

# Quantifying Suppression in Anisometropic Amblyopia With VTS4 (Vision Therapy System 4)

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**Purpose:** Visual acuity (VA) of the amblyopic eye is usually considered for monitoring improvement with therapy. However, participation of the amblyopic eye under binocular viewing conditions is also important. This study investigated the use of a clinically available tool VTS4 (Vision Therapy System 4) to quantify the participation or suppression of the amblyopic eye under binocular viewing conditions.

**Methods:** A cross-sectional study on patients with anisometropic amblyopia was undertaken. Monocular VA was thresholded. Stereo acuity was measured with Randot stereo test. Simultaneous macular perception (SMP) targets in VTS4 were dichoptically presented. SMP target size was reduced till the amblyopic eye's target disappeared (suppression scotoma size). An average of three measurements was taken for the suppression scotoma size.

**Results:** Twenty-eight patients participated (aged 6 to 21 years). The mean interocular VA difference was  $0.50 \pm 0.27$  logMAR. The mean scotoma size was  $8.2^\circ \pm 5.4^\circ$ . Mean stereo acuity was  $2.06 \pm 0.34$  log arc seconds from 21 patients on whom stereopsis could be measured. Suppression scotoma size showed a significant ( $P < 0.001$ ) positive correlation with both interocular VA difference ( $r = 0.59$ ) and stereoacuity ( $r = 0.72$ ).

**Conclusions:** Participation of the amblyopic eye under binocular viewing condition can be assessed by measuring the suppression scotoma size in VTS4, even when stereoacuity is poor or not measurable. Smaller the suppression scotoma, better is the amblyopic eye's participation.

**Translational Relevance:** VTS4 can be used in monitoring amblyopia therapy by quantifying suppression of the amblyopic eye.

## Introduction

Unequal visual acuity between the two eyes in early childhood can disrupt binocular visual experience and can result in the neurodevelopmental disorder called amblyopia. Monocular visual acuity of the amblyopic eye is typically considered for deciding the course of occlusion therapy in amblyopia management.<sup>1</sup> However, the measure of participation of the amblyopic eye, in the presence of the dominant eye, that is, under binocular viewing condition, is the real indicator for success in amblyopia management.<sup>2</sup> Such binocular viewing conditions have been elegantly implemented in psychophysical tests that include dichoptic motion coherence task,<sup>3</sup> global orientation task,<sup>4</sup> and contrast

balancing.<sup>5,6</sup> These tests quantify the depth of suppression of the amblyopic eye under the binocular viewing conditions. However, these psychophysical tests are not yet commonly used in clinical practice.

In the commonly used clinical tests, the three grades of binocular vision<sup>7</sup> (i.e., simultaneous macular perception—first grade, fusion—second grade, and stereopsis—third grade) are assessed to determine binocular participation. These tests include Bagolini striated lenses that evaluates the first grade of binocular vision, Worth 4-Dot Test that evaluates both first and second grades and stereoacuity tests that evaluates the third grade of binocular vision.<sup>8,9</sup> The quantification of suppression is not possible with the Worth 4-Dot test or Bagolini striated lenses because they only qualitatively indicate the presence or absence of

suppression. Although the viewing distance in the Worth 4-Dot test could be changed to calculate the visual angle of suppression to quantify suppression, it could be a time-consuming endeavor.

Stereoacuity is related to measures of suppression.<sup>10</sup> The underlying assumption is that better the stereoacuity, less is the suppression of the amblyopic eye. However, conventional stereoacuity tests used in the clinics do not give equal or fine step sizes to measure stereopsis. For example, the Stereo Fly Test (Stereo Optical Inc., Chicago, IL, USA) starts with 3500 arc seconds, and the next level of stereoacuity that can be measured is 800 arc seconds. Also, these tests can be used only if the patient has reasonably good visual acuity to view the targets. Additionally, to comprehend this test can be a challenge, particularly for young children.<sup>11</sup> If the patient has never experienced stereopsis, they probably will have difficulty to understand terms like “floating up” or “popping out” or will be using monocular cues.<sup>12</sup>

