Symposium - TRIP

Comparison of saccadic reaction time between normal and glaucoma using an eye movement perimeter

Deepmala Mazumdar[1,2,3], JJ M Pel[4], Manish Panday[1], Rashima Asokan[1,2,3], L Vijaya[1], B Shantha[1], Ronnie George[1], J van der Steen[4]

Aim: To compare the saccadic reaction time (SRT) in both the central and peripheral visual field in normal and glaucomatous eyes using eye movement perimetery (EMP). **Materials and Methods:** Fifty-four normal and 25 glaucoma subjects underwent EMP and visual field testing on the Humphrey Field Analyser (HFA) 24-2 program. The EMP is based on infrared tracking of the corneal reflex. Fifty-four test locations corresponding to the locations on the 24-2 HFA program were tested. SRTs at different eccentricities and for different severities of glaucoma were compared between normal and glaucoma subjects. **Results:** Mean SRT was calculated for both normal and glaucoma subjects. Mann-Whitney U test showed statistically significant ($P < 0.001$) differences in SRT's between normal and glaucoma subjects in all zones. **Conclusion:** SRT was prolonged in eyes with glaucoma across different eccentricities.

Key words: Eye movement perimeter, glaucoma, saccadic reaction time

Access this article online

Website: www.ijo.in

DOI: 10.4103/0301-4738.126182

Quick Response Code:

Glaucoma is the second leading cause of blindness worldwide.[1,2] It is a chronic progressive optic neuropathy which starts with damage to the retinal ganglion cells.[3,4] Ganglion cell damage or loss is clinically assessed by measuring visual thresholds.[4] Standard automated perimetry (SAP) is currently the most common and frequently using diagnostic procedure to assess visual field damage. SAP is based on human perceptual performance. During SAP the subject is required to maintain fixation on the central fixation stimulus, while visual stimuli of varying light intensities are presented for a brief period of time in the peripheral visual field. The subject is required to acknowledge seeing the stimulus by pressing a button. The weakest intensities perceived are used to produce the visual sensitivity threshold plot. SAP requires a high level of cooperation, attention, and effort from the subject to maintain central fixation throughout the test and to suppress the tendency to make reflexive eye movements each time a new peripheral visual stimulus is presented. Since the test result is based on human performance thus discomfort, anxiety, and fatigue can compromise reliability of the test result.[5-7]

Eye movement perimetry (EMP) measures saccadic eye movement towards the presented target, using these responses to map the visual field, without inhibiting the reflexive response of oculomotor control system.[8,9]

The EMP algorithm measures a saccade as "seen or not seen". In addition the saccadic reaction time (SRT), the time taken to process visual information and to activate the ocular motor system, is also measured. The SRT is used to plot the visual threshold on the visual field.[8-10]

Saccades are affected in various optic nerve diseases.[11,12] Delayed saccadic latency has been reported in optic nerve conditions such as optic neuritis and glaucoma.[10] Kanjee *et al*., and Lamirel *et al*., have reported that there is a delay in saccadic eye movement initiation in glaucomatous optic neuropathy. In both mild and advanced glaucoma there is an increase in SRT compared to normal.[13,14] Most existing studies have shown the behavior of saccades in the central visual field. There is little published literature on peripheral saccades.

We report the SRTs in both the central and peripheral field in normal and glaucomatous eyes using EMP.

Materials and Methods

Participants

Normal subjects aged between 30 and 70 years were recruited for the study. The participants were recruited from the patients seen in the outpatient clinic of our hospital and volunteers. Written informed consent was obtained from each participant. Each subject underwent a complete ophthalmic eye examination and subjects with spherical ametropia greater than ± 5.00 Dsph and/or cylindrical ametropia of more than − 2.00 diopter sphere (Dsph), best corrected visual acuity less than 20/40, N6, presence of strabismus, amblyopia, any oculomotor restriction, nystagmus, nerve palsy, pupil size less than 3 mm, lens opacities more than N2, C1, P1 based on LOCS II,[15] any history of ocular surgery or any retinal pathology were excluded.

