RESEARCH ARTICLE

Delicate balance: the relationship between internal astigmatism and lens astigmatism [version 1; peer review: 2 not approved]

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V1 First published: 01 Jul 2021, 10:527
<https://doi.org/10.12688/f1000research.54045.1>
 Latest published: 20 Sep 2021, 10:527
<https://doi.org/10.12688/f1000research.54045.2>

Abstract

Background: Due to lack of equipment for directly measuring crystal morphology, there has been little research on crystal astigmatism. The purpose of this study was to accurately explore the correlation between internal astigmatism and lens astigmatism in patients with ametropia.

Methods: This is a cross-sectional study conducted in the Affiliated Hospital of North Sichuan Medical College, China, in September 2020. Diopter values (refractive astigmatism, RA) of patients with ametropia was recorded, and the corneal and lens biological parameters were measured by CASIA2 (corneal/anterior segment optical correlation tomography analyzer). Biometric parameters, including the total corneal astigmatism (TCA), anterior and posterior curvature radius of the lens (ACL, PCL), internal astigmatism (IA), anterior and posterior astigmatism of the lens (AAL, PAL) were measured. Grouping and comparisons were made according to gender and age.

Results: In total, 151 participants (293 eyes) were included in the analysis. There were significant ($P < 0.05$) differences in the IA ($Z = -2.194$, $P = 0.028$) according to gender, but not in the other parameters. By age group, there were statistically significant differences in the TCA ($H = 10.609$, $P = 0.005$), IA ($F = 3.722$, $P = 0.025$), and PAL ($H = 8.254$, $P = 0.016$), but not in the others. The IA was positively correlated with the age ($r = 0.155$, $P = 0.008$), RA ($r = 0.534$, $P < 0.001$), AAL ($r = 0.308$, $P < 0.001$), and was negatively correlated with the TCA ($r = -0.244$, $P < 0.001$). The regression equation between the IA and AAL was: $Y(\text{IA}) = -0.626 + 0.447 X(\text{AAL})$.

Conclusions: There is a delicate balance between internal astigmatism and intraocular astigmatism. There were no significant

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Approval Status ? X

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version 1 01 Jul 2021	 view	 view

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Any reports and responses or comments on the article can be found at the end of the article.

differences in the other parameters except IA for different gender groups. For different ages, there are symbol differences in the TCA, IA and PAL, but not in the other parameters. In the analysis of IA with lens astigmatism, it was found that internal astigmatism was mainly related to AAL, but not to PAL.

Keywords

Astigmatism, Internal astigmatism, Lens astigmatism, Corneal astigmatism, Refractive error

This article is included in the **Eye Health** gateway.

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Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Liu M, Dai C, Zhou G *et al.* **Delicate balance: the relationship between internal astigmatism and lens astigmatism [version 1; peer review: 2 not approved]** F1000Research 2021, 10:527 <https://doi.org/10.12688/f1000research.54045.1>

First published: 01 Jul 2021, 10:527 <https://doi.org/10.12688/f1000research.54045.1>

Introduction

Astigmatism is the most common refractive error in the world, which may come from congenital or acquired factors¹. Astigmatism can change from birth, and its development is influenced by many factors such as heredity, extraocular muscle tension, visual feedback and eyelid pressure². According to World Health Organisation (WHO) statistics in 2018, the prevalence rates of astigmatism in children and adults are 14.9% and 40.4%, respectively³. Similarly, studies have found that 47% of cataract patients suffer from astigmatism ≥ 1 degree⁴. Uncorrected ametropia is the second leading cause of blindness in the world, and astigmatism is a major factor that damages human vision⁵. At present, we have a clear understanding of the detection of refractive astigmatism and corneal astigmatism, but due to the lack of methods to observe crystal morphology, there are few studies on lens astigmatism. The CASIA2 (Tomey Corp., Nagoya, Japan) system is a new type of anterior segment scanner. This novel device can provide accurate measurement of anterior segment parameters, and has good repeatability and reproducibility^{6,7}. Based on the advantages of the CASIA2 system, this paper combines corneal and lens parameters and optometry data to analyze the correlation between internal astigmatism and lens astigmatism.

Methods

Subjects

All the subjects were ametropia patients who came to the Affiliated Hospital of North Sichuan Medical College naturally. The experimenter (Meng Liu) explained this study and examined it with the permission of the patients. Since this research does not infringe on any rights and interests of patients, it can be conducted with the authorization of the Ethics Committee of North Sichuan Medical College. In order to reduce bias, we carefully screened the subjects. All patients had simple ametropia. Patients with organic diseases, such as those affecting the ocular surface and fundus, and patients who had undergone operations affecting refraction, the ocular surface or the fundus in the past were excluded.

