Structural and Optical Changes in Keratoconus

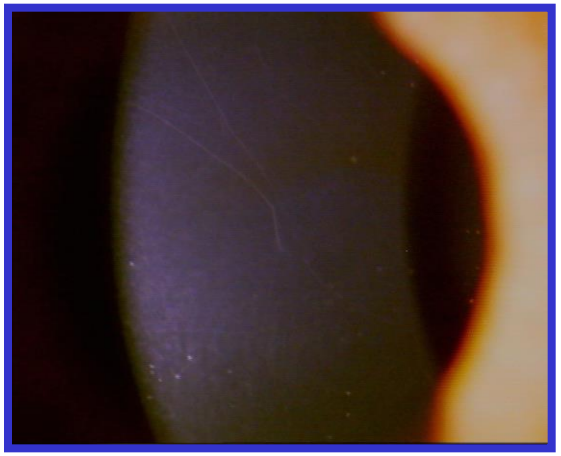
Structural & Optical Changes in Keratoconus

Clare O'Donnell

Amit Jinabhai, Hema Radhakrishnan,
Luisa Simo-Mannion, Cindy Tromans, Arun Brahma

The University of Manchester, Manchester Royal Eye Hospital

Corneal nerves



- Histological studies of KC corneas revealed abnormalities
  - In nerve architecture, especially at the cone apex
    - e.g. thickening, tortuosity, loss of radial orientation (Al-Aqaba 2011)
  - But tend to report only on advanced KC and subject to artefacts
- *In vivo* CM studies have also shown alterations to NFs in KC
  - Unclear at what stage these changes occur or how they relate to reported changes in corneal sensitivity

Aim

To investigate corneal nerve structure and sensitivity in keratoconus

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An evaluation of corneal nerve morphology and function in moderate keratoconus

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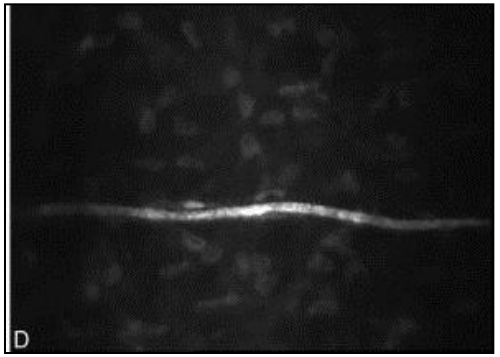
[b] Manchester Royal Eye Hospital, Manchester, UK

Methods

- 44 KC and 44 control subjects recruited
  - 8 mild (k≤45D), 26 moderate (45<k≤52D), 10 severe (k>52D)
  - Mean age 32 ± 9 years (both groups)
  - Also matched for gender, iris colour, mode of correction
- Morphology of stromal and sub-basal nerves
  - ConfoScan 3 confocal microscope, image analysis software
    - Density (length fibres/total area) and thickness (mean of 10)
- Corneal sensitivity assessed using Cochet-Bonnet
  - Centrally and at 4 peripheral locations (1mm from limbus)

Stromal nerves

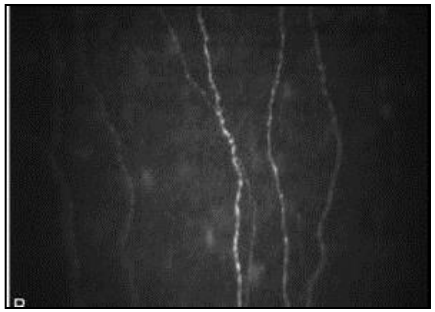


	KC	CTRL	p-value
Density ($\mu m/mm^2$)	429.5 ± 108.0	390.4 ± 100.4	0.106
Thickness (μm)	8.62 ± 4.53	5.25 ± 1.92	0.009*

* Statistically significant difference

Two sample t-test

Sub-basal nerves



	KC	CTRL	p-value
Density ($\mu m/mm^2$)	1094.9 ± 459.6	1846.2 ± 527.5	<0.001*
Thickness (μm)	1.77 ± 0.06	1.82 ± 0.05	0.29

* Statistically significant difference

- NF density decreased as cornea steepened (R^2=0.2, p=0.006)

Two sample t-test

Corneal sensitivity

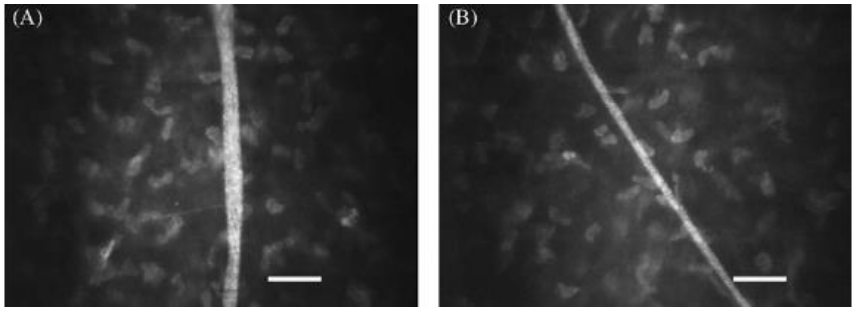
	Central	Superior	Inferior	Nasal	Temp
KC (g/mm^2)	1.11±0.05	1.50±0.16	1.06±0.02	1.02±0.07	1.02±0.11
CTRL (g/mm^2)	1.01±0.33	1.31±0.07	1.11±0.05	1.04±0.16	1.04±0.02
p-value	0.005*	0.976	0.582	0.942	0.652

* Statistically significant difference

- Significant reduction in KC at central location only
- Sensitivity reduced as cornea steepened (R_s=0.44, p=0.003)

Discussion

- Confirm alterations to architecture and function
  - Thickening of stromal NFs seems to occur early
  - Reduced sub-basal nerve density and reduced sensitivity more apparent as disease progresses



