Clinica Oculistica
Dipartimento di Chirurgia e Medicina Traslazionale
Dir. Prof. S. Rizzo

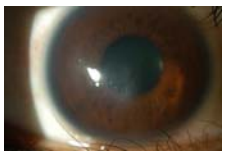
Azienda Ospedaliero Universitaria Careggi

Qualità della visione nella patologia corneale ed impatto della terapia chirurgica

Eleonora Favuzza
Rita Mencucci

- Cornea (or more precisely the anterior ocular surface, including the tear film):
  - is the main determinant of the optical power of the eye (approximately 70%).
  - Is also the main responsible for aberrations (especially astigmatism and asymmetric high-order aberrations like coma)

- Corneal diseases, such as **keratoconus** or **corneal dystrophies** may significantly affect visual performance because of:
  - the reduction in corneal transparency typical of the advanced stages
  - the increased amount of corneal higher-order aberrations(also in the initial stages of the diseases)



Visual acuity vs visual quality

- Visual acuity is an important component of visual quality, but quality of vision in corneal diseases can also be influenced by several other factors:

  - contrast sensitivity
  - anterior and posterior corneal aberrations
  - corneal haze (backscatter, decrease the transmission of light to retina)
  - forward light scatter (straylight)-> glare, halos
  - Neural compensation

Lombardo M J Cataract Refract Surg 2010; 36:313–31
Turnbull, Surv of Ophthalmol, 61 (2016) 257e271

- In presence of a corneal pathology, the neural adaptation can only partially supply and overcome the optical defects of the eye, still increasing the performance of the affected visual system to a certain degree.

Wacker K et al 2015, van der Meulen IJE et al 2011)

Fuchs'endothelial dystrophy

- Fuchs' endothelial corneal dystrophy (FECD) is a bilateral corneal disease characterized by :
  - **focal posterior collagenous excrescences (guttae)**
  - **progressive corneal edema,**

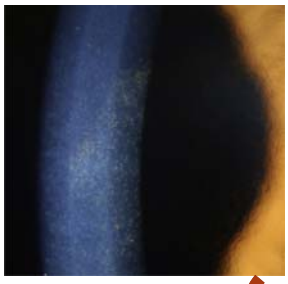
➢ resulting in reduced corneal transparency and impaired vision.

Wacker K, Ophthalmology 2015;122:1645-1652

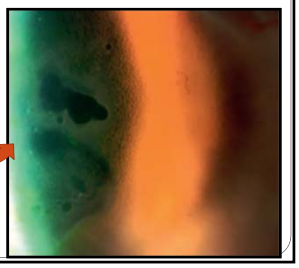
Fuchs endothelial dystrophy

- The most common endothelial dystrophy
- Prevalence: 4% in the USA population >40 ys old. F>M
- Onset: typically sixth decade.
- Most cases sporadic; familial cases with AD inheritance
- Early onset cases (++ familial cases)
- Together with pseudophakic bullous keratopathy (PBK) accounts for over one-third of corneal transplants

Zhang J, Exp Eye Res 130 (2015) 97e105

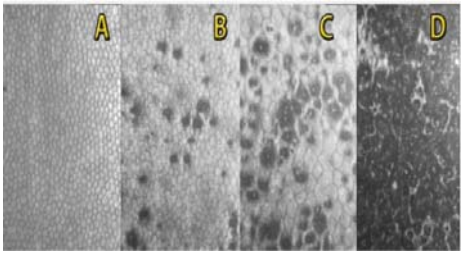


"beaten metal" endothelial appearance associated with guttae



Corneal edema, bullous keratopathy, disorganization of corneal stromal collagen fibrils and keratocytes, fibrosis

Fuchs endothelial dystrophy



Fuchs endothelial dystrophy: symptoms

- Asymptomatic at earliest stages
- Blurred vision in the morning after awakening (corneal sub-edema)
- Visual impairment in latest stages
- Often concomitant cataract (age)

JAMA Ophthalmol. 2015;133(4):e145353.

