ORIGINAL ARTICLE

# Prospective Comparison of VisuALL Virtual Reality Perimetry and Humphrey Automated Perimetry in Glaucoma

Jeffrey M Griffin[1], Grant T Slagle[2], Truong A Vu[3], Ainsley Eis[4], William E Sponsel[5]

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## Abstract

**Aim and background:** Automated perimetry plays an important role in the diagnosis and monitoring of glaucoma patients. The purpose of this study is to prospectively determine parity between Humphrey visual field analyzer (HVFA) perimetry (the current gold standard) and the VisuALL virtual reality perimeter (VRP).

**Materials and methods:** In this prospective fully paired diagnostic accuracy study, patients with stable, long-term HVFA visual fields (horizontal dots for ≥4 consecutive visits on progression analysis) with preperimetric, mild, moderate, or severe visual field loss were familiarized with the VRP and then tested using its proprietary software. These results were used for point-by-point comparison with a contemporaneous HVFA test. This study was approved by the Institutional Review Board (IRB) of the University of the Incarnate Word, San Antonio, Texas, United States of America (IRB approval #20-06-002).

**Results:** The prospective study analyzed 43 eyes of 24 glaucoma patients. Spearman's correlation of mean deviation (MD) revealed a strong correlation between HVFA and VRP with $r_s(41) = 0.871$, $p < 0.001$. The overall mean difference in locus–locus sensitivity between the devices was −0.4 ± 1.5 dB but varied for different visual field locations and glaucoma severity.

**Conclusion:** The parity between the VRP and HVFA was remarkably strong for mild and moderate glaucoma. Given its portability, ease of use, space efficiency, and low cost, the VRP presents a viable alternative.

**Clinical significance:** Automated perimetry, specifically the HVFA, has been the gold standard for visual field assessment since its introduction. The recent COVID-19 pandemic has illuminated the advantages of the VRP, allowing for safer visual assessment for both patient and clinician alike. Our study hopes to establish parity between these systems, allowing for the efficient integration of a novel head-mounted perimetry system that can safely diagnose and monitor glaucomatous progression in clinical practice.

**Precis:** Investigation of parity between Olleyes VisuALL virtual reality perimetry (VRP) and existing standard HVFA perimetry is essential to the diagnosis and management of glaucoma. Linear correlations between the two were established from 43 glaucomatous eyes. Parity was strong for mild and moderate glaucoma, presenting VRP as a viable alternative.

**Keywords:** Glaucoma, Humphrey visual field, Perimetry, Virtual reality perimetry, Visual field analysis.

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## Introduction

Visual field testing is an essential tool in the diagnosis and management of glaucoma. In North America, the Humphrey visual field analyzer (HVFA) (HVFA; Carl Zeiss Meditech, Dublin, California, United States of America) has been the gold standard for visual field analysis for more than three decades since its development.[1] The recent COVID-19 pandemic produced conditions that forced clinicians and patients to adapt and develop alternative approaches to longstanding standard procedures. Traditional automated perimetry is typically conducted one-on-one, often in a relatively small, enclosed space, with the patient undergoing testing and an experienced technician inevitably in close proximity.[2]

The idea of performing perimetry with virtual reality goggles [virtual reality perimeter (VRP)] is not new. The original United States patent was filed in 1998.[3] Even after that patent lapsed and the concept entered the public domain in 2016, there was little or no real progress in this area. The COVID-19 pandemic provided the catalyst for the rapid development of various systems that (1) could be performed simultaneously on multiple patients in various spaces in the clinic and (2) could potentially be used by patients in their own homes as an adjunct to telemedicine monitoring.

These newer VRP methods now appear to have numerous potential advantages over traditional automated perimetry. A single server can conduct testing on a multitude of patients in

[1]Department of Ophthalmology and Visual Sciences, John Sealy School of Medicine, University of Texas Medical Branch, Galveston, Texas, United States

[2]Department of Ophthalmology, HCA Florida Bayonet Point Hospital, Hudson, Florida, United States

[3]Department of Ophthalmology, School of Osteopathic Medicine, University of the Incarnate Word, San Antonio, Texas, United States

[4]Department of Neuroscience, Trinity University, San Antonio, Texas, United States

[5]Department of Vision Science, University of the Incarnate Word, San Antonio, Texas, United States

**Corresponding Author:** Grant T Slagle, Department of Ophthalmology, HCA Florida Bayonet Point Hospital, Hudson, Florida, United States, Phone: +1 (727) 409-3020, e-mail: slaglegrant@gmail.com