Ethical considerations

Written informed consent was provided by the patient or their family/guardian if under the age of 18 years. As this study is an extended retrospective study of relevant prospective approved studies⁸ [approval number 2020ER(A) 068] and does not harm the interests of patients, it received an exemption by the Ethics Committee of North Sichuan Medical College.

Procedure

Biometric parameters of the lens were measured by the same experimenter (ML). An ARK-510A autorefractor (NIDEK, Co.,

Ltd, Gamagori, Japan) and DK-700 optometry system (Topcon, Japan) were used to perform standardized optometry, and the CASIA2 system (Tomey Corp., Nagoya, Japan) was applied to obtain other measurements.

Outcome parameters

Outcome parameters included the following: (1) Sex and age; (2) RA: The refractive astigmatism obtained by optometry; (3) TCA, ACL and PCL directly recorded by the CASIA2 system; (4) IA calculated by RA minus TCA; (5) AAL, PAL: Convert radius of curvature to curvature by formula⁹

$(\emptyset = \frac{n' - n}{r})$, $\emptyset$ = curvature; n' = Exit square refractive index; n = Incident square refractive index; r = the radius of curvature). The default refractive index of CASIA2 crystal is 1.4085, and the refractive index of aqueous humor is 1.336. The radius of the anterior and posterior curvature of the lens can be obtained directly from CASIA2.

Statistical analysis

The sample size was estimated by Stata 16.0 software. The test efficiency $\beta = 0.1$, $\alpha = 0.05$, bilateral test, and the correlation coefficient is 0.3. The calculated sample size is estimated to be 112. SPSS 25.0 statistical software was used for analysis. All data were first tested by the Kolmogorov-Smirnov (K-S) goodness-of-fit normality test before comparisons. Data with a normal distribution were compared using a paired sample t test or ANOVA analysis. If the distribution was not normal, a nonparametric test was used for comparison. In the correlation analysis (Internal astigmatism with Age, Refractive astigmatism, Total corneal astigmatism, Anterior astigmatism of the lens, Posterior astigmatism of the lens), data with a normal distribution are presented as the mean $\pm$ standard deviation ($\bar{X} \pm S$), a Pearson correlation analysis was applied, and a scatter plot was used to describe the correlation. If the data did not conform to a normal distribution, the median $\pm$ quartile spacing ($M \pm Q$) was used, and a Spearman correlation analysis was carried out. Multivariate linear regression analysis was performed for parameters with multiple correlations. $P < 0.05$ was considered to indicate statistical significance.

Results

Participants

This was a cross-sectional study of 151 patients (293 eyes, 77 males and 74 females), including 93 patients with 179 eyes aged 4–12 years, 17 patients with 32 eyes aged 13–18 years and 41 patients with 82 eyes aged 19–40 years²⁶.

Comparison of all parameters by gender

Table 1 shows the comparison results of all parameters grouped by gender. It can be seen that there is no statistical difference in other parameters except IA ($Z=-2.194$, $P=0.028$).

Comparison of all parameters by age

Comparison of all parameters by age group is shown in Table 2. It can be seen that there are statistically significant differences in TCA ($H=10.609$, $P=0.005$), IA ($F=3.722$, $P=0.025$), and PAL ($H=8.254$, $P=0.016$), and others have no statistically significant differences.

Correlation analysis between internal astigmatism and lens astigmatism

After K-S test, the IA and the AAL showed normal distribution, so Pearson correlation analysis was used to analyze the correlation between them. Other parameters had non-normal distribution, so Spearman correlation analysis was used, and the results are shown in Table 3.

The IA was positively correlated with the age ($r=0.155$, $P=0.008$), RA ($r=0.534$, $P<0.001$), and was negatively correlated with the TCA ($r=-0.244$, $P<0.001$). It can be seen that in the correlation analysis between IA and lens astigmatism, IA was positively correlated with AAL ($r=0.308$, $P<0.001$), but not with other lens astigmatism parameters. Therefore, for the regression analysis of IA and AAL, the regression equation is $Y(IA) = -0.626 + 0.447 X(AAL)$ ($F=30.461$, $P<0.001$, $R^2=0.095$) (Figure 1).