Relationship between Corneal Guttae and Quality of Vision in Patients with Mild Fuchs' Endothelial Corneal Dystrophy

Shinya Watanabe, MD, Yoshinori Oie, MD, PhD, Hisataka Fujimoto, MD, PhD, Takeshi Soma, MD, PhD, Shizuka Koh, MD, PhD, Motokazu Tsujikawa, MD, PhD, Naoyuki Maeda, MD, PhD, Kohji Nishida, MD, PhD

Conclusions: Corneal guttae without edema caused the QOV to deteriorate in eyes with FECD. Patients with higher straylight had worse CDVA or LCS. Intraocular forward light scatter caused by corneal guttae may result in visual disturbances. Quantification of corneal guttae can be useful to evaluate the effect of guttae on the QOV and determine the surgical indications of endothelial keratoplasty for eyes with mild FECD. *Ophthalmology 2015;122:2103-2109 © 2015 by the American Academy of Ophthalmology.*

- LCS: letter contrast sensitivity (CSV-1000RN Letter chart)
- Straylight was examined using the C-Quant Straylight Meter (Oculus, Wetzlar, Germany)
- High order aberrations (HOAs): no correlations with guttae

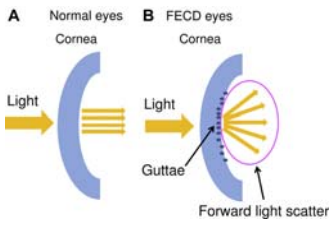


Figure 6. Illustrations showing forward light scatter resulting from corneal guttae.
A, No significant forward light scatter is generated in normal eyes without corneal guttae.
B, Forward light scatter increases because of corneal guttae in eyes with Fuchs' endothelial corneal dystrophy (FECD).

Ophthalmology 2015;122:2103-2109

Corneal Densitometry, Central Corneal Thickness, and Corneal Central-to-Peripheral Thickness Ratio in Patients With Fuchs Endothelial Dystrophy

Maged Alnawaiseh, MD, Lars Zumhagen, MD,* Gabriele Wirths, MD,* Maria Eveslage,† Nicole Eter, MD,* and André Rosentreter, MD**

Conclusions: Corneal light backscatter in the central cornea was greater in patients with FED than in normal subjects. Corneal densitometry enables us to evaluate the optical quality of the cornea in different corneal layers and in different annuli. It is a useful, objective method that, in combination with central corneal thickness and corneal central-to-peripheral thickness ratio, can help to quantify FED severity.

Corneal densitometry: Scheimpflug camera

Corneal Abnormalities Early in the Course of Fuchs' Endothelial Dystrophy

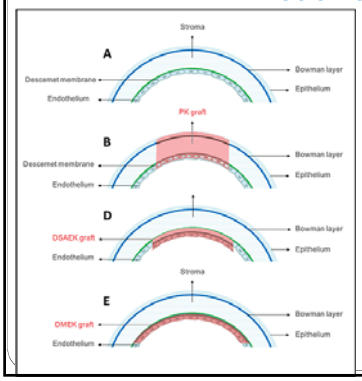
Sejal R. Amin, MD, Keith H. Baratz, MD, Jay W. McLaren, PhD, Sanjay V. Patel, MD

Results: Anterior corneal backscatter was 18% to 67% higher in eyes with moderate and advanced Fuchs' dystrophy compared with normal eyes ($P \leq 0.003$); a similar trend was noted in mild Fuchs' dystrophy eyes compared with normal eyes ($P = 0.08$). Stromal cell density and the absolute number of stromal cells in the anterior 10% of the stroma were approximately 20% and 27% lower, respectively, in Fuchs' dystrophy (regardless of severity) compared with normal ($P < 0.001$). Abnormal subepithelial cells were visible in 9%, 19%, and 30% of corneas with mild, moderate, and advanced Fuchs' dystrophy, respectively. Only corneas with advanced Fuchs' dystrophy were thicker than normal ($P < 0.001$).

Conclusions: Anterior corneal cellular and structural abnormalities begin early in the course of Fuchs' dystrophy, before the onset of clinically evident edema. The chronicity of these changes can explain their incomplete resolution after endothelial keratoplasty, and understanding the onset of these may help to determine the optimal time to intervene to achieve best outcomes. *Ophthalmology 2014;121:2325-2333 © 2014 by the*

Corneal backscatter: in vivo confocal microscopy

Fuchs'endothelial dystrophy Treatment

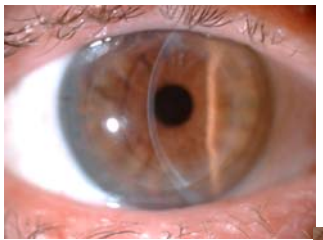


- Cheratoplastica perforante (PK) (--)
- Cheratoplastica lamellare endoteliale (++):
  - **DSAEK** (Descemet stripping automated endothelial keratoplasty)
  - **DMEK** (Descemet membrane endothelial keratoplasty)

What happens after endothelial keratoplasty?

