Cornea Update

DALK & Endothelial Keratoplasty

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

DEEP ANTERIOR LAMELLAR KERATOPLASTY

CENTRE FOR SIGHT

Indications for Lamellar Keratoplasty

"WHENEVER THE ENDOTHELIUM IS NORMAL"

CENTRE FOR SIGHT

Anterior Lamellar Keratoplasty

- **Advantages**
  - Retains endothelium
  - Reduces risk of corneal blindness
- **Disadvantages** (previously)
  - Poor Vision
    - Interface opacification
    - Regular and Irregular Astigmatism
  - Technical skill
    - Perforation

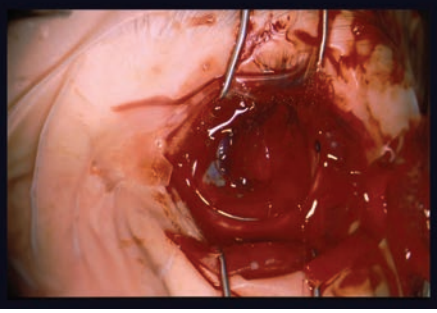
CENTRE FOR SIGHT

DALK – Why ?

- "Primo No Nocere"
- SAFETY
- SURVIVAL – long term
- OTHER...

CENTRE FOR SIGHT

PK can be HAZARDOUS !!!



CENTRE FOR SIGHT

PK – Hazards...

- Expulsive Choroidal Haemorrhage 0.56*-1%
- Rejection & Failure
- Reduced survival of Regrafts
- Glaucoma 19- 30%
- Cataract
- Endophthalmitis

- Speaker MG, Guerriero PN, Met JA, Coad CT, Berger A, Marmor M. A case-control study of risk factors for intraoperative suprachoroidal expulsive hemorrhage. *Ophthalmology 1991 Feb;98(2):202-9;*

CENTRE FOR SIGHT

PK – long term...

EXTENDED REPORT

Penetrating keratoplasty: outcomes from a corneal unit compared to national data

P Beckingsale, I Mavrikakis, N Al-Yousuf, E Mavrikakis, S M Daya

Br J Ophthalmol 2006;90:728–731. doi: 10.1136/bjo.2005.084072

Table 1 Three year graft survival rates for national outcome data (UKT) and Queen Victoria Hospital (QVH)

Diagnosis	UKT 3 year graft survival rates (%)	QVH 3 year graft survival rates (%)	p Value
Keratoconus	93	98	0.019
PBK	85	90	0.00003
Fuchs' dystrophy	87	90	0.47
Viral keratitis	77	95	0.002
Regrafts	57	67	0.002
Total	79	81	0.15

CENTRE FOR SIGHT

DALK - Techniques

- Injection of air into the stroma – big bubble
- Injection of water / viscoelastics
- Stromal Air Injection
- Ferrara Ring Dissection
- Optical recognition - Melles
- Modification of Melles's technique

CENTRE FOR SIGHT

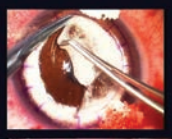
'DALK and Endothelial Keratoplasty'

(slides 1-16)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

DALK – How ?

- Descemet's
  - Big Bubble – *Anwar*
  - Viscodissection
- Pre-Descemet's
  - Optical Recognition – *Melles*
- Femtosecond Assisted



CENTRE FOR SIGHT

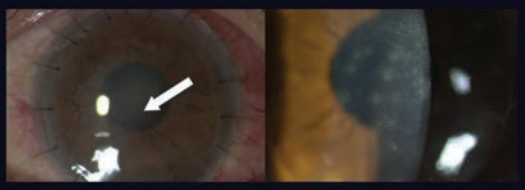
Deep Anterior Lamellar Keratoplasty

Sheraz Daya MD

www.centreforsight.com

CENTRE FOR SIGHT

Do Lamellars Reject ?



Epithelial Rejection

Sub-epithelial Rejection

CENTRE FOR SIGHT

DALK vs PK for Keratoconus

Authors	Number of eyes	BCVA ? 20/40	BCVA ? 20/30
Deep Anterior Lamellar Keratoplasty for keratoconus			
This study	50	74.2%	56%
coombes et al [4]	37	80%	64%
Watson et al [5]	25	87.5%	N/A
Anwar et al [1]	181	89%	27%
Funnel et al[6]	20	78%	N/A
Penetrating Keratoplasty for keratoconus			
Buzard et al[7]	104	88%	88%
Lim et al[8]	93	87%	N/A
Watson et al[5]	22	95%	N/A
Funnel et al[6]	20	85%	N/A

CENTRE FOR SIGHT

Indications for Lamellar Keratoplasty

- "WHENEVER THE ENDOTHELIUM IS NORMAL"

CENTRE FOR SIGHT

POSTERIOR LAMELLAR KERATOPLASTY

CENTRE FOR SIGHT

POSTERIOR LAMELLAR KERATOPLASTY

- ENDOTHELIAL FAILURE
- Cornea Oedema
  - Fuchs Endothelial Dystrophy
  - Pseudophakic Bullous Keratopathy
  - ICE Syndrome – endothelial failure

CENTRE FOR SIGHT

FUCHS DYSTROPHY

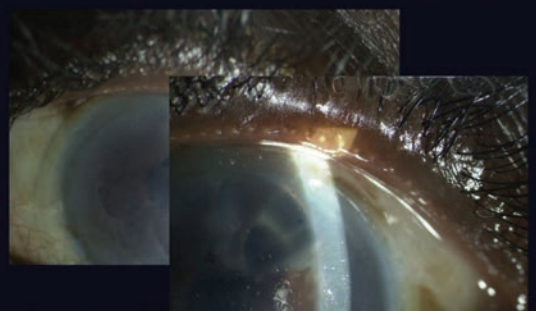
CENTRE FOR SIGHT

'DALK and Endothelial Keratoplasty'

