistical analysis. The mean age was 35.8 (std = 14) and nearly 70% of the sample was female.

Results

This study demonstrated that kinetic visual field sizes across all four color isopters are not influenced by gender (p = 0.96) nor eye tested (p = 0.46). Only a slight difference in mean visual field sizes was found between the three clinical sites ranging from less than 2.5 degrees when the target was blue or green to less than 1.5 degrees for white or red targets. Overall, age had limited, yet significant, influence on kinetic field sizes likely related to the relatively young age of our participants. A significant difference in mean field size existed when comparing the four color isopters with an ascending order of green, red, blue, and white. This pattern was consistent across the three testing sites. Variability in field size for each color isopter was slight across the three clinical sites.

Conclusion

The present pilot study shows promise that a protocol can be established to provide reproducible data and normative trends in kinetic color visual field testing. The authors recognize that this should be achievable with further refinement of the current testing protocol.

BACKGROUND

Visual field evaluation, also known as perimetry or campimetry, is the method of measuring the ability of the peripheral portions of the eye to discern form, motion, and color.[1] It is an assessment of the patient's use of projections of variable contrast across the visual field for detection and representation of the spatial layout of the visual scene.[2] Visual field evaluation has been in existence since 150 B.C. However, it was not until 1602 that the first visual field illustration was recorded. In 1856, Albrecht von Graefe was one of the first to bring visual field testing into clinical practice. Decades later, Jannik Bjerrum introduced the use of color targets in kinetic campimetry to measure the central 30 degrees of a patient's visual field. He also popularized the use of different target sizes. In the 1940's, Hans Goldmann exponentially advanced the knowledge of visual field testing, including both static and kinetic perimetry.[3] Many today continue to consider the manual Goldmann apparatus as a gold standard for kinetic perimetry.[4]

Static perimetry is performed using a stationary test object of variable test value, whereas kinetic perimetry employs the technique of moving a test object of constant stimulus value. Both methods are performed while the patient maintains central fixation. Static testing is quantitative in nature and kinetic testing is qualitative.[1] In the late 1960s and early 1970s, the first automated perimeters were developed by doctors John R. Lynn, George W. Tate, and Franz Fankhauser. Fankhauser produced the first automated perimeter known as the Octopus. Their work paved the way for the advent of automated perimetry which is now far more common than performing manual visual fields.[5] Many more automated perimeters have been developed in recent decades, including both static and kinetic measures. Since this study involves only kinetic perimetry, this manuscript will further reference only kinetic testing.

The challenge for manufacturers has been to create an automated kinetic perimeter that can be as sensitive as the manual Goldmann perimeter. The impetus for the development of automated testing is reduction of human influence on outcomes, thereby supporting what modern research strives for: reproducible data and quality studies that lead to better clinical practices.[6] Several studies have suggested that automated kinetic perimetry may be more reliable, repeatable, and efficient in comparison to manual kinetic perimetry.[7,8,9] In contrast, another study found no significant difference between manual and automated methods of kinetic perimetry.[10] Manual perimetry, such as Goldmann, has disadvantages including examiner bias, and intra-examiner differences in stimulus velocity.[11] Stimulus velocity has been shown to be an important factor in kinetic perimetry and recommended velocities may vary from 2°/s[12] to 4°/s.[7] A study that evaluated manual kinetic perimetry where a velocity of 2 degrees/s was recommended found that this velocity was often exceeded in daily clinical practice.[7] As a result, the investigators proposed that automated kinetic perimetry could ensure a constant lower velocity and thus improve standardization. The rate of target movement has implications for reaction time, perceptual smear, variability, and hence isopter limits.[13]

Four currently available automated kinetic perimeters were evaluated in a 2017 study by Hashimotor, et al.[14] The Octopus GKP was found to be a very comparable device to the Goldmann manual perimeter, while the others had various flaws. These investigators reiterate that examiner skill level and experience substantially affect the test precision of manual perimetry. Such problems can only be solved by the establishment of a fully automated kinetic method, a system completely free from examiner bias, which they discovered is possible with the Octopus GKP. The primary disadvantage of currently available automated perimeters is that they are unable to test the extended periphery as can be accomplished with the manual Goldman apparatus.