Discussion

The types of astigmatism in human eyes include refractive astigmatism, corneal astigmatism, internal astigmatism and lens astigmatism. Internal astigmatism compensates for corneal

astigmatism from birth, but the efficiency of its decreases with age¹⁰. The active compensation between corneal astigmatism and internal astigmatism in childhood helps maintain refractive stability, which is mainly due to the high convergence of the wavefront incident on the lens due to corneal refraction^{11,12}. However, due to the lack of precise equipment for observing anterior segment, the relationship between internal astigmatism and lens is still controversial. For instance, one study found that internal astigmatism gradually increases with age, and it mainly comes from lens¹³. Nevertheless, some studies believe that the prevalence rate of astigmatism increases with age, and the refractive and corneal astigmatism shift to ATR (against-the-rule). But the continuous corneal changes seem to be the cause of the age trend of refractive astigmatism, and the severity of lens opacity plays a small role in the change of internal astigmatism¹⁴. Therefore, based on the advantages of the CASIA2 system, this paper comprehensively analyzed the correlation between internal astigmatism and lens astigmatism by combining corneal and lens parameters. Inevitably, our research also has certain limitations. Because of the complexity and instability of astigmatism, this study only analyzed the power of astigmatism, but did not involve the axial direction. However, through this article, we have made clear the quantitative relationship between internal astigmatism and lens astigmatism, and lens astigmatism mainly comes from the anterior surface of the lens. This can provide reference and ideas for more accurate research on astigmatism.

According to gender, there were statistical differences in internal astigmatism, which were lower in boys than girls, but not in other parameters. Li *et al.*¹⁵ found that corneal astigmatism and internal astigmatism seemed to be higher in girls than in boys. Similarly, Liu *et al.*¹⁰ also found that girls had greater internal astigmatism than boys. This may be due to the fact that

Table 1. Comparison of all parameters by gender.

Gender(eyes)	Age (M±Q)	RA (M±Q)	TCA (M±Q)	IA (M±Q)	AAL (M±Q)	PAL (M±Q)
Male(149)	12±12	0.50±0.75	0.95±0.74	-0.27±0.50	0.69±0.36	0.95±0.85
Female(144)	11.00±12	0.50±0.50	0.98±0.65	-0.41±0.57	0.67±0.48	0.88±0.74
Z/P	-0.028/0.977	-1.744/0.081	-0.553/0.58	-2.194/0.028*	-0.581/0.561	-1.935/0.053

* indicates that the comparison is statistically significant. RA: refractive astigmatism; TCA: total corneal astigmatism; IA: internal astigmatism; AAL: anterior astigmatism of the lens; PAL: posterior astigmatism of the lens.

Table 2. Comparison of all parameters by age.

Years(eyes)	RA (M±Q)	TCA (X±S/M±Q)	IA (±S)	AAL (X±S/M±Q)	PAL (M±Q)
≤12(179)	0.50±0.50	0.99±0.60	-0.35±0.04	0.69±0.02	0.94±0.77
13–18(32)	0.75±0.50	1.06±0.07	-0.35±0.04	0.68±0.04	1.15±0.99
≥19(82)	0.50±0.75	0.80±0.73	-0.19±0.05	0.70±0.45	0.80±0.87
P	0.256	0.005*	0.025*	0.713	0.016*

* indicates that the comparison is statistically significant. RA: refractive astigmatism; TCA: total corneal astigmatism; IA: internal astigmatism; AAL: anterior astigmatism of the lens; PAL: posterior astigmatism of the lens.

Table 3. Correlation analysis among all parameters.

	Age(r/P)	RA(r/P)	TCA(r/P)	AAL(r/P)	PAL(r/P)
IA	0.155/0.008*	0.534/<0.001*	-0.244/<0.001*	0.308/<0.001*	0.032/0.591

* indicates that the comparison is statistically significant. RA: refractive astigmatism; TCA: total corneal astigmatism; IA: internal astigmatism; AAL: anterior astigmatism of the lens; PAL: posterior astigmatism of the lens.

girls' physical development is earlier than boys', and the difference caused by the growth rate of the axial length. Gender is highly correlated with the growth of the axial length, and the growth of the axial length has also been proved to be related to internal astigmatism¹⁶.