Earlier studies on suppression mapping have used perimetric techniques mainly for patients with strabismic amblyopia<sup>13,14</sup> than for patients with anisometropic amblyopia.<sup>15</sup> Attempts have also been made to clinically quantify suppression using devices that alter the retinal illuminance in the dominant eye such as Sbisabar,<sup>16</sup> Bagolini filter,<sup>17</sup> or neutral density filters.<sup>18,19</sup> Couple of head-mounted devices with a dichoptic viewing condition was developed for clinical use<sup>20,21</sup> but has not been available commercially. One of the commercially available clinical devices/software is the VTS4, that is, Vision Therapy System version 4 (HTS Inc., Gold Canyon, AZ, USA). VTS4 is commonly used in optometric/ophthalmologic practices that specialize in binocular vision, at least in India. VTS4 is used for both diagnosing (e.g., vergence anomalies) and for managing (e.g., antisuppression exercises for amblyopia) binocular vision anomalies. VTS4 provides dichoptic viewing using stereo goggles that synchronize the refresh rate of the goggles with that of the screen refresh rate.<sup>22</sup> The software also has targets presented for the three grades of sensory fusion and gives the flexibility to reduce target size or contrast. Given this flexibility, this software therefore could be used as a tool to quantify suppression of the amblyopic eye. Specifically, a dichoptic stimulus could be presented, and its size can be reduced until the patient reports that one of the targets has disappeared. Usually it will be the target seen by the amblyopic eye. The disappearance of the target in the amblyopic eye is labeled as “suppression scotoma” because the target in the dominant eye is still visible, whereas the amblyopic eye has been suppressed and its target has fallen into a “blind zone.” The size of the target at which it disap-

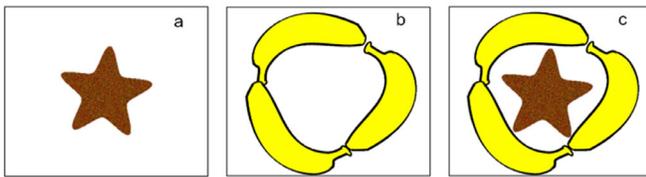
pears can be considered as the suppression scotoma size.

The testing hypothesis in this study is that the measured suppression scotoma size would be larger in those patients with poorer stereopsis and greater interocular visual acuity difference. This would indicate a deep suppression of the amblyopic eye. Thus the purpose of this study was to quantify suppression of the amblyopic eye under binocular viewing conditions with the VTS4. Such an attempt of using the VTS4 to quantify suppression has never been reported before. The outcome of this study can help provide better assessment for binocularity in patients with amblyopia with a readily available clinical tool.

## Methods

A cross-sectional study was conducted after the protocol was approved by the institutional review board of L V Prasad Eye Institute, Hyderabad. The protocol followed the tenets of declaration of Helsinki. All patients and participants were enrolled with written informed consent. Informed consent was obtained from the parents/guardians for children up to age 16 years. Verbal assent was also obtained from children. For the purpose of this study, anisometropia was defined as a difference in refractive error between the two eyes to be  $\geq 1.00$  D of spherical equivalent or  $\geq 1.50$  D of astigmatism.<sup>23,24</sup> Amblyopia was defined as visual acuity difference between the two eyes to be  $\geq 2$  lines<sup>25</sup> from their clinical records, on the day of testing. Patients with diagnosis of anisometropic amblyopia and age greater than four years were enrolled from the pediatric and neuro-ophthalmology clinics of L V Prasad Eye Institute. Patients with other causes for amblyopia (e.g., deprivational, strabismus, etc.) or with any other known systemic diseases were excluded.

All enrolled patients wore their appropriate refractive correction for a minimum of 3 months and were visiting the clinics for follow up visits. Upon enrollment into the study, stereoacuity with Randot stereo test (Stereo Optical Inc.) was measured first, followed by visual acuity thresholding with single optotypes using COMPLog (Ver. 1.3.25.0, Bristol, UK) computerized visual acuity chart. Single optotypes were used to determine the maximum visual acuity potential of the amblyopic eye by eliminating the effect of crowding.<sup>26</sup> Monocular visual acuity thresholding was done first in the dominant eye followed by the amblyopic eye. Visual acuity thresholding was automated in the



**Figure 1.** Top image shows the VTS4 setup. Bottom panel is an illustrative representation of SMP dichoptic targets in VTS4 while viewing through the stereo goggles. Target in (a) was seen by the amblyopic eye, target in (b) was seen by the dominant eye. Target (c) was the binocular view, if the amblyopic eye was not suppressed. If the amblyopic eye was suppressed the view would appear like in (b).

