Correction of perceived visual distortions using a software application and correlation to age-related macular degeneration

Muhammad Hassan (iD), **Adithi D. Chakravarthy** (iD), **Mahadevan Subramaniam,**
Parvathi Chundi, Mohammad Ali Sadiq, Muhammad Sohail Halim, Rubbia Afridi,
Anh N.T. Tran, Yasir J. Sepah, Diana V. Do and Quan Dong Nguyen

Abstract

Purpose: To investigate the use of software-generated corrections in neutralizing perceived distortions in age-related macular degeneration.

Methods: A tablet-based application was utilized to elicit distortions. Five subjects (seven eyes: neovascular age-related macular degeneration and three eyes: non-neovascular age-related macular degeneration) traced the reference lines, and their distortion traces were recorded. To counter distortion, a software-generated trace was re-traced by subjects to produce a corrected trace. Final traces were superimposed on optical coherence tomography images and following distances calculated: (a) dDT: distance between distortion trace and reference line; (b) dGT: distance between software-generated trace and corrected trace; (c) dCT: distance between corrected trace and reference line. Mean percent improvement in distortion was reported. Mean effectiveness of correction was also reported by utilizing *t* test to compare dDT and dCT. The number of distortion traces with underlying lesions on optical coherence tomography was also analyzed.

Results: Mean age of the subjects was 76.6 ($\pm$9.5) years. Each patient traced six reference lines and each was considered a separate case. Out of 30 cases, 17 (56.6%) elicited distortion. Mean percent improvement in distortion was 71.3 $\pm$ 23% ($p < 0.05$). Twelve cases (70.6%) had an underlying lesion (eight cases: disrupted photoreceptor layer and four cases: normal photoreceptor layer). Mean percent improvement in cases with normal photoreceptor layer (90.8 $\pm$ 5.45%) was higher than with abnormal photoreceptor layer (58.5 $\pm$ 7.17%) ($p < 0.05$). Five cases with distortion had no associated underlying lesion. Mean percent improvement in these subjects was significantly higher than those with photoreceptor layer disruption.

Conclusion: Software-generated corrections can potentially correct for perceived distortions in patients with age-related macular degeneration, especially in cases with preserved photoreceptor layer.

Keywords: age-related macular degeneration, metamorphopsia, visual distortion

Correspondence to:
Quan Dong Nguyen
Mary M. and Sash A.
Spencer Center for
Vision Research, Byers
Eye Institute, Stanford
University, 2370 Watson
Court, Suite 200, Palo Alto,
CA 94303, USA.
ndquan@stanford.edu

Muhammad Hassan
Mary M. and Sash A.
Spencer Center for
Vision Research, Byers
Eye Institute, Stanford
University, Palo Alto, CA,
USA

Adithi D. Chakravarthy
Mahadevan Subramaniam
Parvathi Chundi
College of Information
Science & Technology,
University of Nebraska
Omaha, Omaha, NE, USA

Mohammad Ali Sadiq
Kentucky Lions Eye
Center, University of
Louisville, Louisville, KY,
USA

Muhammad Sohail Halim
Rubbia Afridi
Anh N.T. Tran
Yasir J. Sepah
Diana V. Do
Mary M. and Sash A.
Spencer Center for
Vision Research, Byers
Eye Institute, Stanford
University, Palo Alto, CA,
USA

Introduction

Age-related macular degeneration (AMD) is among the leading causes of blindness in the developed world, especially in the population above 65 years of age.[1] It accounts for approximately 12–21% of all cases of legal blindness and as many as 30% of adults over the age of 75 develop signs of senile retinal degeneration.[2]

AMD can be classified into two subcategories: non-neovascular and neovascular. Two of the parameters used for assessment of visual function

in subjects with AMD are visual acuity and degree of spatial distortion (metamorphopsia). Improvement in visual acuity is one of the major targets of therapies for AMD. Recent advances in the management of AMD, especially the advent of anti–vascular endothelial growth factor (anti-VEGF), have revolutionized therapy for this condition.[3] Approximately one-third of subjects receiving treatment with anti-VGEF agents demonstrate significantly improved visual acuity. However, metamorphopsia is less commonly used as an outcome parameter for clinical studies and may persist even after improvement in visual acuity.[4,5] Therefore, it has significant consequences on patient autonomy and quality of life.[5]

