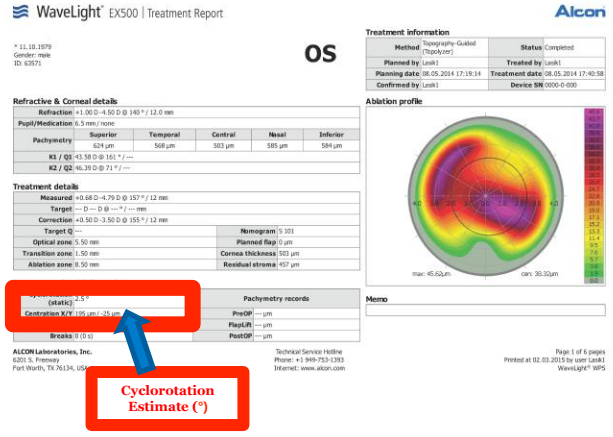
Modified Athens Protocol for Keratoconus
Topo-guided partial PRK normalization and variable pattern and fluence CXL (Refractive CXL-PiXL)



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Methods:

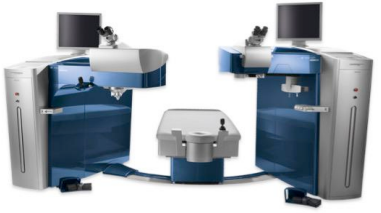
45 consecutive cases treated with the EX500 Wavelight excimer, part of the Refractive Suite and the KXL II CXL device with the following Steps: 1. Partial topography-guided excimer-laser PRK ablation 2. PTK Excimer-laser ablation to account for epithelial removal, employed AFTER the step #1 (50-µm, 8.00-mm zone). 3. variable higher-fluence and variable shape Customized UV-A delivered in custom-designed CXL pattern Long-term stability assessed with refraction, keratometry, Placido topography, Anterior-Segment-OCT, and and Scheimpflug imaging

Results:

All cases had one-year refractive, keratometric, and anterior-surface irregularity indices improvement superior to our previously published standard Athens Protocol results. Average Keratometry improvement: from 51.5 Diopters to 45.4 D, UDVA: from 20/70, to 20/40, CDVA from 20/40 to 20/25, Index of Height Decentration (IHD): from 0,155 to 0,042. Keratoconus stage (1-4): from 3 to 1-2 in average.

Novelty points of the 2014 Modified Athens Protocol

1-Perform the partial topography-guided PRK FIRST (prior to the 50um PTK to remove epithelium) so to achieve better tracking

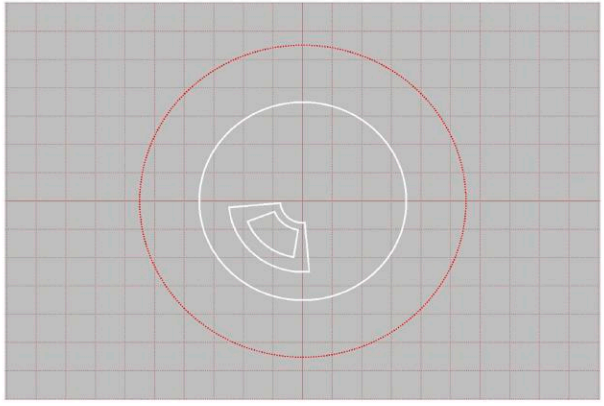


2-EX500 excimer laser with cyclorotation compensation for the partial topo-guided PRK

