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Biomechanics meets tomography. Corvis ST meets Pentacam AXL

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New Belin ABCD keratoconus classification/grading					
ABCD criteria	**A**	**B**	**C**	**D**	
	ARC (3 mm zone)	PRC (3 mm zone)	Thinnest pach um	BDVA	Scarring
STAGE 0	> 7.25 mm (< 46.5 D)	> 5.90 mm	> 490 um	≥ 20/20 (≥ 1.0)	-
STAGE I	> 7.05 mm (< 48.0 D)	> 5.70 mm	> 450 um	< 20/20 (< 1.0)	-, +, ++
STAGE II	> 6.35 mm (< 53.0 D)	> 5.15 mm	> 400 um	< 20/40 (< 0.5)	-, +, ++
STAGE III	> 6.15 mm (< 55.0 D)	> 4.95 mm	> 300 um	< 20/100 (< 0.2)	-, +, ++
STAGE IV	< 6.15 mm (> 55.0 D)	< 4.95 mm	≤ 300 um	< 20/400 (< 0.05)	-, +, ++

Figure 1. New Belin classification system

Source: Michael Belin, MD

OCULUS (Wetzlar, Germany) hosted a lunch symposium at the 31st APACRS Annual Meeting in Chiang Mai, Thailand, on 19 July 2018. The symposium introduced updates to the company's Corvis ST and Pentacam AXL platforms designed to enhance the safety and efficacy of refractive surgery.

Michael Belin, MD, began by discussing "Clinical applications of the Belin ABCD Progression Display."

Dr. Belin compared the current approach to the evaluation of patients with keratoconus to what is called an "idiot light" in the automotive industry—an indicator that by the time its alarm goes off is already too late. This is particularly the case, he said, when using Kmax.

"If you get changes on the anterior surface, you get changes in Kmax, it means your refracting surface is already compromised," Dr. Belin said. Rather than an idiot light, what is needed is a way to monitor progression and see changes to the cornea early, not when it has already started decreasing vision.

This is particularly relevant owing to advances in the management of keratoconus. Whereas until recently the two treatments had been penetrating keratoplasty and rigid contact lenses, used only when the severity of the disease had created anterior surface changes, these days we have crosslinking, a treatment that requires identification and characterization of the disease as early as possible—*before* the patient has loss of vision.

Previously, Dr. Belin had developed the Belin-Ambrosio Display, which uses an enhanced reference surface that is normalized by removing a 3-mm exclusion zone centered on the thinnest point of the cornea from analysis.

However, to characterize the disease, Dr. Belin said that rather than removing the exclusion zone, "let's actually look at that zone."

Dr. Belin developed a new classification called the ABCD classification: A for anterior radius curvature at the thinnest point (not the apex); B for "back" or posterior radius curvature at the thinnest point; C for corneal thickness at the thinnest point; and D for distance visual acuity.

The classification system consisted of five stages, adding a stage 0 to the old Amsler-Krumeich classification (Figure 1). Using this system, each layer is graded independently.

The system is currently available on the Pentacam as part of the Topometric Keratoconic Staging Display.

The goal of the classification system was to develop a way to determine when and if true progression occurs. What Dr. Belin and his colleagues have come up with is the ABCD Progression Display. The display shows up to eight exams over time, analyzes the ABCD parameters and displays both 80% and 95% one-sided confidence intervals.

"If you seek statistically significant change here, it's an indication to treat in spite of the fact that the patient retains good vision," Dr. Belin said. "We should not be waiting until loss of vision occurs. We should be looking for true progression and intervening at the earliest possible stage."

The tomography-based progression display documents statistically significant change and allows timely crosslinking, also showing crosslinking efficacy.

In his talk, **Fritz Hengerer, MD**, discussed "Patient screening and IOL calculation with Pentacam AXL and Keratograph 5M," providing an overview of what they do in Heidelberg with their IOL patients.

