



Comparative Analysis of 10-2 Test on Advanced Vision Analyzer and Humphrey Perimeter in Glaucoma

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Purpose: To evaluate diagnostic precision and prove equivalence of 2 devices, Advanced vision analyzer (AVA, Elisar Vision Technology) and Humphrey field analyzer (HFA, Zeiss) for the detection of glaucoma on 10-2 program.

Design: Prospective, cross-sectional, observational study.

Participants: Threshold estimates of 1 eye each of 66 patients with glaucoma, 36 control participants, and 10 glaucoma suspects were analyzed on 10-2 test with AVA and HFA.

Methods: Mean sensitivity (MS) values of 68 points and central 16 test points were calculated and compared. Intraclass correlation (ICC), Bland–Altman (BA) plots, linear regression of MS, mean deviation (MD), and pattern standard deviation (PSD) were computed to assess the 10-2 threshold estimate of the devices. Receiver operating characteristic curves were generated for MS and MD values, and the area under the curve (AUC) was compared with assessing diagnostic precision.

Main Outcome Measures: Mean sensitivity values of 68 points and central 16 points, AUC for MS and MD values, ICC values, BA plots, and linear-regression analysis.

Results: Bland–Altman plot showed significant correlation for MS, MD, and PSD values for both devices. For MS, the overall ICC value was 0.96 (P < 0.001) with a mean bias of 0.0 dB and limits of agreement range of 7.59. The difference in MS values between both devices was -0.4760 ± 1.95 (P > 0.05). The AUC for MS values for AVA was 0.89 and for HFA was 0.92 (P = 0.188); whereas it was similar at 0.88 for MD values (P = 0.799). Advanced vision analyzer and HFA identically discriminated between healthy and patients with glaucoma (P < 0.001), although HFA denoted marginally greater ability (P > 0.05).

Conclusions: Statistical results denote adequate equivalence between AVA and HFA because threshold estimates of AVA strongly correlate with HFA for 10-2 program.

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Supplemental material available at www.ophthalmologyscience.org.

In a conventional 30-2 or a 24-2 program of Humphrey field analyzer (HFA; Carl Zeiss Meditec), fewer test locations are included within the central 10° zone. The 30-2 and 24-2 testing patterns assess a total of 76 and 54 points, respectively, with 12 points within the central 10° and merely 4 of these points being actually located within the macular region (the central 8°). The macular area represents approximately 40% of the total retinal ganglion cells and 60% of the visual cortex area.¹⁻⁴ A 10-2 test pattern assesses 68 points within the central 10° zone with each point being placed 2° apart. Hence, the detection of central and paracentral scotomas is one of the major benefits of performing a 10-2 visual field test. The development of a central visual defect in a certain subgroup of patients can be a hallmark of the onset of glaucoma with no effective peripheral visual field defects.⁵ Evidence from studies that employed OCT, OCT angiography, and microperimetry suggests the development

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of macular damage during the early stages of glaucoma.^{6,7} Further, a 10-2 test is crucial to monitor the progression of glaucoma in advanced cases.

Advanced vision analyzer (AVA) is a virtual reality (VR) perimeter documented to have substantial equivalence with HFA in an observational study that incorporated a comparative analysis on a 24-2 program.⁸ Because a 10-2 program has a higher cluster of test locations in the central field, we decided to study the correlation between both devices for the detection of central visual field defects. The objective of the study was to assess the diagnostic precision and concordance of visual field results achieved on a 10-2 program with AVA and HFA in patients with glaucoma, glaucoma suspects, and a control group. We compared and analyzed the test duration, receiver operating characteristics (ROCs) curve and area under the curve (AUC), pointwise sensitivity,

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and global indices in identifying and characterizing the visual field defects.