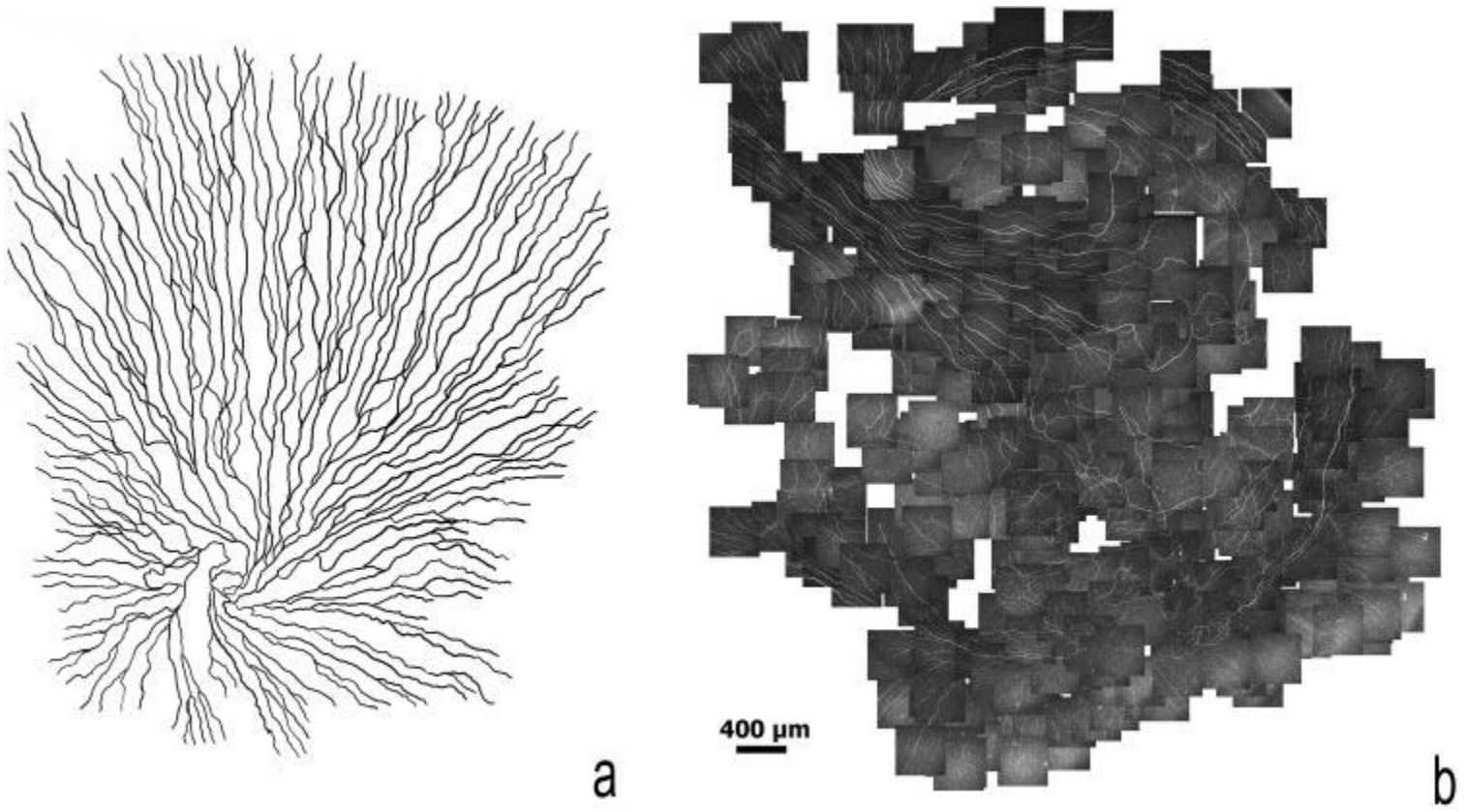
KC CTRL

(Bron 1984; Kinoshita et al., 1999)

Discussion

- Possible causes of stromal nerve thickening
  - Over-expression of nerve growth factor/proliferation Schwaan cells
    - Accumulation of secreted substances due to altered metabolism
- Unclear if NF alterations *causative* or secondary
  - Refinement of *in vivo* techniques should improve understanding of nerve morphology

Especially with full-field image capture and analysis



Normal (schematic)

Keratoconus

Patel and McGhee (2006)

Corneal thinning

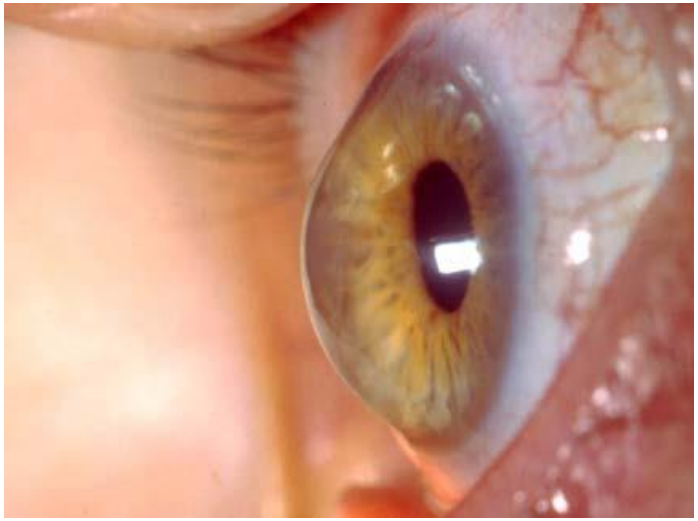
- Aetiology of KC not fully understood, caused by stretching or by loss of tissue?
  - Is protrusion secondary to stromal thinning?
  - Or does reduced strength result in thinning and protrusion
- Loss of tissue might be detected by analysing corneal volume in KC corneas
  - Advances in technology enable assessment of volume in-vivo

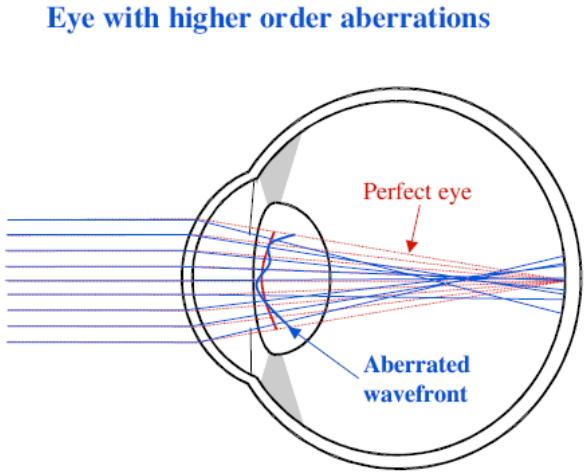
Visual performance with aberration controlling soft contact lenses in keratoconus

Introduction

- Irregular corneas in keratoconus lead large magnitudes of irregular astigmatism and ocular aberrations (particularly vertical coma).

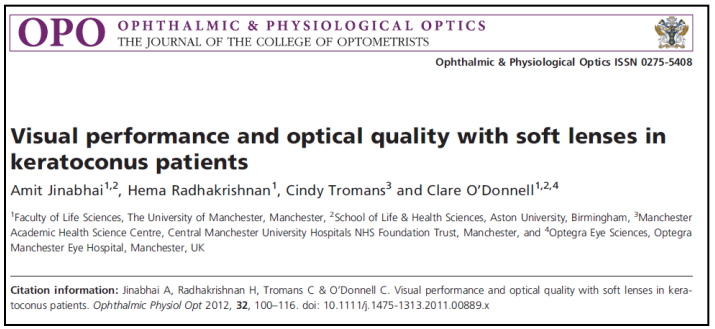
- RGP contact lenses mask most of the induced anterior corneal surface aberrations.