A 53-year-old woman with visually significant Fuchs endothelial dystrophy in both eyes underwent phacoemulsification, an intraocular lens implant, and Descemet stripping endothelial keratoplasty of the left eye.
Before undergoing Descemet stripping endothelial keratoplasty of the right eye, she composed images in Adobe Photoshop 5 comparing the vision in her operated eye (A) with the vision in her unoperated eye (B).

JAMA Ophthalmol. 2015;133(4):e145353



DSAEK

DMEK

Visual acuity

- DSAEK: only approx 25% of DSAEK patients achieves VA >20/25 at 12 months follow-up, despite having otherwise healthy eyes and clear corneas with no evidence of graft failure
- DMEK superior visual outcome:40% -50% of patients 20/20 or better 6 months after surgery

Still fewer patients than expected achieve best corrected visual acuity of 20/20 despite healthy grafts and no ocular comorbidities!!!

Major review

Determinants of visual quality after endothelial keratoplasty

Andrew M.J. Turnbull, BM[a,c], Michael Tsatsos, FRCOphth[b,c], Parwez N. Hossain, PhD, FRCOphth[b,c], David F. Anderson, PhD, FRCOphth[b,c]

- The reasons for this suboptimal visual outcome are still unclear:
  - the age of patients
  - the stage and the duration of the disease at the time of surgery
  - anterior stromal changes
  - graft thickness (the thinner the better?)
  - the characteristics of graft-host interface
  - induced higher-order aberrations

Optical Quality of the Cornea After Descemet Membrane Endothelial Keratoplasty

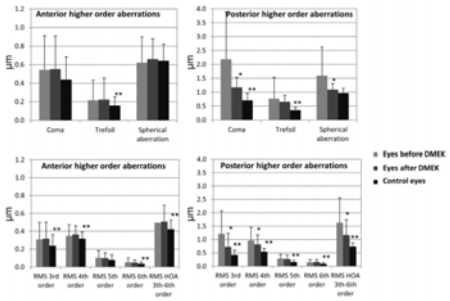
KORINE VAN DIJK, KONSTANTINOS DROUTSAS, JINGZHEN HOU, SASSAN SANGSARI, VASILIOS S. LIARAKOS, AND GERRIT R.J. MELLES

Am J Ophthalmol 2014;158:71–79

CONCLUSIONS:

Anterior and posterior corneal HOAs, as well as backscattered light from the cornea, were elevated in eyes suffering from Fuchs endothelial dystrophy and remained higher throughout 6 months after DMEK.

If present, anterior surface irregularities and anterior corneal haze may be the most important limiting factors in visual rehabilitation after DMEK.



(Top left, Bottom left) The anterior corneal HOAs remained unchanged from before to after Descemet membrane endothelial keratoplasty (DMEK) and sustained higher than the control group.
Instead, (Top right, Bottom right) the posterior HOAs decreased from preoperative to postoperative, although they were still elevated compared to controls.

Quality of Vision in Patients With Fuchs Endothelial Dystrophy and After Descemet Stripping Endothelial Keratoplasty

Arch Ophthalmol. 2011;129(12):1537-1542

Ivanka J. E. van der Meulen, MD; Sanjay V. Patel, MD; Ruth Lapid-Gortzak, MD, PhD; Carla P. Nieuwendaal, MD; Jay W. McLaren, PhD; Thomas J. T. P. van den Berg, PhD

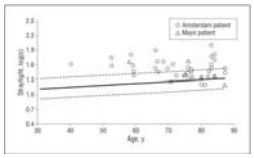


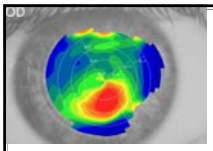
Figure 3. Straylight as a function of age for the Amsterdam and Mayo patients with pseudophakic eyes and Fuchs endothelial dystrophy.

Conclusions: Quality of vision is severely impaired in patients with Fuchs dystrophy and improves significantly after DSEK. Straylight improves more in younger than in older eyes after DSEK. Preoperative straylight can be a useful clinical metric to predict postoperative improvement, especially in cases where preoperative visual acuity is close to 20/20.