COMPLog software, that is, optotype of 0.8 LogMAR is shown and with correct response, optotype size steps down in 0.2 logMAR units until the first mistake, after which a larger optotype size is shown and the step size is changed by 0.1 logMAR. Visual acuity threshold stopping criteria is three mistakes for the same optotype size.<sup>27–29</sup>

## Quantifying Suppression

We used the Vision therapy system, VTS4 system (HTS Inc., Gold Canyon, AZ, USA) to quantify suppression. The VTS4 provides dichoptic targets (each eye sees its own target) for measuring the three grades of binocular vision. The system uses a LCD stereo television (SONY, 48 inches, 1280 × 720 with refresh rate of 60 Hz) that is synced with liquid crystal shutter goggles (Samsung 3D Active glasses, SSG-5100GB; Samsung, Seoul, South Korea) to present dichoptic targets. The VTS4 software has a variety of targets that comprises of pictures of fruits, animals or other objects to choose from. For the purpose of this study, target A1 of simultaneous macular perception (SMP) was chosen (Fig. 1) to be viewed from 33 inches. This target consisted of a brown starfish (25.7 cd/m<sup>2</sup>) for one eye and three yellow bananas (30.5 cd/m<sup>2</sup>) forming a circle for the other eye.

The luminance of the white background was 37.9 cd/m<sup>2</sup>. All of the luminance values were measured through the shutter goggles with a photometer (LS-100; Konica Minolta Photometer, Ramsey, NJ, USA). When aligned in the macula of each eye, a perception of the starfish inside the bananas will be appreciated in binocular viewing conditions (Fig. 1c). If one of the eyes is suppressed, only one target will be appreciated. In our study, the starfish was always presented to the amblyopic eye, to quantify the central suppression scotoma size. By default, the SMP target gets presented at 48.8% scale value (8° visual angle). This scale value is an arbitrary value indicating the size of the target, with a larger value for a larger target size. If both dichoptic targets (starfish and bananas) are detected on presentation at the default size, the target size was reduced by pressing the down arrow key on the keyboard. This key press will reduce the size of both the targets simultaneously by the same amount (can step down by fine steps of 0.1% scale value). At the size where the patient reports the disappearance of the star (i.e., amblyopic eye gets suppressed), the scale value was noted. If the star (amblyopic eye target) was not visible at 48.8% (8°) scale value, then the scale value was increased to 100% (16°, maximum size), and then the size was reduced. The procedure of measuring the scale value was repeated thrice, and the average value was calculated for each patient. The average scale value was converted to visual angles in degrees by using a linear regression model. The linear regression model was established by making measurements at different scale values and physically measuring the size of the targets on the display monitor (star inside the banana). Because the VTS4 only presents the scale value, this linear regression model was useful to determine the scotoma size in visual angles, calculated in degrees. The measurement was taken from the topmost edge of the banana to the bottommost edge of the banana. It can be seen that the star is smaller than the banana. The size difference decreased with the scale value (4.9° at 100%, 2.5° at 48.8%, and 0.14° at 1% scale value). The size difference was ignored in our calculation.

One limitation of the VTS4 stereo goggle is the “leakage” or cross-talk. In the presence of leakage, the dichoptic target presented to the fellow eye could appear “white.” We have noticed from our clinical experience that not all patients report this leakage. Why only some patients report this is unclear to us. To circumvent this limitation, patients in this study were first asked to report what targets they were seeing and the color of the targets. Then they were instructed to report the disappearance of the “brown” starfish.

## Data Analysis

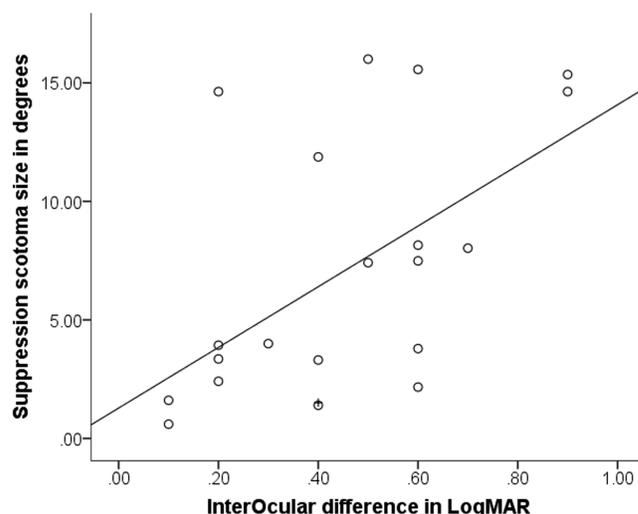
The primary outcome measure from this study was suppression scotoma size. This outcome variable was correlated with interocular visual acuity difference and stereoacuity. Correlations were also computed between the interocular visual acuity difference and stereoacuity. Depending on the distribution of the data, either parametric or nonparametric correlation coefficient was chosen. Stereoacuity data were transformed to log units to normalize the data. All statistical analysis was performed using SPSS 21.0 software (IBM SPSS Statistics, Version 21.0; IBM, Armonk, NY, USA).