Introduction

- Soft contact lenses offer certain advantages over RGPs and can mask irregular corneal astigmatism to a limited extent.



OPO OPHTHALMIC & PHYSIOLOGICAL OPTICS
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Visual performance and optical quality with soft lenses in keratoconus patients

Amit Jinabhai[1,2], Hema Radhakrishnan[1], Cindy Tromans[3] and Clare O'Donnell[1,2,4]

[1]Faculty of Life Sciences, The University of Manchester, Manchester, [2]School of Life & Health Sciences, Aston University, Birmingham, [3]Manchester Academic Health Science Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, and [4]Optegra Eye Sciences, Optegra Manchester Eye Hospital, Manchester, UK

Citation information: Jinabhai A, Radhakrishnan H, Tromans C & O'Donnell C. Visual performance and optical quality with soft lenses in keratoconus patients. *Ophthalmic Physiol Opt* 2012, **32**, 100–116. doi: 10.1111/j.1475-1313.2011.00889.x

- Technology available to make *customised* aberration-controlling soft contact lenses (ACCLs) to reduce ocular aberrations in keratoconic patients.

Aim

- To investigate how toric soft CLs and customised ACCLs alter higher order aberrations and visual performance in keratoconus compared to patient's habitual correction.

- Customised ACCLs were designed either to fully (100%) or partially (50%) correct the third order coma aberrations.

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Optical quality and visual performance with customised soft contact lenses for keratoconus

Amit Jinabhai[1], Clare O'Donnell[1,2,3], Cindy Tromans[1,4] and Hema Radhakrishnan[1]

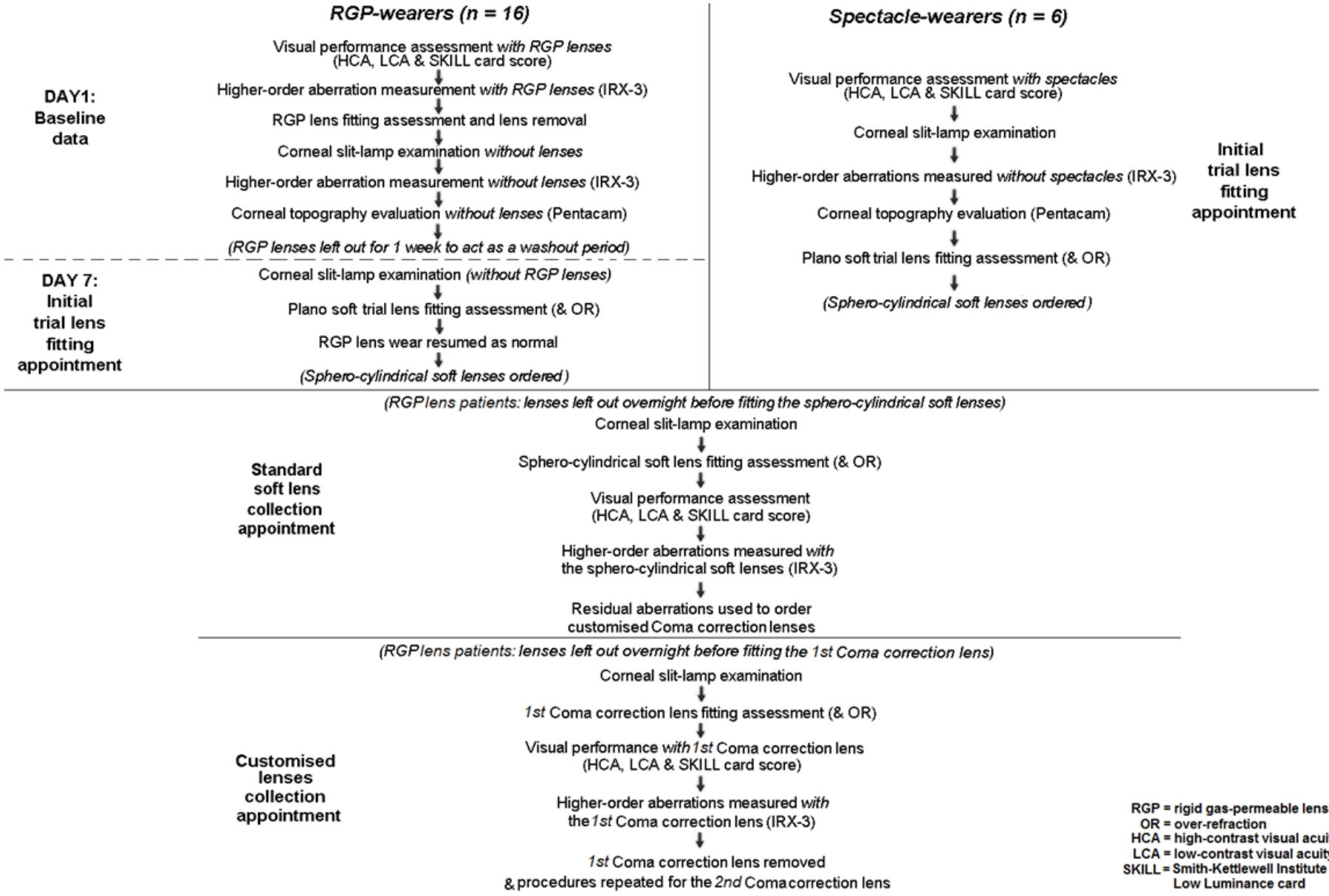
[1]Faculty of Life Sciences, The University of Manchester, Manchester, UK [2]Optegra Eye Sciences, Optegra Eye Hospital, Manchester, UK [3]School of Life and Health Sciences, Aston University, Birmingham, UK and [4]Manchester Academic Health Science Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK

Citation information: Jinabhai A, O'Donnell C, Tromans C, Radhakrishnan H. Optical quality and visual performance with customised soft contact lenses for keratoconus. *Ophthalmic Physiol Opt* 2014. doi: 10.1111/opo.12133

Methods

- 22 keratoconic participants took part in the study
  - 14 moderate, 7 severe, 1 mild KC
- Data collected from one eye for each patient.
- 16 participants were habitual RGP wearers and 6 were spectacle wearers.
- Mean age 34 years (range 19-55 yrs).
- High contrast (95%) and low contrast (15%) visual acuities were measured with Bailey-Lovie logMAR charts.
- Ocular aberrations were measured with a Shack-Hartmann aberrometer (IRX3, Imagine Eyes, Paris)