Currently, there are no standard rehabilitation procedures for the problems that patient face secondary to metamorphopsia. Most of the rehabilitative programs focus on helping patients improve their reading skills. These approaches include the use of visual aids and different visual learning techniques.[6–10] Although these procedures have shown promise in helping patients with AMD, these approaches are not easy to teach and require constant supervision in initial stages. In this pilot study, we aim to investigate the effects of an Android® tablet-based software-generated corrections in canceling the perceived distortions experienced by subjects with AMD and to find an association between perceived distortions and underlying anatomic abnormalities in these subjects.

Methods

The index study employed a cross-sectional design. All the subjects were selected from a tertiary care ophthalmology clinic and fulfilled the study inclusion and exclusion criteria. The study was conducted in compliance with the Declaration of Helsinki, the US Code of Federal Regulations Title 21, and the Harmonized Tripartite Guidelines for Good Clinical Practice (1996). The study was approved by University of Nebraska Medical Center Institutional Review Board (Omaha, Nebraska). A written (signed) informed consent was obtained from all the study subjects.

Inclusion and exclusion criteria

Subjects were included in the study if they fulfilled the following criteria: (a) age ⩾55 years; (b) established diagnosis of age-related macular degeneration; (c) best-corrected visual acuity of 20/40 to 20/125; (d) visual distortions present in at least one eye as determined by Amsler grid; (e) have had a macular region spectral domain optical coherence tomography (SD-OCT) scan performed within 1 month of the current visit. Subjects were excluded from the study if they (a) had visual loss secondary to any disease other than AMD; (b) had visual distortions secondary to conditions other than AMD such as vitreomacular traction and epiretinal membrane; (c) had visual acuity better than 20/40 and worse than 20/125; (d) had an intention tremor more than physiologic tremor and would preclude patients from tracing the lines; and (e) had trouble understanding or using an Android tablet.

Distortion elicitation and correction procedure

An Android tablet-based application was developed using Android 4.4.2 KitKat SDK in Java to elicit and record distortions in images as perceived by the study subjects. A Samsung Galaxy Tab 4.10.1 with 10.1-in touch screen was used for this study. The application software would record distortions perceived by each subject and automatically apply corrective actions to the original image seen by the study subject in accordance with the amount of distortion perceived by the subject. The details of the algorithm utilized by the application for eliciting and recording distortions as well as generating and recording correction data have been published by our group previously.[11] A summary of the actual procedure of recording patient input is described. All the lines seen by the subjects were black on a white background screen. However, in this article, color references are used for the ease of explanation.

Gesture calibration. For each subject, a gesture calibration was performed as the first step to allow effective and robust input capture during the testing phase. This also allows the software to calculate and account for the jitter in the hand motion of each study subject during the active testing phase.

Recording distortion trace. Following calibration, each subject was shown three horizontal equally spaced reference lines (RL) (Figure 1(a) and (e), black line) with a center point of fixation midway across the center line. While focusing on the center point of fixation, each subject was asked to trace the three RLs. As the subjects trace the RLs, their distortion trace (DT) was recorded (Figure 1(b) and (e), green line) by the software without any manual manipulation. Study subjects were
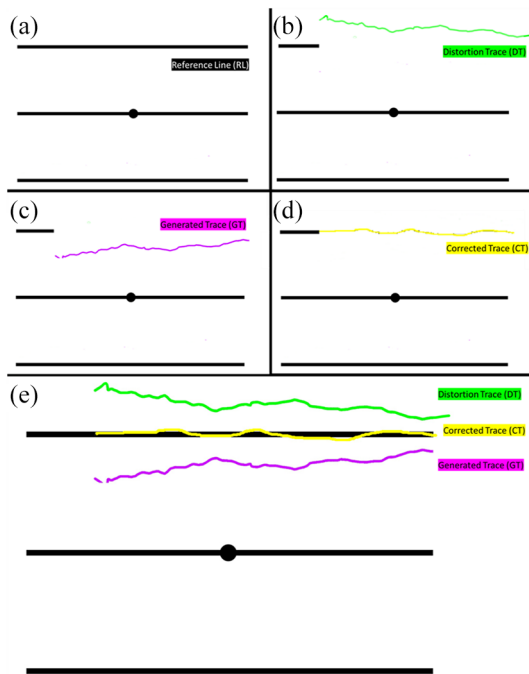
Figure 1. (a) Reference lines (RL; black lines) as seen by the study subject, (b) distortion trace (DT; green line) as drawn by the study subject, (c) software-generated trace (GT; purple line) derived using the data obtained from DT, (d) corrected trace (CT; yellow line) drawn the subject while looking at the GT, (e) DT, GT, and CT drawn on top of RL to show association between the traces in reference to RL.

