# NIIOSNEWSLETTER

Netherlands Institute for Innovative Ocular Surgery Volume 17 | English edition no 33 | March 2020

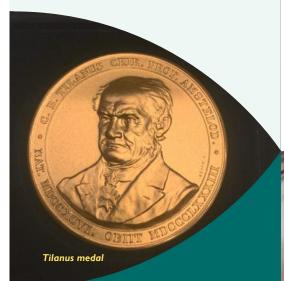


• Bowman layer onlay graft as a potential new alternative to keratoplasty

#### PAGE 3

- NIIOS-USA Cornea Evening in Boston and NIIOS Cornea Evening in Amsterdam (preceding 2020 ASCRS and 2020 ESCRS)
- Dr. Melles gives Tilanus lecture
- E-device for slit-lamp self-imaging by patient developed in collaboration with UCSD/CMRR

- Global interest in endothelial cell culture and cell modification techniques
- Advanced keratoplasty wetlab courses in Rotterdam, The Netherlands
- Melles Research Fund thanks 2019 sponsors



## **REFERRALS TO MELLES CORNEA CLINIC ROTTERDAM**

For referrals to Melles Cornea Clinic Rotterdam, please

- Email to info@corneaclinic.nl
- or use the referral form enclosed, which can be faxed to +31 10 297 4440 and one of our international secretaries will make further arrangements.

## NIIOS 20 years

Being established in the year 2000, NIIOS' 20 year anniversary will be held in 2020. In 2000, the aim was that in 2020, every ophthalmologist would use at least one NIIOS technique in 2020

The papers to establish NIIOS were all signed, sealed and delivered in 1999, but a contemplating attorney in charge of submitting the articles required another year to actually file them. In retrospect, one wonders if this was just juridically transcending talent or divine intervention, because - especially within the field of Ophthalmology - 2020 is a far better year to celebrate our 20 year anniversary than 2019.

#### Our aim: Every eye doctor using a NIIOS technique in 2020

At the start of NIIOS in 2000, the ambition was guite simple: every ophthalmologist worldwide should be using at least one of NIIOS' techniques in 2020, none excepted. Looking back, the goal was well defined and realistic, without aiming too high. So as soon as we emptied our glass of champagne at the very beginning of this year, all of NIIOS was geared up and ready to check and find out if the ophthalmic community met up with our expectations. However, we needed another sip of champagne when we came to realize that it might be somewhat difficult to exclude any outliers.

Of course, educated readers may rebuke our concern with the consideration that it would be hard to imagine, highly unlikely and virtually impossible that any eye doctor would dare to be so deviant. But how about more remote and secluded areas, completely unaware of NIIOS' endeavors, like the North Sentinel Islands or downtown Birmingham, Alabama? That being said, our hopes are still high as well as the confidence in our peers.



NIIOS 2000-2020 Netherlands Institute for Innovative Ocular Surgery













#### Cornea & Research fellows 2018-2019











Left to right: Daniele Spinozzi, Italy; Diana Santander Garcia, Spain; Rénuka Birbal, Netherlands; Diana Dragnea, Romania, Aytan Musayeva, Azerbaijan; Marina Krijgsman, Netherlands

#### 2020

- Parker JS, Ham L, Parker CP, Parker JS,
   Dockery PW, Melles GRJ. DMEK in superseniors: clinical outcomes of Descemet
   membrane endothelial keratoplasty performed
   in patients ≥ 90 years old. Curr Eye Res. 2020.
   Accepted.
- Dapena I, Musayeva A, Dragnea DC, Groeneveld-van Beek EA, Ni Dhubhghaill S, Parker JS, van Dijk K, Melles GRJ. Bowman layer onlay transplantation to manage Herpes corneal scar. Cornea. 2020. Accepted.
- Parker JS, Parker JS, Melles GRJ. Doublebubble Descemet membrane endothelial keratoplasty unfolding in eyes with deep anterior chambers and anterior chamber intraocular lenses. Cornea. 2020. Accepted.
- Dragnea DC, Ni Dhubhghaill S, Bourgonje VJA, Dapena I, Oellerich S, Melles GRJ, Lavy I. Invitro evaluation of the feasibility of slit-lamp Nd:YAG-laser descemetorhexis. Cornea 2020;39:229-33.
- Birbal RS, Baydoun L, Ham L, Miron A, van Dijk K, Dapena I, Jager MJ, Boehringer S, Oellerich S, Melles GRJ. Effect of surgical indication and preoperative lens status on Descemet membrane endothelial keratoplasty outcomes. Am J Ophthalmol. 2020. Accepted.
- Birbal RS, Parker JS, van Dijk K, Oellerich S, Dapena I, Melles GRJ. Hydrops after corneal perforation during manual deep anterior lamellar keratoplasty (DALK) for keratoconus. Acta Ophthalmol. 2020. Accepted.
- Oellerich S, Ham L, Frank LE, Gorges S, Bourgonje VJA, Baydoun L, van Dijk K, Melles GRJ. Parameters associated with endothelial cell density variability after Descemet membrane endothelial keratoplasty. Am J Obhthalmol. 2020. Accepted.
- Baydoun L, Bruinsma M, Santander-Garcia D, Ham L, Oellerich S, Melles GRJ. Combined specular microscopy and Scheimpflug imaging to improve detection of an upcoming allograft rejection after DMEK. Acta Ophthalmol. 2020. Accepted.
- Birbal RS, Ni Dhubhghaill S, Baydoun L, Ham L, Bourgonje VJA, Dapena I, Oellerich S, Melles GRJ. Quarter-Descemet membrane endothelial keratoplasty: 1-2 year clinical outcomes. Cornea. 2020. Accepted.
- Birbal RS, Ni Dhubhghaill S, Bourgonje VJA, Hanko J, Ham L, Jager MJ, Boehringer S, Oellerich S, Melles GRJ. Five-year graft survival and clinical outcomes of 500 consecutive cases after Descemet membrane endothelial keratoplasty. Cornea. 2020. Accepted.