Although the advancement of automated kinetic perimetry is impressive, the availability of color targets in automated kinetic perimeters has, until recently, remained absent. The field of optometric phototherapy, or syntonic optometry, has long relied upon the inclusion of color targets during kinetic perimetry in patient care.[15] Syntonics or optometric phototherapy is the branch of ocular science dealing with the application of selected light frequencies through the eyes. It has been used clinically in optometry for over 80 years.[16] In 1933, Dr. Harry Riley Spitler, established the College of Syntonic Optometry to encourage education and research related to the therapeutic application of light and color to the visual system.

Providers of optometric phototherapy observe patient responses to both movement and location of four targets (i.e., green, red, blue, and white) during kinetic perimetry to assist them with diagnosis and treatment management. Periodically throughout treatment, kinetic color perimetry is repeated to help determine when to modify and or discontinue the phototherapy treatment protocol. However, numerous variations of the kinetic color perimetry technique exist in the literature and amongst practitioners. These variations include target size, testing distances, velocity of target presentation, direction of target presentation (i.e., seeing to non-seeing or non-seeing to seeing), number of meridians tested, illumination of the target background, and the room illumination.[1,17] The authors propose that the FCFTester may provide an opportunity for enhanced universalization of kinetic color field perimetry by facilitating control of these many variables. By controlling the variables mentioned above from clinic to clinic, this will help to minimize discrepancies to promote a more standardized approach.

The current study was conducted to investigate a protocol for clinically measuring kinetic color visual fields utilizing the automated FCFTester. The primary objective was to determine if normative data and reproducibility can be established for values, in degrees, of the isopters representing four colored stimuli: green, red, blue, and white. The study also provided observations of the role that age, sex, and eye to eye comparison play in establishing these values.

METHODS

Subjects

116 healthy adults (18 years of age or older), both male and female (32.8% and 67.2%, respectively), were recruited to participate in this study. To limit confounding factors such as certain participant medications and various medical histories, the authors developed a complete list of inclusion and exclusion criteria (Table 1). This pilot study recruited participants by convenience sampling at the authors' (AN, RS, SC) private clinics.

Table 1: Inclusion and Exclusion Criteria for Participants

Inclusion	Exclusion
Males and Females >18 years of age	• Use of systemic medications including: sympathomimetics (e.g., phenylephrine), sympatholytic (e.g., beta-blockers), parasympathomimetic (e.g., pilocarpine), anticholinergics (e.g., atropine) • History of strabismus, amblyopia, diplopia, other ocular pathology, or surgery on or around the eye • Visual acuity >20/40 OD or OS • Acquired brain injury or traumatic brain injury (mild, moderate, or severe) within 3 years of enrollment date • Neurodegenerative diseases (e.g., Parkinson's disease) • Answered yes to color vision deficiencies as indicated by response on the initial questionnaire • History of optometric phototherapy treatment within the last year

Participants who met the criteria for the study were given the opportunity to read the IRB consent document and study protocol. Written informed consent was obtained from all participants prior to their participation. The study did not pose any potential side effects or adverse effects that could harm the participants. The study was approved by the Advarra Institutional

Review Board (IRB) and in adherence to the Declaration of Helsinki.

Instrumentation

All testing was performed using a ViewSonic® VG2239m-LED LCD 22" monitor (ViewSonic Americas, Brea, CA, USA) and the FCFTester software (available through Bernell Corporation, Mishawaka, IN, USA) at each clinical site. The chosen FCFTester settings were based upon the authors' prior clinical experience (Table 2). As such, the data is only relative when using the software settings of the current study.