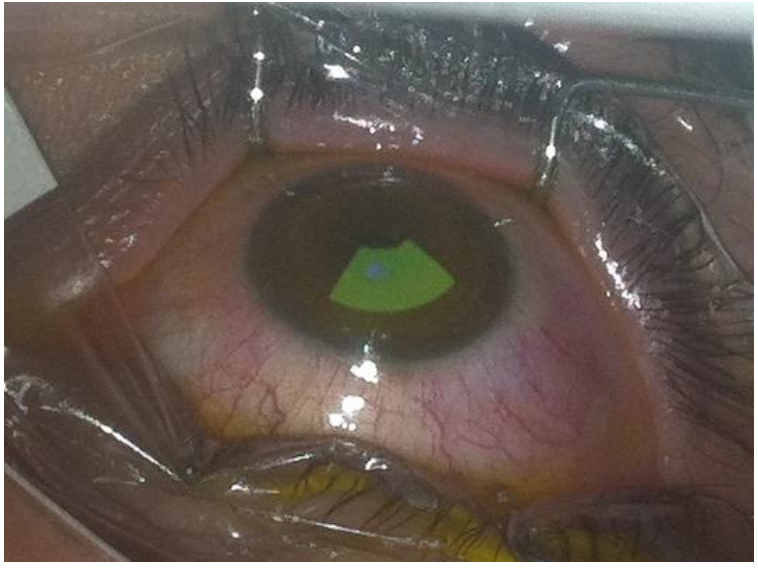
3-Instead of applying uniform higher fluence CXL (6mW/cm2 for 15') variable pattern and variable fluence REFRACTIVE CXL was applied with the KXL-II device by Avedro

Novelty points of the 2014 Modified Athens Protocol

- Instead of applying uniform higher fluence CXL (6mW/cm2 for 15') variable pattern and variable fluence REFRACTIVE CXL was applied with the KXL-II device by Avedro
- The CXL treatment parameters are noted in the treatment plan bellow



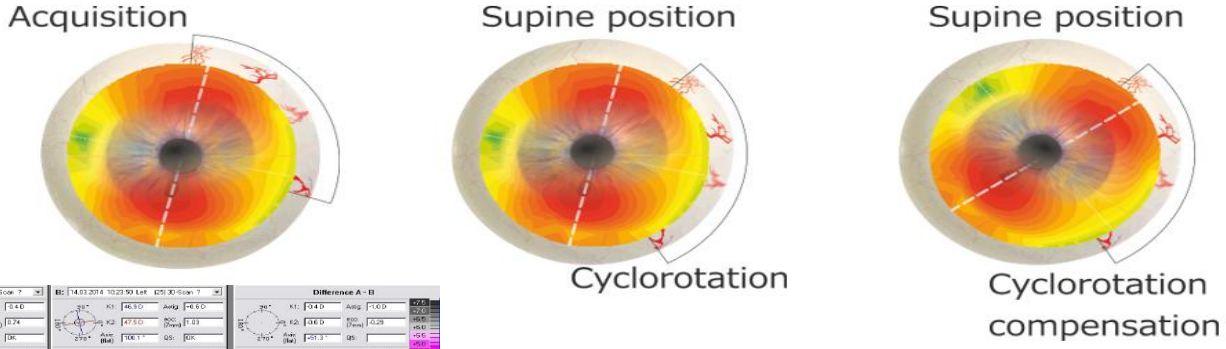
No.	Shape Type	Time (mm:ss)	Total Energy (J/cm²)	X Position (mm)	Y Position (mm)	Axis (degs.)	Dim. 1 (mm)	Dim. 2 (mm)	Arc (degs.)
1	Arc_Single	5:33	15.0	0.0	-0.0	231	4.0	1.0	60
2	Arc_Single	3:42	10.0	0.0	-0.0	230	5.0	1.7	90
3	Circle_7mm	1:29	4.0	0.0	-0.0		7.0		

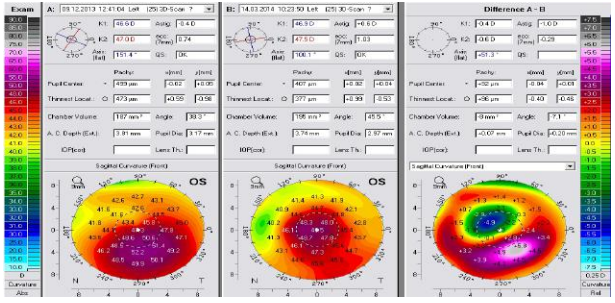


Cyclorotation Compensation

- Combination of iris and limbal blood vessel pattern matching to compare a pre-operative upright reference image with a pre-operative sample supine image.
- Enabled by novel Placido Topography infrared auxiliary imaging (WaveLight Vario).
- The treatment planning is appropriately rotated to compensate for any cyclorotation between the two states.

