**Should the Corvis Biomechanical Index (CBI) Include Corneal Thickness Parameters?**

We read with great interest the article by Steinberg et al.\(^1\) regarding a modified Corvis Biomechanical Index (named aCBI in the article) with the elimination of corneal thickness data, including the Ambrósio’s Relational Thickness in the horizontal profile (ARTh). The aim of the cited article was to provide a proof of concept of whether corneal deformation (biomechanics) alone would be sufficient to separate normal patients from patients with keratoconus.\(^3\) This was accomplished by creating the aCBI algorithm without the ARTh in a pairwise matching of normal and keratoconic eyes with regard to their central corneal thickness (CCT) and corrected intraocular pressure (IOP) (Dresden correction). They further compared the accuracy of the new aCBI and the one obtained with the current CBI that includes the ARTh.\(^2,3\)

The authors found that the aCBI was more sensitive and more specific than the CBI in the training sample, having a higher area under the receiver operating characteristic (ROC) curve (area under the curve [AUC] 0.986 × 0.961). However, the current study had a relatively small sample size and lacked a validation population to test the algorithm, which are important limiting factors. Interestingly, as the authors correctly stated, the design of the study does not allow the possibility to judge whether the aCBI would be better in clinical practice because all patients were matched in thickness, which, by definition, eliminates the need to have thickness inside the algorithm. Furthermore, the patients were also matched in the Corvis IOP (Dresden correction), which should be more correlated with age and biomechanics compared to the biomechanically corrected IOP\(^4,5\) and might cause a bias. When we designed the CBI, we tried many combinations of parameters, with and without the ARTh, and the published outcomes were always better when including thickness profile data.\(^2,3\)

We agree with Steinberg et al. that it is an important finding to demonstrate that corneal deformation or biomechanical response alone is able to differentiate normal patients from those with keratoconus, which is a current project for improving Corvis functions. In addition, we believe it is important to demonstrate that the CBI is able to separate patients with keratoconus more efficiently compared to the aCBI, when considering a larger dataset.

The aim of this correspondence is to demonstrate the results of applying the aCBI\(^1\) to the two large datasets used in the original CBI study\(^2\) and to compare its performance to the published and validated CBI.

We employed the same published population of 658 patients from two clinics: 329 patients (227 healthy and 102 keratoconic) were included from Rio de Janeiro Corneal Tomography and Biomechanics Study Group, Rio de Janeiro, Brazil (Database 1) and 329 patients (251 healthy and 78 keratoconic) from the Vincieye Clinic in Milan, Italy (Database 2). Subsequently, the aCBI and CBI were validated using Database 2. Statistical analysis was clearly described in our study.\(^2\)

The ROC curve investigation of the training Dataset 1 displayed an AUC of 0.964 for the aCBI and 0.977 for the CBI (Figure 1A). Similarly, in the validation Dataset 2, the AUC was 0.969 for the aCBI and 0.998 for the CBI with the same cut-off points (Figure 1B). With the cut-off of 0.5 of the aCBI in Dataset 1, the sensitivity was 90.2% and specificity 92.1%; conversely, in the validation dataset (2) they were 92.1% and 88%, respectively. We previously published\(^2\) 94.1% sensitivity and 100% specificity for the CBI in Dataset 1. Similarly, the same cut-off point provided 100% sensitivity and 98.4% specificity in Dataset 2. There was a significant difference between the ROC curves (\(P = .0141\), De Long’s test).

We commend Steinberg et al. for demonstrating that it is possible to establish a pure biomechanical algorithm for distinguishing normal patients from those with keratoconus. Nevertheless, we still recommend the use of the validated CBI in clinical practice because it was shown to provide better accuracy compared to the aCBI. The superiority of the CBI is explained by the fundamental double role of the ARTh as a correction parameter for thickness and as an independent factor alone for the separation.
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REFERENCES


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Reply

We were honored to read the comments by Vinciguerra et al. as a response to our recent “proof-of-concept” study. First, we congratulate them for their outstanding work in the field of biomechanical analyses and for continuously improving keratoconus screening with their concepts and scientific impulses.