Table 2: Protocol for the FCF Tester Software

Parameters	
Form field target size:	3.0mm
Color field target size:	2.0mm
Blind spot target size:	1.4mm
Target speed:	27mm/sec
Color brightness:	176
Show meridians	15-degrees
Meridian frequency:	30-degrees
Test colors start at:	30-degrees
Central stimulus:	Numbers
Frequency	1500msec between flashes
Testing distance	20cm

Testing Procedure

The authors or trained assistants (examiners) performed the testing by following the protocol in Figure 1. Visual acuity was taken using automated or projected Snellen letters with best corrected prescription (if any) for distance and near. Cover test was performed to rule-out strabismus. Participants wore their habitual near correction, which if indicated, was refined for a 20cm working distance to provide clarity of the 5 and 10-degree circles and numbers. The right eye was measured first followed by the left eye. The participants placed their eyes to the viewing apparatus and were instructed to maintain fixation on the central circle. The participants were informed that during the test random numbers would be flashing in the central circle during the test to help them maintain central fixation. The participants were briefed that each target would be approaching from the periphery (i.e., non-seeing to seeing) and they were to verbalize the target color (i.e, white, green, red, or blue) once they could confidently identify it. If the target color was correctly identified, the examiner clicked the computer mouse which caused the software to register that location point. The software then automatically began another peripheral target presentation. If the participant called the wrong color, the examiner allowed the target to reach the central point (zero degrees) because the software is programmed to repeat this meridian and target color at a random time later during the test. The same process was followed if the participant failed to maintain central fixation. The software presented the targets in a random fashion for both color and meridian being tested. To ensure central fixation, the examiners watched the participant's eye from the side while being kept informed of the target color via a convenient grid at the edge of the monitor screen.

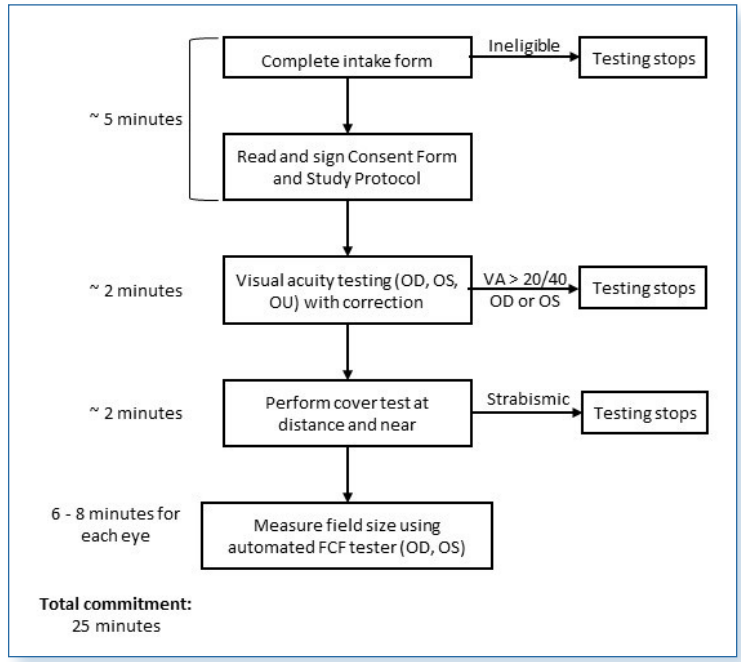

Figure 1. Flow Chart of the study protocol

Statistical Methods

All statistical testing was accomplished using SAS (Version 9.4) statistical software. The distribution of field size measurements was assessed using a Komolgov-Smirnov test. Descriptive statistics for kinetic field size were generated and are reported as mean and

standard deviation. Methodology as described by Bland and Altman[18] was used to assess repeatability of between-eye measurements obtained from right and left eye. Bland and Altman methodology defines the coefficient of repeatability (CoR) as 1.96 x standard deviation of between-eye differences and the 95% Limits of Agreement (LoA) as the mean between-eye difference ± the CoR. The LoA describes the expected range of 95% of repeatability values (OD-OS) when testing both the right and left eye. A mixed linear model controlling for the repeated observations on each participant was completed. Factors in the model included target color, eye tested, patient age and sex, and enrollment site. Estimates of adjusted means with 95% confidence interval (CI) are reported from the mixed model. The overall error-rate for pairwise comparisons of target colors was controlled using the method described by Tukey-Kramer.[19]