(slides 17-32)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

Pseudophakic Bullous Keratopathy



CENTRE FOR SIGHT

Endothelial Failure

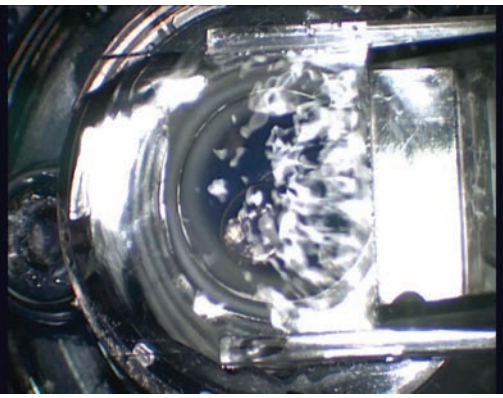
- Traditional approach = Penetrating keratoplasty
- Problems
  - Sutures & suture related problems
  - Rehabilitation – 1 year approx
  - Frequent follow up
  - Open-sky – hazardous
  - Astigmatism – regular & irregular

CENTRE FOR SIGHT

Endothelial Failure

- Why not just replace the endothelial layer ?
  - Anterior corneal stroma is normal
  - Smaller incision outside cornea
  - Less astigmatism
  - More rapid rehabilitation
- CHALLENGE:
  - Keep the endothelial cells in place
  - Graft survival

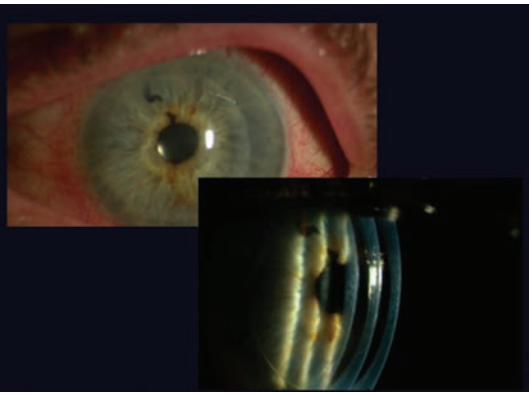
CENTRE FOR SIGHT



CENTRE FOR SIGHT

CENTRE FOR SIGHT

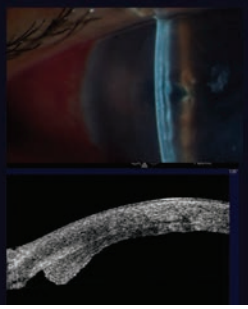
CENTRE FOR SIGHT



CENTRE FOR SIGHT

DSAEK ISSUES

- DISLOCATION
  - Good air Fill
  - No Healon
  - Technique
- ENDOTHELIAL FAILURE
- Technique



CENTRE FOR SIGHT

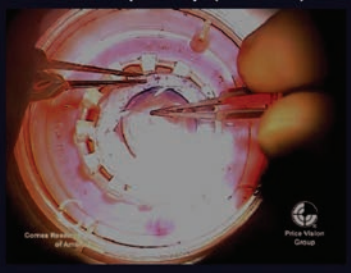
DSAEK ISSUES

- ENDOTHELIAL FAILURE - avoidance
  - Young Donor preferable
  - Single point fixation of Folded Donor
  - Increase incision size

CENTRE FOR SIGHT

CENTRE FOR SIGHT

Descemet's Membrane Endothelial Keratoplasty (DMEK)



CENTRE FOR SIGHT

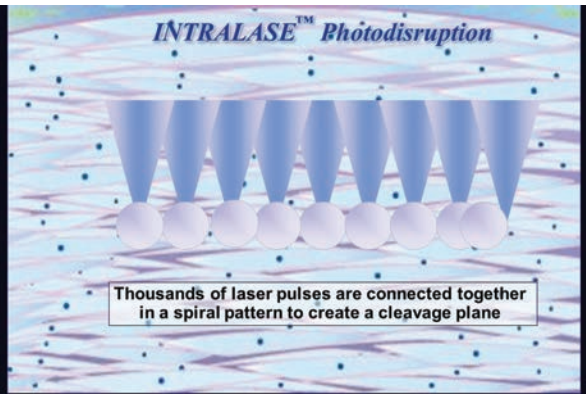
INTRALASE
and Corneal Grafting

CENTRE FOR SIGHT

Intralase & Corneal Grafts

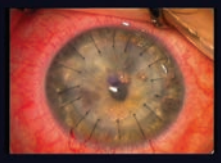
- Intralase Femtosecond Laser
  - CE marked for making PRECISE cuts in corneal tissue
  - Principally used for Flap creation in Lasik
  - Applications in Grafting
    - Anterior Lamellar Keratoplasty
    - Posterior Lamellar Keratoplasty (DSIEK)
    - Penetrating Keratoplasty