[1]Sri Jadhavbhai Nathmal Singhvi Department of Glaucoma, Medical and Vision Research Foundation, Chennai, Tamil Nadu, [2]Elite School of Optometry, Chennai, [3]Birla Institute of Technology and Science, Pilani, Rajasthan, India, [4]Department of Neuroscience, Vestibular and Ocular Motor Research Group, Erasmus MC, Rotterdam, Netherland

Correspondence to: Dr. Ronnie George, Director-Research, Senior Consultant, Sri Jadhavbhai Nathmal Singhvi Department of Glaucoma, Medical and Vision Research Foundation, Sankara Nethralaya, 18, College Road, Chennai - 600 006, Tamil Nadu, India. E-mail: drrg@snmail.org

Manuscript received: 24.10.13; Revision accepted: 14.12.13

Subjects with glaucoma were recruited from the outpatient glaucoma clinic of the same hospital. Subjects with primary open angle or angle closure glaucoma who had glaucomatous optic disc changes and corresponding reliable, repeatable visual field defects on SAP (Humphrey Field Analyzer (HFA)) (model 750; Carl Zeiss Meditec) were included. Reliability criteria were as recommended by the instrument's algorithm (fixation loss, <20% and false positive and false negative, <33%). Subjects with glaucoma were also classified into early, moderate, and severe defects based on visual field defect meeting Hodapp, Parrish, and Anderson's classification.[16]

The experimental procedures were reviewed and approved by the Institutional Review Board and the Medical Ethics Committee of Vision Research Foundation, Chennai.

Instrument description and procedure

The EMP setup comprised of a laptop, a 17 inch monitor with an in built eye tracking device with a refresh rate of 120 Hz (Tobii120, ELO Intellitouch System). The eye tracking device works on the principle of corneal-reflection tracking. Fig. 1 shows an EMP display screen showing the tracking status.

Subjects were instructed to place their chin on a chinrest placed at 60 cm distance from monitor. No refractive correction was used while performing the test. The test was performed uniocularly. However, since it is necessary for the eye tracker to perceive both the eyes in order to maintain accurate gaze, the non-tested eye was covered with a polymethyl methacrylate (PMMA) blocker which allows only infrared rays to be transmitted. This allows monitoring of both eyes simultaneously by the gaze tracker without the stimuli on the screen being visible. Fig. 2 shows the testing setup of EMP.

Each measurement started with a nine-point calibration procedure, which involves following a circular blue colored stimulus which moves at 15 degree angle up, down, left, and right from the center of the display screen. This procedure is necessary to obtain accurate gaze data.

After calibration the test begins with a central fixation stimulus displayed on the center of the screen. Fifty-four points are tested in the visual field at four different contrast levels against the background illumination of 140 cd/m^2. Thus, the total number of points tested is 216. By using eccentric positions of the central target, the maximum visual angles were up to 27 degrees in horizontal and 21 degrees in vertical direction, a visual field of a total 54 × 42 degrees (horizontal × vertical) was tested.

At each location four similar stimuli varying in brightness levels were plotted: 70% brightness (150 cd/m^2), 80% brightness (162 cd/m^2), 90% brightness (175 cd/m^2), and 100% brightness (190 cd/m^2). These different levels are denoted as increasing contrast levels 0.7, 0.8, 0.9, and 1.0. The locations tested in EMP exactly resemble the visual location tested in 24-2 SITA standard strategy of automated HFA. Visual targets used during the test were of Goldmann size III (0.43 degrees angular diameter).

Subjects were asked to fixate at the central stimulus. Next, the peripheral stimuli were randomly presented one by one for a maximum duration of 1.2 s with a gap of 0.2 s between stimuli. The subjects were encouraged to look at each visual target on detection and then return back to the fixation target. Instructions were given to avoid searching for stimuli.

Saccadic responses at each of the 216 gaze data points of each subject were visually inspected and analyzed using customized software.