asked to repeat the step three times to record a mean DT and ignore the outliers in the recorded data. Each time a new set of three horizontal lines was presented to the subject and the previous trace was wiped from the screen.

Generation of correction trace. The *correction algorithm*, using the data obtained from the DT drawn by the subject, produces a software-generated trace (GT) (Figure 1(c) and (e), purple line) to counter the distortions seen by the study subjects. Once again, three new horizontal RLs are presented to the subject but with the correction algorithm applied to them. These traces were labeled as GT to differentiate from the initial reference lines in the data stored by the software. The study subject was asked to focus on the center point of fixation and trace the GT lines and their final traces were recorded by the software. These final traces were labeled as correction trace (CT) (Figure 1(d) and (e), yellow line). This step was repeated three times and each time a new set of GT was presented and a new set of CT was

recorded. The mean CT was recorded by the application for comparison with the original RLs.

SD-OCT
SD-OCT scans captured using Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) within the last 1 month of the study visit were analyzed. Macular scans consisting of either 25 or 49 B-scans were selected for this study.

Mapping DT, GT, and CT on SD-OCT en face image
A flipped and laterally inverted image of the tablet interface with RL and mean DT, GT, and CT on a single image from each subject was superimposed on the *en face* image of the OCT scan from the same subject using MATLAB (Figure 2(a)). The details of the mapping methodology have been described by our group separately.[11] Best corrected lines were drawn passing through the DT, GT, and CT (Figure 2(b)) and the following mean distances were calculated: (a) dDT: distance between DT and RL (Figure 2(c)), which is the distance by which original RL was perceived as distorted by the subject; (b) dGT: distance between GT and CT (Figure 2(c)), which is the distance by which the software generated GT was able to correct the perceived distortion; (c) dCT: distance between CT and RL (Figure 2(c)), which is the distance between the remaining distortion and reference line that may persist even after the subject was presented with GT. The mean distances calculated in the study were average of distances between each pixel along the similar points on the best fitted lines.

Correlating distortion and correction to the SD-OCT findings
During the superimposition on the en face SD-OCT image the center of the fovea was aligned with the center of the fixation spot of the RLs. Three B scans corresponding to the three superimposed RL were selected for each patient. Heidelberg Eye Explorer was used to correlate the area of distortion in the DT to the lesion as seen on the B scan by two independent graders (S.H. and R.A.). Any discrepancy between the graders was resolved by a senior grader (M.H.). If a lesion was present corresponding to area of distortion, presence or absence of disruption of the photoreceptor layer (PRL) overlying the lesion was also noted.
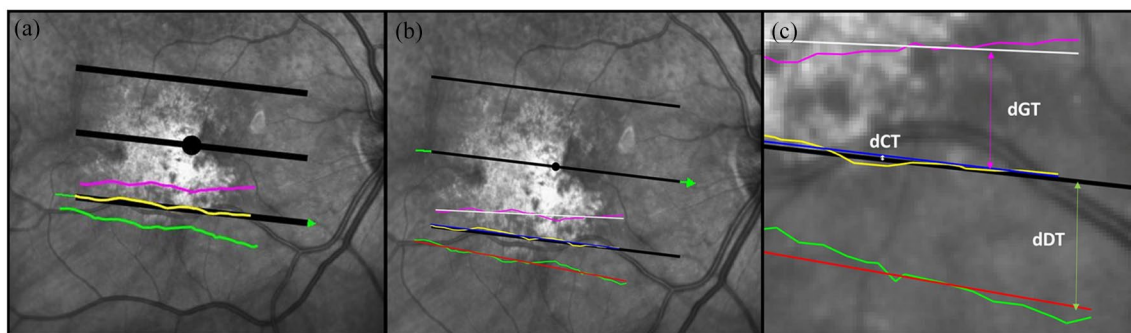
Figure 2. (a) Mapping reference lines (RL, black lines), distortion trace (DT; green line), software-generated trace (GT; purple line), and correction trace (CT: yellow line) to spectral domain optical coherence tomography (SD-OCT) en face image; (b) Best-fit lines through the DT (red), GT (white), and CT (blue); (c) outlining dDT: distance between DT and RL, dGT: distance between GT and CT, and dCT: distance between CT and RL.

