Can the Corvis ST Estimate Corneal Viscoelasticity?

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Conflict of Interest Statement

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We have read with interest Francis et al.'s article "Corneal viscous properties cannot be determined from air-puff applanation" where the Corvis ST output for 312 healthy eyes, 107 fellow eyes of patients with keratoconus, and 289 keratoconic eyes was fitted to mathematical models to assess whether the cornea's viscous properties can be measured with air-puff. While we agree with many of the study's findings as reported in the article, we would like to use this opportunity to discuss some aspects of the study that generated flaws, including the lack of validation, and present our views on the central question of the study

First, about the analysis method. We agree with the authors' assertion that "two classes of mathematical approaches are available for the calculation of biomechanical properties from the deformation amplitude: rheological closed-form analytical and inverse finite element methods. The rheological models are simpler, computationally non-intensive, and fast."

While these statements are correct, they do not present a balanced assessment of the two approaches and lack appreciation of the shortfalls of closed-form analysis, in comparison to inverse FE analysis. Closed-form analysis requires the essential introduction of simplifications, and these will affect the results, which is why validation is required. As this form of analysis was selected for the study, a detailed assessment of their approximations, and the subsequent effect on study outcomes, should have been included. A validation study of the reliability of the closed-form analysis should also have been presented. Without these two critical components, it is impossible to assess the applicability of the analysis results.

We also would like to note a few apparent omissions that may have affected the results. These include the inertia or the mass force, which would be difficult to justify ignoring given the dynamic nature of the air puff excitation, especially when the main objective is to assess viscous response. Further, the primary input to the model, $F_{air\text{-}puff}$, was not given in the paper. When we searched the previous publication [1] as the authors instructed, we noticed that the authors calculated the cross-sectional area of the air-puff with a diameter d as πd^2, not $\pi d^2/4$.

If the cross-sectional area was wrongly estimated 4 times bigger, the force must have been estimated 4 times more propeminent as well. This would undoubtedly impact the results.

Our second point is about the method adopted to estimate corneal viscoelasticity. Viscoelasticity is time-dependent elasticity, which shows in four different ways in mechanical behavior. These are (1) creep (gradual growth in deformation under a constant load), (2) stress-relaxation (gradual reduction in stress under a constant deformation), (3) loading or strain rate dependency (producing higher stiffness under faster loads or faster deformation), and (4) hysteresis (difference in behavior between those experienced under loading and unloading).

With the air-puff devices such as the Corvis ST and the Ocular Response Analyzer (ORA), creep and stress-relaxation cannot be measured as the devices are not designed to apply a constant load or a constant deformation in any stage of the air-puff application. On the other hand, the loading or strain rate dependency means that the corneal material behavior that applies is specific to the loading or strain rate of the air-puff device. This means that if we were to determine corneal viscoelasticity through the loading or strain rate dependency route, the device would have to apply different loading rates or strain rates. However, since this is out of the scope of the current devices, this route is also not feasible.

The remaining sign of viscoelasticity is the hysteresis which can be easily determined from the pressure-deflection behavior recorded by both the Corvis ST and the ORA, and this in our view is the most straightforward route that could be taken to determine corneal viscoelasticity. This route had been adopted by the ORA and resulted in the Corneal Hysteresis (CH) parameter denoting the difference between applanation pressures recorded during the loading and unloading stages[2]. This parameter was used in earlier studies to show significant differences between more significant and healthy corneas[3]. Another parameter (the

Hysteresis Loop Area, HLA) based on the ORA output developed by Hallahan et al.[4] was also successful in differentiating keratoconic and healthy corneas.

We would like to make a further point concerning the study methodology. While we agree with using one eye from normal and keratoconus patients, the inclusion of the "107 fellow eyes of patients with asymmetric keratoconus as a subset of 107 of 289 patients with keratoconus" is confusing as this is not clear. We may assume these have normal topography. In fact, the normal topography eye from patients presenting with very asymmetric ectasia (VAE) have been extensively studied for enhancing ectasia detection[5]. Considering these cases as keratoconus is not in full agreement with the current concepts that keratoconus is a bilateral but asymmetric disease, and that ectasia may occur unilaterally secondary to biomechanical impact from the environment.

In summary, any computational approach to modeling corneal behavior requires validation to demonstrate that appropriate assumptions have been made and the results are sound. Without validation, the results cannot be meaningfully interpreted. The unknown error of fit may be acceptable or alternatively, quite large. This remains unknown for the current study.

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