To analyze gaze data a decision algorithm was developed which classified each stimulus as 'seen' or 'not seen' depending on the eye movement pattern. This decision algorithm was based on a previously reported study on structural eye movement analysis.[8] An event was classified as 'unseen' if, during the presentation of the peripheral target, no eye movements were made towards the target or the first saccade was not in the direction of the target. The event was labeled as 'unknown' when no eye movement data were available due to blinking or pupil detection failure. Events where clear saccadic movements were made towards the presented visual target were considered as 'seen'. Fig. 3 shows eye movement pattern in Matlab window where eye movement starting in the center was made towards the peripheral target in the lower left field. For each 'seen' target the SRT was calculated as the time difference between stimulus presentation and the onset of the saccadic eye movement to the target. Fig. 4 illustrates calculation of SRT corresponding gaze velocity.

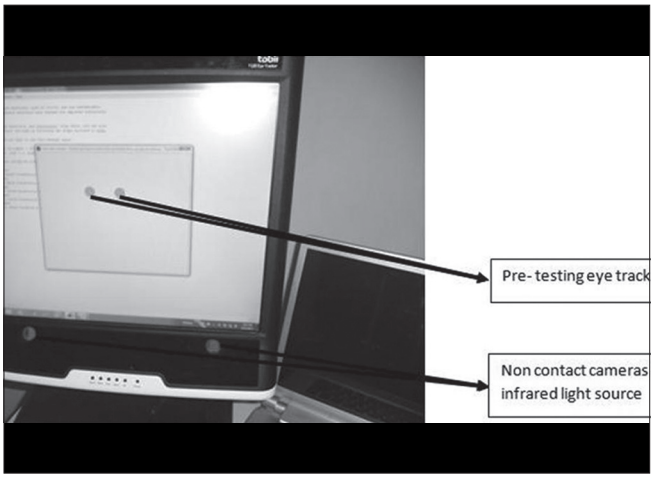

Figure 1: Eye movement perimeter display screen showing the tracking status for both eyes

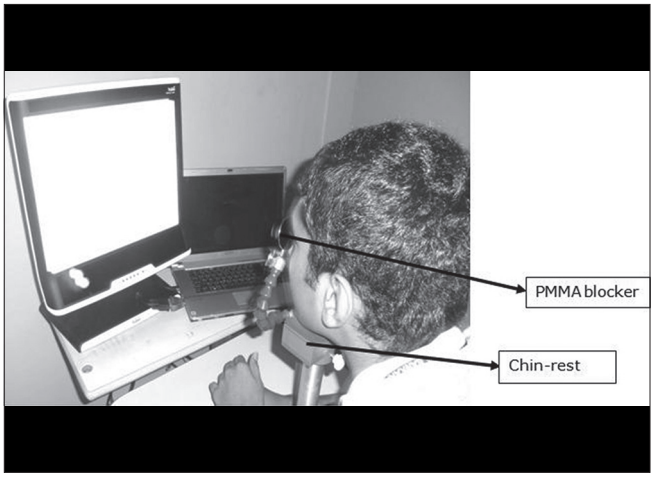

Figure 2: Eye movement perimeter setup used for the study

Statistical analysis was carried out with SPSS 15.0 version (Statistical Package for Social Sciences Inc) and MS Excel 2007. We used responses at Contrast Level 0.8 (162 cd/m^2) and only the right eye was considered for statistical analyses. SRT was converted to milliseconds. Since the SRT data was of wide range therefore for ease of analysis the data was transformed to $\log_{10}$. Tests for normality were carried out for each quantitative variable and appropriate parametric/nonparametric analyses were utilized. Type I error was kept at the 5% level.

The stimulus locations was clustered and divided into different zones considering equal distances from central stimulus. Calculating stimulus locations which are equidistant from the central fixation point eight zones were identified. Fig. 5 represents the zonal divisions of the tested field of vision.

Results

A total of 79 subjects were recruited in the study which included 54 normals and 25 glaucoma subjects. The demographic details of the subjects recruited are given in Table 1.