CENTRE FOR SIGHT



CENTRE FOR SIGHT

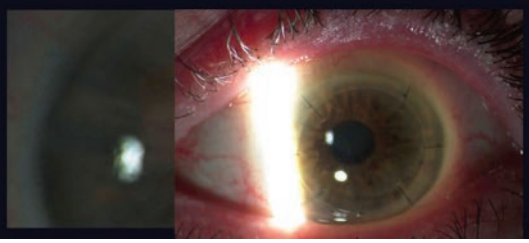
Anterior Lamellar Keratoplasty



CENTRE FOR SIGHT

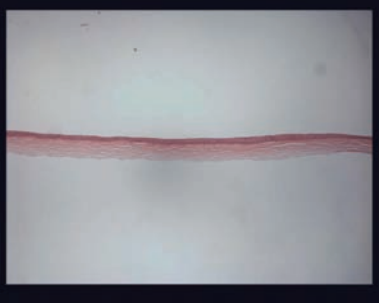
LAMELLAR GRAFTS

- Anterior Basement Membrane Dystrophy – Familial

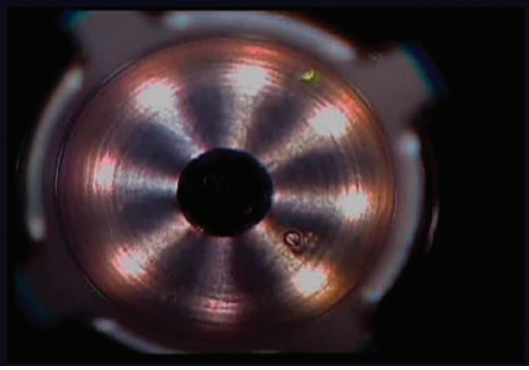


CENTRE FOR SIGHT

HISTOLOGY



CENTRE FOR SIGHT



CENTRE FOR SIGHT

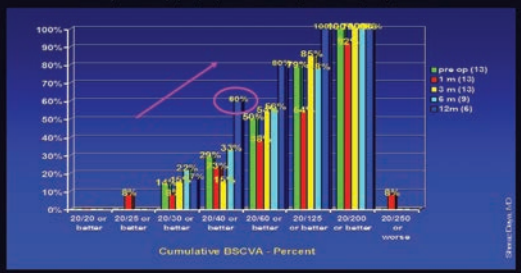
'DALK and Endothelial Keratoplasty

(slides 33-48)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

RESULTS

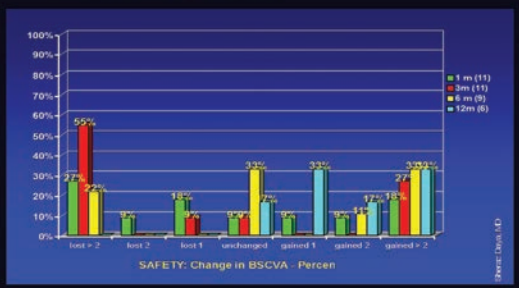
- BSCVA
  - One eye = Amblyopic (improved from 20/200 to 20/100) excluded



CENTRE FOR SIGHT

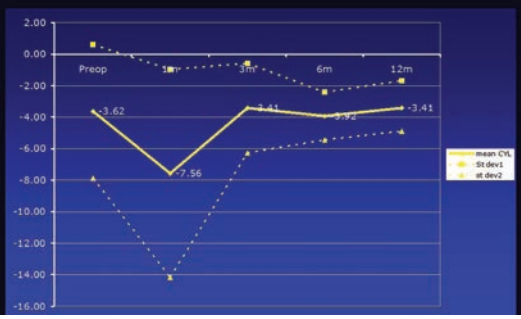
RESULTS

- BSCVA - lines gained /lost



CENTRE FOR SIGHT

RESULTS - Keratometric Astigmatism



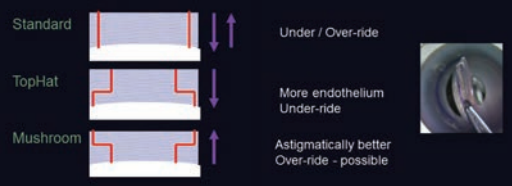
CENTRE FOR SIGHT

Complications

- Compression Striae -recovered following suture removal
- Replacement in one case
  - Polyopia and high astigmatism (graft oversized)
- Residual refractive error
  - May need supplemental LASIK

CENTRE FOR SIGHT

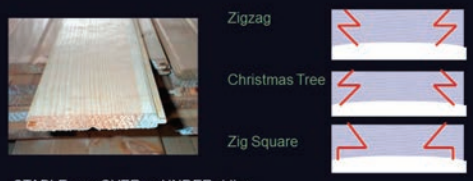
GEOMETRIC PATTERNS - I



CENTRE FOR SIGHT

GEOMETRIC PATTERNS - II

•"Tongue & Groove" !

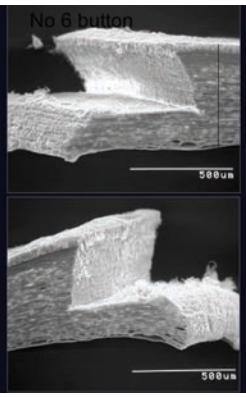


•STABLE - no OVER or UNDER riding
•ANTERIOR ANGLE (ZIG) = smooth anterior join / surface

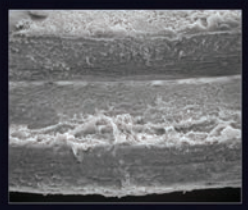
CENTRE FOR SIGHT

Femtosecond PK

CENTRE FOR SIGHT



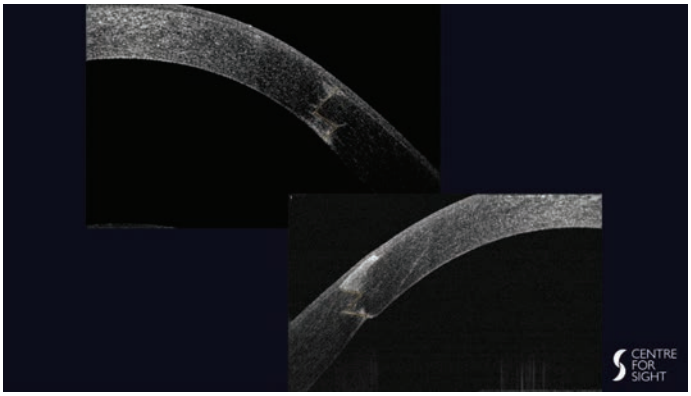
ZIG- SQUARE
(recipient button)

