

## It is time for a Turning Point in Keratoconus

Keratoconus (KC) is no longer a rare disease<sup>1</sup>, especially in certain geographical areas it reaches peaks of endemic value. The therapies and innovations of the last years', starting with *crosslinking*, have drastically changed the prognosis and quality of life of our patients.

New combined therapies, minimally invasive refractive enhancement treatments, have changed and are changing history.<sup>2</sup>

Increasingly sophisticated diagnoses, intelligent CT scanners, machine learning and artificial intelligence are at the service of ophthalmologists who are passionate about the subject and of patients for higher, refined and early diagnoses.<sup>3</sup>

This has made keratoconus a subspecialty of modern ophthalmology and poses ever new and exciting challenges in the clinical, diagnostic, and therapeutic fields. There was a need for an international society dedicated to this disease, distinct and separate, but which is open to dialogue with the most important international societies of refractive and anterior segment eye surgery.

Thus, the IKS (International Keratoconus Society) was finally born, the home of ophthalmologists who deal with keratoconus and of all those who want to dedicate themselves to this fascinating sector of ophthalmology.

Such an important Society could not fail to have an equally important scientific Journal, and we have the honor of having *the International Journal of Keratoconus and Ectatic Corneal Diseases* (IJKECD) as our official IKS scientific Journal.<sup>3</sup>

I cannot hide a certain emotion, because it was precisely in this Journal that the M nomogram<sup>4,5</sup> for the standardized treatment of individualized crosslinking of ectatic corneas of all thicknesses was born, as awarded in the ESCRS Congress in 2019 in Paris with the "Joseph Colin Prize" for innovating therapies in the field of Keratoconus.<sup>4,5</sup>

The "M nomogram" allows safe and effective setting of CXL parameters based on thickness minimum preoperative corneal membrane, also allowing the standardized treatment of thin and ultrathin ectatic corneas with a minimum thickness between 250 and 400  $\mu\text{m}$ , keeping the fluence standardized in the Dresden Protocol constant (5.4 J/cm<sup>2</sup>).<sup>4,5</sup>

Actually, the preliminary results on new epithelium-on accelerated CXL protocols with progressively higher fluence and pulsed light show that a new pachymetry-based PFPL M Epi-on ACXL nomogram stabilizes ectasia progression.<sup>6</sup> Higher fluence Epi-on ACXL increases CXL penetration, with better functional outcomes in the absence of complications, thus paving the way to a replacement of epithelium-off crosslinking treatments. From a clinical and practical perspective, a safer and faster transepithelial crosslinking treatment with an efficacy profile comparable to Epi-off CXL, with no adverse events and capable of quickly rehabilitating patients with progressive KC to resume their school or work activities, represents a great challenge and a highly interesting goal. The early evidence of my recent studies will allow surgeons to extend the indications for the photodynamic variable fluence ACXL protocol to increasingly younger patients, potentially to treat developmental ectasias even in the pediatric age, before or after intrastromal refractive surgery procedures (LASIK and ReLEx). It may also allow them to perform bilateral treatments when needed, with much-improved patient compliance and clinical workflow, including the possibility of outpatient treatments conducted on the same day to reduce the burden of time and organization for both the patient and the surgeon. Moreover, this treatment protocol can be repeated if the progression of ectasia restarts during the follow-up, and the advantages of Epi-on procedures can still be retained in terms of excellent compliance and the absence of infectious and uncontrolled corneal scarring.<sup>6</sup>

*The Journal of Keratoconus and Ectatic Corneal Diseases* has the honor and task of hosting present and future innovations in clinical and surgical research, in keratoconus diagnostics and in everything relating to genetic, hormonal, inflammatory, environmental and biochemical aspects, including new research topic in ocular microbiota.<sup>7,8</sup>

All ophthalmologists of good will are invited to contribute with their studies to the success of the IJKECD, owned and managed by Jaypee Brothers Medical Publishers (P) LTD.

In recent years we have witnessed and contributed to a revolution in the knowledge of the pathophysiology of keratoconus, of the clinic and of pathophysiological optics, thanks to machines such as Scheimpflug-based and now OCT-based tomography. Furthermore, the biomechanics of the cornea is increasingly closer, especially motion-tracking Brillouin Microscopy, surely it will contribute to many new discoveries and increasingly earlier diagnoses of ectatic diseases. Crosslinking protocols have been optimized to benefit the patient's compliance by reducing the treatment time to 20 minutes without giving up effectiveness.<sup>9,10</sup>

Actually, beyond crosslinking, there are surgical options that allow us to correct, partially or totally, the induced refractive error. Intracorneal ring segments (ICRS) implantation represents a minimally invasive surgical option that improves visual acuity by modifying the corneal geometry. The success rate after ICRS implantation is high, and most importantly, the overall complication rate is low with new customized design.<sup>2</sup>

We have witnessed the birth of a new therapy that promises great results, the corneal allogenic intrastromal ring segments consisting of ring segments derived from allogenic eye bank-processed donor corneas that can be combined simultaneously or sequentially with corneal crosslinking (CXL) procedure in keratoconic patients intolerant to rigid gas permeable contact lenses.<sup>2</sup>