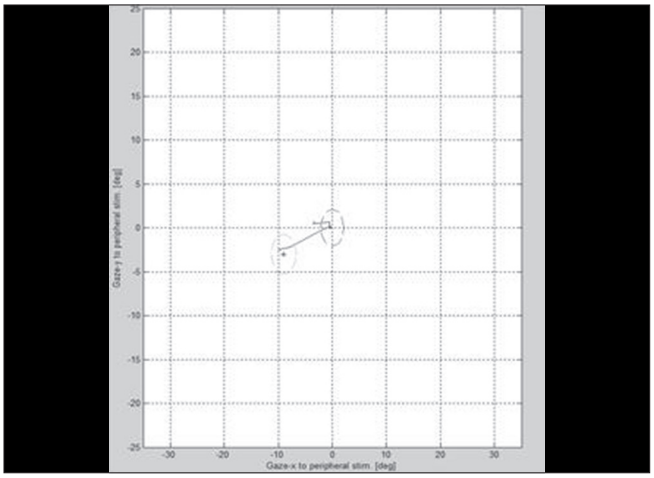

Figure 3: Eye movement pattern in a Matlab window where a saccadic eye movement was made from the center towards a peripheral target in the lower left field

Mean SRTs was found significantly longer in glaucomatous eye in each age cohort [Table 2].

When SRT's were was compared across each of the eight zones classified based on eccentricity the difference between normals and glaucoma was significant [Table 3 and Fig. 6] with glaucomatous eyes having longer SRT as compared to normal. A trend towards increasing SRTs with increasing disease severity was also noted when SRT was compared in mild, moderate, and severe glaucoma. This difference with increasing severity of glaucoma was also apparent for the different eccentricities [Fig. 7].

The EMP has been evaluated as a potential device to test for glaucomatous visual field damage in the past. Kim *et al*., had reported consistency of seen/unseen responses on EMP compared with SAP.[9] They reported good concordance in a group of nine subjects with glaucomatous field damage and 10 normals. Murray *et al*., studied the ability of EMP to detect visual field defects.[17] They tested locations based on the HFA C-40 test using a suprathreshold test strategy and reported excellent concordance with SAP suprathreshold results with the percentages of points in agreement ranged between 90 and 99%. In a pilot study Pel *et al*., (ARVO 2012, abstract no. 4812) showed that visual field sensitivity assessed with SAP correlated with visual field responsiveness assessed with EMP.[18]

SRTs have been reported to be altered in glaucoma. Lamirel *et al*., compared eight primary open angle glaucoma (POAG) and four normal controls.[14] They reported increased SRT values in glaucomatous eyes. However, points till only 7 degrees of eccentricity were tested. Kanjee *et al*., tested 16 glaucomatous and 21 normal eyes up to 10 degrees of eccentricity.[13] Median SRT values were significantly increased in glaucomatous eyes as well as a decrease in the number of express saccades in this group. In this report we found significantly increased SRT values compared to normal eyes. This was consistent across different eccentricities based on the HFA 24-2 test locations. This has important implications for EMP testing in glaucoma since detection of peripherally affected points is important for any perimetric test in glaucoma. SRT values also showed differences across different severity of glaucoma with increasing SRTs being seen with worsening glaucomatous severity. This is again consistent with Lamirel *et al*., who reported that SRT values