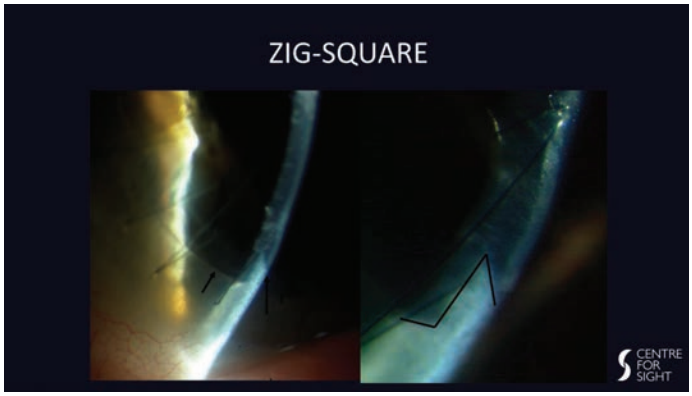


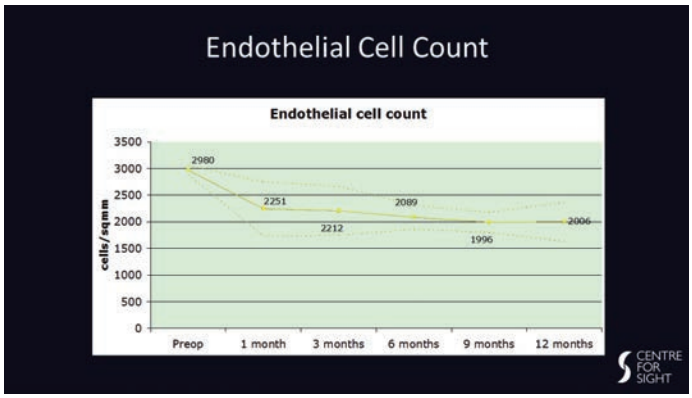
Electron microscopy performed at St Thomas's Hospital - John Marshall PhD

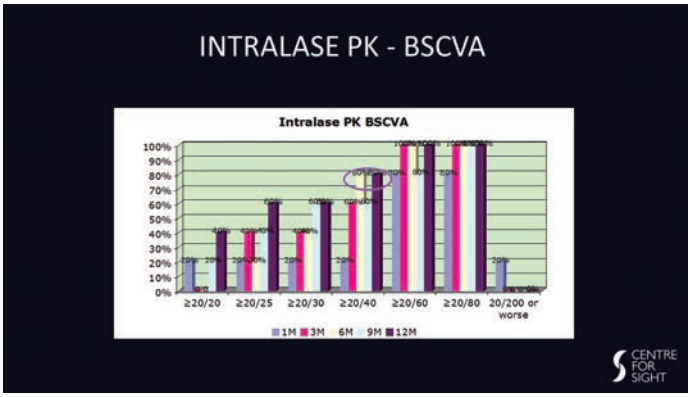
CENTRE FOR SIGHT

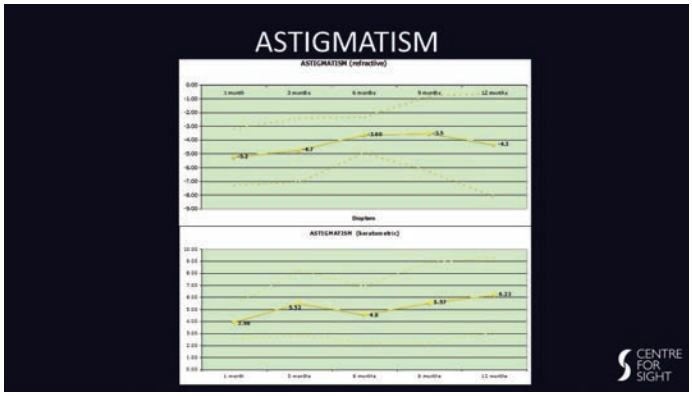
CENTRE FOR SIGHT

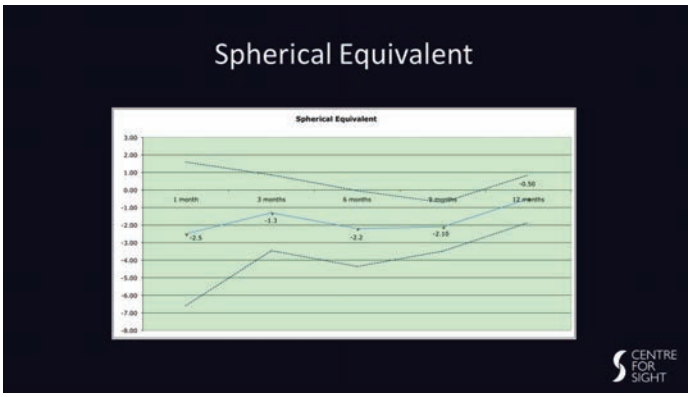


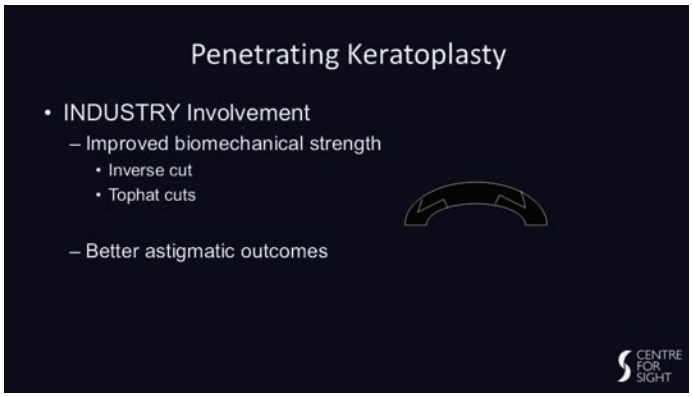










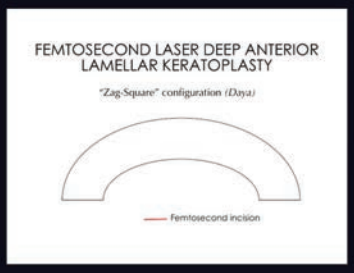


‘DALK and Endothelial Keratoplasty’

(slides 49-54)

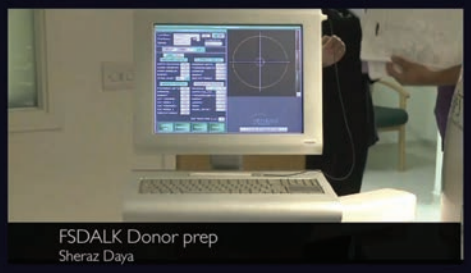
Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