Then, we found that corneal astigmatism, internal astigmatism and posterior astigmatism of lens were different according to age. Firstly, corneal astigmatism has been changing since birth. Naeser *et al.*¹⁷ proved that corneal astigmatism is not stable until the age of 50. Under normal circumstances, corneal astigmatism changes regularly by 0.25 D every 10 years. Secondly, the compensation effect of internal astigmatism on reducing corneal astigmatism is very significant among preschool children, and then this compensation effect gradually weakens with age^{18,19}. Finally, we found that there were differences in the posterior astigmatism of lens, but there was not in the anterior. Birkenfeld *et al.*²⁰ have also found that with the increase of age, the astigmatism of the lens changes significantly, but the difference is that they have significant changes in the anterior

lens. We all know that the curvature of the anterior lens changes more than posterior in the process of accommodation²¹, but this is not completely equivalent to the greater astigmatism of the anterior surface with the change of age, which is the direction for further research.

It can be seen that internal astigmatism is highly correlated with the anterior astigmatism of the lens, but not with the posterior and the internal astigmatism increases with the increase of anterior astigmatism of the lens. Although the refractive index of lens is gradient, its astigmatism is close to anterior surface astigmatism²⁰. However, this does not mean an absolute correlation between internal astigmatism and the anterior astigmatism of the lens, because the state of the lens is unstable. For example, Pérez *et al.*²² found that in the relaxed state, spherical terms account for the majority of anterior lens surface irregularity (47%) and posterior lens astigmatism (70%); however, in the accommodation lens, astigmatism is the main irregularity of anterior lens surface (90%). The optical characteristics of the lens depend on its shape and refractive index

Figure 1. Linear regression graph of the internal astigmatism (IA) and the anterior astigmatism (AAL) of the lens.

distribution²³, which can affect its astigmatism to a great extent, thus further causing internal astigmatism to change. It seems that corneal and internal astigmatism cancel each other out²⁴. The unity of changes among corneal astigmatism, lens astigmatism and refractive astigmatism, do not occur individually²⁵.

To sum up, we found that there are gender and age differences in some astigmatism parameters and the relationship between internal astigmatism and lens astigmatism is clarified. Internal astigmatism increases with the increase of lens astigmatism, and the source of lens astigmatism is mainly the anterior. However, further research is required to determine whether lens astigmatism can be equated with internal astigmatism, and the correlation between internal astigmatism and anterior astigmatism of the lens is related to the mechanism of accommodation.

Data availability

Underlying data

Open Science Framework: Delicate balance: relationship between internal astigmatism and lens astigmatism. <https://doi.org/10.17605/OSF.IO/7X9FD>²⁶.

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

Acknowledgements

The authors thank Professor Changjun Lan (Department of Ophthalmology, Affiliated Hospital of North Sichuan Medical College) for his expert technical assistance.

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<http://www.doi.org/10.17605/OSF.IO/7X9FD>

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Current Peer Review Status:

Version 1

Reviewer Report 01 November 2021

<https://doi.org/10.5256/f1000research.57490.r91892>

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Although this manuscript raised an interesting topic, i.e. the relationship between lens astigmatism and internal astigmatism, it had multiple mistakes in the methods and failed to provide convincing results and logical discussion to prove this relationship. Here are some examples:

- The authors described that the internal astigmatism was calculated by refractive astigmatism minus total corneal astigmatism; however, internal astigmatism should be the vectorial difference between refractive astigmatism and anterior corneal astigmatism. The wrong method for calculating internal astigmatism makes all the following results unreliable.
- All the subjects were ametropia, which might influence the relationship between the lens astigmatism and internal astigmatism, just like age and gender. Its influence should be clarified further.
- Were the subjects under cycloplegia or not when they were taking the examinations? If they were not under cycloplegia, it is necessary to consider whether the accommodation will affect the degree of lens astigmatism and the reliability of the results.
- I noticed that all the correlation analyses were taken without adjusting for confounding factors, which quite impacts the quality of the results. Without adjustment, however, could the authors say "internal astigmatism was mainly related to AAL, but not to PAL"? Although I admit that internal astigmatism mainly comes from a lens, I cannot agree with the conclusion made in the manuscript because of the powerless results.
- "Because of the complexity and instability of astigmatism, this study only analyzed the power of astigmatism, but did not involve the axial direction." However, the axis might play an important role.

- In addition, there are some grammar mistakes.

Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 07 September 2021

<https://doi.org/10.5256/f1000research.57490.r92837>

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Samira Heydarian

Department of Rehabilitation Science, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran

Here are some comments that require clarification as given below.

Abstract:

- It is better to use lenticular astigmatism instead of crystal astigmatism.
- Please clarify what the difference is between internal astigmatism and intraocular astigmatism.

- The conclusion is not appropriate and it is just the repetition of the results.

Introduction:

- "Similarly, studies have found that 47% of cataract patients suffer from astigmatism ≥ 1 degree". What do you mean by "degree"? It seems that it should be changed to "diopter".