## Results

A total of 28 patients (13 females) aged 6 to 21 years were recruited. The mean age  $\pm$  standard deviation was  $11.6 \pm 5.1$  years. The mean logMAR visual acuity of the dominant eye was  $0.04 \pm 0.12$ , and that of the amblyopic eye was  $0.56 \pm 0.23$ . The mean logMAR interocular visual acuity difference was  $0.51 \pm 0.26$ . The mean anisometropia computed from the absolute value of the spherical equivalent was  $4.00 \pm 1.51$  diopters [range, 1.00 DS to 6.50 DS]. On seven patients stereoacuity was not measurable with the Randot stereo test (worse than 500 arc seconds). Within this group, four had suppression of the amblyopic eye detected by their inability to identify one of the letters and lines in the “R + L” vectogram, in the Randot stereo test, indicating deeper suppression, whereas in the remaining three this identification was present, indicating partial suppression. For these three patients an arbitrary value of 3 was assigned for the log stereoacuity and for the remaining four patients a log value of 4 was assigned. These values were used only for graphical visualization. These seven patients were excluded from analyses that involved stereoacuity. For all the other analyses all the 28 patients were included. The mean stereoacuity from the remaining 21 patients was  $160.47 \pm 130.82$  arc seconds ( $2.07 \pm 0.35$  log arc seconds).

## Suppression Scotoma Size

All the patients were able to understand and perform the VTS4 SMP task for measuring the suppression scotoma size. For 15 patients the starting scale value of VTS4 was at 100% ( $16^\circ$  visual angle) and for the remaining patients the starting scale value was 48.8% ( $8^\circ$  visual angle). The average variability, measured by taking the mean of all the patient's standard deviation was  $2.1\% \pm 1.9$  scale value. The



**Figure 2.** Scatter plot showing the correlation between suppression scotoma size measured with the VTS4 and interocular visual acuity difference between the two eyes. The linear fit line ( $r = 0.59$ ) is shown in black solid line. The plus sign inside or over a circle represents overlapping data points.

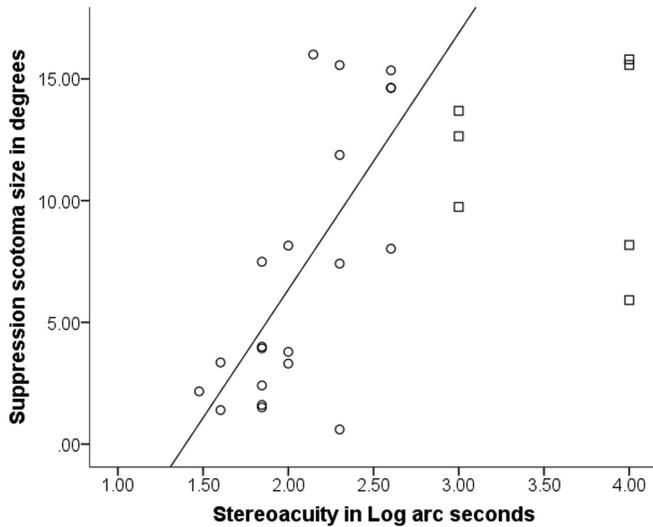
average scotoma size for 28 patients was  $47.46\% \pm 33.9\%$ , converted to visual angles these were  $8.2^\circ \pm 5.4^\circ$ .

One sample Kolmogorov-Smirnov test showed that all the outcome measures were normally distributed ( $Z$ -score  $> 0.7$ ,  $P > 0.31$ ), this was also confirmed by examining the Q-Q plot. Therefore Pearson's correlation coefficient was computed. Suppression scotoma size showed a significant positive correlation with both interocular visual acuity difference ( $r = 0.59$ ,  $df = 26$ ,  $P = 0.001$ ; Fig. 2) and stereopsis ( $r = 0.72$ ,  $df = 19$ ,  $P < 0.001$ ; Fig. 3). The correlation between interocular acuity difference and stereopsis on the other hand showed a borderline significance ( $r = 0.41$ ,  $df = 19$ ,  $P = 0.059$ ; Fig. 4).