FEMTOSECOND DALK



CENTRE FOR SIGHT

FSDALK – Donor Preparation

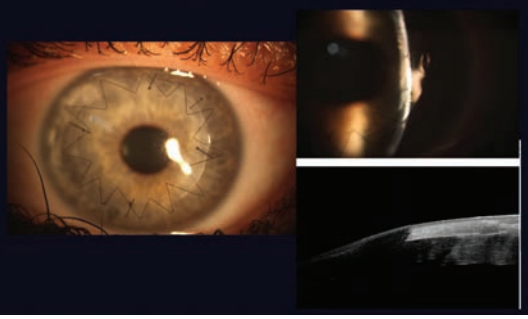


CENTRE FOR SIGHT

FSDALK - Recipient

CENTRE FOR SIGHT

Postoperative 6 weeks



CENTRE FOR SIGHT

Conclusion

- Selective Keratoplasty
  - Superficial Anterior Lamellar Keratoplasty
    - Microkeratome
    - Femtosecond Laser
  - Deep Anterior Lamellar Keratoplasty
    - Manual
    - Big bubble
    - Femtosecond laser

CENTRE FOR SIGHT

Thank you

CENTRE FOR SIGHT

CENTRE FOR SIGHT

Dry Eye Update

Dry Eye - Our approach...

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

CENTRE FOR SIGHT

Dry Eye - Our Approach

SHERAZ DAYA
MD FACP FACS FRCS(Ed) FRCOphth

CENTRE FOR SIGHT

Financial Disclosure

	Company	Code
1.	Abbott Medical Optics Inc.	S
2.	Allergan	L
3.	Bausch + Lomb	C,L
4.	Carl Zeiss Meditec	C
5.	Clarvista	C
6.	Ellex	L
7.	Excellens	C, O
8.	LinCor Biosciences	C
9.	Lumenis	C
10.	Medicem	C
11.	Nidek, Inc.	C,L
12.	Omeros	C
13.	Physiol	L
14.	PRN	O
15.	STAAR Surgical	C,O
16.	Strathspey Crown	C
17.	Scope Pharmaceuticals	C
18.	Rayner	C

C = Consultant / Advisor
E = Employee
L = Lecture Fees
O = Equity Owner
P = Patents / Royalty
S = Grant Support

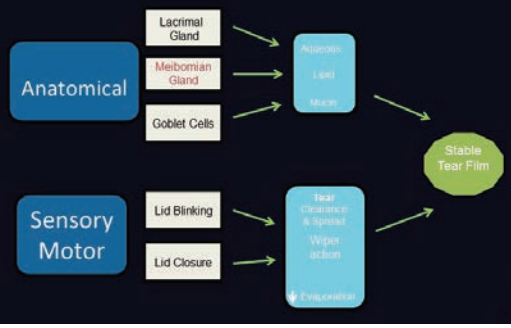
CENTRE FOR SIGHT

TFOS II

"Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."

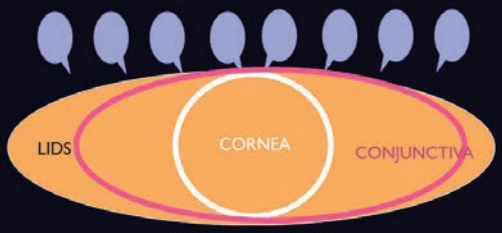
CENTRE FOR SIGHT

Stable Tear Film Maintenance



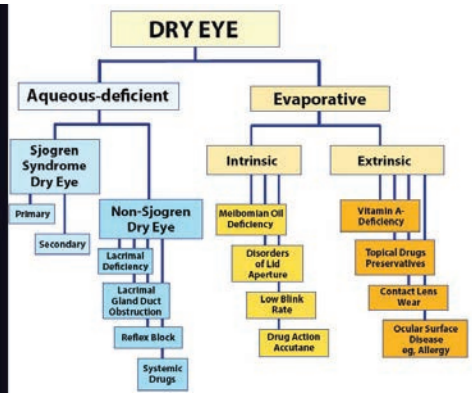
CENTRE FOR SIGHT

OCULAR SURFACE RELATIONSHIPS

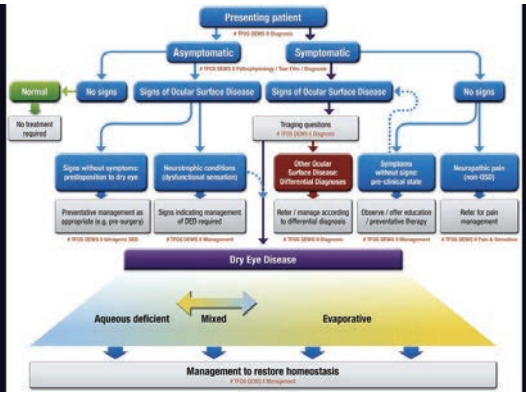


PRESERVE CORNEAL CLARITY

CENTRE FOR SIGHT



CENTRE FOR SIGHT



CENTRE FOR SIGHT

My approach to Dry Eye

- History
- Diagnosis
- Management
  - Emphasis on Evaporative Dry Eye

2007 DEWS REPORT:

"Meibomian gland dysfunction is a condition of meibomian gland obstruction and is the most common cause of evaporative dry eye."

CENTRE FOR SIGHT

'Dry Eye - Our approach...'