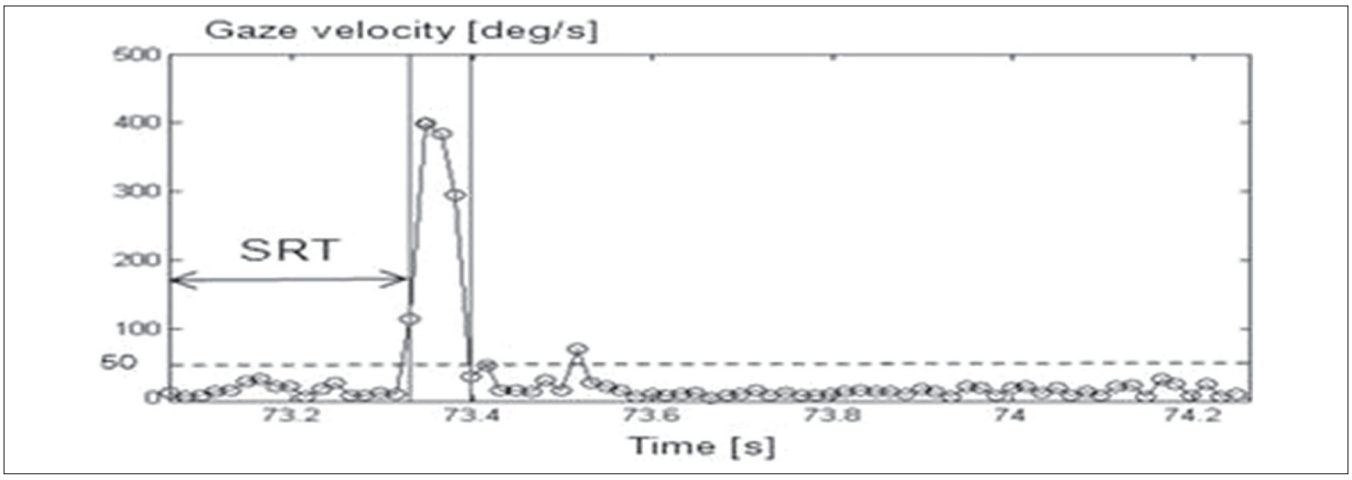

Figure 4: Measurement of saccadic reaction time from tracking data

were increased among moderate glaucoma as compared to those with pre-perimetric disease.

EMP allows natural ocular motor eye movements on perceiving of a stimulus and continuous monitoring of eye movements, which eliminates false positive calls and hence improving test precision. Kim *et al.*, reported that subjects reported alleviation of some of the stress and tedium associated with SAP. Our own (anecdotal) experience was the same with most subjects being more comfortable with EMP testing in spite of the increased testing times.

Since the entire range of thresholds on SAP cannot be reproduced using a single contrast level on EMP we tested at four contrast levels. For the purpose of this analysis only the 0.8 contrast level was used. While using all four contrast levels may help discriminate between small threshold variations even testing at a single contrast level could help discriminate between different severities of glaucoma.

Our study demonstrates that SRT values show significant differences in glaucomatous eyes. However, creation of age-specific normative databases will be required to classify individual locations as diseased. In addition test duration would have to be shortened and a wider threshold would

