Classification of keratoconus and pellucid marginal degeneration by corneal wavefront aberrations

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Background

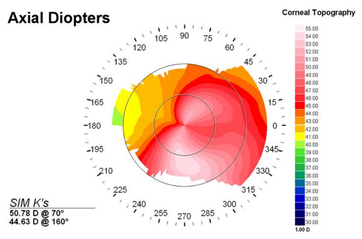
The topic of keratoconus (KC) and pellucid marginal degeneration (PMD) being two different non-inflammatory ectatic disorders or PMD being a KC subgroup is currently discussed and a final decision is not in sight yet. Several research groups accomplished studies to evaluate the characteristics of KC and PMD for better differentiation between them using videokeratography, mean curvature maps or Zernike vector analysis.[1-3] There is still a demand for reliable clinical classifiers for differentiation between KC, PMD and normal eyes.

Purpose

To assess the ability of anterior and posterior corneal wavefront aberrations of eyes with KC, PMD and normal eyes to identify groups and to classify them without a priori classification.

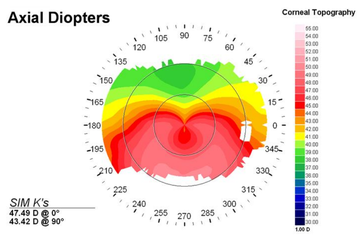
Patients and Methods

A priori classification was accomplished using the qualitative topography classification system for corneal topography by Bogan et al.[4]



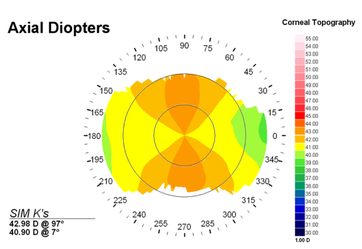
Group 1: 55 eyes of 32 patients with early KC

- Corneal topography with an asymmetric bow-tie and skewed radial axes
- No corneal scarring or other surface irregularities
- Discontinuation of contact lenses for at least 2 weeks



Group 2: 60 eyes of 43 patients with early PMD

- Corneal topography with inferior steepening and flattening of the central corneal curvature along a vertical axis
- No corneal scarring or other surface irregularities
- Discontinuation of contact lenses for at least 2 weeks



Group 3: 64 healthy pre-LASIK eyes of 32 patients

- Corneal topography without any asymmetry suspicious for KC or PMD
- Uncomplicated follow-up after LASIK of at least 12 months, no signs or symptoms of keratectasia
- Discontinuation of contact lenses for at least 2 weeks

From axial-keratometric data of the anterior corneal surface and elevation data of the posterior corneal surface a Zernike decomposition was performed

Corneal topography: measurements were performed with the Orbscan IIz (Bausch & Lomb, Rochester, NY, USA)

Anterior corneal surface wavefront reconstruction:

- Axial-keratometric data of the anterior corneal surface (Placido-based)
- 2nd-7th order Zernike polynomials
- 6 mm pupil diameter
- VOL-Pro 7.14

Posterior corneal surface wavefront reconstruction:

- Elevation data of the posterior corneal surface (Scheimpflug-based)
- 2nd-7th order Zernike polynomials
- 6 mm pupil diameter
- MATLAB 7.0

Statistical Analysis

Due to limitations caused by the a priori classification further statistical analyses were necessary to receive an objective classification of KC, PMD and normal eyes[5]

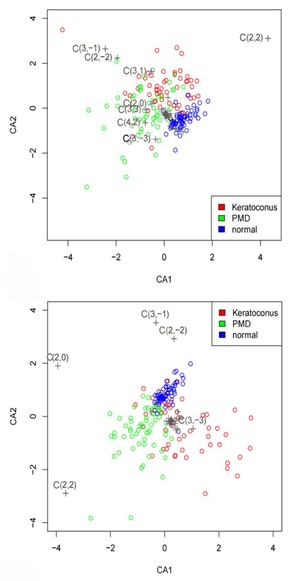
Anterior and posterior corneal wavefront aberration data was analysed using:

1. **Correspondence analysis** to detect the most influential Zernike coefficients (ZC) for separation between KC, PMD and normal eyes..
2. **Hierarchical cluster analysis** to explore group structures without *a priori* classification.
3. **Receiver operating characteristic curve (ROC) analysis** to determine individual ZC with the highest discriminative ability to distinguish between KC, PMD and normal eyes.
4. **Support vector machine (SVM) classification with linear and gaussian kernel** to derive a decision rule with high generalisation ability to classify patient eyes into groups. Cross-validation was used to estimate the classification error on unseen data.

Statistical analyses (1-4) were performed with *R version 2.11.0.* Kernel implementations (4) as contained in *kernlab*.

Results

2nd and 3rd order ZC were most influential for separation between KC, PMD and normal eyes