Methods

Algorithm

The Elisar standard algorithm is a novel algorithm that has been described before⁸ as being a hybrid of a 4-2 staircase with Bayesian-update stopping rules. The final threshold resembles QUEST, as the mode of probability density function is chosen as the final estimate.⁸

Elisar standard algorithm uses 2 prior curves that are built using results recorded from a set of 100 subjects. These curves describe the probability distribution of threshold sensitivities of normals and abnormals, the method being similar to that described by Turpin et al.⁹ The 68 points are divided into 4 quadrants and each quadrant has a seed point located 3° apart from fixation. The test starts at 4 seed locations based on the age-corrected normal mean value for that location. The test eventually proceeds as per the HFA 10-2 growth pattern. Subsequent stimulus intensities are determined based on a 4-2 dB staircase procedure. The algorithm uses initial step sizes of 4 dB that is followed by 2 dB after the first reversal. Although the staircase is running, the probability curves of threshold estimates are regenerated based on the response to the stimulus (seen/not seen). The new probability curves are determined by multiplying the old prior curves by a likelihood function that is similar in nature to the Zippy estimation by sequential testing algorithm. The testing at the seed points is terminated if: (1) there are 2 reversals of the staircase, (2) maximum threshold value is recorded as seen at least twice for each seed point, or (3) minimum threshold value is recorded as seen at least twice or more for a particular seed point. The testing for other 64 points is terminated if: (1) either of the probability curves of threshold estimates has a standard deviation that is below a predetermined level and if there is a reversal of the staircase (the level varies linearly from 2.5 dB for threshold estimates near 0 to 1.2 dB for threshold estimates near 40 dB) or (2) if there are 2 reversals of the staircase. The final threshold estimate is determined by considering the higher of the modes of final probability curves of the threshold.

The 10-2 program installed on AVA tests 68 points that are placed at 10° from the central field where the probability curve obtained from the normative data and the patient's response generates a new probability curve. Fail-safe value limits the gap between the initial and final threshold value. If the resulting threshold value for any test-point has a difference of > 4 dB (for central 16 points) or 8 dB (for 52 points) from the initial value at that point, the test is rerun. The test then begins from the result value and the final threshold value is calculated as the average of 2 test-runs. Specific to the 10-2 pattern test on AVA, threshold measurement values are represented as 0 dB, < 8 dB or in numerical values from 8 to 40 dB. Elisar standard algorithm strategy does not present any stimuli in the range of 1 to 7 dB. If the patient perceives 0 dB and does not perceive 8 dB, then it is assumed that the threshold value at that point lies in the range of 1 to 7 dB. This is clinically represented as < 8 dB on the visual field chart.

The luminance scale of AVA is designed to be as close as possible to the luminance scale of HFA. The background luminance for AVA was kept at 9.6 cd/m². For stimulus luminance (L_s) and background luminance (L_b), the contrast level is defined by the formula (contrast at stimulus level $S = [L_s - L_b] / L_b$) that is in line with the ISO standards (https://www.iso.org/obp/ui/#iso:std:iso:12866:ed-1:v2:en). The perimetry dB scale is given by the formula S (in dB) = 10 * log₁₀([Lmax - L_b]/[L_s - L_b]) where Lmax is the maximum luminance that can be generated by a

particular instrument. To keep the differential light sensitivities similar for both the devices, grey levels on AVA were chosen such that the contrast generated by stimulus at a certain decibel value was similar to the contrast generated by the corresponding stimulus on HFA.

The brightest stimulus that can be delivered on AVA by changing the grey levels is 9 dB (corresponding to a luminance value of 400 cd/m²). To measure threshold at contrast levels that are > 9 dB, stimuli sizes are increased, whereas the luminance is maintained at 9 dB. Consequently, the stimulus size used to achieve 0 dB for AVA corresponds to the luminance that is equivalent to 3200 cd/m². The approach used to determine stimuli sizes is similar to the procedure described by Gonzalez et al.¹⁰ In addition to this, a color bit-stealing routine¹¹ is used to improve the luminance resolution of the device at the higher end of the dB scale.

The eye-tracking subsystem consists of 2 infrared complementary metal—oxide—semiconductor cameras placed for each eye and an array of infrared light-emitting diodes (LEDs) are used to illuminate the pupil. The images of the pupil captured by the eyetracking subsystem are wirelessly transferred to the test controller device where the operator can monitor the gaze of the patient for the qualitative assessment. The screen calibration for AVA is performed with a complementary metal—oxide—semiconductor camera that is regularly calibrated with a photometer.

Study

The study adhered to the tenets of the Declaration of Helsinki and was approved by local institutional review and ethics board at Dr. Agarwal's Eye Hospital & Research Centre. The subjects provided written informed consent before inclusion in the study. The recruited subjects underwent 10-2 threshold with HFA (SITA-Standard) and AVA (Elisar standard)⁸; the order of the tests was randomized. The patients with glaucoma were well versed with perimetry, whereas a trial run was arranged 2 days before the actual test for the control group and glaucoma suspects. A gap of at least 1 hour occurred between the 2 tests.