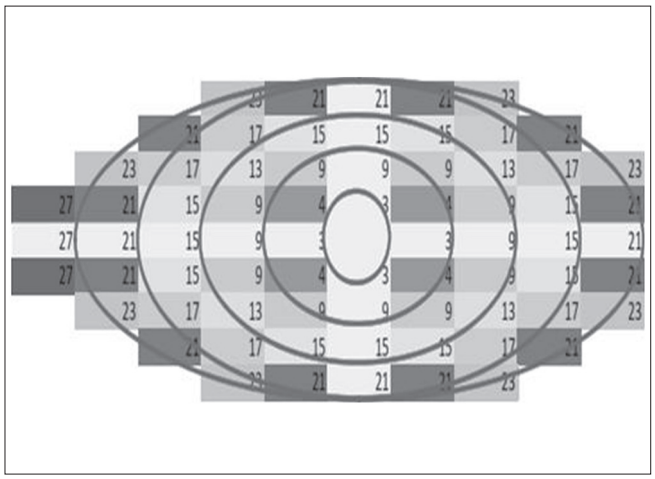

Figure 5: Division of tested points into eight zones equidistant from the center

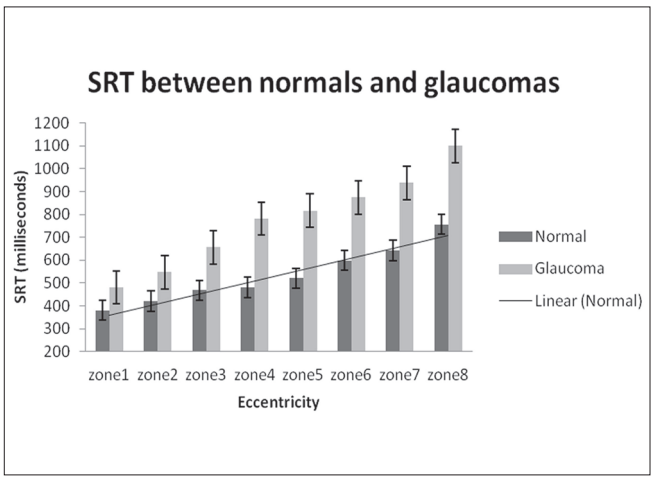

Figure 6: Comparison of saccadic reaction times between normal and glaucoma at varying eccentricities (mean, error bars show standard errors)

Table 1: Demographics of the study population

Subject characteristics	Normals (*n*=54)	Glaucoma (*n*=25)
Age range (in years)	30–70	30–70
Mean age (SD)	42.0±13.3	54.2±11.6
Gender (in percentage)	Male-53.52	Male-66.7
	Female-46.48	Female-33.30

SD: Standard deviation

Table 2: Global mean SRT between normal and glaucoma subjects

Age (in years)	SRT (mean±SD) (in milliseconds)		*P* value
	Normal	Glaucoma	
30-39	597±200 (18)	767±246 (11)	0.01
40-49	606±249 (16)	834±279 (6)	0.04
50 and above	674±288 (20)	934±307 (8)	0.02

SD: Standard deviation, SRT: Saccadic reaction time

Table 3: Mean SRT in normals and glaucoma in all eight zones for contrast level 0.8

Eccentricity	SRT (in milliseconds) in normal			SRT (in milliseconds) in glaucoma			*P* value
	Mean±SD	95% CI		Mean±SD	95% CI		
		Lower limit	Upper limit		Lower limit	Upper limit	
Zone 1	380±282	336	426	480±378	408	553	<0.001
Zone 2	420±269	395	445	546±377	496	597	0.04
Zone 3	467±268	436	500	656±361	608	705	<0.001
Zone 4	480±287	448	513	781±346	719	844	<0.001
Zone 5	520±238	492	549	816±345	770	862	<0.001
Zone 6	598±268	573	624	874±339	834	914	0.02
Zone 7	641±259	612	672	937±330	892	983	<0.001
Zone 8	756±288	692	822	1,100±242	1,053	1,147	<0.001

SD: Standard deviation, SRT: Saccadic reaction time, CI: Confidance interval

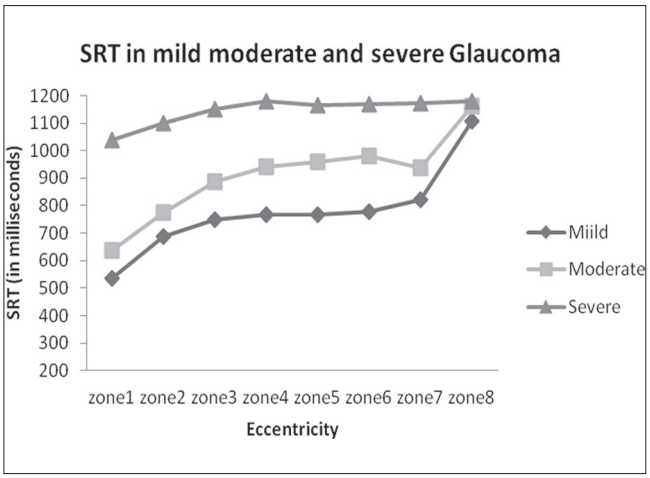

Figure 7: Mean SRT in mild, moderate, and severe glaucoma at different eccentricities

need to be tested for full comparison with SAP. While the test eliminates the need for testing for false positives an algorithm for testing false negatives would be required. Plotting visual field using reflexive eye movement might reduce the factors affecting visual field test results. SRTs in glaucoma provides one more parameter that can be suggestive of glaucomatous damage on perimetry.

