Correlation between overall epithelial thickness in normal corneas, ectatic and ectatic previously treated with CXL corneas:

Can overall corneal epithelial thickness become a very early ectasia prognostic factor?
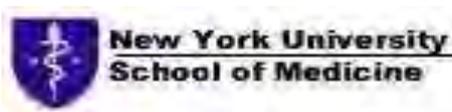
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Introduction:

To determine the efficacy of epithelial corneal thickness (pachymetric) measurements taken with a digital arc scanning very high frequency ultrasound biomicroscopy (HF UBM) imaging system (Artemis-II), and compare mean, central and OVERALL epithelial thickness over normal, keratoconic, non-treated eyes, and keratoconic eyes treated with collagen cross-linking (CXL).
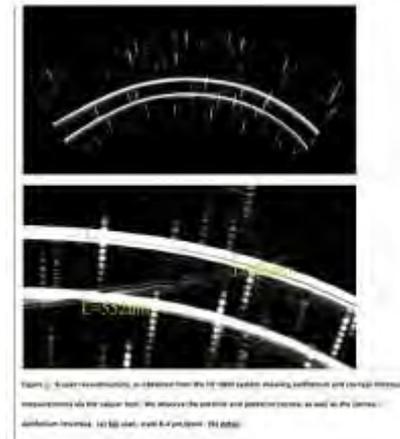
Epithelial pachymetry measurements (topographic mapping) were conducted on one hundred subjects via high-frequency digital arc scanning biomicroscopy. Three groups of patients were formed, namely normal, keratoconic with no treatment, and those with keratoconic eyes treated with CXL. Central, mean, and peripheral corneal epithelial thickness was examined for each group, and statistic study was conducted.

Methods:
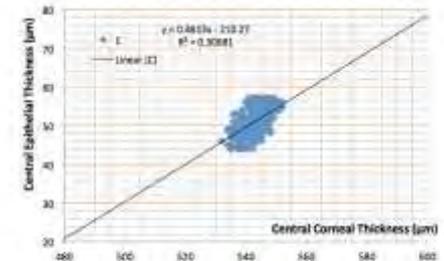
Figure 2. Central epithelial thickness versus central corneal thickness of the same data points as produced by 540 different combinations of latest meridional scans. All data correspond to the same eye.

- Epithelial pachymetry measurements (topographic mapping) were conducted on one hundred subjects via high-frequency digital arc scanning biomicroscopy. Three groups of patients were formed, namely normal, keratoconic with no treatment, and those with keratoconic eyes treated with CXL. Central, mean, and peripheral corneal epithelial thickness was examined for each group, and statistic study was conducted.

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Results:

- Mean central, and transitional zone (peripheral) corneal epithelial thickness was compared between the three groups of patients. The control group displays consistently a thicker epithelium over the pupil center a point that was usually not the peak of the cone, where the cornea is thinner. Epithelium thickness varied substantially in the keratoconic group, and in some cases this may have presented a difference of up to 20 μm between various points of the same eye, and often enough, the thinner epithelium coincided with the thinner cornea.
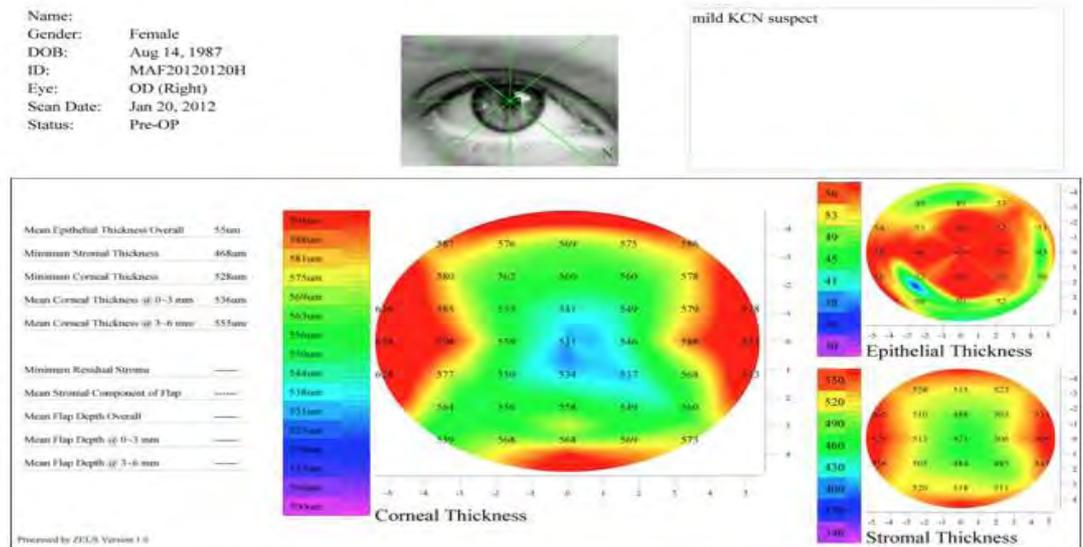
KCN example

Figure 3: Corneal and epithelial thickness maps a KCN patient. A significantly thicker epithelium over the pupil center is observed to "mask" the cone apex just inferior to this. The overall epithelial thickness is thicker than normal studied and KCN eyes that had undergone previous CXL.