Methods


RGP-wearers (n = 16)
Spectacle-wearers (n = 6)
DAY1: Baseline data
Visual performance assessment with RGP lenses (HCA, LCA & SKILL card score)
Higher-order aberration measurement with RGP lenses (IRX-3)
RGP lens fitting assessment and lens removal
Corneal slit-lamp examination without lenses
Higher-order aberration measurement without lenses (IRX-3)
Corneal topography evaluation without lenses (Pentacam)
(RGP lenses left out for 1 week to act as a washout period)
DAY 7: Initial trial lens fitting appointment
Corneal slit-lamp examination (without RGP lenses)
Plano soft trial lens fitting assessment (& OR)
RGP lens wear resumed as normal
(Sphero-cylindrical soft lenses ordered)
Visual performance assessment with spectacles (HCA, LCA & SKILL card score)
Corneal slit-lamp examination
Higher-order aberrations measured without spectacles (IRX-3)
Corneal topography evaluation (Pentacam)
Plano soft trial lens fitting assessment (& OR)
(Sphero-cylindrical soft lenses ordered)
Initial trial lens fitting appointment
(RGP lens patients: lenses left out overnight before fitting the sphero-cylindrical soft lenses)
Standard soft lens collection appointment
Corneal slit-lamp examination
Sphero-cylindrical soft lens fitting assessment (& OR)
Visual performance assessment (HCA, LCA & SKILL card score)
Higher-order aberrations measured with the sphero-cylindrical soft lenses (IRX-3)
Residual aberrations used to order customised Coma correction lenses
(RGP lens patients: lenses left out overnight before fitting the 1st Coma correction lens)
Customised lenses collection appointment
Corneal slit-lamp examination
1st Coma correction lens fitting assessment (& OR)
Visual performance with 1st Coma correction lens (HCA, LCA & SKILL card score)
Higher-order aberrations measured with the 1st Coma correction lens (IRX-3)
1st Coma correction lens removed & procedures repeated for the 2nd Coma correction lens
RGP = rigid gas-permeable lens
OR = over-refraction
HCA = high-contrast visual acuity
LCA = low-contrast visual acuity
SKILL = Smith-Kettlewell Institute Low Luminance card

Results

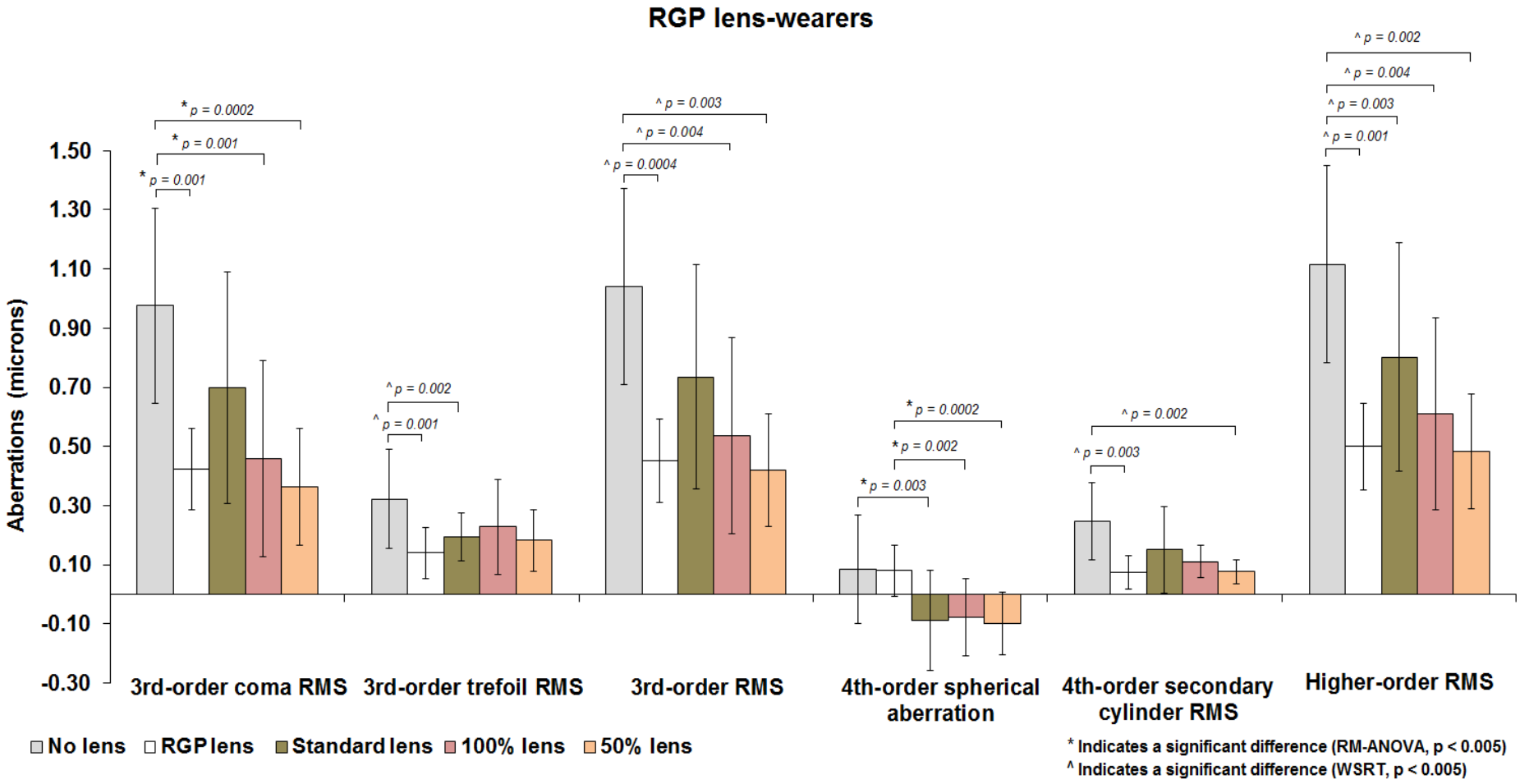
Patient ref.	*Flat K (D)*	*Steep K (D)*	*Central corneal thickness (microns)*	*CLEK severity grade*	*Vogt's striae*	*Apical scarring*	*RGP lens fitting grade*
1	49.8	56.0	455	Severe	Present	Absent	DAT
2	45.6	50.0	451	Moderate	Absent	Absent	AT
3	42.8	45.1	440	Moderate	Absent	Absent	AT
4	45.6	48.4	434	Moderate	Absent	Absent	AC
5	58.2	61.8	324	Severe	Present	Present	AT
6	45.6	47.3	505	Moderate	Absent	Absent	AT
7	47.8	52.0	419	Moderate	Present	Present	DAT
8	52.2	55.9	503	Severe	Present	Present	DAT
9	44.2	48.0	453	Moderate	Present	Absent	DAT
10	44.1	49.2	461	Moderate	Absent	Absent	DAT
11	43.9	49.4	386	Moderate	Present	Present	DAT
12	48.6	51.9	415	Moderate	Present	Present	DAT
13	43.4	47.3	484	Moderate	Present	Absent	AT
14	51.4	56.4	416	Severe	Present	Present	DAT
15	49.1	52.9	435	Severe	Present	Present	DAT
16	47.7	53.2	420	Severe	Present	Absent	DAT
17	43.9	46.9	422	Moderate	Present	Absent	-
18	50.7	53.0	494	Severe	Present	Present	-
19	44.9	48.0	477	Moderate	Absent	Absent	-
20	43.2	46.7	462	Moderate	Present	Absent	-
21	45.7	49.3	432	Moderate	Absent	Absent	-
22	42.7	43.4	514	Mild	Absent	Absent	-

