Using corneal first surface wavefront to detect Keratoconus

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Why detect keratoconus?

- Keratoconus detection is important in routine clinical care in ophthalmology and optometry.
- Keratoconus is a rare disease, affecting ~150,000 Americans.
- Keratoconus causes myopia and astigmatism in its early stages, so patients present disproportionately often for refractive surgery.
- Refractive surgery on an eye with Keratoconus causes rapid acceleration of the disease leading to severe vision loss.
Post-LASIK ectasia
Screening for Keratoconus

- Keratoconus screening is an important part of pre-refractive surgery assessment.
- Screening is typically done qualitatively – clinical acumen required – using clinical examination and corneal topography.
- Qualitatively assess asymmetry.
- Consider maximum corneal power.
Axial Diopters

dist 1.41 mm  
axis 268°  
value 51.30 D

Optical zone
Min Pwr 45.98  
Max Pwr 46.94  
Mean Pwr 46.59  
Min Radius 0.40  
Max Radius 1.36  
Mean Radius 0.69  
OZ Area 1.50

SIM K's
47.41 D @ 106°  
44.06 D @ 16°
Axial Diopters

dist  1.66 mm
axis  266°
value 44.41 D

Corneal Topography

Optical zone
Min Pwr  42.45
Max Pwr  43.44
Mean Pwr  42.75
Min Radius  0.45
Max Radius  3.60
Mean Radius  1.08
OZ Area  3.64

SIM K's
43.25 D @ 123°
42.05 D @ 33°

1.00 D
Automated quantitative screening

- Tremendous effort has gone into the development of quantitative indices of Keratoconus risk
- Quantify asymmetry or other factor
- Automate detection
- Developed indices are topographer specific
- Many topographers do not have a keratoconus detection schema
Topographer-based screening

- Inferior – Superior (I-S) scheme: 6 points, basic asymmetry test
- I-S + corneal power, KISA % (Rabinowitz test)
- Klyce/Maeda Keratoconus Index (KCI)
- Holladay Diagnosis Summary Indices
- Classification neural network
- Others proposed – thickness, posterior elevation, rate of steepening etc
- Most successful schema basically detect asymmetry within the topography pattern
Wavefront sensor-based screening

- Why not use wavefront error?
- At least 7 wavefront sensors are available on the market
- None have detection schema
- New detection schema could readily find a platform for application
Wavefront to detect keratoconus

• The first publication on Keratoconus detection from corneal topography height data using components of a Zernike expansion (Schwiegerling J, Greivenkamp JE. Keratoconus detection based on videokeratoscopic height data. Optom Vis Sci. 1996 Dec;73(12):721-8.) showed it was more effective than existing schema e.g. I-S index.
• Index used Coma and Trefoil only
How good are existing schema?

• **Langenbcher et al** (Langenbcher A, Gusek-Schneider GC, Kus MM, Huber D, Seitz B. [Keratoconus screening with wave-front parameters based on topography height data] [Article in German] Klin Monatsbl Augenheilkd. 1999 Apr;214(4):217-23.) extended Schwiegerling’s 2 term model to include 4 terms and showed that this was better again.

• Added secondary coma and secondary trefoil to the index.
Zernike decomposition

• Agree with Schweigerling and Langenbucher
• Zernike decomposition provides a convenient way to identify disease specific patterns
• Other basis functions may be equally suitable
Our approach

- Ten order Zernike polynomial fit to the wavefront for a 5 mm pupil, VOLPro v 6.71
- Investigate all 66 terms for ability to detect Keratoconus
- Investigate 30 modal pairs
- Using better performed terms or pairs, investigate combinations
- Progressively more complex combinations
- Report Zernike terms in single index form
Methods – population 1

- Population selection is all important and controversial
- Eyesys topographies
- All subjects examined by 1 investigator (KP)
- Careful diagnosis into 4 categories: normal keratoconus, forme fruste keratoconus, normal fellow eye of keratoconus eye*

Forme Fruste Keratocono

Axial Diopters

- dist: 1.19 mm
- axis: 316°
- value: 45.98 D

Corneal Topography

Optical zone:
- Min Pwr: 45.00
- Max Pwr: 45.92
- Mean Pwr: 45.14
- Min Radius: 0.42
- Max Radius: 3.84
- Mean Radius: 2.16
- OZ Area: 14.65

SIM K's
- 45.57 D @ 120°
- 45.02 D @ 30°

0.10 D
Normal fellow eye

Axial Diopters

- Dist: 2.85 mm
- Axis: 318°
- Value: 44.22 D

Optical zone

- Min Pwr: 43.44
- Max Pwr: 44.35
- Mean Pwr: 43.74
- Min Radius: 1.98
- Max Radius: 3.58
- Mean Radius: 2.90
- OZ Area: 26.34

