The Science of Overnight Orthokeratology

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Definition of orthokeratology (OK)

- "...the reduction, modification or elimination of refractive anomalies by the programmed application of contact lenses" *(International Orthokeratology Section of NERF, 1971)*

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Modern OK

- specially designed rigid contact lenses
  - reverse geometry design
- worn overnight only
  - no lens wear during the day
- provide temporary correction for refractive error
  - effect is reversible if lens wear ceases
- mainly used for low-moderate myopia

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Modern OK

- reverse geometry lenses
- corneal topography
- overnight OK

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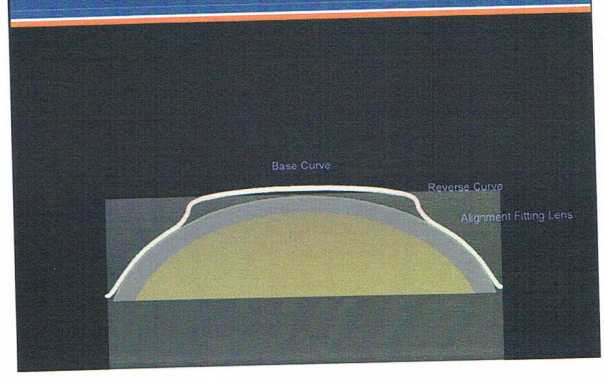
OK lens design



OK lens - fluorescein pattern

Modern OK

- reverse geometry lenses
- corneal topography
- overnight OK

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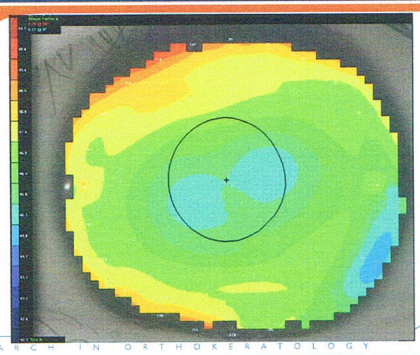
Modern OK



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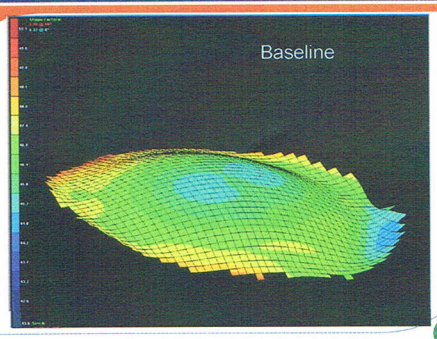
Modern OK



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Modern OK

- reverse geometry lenses
- corneal topography
- overnight OK

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Overnight OK

- overnight OK is the clinical protocol of choice
  - lenses are worn overnight only
  - lenses removed during waking hours
- overnight OK fulfils a desired clinical aim
  - to achieve clear vision through waking hours without the need to wear refractive correction

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Research questions

- Does OK work?
- How does OK work?
- Is OK safe?
- What of the future?

RESEARCH IN ORTHOKERATOLOGY

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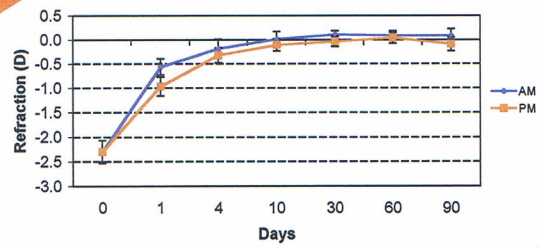
Change in refraction



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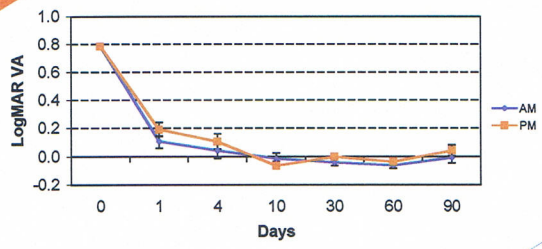
Change in logMAR VA



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Does OK work?

Author	Px	Lens type	Wear time	Mean Rx change
Mountford (1997)	60	Contex OK	≈2 mths	2.19 ± 0.57 D
Nichols et al (2000)	8	Contex OK	2 mths	1.83 ± 1.23D
Rah et al (2002)	31	Fargo/CRT	3 mths	2.08 ± 1.11D
Soni et al (2003)	8	Contex OK	3 mths	2.12D
Tahhan et al (2003)	46	Various	1 mth	2.00 ± 0.34D
Alharbi (2003)	18	BE	3 mths	2.63 ± 0.57D
Sorbara et al (2005)	23	Paragon CRT	1 mth	2.59 ± 0.77D

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Short-term OK lens wear

- significant corneal changes within minutes of OK lens insertion
- changes progress with longer lens wear period
  - corneal apex flattens
  - treatment zone diameter increases
  - unaided visual acuity improves
- 75% of effect apparent after first night

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Research questions

- Does OK work?
- How does OK work?
- Is OK safe?
- What of the future?

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Research answers

- overnight OK is effective for temporary reduction of low to moderate myopia
  - current limit about -4.00D (to -6.00D?)
- most change after 1st night of lens wear
  - endpoint after 7-10 nights of lens wear
- regression of effect during the day
  - approximately 0.25 to 0.75 D

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Research questions

- Does OK work?
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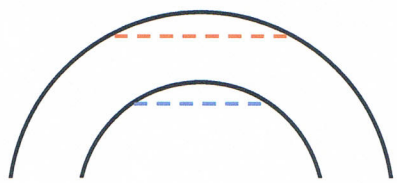
Corneal curvature changes



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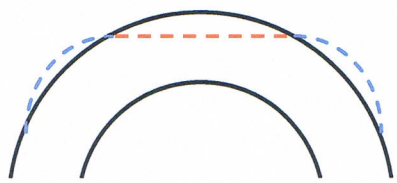
Corneal curvature changes



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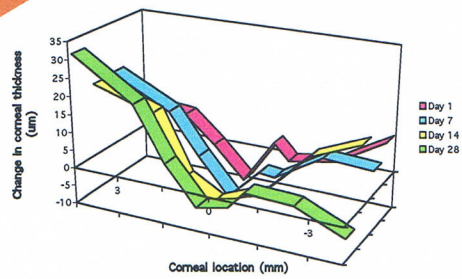
Changes in corneal thickness

(Swarbrick, Wong & O'Leary, 1998)



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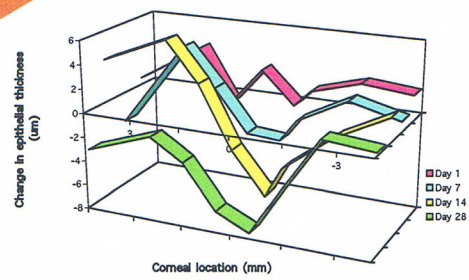
Changes in epithelial thickness

(Swarbrick, Wong & O'Leary, 1998)



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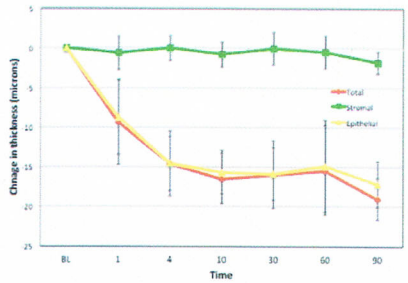
Central corneal thickness
(Alharbi and Swarbrick, 2003)