In AVA, the lens holder has a provision for placing lenses to correct refractive error of the eyes being tested. The subjects underwent refractive correction with full-aperture lenses, the power of which was based on correction for the distance of 70 cm with agebased near correction.

Patient Selection. The candidates for the control group were chosen from the outdoor patient department and comprised those who were willing to participate, were normal, and were not relatives of patients with glaucoma. The inclusion criteria for the healthy control group were as follows: (1) age > 18 years, (2) best-corrected Snellen visual acuity of 20/40 or better, (3) normal visual field test results, and (4) intraocular pressure ≤ 21 mmHg. The exclusion criteria were as follows: (1) refractive error > 6 diopters (D) equivalent sphere or 3 D of astigmatism, (2) amblyopia or any other ocular disease, and (3) a systemic or neurologic disorder that would confound the visual field test results.

Case sheets of patients with glaucoma were reviewed for potential participation, the inclusion criteria being as follows: (1) age > 18 years; (2) best-corrected visual acuity of 20/40 or better; (3) confirmed clinical diagnosis of open-angle glaucoma with evidence of changes in the optic nerve head, retinal nerve fiber layer, and visual field defects detected on a 24-2 test; and (4) glaucoma hemifield test results outside normal limits. Of 66 glaucomatous eyes, 41 eyes had paracentral VF damage on 24-2 test, defined as the presence of at least 1 test location at *P* value of < 0.05 within the central 16 test points. The exclusion criteria designated for patients with glaucoma were similar to those mentioned for the healthy control group except for the presence of glaucoma. If the subject had glaucoma in both the eyes; 1 eye was randomly chosen;

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		Mean Va	alue (dB)	Range	e (dB)	Mean		
	No. of eyes	HFA	AVA	HFA	AVA	HFA	AVA	P Value
Overall	112	28.09	28.09	4.38, 36.04	01.97, 34.62	28.08 ± 6.83	28.08 ± 6.86	0.977
Normal	36	32.69	33.21	24.12, 36.04	24.68, 34.62	32.69 ± 2.50	32.21 ± 1.92	0.476
Glaucoma	66	24.30	24.84	4.38, 32.78	01.97, 34.27	24.29 ± 7.15	24.83 ± 7.86	0.102
Glaucoma suspect	10	32.12	31.54	27.21, 35.18	28.84, 33.11	32.17 ± 2.14	31.53 ± 1.25	0.422

Table 2. Comparative Values of Mean Sensitivity for 68 Points on 10-2 Program

AVA = Advanced vision analyzer; CI = confidence interval; dB = decibels; HFA = Humphrey field analyzer; SD = standard deviation.

whereas if glaucoma was detected in 1 eye, it was included in the study.

Glaucoma-suspect candidates had signs of glaucoma as per current clinical guidelines¹² but were insufficient to confirm the diagnosis.

The Goldmann size III target was adopted, and reliability indices were set at false-positive rates, false-negative rates, and fixation losses of $\leq 20\%$. Mean sensitivity (MS) was measured on threshold printouts, and overall MS was calculated as the average of visual field sensitivities at the 68 points. Additionally, MS values were separately calculated for 16 central test points of the macular program for comparison and analysis. The mean deviation (MD) and pattern standard deviation (PSD) were also calculated and analyzed. Pointwise sensitivity analysis was performed for the control group (68

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Figure 1. Details of pointwise threshold sensitivity values for control group. (A) Pointwise mean sensitivity threshold for Humphrey field analyzer (HFA). (B) Pointwise mean sensitivity threshold for Advanced vision analyzer (AVA). (C) Difference in mean sensitivity values between HFA and AVA. (D) Difference in standard deviation values between HFA and AVA.

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Figure 2. Details of pointwise threshold sensitivity values for the glaucoma group after censoring 1- to 7-decibel values on Humphrey field analyzer (HFA). (A) Pointwise mean sensitivity value at each stimuli location for HFA. (B) Pointwise mean sensitivity at each stimuli location for Advanced vision analyzer (AVA). (C) Difference in mean sensitivity at each stimuli location between HFA and AVA. (D) Correlation coefficient (r) for glaucoma cases.

points) and compared for both devices. For cases with glaucoma and glaucoma suspects, pointwise sensitivity for the 68 points and the central 16 points was calculated after censoring 1 to 7 dB values on HFA. To assess diagnostic precision, ROCs were generated and AUC was calculated for MS and MD values for both devices.