SIM K's

- 43.94 D @ 40°
- 43.83 D @ 130°
Population 1 – Eyesys

- N=176
- Normal = 60
- Keratoconus = 104
- Forme Fruste = 6
- Normal fellows of keratoconus = 6
Analysis

- Receiver operating characteristic (ROC) analysis using Analyse-it v1.71 Analyse-it Software Ltd, Leeds, UK
- Determines the ability of a metric to separate 2 groups
- Main outcome measure is the area under the curve (AUC) where 1.0 is perfect separation and 0.50 is random
- Also false positives (FP), false negatives (FN), sensitivity, specificity and separation from next case

AUC=0.953, Optimum 0.397, FP=3, FN=10, Sensitivity=91.5, Specificity=95.2, Separation=0.018
Results – Population 1 (Eyesys)

- Analysed 66 Zernike terms
- 10 best discriminators

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<td>49</td>
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<tr>
<td>17</td>
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Results – Population 1 (Eyesys)

- Analysed 30 Zernike pairs
- 10 best discriminators

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<tr>
<td>17&amp;18</td>
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<td>16&amp;19</td>
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<td>23&amp;25</td>
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<td>30&amp;33</td>
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<td>31&amp;32</td>
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Results – Population 1 (Eyesys)

- Combination metrics
- 7,8,11,12,13,17,18,23,24,25,31,32
  AUC = 1.0 FN=0, FP=0, separation 0.037 _m
- 1,2,6,7,8,9,11,12,13,17,18,23,24,25,31,32,39,40,41,49,50,59,60,61
  AUC = 1.0 FN=0, FP=0, separation 0.049 _m
### Results – Population 1 (Eyesys)

<table>
<thead>
<tr>
<th>Zernike terms included</th>
<th>AUC</th>
<th>FN</th>
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Schwiegerling metric

• AUC = 0.895
Langenbucher metric

- AUC = 0.862
Keratoconus vs. topographically normal fellow eye

- Keratoconus n=104
- Normal fellow n=6
- 7,8,11,13,17,18,23,25,31,32
- AUC=1.00
- Normal eyes are normal!
- Even if keratoconus in the other eye
Normal vs forme fruste

- Normal n=60
- Forme fruste n=6
- 7,8,11,13,17,18,23,25,31,32
- AUC=0.956, FN=2
- Some overlap inevitable
- Depends on definition
Population 2 - Eyemap

- Diagnosis based solely of appearance of corneal topography
- N=105
- Normal = 53
- Keratoconus = 49
- Forme Fruste = 0
- Normal fellows of keratoconus = 3
- Repeat testing of candidate metrics
## Results – Population 2 (Eyemap)

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Population 3 - Orbscan

- Placido data (not scanning slit) used
- Diagnosis based solely of appearance of corneal topography
- N = 295
- Normal = 226
- Keratoconus = 63
- Forme Fruste = 3
- Normal fellows of keratoconus = 3
- Repeat testing of candidate metrics
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<th>FP</th>
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Comparison of three topographers

- Same metrics, same efficiency
- Orbscan – more normals, less metrics effective, more specific metrics
- Point of discrimination same for Eyesys and Eyemap but 25% higher for Orbscan
- E.g. for 7, 8, 11, 13, 17, 18, 23, 25 discriminator was 0.257 for Orbscan, but 0.212 for Eyesys and 0.217 for Eyemap
Discussion

• We extend the approach of Schwiegerling and Langenbacher to more complex combinations of Zernike elements
• Looking at all 66 terms, and 30 pairs led us to 6 to 8 metrics with high sensitivity to the detection of Keratoconus
• Larger population (normals, mild cases), no normalising factor
• More terms are helpful
Limitations

• There is no way to use wavefront data to detect keratoconus in the topographically normal fellow eye of a keratoconus eye.
• Therefore abnormal in 1 eye is enough to diagnose keratoconus.
• Corneal topography data so far, need to test on wavefront sensor data.
Discussion

• Not directly tested against all existing schema
• But superior to existing Zernike-based schema, which are in turn superior to existing schema
• It is likely that our approach is better or at least as good as all existing schema
• Even if our approach is not better than all existing schema, these are proprietary to certain topography systems and there are many existing topographers and wavefront sensors that need a Keratoconus detection schema
Other applications

- This approach could be used for the detection of other conditions (Klyce, Italy, September 2004)
- For example: PMD, TMD, Pterygium etc
  LASIK, PK, contact lens warpage, etc
  Cataract, Lenticonus, microspherophakia, etc
- Ophthalmic conditions tend to cause specific types of visual disturbances, so multiple schema could be built up into a diagnostic paradigm to assist the clinician with objective diagnosis likelihood output