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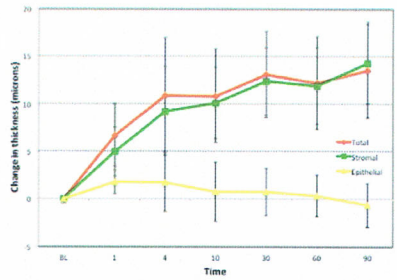
Midperipheral corneal thickness
(Alharbi and Swarbrick, 2003)



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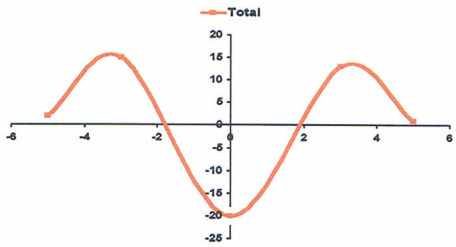
Total corneal thickness



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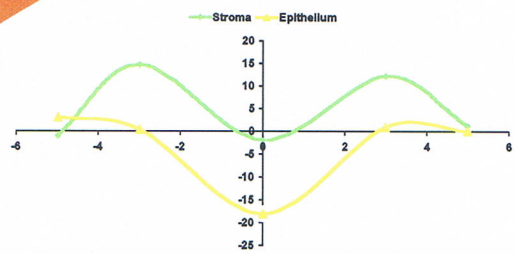
Stroma and epithelium



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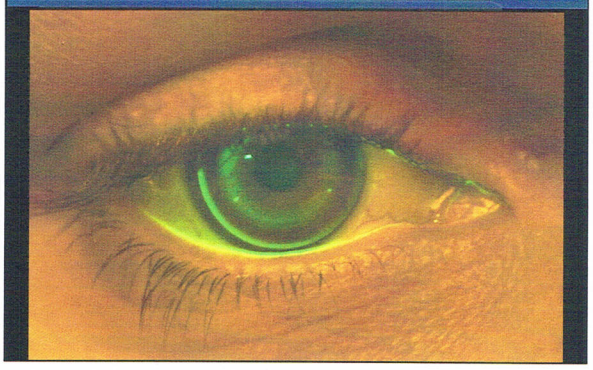
OK - fluorescein pattern



Central epithelial thinning

- histological evidence for central epithelial thinning in OK
  - Matsubara et al (2004) - rabbit model
  - Choo et al (2007) - cat model
  - Cheah et al (2008) - primate model

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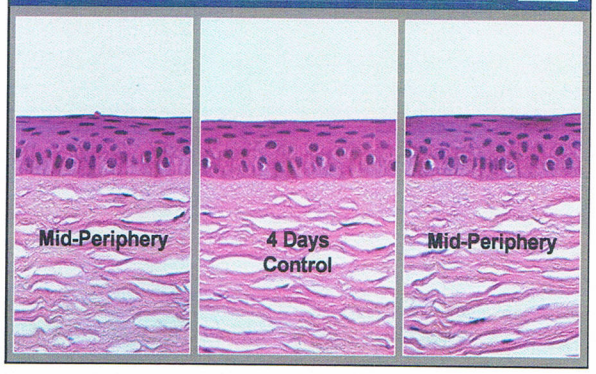
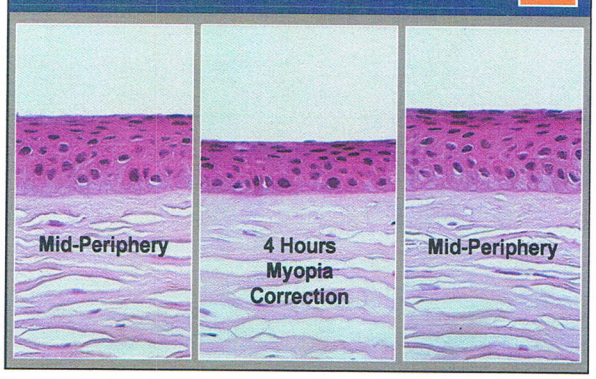
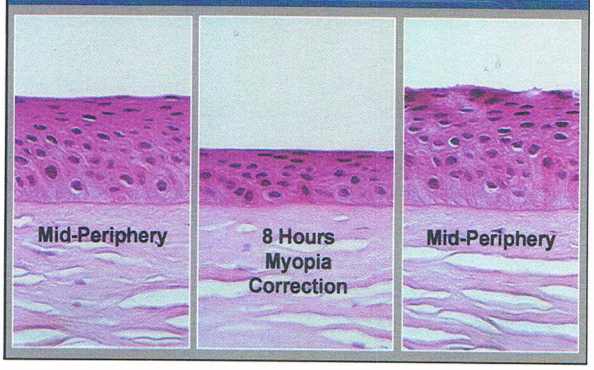
Normal cat cornea
(Choo et al, 2007)



4 hours myopia correction
(Choo et al, 2007)



8 hours myopia correction
(Choo et al, 2007)



Central epithelial thinning

- supporting evidence from clinical studies of overnight OK
  - Nichols et al (2000) - Orbscan
  - Soni et al (2003) - Orbscan
  - Haque et al (2004) - OCT
  - El Hage et al (2007) - confocal
  - Knappe et al (2007) - confocal with Rostock cornea module
  - Reinstein et al (2009) - Artemis

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Analysis of thickness changes

Munnerlyn's formula (Munnerlyn et al, 1988)

$$t = -S^2 D / 8 (n-1)$$

- t = ablation depth (um)
- S = optic zone diameter (mm)
- D = refractive change (D)
- n = refractive index of tissue

- used to calculate ablation depth in PRK
- assumes that posterior corneal curvature does not change

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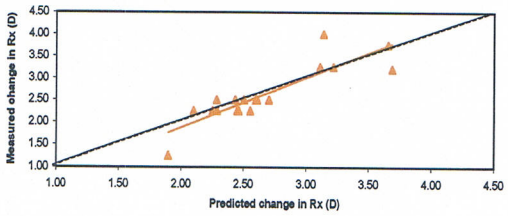
Analysis - Munnerlyn's formula
(Alharbi and Swarbrick, 2003)



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Research questions

- Does OK work?
- How does OK work?
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- What of the future?

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Corneal thickness changes in OK

- corneal thickness changes with:
  - daily wear OK *(Swarbrick, Wong, O'Leary 1998)*
  - overnight OK *(Alharbi and Swarbrick 2003)*
- central epithelial thinning
- midperipheral stromal thickening
- topographic thickness changes explain the refractive effect in OK
  - no corneal bending

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ON edema and OK outcomes

- OK lenses are quite thick (>0.2mm)
  - nominal BE lens Dk/t in Boston XO = 45
  - overnight edema would be expected
- Does ON edema influence clinical outcomes in ON OK?
- Does lens Dk/t influence clinical outcomes in ON OK?