KERATOCONUS

- Keratoconus is the most common primary ectasia.
- It is a **bilateral** and **asymmetric** corneal degeneration characterized by localized corneal thinning which leads to protrusion of the thinned cornea.
- Corneal thinning normally occurs in the infero-temporal as well as the central cornea, although superior localizations have also been described
- Corneal protrusion causes high myopia and irregular astigmatism, affecting visual quality

Romero-Jimenez M, Contact Lens & Anterior Eye 33 (2010) 157–166



KERATOCONUS

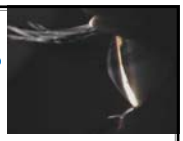
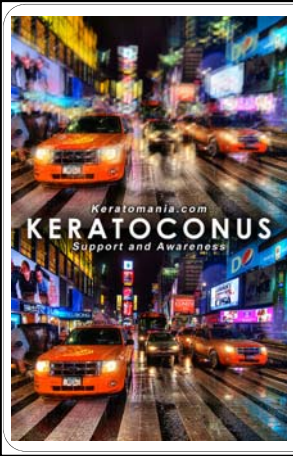
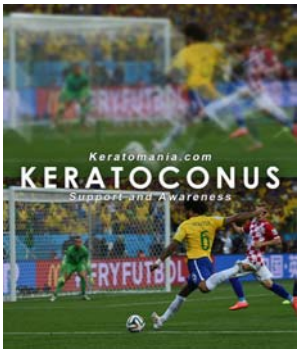


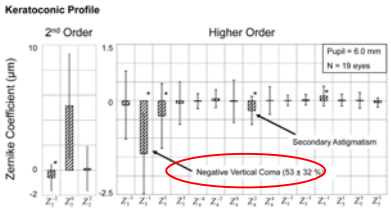
Table 1
Keratoconus classification based on disease evolution. VA, visual acuity; D, dioptres.

Stage	Description
1	Frustre or subclinical form; diagnosed by corneal topography; ~6/6 VA achievable with spectacle correction.
2	Early form; mild corneal thinning; corneal scarring absent.
3	Moderate form; corneal scarring and opacities absent; Vogt's striae; Fleischer's ring; <6/6 VA with spectacle correction, but ~6/6 VA with contact lens correction; irregular astigmatism between 2.00–8.00 D; significant corneal thinning.
4	Severe form; corneal steepening >55.00 D; corneal scarring, <6/7.5 VA with contact lens correction; severe corneal thinning and Munson's sign.





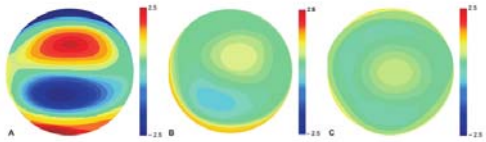
Keratoconus
higher order aberrations



Eyes with KC have higher-order aberrations that are approximately 5.5 times more than what is typical in normal eyes. Vertical coma is the dominant higher-order aberration in people with KC

Pantanelli S, Ophthalmology 2007;114:2013–2021

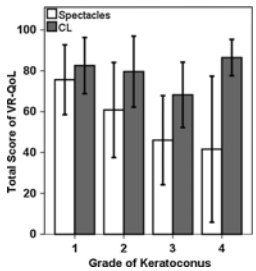
Keratoconus
higher order aberrations



Figs 3A to C: Corneal HOAs measured by the Orbscan appliance. The left circle belongs to the early-stage KC. It is apparent that the coma aberration is very dominant. The center circle represents the fellow eye of patients from the first group of KC patients. This eye has suspected KC with no clinical signs. Using this examination, it is possible to see a small amount of coma aberration, even at a very early stage when there is only suspected KC. The right circle represents the control group with healthy eyes, showing no sign of the aberration[5]

Hefner-Shahar H, Int J Ect Cor Dis 2016;5(3):128-31

Keratoconus: quality of life



Total score of NEI-VFQ-25 and all subscales scores were lower in the keratoconus group than in the healthy group with both refractive corrections (spectacles and CLs)

Fig. 1 NEI-VFQ-25 total score in the different grades of keratoconus with spectacles and CL correction. The CL score was not significantly different (P = 0.06 Kruskal–Wallis ANOVA) for different kerato- conus degrees; however, the spectacles score decreased significantly with the stage of keratoconus

Ortiz-Toquero S, Qual Life Res (2016) 25:1043–1051

Cornea

Impact of Keratoconus in the Better Eye and the Worse Eye on Vision-Related Quality of Life

Srujana Sahebjada,[1,2] Eva K. Fenwick,[1,2] Jing Xie,[1,3] Grant R. Snibson,[1,3] Mark D. Daniell,[1,3] and Paul N. Baird[1,3]

IOVS 2014, 55:412-416

Vision and Quality of Life Index

TABLE 1. The Six Items in the VisQoL

Item	Response Options
Likely to injure self	1-Unlikely to 5-Almost certainly
Coping with life demands	1-No effect to 6-Unable
Ability to have friendships	1-Easier to 6-Unable, plus a n/a option
Organizing assistance	1-No difficulty to 6-Unable, plus a n/a option
Difficult to fulfill roles	1-No effect to 6-Unable
Confidence to join activities	1-More confident to 6-Not confident at all

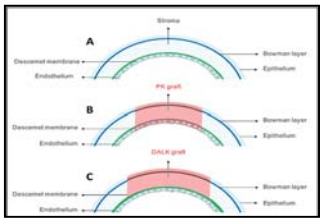
n/a, not applicable.