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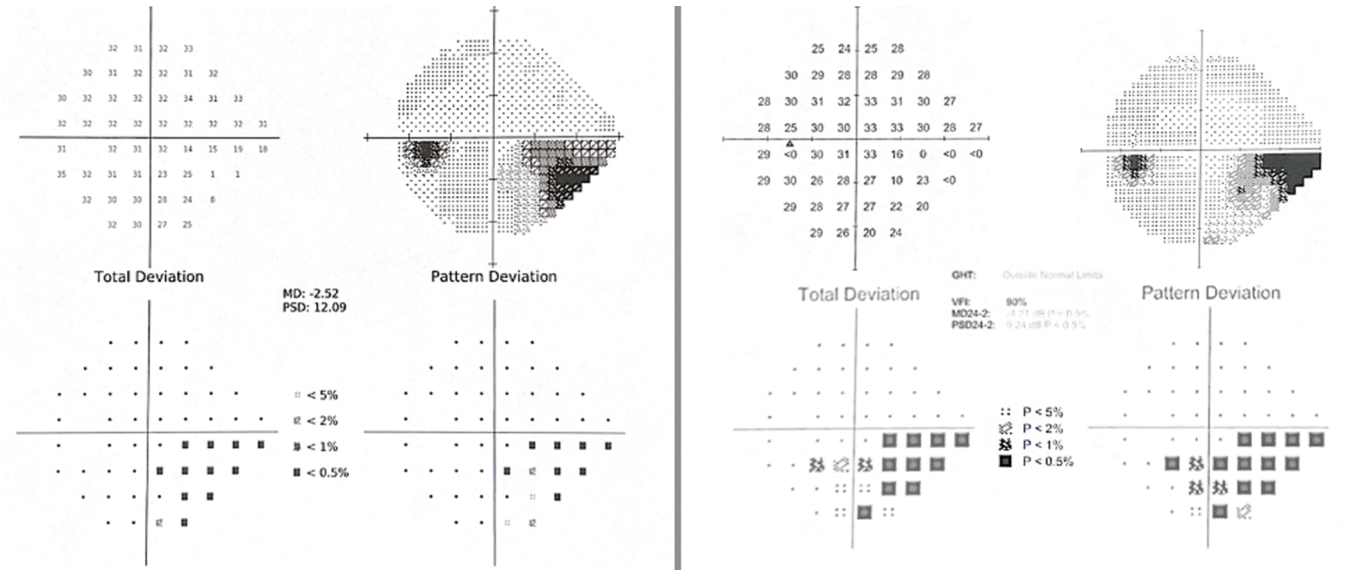



**Fig. 1:** Comparison of readouts from VRP (left) and HVFA (right) in a patient with mild glaucoma. VRP, VisuALL virtual reality perimeter; HVFA, Humphrey visual field analyzer

various clinics simultaneously, integrating their output seamlessly with electronic medical recordkeeping systems. Indeed, the system being evaluated below provides instantaneous direct access to assist with the interpretation of visual field data from our North American, Central African, and Central American clinics.

The VRP goggles produce a microenvironment in which ambient light levels in the testing space are of no consequence. Trial frame lenses and eye patches are not required. The patient has total freedom of movement; they can sit or stand, remain stationary or move around, tilt their head, and so on, with no associated loss of fixation or production of visual field artifacts associated with inadequate positioning or head movement.[4] Immobilized patients in wheelchairs and those afflicted with severe arthritis can perform testing as easily as ambulatory patients.

Perhaps one of the best surprises with the system evaluated below was our sudden realization that highly reproducible visual fields could be obtained for the first time from low-vision eyes. Because the testing algorithm alternates rapidly between the left and right eyes to compile both fields at once, as long as one eye has the capacity for fixation, the fellow eye without macular function remains in neutral gaze and large areas of extant visual function, often contributory to the fullness of the binocular field, can be reliably mapped and monitored.