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Lens Dk/t and OK outcomes

- comparison of clinical outcomes with OK lenses of different Dk/t:
- two separate contralateral eye studies
  - low (Boston EO) vs. moderate (Boston XO)
  - moderate (Boston XO) vs. high (Boston XO_2)
- matched lens designs and fits
- 2 weeks of overnight OK lens wear

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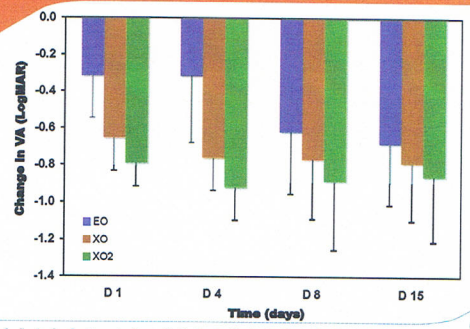
Change in visual acuity
(Lum and Swarbrick, 2007)



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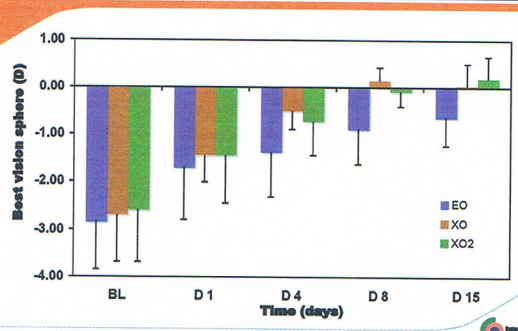
Change in refraction
(Lum and Swarbrick, 2007)



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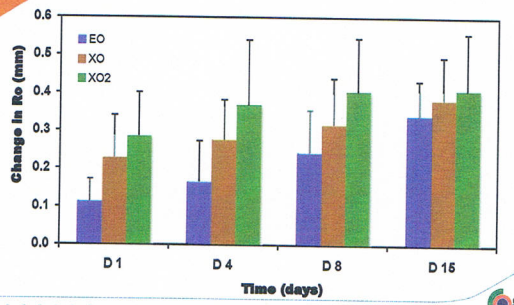
Change in apical radius
(Lum and Swarbrick, 2007)



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Lens Dk/t and OK outcomes

- lens Dk/t influences clinical outcomes in ON OK
  - more rapid rate of onset of effect with lenses of higher Dk/t
  - differences after longer lens wear?
- use high Dk/t lenses for ON OK
  - to promote corneal health
  - to optimize clinical outcomes

RESEARCH IN ORTHOKERATOLOGY

Research questions

- Does OK work?
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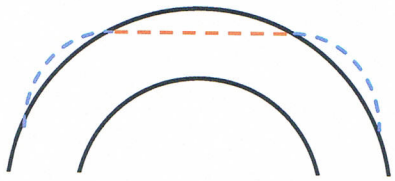
Research answers



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Research answers

- lens-induced pressures associated with reverse geometry lens wear:
  - thin the central epithelium
  - thicken the mid-peripheral stroma
- lens Dk/t affects the clinical outcomes of ON OK

RESEARCH IN ORTHOKERATOLOGY

Research questions

- Does OK work?
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Is OK safe?

- OK effect is achieved by:
  central epithelial thinning
- does this epithelial thinning compromise epithelial barrier function?
- does this epithelial thinning predispose the cornea to microbial keratitis (MK)?

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MK in OK - worldwide experience

Watt and Swarbrick, 2008

- analysis of 129 reported cases of MK in ON OK
  - all cases reported from 2001 to 2008
  - demographics of patients
  - clinical features of infection
  - trends in MK in OK

Kathleen Watt

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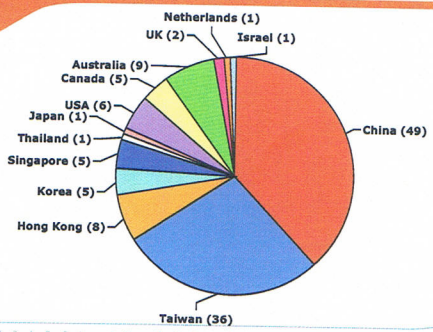
Country of report (n = 129)

(Watt and Swarbrick, 2008)



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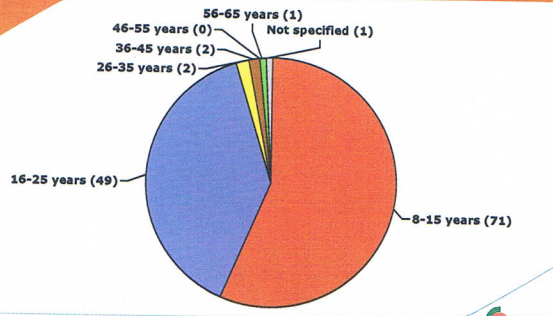
Age of patients (n = 126)

(Watt and Swarbrick, 2008)



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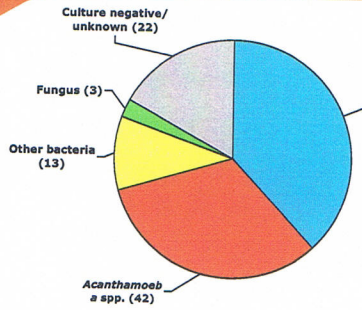
Causative organism (n = 129)

(Watt and Swarbrick, 2008)



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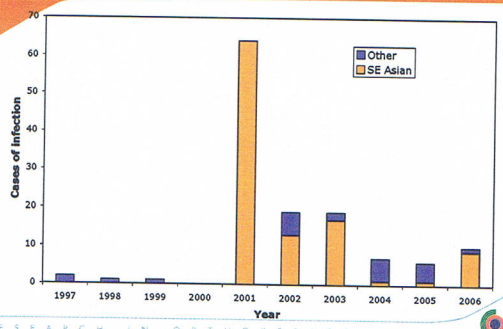
Year of infection - country

(Watt and Swarbrick, 2008)



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Lessons learnt

- practitioner education is essential
  - professional competence and training
  - knowledge of correct lens fitting procedures
  - use of appropriate instrumentation
  - use of appropriate lens designs and materials
  - careful patient instructions

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Lessons learnt

- practitioner education is essential
- patient compliance is critical
  - follow lens wear and care instructions
  - **avoid use of tap water**
  - hygiene and replacement of lens cases and accessories
  - report any problems early
  - attend regular aftercares

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Lessons learnt

- practitioner education is essential
- patient compliance is critical
- aftercares are essential
  - monitor corneal topographic outcomes
  - monitor corneal health
  - reinforce patient compliance

RESEARCH IN ORTHOKERATOLOGY

Safety of OK - unanswered questions

- is ON OK lens wear inherently unsafe?
- risk factors:
  - lens wear in closed eye
  - central epithelial thinning
  - potential for epithelial compromise (e.g. lens binding, staining, hypoxia)

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Safety of OK - unanswered questions

- what is the overall incidence/relative risk of MK in ON OK?
  - number of ON OK wearers unknown
  - number of ON OK wearers has varied over time
  - few recent reports of MK in ON OK
- recent estimates suggest no greater risk than other ON lens wear modalities (Bullimore et al)

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Ensuring safety in ON OK

- Careful fitting of OK lenses required
- Use high Dk materials for ON OK
- Corneal topographer is essential to monitor outcomes and trouble-shoot
- No tap water to be used with OK lens cleaning regimens
- Patient compliance is essential
- Continue regular aftercares

RESEARCH IN ORTHOKERATOLOGY

Research questions

- Does OK work?
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- What of the future?

