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Glaucoma

Evaluation of Virtual Reality Perimetry and Standard Automated Perimetry in Normal Children

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Purpose: The Olleyes VisuALL-K is a pediatric videogame-based static threshold perimeter using a virtual reality headset. We determined normal threshold sensitivities for the 24-2 test locations using the virtual reality perimetry (VRP) and also tested patients on the Humphrey Field Analyzer (HFA). Patient satisfaction for the two instruments was compared.

Methods: This exploratory study tested 50 normal pediatric participants aged 8 to 17 years on the HFA and VRP. The main outcome measure was threshold sensitivity at the 24-2 test locations for the two instruments.

Results: The mean participant age was 13.0 $\pm$ 2.6 years; 50% were female. The threshold values for VRP are reported as measured on the device and after conversion to an HFA-equivalent scale. Age-adjusted thresholds showed a mean sensitivity of 31.8 $\pm$ 1.1 dB (46.1 $\pm$ dB HFA equivalent) diminution from the maximum light intensity in the VRP and 31.0 $\pm$ 1.5 dB diminution from the maximum light intensity in the HFA; interparticipant variability in mean threshold sensitivity was 2.7 $\pm$ 0.4 dB for the VRP and 2.7 $\pm$ 0.6 dB for the HFA. The HFA demonstrated decreased threshold sensitivity with increasing eccentricity, whereas the VRP threshold did not seem to vary with eccentricity. Mild age effects on threshold sensitivity were seen in the VRP and the HFA ($R^2 = 0.11$, $P < 0.001$ and $R^2 = 0.05$, $P < 0.05$, respectively). The mean time to completion for VRP and HFA was 7.6 $\pm$ 1.5 and 5.3 $\pm$ 0.9 min/eye, respectively ($P < 0.0001$). Patient satisfaction scores favored VRP ($P < 0.01$) despite the longer test duration.

Conclusions: The Olleyes game-based VRP and HFA can be used to map out the peripheral vision in normal children. The VRP has a higher patient satisfaction when used in children than the HFA. The portability of the test allows it to be performed in a myriad of environments, lending a flexibility that can benefit this population.

Translational Relevance: This virtual reality perimetry device provides an alternative to the Humphrey Field Analyzer for children.

Introduction

Perimetry, or mapping of the visual field (VF), provides valuable information regarding the integrity of the afferent visual pathways.[1] Standard automated perimetry (SAP) is the most common form of VF testing. SAP determines the visual threshold for the detection of static stimuli at various locations throughout the central retina. A lower threshold value at a test location indicates a less sensitive visual system at that location. Without perimetry, conditions that impact optic nerve function, such as glaucomatous and nonglaucomatous optic neuropathies, brain tumors, strokes, and infiltrative diseases run the risk of either going unmonitored or undiagnosed.[2]

Perimetry in children can be challenging for many reasons. Some children are unable to maintain attention to task for the duration of the test, especially those under 8 years old.[3] The test is monotonous, and the

machines are built to accommodate adults, which may result in incorrect positioning and discomfort. These limitations may lead to poor performance by children or sometimes preclude testing altogether.

A more versatile format may better capture the participation and engagement of children who need to perform perimetry. The development of extended reality technology has produced engaging and immersive experiences across the entertainment industry. Although most extended reality systems are designed for recreation, this technology has been leveraged for medical diagnostic use. Virtual reality perimetry (VRP) uses virtual reality technology as part of an innovative platform that can be used to map VF defects. This study looked at the ability of a commercially available VRP to determine VF threshold values in normal children, and evaluated patient satisfaction with this device compared with the industry standard perimeter Humphrey Field Analyzer (HFA) (Zeiss Meditech, Inc, Dublin, CA). In this study, we assessed the ability of children aged 8 to 17 years to complete the test. We wanted to capture a group that has been shown to demonstrate reliable testing on other SAP[4,5] and to include more mature pediatric patients who are expected to perform similarly to adults. Therefore, we expected most of the children in our study to have sufficient attention to task owing to their age.

Materials and Methods

This prospective cohort study was approved by the Institutional Review Board at Vanderbilt University Medical Center (Clinicaltrials.gov identifier: NCT04175444). The study protocol adhered to the tenets of the Declaration of Helsinki. All participants were informed of the potential risks and benefits, and parents or guardians of all participants signed an informed consent form before enrollment. We recruited healthy pediatric volunteers to create a normative database for the game-based VF test on the VisuALL K VRP (Olleyes, Inc., Summit NJ). Participants were tested using the VRP instrument as well as the HFA.