The new systems are also inexpensive. So now that this new paradigm exists, with its many apparent potential advantages, the one major impediment to the general adoption of this very promising emerging technology would be the lack of parity with the prevailing gold standard, the HVFA. This study has been undertaken to determine to what extent visual field data obtained using the Olleyes VRP system's commercially available platform (VisuALL™ S; Olleyes Inc., Summit, New Jersey, United States of America) correlates with data obtained from the same patient using the HVFA. Glaucoma patients with normal fields (preperimetric glaucoma) and similar numbers with mild, moderate, and severe glaucomatous visual field defects were assessed. All participants had demonstrated visual field stability for at least four prior visits using HVFA to minimize the effects of progression, recovery, or testing performance inconsistency on the HVFA/VRP comparison. An example readout showing the similarities in grayscale readouts between the VRP and HVFA has been provided (Fig. 1) to emphasize its similarity to the existing standards of perimetry.

The present prospective fully paired diagnostic accuracy study compares locus–locus sensitivity scores, and mean deviation (MD) scores in patients with glaucoma obtained through both HVFA and VRP testing to develop an algorithmic approximation of HVFA from VRP results.

## Materials and Methods

### Participants

Criteria for inclusion were adults aged greater than 18 with a glaucomatous appearing optic nerve and/or retina and abnormal perimetry results, which were consistent with the pattern of glaucoma or preperimetric glaucoma diagnosed by evaluating optic nerve appearance and retinal nerve fiber layer thickness by optical coherence tomography. Glaucoma was stratified into consolidated stages (CS) described as preperimetric (CS1, no visual field defect), mild (CS2, early/mild visual field defect), moderate (CS3, defect in one hemifield but not within 5° of fixation), or severe (CS4, defect in two hemifields or within 5° of fixation).[5] Criteria for exclusion included spherical refraction outside ± 5.0 D and cylinder correction outside 2.0 D, unreliable perimetry (false positives, fixation losses, and false negatives > 25%), unreliable VisuALL™ S (> 25% false positives, fixation losses), perimetry abnormality with a pattern other than glaucoma, intraocular surgery in the study eye (except for noncomplicated cataract or refractive surgery that occurred >6 months before study enrolment), history of systemic condition or medication known to affect visual function, and known infection or signs of COVID-19. This study was approved by the Institutional Review Board (IRB) of the University of the Incarnate Word, San Antonio, Texas, United States of America (IRB approval #20-06-002). Written informed consent was obtained from all participants, and no compensation was given.

### Statistical Analysis

A total of 52 corresponding loci were identified between HVFA and VRP. These were mapped, and a number for each locus was assigned. Corresponding loci in the right or left eye were treated

equally in the analysis, as has been done elsewhere.[6] For example, the superior temporal-most locus in the right eye was designated with the same locus number as the left eye's superior temporal-most locus. Note that all comparisons were made between HVFA and VRP using only the same eye.

Locus–locus comparison between HVFA and VRP was done separately for each stage of glaucoma, including preperimetric, mild, moderate, and severe disease. Bland–Altman plots were created to compare differences and evaluate the relationship between the two testing modalities.

Prior to analysis, a Shapiro–Wilk test was used to determine the normality of the MD scores obtained from each visual field test. Results indicated that the scores obtained from both the HVFA; $W(43) = 0.948$ and $p = 0.049$, and the scores obtained through VRP; $W(43) = 0.884$ and $p = 0.0004$, were not normally distributed. Due to the departure from normality, Spearman's rank correlation was used to determine the relationship between HVFA and VRP MD scores.

### Procedures

Following a complete ophthalmic examination, participants completed two vision tests—the Humphrey automated 24-2 SITA standard perimetry test and the VisuALL™ S T-24 perimetry test. The tests were presented in a random sequence before proceeding to full visual field evaluation. At least a 5-minute rest between tests was implemented to prevent testing fatigue. Participants were familiarized with the VisuALL VRP by performing an abbreviated suprathreshold test, and a tester verified participants' understanding of the device's function. Then, testing using the VisuALL™ S T-24 protocol was completed. After another 5-minute rest period, testing was again completed using the VisuALL™ S T-24 protocol. Results from this second test were used for data analysis.

### Humphrey Automated Perimetry 24-2 Protocol

The threshold visual field was assessed using the Humphrey field analyzer and the 24-2 SITA standard protocol. A bowl perimeter was used to project a small spot of light onto a surface 33 cm from the participant's eye in various locations within the visual field, and the patient was asked to press a button whenever they perceived the light. The intensity of the light stimulus was varied, and the dimmest intensity perceived at a series of predetermined locations was recorded as the test result.

### VisuALL™ S T-24 Protocol

The threshold visual field was assessed using the VisuALL™ S head-mounted virtual reality display and a 24-2 protocol. The light stimulus was displayed within the virtual reality display. The intensity of the light stimulus was varied, and the dimmest intensity perceived at a series of predetermined locations was recorded as the test result.