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What of the future?

- myopia control
  - current evidence?
  - mechanism?
  - future studies
- ON OK for other refractive errors
  - hyperopia
  - presbyopia
  - astigmatism

RESEARCH IN ORTHOKERATOLOGY

What of the future?

- myopia control
  - current evidence?
  - mechanism?
  - future studies
- ON OK for other refractive errors
  - hyperopia
  - presbyopia
  - astigmatism

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Myopia correction *vs* control

- myopia <u>correction</u> is what we do every day to provide clear vision for myopes
  - spectacles, contact lenses
  - orthokeratology
  - refractive surgery
- myopia <u>control</u> refers to the reduction or elimination of ***progression*** of myopia in developing myopes

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Myopia control with OK lenses

- anecdotal evidence abounds that OK may slow progression of myopia
- thousands of children in East Asia are wearing ON OK specifically for myopia control
- how could OK work to control myopic progression?

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Role of peripheral refraction

- progressing myopes tend to show relatively hyperopic peripheral refraction

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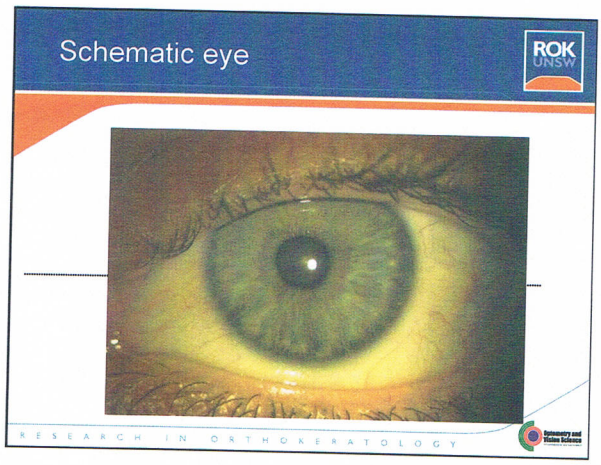
Schematic eye
ROK UNSW
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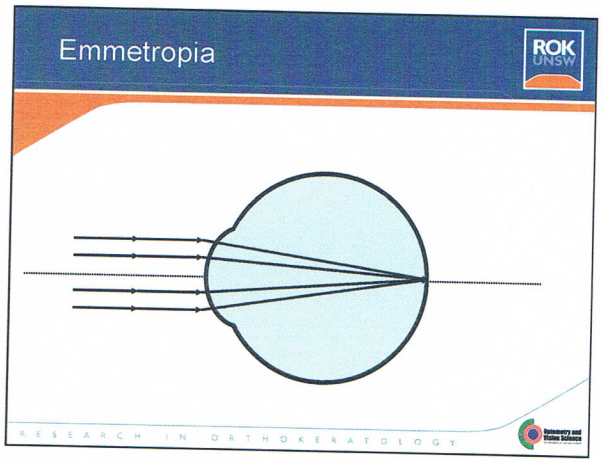
Emmetropia
ROK UNSW
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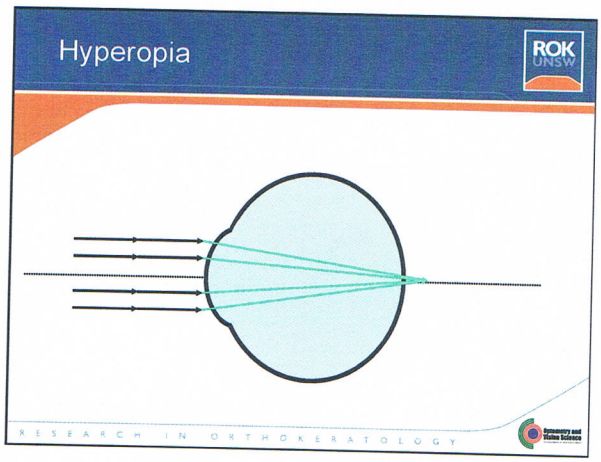
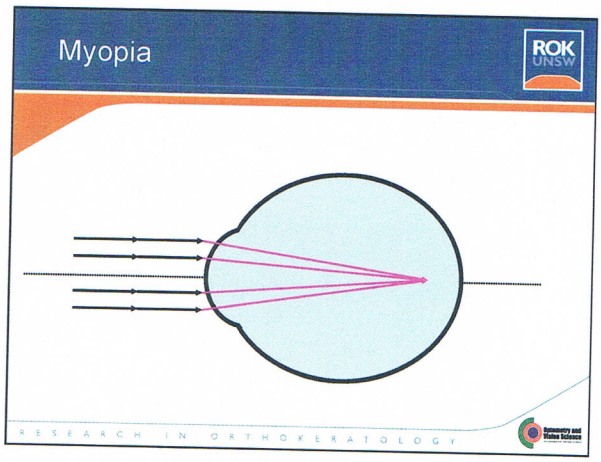
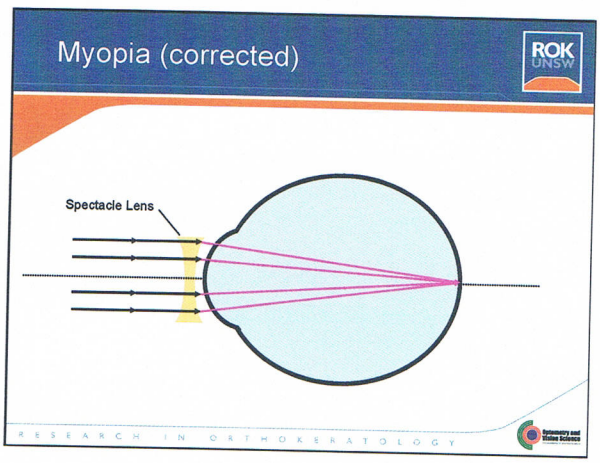
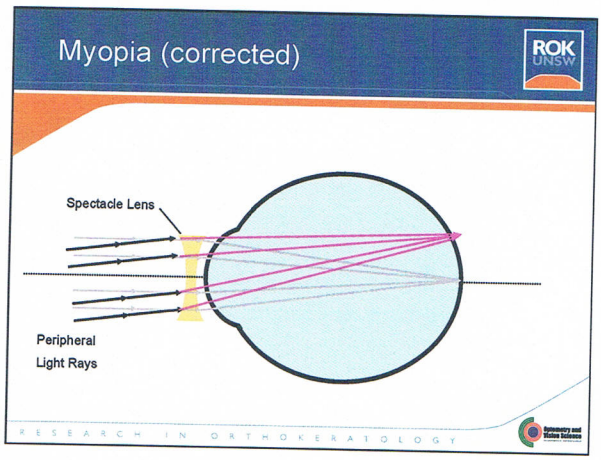

