• Clinical Research •

Validity of autorefractor based screening method for irregular astigmatism compared to the corneal topography- a cross sectional study

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Abstract

● AIM: To present a method of screening for irregular astigmatism with an autorefractor and its determinants compared to corneal topography.

● METHODS: This cross-sectional validity study was conducted in 2013 at an eye hospital in Spain. A tabletop autorefractor (test 1) was used to measure the refractive status of the anterior surface of the cornea at two corneal meridians of each eye. Then corneal topography (test 2) and Bogan's classification was used to group eyes into those with regular or no astigmatism (GRI) and irregular astigmatism (GRII). Test 1 provided a single absolute value for the greatest cylinder difference (Vr). The receiver operating characteristic (ROC) were plotted for the Vr values measured by test 1 for GRI and GRII eyes. On the basis a Vr value of 1.25 D as cut off, sensitivity, specificity were also calculated.

● RESULTS: The study sample was comprised of 260 eyes (135 patients). The prevalence of irregular astigmatism was 42% [95% confidence interval (CI): 36, 48]. Based on test 2, there were 151 eyes in GRI and 109 eyes in GRII. The median Vr was 0.75 D (25% quartile, 0.5 D) for GRI and 1.75 D (25% quartile, 1.25 D) for GRII. The area under curve was 0.171 for GRI and 0.83 for GRII. The sensitivity of test I was 78.1% and the specificity was 76.1%.

● CONCLUSION: A conventional autorefractor can be effective as a first level screening method to detect irregular corneal astigmatism in places where corneal topography facilities are not available.

● KEYWORDS: screening; irregular astigmatism; autorefractor; corneal topography; cornea; validity

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INTRODUCTION

The volume of refractive surgery has steadily increased over time. Hence, detection and management of irregular astigmatism has become crucial for improving outcomes and for patient satisfaction. However, as the volume of refractive surgery increased over the last 2-3 decades, a diagnosis of irregular astigmatism has become more common[1-2]. Additionally, better detection of irregular corneas has become paramount for modern cataract surgery.

Prior to the introduction of corneal topography, irregular astigmatism was diagnosed with scissors movement on retinoscopy and/or deformation of the mires during manual keratometry[2]. However, a keratometer only provides a crude, qualitative measure of irregular astigmatism, subjectively judged by distortion of the mires[3]. Although keratometry provides information on corneal image forming properties, such as corneal astigmatism, it is inaccurate for irregular astigmatism. Irregular astigmatism can also be suspected in cases with impaired vision that is corrected by placement of rigid contact lenses[2]. However, rigid contact lens fitting causes patient discomfort and involves significant patient chair time precluding its use as a diagnostic test for irregular astigmatism. Proper placement of a pinhole to align with the visual axis can yield accurate visual acuity. However, this is a subjective test that precludes diagnosis of peripheral irregularities and