**Table 1:** Baseline and demographic data

| *Baseline demographics* | |
|---|---|
| Age (± SD) | 69.1 ± 16.5 |
| Biological sex (male/female) | 11/13 |
| Race | |
| Hispanic | 13 |
| Caucasian | 10 |
| Black | 1 |
| Eye (OD/OS) | 23/20 |
| Glaucoma severity (#of eyes) | |
| Preperimetric | 10 |
| Mild | 9 |
| Moderate | 10 |
| Severe | 14 |

SD, standard deviation

## Results

A total of 43 eyes from 24 glaucoma patients between the ages of 20 and 90 years [MD = 69.1, standard deviation (SD) = 16.5] were included in the study. A table demonstrating baseline characteristics is included in Table 1. Median MD was −8.82 dB for HVFA and −8.34 dB for VRP, and because of the wide range of glaucoma severity included, MD values varied widely (range +1.42 to −25.53 dB, and +0.6 to −41.18 dB, for HVFA and VRP, respectively).

Spearman's correlation revealed that there was a strong positive correlation between the MD scores, $r_s(41) = 0.871$, $p < 0.001$ (Fig. 2). SPSS™ (IBM, Endicott, New York) statistical software analysis was used to generate a correction factor for locus–locus correlation. For mild, moderate, and severe glaucoma, these were [y-intercept (dB)/slope/R]—mild (−1.4/1.1/0.64), $p = 0.063$; moderate (+1.6/0.9/0.67), $p = 0.034$, and severe (+0.6/0.5/0.44), $p = 0.12$. With corrected analysis, high parity was observed in the preperimetric and mild glaucoma groups. The correlation was lower in the severe glaucoma group.

Mean differences in locus-specific sensitivity between HVFA and VRP were close to 0 for all stages of glaucoma. They were as follows for preperimetric, mild, moderate, and severe glaucoma, respectively—[sensitivity (dB) ± SD] −0.10 ± 3.8 dB, −1.6 ± 4.9 dB, −0.42 ± 8 dB, and 0.10 ± 8 dB. Bland–Altman plots for all four stages are shown in Figure 3. The plots demonstrate minimal mean differences with good correlation for preperimetric and mild glaucoma, but moderate and severe glaucoma show significant funneling.

Comparison of locus–locus differences, including all glaucoma severities, was excellent, with a median difference of −0.3 ± 1.5 dB