SRTs are significantly increased in glaucoma subjects across the tested field of vision. This combined with the technique of test administration makes EMP a promising candidate for assessing visual field defects in glaucomatous eyes. Further studies are needed to collect a normative database for the test and to investigate the influence of contrast levels of the presented stimulus on SRT.

Acknowledgements

Authors thank the 'Department of Science and Technology, Government of India' [DST/INT/NL/Biomed/P (2)/2011(G)] and 'Netherlands Organization for Scientific Research' (NOW) for their financial support.

References

1. George Re, Ve RS, Vijaya L. Glaucoma in India: Estimated burden of disease. J Glaucoma 2010;19:391-7.
2. Bourne RR, Foster PJ, Bunce C, Peto T, Hitchings RA, Khaw PT, *et al*. The morphology of the optic nerve head in the Singaporean Chinese population (the Tanjong Pagar study): Part 1-Optic nerve head morphology. Br J Ophthalmol 2008;92:303-9.
3. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90:262-7.
4. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol 2002;86:238-42.
5. Toepfer A, Kasten E, Guenther T, Sabel BA. Perimetry while moving the eyes: Implications for the variability of visual field defects. J Neuroophthalmol 2008;28:308-19.
6. Heijl A, Lindgren G, Olsson J. The effect of perimetric experience in normal subjects. Arch Ophthalmol 1989;107:81-6.
7. Wild JM, Dengler-Harles M, Searle AE, O'Neill EC, Crews SJ. The influence of the learning effect on automated perimetry in patients with suspected glaucoma. Acta Ophthalmol (Copenh) 1989;67:537-45.
8. Jernigan ME. Structural analysis of eye movement response to visual field stimuli. Comput Biol Med 1980;10:11-22.
9. Kim DE, Eizenman M, Trope GE, Kranemann C. Eye movement perimetry. In Engineering in Medicine and Biology Society, IEEE 17th Annual Conference 1995;2:1629-30.
10. Trope GE, Eizenman M, Coyle E. Eye movement perimetry in glaucoma. Can J Ophtalmol 1989;24:197-9.
11. Brigell MG, Goodwin JA, Lorance R. Saccadic latency as a measure of afferent visual conduction. Invest Ophthalmol Vis Sci 1998;29:1331-8.
12. Reulen JP. Latency of visually evoked saccadic eye movements. I. Saccadic latency and the facilitation model. Biol Cybern 1984;50:251-62.
13. Kanjee R, Yücel YH, Steinbach MJ, González EG, Gupta N. Delayed saccadic eye movements in glaucoma. Eye 2012;4:63-8.
14. Lamirel C, Milea D, Cochereau I, Duong MH, Lorenceau J. Impaired Saccadic Eye Movement in Primary Open-angle Glaucoma. J Glaucoma 2014;23:23-32.
15. Chylack LT Jr, Leske MC, McCarthy D, Khu P, Kashiwagi T, Sperduto R. Lens opacities classification system II (LOCS II). Arch Ophthalmol 1989;107:991-7.
16. Hitchings RA, Spaeth GL. The optic disc in glaucoma. I: Classification. Br J Ophthalmol 1976;60:778-85.
17. Murray IC, Fleck BW, Brash HM, MacRae ME, Tan LL, Minns RA. Feasibility of saccadic vector optokinetic perimetry: A method of automated static perimetry for children using eye tracking. Ophthalmology 2009;116:2017-26.
18. Pel JJ, Vermeer KA, Van BM, Lemij HG, Van der Steen J. Correlation between reduced visual field sensitivity and saccadic reaction times. ARVO 2012.

Cite this article as: Mazumdar D, Pel JM, Panday M, Asokan R, Vijaya L, Shantha B, *et al*. Comparison of saccadic reaction time between normal and glaucoma using an eye movement perimeter. Indian J Ophthalmol 2014;62:55-9.

Source of Support: Nil. **Conflict of Interest:** None declared.