## Comment on: Corneal Epithelial Thickness Measured Using AS-OCT as a Diagnostic Parameter for Limbal Stem Cell Deficiency

EDITOR:

WE READ WITH INTEREST THE ARTICLE BY LIANG AND ASSO-ciates that evaluated the diagnostic performance of the corneal epithelium thickness (CET) measured using an anterior segment optical coherence tomography (AS-OCT) and in vivo confocal microscopy (IVCM) in patients with limbal stem cell deficiency (LCSD).[1] The measurements obtained were the average of 3 independent scans performed by 2 independent, masked observers. The authors reported the interobserver variation of these measurements by calculating the interobserver differences only. Furthermore, they analyzed the CET data using a 3-point measurement on the AS-OCT (OCT-CET3) only, but not the 1-point measurement (OCT-CET1) because of the greater correlation with IVCM-CET in the former than the latter CET. We have reservations regarding these statistical approaches.

Multiple measurements were manually obtained by 2 observers from the AS-OCT and IVCM. The reliability of these measurements should be assessed by both the inter-rater reliability and intrarater reliability using the intraclass correlation coefficient (ICC). The repeatability coefficient (RC), defined as $1.96 \times \sqrt{(2 \times \text{within-subject variance})}$, is the 95% confidence limit of the difference of measurements between examinations. RC is another reliability index that should be considered because it lends itself to easy clinical interpretation, since it is quantified in the same unit as the measurement device. Without the ICC and/or RC reliability evaluations, it is difficult to interpret the results presented by the authors in a clinically meaningful context.

Although the authors found a higher correlation between IVCM-CET with OCT-CET3 than OCT-CET1, a higher correlation does not imply there is a better agreement between these 2 methods. This concept has been discussed in detail by Bland and Altman in their article, one of the most highly cited papers in medical research, highlighting that the correct approach is to calculate the limits of agreement and not correlation.[2] Without considering the limits of agreement, systemic bias, and scaling bias between these 3 measurements, the OCT-CET1 data should not have been disregarded entirely in their analysis, as it might have been a useful diagnostic and staging biomarker.

Lastly, without calculating the area under the receiver operator characteristic curve (AUC) for OCT-CET1 or IVCM-CET and comparing these AUCs with OCT-CET3 using a statistical test (ie, DeLong's test[3]), it is premature to state that OCT-CET3 has the highest diagnostic value for LSCD in the present study. It would be of interest if the authors could provide the analyses described above so that the results can be better put into a clinical perspective to address the question the authors set out to answer.

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REFERENCES

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REPLY

WE SINCERELY THANK DR. WAN AND COLLEAGUE FOR THEIR interest in our recent article, entitled "Corneal Epithelial Thickness Measured Using AS-OCT as a Diagnostic Parameter for Limbal Stem Cell Deficiency",[1] and for giving us the opportunity to further elaborate on our study. We previously showed that central corneal epithelial thickness (CET) obtained using in vivo confocal microscopy (IVCM-CET) decreased substantially in eyes with limbal stem cell deficiency (LSCD).[2,3] In addition, the degree of epithelial thinning in the central cornea reflected the global function of limbal stem cells. The purpose of our recent study was to develop the methodology of CET measurement using anterior segment optical coherence tomography (OCT) as a diagnostic test for LSCD. Our decision to