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Keratoconus

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Pathophysiology of Keratoconus: What we know and what we are learning

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Keratoconus (KC) is a complex, multifactorial, corneal disease that remains a mystery, in the context of its onset, rate of progression, and underlying pathobiology. Progressive ectasia, corneal thinning, and scarring are the hallmarks of KC, known to affect both males and females. Prevalence has been increasing steadily, going from 1:2000 back in the 1980s to 1:350 in the 2000s worldwide, perhaps due to technological advancements and better diagnostics. Hunting for an etiology for the appearance and progression of KC, studies have been reporting a slew of contributing factors including genetics, environmental conditions, eye rubbing, and hormonal imbalances; however, the pathophysiology of KC remains poorly understood.

The socioeconomic impacts of the disease are harder to compute, but KC is known to disqualify individuals from securing various jobs as well as joining the military. Worldwide, KC remains one of the most common indications leading to corneal transplants. KC was documented, for the first time ever, more than 150 years ago. Despite significant progress, the mechanisms/factors that contribute to the structural and molecular abnormalities in KC are still unclear. Our group has focused on hormonal imbalances and their role in KC; a research direction justified by the manifestations seen in clinics.

Detecting Keratoconus: Advances in corneal imaging and early diagnosis

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Historical Evolution of Corneal Imaging

Corneal imaging has evolved over four centuries from purely qualitative reflection-based methods to sophisticated quantitative tomographic systems. Early developments, from Father Christopher Scheiner's calibrated spheres (1600s), AntonioPlacido's disk (1800), Hermann von Helmholtz's ophthalmometer (1854) to more recent Placido based videokeratoscopes provided only anterior curvature information.

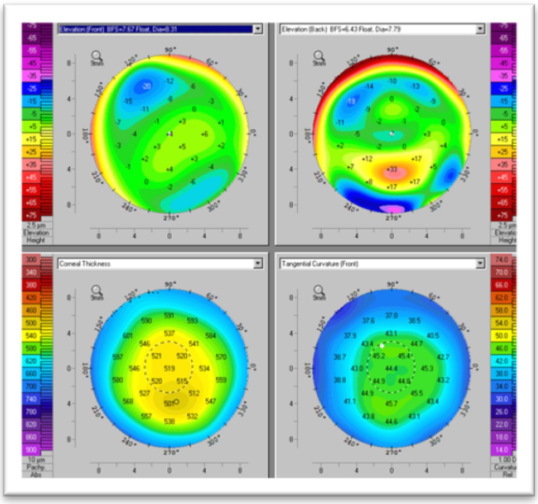

Fig. 1: Subclinical keratoconus – The anterior curvature map (bottom right) is normal, while there is a prominent posterior ectasis (posterior elevation – upper right)

Limitations of Anterior Surface Parameters

Historically, Kmax and related anterior curvature indices were used to identify keratoconus. While these parameters were adequate when treatments were limited to spectacles, contact lenses, or penetrating keratoplasty, they lacked the ability / sensitivy to detect early or subclinical disease. Reflective systems assess only 60% of the anterior corneal surface, leaving the posterior surface and pachymetric progression unmeasured. Figure 1 shows subclinical keratoconus, characterized by a normal anterior curvature map (bottom right), while the posterior elevation map (top right) reveals a distinct posterior ectasia, indicating early corneal changes not yet detectable on the anterior surface.

Tomography and the ABCD Classification

Modern Scheimpflug and anterior segment OCT imaging systems provide three-dimensional corneal maps including both anterior and posterior curvature and full-thickness pachymetry . The ABCD classification was developed to address the limitation of the 75 year-old Amsler-Krumeich classification. It evaluates anterior and posterior radii of curvature taken from a 3 mm optical zone centered on the thinnest point, minimum corneal thickness, and best-corrected visual acuity and allows for a detailed anatomic description (figure 2).