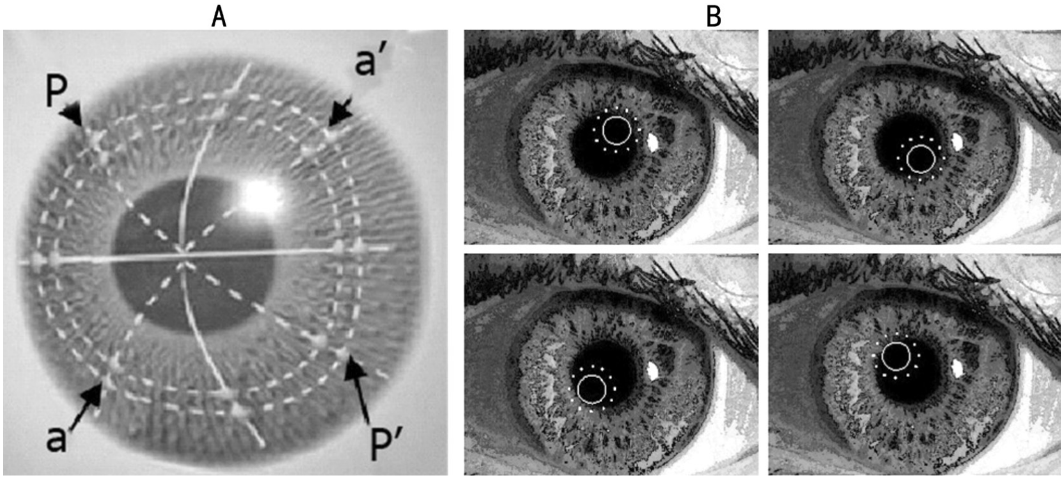

Figure 1 Schematic drawing of test 1 methods A: Each meridian of a cornea formed of two semi-meridians symmetrical from the optical axis, any two points *P* and *P'* of these semi-meridians located at the same distance from the corneal apex has the same curvature; B: Four measurements were performed within the pupillary area near the iris sphincter at 45°, 135°, 225° and 315° meridians.

is influenced by other conditions such as retinal damage and cataracts[4].

Corneal topography provides the most comprehensive information on corneal regularity and curvature for the diagnosis of irregular astigmatism[3,5-8]. However, availability, cost and the ability to interpret the outcomes is a challenge in all ophthalmic clinics. A tabletop autorefractors is available in most ophthalmic and optometric clinics. Autorefractors acquire measurements rapidly and are patient friendly to use compared to topography[9-10]. The aim of this study is to validate a quantitative test for irregular astigmatism using an autorefractor compared to conventional topography.

SUBJECTS AND METHODS

This was a non-randomized, cross sectional study of consecutive patients who presented to a public general ophthalmology outpatient clinic in Valladolid, from January to December 2013. This study adhered to the tenets of the Declaration of Helsinki. Patients were included after informed consent was obtained. Patients were excluded if they had mental or physical disability, uncooperative, history of recent ocular surgery, corneal scars or acute ocular pathology at examination.

All patients were first examined by an ophthalmologist before being sent for consultation to an optometrist to ensure that patients met the inclusion criteria and could be enrolled in the study. Patients' data were collected on demographics such as age, gender and laterality of the condition and the distance visual acuity with and without spectacles. Distance vision was tested monocularly using a Snellen illiterate E visual acuity chart held at 6 m distance. An optometrist performed dynamic refraction for each eye without pharmacologic cycloplegia.

Methods to Detect Irregular Astigmatism Test 1: Astigmatism evaluation using an objective asymmetric refractometer was performed with a tabletop autorefractor (Canon R-20; Canon Inc., Tokyo, Japan) to determine the refractive status of anterior surface of the cornea in two meridians that pass through the pupil. *P* and *P′* are symmetrical points located at opposite ends of a symmetric corneal parallel. Stated differently, *P* and *P′* are diametric opposite ends of an ellipse, hence, both have the same curvature as the parallel. Consequently, if two symmetrical points of a cornea have the same radius as the meridian and also the same radius as the parallel, its astigmatism will be regular.

Four measurements were performed within the pupillary area near the iris sphincter at 45°, 135°, 225° and 315° meridians (Figure 1). All measurements were obtained by an experienced operator using the same machine and procedure. Subjects were instructed to look at an optically distant target displayed in the autorefractor and keep their eyes wide open during this measurement. All refractions were noted in negative cylinder notation. The readings were recorded, 1-2s after a blink. Average values of the refraction measurements were printed from the auto refractor and were recorded using an absolute magnitude of cylinder notation.

At the 45° meridian, we performed measurements number 1 and 3 (45º and 225º). We termed this V_{45} which was the absolute value of the difference between the first measurement of astigmatism (Cyl_1_{45}) and the third (Cyl_3_{225}) so that $V_{45}=Cyl\_1_{45}-Cyl\_3_{225}$.

At the 135º meridian, we performed measurements number 2 and 4 (135º and 315°). This was termed V_{135}, the absolute value of the difference between the astigmatism of the second measurement (Cyl_2_{135}) and the fourth (Cyl_4_{315}) so that $V_{135}=Cyl\_2_{135}-Cyl\_4_{315}$.