The VisuALL is a U.S. Food and Drug Administration–registered, VR-based, VF platform (Fig. 1). It was designed to emulate the other commonly used automated perimeters. The head-mounted device (HMD) weighs 276 g and includes a quad high-definition liquid crystal display with a resolution of 3840 × 2160 pixels and a refresh rate of 75 Hz. The display is divided into two halves (one for each eye), with a resultant resolution of 1920 × 2160 pixels on each half. The display measures 125.40 × 70.56 mm and is placed at a distance that subtends a field of view of approximately 100°. The HMD includes several tracking systems, inertial measurement units consisting of gyroscopes and accelerometers, and infrared-based position tracking with two arrays of six infrared-based sensors.

The VisuALL K uses a cloud-based server and an Olleyes web application, which is how the doctor interacts with the platform. The cloud and web applications are all compliant with the Health Insurance Portability and Accountability Act. For increased security and for compliance with the Health Insurance Portability and Accountability Act, patient data are not stored in the HMD and are instead stored in a cloud-hosted back-end site. Additional technical details of the headset and test strategy are described elsewhere.[6]

To measure the luminance, the HMD was fixed in a horizontal position and a Mavomonitor USB Luminance Meter (Hotek Technologies, Inc., Yelm, WA) was superimposed on the right HMD lens. The luminance values were obtained from an illuminated circle, located in the center of the tested screen,

Figure 1. Olleyes Headset and wireless remote (A). A 9-year-old child completing the VRP in clinic (B).

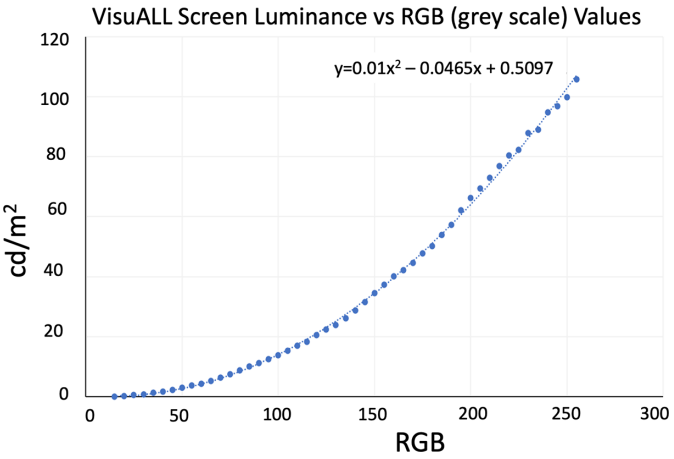

Figure 2. VisuALL screen luminance (cd/m2) vs RBG (gray scale) values.

and having a diameter of 500 pixels. This luminance calibration process assumes uniformity across the display. To the extent that the display was spatially nonuniform, some systematic and/or random measurement error may have been introduced as a result (e.g., particularly at peripheral test locations). The luminance test was performed in a room with all lighting switched off.

A single VRP device was used in all the testing and was calibrated before delivery; the screen was not recalibrated between tests. To monitor calibration, a sample device was kept in house and tested every 6 months to confirm the stability of the screen properties and significant changes were addressed online if found.

The VisuALL software uses a gray scale (RGB scale) for display adjustment. Forty-nine central circumferences were shown with variable pixel intensities (5-pixel intensity interval) between 0 pixels (black, 0.049 cd/m^2) and 255 pixels (white, 120 cd/m^2, 0 dB). Figure 2 plots the values, and although 120 cd/m^2 is the theoretical maximum, it seems that the actual maximum is closer to 105 cd/m^2. The LCD screen always has LEDs backlit. The minimum luminance recorded is 0.049 cd/m^2. The background luminance used in the VisuALL is 1 cd/m^2. The number of dBs that correspond with 120 cd/m^2, the maximum luminance available in the VisuALL is determined for each location. The resultant dB range is 0.14 to 35.00 dB.

The VisuALL K strategy has been modified for the pediatric population to create the feeling of playing a video game and tests both eyes simultaneously (binocularly). The test begins with a central red fixation target described as the "planet of Mars." A handpiece (placed in the child's dominant hand) controls the movement of a spaceship. The spaceship hovers over Mars (central fixation target) until a "shooting star" (a stationary Goldmann III stimulus) is seen and the child moves the spaceship toward the flash. The child then returns the spaceship to Mars to await the next stimulus. The requirement for returning the spaceship to Mars ensures that the child is fixating on the central target before the subsequent stimulus is presented. This strategy eliminates the need to record fixation losses. Moving the handpiece toward the stimulus also eliminates the need to record false positives or negatives because the system records whether the patient moved the spaceship toward an actual stimulus position. The threshold values are determined by a single crossing from seen to unseen (or vice versa). Moving the handpiece instead of clicking a button increases the time between stimuli, but gives greater confidence in the results, because it requires localization of the movement toward the target.