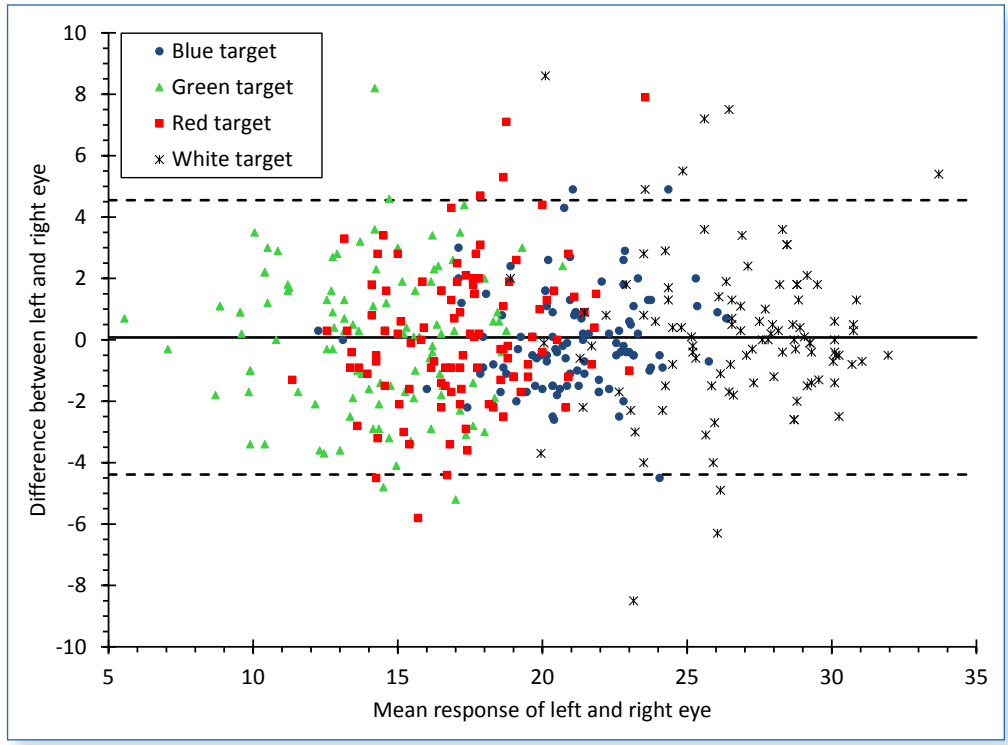

Figure 2. Bland-0Altman plot

RESULTS

Participants (n=116) were enrolled at three clinical sites (A, B, and C). Only those participants who reported White race (n=106) were used in analyses. The 10 non-White participants were excluded from all analyses as no previous research has been completed to investigate the impact of race on field size. The mean age was 35.8 years (std = 14.0) but varied significantly across sites (p = 0.002). The youngest participants were enrolled at Site C (mean = 31.8 years; std = 11.9). At Site A, the mean age was 32.5 years with a standard deviation of 12.6. The oldest participants were enrolled at Site B (mean = 41.4 years; std = 15.8). Slightly more than two-thirds of the participants were female (69.8%) and the distribution did not vary across sites (p = 0.077). There was no significant difference in the field size of males and females (p = 0.96) nor did the effect of sex vary across target color (interaction p = 0.18) or site (interaction p = 0.18).

The mean difference between right and left eyes was small (0.080 degrees) and non-significant (p = 0.46). The coefficient of reliability was 4.47 degrees with 95% limits of agreement from -4.40 to +4.55. A Bland Altman plot of the between-eye difference in relation to the mean response is shown on Figure 2. While 95% of difference values were ± 4.5 degrees, nearly 71% had between-eye difference values within ± 2 degrees. While the magnitude of the measurements varied across target colors, the observed difference in right and left eyes was not related to target color (p = 0.72; Figure 2). There was a slight, yet statistically significant (p < 0.001) effect of enrollment site on the difference between right and left eyes, however, these between-site differences were all less than 1.5 degrees which is well within the 95% limits of agreement.