Statistical Tests. Statistical analyses were performed using STATA software version 12.0 (Stata Corp). Statistical significance was defined as P value of < 0.05. Descriptive statistics were applied to analyze the demographic characteristics of the cohorts. The quantitative data were assessed for normality with parametric

and nonparametric tests. The Mann–Whitney U test was used to analyze the test-duration values. Bland–Altman analysis was performed using Python 3.4.3 software, and charts were plotted to derive the limits of agreement (LOA) with the 95% confidence interval (CI). Linear regression was used to predict the relationship between 2 variables. Intraclass correlation (ICC) values were derived using R-studio 4.0.3 software to understand the correlation between both devices. Significance of the difference in the MS values was tested by using the student t test, and mean bias (MB) was calculated.

	Table 4.	Comparative	Values of Mean	Deviation and	Interpretation o	of Bland–Altm	an Plots and	Intraclass	Correlation
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		Mean Va	alue (dB)	Rang	ge (dB)	Me	dian			
	No. of Cases	HFA	AVA	HFA	AVA	HFA	AVA	ICC (95% CI)	Bias	95% LOA
Overall	112	-4.69	-4.94	-28.49, 6.70	-31.15, 1.24	-2.16	-22.16	0.95	0.24	4.33, -3.84
Normal	36	-0.87	-0.97	-8.56, 1.75	-8.32, 1.24	-0.63	-0.58	0.51	0.09	3.82, -3.63
Glaucoma Glaucoma suspect	66 10	$-8.08 \\ -0.07$	-8.09 -1.50	-28.49, 0.65 -5.42, 6.70	-31.15, 1.02 -4.39, - 0.10	$-6.02 \\ -1.32$	$-5.39 \\ -1.27$	0.96 0.24	0.01 1.42	3.89, -3.87 6.93, -4.08

AVA = Advanced vision analyzer; CI = confidence interval; dB = decibels; HFA = Humphrey field analyzer; ICC = intraclass correlation; LOA = limits of aggreement.

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Table 5. Comparative Values of Pattern Standard Deviation and Interpretation of Bland-Altman Plots and Intraclass Correlation

	No. of Cases	Mean Value		Ra	Me	dian				
		HFA	AVA	HFA	AVA	HFA	AVA	ICC (95% CI)	Bias	95% LOA
Overall	112	4.02	4.26	0.89, 16.99	0.96, 14.41	1.62	2.13	0.96	0.24	1.54, -2.02
Normal	36	1.47	1.79	0.92, 3.29	0.96, 4.08	1.22	1.71	0.52	-0.32	0.62, -1.26
Glaucoma	66	6.11	6.23	0.89, 16.99	1.26, 14.41	6.19	5.12	0.96	-0.12	1.95, -2.19
Glaucoma suspect	10	1.32	2.03	1.04, 1.68	1.29, 3.91	1.24	1.79	0.04	-0.71	0.78, -2.21
AVA – Advanced	vision analyzer: CI	– confide	ence interv	al· HFA — Hun	unbrev field anal	vzer: ICC	– Intrac	ass correlation I OA	— Limits	of aggreement

Results

After fulfilling the exclusion and inclusion criteria, data of 112 eyes were included for analysis. The mean age of the control group was 41.69 ± 15.86 years, the mean age of the glaucoma group was 61.08 ± 14.46 years, and the mean age of the glaucoma suspects was 51.4 ± 11.22 years. The ratio of males to females for the control group was 16:20, for the glaucoma group was 40:26, and for the suspects group was 6:4. The overall mean test time (minutes:seconds) for HFA was $6:28 \pm 1:26$ and for AVA was $7:14 \pm 1:46$ (P = 0.0006). There was a significant difference in test time between both devices for the control and glaucoma groups (Table S1, available at www.ophthalmologyscience.org).