Participants included pediatric volunteers aged from 8 to 17 years. Inclusion criteria included a best corrected visual acuity of 20/30 or better in each eye and no afferent defect. Exclusion criteria was spherical refraction of more than ±3.0 D or cylinder correction or more than 2.0 D, a history of intraocular surgery, a history of systemic condition known to affect visual function, or a history of medication use known to affect visual function. Participants and guardians or parents were also questioned regarding medical and ocular history to ensure all participants met criteria.

Participants were recruited from friends and family of Vanderbilt University Medical Center employees. Participants were all tested at the main campus location of the Vanderbilt Eye Institute. Best-corrected visual acuity at 20 feet was determined using a standard Snellen vision chart. Pupils were evaluated for afferent defects with a Finhoff transilluminator, and a pen light was used to evaluate anterior segment structures. Dilated fundus examination and cycloplegic retinoscopy were not performed.

A flip of a coin was used to randomize the participants to the order of test device. For children randomized to begin with the HFA, the participant's glasses were measured and the refractive error, if any, was documented. The child was then seated in front of the machine and his or her chin was guided into the chin rest. The HFA was then conducted by an experienced ophthalmic technician one eye at a time using the Swedish Interactive Thresholding Algorithm (SITA) Standard 24-2 testing strategy. The right eye was done first followed by the left eye, with the foveal threshold being determined at the beginning of each test. Once the test concluded, participants were encouraged to stand up and stretch before beginning their second test.

If the child was randomized to the HFA first, they did the VisuALL K second (vice versa if randomized to VisuALL K first).

The entirety of the HMD was sanitized using alcohol preparation pads before each use. Participants were instructed to wear glasses as needed during the test. All glasses fit comfortably under the headset. Face masks were kept in place and the top of the mask was taped to prevent screen fogging. The children were asked to place the headset over their head and the clinician adjusted the straps for the proper fit. Participants were instructed to remain seated for the duration of the test. Securing the HMD snugly was important so the images were crisp on the screen. The handpiece was placed in the participant's dominant hand and the participant was shown the select button. A Pediatric 24-2 Threshold test was conducted. This test is a modification of the standard automated 24-2 test using a game-based format as described elsewhere in this article.

After the tests were completed, each child was provided and completed a survey with four questions on a Likert scale of 1 to 5 regarding his or her testing preferences.

Primary outcomes were the normative threshold sensitivities for each test location, and patient satisfaction score, measured on a scale of 1 to 5, with the Wilcoxon matched pairs signed rank test. Secondary outcomes were test time and the effects of age, gender, and ethnicity. Threshold values for each test location for the HFA and VRP were calculated, and both mean- and pointwise- threshold sensitivities were compared between devices with standardized main axis regression. Normative threshold sensitivities were established by percentile rank. The mean interparticipant variability was measured by Gini's mean difference. Statistical analysis was done with RStudio (Version 1.3.1073; RStudio, PBC, Boston, MA) and GraphPad Prism (version 7.00; GraphPad Software, Inc, La Jolla, CA).

Results

Fifty participants aged 8 to 17 years (mean, = 13.0 ± 2.6 years; 50% female) (Table) were enrolled. The children performed both the HFA SITA Standard 24-2 and Olleyes VisuALL K, or VRP, 24-2 pediatric threshold perimetry on the same clinic visit.

Each participant's data are plotted to illustrate the threshold sensitivity distributions in each modality (Fig. 3). It is important to note the sensitivity values of each device are measured on separate scales based on the luminance of the presented stimuli compared with the theoretical maximum stimulus luminance that the device can generate. To assist in reader interpretation, the values for the VRP are presented using the threshold scale from the device and also using an