Results

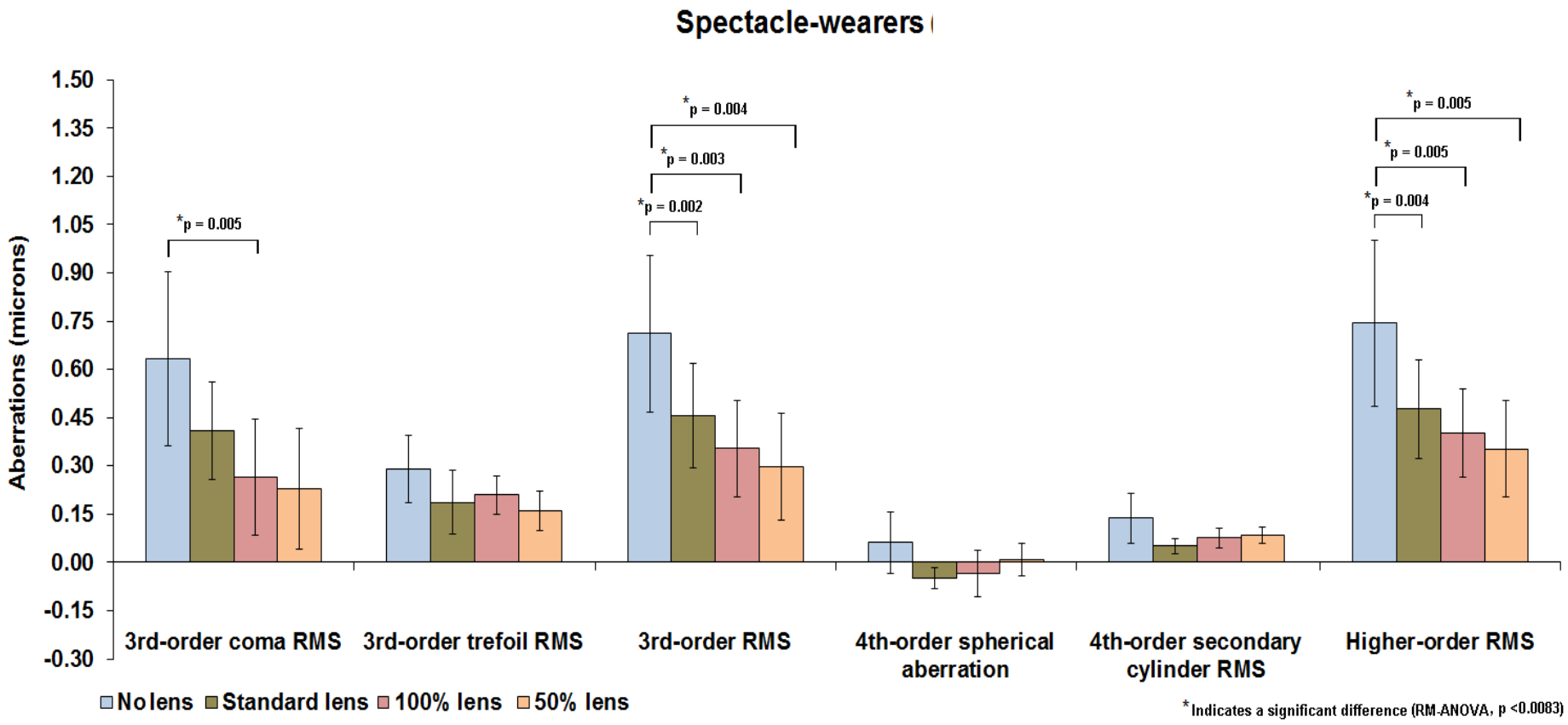
- Compared to when uncorrected and compared to all three soft study lenses, RGP lenses significantly reduced 2nd-order cylinder RMS.

- Compared to when uncorrected, there was significantly lower coma RMS with RGP lenses ($p=0.001$), 100% lenses ($p=0.001$) and 50% lenses ($p=0.0002$).