Table 1. Demographic Characteristics of the Study Population.

Number of lines (eyes), [patients]	30 (10), [5]
Mean age (years) (±SD)	76.6 ± 9.5
Females	100%
Diagnosis (number of eyes) (%)	
Neovascular AMD	7 (70%)
Non-neovascular AMD	3 (30%)

AMD, age-related macular degeneration; SD, standard deviation.

Improvement in distortion

Percent improvements in distortion were calculated by comparing the dGT and dDT values in each subject. Effectiveness of correction was also determined by comparing dGT and dCT values.

Outcome measures

Mean percent improvement in distortion was reported for the study population. Mean effectiveness of correction was also calculated for the study population. The DTs were further classified as having as associated underlying lesion on the B scan and without any associated lesion. The cases with associated lesions were further classified into groups with or without PRL disruption. Mean percent improvement in distortion and effective of correction values were also calculated and compared for these subgroups.

Statistical analysis

Stata V14.1 (Stata Corp, TX) was used for all statistical analysis. Mean percent improvement in distortions along with standard errors were calculated. *T*-test was utilized to calculate the effectiveness of correction in the study subjects. A *p* value of <0.05 was deemed significant.

Results

Patient characteristics

Ten eyes (five subjects) which fulfilled the study inclusion and exclusion criteria were included in the study. Table 1 outlines the baseline demographic characteristics of the study subjects. Each subject had to trace six RLs in total (three per eye). In this study, we treated each RL traced as a separate case. Therefore, a total of 30 cases were analyzed.

Distortion and correction analysis

Out of 30 cases analyzed, 17 cases (56.6%) elicited distortion. The mean percent improvement in distortions was $71.3 \pm 23\%$. The effectiveness of correction was determined to be statistically significant ($p < 0.05$). These 17 cases were further analyzed for any underlying lesion present on the SD-OCT.

Correlating distortion and correction to the SD-OCT findings

Twelve (70.6%) out of 17 cases which elicited distortion had an underlying lesion (Figure 3(a)). In eight of these subjects, there was disruption of PRL, while in four cases, PRL was intact. The mean percent improvement in distortions in cases with PRL disruption was $58.5 \pm 7.17\%$. However, the mean percent improvement in distortions in cases without PRL disruption was $90.8 \pm 5.45\%$.
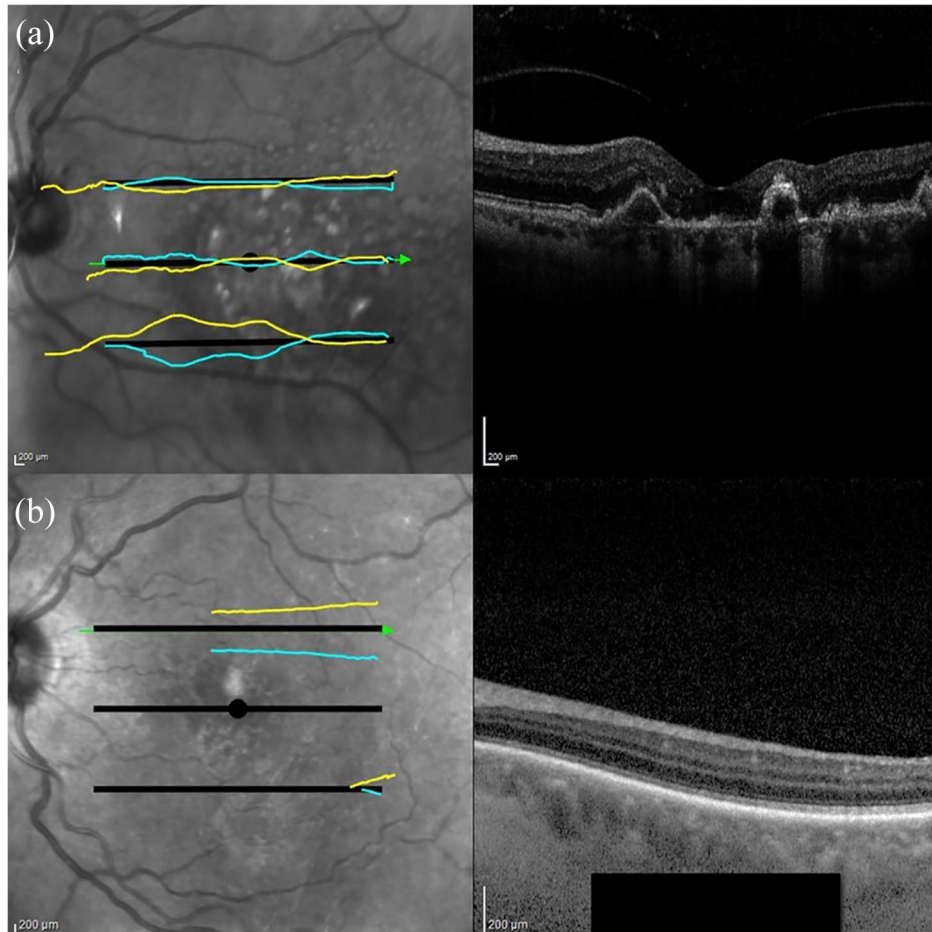
Figure 3. (a) A case where distortions seen by the patients were associated with underlying lesions on the spectral domain optical coherence tomography (SD-OCT) B scan. (b) A case where distortion was not associated with an underlying lesion on the SD-OCT B scan.