Table. Breakdown by Age of Participants

Age (Years)	No.
8–11	18
12–14	18
15–17	14

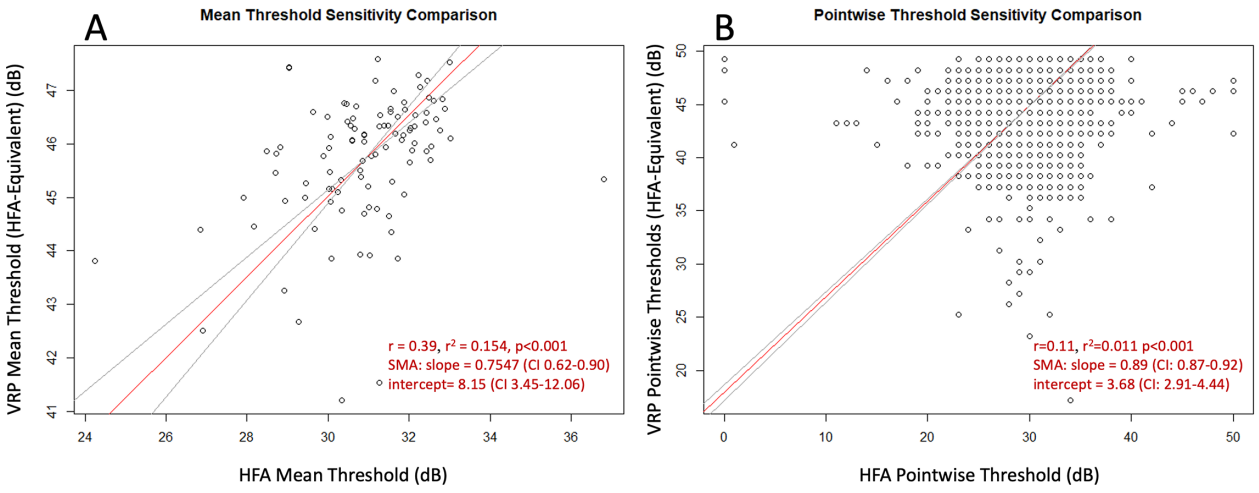

Figure 3. Scatterplot comparison of mean threshold sensitives in each eye on the HFA and VRP (A) and the pointwise threshold comparison in dB for corresponding points on the VRP and the HFA (B). The plots are fit with standardized major axis (SMA) regression lines (red) with 95% confidence intervals (CI). The blue dotted lines are a slope of 1. The VRP is plotted on a HFA-equivalent dB scale on the *y* axis to provide a comparison.

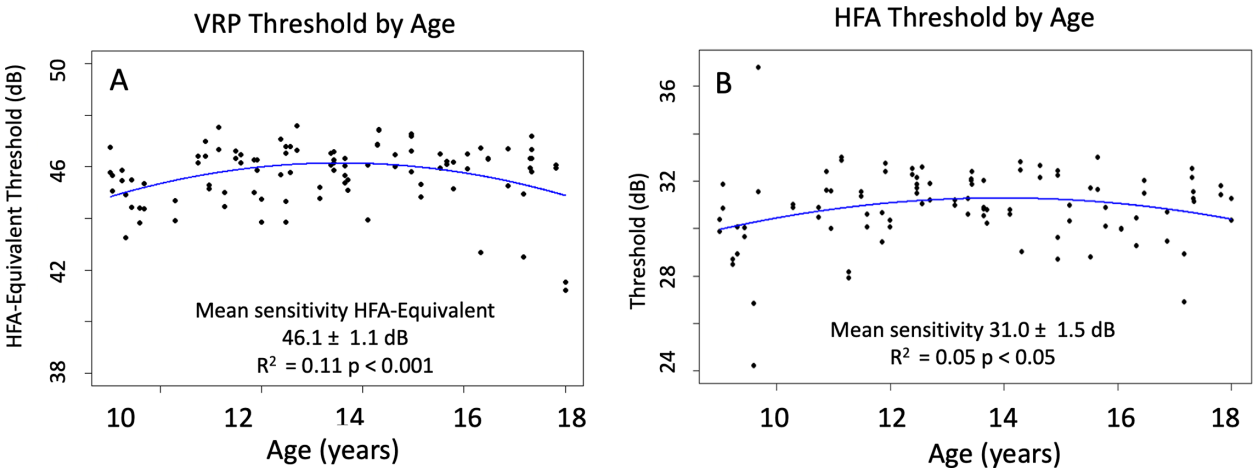

Figure 4. Parametric regression of mean threshold sensitivity by age found small age effects with the VRP (A) and HFA (B) devices. The VRP values here are reported in HFA-equivalent threshold values, to provide a comparison.