The details of MS values for all 68 points in a 10-2 program are listed in Table 2. The MS values of the 68 points for the control group were 32.69 ± 2.50 dB with HFA and 32.21 ± 1.92 dB with AVA (P = 0.476), whereas for the glaucoma group, the MS values were 24.29 ± 7.15 with HFA and 24.83 ± 7.86 with AVA (P = 0.102). Mean sensitivity values for 112 eyes had an

ICC value of 0.96, LOA was 7.59 with MB of 0. An individual analysis of MS of the central 16 test points was performed. The MS values of the control group for the central 16 test points for HFA was 33.93 ± 2.34 and for AVA was 33.49 ± 1.68 (P = 0.287), whereas for the glaucoma group, it was 26.56 ± 6.72 for HFA and 27.26 ± 7.14 for AVA (P = 0.09). Additional details are listed in Table S3 (available at www.ophthalmologyscience.org). The MS analysis of the central 16 test points depicted an ICC value of 0.94; the range of LOA varied from 4.059 to -4.287 (95% confidence interval were within LOA) with a MB of -0.11. Pointwise sensitivity of the control group was analyzed, and the details are depicted in Figure 1. The difference in measurements (AVA – HFA) was -0.4760 ± 1.95 dB (P > 0.05).

Sensitivity after Censoring 1 to 7 dB Values on HFA

Mean sensitivity values of the 68 points for subjects with glaucoma with HFA and AVA were 27.37 ± 1.99 and 28.20



Figure 3. Bland–Altman plot and linear-regression analyses of global indices: mean sensitivity (**A**), mean deviation (**B**), pattern standard deviation (**C**) for Humphrey field analyzer (HFA) and Advanced vision analyzer (AVA). The top row shows Bland–Altman plots with mean bias values (dotted central line) and limits of agreement (LOA). The bottom row depicts linear-regression analyses with R^2 , slope, and probability *P* values. A positive linear relationship is seen between mean sensitivity (MS), mean deviations (MD), and pattern standard deviation (PSD) values of HFA and AVA.



Figure 4. Receiver operating characteristic curve of the mean sensitivity (A) and mean deviation (B) values of Humphrey field analyzer (HFA) and Advanced vision analyzer (AVA).

 \pm 2.02, respectively, and the difference between measurements (AVA-HFA) was 0.8282 ± 0.69 . Mean sensitivity values for central 16 points for glaucoma subjects with HFA was 29.09 \pm 1.11 and with AVA was 29.95 \pm 1.34 with the difference between values (AVA - HFA) being 0.8656 \pm 0.76. Similarly, MS values of the 68 points for glaucoma suspects with HFA and AVA were 32.11 ± 1.04 and 31.57 \pm 1.45, respectively, and the difference between both measurements (AVA-HFA) was -0.5391 ± 0.91 . Mean sensitivity values for the central 16 points for glaucomasuspect subjects was 33.26 ± 0.41 with HFA and was 32.97 ± 0.78 with AVA; the difference between the measurements (AVA – HFA) being -0.2948 ± 0.94 . Pointwise sensitivity for the glaucoma group was analyzed after barring 1 to 7 dB values on HFA. The details are depicted in Figure 2.

Tables 4 and 5 highlight the MD and PSD values, respectively, for both devices. Bland–Altman graphs were plotted to understand the agreement between HFA and AVA. The MB values and LOA were within the prescribed limits in overall fields. Figure 3 depicts the Bland–Altman and linear-regression plot for global indices. A total of 95% of the data points were within the upper and lower LOA. For the values of MS, MD, and PSD, a positive linear relationship was observed between HFA and AVA.

Receiver operating characteristic curves were plotted and for MS values. Our study yielded an AUC of 0.92 for HFA and 0.89 for AVA (P = 0.187; Fig 4A). The graph depicted marginally greater ability of HFA to discriminate between normal patients and patients with glaucoma, although the P value was not significant. For the ROC curve depicting the MD values, AUC for both HFA and AVA was found to be 0.88 (Fig 4B). Both devices showed a good ability to discriminate between controls and patients with glaucoma (P < 0.001).