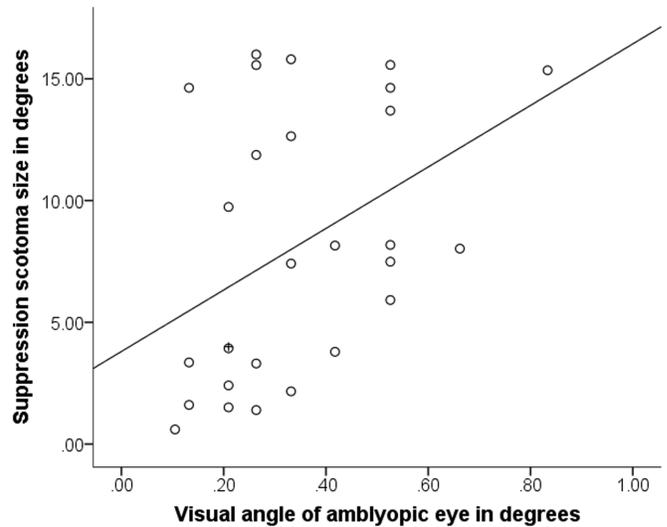
We also plotted the correlation between the suppression scotoma size and the visual angle ( $r = 0.416$ ,  $df = 26$ ,  $P = 0.028$ ; Fig. 5). The visual angle denotes the size of the smallest letter that was read by the amblyopic eye. The size is calculated from the equation:  $5 \times$  Minimum angle of resolution. Therefore if the visual acuity of the amblyopic eye was 0.4 logMAR, then the visual angle would be  $0.21^\circ$ .

## Discussion

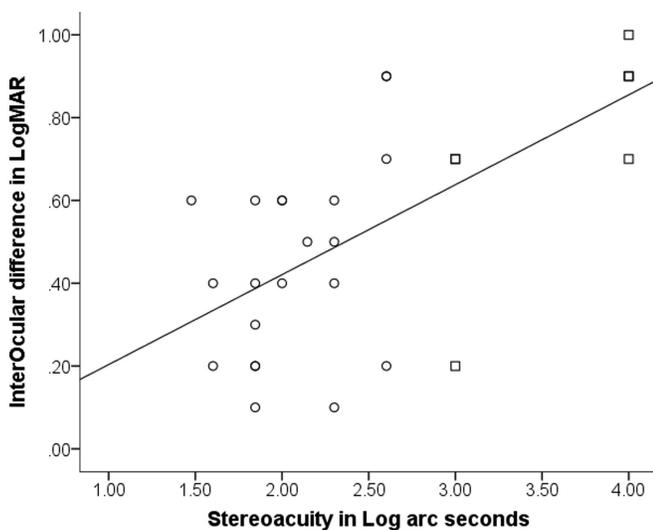
This study provides evidence that a clinical tool like the VTS4 system can be adapted to quantify suppression of the amblyopic eye under binocular viewing condition. This was achieved by measuring the suppression scotoma size with dichoptically viewed



**Figure 3.** Scatter plot showing the correlation between suppression scotoma size measured with the VTS4 and stereoacuity in log arc seconds. The linear fit line ( $r = 0.72$ ) is shown in *black solid line*. *Square symbols* represent the subjects for whom stereoacuity was not measurable and an arbitrary value has been assigned.



**Figure 5.** Scatter plot showing the correlation between suppression scotoma size and visual angle of the smallest letter read by the amblyopic eye. The linear fit line ( $r = 0.42$ ) is shown in *black solid line*. The *plus sign* inside or over a *circle* represents overlapping data points.



**Figure 4.** Scatter plot showing the correlation between interocular visual acuity difference in logMAR and stereoacuity in log arc seconds. The linear fit line ( $r = 0.41$ ) is shown in *black solid line*. *Square symbols* represent the subjects for whom stereoacuity was not measurable and an arbitrary value has been assigned.

size. This indicates that the suppression scotoma size measurement can be implemented in the clinics for monitoring and managing amblyopia, similar to how stereoacuity values are used.