HFA-equivalent scale. Of note, the VRP thresholds are measured against a background illumination that is 10 times dimmer than used by the HFA. Because threshold sensitivity is related to the contrast ratio of stimulus to background luminance, threshold stimulus luminance (and by extension the HFA-equivalent scale value) is expected to be much dimmer with the VRP. The maximum stimulus intensity also differs substantially. Age-adjusted thresholds with the VRP showed a mean sensitivity of 31.8 ± 1.1 dB (46.1 dB HFA equivalent) diminution from the maximum light intensity of 120 cd/m^2, and 31.0 ± 1.5 dB diminu-

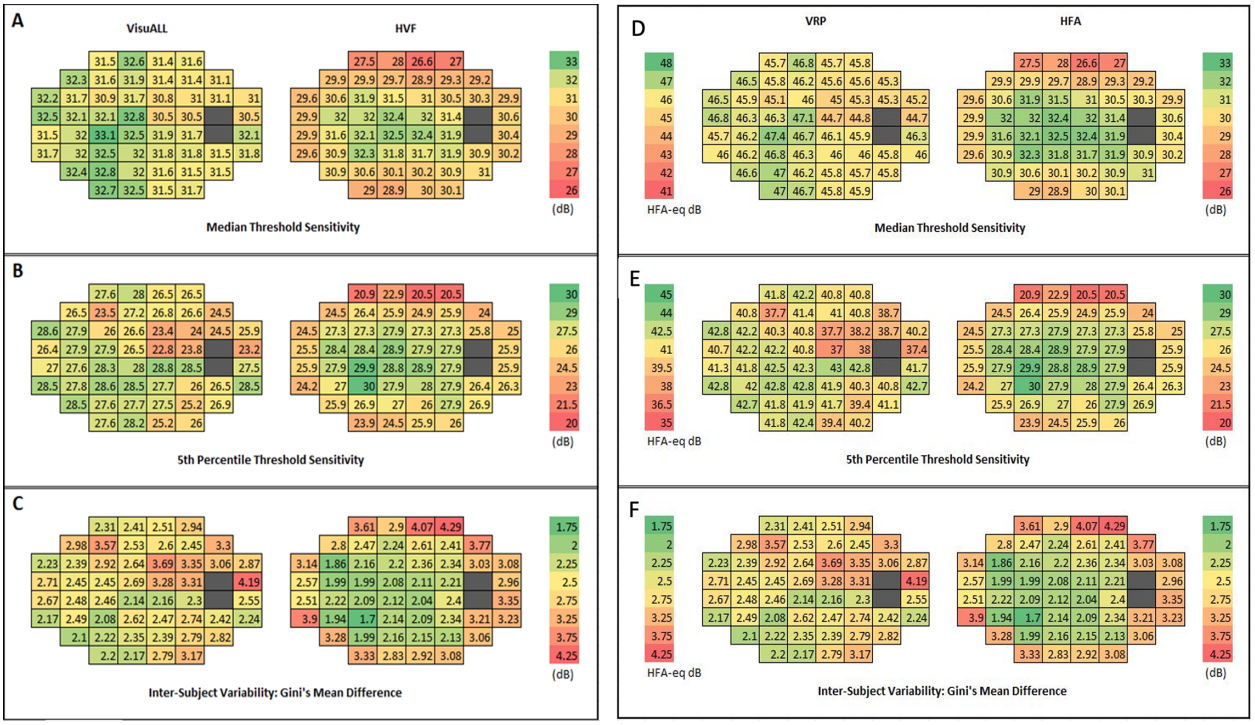

Figure 5. Heatmap of the distribution as represented by (A) median threshold sensitivity at each location; (B) fifth percentile threshold sensitivity; and (C) interparticipant variability of threshold sensitivity at each location. There was no significant difference in overall interparticipant variability ($P > 0.25$) between the devices. (D–F) A map of the same values as (A–C), but the VRP thresholds have been converted to an HFA-equivalent scale. The values of each threshold point on the VRP are higher but the same general pattern is demonstrated.