Effect of Age

The relationship between age and kinetic field size was dependent on target color (interaction p = 0.017). As shown on Figure 3, there are slight differences in the slope estimates. Field

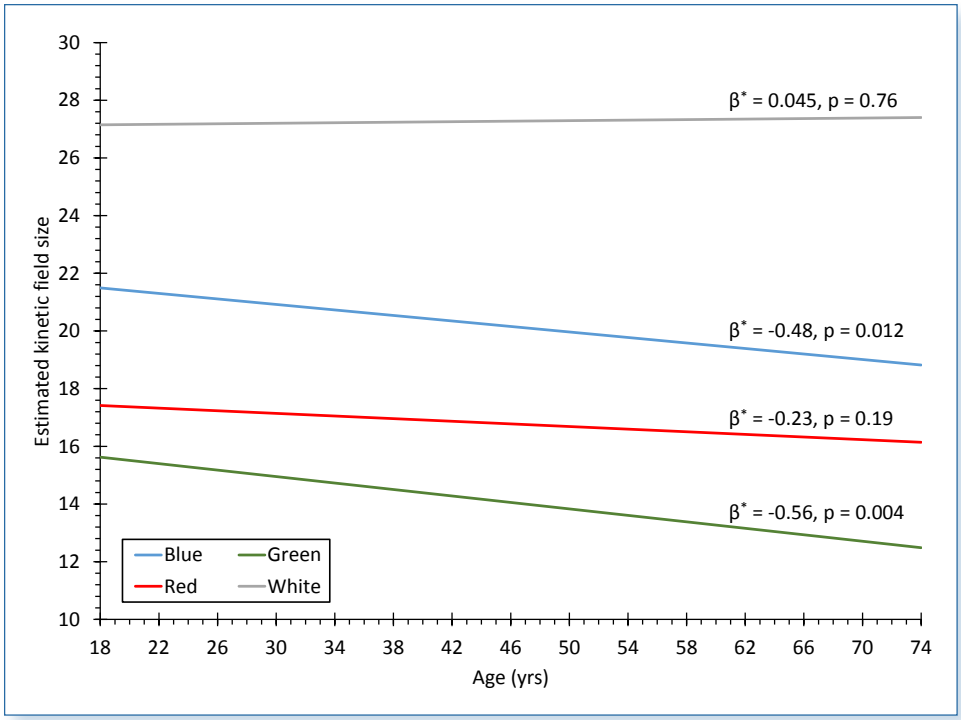

Figure 3. Relationship between kinetic field size and age of participants, by target color *Per Decade of Age

Table 3: Adjusted* mean (95% CI) kinetic field size, by target color and site

Site	Green	Red	Blue	White
A	15.2 (14.3, 16.2)	17.9 (16.9, 18.8)	22.7 (21.8, 23.7)	25.8 (24.9, 26.8)
B	12.7 (12.1, 13.3)	17.2 (16.6, 17.8)	20.6 (19.9, 21.2)	26.4 (25.8, 27.0)
C	14.7 (14.1, 15.2)	17.0 (16.5, 17.6)	20.7 (20.1, 21.3)	27.3 (26.7, 27.9)
Overall	14.2 (13.8, 14.6)	17.4 (16.9, 17.8)	21.3 (20.9, 21.7)	26.5 (26.1, 26.9)

