



## Let's detect progressive keratoconus correctly



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On November 5, 2021, Ingemar Gustafsson defended his thesis “The Assessment of Disease Progression in Keratoconus and Corneal Crosslinking in Thin Cornea” at the Department of Clinical Sciences, Lund University, Sweden. His main supervisor was Anders Bergström, Department of Clinical Sciences, Lund University, Lund Sweden. His three co-supervisors were Jesper Hjortdal, Anders Ivarsen, and Anna Cardiakides.

Keratoconus generally manifests in adolescents and can progress to severely impaired vision. The risk of progression is inversely correlated to age; thus, younger patients are at higher risk than older ones. Progressive keratoconus can be halted by corneal crosslinking (CXL). The general indication for CXL is progressive keratoconus, although children are commonly treated with CXL upon initial diagnosis. Tomography is used to assess progression. Measurements made during different visits are compared to determine whether the patient's keratoconus has progressed and if they should be referred for CXL. However, there is no consensus on which parameters should be used or the magnitude of the change in these parameters that indicates progression. An increase in the curvature power of the steepest point on the anterior surface (Kmax) of 1.0 diopters is commonly used for all patients. However, there is little evidence that this is appropriate. Furthermore, inconsistent results have been presented regarding the magnitude at which progression can be detected. Such studies are often based on determinations of the repeatability of measurements made on one occasion. However, the

progression of keratoconus is evaluated from measurements made on different occasions, and it is reasonable to assume that measurements obtained on different days will be subject to greater variation due to the biomechanical instability of the cornea caused by keratoconus. Additionally, it has been suggested in studies that the repeatability of measurements is lower in subjects with more severe keratoconus. Because keratoconus is a thinning disorder, a minimum corneal thickness of 400  $\mu\text{m}$  has been suggested for the safe performance of CXL. Thus, a significant proportion of keratoconus patients are excluded from the standard CXL treatment protocol.

In the first study of this thesis, we elucidated the association between measurement error and disease severity. In the second investigation, we tested the inter-day repeatability of measurements, and in the third, we examined the Belin ABCD Progression Display. Finally, we assessed a protocol in which sterile water was added during the crosslinking procedure to increase the corneal thickness. We found that the measurement error was associated with the disease severity and that progression should be defined by limits of inter-day measurements. The results also

### Key points:

- Take disease severity into account when diagnosing progression.
- Consider whether to use one or the mean of several measurements.
- The ABC(D) Progression Display appears to over-diagnose subjects as progressive.
- The use of sterile water during CXL appears to be efficacious in halting disease progression.

suggest that the diagnosis of progressive keratoconus by the Belin ABCD Progression Display led to over-diagnosis of progression. Further, the addition of sterile water was effective in increasing the corneal thickness above the suggested safety limits.

These results have important clinical implications. The limits at which progression is defined should be stratified according to the severity of the disease. Patients with less advanced keratoconus are underdiagnosed as progressive if commonly used parameters are not stratified according to disease severity. This could lead to delayed referral for CXL, resulting in an avoidable risk of deterioration in vision. Patients with more advanced keratoconus, on the other hand, would be over-diagnosed as progressive, which could lead to unnecessary CXL, subjecting the patient to discomfort and possible treatment-associated complications. This risk of over-diagnosis is also relevant when using the Belin ABCD Progression Display. Finally, the data suggest that a simple measure, such as adding sterile water during corneal crosslinking, could enhance the corneal thickness to improve the safety of the treatment.

### Future directions:

- Using artificial intelligence to diagnose progressive keratoconus
- Further randomized clinical trials on the treatment efficacy of using sterile water in different CXL-protocols

### References

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