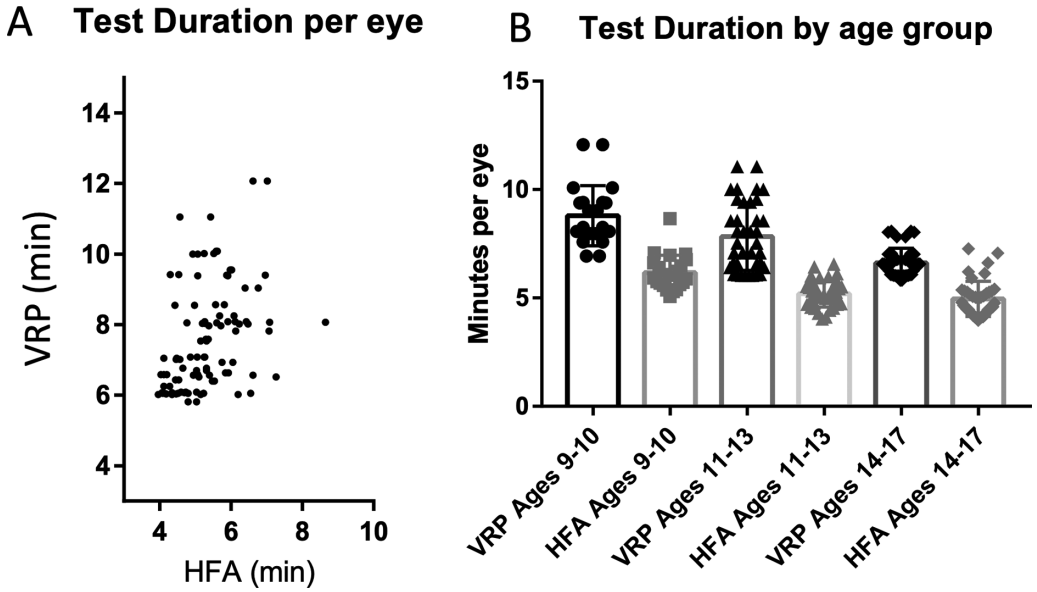

Figure 6. Scatterplot of test duration of each participant on the VRP and the HFA (A) and mean minutes per eye broken down by age on the VRP (black) and the HFA (gray) (B). Of note, the VRP device tests both eyes simultaneously so the time is total time divided in half.

tion from the maximum light intensity in the HFA of 3183 cd/m^2 (Fig. 4). The mean sensitivity mildly increased as a factor of age in both groups (R^2 = 0.11, $P < 0.001$ for the VRP; $R^2 = 0.05$, $P < 0.05$ for the HFA). The standardized main axis regression of the mean thresholds between VRP and HFA showed a positive relationship of slope 0.75 (95% confidence interval, 0.62–0.90) with an R^2 of 0.15, and point-wise standardized main axis regression of thresholds at each location for each subject for the VRP versus the HFA showed a positive relationship with a slope pf 0.89 (95% confidence interval, 0.87–0.92; $R^2 = 0.15$) (Fig. 3). The HFA demonstrated a decreased threshold sensitivity with increasing eccentricity, whereas the VRP threshold did not seem to differ with eccentricity (Figs. 5A, 5D).

The interparticipant variability in mean threshold sensitivity as measured by Gini's mean difference was 2.7 ± 0.4 for the VRP and 2.7 ± 0.6 for the HFA (Figs. 5C, 5F). Fifth percentile values were derived empirically at each location to establish the bounds of normal threshold sensitivity values (Figs. 5B, 5E).

The mean time to completion for VRP and HFA was 7.56 ± 1.49 and 5.31 ± 0.87 min/eye, respectively ($P < 0.0001$) (Fig. 6). Patient satisfaction scores favored the VRP device experience (Likert scale of 1–5), with a mean satisfaction score of 3.26 ± 0.9 and 4.12 ± 0.8 for the HFA and the VRP, respectively (Fig. 7). The Wilcoxon matched-pairs signed rank test P value was less than 0.01.

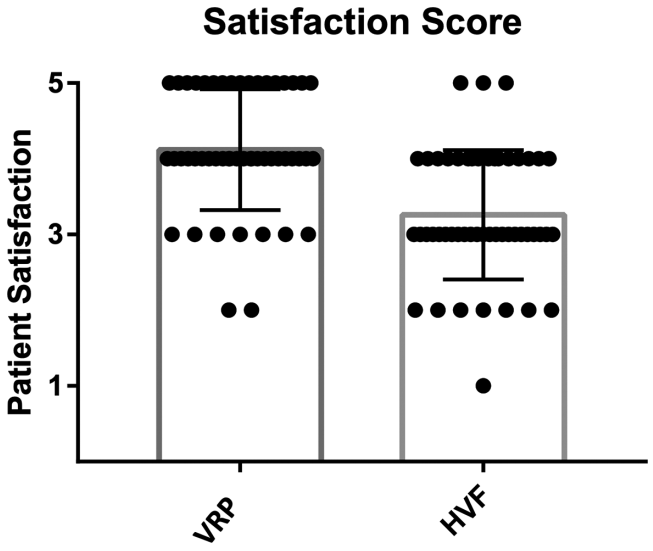

Figure 7. Box plot of patient satisfaction scores. Scores were measured on a 1 to 5 Likert scale. Patient satisfaction scores favored the VRP device experience ($P < 0.01$).