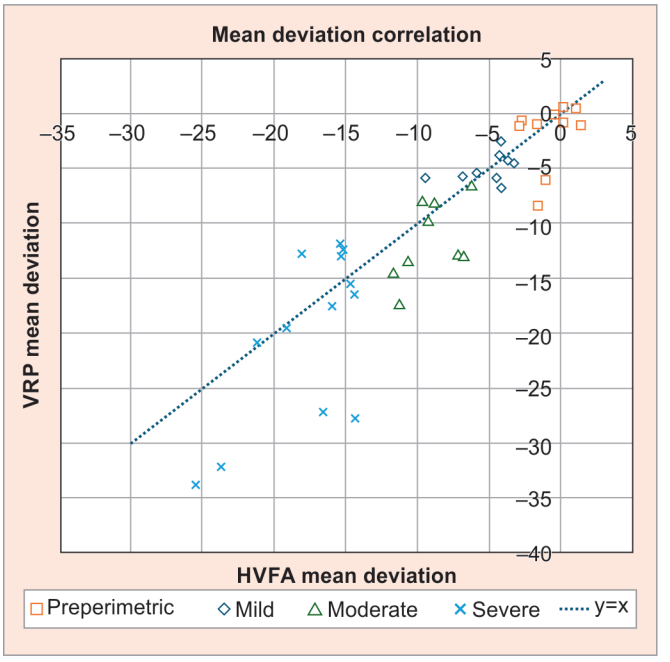
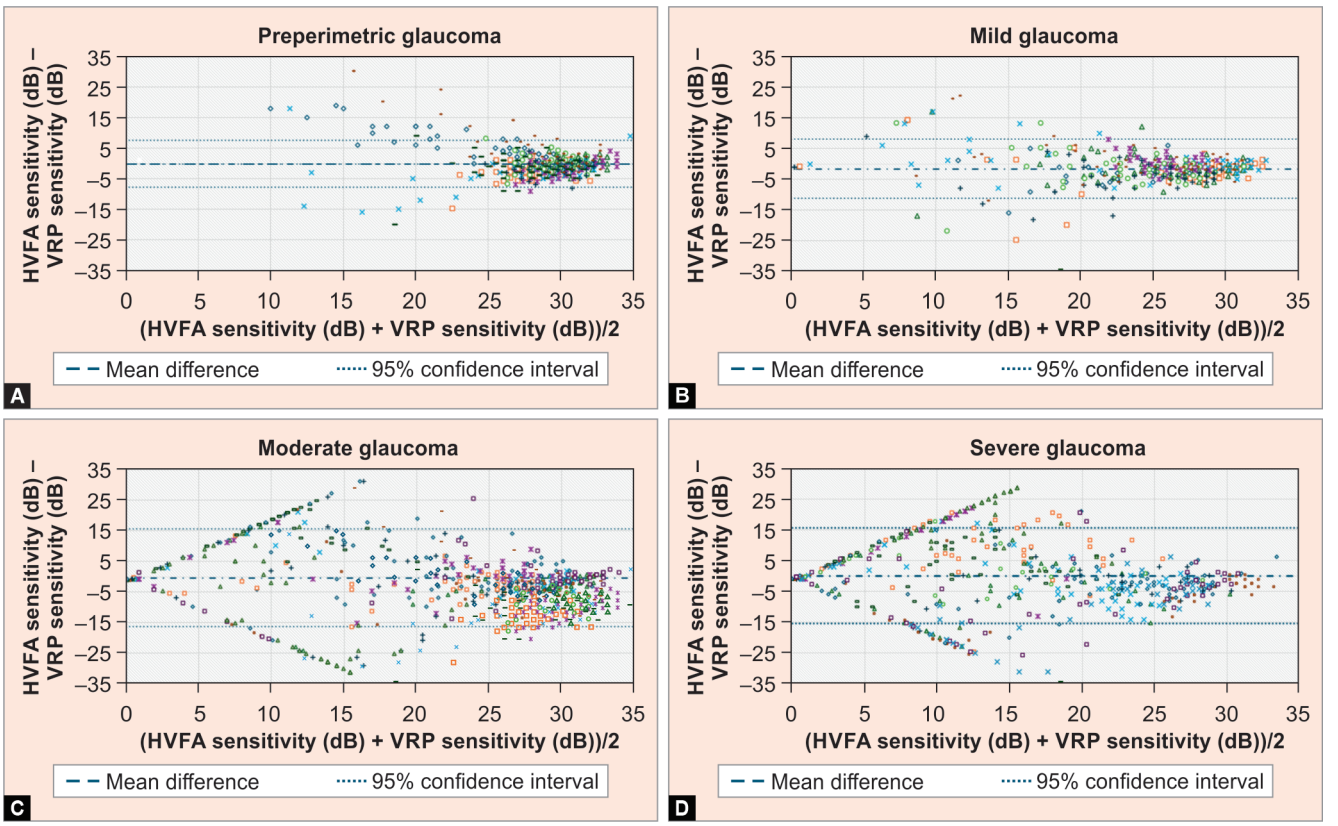



**Fig. 2:** A high correlation between visual field MD results is observed in the preperimetric, mild, and moderate glaucoma groups. Correlation weakens in the severe glaucoma group. MD, mean deviation; VRP, VisuALL virtual reality perimeter; HVFA, Humphrey visual field analyzer




**Figs 3A to D:** Bland–Altman plots show locus–locus comparison of differences in visual field sensitivity (dB) between HVFA and VisuALL VRP separated into: (A) preperimetric glaucoma; (B) mild glaucoma; (C) moderate glaucoma; (D) severe glaucoma. Mean differences in sensitivity are close to 0 dB for all stages, but significant funneling appears for moderate and severe glaucoma. Data were subjected to horizontal jitter to prevent overplotting

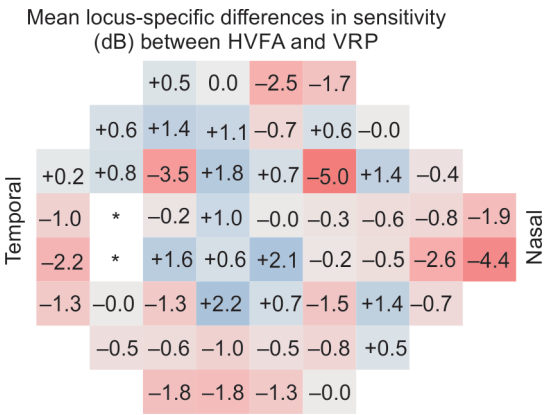



**Fig. 4:** Mapped mean differences of locus–locus comparison of HVFA and VisuALL VRP with all stages of glaucoma included. Values are derived from HVFA sensitivity minus VRP sensitivity; asterisks indicate loci not included due to algorithmic constraints

(range –5.0 to +2.2 dB). Figure 4 illustrates locus-specific mean differences between HVFA and VRP for all eyes used in the study.