For preoperative cataract screening, Dr. Hengerer performs ocular surface analysis with the Keratograph 5M (OCULUS) before Pentacam analysis. Measurements are taken before any eye drops are applied.

The Keratograph can demonstrate diminished tear breakup time despite a normal looking slit lamp corneal reflex and can be used to help patients understand the need for steroid treatment to manage postop dry eye. Meanwhile, the Pentacam—originally named for measuring five parameters—measures various parameters including axial length, keratometry, pachymetry, pupil diameter, natural lens densitometry, keratoconus screening, index reporting, and IOL calculation.

Prof. Naoyuki Maeda established an algorithm to develop preop assessment of corneal optical properties for premium IOL selection using four-step criteria on the Pentacam's Cataract Preop Display: (1) evaluation of HOAs; (2) corneal shape assessment; (3) evaluation of corneal spherical aberrations (Z4,0); and (4) evaluation of corneal astigmatism, including magnitude and axis.

"With the latest software update of the Pentacam AXL, we can assume that it is faster, the measurements are more precise, can measure denser cataracts," Dr. Hengerer said.

Furthermore, he said, the software makes it feasible to compare with the IOLMaster 700 (Carl Zeiss Meditec, Jena, Germany), which uses a completely different approach to evaluating the cornea.

Heidelberg University undertook a large comparative prospective trial comparing the IOLMaster 700 and Pentacam AXL using the most recent software versions of both devices.

Evaluating 158 eyes from patients who fulfilled inclusion criteria and consented and who underwent three exams per eye with the IOLMaster 700 and Pentacam AXL, Dr. Hengerer and his colleagues looked at: (1) success rate of axial length measurements—quality scan = OK for the Pentacam, no exclamation mark for the IOLMaster; (2) comparison of three repeated exams taken with both devices for the same eye regarding repetition of axial length, keratometry, astigmatism and axis, anterior chamber depth, horizontal corneal diameter (HWTW); (3) coefficient of repeatability, the standard deviation and mean.

Dr. Hengerer and his colleagues found that the Pentacam AXL had a higher success rate for axial length measurements (Figure 2), with higher repeatability for axial length, keratometry, astigmatism, axis, and HWTW measurements. The IOLMaster, on the

Axial length [mm]									
	n	**[%]**	**Mean**	**Min**	**Max**	**COR**	**Max. diff 1. vs 3. exam**	**Max. diff 1. vs. 2. exam**	**Max. diff 2. vs. 3. exam**
IOLMaster 700	117	72,84	23,41	21,02	28,11	**0,027**	0,08	0,07	0,071
Pentacam AXL	128	80,5	23,6	20,988	34,17	**0,022**	0,051	0,078	0,078
IOLMaster 700, inkl. (!)	156	98,11	23,74	21,02	34,2	**0,050**	0,3	0,3	0,1

Figure 2. Comparison of success rates between the IOLMaster and Pentacam AXL for axial length measurements

Source: Fritz Hengerer, MD

AUC and pAUC With Specificity ≥ 80% for Classification Between Normal and Subclinical Keratoconus

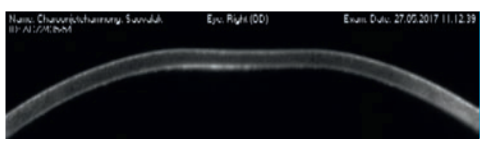
Parameter[a]	AUC	pAUC	Cut-off	Specificity	Sensitivity
TBI	0.925	0.150	0.16	82.4%	84.4%
Corvis ST					
ARTh	0.836	0.129	444.0	82.4%	81.3%
Max inv rad	0.754	0.079	0.19	82.4%	59.4%
A1T	0.750	0.052	7.18	82.4%	46.9%
RC	0.736	0.094	6.78	82.4%	62.5%
Pentacam					
BAD final D	0.786	0.088	1.38	85.3%	53.1%
IVA	0.781	0.125	0.15	88.2%	68.8%
ARTmax	0.759	0.095	386.5	82.4%	65.6%
CTapex	0.722	0.058	534.5	82.4%	37.5%
CTmin	0.710	0.059	529.5	82.4%	43.8%