(slides 1-16)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

Simplified

HISTORY

- Symptoms
  - Grittiness
  - Burning
  - Itching
  - Lid stuck to eye on awakening
  - Photophobia
  - Eye Fatigue
  - Excessive Tearing (windy environment)
- Drugs

Questionnaires

- SPEED
- OSDI

- Useful for subjective scoring
- Interval change
- Content – serves as a guide to type of dry eye

Clinical Evaluation

- Lid Closure
- Blink Rate
- Puncti

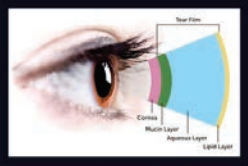
- LID MARGINS
  - Collarettes – scurf, basal, sleeves
  - Meibomian Gland orifices
  - Meibum quality
  - Level of inflammation

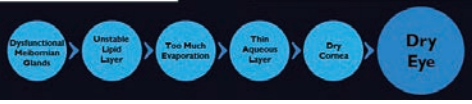
CLINICAL EVALUATION

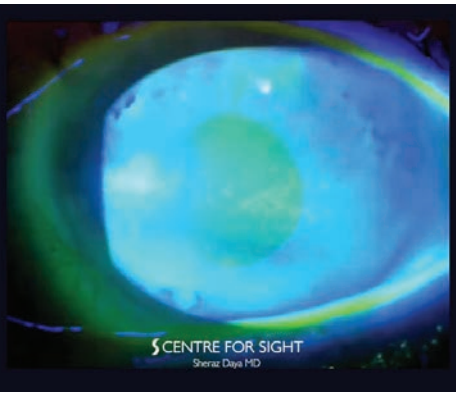
- CONJUNCTIVA
  - Bulbar
  - Palpebral
- FLUORESCEIN
  - Lid "Wiper" Action
  - Quality of tear surface
  - Tear Meniscus
  - Corneal & Conjunctival Stain
- Rose Bengal / Lissamine Green

Evaporative DED accounts for 86% of DED

The number of Meibomian glands is relatively small, any dropout has a significant impact







Investigations

- Tear Break Up Time (TBUT)
- Schirmer's (with topical anesthetic)

- Lipiview
- Meibography
- Tear Osmolarity
- Surface irregularity
- HD Analyzer

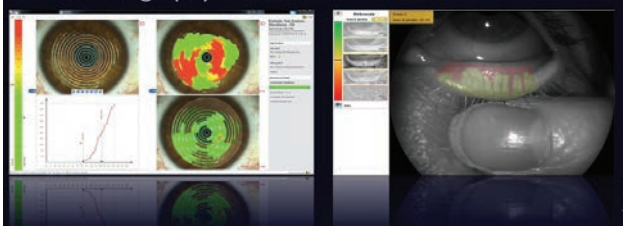
'Dry Eye - Our approach...'

(slides 17-32)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

ANTARES

- Tear break up time
- Meibography



TearScience® Solution

TearLab® Osmolarity System

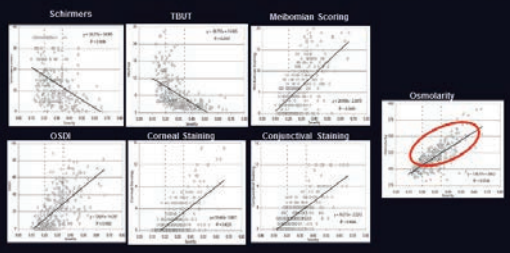
What does the TearLab system measure?

Blinking, aqueous tearing (mixing), increased lipid secretion excretion - all lower osmolarity transiently and asymmetrically

< 5 mOsm/L Variability
mOsm/L ≥ 20 mOsm/L

A Bron, et al. The Ocular Surface 2009 Apr;7(2):78-92.
A Keech, et al. Curr Eye Res 2013 Apr;38(4):428-36.

Osmorality is the best single predictor of DED severity



Sullivan BD, et al. *Invest Ophthamol Vis Sci.* 2010 51:6125-6130.

Tearlab - Discovery

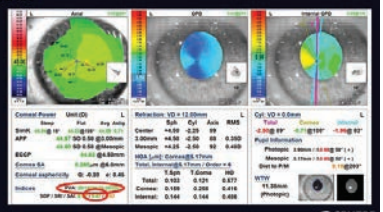
- Osmolarity
- Interleukin-1 receptor antagonist (IL-1Ra)
- Matrix metalloproteinase 9 (MMP-9)

Indications	Asymptomatic	Symptomatic	P-values
Osmolarity (mOsm/L)	303.1±10.2	313.9±24.5	0.034
IL-1Ra (ng/mL)	279.3±509.5	342.3±472.9	0.566
MMP-9 (ng/mL)	100.5±131.0	319.1±565.5	0.058
TBUT (sec)	10.1±4.5	8.3±4.5	0.078
CFS	0.4±0.8	0.6±1.0	0.289

Francesco Carones MD[2], Béatrice Cochener MD[3], Sheraz M. Daya MD[4], Erik L. Mertens MD[5], Thomas Kohnen MD, PhD, FEBO[1]

OPD 3

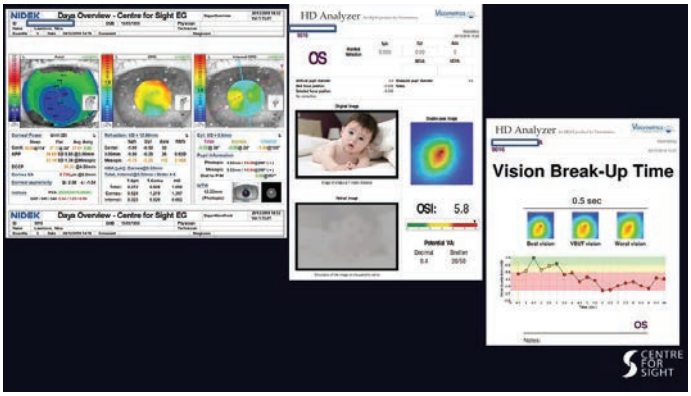
Surface Regularity Index
Irregular astigmatism
Visual Potential



HD Analyzer

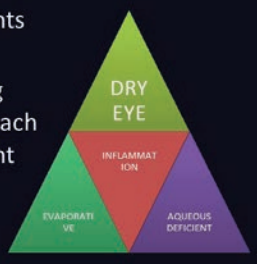
- Measures scatter
  - Tear film
  - Cornea
  - Lens
  - Vitreous