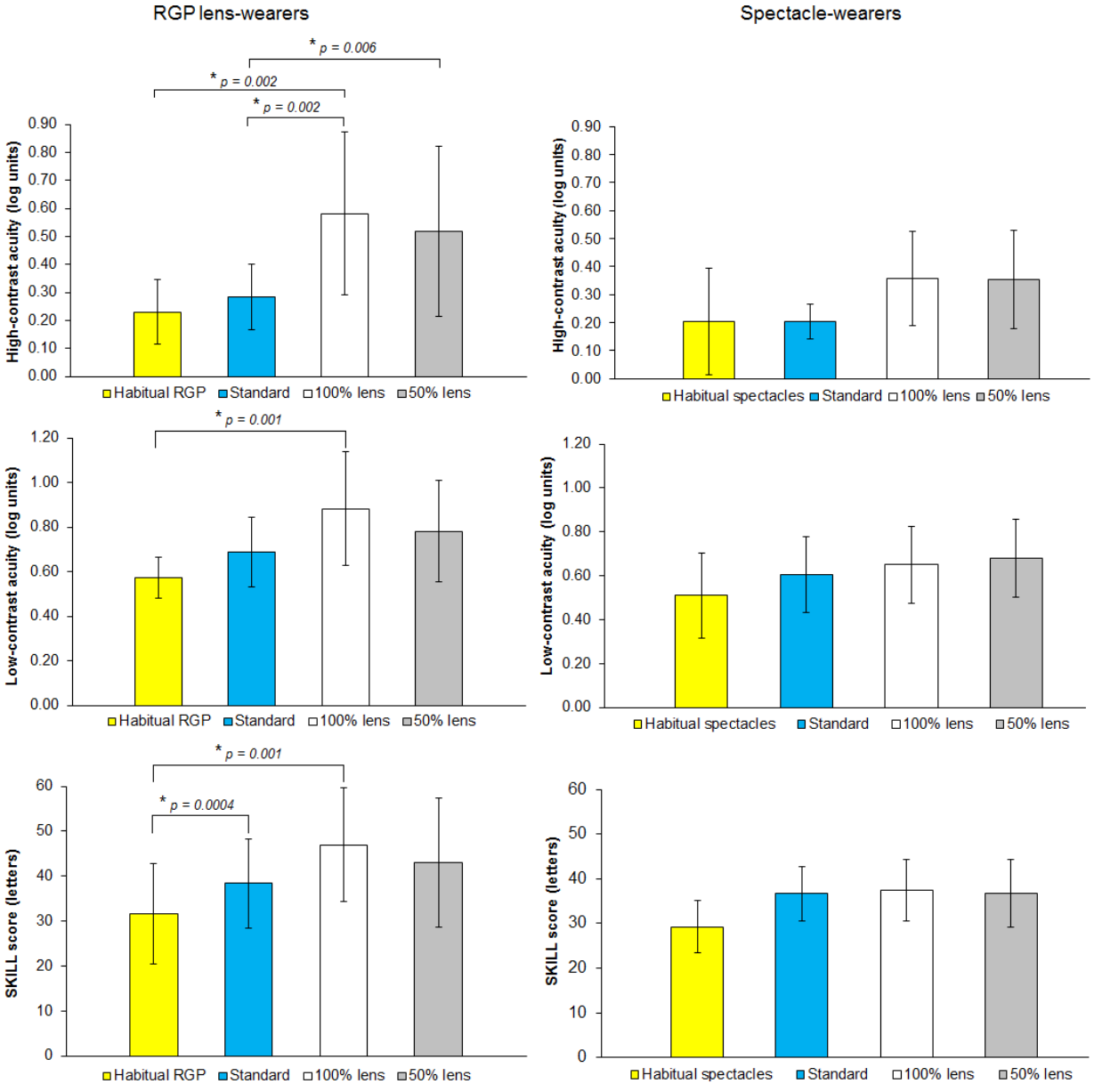
Results


RGP lens-wearers
Aberrations (microns)
1.50
1.30
1.10
0.90
0.70
0.50
0.30
0.10
-0.10
-0.30
* p = 0.0002
* p = 0.001
* p = 0.001
^ p = 0.002
^ p = 0.001
^ p = 0.003
^ p = 0.004
^ p = 0.0004
* p = 0.0002
* p = 0.002
* p = 0.003
^ p = 0.002
^ p = 0.003
^ p = 0.002
^ p = 0.004
^ p = 0.003
^ p = 0.001
3rd-order coma RMS
3rd-order trefoil RMS
3rd-order RMS
4th-order spherical aberration
4th-order secondary cylinder RMS
Higher-order RMS
No lens
RGP lens
Standard lens
100% lens
50% lens
* Indicates a significant difference (RM-ANOVA, p < 0.005)
^ Indicates a significant difference (WSRT, p < 0.005)

Results


Spectacle-wearers
Aberrations (microns)
1.50
1.35
1.20
1.05
0.90
0.75
0.60
0.45
0.30
0.15
0.00
-0.15
-0.30
*p = 0.005
*p = 0.002
*p = 0.003
*p = 0.004
*p = 0.004
*p = 0.005
*p = 0.005
3rd-order coma RMS
3rd-order trefoil RMS
3rd-order RMS
4th-order spherical aberration
4th-order secondary cylinder RMS
Higher-order RMS
No lens
Standard lens
100% lens
50% lens
*Indicates a significant difference (RM-ANOVA, p <0.0083)

Results


RGP lens-wearers
Spectacle-wearers
* p = 0.006
* p = 0.002
* p = 0.002
High-contrast acuity (log units)
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
Habitual RGP
Standard
100% lens
50% lens
Habitual spectacles
* p = 0.001
Low-contrast acuity (log units)
1.20
1.00
0.80
0.60
0.40
0.20
0.00
* p = 0.001
* p = 0.0004
SKILL score (letters)
60
50
40
30
20
10
0
* Indicates a significant difference (RM-ANOVA (p < 0.0083)

Summary and discussion

- As expected, RGP lenses provided better visual performances than conventional toric SCLs for keratoconic patients.

- RGP lenses on eye also showed some residual aberrations, which are likely to be due to topographical alterations at the posterior corneal surface.

Summary and discussion

- The 100% lenses, on average, overcorrected vertical coma, resulting in positive residual aberration.
- The 50% lenses, on average, provided either negative residual vertical coma aberration (contact lens group) or values close to zero (spectacle group).
- Wavefront sensor errors occur through overlapping spot images, spot image crossover or missing spots and scatter.
- With customised ACCLs, superfluous wavefront aberrations can become induced through small lens translations and rotations upon blinking.

Discussion

- LCVA scores measured with toric SCLs or the 50% AC lenses were best for low levels of spherical aberration (of around zero).

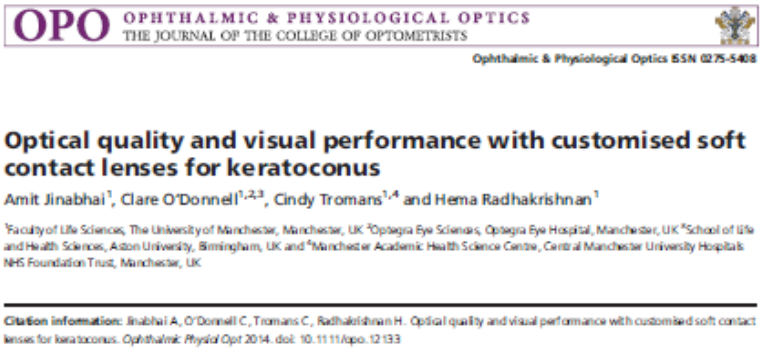
- Visual neural system may compensate for long-term exposure to an asymmetrically blurred retinal image in keratoconic patients.

- Customised lenses should be made with bespoke optic zone diameters to match with the pupil size of the patient.

Conclusions

- The two customised ACCLs reduced uncorrected coma RMS and HORMS error in both groups.

- The patient's habitual RGP lenses gave better visual performances than with either ACCL in the contact lens group.
    - Limiting factors
        - Repeatability and accuracy of aberration measurements
        - Lens stability



