Peer Review File

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Dear Editor and Reviewers:

Many thanks for your letter and the reviewers' comments concerning our manuscript entitled "Determinants of intraocular lens tilt and decentration after cataract surgery (ATM-20-1008)". We have studied the comments carefully and have made revision to our manuscript accordingly. We appreciate the reviewers' suggestions and hope that the revision addresses all the issues.

Our point-by-point responses for reviewers are as follows:

Comment 1: Please explain how the percentage of variability was calculated.

In more specifically, on page 5 line 58, Wang L. et al demonstrated that the tilt of preoperative crystalline lens explained 70.7% of the variability in IOL tilt. This study reported that the decentration of the crystalline lens and AL explained 54.6% of the variability in IOL decentration. How did the authors calculate the values of 70.7% and 54.6%?

Reply 1: We thank the reviewer for this good question. In our study, we used the coefficient of determination (R^2) of regression analysis to interpret the proportion of variability in IOL tilt or decentration that was predicted from preoperative crystalline lens tilt or decentration. For example, we found the tilt of preoperative crystalline lenses had an R^2 of 0.512 in the univariate analysis of IOL tilt, which means the tilt of

preoperative crystalline lenses can explain 51.2 % of the variability in IOL tilt. In univariate regression analysis for IOL decentration, the R^2 value of preoperative crystalline lens decentration was 0.214, and the R2 value of axial length was 0.332, thus preoperative crystalline lens decentration and axial length explained 54.6% of the variability in IOL decentration together.

In Wang L. et al's study, they used correlation analysis to assess the relationship in tilt and decentration of crystalline lens and IOL, and they found there was a strong correlation between the magnitude of preoperative crystalline lens and IOL tilt (r = 0.707). However, that can not to be used to illustrate the tilt of preoperative crystalline lens explained 70.7% of the variability in IOL tilt. We are sorry for confounding the correlation coefficient and coefficient of determination (R^2) of regression analysis. We have modified the statement in our revised manuscript (Page 6, Paragraph 2, line 84).

Changes in the text: However, Wang L et al demonstrated that the tilt of preoperative crystalline lenses was correlated with IOLs tilt strongly (r=0.707). (Page 6, Paragraph 2, line 84).

Comment 2: In page 7, line 99, the analysis results of tilt and decentration were generated directly by the built-in software. Please add the software version, since according to Tomey Corp, the CASIA2 angle analysis algorithm may differ depending on its software version.

Reply 2: We appreciate the reviewer for your suggestion. We have added the software

version (Version SS2000) in the revised manuscript (Page 8, Paragraph 1, line 124).

Changes in the text: The outlines of crystalline lenses and IOLs were automatically recognized, and 3-dimensional analysis results of tilt and decentration were generated directly by the built-in software (Version SS2000) relative to the corneal reflection dot axis. (Page 8, Paragraph 1, line 124).

Comment 3: In the caption of Figure 1, the explanation of R, Rs, and Rf should be similar for both anterior (Front) and posterior (Back). Therefore, I suggest changing the explanation as follows.

R = radius of curvature; Rs = steep radius of curvature; Rf = flat radius of curvature, for front and back surfaces, respectively; Decent. = decentration; LT = lens thickness (thickness of the crystalline lens); LE-Dia. = lens equator diameter (equatorial diameter of the crystalline lens).

Reply 3: We thanks so much for your suggestion. We have changed the corresponding explanation in the caption of Figure 1 in our revised manuscript (Page 19, Paragraph1, line 341-345).

Changes in the text: Figure 1. The representative images show 3 dimensional results of crystalline lens and IOL. The optic axis of IOL (yellow dot line) and the visual line (blue dot line) are automatically generated by the built-in software. R= radius of curvature, Front R= radius of curvature for lens front surface; Rs=steep radius of curvature; Rf=flat radius of curvature; Back R= radius of curvature for lens back surface; Decent. = decentration; LT=lens thickness (thickness of the crystalline lens); LE-Dia.= lens equatorial diameter (equatorial diameter of the crystalline lens). (Page

19, Paragraph1, line 341-345).