•Worse vision in the better eye (but not the worse eye) was associated independently with a reduction in VisQoL utilities, suggesting that considering VisQoL utilities based on vision in the better eye is an important estimate of the impact of keratoconus from the patients' perspective.

•Treatment and rehabilitation interventions to retard the progression of vision impairment in the better eye resulting from keratoconus would be most efficacious at an early stage to improve QoL outcomes for patients with this disease.

Keratoconus: surgical treatment

- INTACS
- PK (Penetrant Keratoplasty)
- DALK (Deep Anterior Lamellar Keratoplasty)



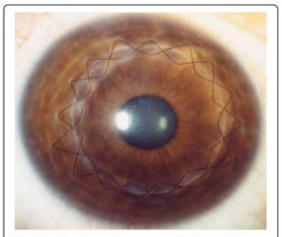
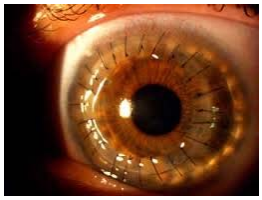


Fig. 2 Slit-lamp image of a keratoconic eye after penetrating keratoplasty with a double continuous suture



Amalich-Montiel *et al. Eye and Vision* (2016) 3:2

Keratoconus: surgical treatment

- Excellent postop visual acuity (20/25-20/20)

Despite anatomical clarity, the transplanted eye may be optically degraded due:

- Astigmatism (suture adjustment/removal, ~1 year follow-up)
- higher-order wavefront aberrations (++trefoil)
- Interface haze (DALK)

Tamaguchi T, Cornea 2015;34(Suppl):S128–S135

DALK vs PK

- DALK: retention of healthy recipient corneal endothelial cells
  - ➢absence of corneal endothelial cell immune rejection
- Similar postoperative visual outcome (especially with bared Descemet), but sometimes DALK<PK, even in presence of transparent graft
- DALK: more challenging for the surgeon

Tamaguchi T, Cornea 2015;34(Suppl):S128–S135

An Analysis of Factors Influencing Quality of Vision After Big-Bubble Deep Anterior Lamellar Keratoplasty in Keratoconus

SEPEHR FEIZI, MOHAMMAD ALI JAVADI, AND HOSSEIN MOHAMMAD-RABEI

Am J Ophthalmol 2016;162:66–73

- Postoperative BSCVA demonstrated no significant association with postoperative keratometric astigmatism, irregularity index, HOAs, or interface haze
- **Optical aberrations and surgical interface haze were the main reasons for decreased contrast sensitivity** . The surgical interface was characterized by the presence of reflective particles and amorphous materials, despite achieving a bare Descemet membrane during the surgery.

RESEARCH ARTICLE

Corneal Transplantation in Disease Affecting Only One Eye: Does It Make a Difference to Habitual Binocular Viewing?

Praveen K. Bandela[1,2], PremNandhini Satgunam[1,2], Prashant Garg[1,3], Shrikant R. Bharadwaj[1,2]*

Background

Clarity of the transplanted tissue and restoration of visual acuity are the two primary metrics for evaluating the success of corneal transplantation. Participation of the transplanted eye in habitual binocular viewing is seldom evaluated post-operatively. In unilateral corneal disease, the transplanted eye may remain functionally inactive during binocular viewing due to its suboptimal visual acuity and poor image quality, vis-à-vis the healthy fellow eye.

Conclusions

In unilateral corneal disease, the transplanted eye does participate in gross binocular viewing but offers limited support to fine levels of binocularity. Improvement in the transplanted eye's optics enhances its participation in binocular viewing. Current metrics of this treatment success can expand to include measures of binocularity to assess the functional benefit of the transplantation process in unilateral corneal disease.

PLoS ONE 11(3): e0150118.

Conclusion

- Visual quality (not only visual acuity) should be considered especially in the initial stages of corneal diseases
- Surgery improves visual function, still worse than normal eyes

- Fuchs'endothelial dystrophy: the longer the disease duration at the time of surgery, the poorer the visual outcome
- Keratoconus: DALK good outcome also for young patients