Discussion

Although the HFA and Octopus (Haag-Streit Diagnostics; Bern, Switzerland) are the most widely recognized instruments for performing static automated perimetry, both have inherent limitations.[3,7–9] The machines are large and immobile. The instrument is confined to a single location, restricting its use to patients healthy enough to present to

an outpatient clinic. Additionally, test reproducibility is highly dependent on a patient's head position. Patients with mobility-limiting conditions or small stature may find the positioning difficult, if not impossible. A patient's comfort may negatively influence the test reliability and inflate fixation errors, as well as the percentage of false-positive or false-negative responses. The impact of each of these factors is amplified when applied to children, especially because most perimetry machines are located in adult ophthalmology clinics. Most clinics are set up for adult patients, so the chairs are not calibrated to a child's height or weight, which results in dangling feet and uncomfortable positioning. In addition, the large bowl that surrounds the front of children's faces on the HFA can be intimidating. Factors that contribute to the reliability of the test affect reproducibility.[10] Repeat testing has been demonstrated to produce improved reliability, likely owing to a learning effect. However, in children, fatigue can contribute to more abnormal testing and poor repeatability.[11]

There have been several perimetry modalities attempted for use on very young children, including the "pediatric perimeter" in infants aged 2 to 12 months using light-emitting diodes and measured reaction time toward the stimulus.[12] This procedure may estimate the VF extent, but is limited on quantifiable field information. Normative values of infant reaction times have been established.[13] Another perimetry method children is with the saccadic vector optokinetic perimeter.[14,15] This suprathreshold test measures the central 30° of vision and uses infrared eye tracking to produce objective data without limitation of the head position or requiring a single fixation point. This technique has limitations for children with nystagmus as seen in poor vision and cannot produce threshold values. It may be valuable in children in whom other field assessment is not possible.

Frequency doubling technology perimetry has also been tested in children.[16–19] Nesher et al.[18] demonstrated the ability of healthy children as young as 5 years of age to perform the test. They pointed out that patient selection is important because not all children in the lower age range are cooperative. Quinn et al.[19] looked at normative values for children compared with adults. They found that children 15 years and older had threshold values similar to those found for adults, but children ages 14 and younger had mean deviations that decreased with decreasing age.[19] This finding is likely due to the decreased attention to task in children of younger ages, rather than structurally related differences within the afferent visual system. This difference in age groups was supported by our findings of increased threshold values in older children.

Automated perimetry is performed primarily in the adult population, although children with visual pathway disorders also require diagnosis and monitoring.[20] There are several studies that evaluate the performance of children on the HFA.[3,4,21–23] Children begin to perform HFA with acceptable reliability at approximately 7 to 9 years of age. Before this age, they have difficulty with understanding or paying attention to the task. Beyond this point, sensitivity is often prone to overestimation.[24] There are also times when it is challenging to bring children into adult care settings, especially when they have special needs.[25] When there is variable reliability, sensitivity is impacted and can cause fluctuation in VF results.[10] Most of the literature on HFA perimetry in children includes only normal participants, but children with afferent visual pathway disorders have been demonstrated to successfully complete HFA testing within the similar age range.[3]

Although some pediatric patients can produce reliable results on perimetry, success depends on patient selection. When patients are approximately 8 years and younger, their attention span limits their ability to complete the test. Children ages 8 to 10 years may be able to complete the test, but there are children in this age group who have difficulty with completing the task. As literature shows the mean deviation in children increases to a stable point around 12 to 14 years of age,[4] indicating this is the age when most children are able to complete the test competently. There is a need in pediatric clinical care to provide an alternative method for performing perimetry. VRP uses a versatile, portable, technologically advanced device to perform the testing. Because children are widely exposed to digital devices at home and school, the digital features are familiar. The perimetry test format has been altered specifically for the engagement of the pediatric population. A child is free to pause the test, shift positions, and sit however he or she feels most comfortable. Because the headset is mounted to the child's head, small movements of the participant do not result in misalignment and unreliable testing. In addition, both eyes are tested during the same session to limit repositioning.

There have been other attempts to create game-based perimetry tests that are targeted to children. Miranda et al.[16] described a computer game–based perimetry targeting children ages 4 to 16 years. One eye was tested at a time on a flat monitor testing the central 24° as the children were engaged in a quest through obstacles to gather coins. The child progressed through levels as the stimuli were collected. Although threshold sensitivities were similar to those obtained in an adult population, the variability was significantly greater. They also faced the challenge of extended response

time in the video game format, which prolonged the testing time.