Stereoacuity had a better correlation with the suppression scotoma size (Fig. 3) when compared to the interocular visual acuity difference (Fig. 4). This is not surprising because visual acuities are monocular measures, whereas stereoacuity is a better indicator of both eyes functioning together for binocular vision. The suppression scotoma size measurement is a binocular task and can thus be considered as a marker of binocularity similar to stereoacuity. The suppression scotoma size can be measured more easily and can be understood easily in young children as well. Although the youngest in this study was six years old, we have observed from our clinical practice that we could do this procedure on children younger than six years also. Additionally, in the patients ( $n = 7$ ) for whom we could not measure the stereoacuity, a suppression scotoma size measurement was possible. This indicates that suppression scotoma size gives a more continuous and finer scale for measuring the limit of binocular participation (or the beginning of suppression) of the amblyopic eye.

Careful examination of the scatter plot between interocular visual acuity difference and stereoacuity (Fig. 4) reveals that some patients may have a larger interocular acuity difference and yet have a better stereoacuity or vice-versa. This is an important finding and reveals that a mere difference in

SMP targets. For a normally-sighted individual the SMP targets seen by each eye will be visible even at the smallest target size. For an individual with amblyopia the target perceived by the amblyopic eye will disappear at a relatively larger size, indicating the beginning of the suppression scotoma from that size onward, for that eye. We observed a significant positive correlation between stereoacuity and suppression scotoma

visual acuity between the two eyes may not indicate the depth of the suppression in the amblyopic eye. Such a finding has been reported previously between stereoacuity and visual acuity of the amblyopic eye.<sup>30</sup> The reasons for these variations were not explored in the present study. Neither were these patients tested for the presence of microtropia, which is a limitation of this study. The test-retest repeatability for the suppression scotoma size on different days were not undertaken in this study and that is another limitation. Future studies can consider factors such as visual acuity of the dominant and amblyopic eye, amount of anisometropia as random factors or covariates in a larger sample size to use predictive models to study the depth of suppression.

Previous studies quantified suppression and modulated the contrast,<sup>6,31–33</sup> motion coherence,<sup>31,34–36</sup> and optical blur<sup>31,34,37,38</sup> in the dominant eye. In the present study suppression is quantified by modulating the target size. Also, unlike previous studies, there are no competing contours visible to the dominant eye's foveal region in this study. Only a white central region was seen in the dominant eye's stimuli. Such a lack of competing stimuli could have underestimated the scotoma size in the present study. The size of the suppression scotoma indicates the target size (visual angle) at which the dominant eye alone is able to view the scene. The participation of the amblyopic eye in that viewing condition is nil, and this could be because of the limit of the visual acuity threshold in the amblyopic eye or due to the cortical suppression mechanism setting in at that target size. The scatter plot (Fig. 5) between the suppression scotoma size and the amblyopic eye's visual angle shows a positive correlation. Thus a smaller suppression scotoma size will be present in the amblyopic eye with better acuity. The visual angle of the suppression scotoma is, however, larger when compared to the visual angle of the smallest letter seen by the amblyopic eye. This could indicate that greater active cortical inhibition is present in a binocular task when compared to a monocular task such as monocular visual acuity measurement.

There is increasing awareness for binocular exercises to be incorporated in amblyopia therapy either with or without patching therapy.<sup>39,40</sup> Studies have compared evidence of better acuity improvement in therapies involving video games or dichoptic exercises.<sup>41–43</sup> Hence, along with considering visual acuity in the amblyopic eye and stereoacuity, the suppression scotoma size that is a dichoptic measure can also be considered as an outcome parameter in pre and post antisuppression therapy sessions to gauge the improvement in the amblyopic eye. The utility of this

measure can be explored further in both clinical care and research studies.

In this study we measured the suppression scotoma size in patients with anisometropic amblyopia. It is possible to measure the suppression scotoma size in patients with strabismic amblyopia as well using the same method. VTS4 permits measuring the subjective angle of ocular deviation by asking the patient to align the two SMP targets. At this subjective angle of ocular deviation, the size of the SMP targets can then be decreased to determine the suppression scotoma size. It must be noted that if the subjective angle of deviation is zero, it would indicate an anomalous retinal correspondence condition.<sup>44</sup>

In conclusion, VTS4 can be used as a device to measure suppression scotoma size in patients with anisometropic amblyopia. This measurement has a good correlation with stereopsis and interocular visual acuity difference. Therefore scotoma size measurement can also be used as a parameter to quantify the depth of suppression of the amblyopic eye. The scotoma size measure can be a useful measure even when stereopsis measurement is not possible in some patients to assess binocular participation.

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