* Adjusted for eye tested and age

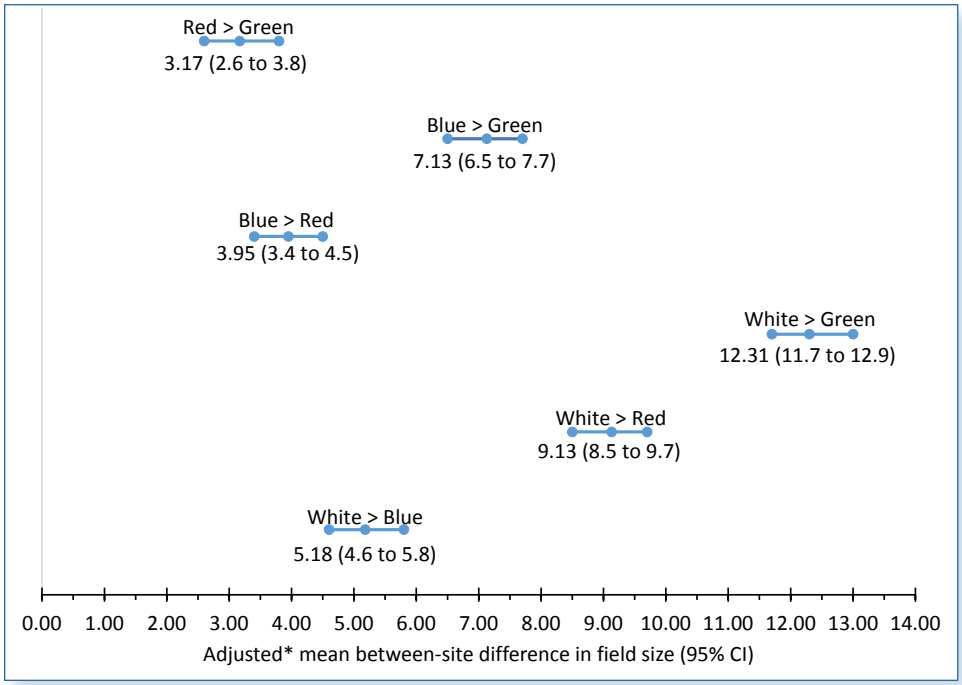

Figure 4. Adjusted* mean (95% CI) between-target color difference in field size
* Adjusted for participant age, eye tested, and site

size was not related to age when the target was red (p = 0.19) or white (p = 0.76). When the target was blue, field size was reduced by 0.48 degrees (p = 0.012) for every decade of life. The greatest impact on field size was observed when the target was green with a 0.56-degree (p = 0.004) reduction per decade of life.

Effect of Target Color

There were significant differences in mean response of the four target colors which depended on the enrollment site (interaction p < 0.001). For each target color, the variability observed between site means was small (Table 3). The site means were nearly identical when the target color was red (between-site σ^2 = 0.28) and white (between-site σ^2 = 0.64). Larger between-site differences were observed when the target was blue (between-site σ^2 = 2.08) and green (between-site σ^2 = 3.02).

The same pattern of increasing means from green through white targets applies to all three enrollment sites (Table 3). The greatest response was observed when the target was white with an adjusted mean of 26.5 degrees (95% CI 26.1 to 26.9). In contrast, the mean response when using a green target was 14.2 degrees (95% CI 13.8 to 14.6).

Regardless of site, the magnitude of between-target color differences was statistically significantly different from zero (Figure 4). The largest difference was observed when comparing the field size responses from green and white targets with an average difference

of more than 12 degrees (mean = -12.3; 95% CI: -13.0 to -11.7). Conversely, slightly more than a 3-degree difference was observed in responses from green and red targets (mean = -3.23; 95% CI: -4.0 to -2.5).

DISCUSSION

The authors created the current pilot study to investigate normative trends and provide early assessments of reproducibility of kinetic color field sizes. Normative data and reproducibility are major areas of focus within evidence-based healthcare. We suggest that the commercially available FCFTester provides a platform to accomplish this via universalized testing with rigid protocols.

For example, there were small differences in field sizes across the three clinical sites that were not statistically significant, however the mean difference was only 1.5 degrees. Future studies will provide data from additional clinic sites allowing for refinement of the estimated repeatability and testing between site differences on a larger scale. Once normative data is established, larger multicenter studies can be designed to provide comparative analysis of normal to abnormal kinetic color fields within various etiological populations.[20,21,22] This study indicated that kinetic color field sizes were not statistically different when comparing males to females, nor right to left eyes.

Our results revealed that green and blue field sizes were influenced by age, while white and red were not. However, the authors caution that our participant group mean age was young, only 32.3 years. Aging is accompanied by changes in the speed and/or mode of information processing in the brain during speed dependent tasks[23] such as kinetic color field testing. Moreover, the effect of age on brain processing becomes progressively more evident with greater task complexity.[24] Additional reasons why field sizes may be smaller with aging include senile miosis, crystalline lens changes, upper lid position changes, and retinal nerve fiber layer thickness decrease.[1,25] Finally, older patients tend to be more cautious than younger patients when performing the field testing to ensure that they are answering correctly.[26] This behavior could result in a later response and thus a smaller isopter.