Hyperopia
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY


Myopia
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY


Myopia (corrected)
ROK UNSW
Spectacle Lens
RESEARCH IN ORTHOKERATOLOGY


Myopia (corrected)
ROK UNSW
Spectacle Lens
Peripheral
Light Rays
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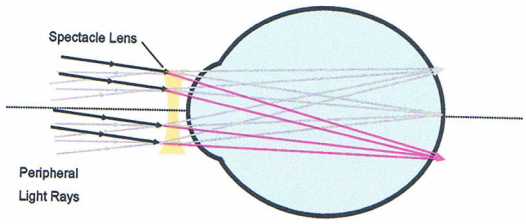
Myopia (corrected)



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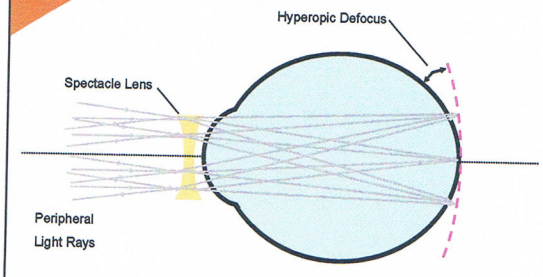
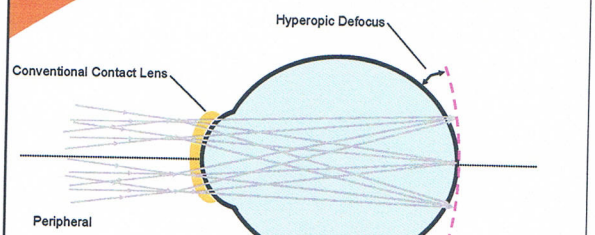
Myopia (corrected)



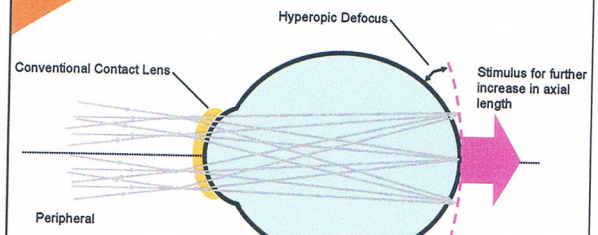
RESEARCH IN ORTHOKERATOLOGY

Myopia (corrected)



RESEARCH IN ORTHOKERATOLOGY

Myopia (corrected)



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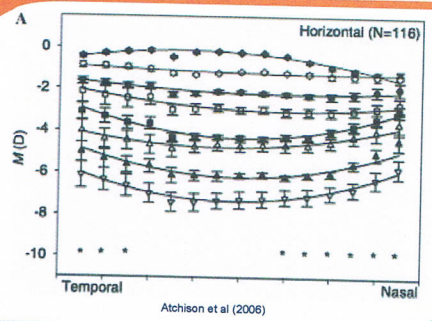
Peripheral refraction in myopia



Atchison et al (2006)

RESEARCH IN ORTHOKERATOLOGY

Role of peripheral refraction?

- progressing myopes tend to show relatively hyperopic peripheral refraction
- manipulation of peripheral refraction towards relative myopia may act to slow myopia progression
  - this may be achievable with orthokeratology!

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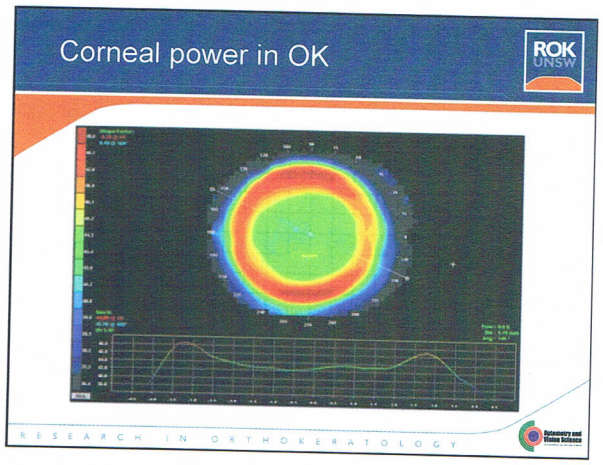
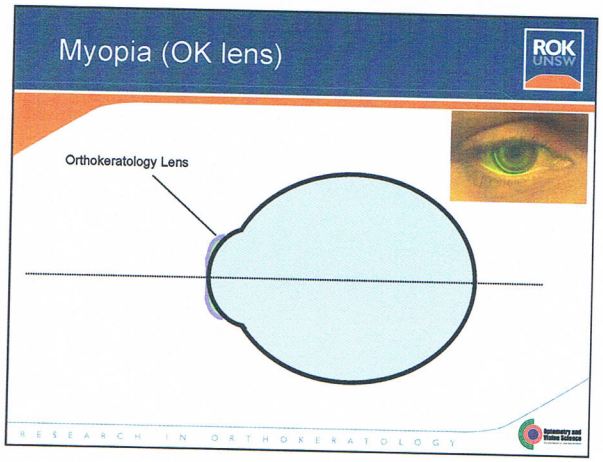
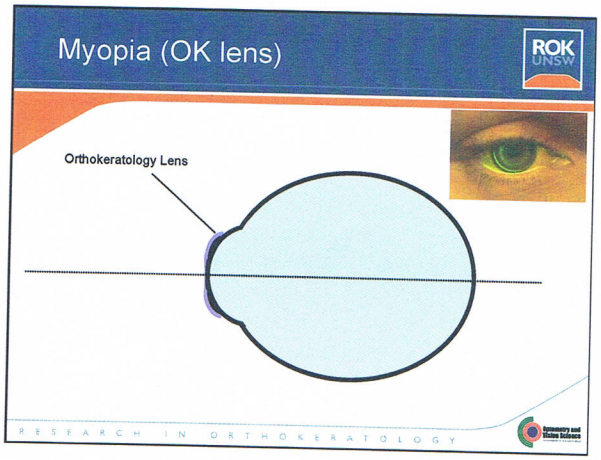
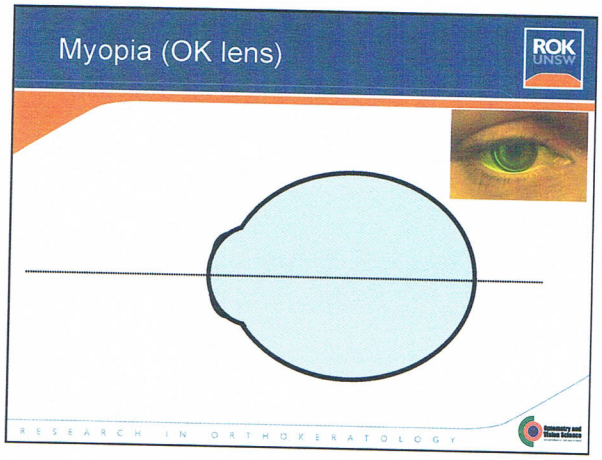
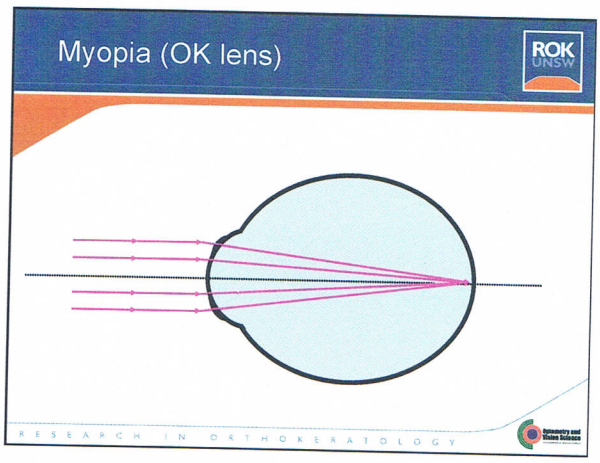
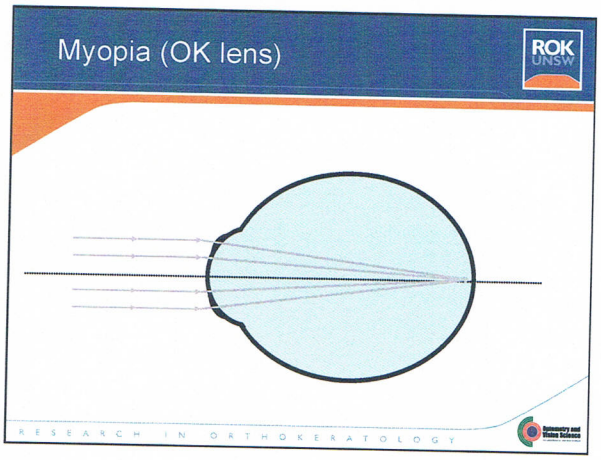