We choose the highest absolute value between V_{45} and V_{135} and termed it Vr. Vr designated the greater asymmetry in the cornea. To obtain a cut-off value, all the Vr values were compared to our topographic classification.

Table 1 Comparison of corneal topography measurements in eyes with and without irregular astigmatism

Topography parameters	Group I (*n*=151)		Group II (*n*=109)		χ^2	*P*
	Median	25% quartile	Median	25% quartile		
V_{45}	0.5	0.25	1.0	0.5	50.8	<0.001
V_{135}	0.5	0.25	1.25	0.5	41.0	<0.001
Vr	0.75	0.5	1.75	1.25	83.5	<0.001

Vr: Greatest cylinder value in two diagonal meridians if it is equal to or greater, suggests irregular astigmatism. *P*<0.05 is statistically significant.

Example for right eye (OD): 1) measurements with refractometer in OD; measure at 45º=-1, -1×45º, measure at 225º=-0.5, -1×225º, measure at 135º=1, -0.5×135º, measure at 315º=-0.5, -2×315º; 2) then we have the absolute value of the cylinder value of each meridian, getting Cyl_{45}=1, Cyl_{225}=1, Cyl_{135}=0.5, Cyl_{315}=2; 3) calculate V_{45}=0, V_{135}=-1.5; 4) calculate Vr, we choose the highest absolute value between V_{45} and V_{135}.

Test 2 (gold standard): corneal topography was performed using EyeSys Windows WorkStation V.2 software topographer (EyeSys Technologies, Houston, TX, USA). This video keratoscope is based on Placido disk corneal topography, where a patient's cornea is illuminated by concentricrings, which create an image that is reflected by the anterior surface of the cornea. The reflected image is computer analyzed, and a color-coded curvature map of the corneal surface is generated[8]. Only topographic images that were well aligned and well focused were selected for evaluation.

The eyes were separated into two groups, based on the corneal topography classification: group I [regular or no astigmatism (GRI)] including eyes with normal or regular astigmatism (round or oval and symmetric pattern); and group II [irregular astigmatism (GRII)], containing eyes with irregular astigmatism (irregular and unclassified) considering asymmetric topographic images[11]. Eyes were qualitatively classified based on Bogan's recommendations[11].

To minimize variation in the results, all measurements were performed between 9 a.m. and 2 p.m. The examiner and participants were masked to the results of the previous measurements obtained from each device. Participants were instructed to blink completely just before each measurement. They were asked to sit back after each repeat measurement, and the device was realigned before each measurement.

Statistical Analysis Statistical analysis was performed using Statistical Package for Social Studies (SPSS 22.0) (IBM Corp., New York, NY, USA). We calculated frequencies and percentage proportions for categorical variables. The distribution of continuous variables was evaluated. If the distribution was normal, we calculated the mean and standard deviation (SD). If they were not normally distributed, we calculated median and 25% quartiles. We used a non-parametric method for comparing the continuous outcome variable (Vr) in GRI and GRII. Two sided Kruskal-Wallis *P* values were estimated for validity of outcomes.

The validity of autorefractors in defining irregular astigmatism in both GRI and GRII was compared to that found by corneal topography was performed using the receiver operator characteristic (ROC) curve. The results of this analysis was used to determine the diagnostic cut-off points (Vr=1.25 D) to determine the overall predictive accuracy of the test as described by the area under the curve (AUC). These curves are obtained by plotting sensitivity against 1-specificity, calculated for each value observed. An area of 100% implies that the test perfectly discriminates between groups. We also used this approach to calculate specificity, sensitivity, and positive [sensitivity/(1-specificity)] and negative [(1-sensitivity)/specificity] likelihood ratios (LR) for cut-off points of irregular astigmatism selected *a priori*, and to identify irregular astigmatism cut-off points that maximized sensitivity and specificity in discriminating irregular astigmatism.

The validity parameters were sensitivity, specificity, positive predictive value, negative predictive value and prevalence of irregular astigmatism. The 95% confidence interval (CI) of the validity parameters was also calculated. *P*<0.05 was considered statistically significant.