Discussion

Standard automated perimetry is crucial to diagnose and monitor patients with visual field defects. The Advanced vision analyzer is a novel VR perimeter designed to perform perimetry in clinics and home-based settings, as well as in individuals who are remotely located, thereby allowing clinicians to take care of their patients. The current study was undertaken to evaluate and analyze the diagnostic precision of AVA against HFA for a 10-2 program. The AUC for MS was higher for HFA and a consistent difference was found in the shape of curve, where the values for AVA trended marginally lower. On the contrary, the AUC for MD was similar between both devices, with ROC curves overlapping and intersecting (Fig 4B), but without significance (P = 0.799). Hence, it can be stated that for diagnostic purposes, the results of both the devices are comparable and similar.

On a VR platform, while recording visual fields, size modulation is essential for decibel values < 8. This eventually increases the chance of inaccuracy. As compared with bowl perimeters, the screen on a VR headset is flat and can result in stimulus aberration.¹³ Additionally, a trade-off is to be achieved between establishing the accuracy of threshold values and the time needed to complete the test. Therefore, sensitivity values that ranged between 0 and 8 dB were listed as < 8 dB, and the test points were not tested specifically for the exact dB values. However, the MS values when compared after censoring 1- to 7-dB values on HFA



Figure 5. Image depicting the visual field printout of Humphrey field analyzer (HFA) (A) and Advanced vision analyzer (AVA) (B) for a 10-2 program in a case of advanced glaucoma. MD = mean deviation; NEG = negative; POS = positive; PSD = pattern standard deviation.

lead to similar results between the devices (Fig 2). The failsafe values of the central 16 test points were set at 4.1 dB, whereas for the remaining 52 points it was set at 8.1 dB to enhance the accuracy of central points that are used to determine macular split in advanced cases. Split fixation was defined as retinal sensitivity of 0 dB on all test locations in at least 1 quadrant of the macular threshold program.¹⁴ We performed a separate comparative analysis of MS for the 68 points and the central 16 test points for normal, glaucoma, and glaucoma suspects group. There was no statistically significant difference between the devices. Hence, we believe that our algorithm accurately detects the visual field defects even in cases with lower sensitivity values. Pointwise sensitivity was not analyzed for glaucoma cases because dB values between 0 and 8 are not listed and are either recorded as 0 dB or < 8 dB. Therefore, the results of pointwise comparison for glaucoma cases would be redundant and serve as a source of error.

For progression analysis with a standard stimulus of size III, monitoring points with lower sensitivity (especially

between 0 and 8 dB) over a period may be a limitation. As suggested by several studies, 10-2 testing with a nonstandard size V stimulus can more reliably measure visual function.^{5,15} For AVA, this aspect needs to be evaluated further. It is essential to state that despite listing dB values between 0 and 8 as < 8, no significant difference was found between the MS and MD analyses for both devices (Fig 5). However, global analyses may not be as sensitive as pointwise analyses for early damage because small changes in dB values may not be reflected in the averaging data across the visual field.

In summary, our study demonstrated that for a 10-2 test, the threshold estimates and global indices derived with AVA correlated well with HFA. The findings suggest the potential use of AVA for performing diagnostic tests in glaucoma. Additionally, as a VR perimeter, its implementation in the office as well as for teleophthalmology can be beneficial to a large group of patients. However, studies with a larger group of patients and detailed follow-up are essential and are underway.

Footnotes and Disclosures

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Disclosures:

All authors have completed and submitted the ICMJE disclosures form.

The authors have no proprietary or commercial interest in any materials discussed in this article.

HUMAN SUBJECTS: Human subjects were included in this study. The study adhered to the tenets of the Declaration of Helsinki and was approved by local institutional review and ethics board at Dr. Agarwal's Eye Hospital & Research Centre. The subjects provided written informed consent before inclusion in the study. No animal subjects were included in this study.

No animal subjects were used in this study.

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Data collection: P. Narang, A. Agarwal, Ashvin Agarwal, Sundaramoorthy Analysis and interpretation: P. Narang, R. Narang, A. Agarwal, Ashvin Agarwal

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Abbreviations and Acronyms:

AVA = Advanced vision analyzer; AUC = area under the curve; BA = Bland-Altman; HFA = Humphrey field analyzer; ICC = intraclass correlation; Lb = background luminance; Ls = stimulus luminance; MB = mean bias; MD = mean deviation; MS = mean sensitivity; PSD = pattern standard deviation; ROC = receiver operating characteristic; LOA = limits of agreement; VR = virtual reality.

Keywords:

Advanced vision analyzer, AVA, HFA, Visual field test, VR perimeter. Correspondence:

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