Corneal power in OK
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY

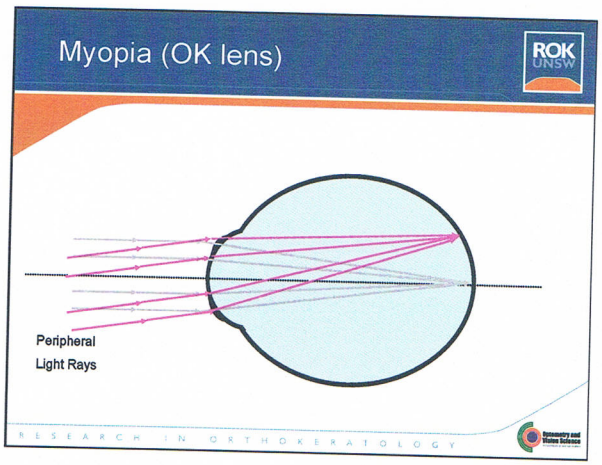

Myopia (OK lens)
ROK UNSW
Orthokeratology Lens
RESEARCH IN ORTHOKERATOLOGY

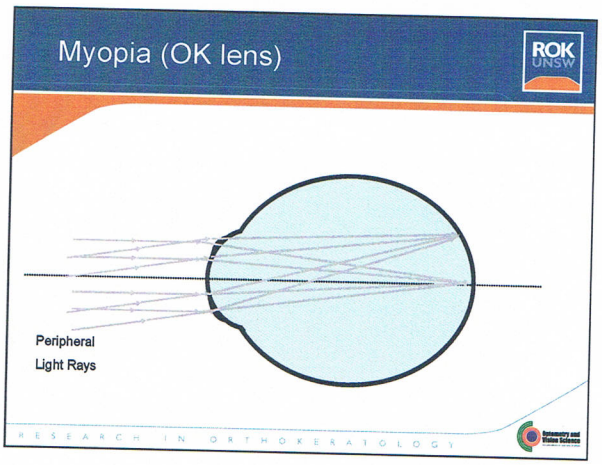

Myopia (OK lens)
ROK UNSW
Orthokeratology Lens
RESEARCH IN ORTHOKERATOLOGY

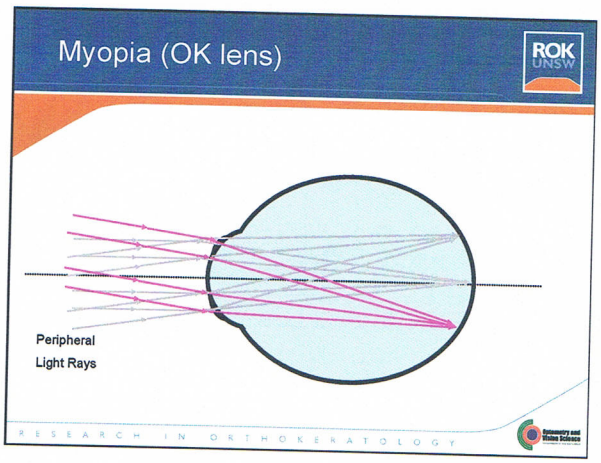

Myopia (OK lens)
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY

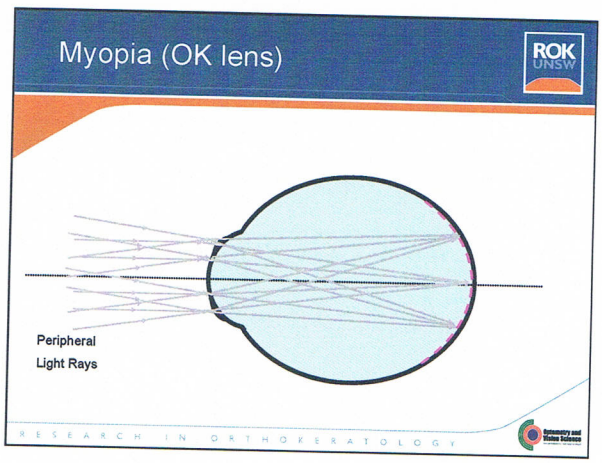

Myopia (OK lens)
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY

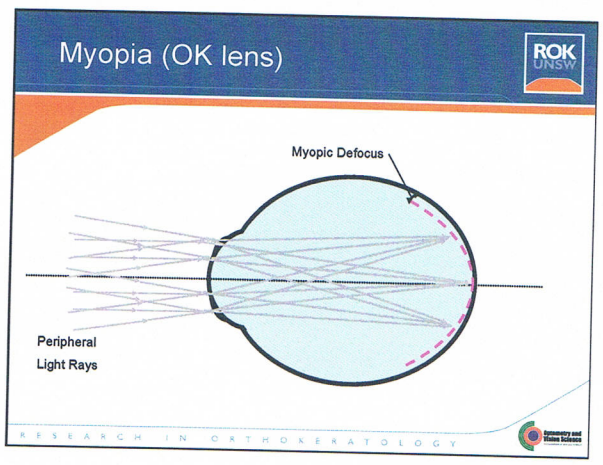

Myopia (OK lens)
ROK UNSW
RESEARCH IN ORTHOKERATOLOGY

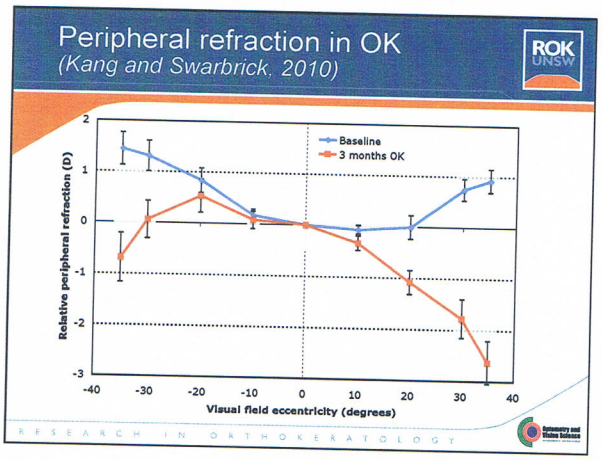

Myopia (OK lens)
ROK UNSW
Peripheral
Light Rays
RESEARCH IN ORTHOKERATOLOGY


Myopia (OK lens)
ROK UNSW
Peripheral
Light Rays
RESEARCH IN ORTHOKERATOLOGY


Myopia (OK lens)
ROK UNSW
Peripheral
Light Rays
RESEARCH IN ORTHOKERATOLOGY


Myopia (OK lens)
ROK UNSW
Peripheral
Light Rays
RESEARCH IN ORTHOKERATOLOGY


Myopia (OK lens)
ROK UNSW
Myopic Defocus
Peripheral
Light Rays
RESEARCH IN ORTHOKERATOLOGY