CENTRE FOR SIGHT



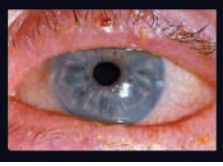
ASSESSMENT of findings

- SCORE components
- Assess underlying cause of each component



Management

GOALS
- Reduce symptoms
  - Lubricants – appropriate
- Treat underlying cause
- ? Treat Inflammation



MANAGEMENT

AQUEOUS DEFICIENT
- Sjogren's
- Non-Sjogren's
  - Drugs
  - Lacrimal Dysfunction
  - Lacrimal Gland Obstruction
  - Reflex Block – denervation *(Laser eye surgery)*

EVAPORATIVE

- Intrinsic
  - Meibomian Gland Dysfunction
  - Lid Closure – lagophthalmos
  - Blink Rate
- Extrinsic
  - Drug Preservatives
  - Ocular surface inflammation – allergy
  - CTL
  - Vitamin A deficiency

Meibomian Gland Disease

LID MARGINS
- Treat underlying lid problem
  - Seborrhea – Nizoral
  - Staph – Fucidic acid
  - Demodex – Tea Tree Oil
- Consider – are the above "Opportunistic" ?

BlephEx™

Meibomian Gland Disease

- Lid Hygiene – Compresses and scrubs
- Inflamed ?
  - Lotemax BID for 3 months
- All should get Re-esterified Omega 3 (PRN Omega Eye)

What are Omega 3s ?

- Polyunsaturated Fatty Acids (PUFA)
  - DHA (Docoshexanoic Acid)
  - EPA (Eicosapantaneoic Acid)
  - DPA (Docospantaneoic Acid)
  - ALA (Alpha Linolenic Acid)
    - flax seeds
    - Requires conversion to EHA & DPA before active

'Dry Eye - Our approach...'

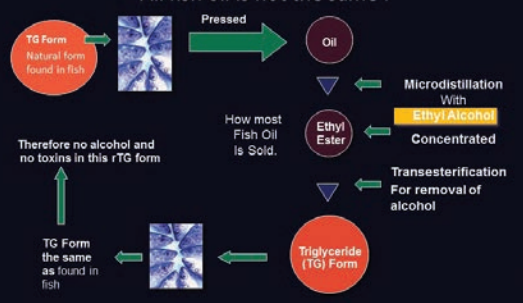
(slides 33-48)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

Why Re-esterified Omega 3?

CENTRE FOR SIGHT

Omega Eye Production – All fish oil is not the same !



CENTRE FOR SIGHT

Dose & Form

- > 2.7g - anti-inflammatory effect

Arthritis Research & Therapy 2006, **8**:202 (doi:10.1186/ar1876)

- We can't get 2-3 grams of EPA & DHA from eating oily fish
- Better absorption in the body with rTG form

The bioavailability of EPA + DHA from reesterified triglycerides was superior (124%)

CENTRE FOR SIGHT

PERSONAL OBSERVATIONS

PRN Omega 3

1. Schirmer's improves after 3 months
   0mm to 4-5mm - !!!!!
2. Blepharitis (Seborrheic, Demodex,) improves
3. Telangiectasia less pronounced
4. Turbid secretions –become Thinner & Clearer

? Poor Meibum causes low grade inflammation

CENTRE FOR SIGHT

Omega 3s and Prostatic Cancer ?

- Brasky et al. Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial.
  - *Journal of the National Cancer Institute*
  - Higher plasma levels of DHA & EPA associated with higher rate of prostate cancer

CENTRE FOR SIGHT

Omega 3s and Prostate Cancer

- Study measured plasma levels
  - Plasma levels fluctuate wildly depending on immediate intake
  - Red blood cell levels – medium term intake
  - EPA + DEA Plasma levels between the two groups:
    - 4.48% no-cancer group
    - 4.66% in total cancer group
    - 4.66% in low grade CA
    - 4.71% in high grade CA

CENTRE FOR SIGHT

Omega 3s & Prostate Cancer

More studies that demonstrate a REDUCTION in Prostate CA with Omega 3

1. Brasky TM, Bistal AR, Navarro SL, Lampe JW, Peters U, Patterson RE, White E. Specialty supplements and prostate cancer risk in the VITamins and Lifestyle (VITAL) cohort. Nutr Cancer 2011;63:573-82.
2. Szymanski KM, Wheeler DC, Mucci LA. Fish consumption and prostate cancer risk: a review and meta-analysis. Am J Clin Nutr 2010;92:1223-33.
3. Terry P, Lichtenstein P, Feychting M, Ahlbom A, Wolk A. Fatty fish consumption and risk of prostate cancer. Lancet 2001;357:1764-6.
4. Leitzmann MF, Stampfer MJ, Michaud DS, Augustsson K, Colditz GC, Willett WC, Giovannucci EL. Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer. Am J Clin Nutr 2004;80:204-16.
5. Mina K, Fritschi L, Johnson KC. An inverse association between preserved fish and prostate cancer: results from a population-based case-control study in Canada. Nutr Cancer 2008;60:222-6.
6. Epstein MM, Kasperzyk JL, Mucci LA, Giovannucci E, Price A, Wolk A, Hakansson N, Fall K, Andersson SO, Andren O. Dietary fatty acid intake and prostate cancer survival in Orebro County, Sweden. Amer J Epidemiol 2012;176:240-52.
7. Fradet V, Cheng I, Casey G, Witte JS. Dietary omega-3 fatty acids, cyclooxygenase-2 genetic variation, and aggressive prostate cancer risk. Clin Cancer Res 2009;15:2559-66. - See more at: http://fpim.org/articles/heart-health/omega-3-fatty-acids-and-risk-for-prostate-cancer/#sthash.Ph2YRibq.dpuf