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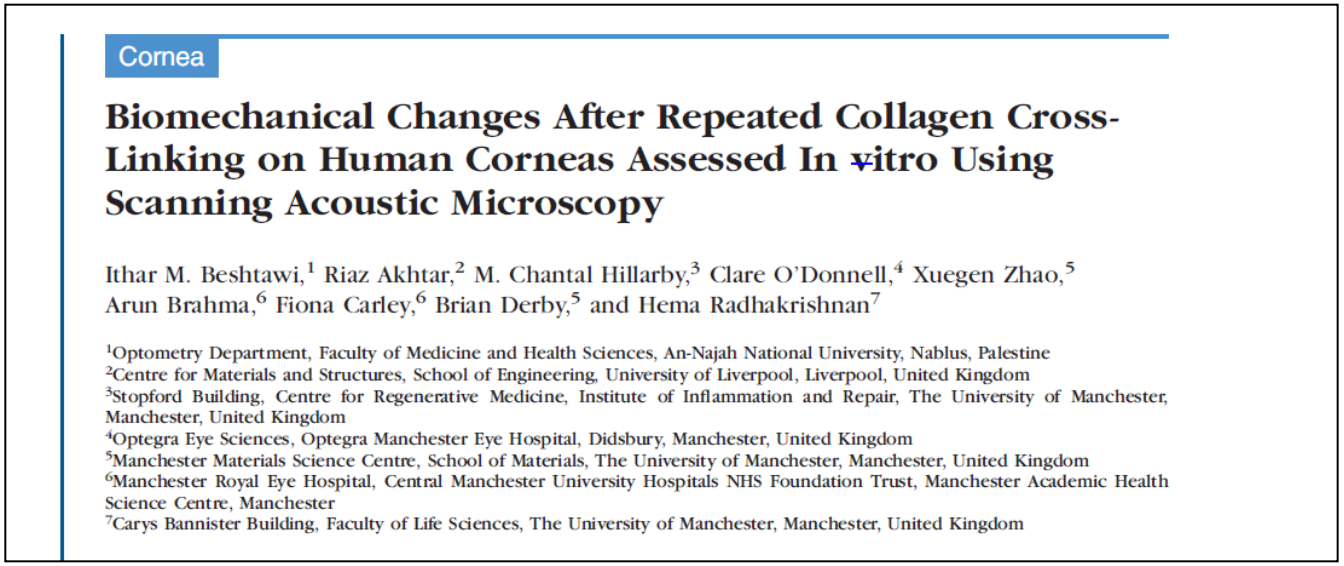
Citation information: Jinabhai A, O'Donnell C, Tromans C, Radhakrishnan H. Optical quality and visual performance with customised soft contact lenses for keratoconus. *Ophthalmic Physiol Opt* 2014. doi: 10.1111/opo.12133

Recent collaborations

- Corneal collagen cross-linking
  - *In-vivo* and *in-vitro*



Cornea

Biomechanical Changes After Repeated Collagen Cross-Linking on Human Corneas Assessed In vitro Using Scanning Acoustic Microscopy

Ithar M. Beshtawi,[1] Riaz Akhtar,[2] M. Chantal Hillarby,[3] Clare O'Donnell,[4] Xuegen Zhao,[5] Arun Brahma,[6] Fiona Carley,[6] Brian Derby,[5] and Hema Radhakrishnan[7]

[1]Optometry Department, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine
[2]Centre for Materials and Structures, School of Engineering, University of Liverpool, Liverpool, United Kingdom
[3]Stopford Building, Centre for Regenerative Medicine, Institute of Inflammation and Repair, The University of Manchester, Manchester, United Kingdom
[4]Optegra Eye Sciences, Optegra Manchester Eye Hospital, Didsbury, Manchester, United Kingdom
[5]Manchester Materials Science Centre, School of Materials, The University of Manchester, Manchester, United Kingdom
[6]Manchester Royal Eye Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester
[7]Carys Bannister Building, Faculty of Life Sciences, The University of Manchester, Manchester, United Kingdom

Manchester Corneal Collagen Cross-Linking Group

Dr Ithar Beshtawi: Today 16.00 Cornea II Session

Acknowledgements

Collaborators

- Dr Hema Radhakrishnan, Dr Luisa Simo-Mannion
- Dr Amit Jinabhai, Dr Cindy Tromans,
- Mr Arun Brahma, Prof WN Charman

Funding

- Vision Centre
- College of Optometrists
- Central Manchester Hospitals Foundation Trust
- UMIP

Aim

To investigate the effect of RGP CL lens fit on ocular HOA and VA in keratcoconus

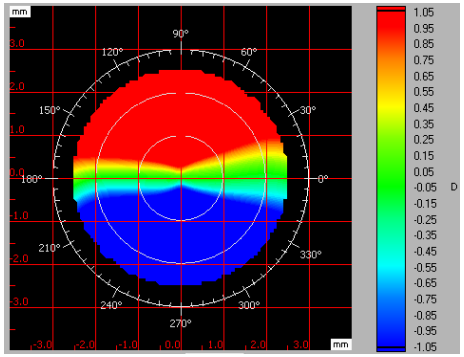
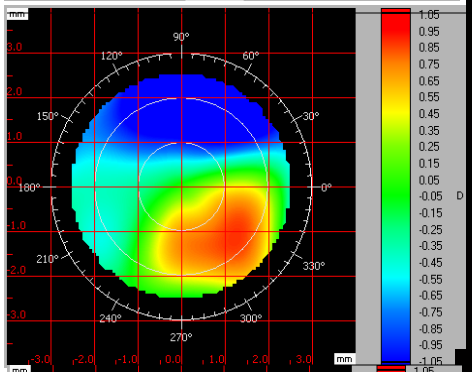
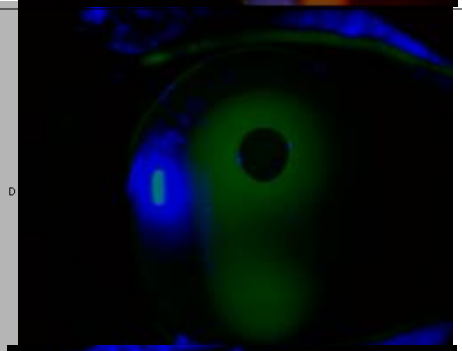
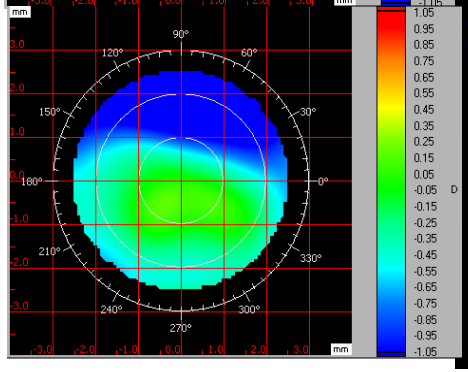
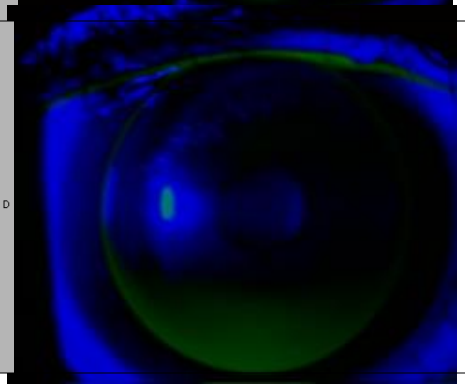
CASE REPORT

Visual Acuity and Ocular Aberrations With Different Rigid Gas Permeable Lens Fittings in Keratoconus