Initial data matching to reference image

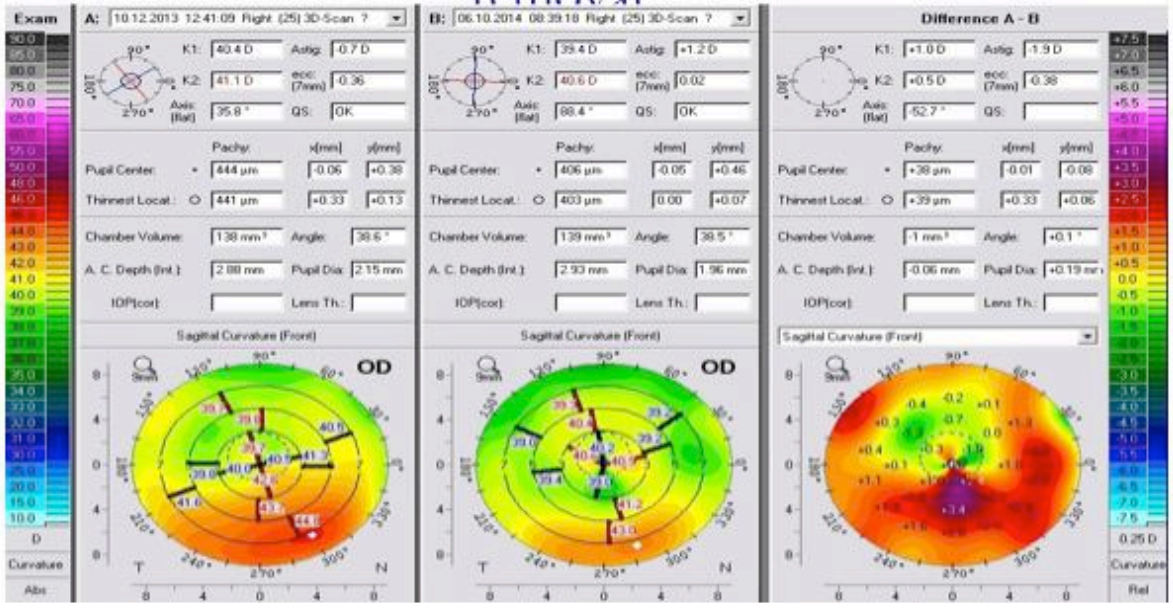




The Scheimpflug-derived difference map

Clinical example, before, after and difference

AP plus PiXL (variable fluence topo-guided CXL)
The advantage is marked normalization with less tissue removal



Analysis

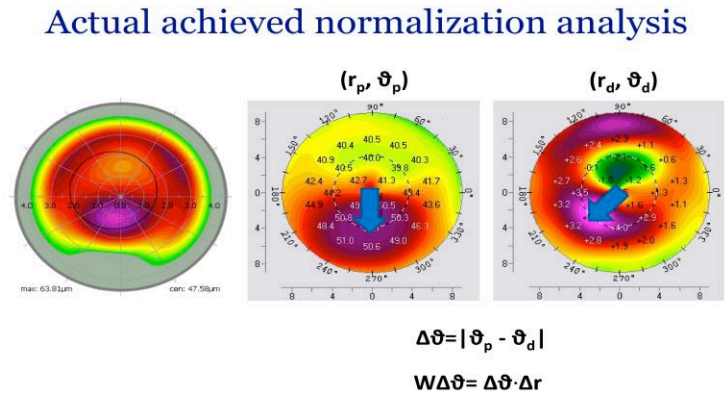
Digital processing of Scheimpflug-imaging derived topographic curvature **difference maps** with the objective to measure angular differences between targeted (surgical planning) and achieved ablation pattern.

Outcomes:

Vector (r, ϑ) corresponding to the steepest (peak topographic) corneal point (cone) on the pre-operative surgical planning map (r_p, ϑ_p) and the curvature difference map (r_d, ϑ_d).

Calculated data:

Differences between the peak topographic angular data: $\Delta\vartheta=|\vartheta_p - \vartheta_d|$ & weighted angular difference $\mathbf{W\Delta\vartheta=\Delta\vartheta \bullet \Delta r}$.