## Discussion

The modern HVFA machine has undergone many design improvements for streamlining and efficiency, but there remain limitations. The HVFA machine is large, heavy, and expensive, which limits its affordability and overall practicality.[7] Additionally, HVFA requires the patient to sit upright and still for several minutes, potentially causing body and eye fatigue in older patients, thus decreasing its reproducibility.[8] Furthermore, the reliability and accuracy of HVFA depend on various factors, including cooperation, understanding, attention, and the limitation of external factors that could disturb the patient's focus.[9] These factors are known as the "learning effect" of HVFA, which typically takes about three repeated tests for accurate results.[10] Moreover, other studies show improved testing outcomes when patients are able to centrally fixate at a point during the test.[11] These concerns should be considered when utilizing HVFA in those patients who may not be capable of enduring the requirements for a reliable test.

Our study was part of an effort to develop an algorithmic approximation of HVFA from VRP results. Locus–locus correlation and correlation of MD scores obtained through the VisuALL™ S VRP 1 (Olleyes, Inc., Summit, New Jersey, United States of America) and the HVFA (Zeiss, Jena, Germany) were utilized in this effort.

This study exclusively examined glaucoma patients, allowing for a detailed investigation into the relationship between VRP and HVFA specific to this particular ophthalmic disorder. Overall, our results suggested a high correlation between results obtained *via* HVFA and those obtained through the VisuALL™ S system. Both MD scores and the sensitivity scores showed a high correlation between the two tests in the mild and moderate glaucoma groups; however, direct parity decreased in the severe disease group. On average, the VRP may slightly overestimate sensitivity (i.e.,

differences in HVFA minus VRP are slightly negative), especially in the nasal region of the visual field. This can be appreciated by observing a concentration of negative values for the nasal loci in Figure 4.

Based on these results, we suggest that the algorithm of the VisuALL™ S should be improved to include calculations that help correct the loss of parity with HVFA in patients with severe impairment of the visual field. Although these corrections should be added, it is important to note that at the clinical level, the most critical diagnostic and treatment decisions are made early on in patient assessments. In mild or moderate glaucoma, the quantitative results of visual field analysis assist providers in clarifying any uncertainty regarding the diagnosis that may remain after an ophthalmic evaluation or from the qualitative field alone. Once the disease has progressed sufficiently to be considered severe, there is little room for uncertainty, and the course of treatment will be the same regardless of how severe the disease is. Thus, parity at the severe level is less crucial than at the mild and moderate levels of glaucoma.

The funneling observed in the Bland–Altman plots, especially for moderate and severe glaucoma, indicates heteroscedasticity. In this case, the variance of locus-specific differences in visual field sensitivity between the two modalities increases with decreasing sensitivity. In other words, as an eye's sensitivity decreases at a particular locus, the agreement in sensitivity measured between the two devices also decreases.

The data points of the Bland–Altman plots for the moderate and severe glaucoma each form a distinct set of straight lines diverging from the origin. These lines correspond to incidences where one device registered a minimum sensitivity (no stimulus seen), and the other device measured a nonminimum sensitivity (stimulus seen) at that corresponding locus. Interestingly, the number of points along this line on the positive side of the vertical axis (refers to VRP recording a "seen stimulus" and HVFA recording a "stimulus not seen" at the same locus) roughly balances with the number of points on the negative side of the vertical axis (refers to HVFA recording "stimulus not seen" and VRP recording "stimulus seen" at the same locus). This may suggest that although these devices may disagree on what sensitivity is at a particular locus in severe disease, these "disagreements" tended to balance out overall. This may be due to slight differences in effective eye position, causing a particular scotoma to affect slightly different loci but ultimately about the same total number of loci when compared to the other device.