Comment 4: In the discussion page 12, line 216, remove the (R2=0.214). Repeating the same information which was explained in the sentence before.

Reply 4: We thanks so much for your advice. We have deleted R2=0.214 in our revised manuscript (Page 13, Paragraph3, line 240-241.)

Changes in the text: Interestingly, axial length is the most highly associated factor for IOL decentration (R^2=0.332, P<0.001), rather than the decentration of preoperative crystalline lens. (Page 13, Paragraph3, line 240-241.)

Comment 5: Current Figure 2 only shows the orientation of tilt and decentration, but no information about the tilt and decentration values. Please revise this figure to include the values and revise also the figure caption in accordance to figure revision. Refer to Figs. 2-5 of Ref. 14 or Fig. 2 of Ref. 16.

Reply 5: We thank the reviewer for this valuable suggestion. We totally agree that figure including the orientations and the values of tilt and decentration is clearer to display the relationship of tilt and decentration between crystalline lenses and the IOLs. We have revised figure 2 refer to Ref. 14 and Ref. 16, and its legend has been also revised in our manuscript (Page 19, Paragraph 2, line 346-352).

Changes in the text: Figure 2. (A) Coordinate graphics show the orientations and the values of the tilt of crystalline lenses and IOLs in the right and left eyes. Preoperative crystalline lens and IOLs both tilt toward inferotemporal direction in both eye (red circle: crystalline lens, n=38; blue circle: IOL, n=18); **(B)** Coordinate graphics show

the orientations and the values of the decentration of crystalline lenses and IOLs in the right and left eyes. Crystalline lenses and IOLs are both more likely to decenter toward temporal direction (red circle: crystalline lens, n=38; blue circle: IOL, n=18). (Page 19, Paragraph 2, line 346-352)

Comment 6: The discussion described several issues that are related to the objectives of the study. These were fine.

If we look at the AS-OCT image (Figure 1), both the crystalline lens and IOL tilt are calculated based on the difference between the optical axis and the corneal vertex axis. However, the optical axis of the cornea is not corneal vertex axis but most probably very close to the crystalline lens optical axis. This issue is very important to the preoperative ocular aberrations as well as postoperative. It means that the crystalline lens tilt and IOL tilt are relative to cornea tilt. I suggest the authors to include this issue in the discussions.

Reply 6: We appreciate the reviewer for this very important issue. After communicating with the manufacturer and checking the instructions, we have made sure that CASIA2 measures the tilt of crystalline lenses and IOLs using visual line as reference, rather than corneal vertex axis. Like other aberration measuring machines, the “visual line” is defined by the point light source and its projection on the cornea. As illustrated in the instructions of CASIA2, tilt means the axis angle between the crystalline lens or IOL axis (yellow dot line) with respect to visual line (blue dot line) (Figure 1). We have revised the statement in our manuscript accordingly (Page 6, Paragraph 1, Line 76-78).

Changes in the text: It can clearly outline crystalline lenses or IOLs, and generate 3-dimensional results of tilt and decentration of crystalline lenses or IOLs using the visual line as reference. Compared to the pupil center, the visual line is considered to be a better reference to assess IOL tilt and decentration since it is not affected by the shape of pupil. (Page 6, Paragraph 1, Line 76-78)

Comment 7: For consistency, change Casia2 on page 12 line 207 to CASIA2.

Reply 7: Thanks for your suggestion. We have changed Casia2 to CASIA2 in our revised manuscript. (Page 13, Paragraph 2, line 232)

Changes in the text: Using CASIA2, we found the mean tilt of crystalline lenses was 4.9 degrees and the mean tilt of IOLs was 4.75 degrees, and the tilt of crystalline lens explained 51.2% of variability in IOL tilt, which were within the range of previous findings. (Page 13, Paragraph 2, line 232)

Comment 8: Please check the English, since there are linguistic errors, such as on page 7, line 102. [An … is showed in Figure 1] should be [An … is shown in Figure 1].

Reply 8: We thanks so much for your suggestion. We have checked the manuscript carefully and corrected them in the revised manuscript.

Changes in the text: We have revised the manuscript thoroughly and modified the text as advised.