Author’s response to reviews

Title: Absolute and estimated values of macular pigment optical density in young and aged Asian participants with or without age-related macular degeneration

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Author’s response to reviews:

The authors’ response letter has been included as a supplementary file together with cover letter to the Editor. Below, we inserted the same contents as the authors' response letter.

Point-by-Point Responses to the Editor’s and the Reviewer’s Comments
Editor Comments:

The authors have submitted a clear, concise manuscript regarding the applicability of the measurement of macular pigment optical density in Asian eyes using a commercially available device.

Thank you for your favorable review and constructive comments, which we believe helped improve the manuscript.

The MPS II contains a +4.00 lens which is not appropriate for eyes with high myopia, which constitutes a substantial proportion of certain Asian populations. The refractive data for the patients included in the study should be discussed in the Subjects section.

Thank you for pointing this out, we agree that the number of high-myopia patients is greater in Asian populations. However, we excluded individuals with high myopia (over -6D in spherical equivalent) from the study. As a result, the refraction error ranged from -5.00 to +3.75D (average -0.66D). We mentioned this criterion in the Methods (Subjects) section:

Page 6, line 128~

Individuals with high myopia (over -6.00D) were excluded.

The decision to perform testing following pupil mydriasis with an anti-cholinergic should be explained and the potential effect this may have had on the results of the study. For subjects in which fundus photography and fluorescein angiography was performed, was MPS II testing performed before or after these studies. If MPS II testing was performed on the same day, after fundus imaging, how much time was given to allow the patient to allow for recovery of photoreceptors.

Thank you for your comment. We measured MPOD at the time of return visit, not the first visit. The measurement was performed before pupil dilation and under non-mydriatic conditions, and before obtaining fundus photographs and angiograms in all subjects. This was mentioned in the Methods (Measurement of MPOD) section:

Page 7, line 141~

The measurement was performed before pupil dilation and obtaining fundus images, and under non-mydriatic conditions.
The last paragraph in the results section contains information in lines 196-202 which would be more appropriately placed in the discussion.

Thank you for this suggestion, we have revised some of the text in the discussion accordingly:

Page 11, line 247~

Moreover, the AMD-related eyes exhibited lower levels of MPOD in estimated value, consistent with a previous report [12]. Eyes with AMD in the fellow eye may have a condition more closely approximating the AMD eyes than the otherwise healthy group (other than cataract), although the AMD lesion had not yet developed. In fact, AMD-fellow eyes are regarded as “risk eyes” [3, 4].

Reviewer reports:

Naoyuki Tanimoto, M.D., Ph.D. (Reviewer 1): In this manuscript by Ozawa et al, absolute and estimated values of macular pigment optical density were measured in healthy volunteers and patients with age-related macular degeneration (AMD) using a commercially available device (MPS II). Absolute values were not detectable in approximately 1/3 to 1/2 of aged cases, even in subjects with normal foveal and parafoveal appearance. In cases in which the both types of values could be estimated, there was a significant correlation between them. Estimated values obtained from AMD and AMD-fellow eyes were lower than control eyes.

Although the cases enrolled in this study were somewhat limited (also mentioned by the authors in the Discussion), the data in this study would be valuable to facilitate further investigations for the topic.

The manuscript is well written, and the data have been treated properly.

Thank you for your gracious comments and insightful advice for future studies.

I have a couple of questions and comments:
1) How is/was the test-retest reliability?

Generally, the test-retest reliability of this method was satisfactory. Absolute and estimated values in individuals from all groups were well correlated in this study, which supports this conclusion. Additionally, participants whose measurement was unsuccessful the first time had a second chance for measurement, as described in the Methods section of the original manuscript. In these participants, the repeat measurements were, in large part, unsuccessful again, which lends support to the good test-retest reliability of the method.

2) Were the measurements performed in miosis or in mydriasis?

The measurements were performed in miosis. This information was included in the Methods (Measurement of MPOD) section:

Page 7, line 141~

The measurement was performed before pupil dilation and obtaining fundus images, and under non-mydriatic conditions.

3) Could lens opacities be the major factor to avoid an estimation of absolute values in the aged subjects in this study? Were there any other possible factors/reasons?

This is an interesting point. We consider that lens opacity and cataract-related reduction in the quality of visual acuity may be one of the major causes as described in the original manuscript (Page 11, line 229~), since aged group without AMD also showed low number of participants whose absolute value was measurable. In addition, we believe that it is possible that older subjects have less capacity for prolonged concentration and, therefore, may more easily abandon the examination. This possibility was also mentioned in the original manuscript:

Page 11, line 235~

Alternatively, age itself may affect an individual’s endurance for concentrated focus on the dark stare point.
4) Not for this manuscript, but it is interesting to compare values between pseudophakic AMD patients and pseudophakic age-matched control subjects with a clear cornea and in conditions after a Nd:YAG posterior capsulotomy, or more simply to examine values pre and post cataract surgery in cases with normal retinal functionality.

Thank you for your comment. We acknowledge this valid point and will consider it in future studies.