The HFA does not have a normative database incorporated into the analysis package, but the OPTIC Study group has established normative values in children 5 to 15 years of age.[23] As noted elsewhere in this article for frequency doubling technology, the normative data applied to the HFA may impact the testing algorithm; sensitivities have been shown to be lower for children ages 14 and younger.[19] The testing strategy for the HFA uses the youngest database age (18 years) when testing a child and the normative values are applied to the thresholds. This study did not assess the mean deviation as calculated by the SITA software on the HFA, but future analyses may show deviations in younger children, as shown on the frequency doubling technology.

In our study, the individual points were analyzed in two ways. One was as raw threshold data for the two devices. Of note, the threshold values are independent values on each machine. Therefore, the values across the two devices cannot be directly compared without a transformation. To give the reader a sense of how the scales compare, we converted the dB threshold values on the VRP with the HFA-equivalent dB values and reported both numbers. The measured threshold values differ significantly in terms of stimulus luminance between the two machines. However, it is important to keep in mind that the background luminance also differs greatly. The background luminance on the VRP is in the mesopic range at 1 cd/m^2, whereas the HFA background luminance is 10 times greater, in the low photopic range at 10 cd/m^2. This difference in background luminance would account for a 10-dB difference in stimulus luminance between the devices if Weber's law held perfectly between the two disparate conditions. We measured on average approximately a 14-dB difference in stimulus luminance at threshold, which corresponds with a 4-dB or 0.4 log unit difference in stimulus contrast at threshold between devices.

Mesopic range backgrounds around 1 to 4 cd/m^2 are common among current microperimetry devices, and they were originally used in SAP by the Octopus perimeter before changing to 10 cd/m^2 for decreased dark adaptation time.[26] Dimmer backgrounds result in smaller decreases in sensitivity with eccentricity compared with the classical photopic hill of vision, which may explain the difference we see with eccentricity between devices. The dimmer background of the VRP presumably was chosen to allow for the maximization of dynamic range in a digital perimeter with limited maximum luminance.

There are some limitations to this study. We only tested healthy children, so we are unable to confirm how the test will perform on children with visual pathway pathology. In addition, each test was performed only once; repeatability data were not collected. We plan to investigate both in future studies. In addition to the difference in background lamination between the devices discussed elsewhere in this article, other reasons for the decrease in threshold sensitivity with increasing eccentricity from fixation may be due to limitations in this technology, an optical effect of the hardware, the thresholding strategy, or some other issue intrinsic to the testing algorithm. Although challenges may arise theoretically during the presentation of the most dim stimuli, this should not explain our relative inability to detect the pinnacle of the "hill of vision." It is unclear if this limitation may impair the ability of the device to detect subtle VF abnormalities. Further study is indicated in this regard.

There are some limitations to the device that were observed. Figure 3 describes the pointwise values of the mean threshold sensitivity for the two instruments. The lack of correlation between the two suggests that the VRP may have more difficulty detecting threshold, possibly owing to either algorithm limitations or hardware limitations related to partial illumination of individual pixels. Alternatively, because our study only included normal individuals, there may be more intrasubject variability between two different types of tests than intersubject variability of normal individuals performing the same test. The details on how the values achieve sufficient diminution to result in a threshold value of 35 dB were proprietary and are not available to us. The pointwise plots do support the presence of a ceiling effect in some locations. Because this is an 8-bit display, the smallest visible stimulus should be visible to normal sighted individuals at all but the peripheral-most locations, somewhat explaining this noticed ceiling effect.

Practically, there are several things to consider with a VR-based system. The portability and the cost-effective nature of the devices is a strong pro. However, a device with a screen is susceptible to the screen losing its calibration over time. The cost is substantially less than conventional perimeters and need less technician time to perform, which makes it more cost effective in labor time.

The Olleyes VRP is novel in that it transforms a cumbersome and monotonous testing strategy into a game-based format that is easy to perform and appealing to children. We believe that this appeal will improve attention and, therefore, reliability. By creating a normative database, we have made possible further research in the diagnosis of visual pathway disorders with VRP. There is more work needed in the validation of this device, specifically testing in children with

visual pathway disorders and in younger children, but it has shown potential to be a powerful tool for assessing visual function in children. We believe this will open the door to facilitate testing outside the clinic, extending the reach of clinicians.

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