ABCD Criteria	A	B	C	D
	ARC (3 mm Zone)	PRC (3 mm Zone)	Thinnest Pach um	BDVA
STAGE 0	> 7.25 mm (< 46.5 D)	> 5.90 mm (< 57.25 D)	> 490 um	= 20/20 (= 1.0)
STAGE I	> 7.05 mm (< 48.0 D)	> 5.70 mm (< 59.25 D)	> 450 um	< 20/20 (< 1.0)
STAGE II	> 6.35 mm (< 53.0 D)	> 5.15 mm (< 65.5 D)	> 400 um	< 20/40 (< 0.5)
STAGE III	> 6.15 mm (< 55.0 D)	> 4.95 mm (< 68.5 D)	> 300 um	< 20/100 (< 0.2)
STAGE IV	< 6.15 mm (> 55.0 D)	< 4.95 mm (> 68.5 D)	= 300 um	< 20/400 (< 0.05)

Fig. 2: Belin ABCD Classification

Detecting Early and Progressive Disease

Early keratoconus can exist with normal anterior surface and vision but marked posterior elevation and asymmetric pachymetric thinning. Progression should be defined by statistically significant changes on tomography rather than visual acuity or Kmax changes. The Belin ABCD Progression Display allows for the identification of statistically significant change (progression) in spite of a stable Kmax and/or a stable anterior surface (figure 3).

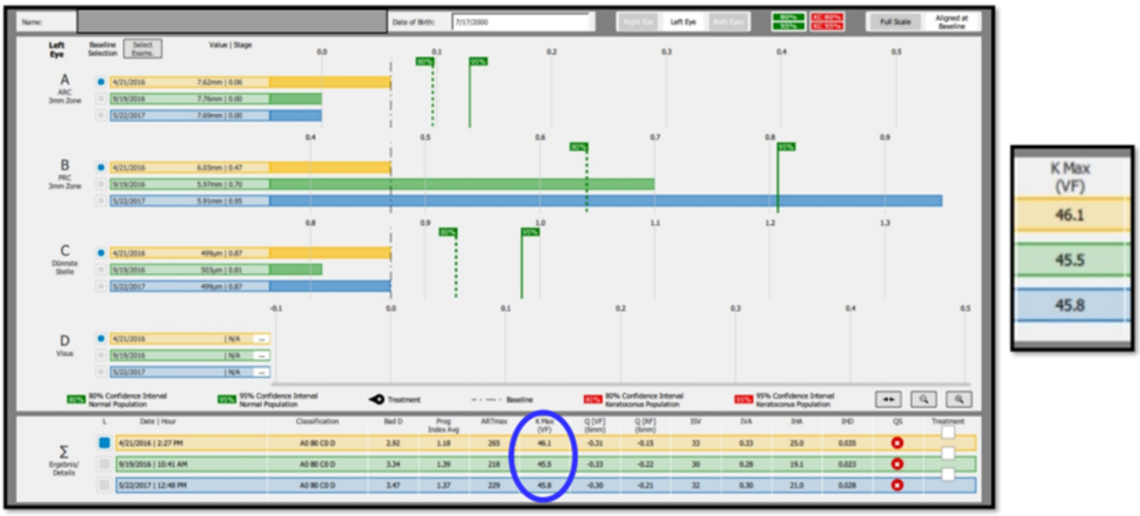

Fig. 3: Stable anterior surface ("A" parameter) and stable Kmax in the presence of marked posterior progression ("B" parameter)

As treatment philosophy has shifted from managing visual loss to preventing progression, the Belin ABCD progression display allows for earlier detection of progressive disease than relying on changes to Kmax. Early identification allows timely crosslinking (CXL) before loss of best-corrected visual acuity.

Conclusion

The paradigm shift in keratoconus diagnosis emphasizes posterior surface analysis and pachymetric progression as key indicators of early disease. Tomographic-based approaches such as the ABCD classification provide earlier detection of ectasia than Kmax-dependent methods.