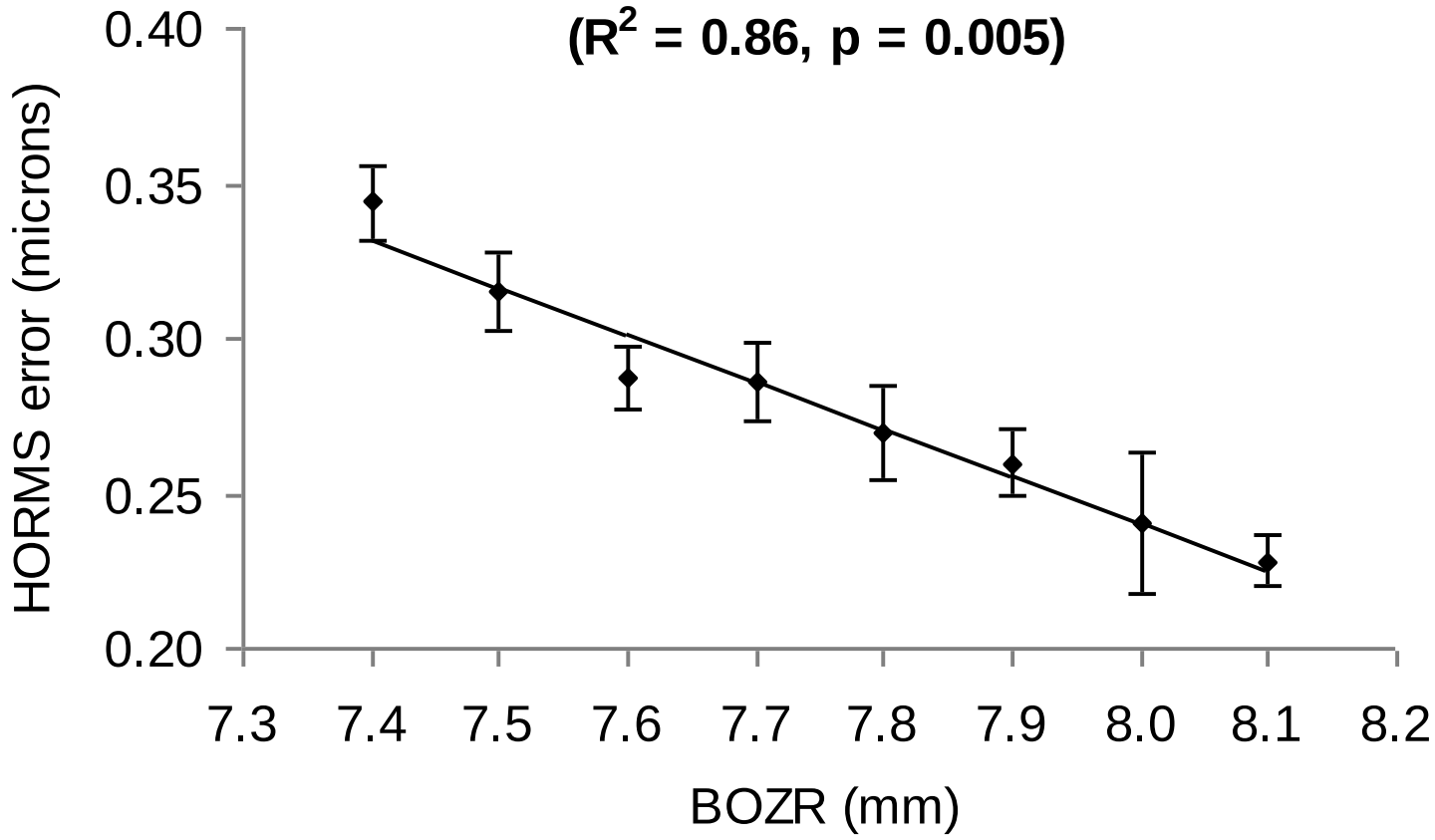
Amit Jinabhai, B.Sc. (Hons), Hema Radhakrishnan, Ph.D., and Clare O'Donnell, Ph.D.

Method

- 25 year old KC patient
  - Bilateral, moderate
- RE systematically fitted with RGP CLs
  - BOZR of 7.40 mm to 8.10 mm, in 0.10 mm steps
  - Menicon-*EX,* same diameter
- VA with over refraction recorded
  - LogMAR
- IRX-3 HOA
  - 5mm pupil, up to 6th Zernike order

Wavefront aberration map	*Slit-lamp appearance*	*RGP lens specification (in mm)*	*Wavefront aberrations (µm)*
		**No contact lens in place** **VA 0.04**	**HORMS = +1.70** **3rd-order RMS = +1.65** **Vertical coma = -1.49**
		**BOZR = 7.40** **VA 0.58** **STEEP**	**HORMS = +0.35** **3rd-order RMS = +0.34** **Vertical coma = +0.34**
		**BOZR = 8.10** **VA -0.30** **FLAT**	**HORMS = +0.23** **3rd-order RMS = +0.23** **Vertical coma = +0.21**

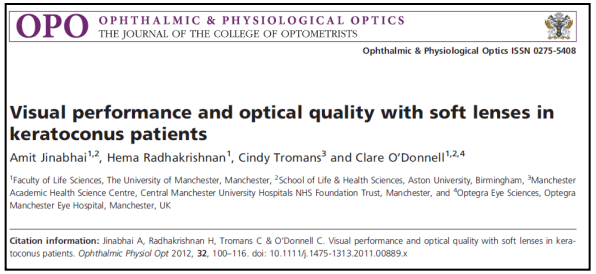
HORMS vs. BOZR



Discussion

- As BOZR flattened from 7.4 to 8.1mm
  - HORMS reduced +0.34 µm to +0.23 µm
  - and VA improved +0.58 to -0.30 log units
- Flatter fits improved visual performance
  - Explain why patients may prefer older lenses
- Flattening and moulding effect improving profile
  - Disadvantages physiologically of this approach
    - Staining and scarring

SCL in KC



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Visual performance and optical quality with soft lenses in keratoconus patients

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- If RGP lens intolerant may refit to SCL
  - Expect compromise in VA
- But if we could correct HOA
  - Visual performance may improve with SCL
- Technology to manufacture lenses exists
  - Customised A-C soft lenses are available
- What happens when KC refitted from RGPs?
  - Is wash-out period necessary?

Aim

To assess the changes in VA, HOA and refraction after suspending RGP CLW for one week in KC patients

Methods

- 16 subjects moderate/severe KC
  - Suspended RGP CLW
- Pentacam
  - Ks and CCT
- IRX-3
- Subjective refraction
- LogMAR VA
- Performed at two visits, 7 days apart after RGP lens removal

Results

- Reductions in VA
  - High (p=0.001) and low contrast (p=0.005)
- Increase in ocular aberrations
  - HORMS (p=0.003)
- Corneal steepening (p=0.02)
- Reduction in CCT (p=0.01)

Conclusion

- Changes in the optical and structure
  - After suspend RGP lens wear
- Stabilisation time will depend on factors
  - Lens fit, duration of wear, topography
- Important to consider
  - When prescribing AC-SCL