AUC = area under the receiver operating curve; pAUC = partial area under the receiver operating curve; TBI = tomographic biomechanical index; ARTh = horizontal Ambrósio's relational thickness; Max Inv Rad = maximum inverse radius; A1T = time from the initiation of air-puff until the first applanation; RC = radius of curvature at highest concavity; BAD final D = Belin/Ambrósio Enhanced Ectasia Display final D value; IVA = index of vertical asymmetry; ARTmax = maximum Ambrósio's relational thickness; CTapex = corneal thickness at apex, CTmin = minimum corneal thickness
[a]Only the highest 5 parameters from each device were selected.
The Pentacam and the Corvis ST are manufactured by Oculus Optikgeräte, Wetzlar, Germany.

Figure 3. TBI had a high AUC for differentiating between normal and subclinical keratoconus.

Source: Tommy Chan, MD

Applanation 1
Inward motion



Parameters	Stage1	Stage2	Stage3	unadjusted		adjusted	
	(n=42)	(n=26)	(n=12)	p[a]	p[b]	p[c]	p[d]
A1- Length (mm)	1.79 ± 0.05	1.84 ± 0.05	1.92 ± 0.09	<0.001	<0.001	0.07	<0.001
A1- Time (ms)	6.89 ± 0.25	6.83 ± 0.23	6.66 ± 0.39	0.31	<0.01	0.24	<0.01
A1- Velocity (m/s)	0.14 ± 0.01	0.14 ± 0.02	0.16 ± 0.03	0.79	0.07	0.88	0.10

General linear mode

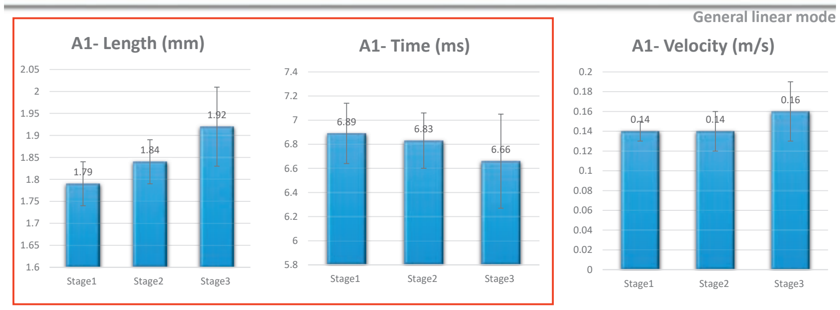


Figure 4. Applanation 1 parameters

Source: Usanee Reinprayoon, MD

other hand, showed higher repeatability for ACD measurements.

Tommy Chan, MD, shifted the discussion to the use of the Corvis ST (OCULUS), discussing "The use of combined tomographic and biomechanical assessment in pre-refractive surgery screening."

Rotating Scheimpflug imaging, he said, provides useful information on the base of tomographic data for diagnosing early ectatic change, contextualizing the importance of this by calling corneal ectasia a "nightmare"—"one of the most devastating complications after corneal refractive surgery" that can occur any time.

While current methods easily differentiate ectatic from normal eyes, more challenging is differentiation between subclinical disease, such as with forme fruste keratoconus, and normal eyes.

"Apart from the tomography, we would like to evaluate the biomechanical properties of the cornea in order to have a complete picture of the cornea, especially since corneal biomechanical failure is the basis of keratoconus," Dr. Chan said. The Corvis ST provides this information.

An ultra high-speed Scheimpflug device, the Corvis ST applies a non-contact tonometer symmetrically metered air pulse to the cornea and scans at 4,330 frames/sec, with 8-mm horizontal coverage.