The 'compare 2 exams' output from the Scheimpflug imaging device.

- Left, the pre-operative sagittal curvature map;
- middle, the post-operative map
- right, the difference of the two maps.

Measurement of axial and radial coordinates of the steepest corneal point (ImageJ Software) corresponding to the pre-operative (left) and difference map (right) also shown above.

The pre-operative map vector had coordinates rp = 1.69 mm, ϑp = 270°.

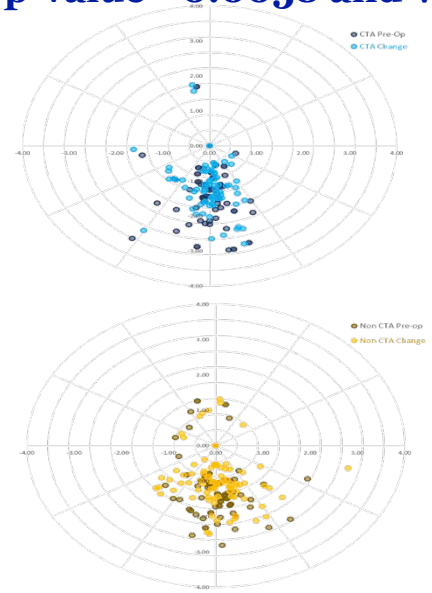
The difference map vector, rd = 1.69 mm, ϑd = 225°, respectively.

There is evident difference between the two maps, which may be attributed to non-compensation of cyclorotation: the $\Delta\vartheta$ (difference between the peak topographic angular data) and W$\Delta\vartheta$ (weighted angular difference) corresponding to these data were 45° and 58.30 mm, respectively.

For **group-A** Athens Protocol cases with cyclo adjustment average Δϑ was 7.18±7.53 (0 to 34) ° and WΔϑ was 3.43±4.76 (0.00 to 21.41) mm.

For group-B (without-cyclo), average Δϑ was 14.50±12.65 (0 to 49) ° and WΔϑ was 10.23±15.15 (0.00 to 80.56) mm.

The group-A Athens Protocol **cases with cyclorotation adjustment had on average smaller angular difference** as well **as weighted angular difference by a statistically significant margi (Δϑ p-value =0.0058 and WΔϑ p-value =0.015).**



	group-A	(Vario/cyclo)	group-B	(Oculyzer II, non-cyclo)
	Δϑ (°)	WΔϑ (mm)	Δϑ (°)	WΔϑ (mm)
average	7.18	3.43	14.50	10.23
st. dev	± 7.53	± 4.76	± 12.65	± 15.15
min	0	0.00	0	0.00
max	34	21.41	49	80.56
Confidence Intervals				
0.95	± 1.77	± 1.12	± 2.64	± 3.21
0.99	± 2.35	± 1.49	± 3.49	± 4.25
p-value between groups	0.0058	0.0015		

Discussion

- In addition to adopting cyclo-tortional compensation, the enhanced Athens Protocol incorporates a change in the ablation pattern sequences, by preceding the PRK step to the PTK step. The rationale for this has been the following: the topography-guided ablation pattern bears the customized part, for which the active eye-tracking should be performing with minimal interference. Thus the partial-PRK step is performed first, to interfere with less ablated debris, and therefore to have the best possible pupil imaging. The PTK step, which was initially designed to ablate a 'uniform' 50 μm thickness over a 8.00 mm zone, to achieve epithelial debridement, may be performed subsequently. This PTK part, by being rotationally symmetric, does not necessitate cyclorotation compensation is not dependent on saccadic motion to the extend the PRK part does
- Incorporation of cyclorotation compensation in customized topography-guided treatments in our Athens Protocol cases with the EX500 excimer laser, leads to **greatly improved objective correlation between targeted and achieved** cylindrical changes.
- The Refractive CXL utilized, enhances the refractive result and minimizes tissue removal
- Topography-guided partial PRK with excimer laser combined with customized variable fluence and pattern UV-A delivery CXL (vCXL) leads to improved visual rehabilitation outcomes with similar stability established, and potentially a more effective normalization with less cornea tissue removal due to the added refractive effect of vCXL.