The difference between the two groups was statistically significant ($p < 0.05$) (Table 2).

In five (29.4%) cases with distortion, an underlying lesion could not be appreciated (Figure 3(b)). The mean percent improvement in distortions in these cases was $86.5 \pm 3.23\%$. The mean percent improvement of distortions in the group with distortions without underlying lesion was significantly higher than that of the group with distortion and an associated lesion with PRL disruption ($p < 0.05$) (Table 3). However, the mean improvement in distortions was not significantly different between groups with distortion without lesion and distortion with lesion but with an intact PRL ($p > 0.05$) (Table 3).

Discussion

Metamorphopsia is one of the hallmark signs of macular diseases. Amsler grid consisting of evenly spaced vertical and horizontal lines is a very low-cost, easy-to-use method utilized universally to test and follow patients with AMD for metamorphopsia.[12] However, due to its high false-negative rate, other methods such as M-chart have been utilized to document the degree of metamorphopsia.[12,13]

With the advent of anti-VEGF therapy, patients with nv-AMD have demonstrated significant improvement in visual acuity in multiple clinical studies.[3] However, metamorphopsia in patients of non-neovascular and neovascular AMD may persist despite improvement in visual acuity. This can have significant effect on the quality of life, especially the reading abilities of these patients as demonstrated by Xu and colleagues.[5]

Therefore, current studies assessing the role of various rehabilitative techniques and devices focus on improving the reading abilities of patients

Table 2. Analysis of Distortions and Corrections in Cases With Associated Underlying Lesion.

Number of cases with distortion with associated underlying lesion, n (%)	12/17 (70.6%)	
Number of cases with PRL disruption, n	8	
Number of cases without PRL disruption, n	4	
Mean percent improvement in cases with PRL disruption (%) (±SE)	58.5 (7.17)	$p < 0.05$
Mean percent improvement in cases without PRL disruption (%) (±SE)	90.8 (5.45)	
PRL, photoreceptor layer; SE, standard error.		

Table 3. Analysis of Distortions and Corrections in Cases Without Associated Lesion and Comparison of These Cases With Distortions Associated With Lesions.