Peripheral refraction in OK
(Kang and Swarbrick, 2010)
ROK UNSW
Baseline
3 months OK
Relative peripheral refraction (D)
2
1
0
-1
-2
-3
-40
-30
-20
-10
0
10
20
30
40
Visual field eccentricity (degrees)
RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK lenses

- anecdotal evidence abounds that OK may slow progression of myopia
- thousands of children in East Asia are wearing ON OK specifically for myopia control
- promising results from early clinical studies of overnight OK

RESEARCH IN ORTHOKERATOLOGY

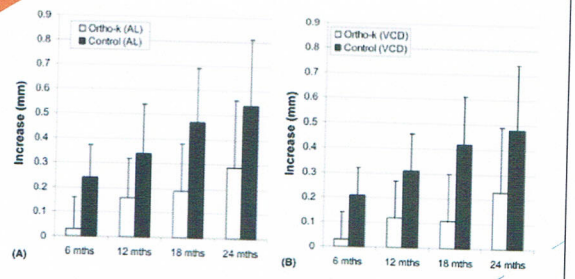
Myopia control with OK lenses

Cho et al (2005) - LORIC Study

- 35 myopic children, 7-12 years
  - control group: 35 spectacle wearers
- 2 years of overnight OK
- axial length and vitreous chamber depth monitored
- reduced eye growth in OK group

RESEARCH IN ORTHOKERATOLOGY

Cho et al (2005)



RESEARCH IN ORTHOKERATOLOGY

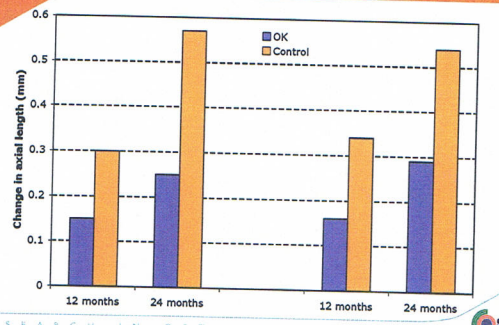
Myopia control with OK lenses

Walline et al (2009) - CRAYON Study

- 28 myopic children, 8-11 years
  - control group: 28 soft contact lens wearers
- 2 years of overnight OK
- axial length and vitreous chamber depth monitored
- reduced eye growth in OK group

RESEARCH IN ORTHOKERATOLOGY

Walline et al (2009)



RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK lenses

- both of these studies showed very promising outcomes
- both of these studies had significant shortcomings in study design
- prospective, randomized clinical trials necessary to confirm this early promise

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

- controlled, prospective, randomized clinical trials are underway worldwide
  - MCOS study (Spain)
  - SMART study (USA)
  - ROMIO study (Hong Kong)
- study design based on comparison between OK and control groups

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

MCOS *(Myopia Control with OK contact lenses in Spain)*

- 2 year study, sponsored by Menicon
- Menicon Z Night lens (similar to CRT); control group in spectacles
- axial length using IOL Master
- 24-month results show AL and Rx differences between groups

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

SMART *(Stabilizing Myopia by Accelerated Reshaping Technique)*

- 5-year multi-centre study in USA, sponsored by Bausch & Lomb
- Emerald OK lenses; control group in PureVision daily wear
- axial length using A-Scan ultrasound
- 24-month results suggest small differences in Rx only between groups

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

ROMIO *(Retardation of Myopia In Orthokeratology)* - Cho et al

- 2 year study, sponsored by Menicon
- NKL OK design in Menicon Z material; control group in spectacles
- axial length using IOL Master
- 12-month results suggest significant AL differences between groups

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

- controlled, prospective, randomized clinical trials are underway worldwide
  - SMART study (USA)
  - MCOS study (Spain)
  - ROMIO study (Hong Kong)
- ROK Group study (UNSW, Sydney)
  - novel contralateral-eye study design

RESEARCH IN ORTHOKERATOLOGY

OK and myopia control: ROK clinical study team

Ahmed Alharbi

Kathleen Watt

Helen O' Shea

RESEARCH IN ORTHOKERATOLOGY

OK and myopia control: ROK clinical study team

Ahmed Alharbi | Edward Lum | Helen O' Shea

RESEARCH IN ORTHOKERATOLOGY

OK and myopia control

- East Asian subjects
  - age 8-16 years
  - progressive myopes
- contralateral-eye study design
  - daily wear GP lens in one eye ("Day Lens")
  - overnight OK lens in other eye ("Night Lens")
- 12 months study
  - lens/eye crossover after 6 months

RESEARCH IN ORTHOKERATOLOGY

Methods - contact lenses

- overnight orthokeratology lenses
  - BE or ABE reverse geometry lenses (Capricornia Contact Lens)
- conventional alignment GP lenses
  - J-Contour aspheric lenses (Capricornia Contact Lens)
- Boston XO_2 material (Dk 141 ISO)

RESEARCH IN ORTHOKERATOLOGY

Methods - measurements

- progression of myopia monitored by measuring changes in axial length
  - Zeiss IOL Master
- study measurements taken after 3, 6, 9, 12 months of lens wear

RESEARCH IN ORTHOKERATOLOGY

Methods - measurements

- objective refractive error measured using Shin-Nippon N-Vision K5001 autorefractor
  - at baseline and following 2-week washout (no lens wear) at 6 and 12 months
  - no cycloplegia
  - spherical equivalent recorded

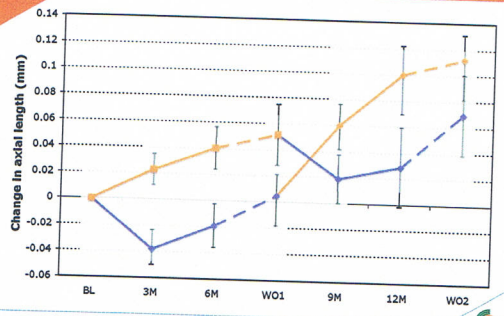
RESEARCH IN ORTHOKERATOLOGY

Subject discontinuations

- 32 subjects commenced study
  - 2 unable to adapt to GP daily wear
  - 1 lens-related discontinuation (GP eye)
  - 2 discontinued because of travel distance
  - data for 1 subject deleted - noncompliance
- 26 subjects completed 6 months
  - 2 discontinued at 6 months because of travel
- 24 subjects completed 12 months