RESULTS

The study sample was comprised of 260 eyes of 135 participants. There were 58 (43%) males and 77 (57%) females. The median age of participants was 35.5y (25% quartile, 25y). There were 132 (50.8%) right eyes and 128 (49.2%) left eyes.

Based on the Bogan *et al*[11] corneal topography classification, 151 (58%) eyes had no astigmatism or regular astigmatism (GRI) and 109 (42%) eyes had irregular astigmatism (GRII).

Comparison of autorefractor measurements in eyes with and without irregular astigmatism is presented in Table 1. The Vr values were significantly higher in GRII compared to GRI. The ROC of GRI and GRII is presented in Figure 2. The AUC in GRI and GRII were 0.17 and 0.83 respectively.

The validity parameters for test 1 were estimated by comparing the presence and absence of irregular astigmatism as defined by test 2. Irregular astigmatism was defined as a Vr value greater than 1.25 D. The sensitivity, specificity, positive predictive value, negative predictive value were calculated using standard formulas (Table 2).

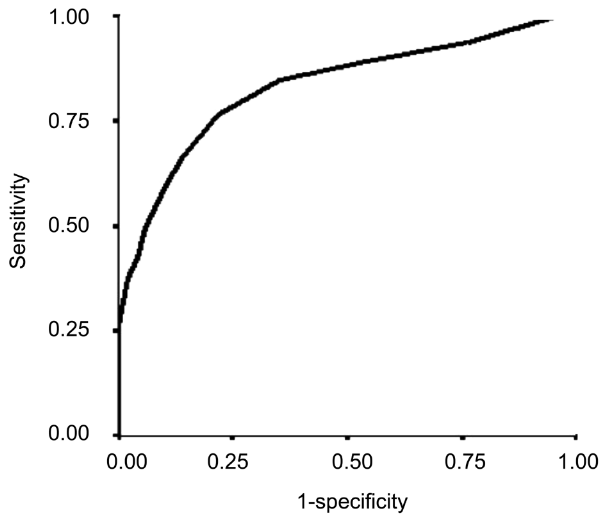

Figure 2 Area of ROC curve (graphical plot of the sensitivity *vs* 1-specificity) for astigmatism The cut-off was Vr 1.25 D, with 78.1% sensitivity and 76.1% specificity.

Table 2 Validity of astigmatism screening by an autorefractor compared to corneal topography

Diagnosis of irregular astigmatism		Topography based Irregular	Topography based Regular	Total patients
Autorefractor based	Irregular	118	26	144
	Regular	33	83	116
Total patients		151	109	260

Sensitivity: 118/151×100%=78.1% (95% CI 73.1, 83.1); Specificity: 83/109×100%=76.1% (95% CI 71.0, 81.3); False positives: 26/144×100%=18.1% (95% CI 13.4, 22.7); False negatives: 33/116×100%=28.4% (95% CI 23.0, 33.9); Positive predictive value: 118/144×100%=81.9% (95% CI 77.3, 86.6); Negative predictive value: 83/116×100%=71.6% (95% CI 66.1, 77.0); Prevalence of irregular astigmatism: 151/260×100%=58.1% (95% CI 52.1, 64.1).

We also studied the influence of age-group, gender and the eye involved on the validity parameters such as sensitivity and specificity of autorefractor screening (test 1) for irregular astigmatism (Table 3). Age group was statistically significantly positively associated to specificity (P<0.001) and negatively associated to sensitivity (P=0.006). However female gender (P=0.008) and left eyes (P=0.05) had statistically significantly higher specificities compared to males and right eyes.