Most influential anterior ZC

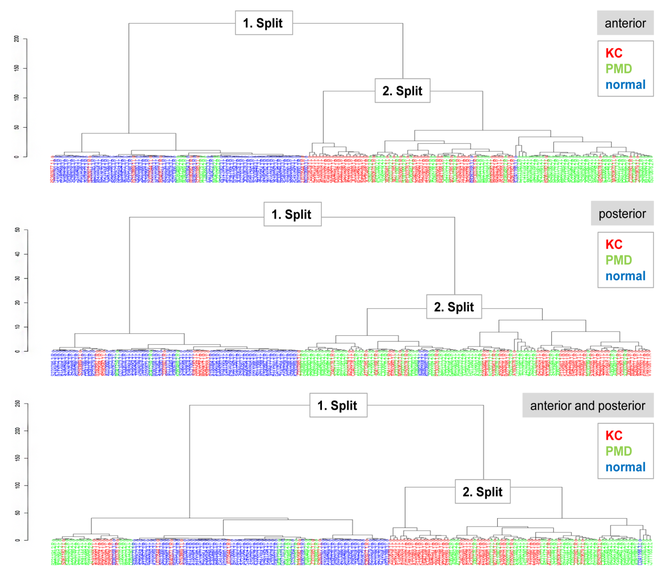
C_2^0 C_2^2 C_3^{-1} C_2^{-2} C_3^{-3}

Most influential posterior ZC

C_3^{-1} C_3^1 C_2^{-2} C_2^2 C_3^{-3}

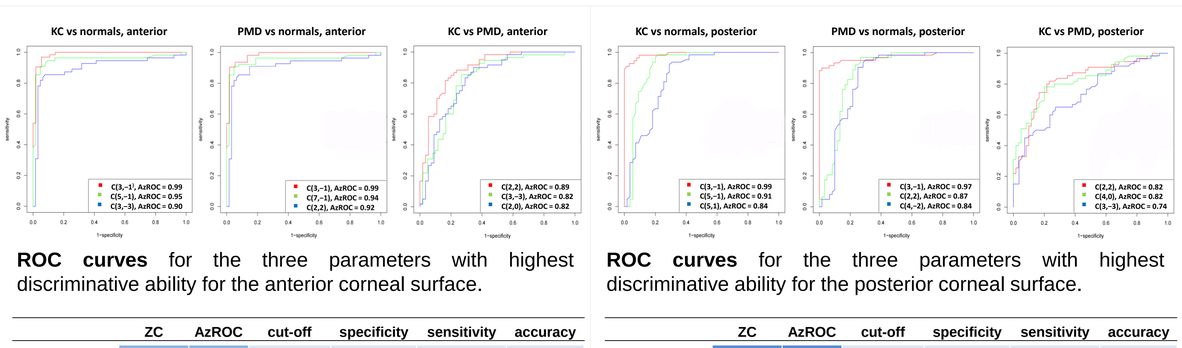
Correspondence analysis of anterior and posterior wavefront data showed a good separation of three groups. The most significant ZC for classification between the three groups were ascertained by sparse principal component analysis.

Clear grouping of patients into three major groups as a result of the first two hierarchical splits



Hierarchical cluster analysis of anterior, posterior and anterior and posterior wavefront data together: dendrogram shows that the first split separates healthy from diseased eyes, the second split separates KC from PMD eyes.

Discriminative ability of anterior and posterior corneal ZC was different for KC, PMD and normal eyes and higher for anterior ZC



ROC curves for the three parameters with highest discriminative ability for the anterior corneal surface.

	ZC	AzROC	cut-off	specificity	sensitivity	accuracy
KC vs normals	**C(3,-1)**	0.986	-0.228	94.5	96.8	95.8
PMD vs normals	**C(3,-1)**	0.991	-0.148	98.3	93.7	95.9
KC vs PMD	**C(2,2)**	0.891	-0.129	83.6	81.7	82.6

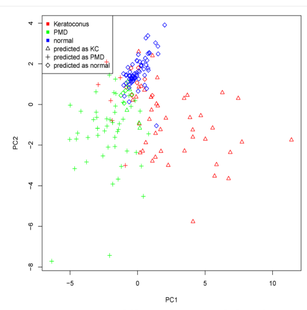
Best three classifying parameters of the anterior corneal surface for discrimination between the groups.

ROC curves for the three parameters with highest discriminative ability for the posterior corneal surface.

	ZC	AzROC	cut-off	specificity	sensitivity	accuracy
KC vs normals	**C(3,-1)**	0.990	0,193	100	89.1	94.9
PMD vs normals	**C(3,-1)**	0.969	0.189	100	88.3	94.3
KC vs PMD	**C(2,2)**	0.824	0.104	83.3	74.5	79.1

Best three classifying parameters of the posterior corneal surface for discrimination between the groups.

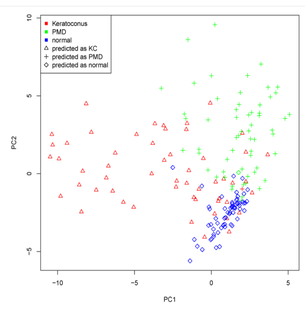
87 out of 100 patients were classified correctly using SVM classification based on all 33 anterior ZC



Data input:
5 anterior and posterior ZC

Training error: 0.13
Cross-validation error: 0.17
CCR: 83%

SVM classification with linear kernel (nu=0.30) based on the 5 most influential anterior and posterior ZC together marked in a plot of the first two principal component (PC) axes.



Data input:
33 anterior ZC

Training error: 0.01
Cross-validation error: 0.13
CCR: 87%

SVM classification with gaussian kernel (nu-SVC: rbf kernel, s=0.0066, nu=0.10) of all 33 anterior ZC achieved the highest correct classification rate (CCR) of 87% for unseen data.

Conclusions

- **Identification of three groups (KC, PMD and normal eyes) without a priori classification based on group specific wavefront patterns.**
- **ZC from the anterior and posterior corneal surface classify between KC, PMD and normal eyes with high accuracy.**
- **Overall anterior corneal aberrations were more powerful than posterior corneal aberrations for classification between the three groups.**
- **Anterior primary vertical coma C_3^{-1} had the highest ability to discriminate between both KC vs. normals and PMD vs. normals.**
- **Anterior primary astigmatism C_2^2 had the highest ability to discriminate between KC and PMD.**

References

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