We are excited that their long-anticipated study “Detection of Keratoconus With a New Biomechanical Index” has been published. They presented the Corvis Biomechanical Index (CBI) as an index to finally enable reliable in vivo keratoconus screening based on biomechanical analyses. This opens the path for new diagnostic modalities because it potentially could improve early keratoconus screening beyond the threshold of pure (static) morphometric analyses. Therefore, and because of many inhomogeneous results of former studies using the CorvisST to improve keratoconus screening, we were thrilled by their results.

As Vinciguerra et al. mentioned correctly, the aim of our study was “to provide a proof of concept whether corneal deformation (biomechanics) alone would be sufficient to separate normal subjects from keratoconic patients.” Therefore, in a first step, we tested their CBI in a critical/artificial setting by strictly pairing normal patients and patients with advanced kera-
toconus regarding their intraocular pressure and central corneal thickness with the intention to exclude potential biasing factors of the in vivo biomechanical analyses. Even using our “overcritical” methodology, the CBI successfully distinguished between both entities with a high accuracy.\(^1\)

Vinciguerra et al. mentioned in their study that: “A possible criticism of our study could be the decision to use ARTh [Ambrósio’s Relational Thickness to the horizontal profile]...because it is already a pure thickness profile with a good AUC [area under the curve]...”\(^2\) They justified the implementation of the ARTh by writing, “However...sensitivity and specificity increased meaningfully with the addition of the other five DCR [dynamic corneal response] parameters, which confirms the importance of biomechanics in evaluating ectasia. Furthermore, ARTh can be considered either a thickness parameter inside the multivariate analysis to separate normal from keratoconic eyes or a correction parameter for the possible difference in thickness between the patients to correctly evaluate biomechanics. It is known that many DCR parameters are correlated with thickness.”\(^2\)

We agree with their conclusions and see the benefits of including the ARTh in the CBI. However, the reader should not underestimate that they compared normal and advanced keratoconic eyes, which typically demonstrate a distinct difference regarding the corneal thickness profile.

We thought it would be interesting in our “proof-of-concept” study to analyze whether biomechanical analyses/parameters alone are able to distinguish between normal and keratoconic eyes. Therefore, we excluded the ARTh from the CBI and thereby “designed” the adjusted Corvis Biomechanical Index (aCBI).

We concluded in our study that the “aCBI analysis could demonstrate that the concept of solely biomechanical differentiation of keratoconic and normal eyes with the CorvisST proved to be successful.”\(^2\) To avoid the misinterpretation of our results, we discussed this topic explicitly in our publication and stated: “The even higher accuracy of the aCBI compared to the CBI should not be misinterpreted because the sensitivity/specificity acquired with our ‘proof-of-concept’ study design is not eligible to be transferred to a ‘real-time’ scenario” and “because of our proof-of-concept study design, it is of utmost importance that reliability and cut-off values for the parameters of interest should not be used in the clinical setting.”\(^1\)

However, we believe Vinciguerra et al.’s additional analyses and our clarification will help the reader to understand the benefits of the CBI designed by their study group.\(^2\) We again congratulate the authors on their important work and are convinced that we could bring additional (and not too disturbing) aspects with our “proof-of-concept” study.\(^3\) Our common message for readers is that biomechanical in vivo analyses to distinguish between normal and (advanced) keratoconic eyes finally works on a robust, reliable, unbiased level. Finally, to improve early keratoconic screening, the question is not tomography OR biomechanical analyses but how to combine both in the most effective way.

As the readers of this journal know, Vinciguerra et al. are working hard to optimize these symbiotic diagnostic tomographic/biomechanical devices.\(^6\) We appreciate their outstanding scientific efforts.

**REFERENCES**


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