Number of cases with distortion with no associated lesion, n (%)	5/17 (29.4%)	
Mean percent improvement distortion in cases with no associated lesion (%) (±SE)	86.5 (3.23)	$p < 0.05$
Mean percent improvement in cases with PRL disruption (%) (±SE)	58.5 (7.17)	
Mean percent improvement distortion in cases with no associated lesion (%) (±SE)	86.5 (7.17)	$p > 0.05$
Mean percent improvement in cases without PRL disruption (%) (±SE)	90.8 (5.45)	
PRL, photoreceptor layer; SE, standard error.		

with AMD. A number of these studies employ the use of optical as well as electronic magnification tools to help patients with low vision. Due to limitations associated with optical magnification such as limited field of view, increased aberrations, limited contrast manipulation, and a steep learning curve, the use of electronic magnifiers has been extensively studied.[6,9] These devices included head-mounted electronic magnifiers, video magnifiers, tablet-based magnification, and portable hand-held magnifiers.[7–10] A number of these devices have shown promising outcomes; however, all of these devices are helpful only in patients with low vision secondary to AMD and are not particularly focused on helping subjects with distortions in their vision.

Another rehabilitative approach is the use of perceptual learning in patients with low vision.[14,15] Perceptual learning is experience-dependent augmentation of ability of the subjects to make sense of what they see and has shown promising outcomes. However, perceptual learning in AMD has its limitations, such as age of the patients, learning curve, and limitations in transport to lab facilities. In addition, it may have a limited role in patients with metamorphopsia as the distortions

in these subjects evolve decreasing efficacy of an experience-dependent rehabilitative system.

In contrast to the above approaches, our study focuses on patients with AMD and visual distortions. We developed and utilized a novel tablet-based application to quantitatively assess the visual distortions perceived by the patients with AMD and apply automatic software-based corrections to help neutralize the effect of these distortions. Our methodology was based on the historical use of Amsler grid to evaluate metamorphopsia in patients with AMD. Similar to the Amsler grid testing, the patient was asked to focus on the center fixation point and trace three horizontal lines. Our software application was able to improve the distortions in our study population by an approximate 70%.

We further explored the association of visual distortions with underlying anatomical lesions using SD-OCT. We noticed that cases experiencing distortions in vision with an underlying associated lesion have greater chances of achieving a correction in distortion if they have an intact PRL compared with those with disruption of the PRL. One of the mechanisms for metamorphopsia reported

in the literature is changes in photoreceptor alignment, location, and structure.[4] Such changes could potentially explain the visual distortions seen in our study subjects with underlying lesions leading to displacement of the PRL. Furthermore, the correction was less effective in subjects where the PRL was disrupted supporting the photoreceptor origin of the symptom.

A subgroup of our study population consisted of cases who experienced distortions without any underlying lesions visible on SD-OCT. The mean percent improvement in distortions in this subgroup of subjects was similar to those cases with underlying lesion but no PRL disruption. We assumed the center of fixation to be the foveal center in all the subjects while superimposing the distortion outcomes on the SD-OCT scans. However, these cases may have an eccentric center of fixation as all of these subjects had foveal lesions.

As with any study, our study has its limitations. The sample size of our study was very small. We did not accurately assess each patient's center of fixation and it was assumed to be the fovea. The axial length of the eyes was not obtained as it could potentially affect the superimposition of the distortion outputs on the retina. Finally, we did not track the gaze of the patient and relied on subjective account of the patient fixating on the center black spot.

Even with the limitations, our study was first of its kind in developing and implementing a novel technique to correct the distortions perceived by the patients with AMD. We are planning to develop and conduct additional studies to improve on this technology and account for the limitations noted in this study like incorporating visual tracking and machine learning algorithms in our technology. The technology illustrated in our study has a vast array of potential implications. Once fully developed, we can incorporate the distortion correction mechanism in the operating system of the tablets used by patients with visual distortions rather than limiting to one application. Such availability would allow these people to use the tablet for their personal use. In addition, as the tablet will calibrate periodically to account for any changes in visual distortions of the subject, this would allow patients as well as health professionals to track changes in visual distortions and the underlying anatomical abnormalities.

In conclusion, our Android software-based application showed promising results in potentially correcting distortions in subjects with AMD. Furthermore, the effectiveness of this software in correcting distortions is more pronounced in cases with intact PRL. On the other hand, disruption of PRL layer is associated with distortions with limited possibilities for improvement.

Conflict of interest statement
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ORCID iDs
Muhammad Hassan https://orcid.org/0000-0001-9033-8117

Adithi D. Chakravarthy https://orcid.org/0000-0001-7064-3376

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