Method:*Subjects:*

- How were the subjects screened to reduce bias? Please clarify more.
- Please add the inclusion criteria. For instance, is there any age limit for the study?

Procedures:

- What are the other measurements that the authors measured using CASIA and what is the standardized optometry?
- Due to the effect of accommodation on the lens and even on corneal curvature, cyclorefraction and comparing changes before and after cycloplegia seems useful.

Outcome parameters:

- As a general rule, all non-standard abbreviations/acronyms should be written out in full on first use (in both the abstract and the paper itself) and followed by the abbreviated form in parentheses. Please consider this point throughout the manuscript.
- Do the authors consider the curvature of the anterior and posterior surface of the lens as AAL and PAL? Astigmatism is the difference between the main curvatures, not just the curvature.

Statistical analysis:

- Please cite the reference that is used for the calculation of the sample size.

Results:

- Please add the mean age of the participants.
- How did they compare astigmatism without considering the effect of the axis? Vector analysis seems necessary for an appropriate comparison.

Discussion

- The discussion is weak and needs to be improved.
- The effect of the posterior surface of the cornea and retinal astigmatism was not considered and discussed throughout the manuscript.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Optometry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 08 Sep 2021

Binzhong Li, North Sichuan Medical College, nanchong, China

Dear Professor Samira Heydarian,

Thank you very much for your many meaningful comments on this article, so as to make changes according to your suggestions. The changes are as follows:

1. Abstract:

1.1 It is better to use lenticular astigmatism instead of crystal astigmatism.

Author response: Thank you for your suggestion, it has been modified.

1.2 Please clarify what the difference is between internal astigmatism and intraocular astigmatism.

Author response: Thank you for your suggestion. As explained in the method and first paragraph of the discussion section, internal astigmatism in this paper is the difference between human total astigmatism (refractive astigmatism) and corneal total astigmatism, which is the overall internal astigmatism including intraocular astigmatism.

1.3 The conclusion is not appropriate and it is just the repetition of the results.

Author response: It has been modified.

2. Introduction:

2.1 "Similarly, studies have found that 47% of cataract patients suffer from astigmatism ≥ 1 degree". What do you mean by "degree"? It seems that it should be changed to "diopter".

Author response: It has been modified.

3. Methods

3.1 How were the subjects screened to reduce bias? Please clarify more.

Author response: Thank you for your suggestion, it has been added.

3.2 Please add the inclusion criteria. For instance, is there any age limit for the study?

Author response: It has been added.

3.3 What are the other measurements that the authors measured using CASIA and what is the standardized optometry?

Author response: It has been modified. That is, the optometry process to obtain the best corrected vision and diopter.

3.4 Due to the effect of accommodation on the lens and even on corneal curvature, cyclorefraction and comparing changes before and after cycloplegia seems useful.

Author response: Yes, your point of view is worth thinking about. As you said, the changes related to adjustment before and after mydriasis are very important, which is worth our next research direction.

3.5 As a general rule, all non-standard abbreviations/acronyms should be written out in full on first use (in both the abstract and the paper itself) and followed by the abbreviated form in parentheses. Please consider this point throughout the manuscript.

Author response: It has been added in the abstract.

3.6 Do the authors consider the curvature of the anterior and posterior surface of the lens as AAL and PAL? Astigmatism is the difference between the main curvatures, not just the curvature.

Author response: We are discussing the main curvature, which has been made clear. Thanks again.

3.7 Statistical analysis: Please cite the reference that is used for the calculation of the sample size.

Author response: It has been added.

4. Results:

4.1 Please add the mean age of the participants.

Author response: It has been added.

4.2 How did they compare astigmatism without considering the effect of the axis? Vector analysis seems necessary for an appropriate comparison.

Author response: It has been added.

5. Discussion

5.1 The discussion is weak and needs to be improved.

Author response: According to your suggestion, the discussion section has been modified.

5.2 The effect of the posterior surface of the cornea and retinal astigmatism was not considered and discussed throughout the manuscript.

Author response: Total corneal astigmatism of CASIA2 is a general index combined with anterior and posterior corneal surfaces. Due to the lack of equipment to detect retinal astigmatism, we did not discuss retinal astigmatism, but under the condition of clear refractive medium it seems that physiological retinal astigmatism is very small, which deserves further study and is also a new direction for us to learn. Thank you for your suggestion.

Best wishes,
Binzhong Li (on behalf of all authors)

Competing Interests: The authors declare that they have no competing interests.

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