These results are highly suggestive that the VisuALL™ S VRP is a reliable substitute for HVFA due to the high agreement between locus–locus correlation and MD scores. Furthermore, VRP testing addresses certain limitations associated with HVFA, such as portability and affordability. The VRP testing protocol limits patient fatigue and improves monovision patients' ability to fixate. During data analysis, many of the participants who were excluded from the analysis due to unreliable perimetry only demonstrated issues with false negatives, false positives, or fixation in the HVFA test. The increased reliability of VRP perimetry in the study further supports the added benefits of the VisuALL™ S system. Overall, these factors should be considered as they may increase accessibility to visual field testing without sacrificing the reliability and reproducibility of data.

### Limitations

This study population only includes glaucoma patients (including preperimetric glaucoma). Consequently, while our findings provide insights into VRP accuracy in glaucoma patients, it is conceivable that this correlation may be different in nonglaucomatous visual field changes. The extent to which our findings can be generalized to the broader population should be considered with this limitation in mind.

Furthermore, the VRP model used in this study does not include eye tracking, which could result in very different visual field results than HVFA if, for example, a participant fell asleep during the test. This may explain some outliers in our results (Fig. 2). However, it is worth noting that newer VRP models now incorporate eye-tracking technology and protocols to address this limitation. Technology and algorithmic advances in the VRP are expected to further improve the accuracy and reliability of future studies utilizing this approach.

Considering the mentioned limitations, the findings of this study still demonstrated the strong potential of VRP in evaluating patients in various stages of glaucoma. These findings underscore the importance and need for future research endeavors to explore the interplay between VRP and the existing gold standard, HVFA, not only in glaucoma but also in other ophthalmic conditions. To situate our findings within the existing body of literature and gain a more comprehensive understanding, a thorough review of relevant studies is essential.

## Literature Review

Our findings align with those of a 2017 study conducted by Tsapakis et al., affirming the consistency of the results, which suggest that virtual reality methods for visual field testing can be considered reliable and promising for clinical use.[3] Our research further expands on the correlation analysis of Tsapakis et al. by examining different subgroups within the study population, specifically categorizing patients into mild, moderate, and severe glaucoma groups based on predefined ranges. This differentiation provides additional insights into the strength and consistency of the correlation in various glaucoma stages, which adds nuance and depth to the findings beyond what is discussed by Tsapakis et al. Although our study focused primarily on glaucoma patients, the implications of VRP testing may extend to other ophthalmic disorders.

In a separate study conducted in 2021, researchers Nanti and Lenoci reviewed patients who underwent virtual visual field testing (VRP) within a 12-month time frame following prior HVFA testing.[12] Inclusion of patients who underwent HVFA testing up to 12 months prior to VRP testing introduces potential confounding factors that could affect the validity of the results. Disease progression, treatment interventions, injuries, or natural fluctuations in the patients' vision can change over a 12-month time frame, impacting their visual field test outcomes. While our results are consistent with Nanti and Lenoci's research, our study distinguishes itself by demonstrating notable differences in methodology.

A study conducted by Stapelfeldt et al. compared the results of visual field testing between a virtual reality Oculus Quest headset and an Octopus 900 as the conventional testing perimeter.[13] Our two studies yielded concordant findings, suggesting that various VRPs can effectively rival various established systems routinely employed in clinical practice, such as the Humphrey and Octopus 900.

## Conclusion and Clinical Significance

A high correlation was observed for measures in patients with preperimetric, mild, and moderate glaucoma from the study data. The two systems showed less parity for patients with severe glaucoma. Our results indicate that the transition to the VRP test is expected to provide reliable identification of early disease and the detection of disease progression.

## Authors Contributions

JMG: Patient recruitment, data collection, analysis, interpretation of data, writing of the report.
GTS: Study design, patient recruitment, data collection, analysis, interpretation of data, writing of the report.
TAV: Analysis, interpretation of data, writing of the report.
AE: Analysis, interpretation of data, writing of report.
WES: Study design, analysis, interpretation of data, writing of the report.

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## Data Availability Statement

Data are available upon request.

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## Ethics Approval and Patient Consent to Participate

This study was approved by the Institutional Review Board (IRB) of the University of the Incarnate Word (IRB approval #20-06-002). Written informed consent was obtained from each participant before data was acquired.

## Orcid

*Jeffrey M Griffin* https://orcid.org/0000-0002-3988-1832
*Grant T Slagle* https://orcid.org/0000-0001-7963-2067

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