DISCUSSION

This study is unique as it attempted to evaluate the utility and reliability of an autorefractor, a commonly available diagnostic tool for basic refractive examination, as a method for screening irregular astigmatism. Autorefractors are inexpensive and routinely used in most clinics. The purpose of our investigation was to show that it can be use in triage to identify patients who require corneal topography to confirm the diagnosis of irregular astigmatism and further management. Astigmatism is a clinically important condition and accounts for about 13% of the refractive errors of the human eye[12]. The prevalence

Table 3 Variation in validity parameters of greatest cylinder value in two diagonal meridians by an autorefractor compared to topography by determinants

Determinants	Sensitivity (%)	Validation (two sided P)	Specificity (%)	Validation (two sided P)
Gender		0.11		0.008
M	82.8		68.1	
F	74.7		82.3	
Eye involved		0.9		0.05
Right	77.9		70.9	
Left	78.4		81.5	
Age group (a)		0.06		<0.001
<20	89.3		50.0	
20 to 39	77.0		67.3	
40 and more	74.2		87.0	

P<0.05 is statistically significant.

of astigmatism (considered cylinder <-1.0 D) varies based on the population studied, from 3.8%[13] in Finland to 44.2% in Koreans[14-17].

Astigmatism greater than 1 D cylinder represent significant irregularity[2,13-14]. In general, irregular astigmatism has been considered an uncommon refractive error. However, after the introduction of corneal topography, the prevalence is reported to be as high as 40%[2]. The prevalence of astigmatism (Cyl≥1.00 D) has been reported in Native American (42%)[18] and Chinese (53%)[19] school children. In our participants 42% had irregular astigmatism but the current study was done using a not randomized population sample and data were based on a convenience sample, composed of individuals who spontaneously requested ophthalmic treatment. Hence the prevalence of astigmatism reported in this study must be interpreted with caution. The high prevalence could be because our ophthalmic clinic is known in the region for its expertise in dealing with keratoconus patients and referral bias may play a role.

In our study there was no association between irregular astigmatism and gender. This result need to be seen with caution since our sample had enrolled more females. However, it remains unclear if gender is determinant in the astigmatism prevalence[20-22] or the preponderance of keratoconus[23-24]. Mainly young patients (below 20y) had high corneal astigmatism that decreased with age[14]. The mean at diagnosis for irregular astigmatism ranged from 2y to 24.05y[20, 25-26].

We elected to study Vr, based on each meridian formed by two semi-meridians symmetrical to the optical axis. These are two points, P and P' of these semi-meridians located at the same distance from the corneal apex and have the same curvature. In a normal cornea all meridians are elliptical curves and the curvature of the meridian varies in a mathematically predictable manner as the distance from the corneal center increases[27]. Additionally, all parallel meridians of a normal cornea are ellipses. In each parallel meridian, the curvature varies according to a mathematical rule between a maximum and a minimum in a sinusoidal fashion with a cycle of 180º[27]. For irregular astigmatism, it is highly unlikely that the radii of curvature of the meridian and the parallel of these two symmetrical points are equal, so we can assume the pairs of symmetric points of a cornea with irregular astigmatism do not have the same astigmatism. As expected, the Vr value in our sample was significantly higher in GRII, the group with irregular astigmatism. GRII had significant differences in cylinder in different point of the cornea, designated by the greater asymmetry in the cornea.

Both eyes had similar Vr enantiomorphism of corneal topographic parameters among fellow eyes has been recently reported[28]. However, we found that Vr was higher in left eyes compared to right eyes. Besides the statistical difference, we cannot explain this observation.

The overall predictive accuracy of Vr, as described by the area under the ROC curve (AROC), was high in GRII (0.83) with values >0.9[29]. Some have reported AROC values of topography-based keratoconus are 0.91[30].

Hence, test 1 with Vr was effective for the screening for irregular astigmatism. The cut-off point of Vr 1.25 D showed high sensitivity and specificity (78.1% and 76.1%, respectively). Lower values for AROC have been reported with other topographic indices derived from Placido disk-based video keratography[31-32], optical coherence tomography pachymetry mapping[30], quantitative analysis of iris parameters using optical coherence tomography[33]. In contrast, our test 1 Vr obtained higher AROC values than Fontes *et al*[34] who compared corneal hysteresis and corneal resistance factor in normal corneas and in mild keratoconus.