Results:

- However, on average, data from the keratoconic group suggest that there is an overall thickening of the epithelium, particularly over the pupil center, while the mean epithelium thickness compared to the control population (P< 0.0001), and the peripheral transitional zone thickness being almost on average the same.

- This thickening is pronounced in the younger patients of the group. Eyes having been treated with CXL show, on average, virtually the same average epithelium thickness (-0.7 μm mean, -0.2 μm over the pupil center, -0.9 over the transitional zone) as the control group.

- The comparison of normal, KCN and KCN treated with CXL corneal epithelial thickness is very impressive:

Table 5 Mean, center, and peripheral epithelium thickness, as examined separately for the five younger and the five elder patients from the KCN group

	Age (years)	Epi mean	Epi center	Epi peripheral 4 mm	Age (years)	Epi mean	Epi center	Epi 4 mm
Average	20.9	52.0	55.9	49.7	33.1	51.4	53.4	49.7
Max		57.0	60.0	55.0		55	58	55.00
Min		48	48	44		46	46	43
SD	3.5	3.1	3.8	3.2	3.8	3.6	3.5	4.2

Abbreviations: Epi, epithelium thickness; SD, standard deviation.

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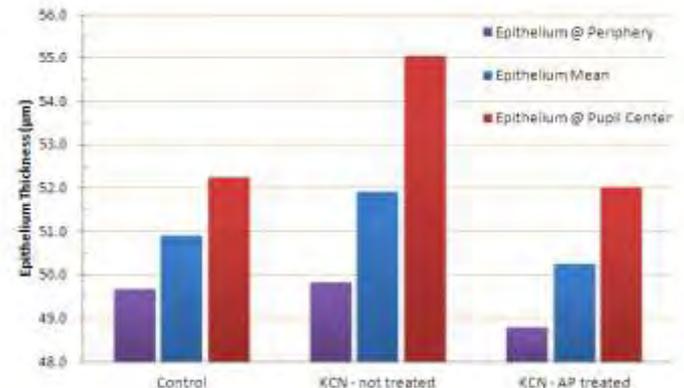
Discussion

- Our study demonstrated that epithelial thickness readings, as obtained by using arc-scanning HF UBM pachymetry, show substantial localized, as well between patients, variation. Eyes not having been subjected to any surgery show a moderate central epithelium thickening. Overall thicker epithelium, with large variations was observed on the KCN patients. This comes in contrast to previously published work and current understanding In many occasions the epithelium was significantly thinner over areas of corneal ectasia. While masked by the uncertainty of the readings, this difference may be particularly helpful in close-call clinical decisions, if prominent enough, and if the differences of the thinner part, which coincides with the corneal protrusion, are large enough to justify a clinical call.

- Patients subjected to CXL-treatment, however, did not show a statistically significant trend towards thicker central epithelium, **supporting our hypothesis of "reactive" epithelial hyperplasia in** biomechanically unstable corneas.

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Discussion

- We feel this may be a significant new finding. Especially in an era when most anterior segment OCT devices will be able to offer detailed and accurate cornea epithelial maps, this theory may provide a very sensitive, pre-ectasia clinical parameter in corneas that have become biomechanically unstable. This **"reactive" epithelial hypertrophy may precede any of the** standard topographic or tomographic cornea findings. For **example "suspect" corneas due to thinner structure, high** astigmatism or even relation to a known KCN patient may be differentiated in regard to their ectasia potential based on the average cornea epithelial thickness.

- **The "normalization" of average epithelial thickness in long** term follow-up of CXL treated ectasia cases, further supports this theory. Further studies are obviously needed to further validate these results.

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Conclusions

- Very high-frequency digital ultrasound topography of cornea may map the epithelium and flap thickness over the entire cornea
- As shown before the epithelium appeared thinner over the keratoconic apex and thicker over flatter areas.
- Highly irregular epithelial thickness may be suggestive of an ectatic cornea,
- We have found herein that overall, there is thicker –on average- epithelium in the ectatic group of patients. This difference, not only appears to be clinically significant, but also appears to reverse in ectatic corneas that have had CXL.
- We theorize that this thickness represents a reactive epithelial hypertrophy to the biomechanical instability that these corneas have to internal and external oscillation(s).
- This novel finding may pioneer epithelial thickness measurements as a very early screening tool of eyes suspected for ectasia. The clinical applications of this theory are enormous considering the evolving ability of cornea OCT devices to offer accurate and easy to obtain epithelial thickness maps.

Kanellopoulos AJ, Aslanides IM, Asimellis G. Correlation between epithelial thickness in normal corneas, untreated ectatic corneas, and ectatic corneas previously treated with CXL; is overall epithelial thickness a very early ectasia prognostic factor? Clin Ophthalmol. 2012;6:789-800.

Kanellopoulos AJ, Asimellis G Correlation between central corneal thickness, anterior chamber depth and corneal keratometry as measured by Oculyzer II (Pentacam HR) and Alcon Biograph (LenStar LS900) in pre-cataract surgery patients. In press J Refract Surg

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