The authors recognize that this study protocol utilized a relatively small target size and the target presentation began at 30 degrees. To measure kinetic color field isopters more peripherally (larger eccentricities), the target sizes need to be larger. This is because color identification throughout the visual field becomes more difficult as eccentricity from the macula increases due to decreasing concentration of cone receptors. Color can be identified up to 50 degrees when the target stimulus is large enough (5-8-degree target sizes).[27] However, when attempting visual field evaluation beyond 30 degrees, the authors caution that test time may be of concern. Longer test durations have potential adverse effects such as inducing patient fatigue or poorer attention span thus possibly affecting reliability.

The results of this study confirm long-standing teachings by the College of Syntonic Optometry that in the normal population, kinetic color field testing produces an ascending order of color field isopters, namely green, red, blue, and white.[28] This trend in the color isopters was consistent at all three clinical sites.

The reason for color visual field size differences is not well known or established, however, The Syntonic Principle, a doctoral thesis by Dr. Harry Riley Spitler, suggests that anatomical and physiological properties of the retinal cones and rods play a role in the color field disparity.[29] However, he does not provide the scientific basis as it was likely unavailable at that time. Today's literature reports that most neural differentiation of visual processing for color occurs at the level of the retina and the retinogeniculate pathway.[30] In the retina there are three cones that perceive color; these cones are known as Long (L or red), Medium (M or green), and Short (S or blue) wavelength cones. L and M cones are most densely concentrated in the foveola and become less so at greater eccentricities; the S cones are absent in the

foveola and increase in density at greater eccentricities.[27,31] This anatomical arrangement may be the neuro-physiological basis for the ascending order of color field isopters being green, red, and blue in our study (Table 3) and in clinical optometric phototherapy practice. The authors suggest future investigation as to the role of retinal cell anatomy in producing these color isopter differences.

CONCLUSION

The results of this study indicate that the automated FCFTester demonstrates potential for utilization as a standardized measurement of kinetic color visual fields. This technology controls many variables including target size, testing distances, velocity of target presentation, direction of target presentation, illumination of the target background, and more. By minimizing inter and intra-examiner variations in technique, this technology potentiates reproducibility, establishment of normative data, and reduces examiner bias (both intentional and unintentional) on clinical measures resulting in improved quality of research, education, and patient care in the practice of vision therapy and optometric phototherapy. Future study designs are intended to include factors such as pediatric populations, racial diversity, various target speeds and sizes, blind spot assessment,[17,32] and the role of retinal anatomy and retinogeniculate pathway on the ascending order of the isopter measures.

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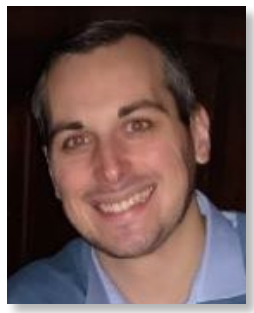

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Dr. Aaron Nichols practices at Excel Neuro-Optometric Rehabilitation Clinic in Shelby Township, Michigan. Dr. Nichols graduated from Ferris State University with a bachelor's degree in 2014 and from the Illinois College of Optometry in 2018. Following his graduation, he completed a residency in vision therapy and rehabilitation at EyeCare Associates, PC in Connecticut. The residency site is affiliated with the State University of New York.

Dr. Nichols gained interest in research during his residency and has since worked with a team of optometrists across the country to advance research and knowledge, as well as awareness, of syntonics or optometric phototherapy. Dr. Nichols and his colleagues have created the Optometric Phototherapy Investigation Team (O.P.I.T).

Clinically, he works with patients all of ages from pediatrics to geriatrics who have acquired or traumatic brain injury, autism, learning disabilities, strabismus and amblyopia, and neuro-degenerative diseases. When Dr. Nichols is not working in clinical he enjoys spending time with his family and friends, golfing, exercising, and playing or watching sports.