Selective ray-tracing-guided sequential and simultaneous excimer laser transepithelial photorefractive or phototherapeutic keratectomy combined with conventional and accelerated CXL is another way in selected cases to improve spectacles-corrected distance visual acuity (CDVA) of keratoconic eyes.<sup>5</sup>



The microphotoablative remodeling of the central corneal profile is generally planned by using ray-tracing-guided excimer laser softwares, optimizing the optical zones, minimizing tissue consumption, and taking into account the contribution of the epithelium and posterior corneal surface thus avoiding overcorrections.<sup>5</sup>

Phakic intraocular lens (PIOL) implant is also considered in patients with stable or stabilized keratoconus, acceptable CDVA and with acceptable anatomical requirements. The two types of pIOLs, depending on their implantation inside the eye, are anterior chamber (AC)-pIOLs which fixate to the anterior surface of the iris by using a polymethylmethacrylate claw at the haptics, and in particular the posterior chamber (PC)-pIOLs, with ICL concentrating almost all available scientific evidence about the use of PC-pIOL in KC.<sup>2</sup>

Patients with both cataracts and KC present unique challenges for the surgeon, given the peculiar optical characteristics of the ectatic corneas. Particularly, the preoperative evaluation draws our attention to the correct IOL power calculation that is difficult to obtain due to the irregular corneal shape and K values. IOL selection is a crucial moment in the surgery. Toric IOL can be used, but carefully judging the tomography, the manifest refraction, the tolerance of RGP contact lenses and the possible need of subsequent keratoplasties.<sup>2</sup>

Ultimately, it is time for a turning point in keratoconus diagnosis and management and all together we can contribute to this turning point.

## References

1. Hashemi H, Heydarian S, Hooshmand E, et al. The prevalence and risk factors for keratoconus: A systematic review and meta-analysis. *Cornea*. 2020;39(2):263–70.
2. D’Oria F, Bagaglia SA, Alio Del Barrio JL, et al. Refractive surgical correction and treatment of keratoconus. *Surv Ophthalmol*. 2023; S0039-6257(23)00125-X. doi: 10.1016/j.survophthal.2023.09.005. Epub ahead of print. PMID: 37774800.
3. Salman A, Mazzotta C, Kailani O, et al. Diagnostic accuracy of corneal and epithelial thickness map parameters to detect keratoconus and suspect keratoconus. *J Ophthalmol*. 2023;6677932. doi: 10.1155/2023/6677932. PMID: 37842327; PMCID: PMC10575749.
4. Mazzotta C, Romani A, Burroni A. Pachymetry-based accelerated cross-linking: the “M Nomogram” for standardized treatment of all-thickness progressive ectatic corneas. *Int J Keratoconus Ectatic Corneal Dis*. 2019;7(2):137–44.
5. Mazzotta C, Stojanovic A, Romano V, et al. Ray-tracing transepithelial excimer laser central corneal remodeling plus pachymetry-guided accelerated corneal crosslinking for keratoconus. *Cornea*. 2023. doi: 10.1097/ICO.0000000000003380. Epub ahead of print. PMID: 37699556.
6. Mazzotta C, Pandolfi A, Ferrise M. Progressive high-fluence epithelium-on accelerated corneal crosslinking: a novel corneal photodynamic therapy for early progressive keratoconus. *Front Med (Lausanne)*. 2023; 10:1198246. doi: 10.3389/fmed.2023.1198246. PMID: 37671401; PMCID: PMC10475938.
7. Mazzotta C, Traversi C, Mellace P, et al. Keratoconus progression in patients with allergy and elevated surface matrix metalloproteinase 9 point-of-care test. *Eye Contact Lens*. 2018;44 Suppl 2:S48–S53.
8. Rocha-de-Lossada C, Mazzotta C, Gabrielli F, et al. Ocular surface microbiota in naïve keratoconus: A multicenter validation study. *J Clin Med*. 2023;12(19):6354. doi: 10.3390/jcm12196354. PMID: 37834997; PMCID: PMC10573816.
9. Mazzotta C, Raikup F, Hafezi F, et al. Long term results of accelerated 9 mW corneal crosslinking for early progressive keratoconus: the Siena Eye-Cross Study 2. *Eye Vis (Lond)*. 2021;8(1):16.
10. Mazzotta C, Pulvirenti MA, Zagari M, et al. Crosslinking for progressive keratoconus: is there room for improvement? *Expert Review of Ophthalmology*, 2023. DOI: 10.1080/17469899.2023.2207010

**Professor Cosimo Mazzotta MD, PhD, FWCRS**

Associate Professor of Ophthalmology

Director and Founder of the Siena Crosslinking Center, Italy

Anterior Segment Eye Surgeon at the Departmental of Ophthalmology Unit,

Tuscany South-East, Alta Val D’Elsa Hospital, Campostaggia (Siena), Italy

Assistant Professor of Ophthalmology, Post-Graduate Ophthalmology School, University of Siena, Italy

Fellow of the World Council of Refractive Surgery and Visual Sciences Co-Founder of the International Keratoconus Society