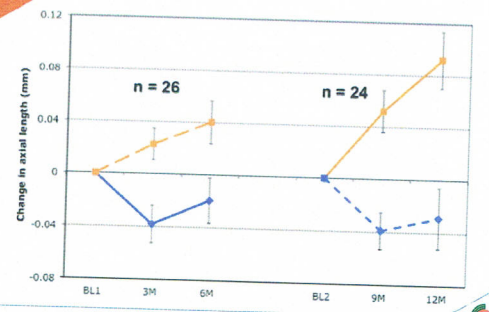
RESEARCH IN ORTHOKERATOLOGY

Change in axial length - OK vs GP
(Swarbrick et al, 2011)



RESEARCH IN ORTHOKERATOLOGY

Change in axial length - OK vs GP
(Swarbrick et al, 2010)



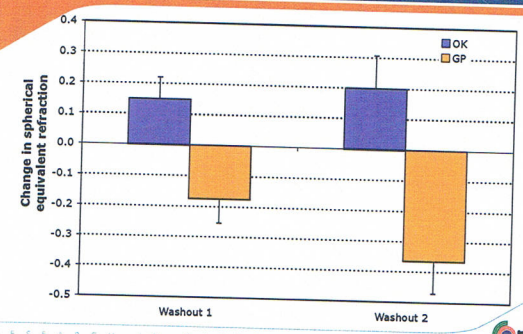
RESEARCH IN ORTHOKERATOLOGY

Change in axial length - OK vs GP

- significantly less axial length growth in OK vs GP eyes (ANOVA; $p<0.02$)
  - progressive axial length growth in GP eyes
  - no difference from baseline in OK eyes at 6 and 12 months
- cross-over effect compelling

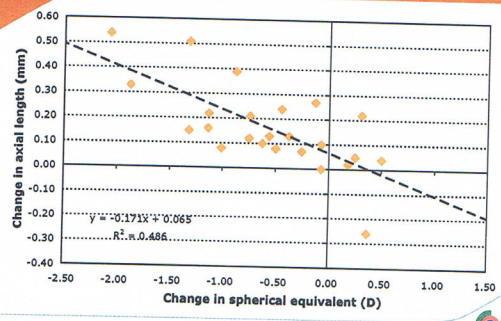
RESEARCH IN ORTHOKERATOLOGY

Change in refraction - OK vs GP
(Swarbrick et al, 2011)



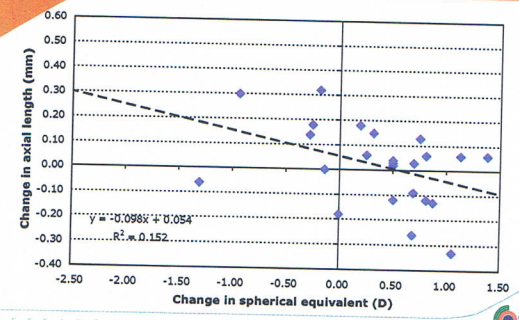
RESEARCH IN ORTHOKERATOLOGY

GP - changes in Rx *vs* axial length
(Swarbrick et al, 2011)



RESEARCH IN ORTHOKERATOLOGY

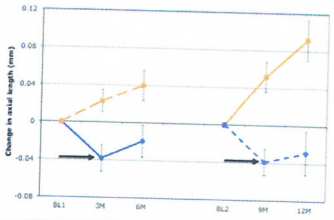
OK - changes in Rx *vs* axial length
(Swarbrick et al, 2011)



RESEARCH IN ORTHOKERATOLOGY

Myopia control in OK - questions

- why the apparent shortening in axial length in the OK eye at 3 and 9 months?



RESEARCH IN ORTHOKERATOLOGY

Myopia control in OK - questions

- why the apparent shortening in axial length in the OK eye at 3 and 9 months?
  - IOL Master measures from corneal front surface to retinal pigment epithelium
  - some apparent shortening is due to central epithelial thinning (about 20 um)
  - some apparent shortening may be due to choroidal thickening

RESEARCH IN ORTHOKERATOLOGY

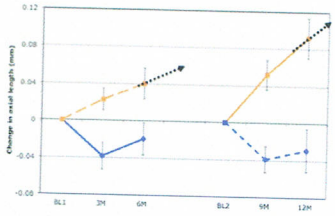
Myopia control in OK - questions

- choroidal thickening?
  - well documented in animal models of myopia (chicken through to primate)
  - choroid thins on application of myopigenic stimulus (e.g. defocus, occlusion)
  - choroid shows rapid thickening (recovery) on removal of myopigenic stimulus
  - implication: OK neutralizes the myopigenic stimulus in progressive myopes

RESEARCH IN ORTHOKERATOLOGY

Myopia control in OK - questions

- why the greater axial length growth in Phase 2 in the GP eye?



RESEARCH IN ORTHOKERATOLOGY

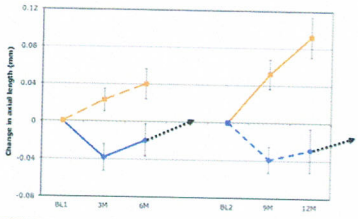
Myopia control in OK - questions

- why the greater axial length growth in Phase 2 in the GP eye?
  - "rebound" effect?
  - what happens if OK lens wear is discontinued?
  - how long must OK lenses be worn to maintain myopia control effect?

RESEARCH IN ORTHOKERATOLOGY

Myopia control in OK - questions

- what happens in the OK eye after 6 months?



RESEARCH IN ORTHOKERATOLOGY

Myopia control in OK - questions

- what happens in the OK eye after 6 months?
  - short-term study, long-term effects unknown
  - is there accrual of effect?
  - follow-up on ROK Group subjects ongoing
  - long-term OK myopia control studies will help to resolve this question

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

- in the short term, overnight OK inhibits axial length growth and myopia progression in myopic children
  - this confirms its potential for myopia control
  - long-term studies are now required to demonstrate effects over time

RESEARCH IN ORTHOKERATOLOGY

Myopia control with OK

- myopia control with OK works better for some children than others
  - can we predict the successful wearers?
  - can we individualize OK lens design to target effective myopia control for all kids?
- myopia control *vs.* myopia prevention?
  - can we prevent development of myopia?
  - what causes myopia in the first place?

RESEARCH IN ORTHOKERATOLOGY

Research questions

- Does OK work?
- How does it work?
- Is it safe?
- What of the future?

RESEARCH IN ORTHOKERATOLOGY

Acknowledgements

- The UNSW ROK Group:
  - Paul Gifford, Edward Lum, Kathleen Watt, Ahmed Alharbi, Pauline Kang, Helen O'Shea, Vinod Maseedupally, Gavin Boneham
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  - Australian Research Council Linkage Project Scheme
    - Bausch & Lomb Boston
    - BE Enterprises Pty Ltd
    - Capricornia Contact Lens Pty Ltd
  - OK Society of Oceania, Contact Lens Society of Australia, Bausch & Lomb (Australia)

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ROK Group

RESEARCH IN ORTHOKERATOLOGY