CENTRE FOR SIGHT

Meibomian Gland Disease

- Lipiflow
- MiboFlo
- Intense Pulsed Light

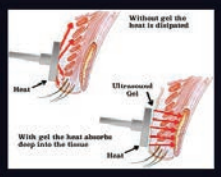
CENTRE FOR SIGHT

CENTRE FOR SIGHT

LipiFlow® Thermal Pulsation System

- Heat applied to the palpebral surfaces of the upper and lower eyelids directly over the meibomian glands
- Graded pulsatile pressure delivered to the outer eyelid

MiBoFlo



IPL - Lumenis M22

Evolved from treating Rosacea

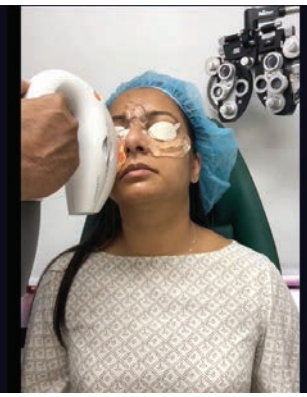
- Rolando Toyos MD
- Discovered Rosacea patients - Dry eye improved

Treatment Protocol

- Treat from Ear to Ear
- Two pass protocol
- Closer to the Lid Margin the better the response
- More pigment in the skin the less energy needed
- Express after each treatment

Courtesy Rolando Toyos MD

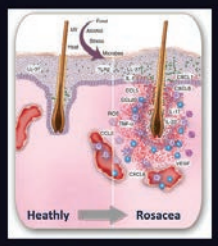
IPL



Skin Rosacea

In skin rosacea, abnormal blood vessels release pro inflammatory agents

Those inflammatory agents propagates to the eyelids via the orbital vasculature*



Courtesy Rolando Toyos MD

'Dry Eye - Our approach...'

(slides 33-48)

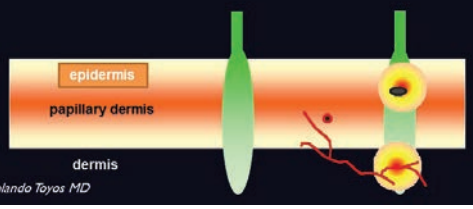
Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

IPL

From 500 nm to 800 nm

penetrates to the deeper dermis

subsurface heating is variable

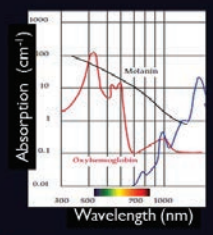


Courtesy Rolando Toyos MD

CENTRE FOR SIGHT

How IPL Works

- A Xenon flashlamp
- Broad Band of Light: 500-1200 nm 500-1200nm
- Cut Off Filter – transmits wavelengths only above some threshold
- Light is pulsed in milliseconds
- Fluence from 10 J/cm² to 30 J/cm² 10 J/cm² - 30 J/cm²



Courtesy Rolando Toyos MD 100 nm 400 nm 700 nm 100,000 nm

CENTRE FOR SIGHT

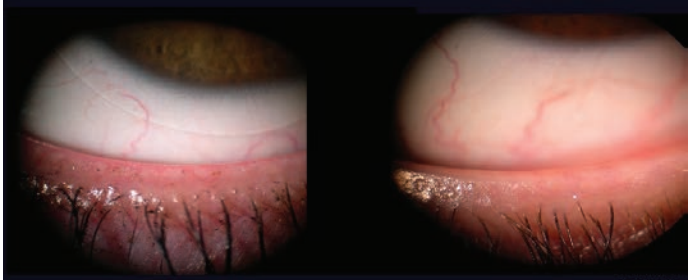
MGD expression

Courtesy Rolando Toyos MD

CENTRE FOR SIGHT

Lid Margin Before IPL

Lid Margin After IPL



Courtesy Rolando Toyos MD

CENTRE FOR SIGHT

IPL for Dry Eye – Mechanism of Action

- Kills Bacteria and Demodex
- Heat and Expression
- Closes abnormal Telangiectasias
- Decreases Inflammatory Mediators on the Skin
- Photomodulation – increase in cellular function (mitochondrial upregulation) – improvement in cellular morphology equals improvement in gland function

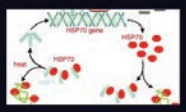
Courtesy Rolando Toyos MD

CENTRE FOR SIGHT

Heat Shock Protein 70

- Expressed in tissues to stress to protect cells against Apoptosis
- Decrease Pathological changes in cells
- Increase expression of HSP70 in Intense Pulse Light treated Skin

Prieto et al – Effects of IPL on Sun Damaged Skin – Histological and Immunohistochemical Analysis – Dermatologic Surgery 2005



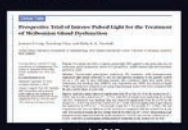
Courtesy Rolando Toyos MD

CENTRE FOR SIGHT

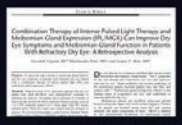
Peer Reviewed Studies

Toyos et al, 2015

Vora and Gupta (Duke), 2015

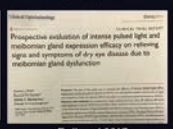


Craig et al, 2015



Shen et al (Mayo Clinic), 2016

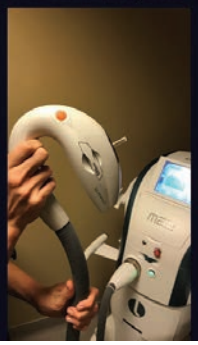
Toyos et al, 2016



Dell et al, 2017

CENTRE FOR SIGHT

Future Improvement - New Tip for Easy Upper Lid Treatment



Optima IPL

Think Outside the Eye

LUMENIS

CENTRE FOR SIGHT

CENTRE FOR SIGHT

Meibomian Gland Disease

- Most common cause of dry eye
- Causes ?
- Principles of management:
  - Replace old oils
  - Reduce inflammation
- How ? – variety of methods…
  - Omega 3s
  - IPL

Thank you…

www.centreforsight.com

'Dry Eye - Our approach…'

(slides 49-58)

Sheraz Daya
MD FACP FRCS(Ed) FRCOphth

CENTRE FOR SIGHT