Although 42% of our study sample had irregular astigmatism, the sensitivity and specificity of the autorefractor test to screen for irregular astigmatism was less than desired.

Unlike Vr, which derives from a single data, most topographic indices derived from Placido disk-based video keratography include multiple parameters, require integration of the data into a decision-making process, such as neural network or automated decision-tree classification or are based on a more sophisticated polynomial analysis[31,35]. This makes our test 1 a very accessible and easy test to perform.

Since this is the only keratometric methods analyzed with AROC, we are unable to compare our study with others. We found age was positively associated to specificity and negatively associated to sensitivity. However female gender and left eyes had significantly higher specificities compared to those of males and right eyes.

Our suggested method is an objective method and there are only a few other objective methods to determine astigmatism[36-39]. Conventional manual, automated keratometers and automatized wavefront measure refraction and anterior corneal curvature[3,40]. However, it was already documented that automatized kerato-refractometer and wavefront under cycloplegia had similar numerical values[41].

The multimeridional keratometry test assess the anterior corneal curvature using standard clinical keratometry technique[36-39]. The two principal meridians are identified and measurements are performed along these meridians[36-39]. However, we believe that in cases with corneal irregularities the steepest and flattest meridians may be impossible to identify. Similar results were obtained by Karabatsas *et al*[42] who evaluated the agreement between the auto-keratometer and corneal topographer devices in highly astigmatic corneas. They found that the two devices showed poor agreement between measurements of corneal astigmatism and axis location, possibly due to an irregular corneal surface[43]. Roh *et al*[3] demonstrated that corneal irregularities significantly impact the assessment of astigmatism with the classic auto-keratometer.

The reliability of astigmatism measurement by the automated keratometry function of the IOLMaster (Carl Zeiss AG, Oberkochen, Germany) is controversial. Shammas and Chan[44] reported that the precision of astigmatism measurements by the IOLMaster was relatively lower for steeper corneas and the difference in corneal astigmatism measurements between IOLMaster and another automated keratometer can increase more in corneas with an asymmetric bowtie pattern than in corneas with a symmetric bowtie pattern[45].

In contrast, our method is an objective quantitative method, which is quick, easy and reliable for screening for irregular astigmatism. We obtained a Vr value which designated the greater asymmetry in the cornea, by only using an autorefractor.

This new proposed method is adequate for primary screening but has some limitations. To perform test 1 correctly, the autorefractor should be directed exactly on 2 pairs of symmetrical points on the cornea in the same meridian. However, we recognize that in practice, perfect symmetry is difficult to achieve. Therefore, we accept that the points can be similar distances from the center of the cornea in the same meridian.

As a consequence of the difficulty in measuring at perfectly symmetric points in the same meridian, applying test 1 to corneas with irregular astigmatism, the possible error will be added or subtracted to the actual differences that may exist. However, this error also exists in corneal topographers, as it is impossible to take two topographies that are precisely aligned[46]. We assume that repeatability of irregularity measurements is worse in eyes with keratoconus than in normal eyes, with any diagnostic technique[5,47-48].

Another limitation of test 1 is the area where the measurement is taken from is the spontaneous papillary area. We concede that the points P and P' are at a distance which may be different for each patient, as the pupil size during refractometry depends on the age of the subject, refractometer light, and accommodation. Nevertheless, we estimate that normal room light during refractometry scanning affects the peripheral aspects of the eye and represent a very small stimulus to miosis.

In conclusion, test 1 is not designed to compete with the topographer. It offers the possibility of a likely diagnosis applicable to all patients presenting to a general ophthalmology clinic. Our method permits the identification of cases suspicious for irregular astigmatism and those should undergo corneal topography. Hence this is a screening tool for patients who require further workup. This optimizes the use of the corneal topographer and allows for greater clinical efficiency.

Although it cannot be concluded from this study that Vr is sufficient alone as a single diagnostic index, it does seem to be very effective in discriminating irregular from regular astigmatism. Thus data concerning Vr >1.25 D should be combined with curvature data in stratifying patients with this condition.

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