Dr. Chan discussed a number of parameters for evaluating corneas and described the Vinciguerra Screening Report, which incorporates seven parameters, including DA ratio, integrated radius, Ambrosio relational thickness (ART), the new corneal stiffness parameter SP-A1, and Corvis biomechanical index (CBI).

The Vinciguerra group used CBI to differentiate keratoconus from normal and found a very high AUC of 0.990 in differentiating keratoconus from normal. Dr. Chan and his colleagues also found an AUC of 0.971 when using CBI to differentiate normal corneas from keratoconus. A comparable AUC was observed between CBI (AUC=0.785) and use of the Belin-Ambrosio Display (BAD, AUC=0.757) (p=0.590) for detection of forme fruste keratoconus with sensitivities of 65% and 53%, respectively, specificity of 80%.

Dr. Chan said that combining tomography and evaluation of the biomechanical properties of the cornea would allow better detection of subclinical or forme fruste keratoconus. OCULUS has thus introduced a new parameter with the Pentacam: the tomography biomechanical index (TBI). New software incorporates the Corvis parameters and the tomography values, generating a TBI at the end.

Dr. Chan and his colleagues analyzed data from 41 keratoconus cases, with 37 controls and 23 subclinical keratoconus. They found a very high AUC of 0.925 with specificity of 82.4%, sensitivity of 84.4% for differentiating between normal and subclinical keratoconus using TBI (Figure 3).

"The combination of corneal tomography and biomechanical properties is a very good tool to enhance the safety and efficiency of your surgery," Dr. Chan concluded.

Also speaking on her experience with the Corvis ST, **Usanee Reinprayoon, MD**, discussed "Clinical applications of corneal biomechanics in corneal diseases."

Dr. Reinprayoon described her conceptual framework as follows: If you do refractive surgery on patients with subclinical keratoconus, the patient may end up with corneal ectasia. Similarly, if you do cataract surgery on patients with Fuchs' endothelial corneal dystrophy (FECD), the patient may end up with corneal decompensation.

FECD, she said, is a progressive loss of corneal endothelial cells leading to corneal thickening and edema that may be focal or diffuse. It requires clinical assessment, with specular microscopy limited to a small central area and high variation in cell count and pachymetry providing an indirect measurement to evaluate endothelial cell function.

In FECD, she said, tissue hydration is increased. How does this affect corneal stiffness and biomechanics?

Dr. Reinprayoon said that corneal biomechanics provides an understanding of the natural history, pathophysiology, and prognosis of FECD. She and her colleagues used the Corvis ST to analyze the corneal biomechanics in 80 FECD patients, looking at various parameters. During the inward motion (Applanation 1), they looked at A1-Time, the time taken for the cornea to reach first applanation; A1-Length, the length of the flattened portion at first applanation; and A1-Velocity, the velocity of inward motion at first applanation. At the point of highest concavity (HC), they looked at HC Time, the time taken for the cornea to reach HC; Peak Distance, the distance between the peaks; HC Radius, the radius of curvature at HC; and Deformation Amplitude (DA), displacement from initial state. Finally, during outward motion (Applanation 2), they looked at A2-Time, the time taken for the cornea to reach second applanation; A2-Length, the length of flattened portion at second applanation; and A2-Velocity, the velocity of inward motion at second applanation.

She said that nearly all corneal biomechanical parameters correlated with clinical staging; compared to the normal population, the FECD patient's cornea is more easily compressed by pneumopressure, and the more advanced the disease, the flatter the cornea. A1-Time and A1-Length seem to be the sensitive parameters among those analyzed (Figure 4).

This understanding will benefit the treatment plan of patients, she said.

In the future, Dr. Reinprayoon said that corneal biomechanics is applicable in the diagnosis of endothelial decompensation from other causes and in the follow-up of patients post-corneal transplantation, for the novel prediction of corneal diseases, and to evaluate the effect of corneal transplantation and donor parameters.