#### 2019

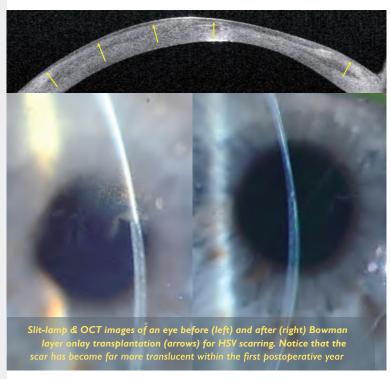
- Miron A, Spinozzi D, Ni Dhubhghaill S, Lie JT, Oellerich S, Melles GRJ. In vitro endothelial cell migration from limbal edge-modified Quarter-DMEK grafts. PLoS One 2019;14:e0225462.
- Tong CM, Parker J, van Dijk K, Birbal RS, Melles GRJ.The Melles technique. In Jacob S (ed.): Mastering DALK: A video textbook on Deep Anterior Lamellar Keratoplasty. 2019; Chapter
- Parker JS, Birbal RS, van Dijk K, Oellerich S, Dapena I, Melles GRJ. Reply to Comment: Are

- Descemet membrane ruptures the root cause of corneal hydrops in keratoconic eyes? Am J Ophthalmol. 2019;205:204-5.
- Birbal RS, Tong CM, Dapena I, Parker JS, Parker JS, Oellerich S, Melles GRJ. Reply to Comment on Clinical outcomes of Descemet membrane endothelial keratoplasty in eyes with a glaucome drainage device. Am J Ophthalmol 2019:208:440-1.
- Parker JS, Birbal RS, van Dijk K, Tong CM, Ambati B, Baydoun L, Dapena I, Melles GRJ. Bowman layer transplantation for advanced keratoconus. In Barbara A (ed.): Controversies in the management of keratoconus. 2019; Chapter 27.
- Tong CM, van Dijk K, Melles GRJ. Update on Bowman layer transplantation. Curr Opin Ophthalmol 2019;30:249-55.
- Luznik Z, Oellerich S, Roesch K, Yin J, Zumbansen M, Franken L, Melles GRJ, Dana R. DMEK failure associated with innate immune activation. Ophthalmology 2019;126:1462-4.
- Parker JS, Birbal RS, van Djik K, Oellerich S, Dapena I, Melles GRJ. Are Descemet membrane ruptures the root cause of corneal hydrops in keratoconic eyes? Am J Ophthalmol. 2019;205:147-52.
- Tong CM, Parker JS, Dockery PW, Birbal RS, Melles GRJ. Use of intraoperative anterior segment optical coherence tomography for Bowman layer transplantation. Acta Ophthalmologica 2019;97:e1031-2.
- Muijzer MB, van Luijk CM, van den Bogaerdt AJ, Kruit PJ, Groeneveld-van Beek E, Melles GRJ, Wisse RPL. Prospective evaluation of clinical outcomes between pre-cut corneal grafts prepared using a manual or automated technique: with one-year follow-up. Acta Ophthalmol 2019;97:714-20.
- Salouti R, Zamani M, Ghoreyshi M, Dapena I, Melles GRJ, Nowroozzadeh MH. Comparison between manual trephination versus femtosecond laser-assisted deep anterior lamellar keratoplasty for keratoconus. Br J Ophthalmol 2019;103:1716-23.
- Sikder S, Melles GRJ. Reflections on the Barcelona Principles-Planning for the Future. Cornea 2019:38:e8.
- Birbal RS, Tong CM, Dapena I, Parker JS, Parker JS, Oellerich S, Melles GRJ. Clinical outcomes of Descemet membrane endothelial keratoplasty in eyes with a glaucome drainage device. Am J Ophthalmol. 2019;199:150-88.
- Spinozzi D, Miron A, Bruinsma M, Dapena I, Lavy I, Binder P, Rafat M, Oellerich S, Melles GRJ. Evaluation of the suitability of biocompatible carriers as artificial transplants using cultured porcine corneal endothelial cells. Curr Eye Res 2019;44:243-9.
- Dragnea DC, Nobacht S, Gericke A, Parker JS, Oellerich S, Ham L, Melles GRJ. Postoperative re-positioning of inverted DMEK grafts.
  Cornea 2019;201938:162-5.
- Santander-García D, Peraza-Nieves J, Müller TM, Gerber-Hollbach N, Baydoun L, Liarakos VS, Dapena I, Oellerich S, van Dijk K, Melles GRJ. Influence of intraoperative air tamponade time on graft adherence in Descemet Descemet membrane endothelial keratoplasty (DMEK). Cornea 2019;38:166-72.

# Bowman layer onlay graft as a potential new alternative to keratoplasty

## Bowman layer onlay transplantation as a potential alternative to keratoplasty

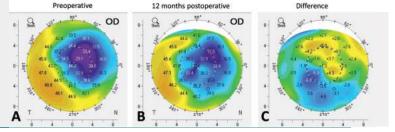
In the past decade, NIIOS has introduced Bowman layer (BL) inlay transplantation, to stabilize eyes with advanced keratoconus (KC), as well as BL onlay grafting for treatment of persistent subepithelial haze after excimer laser surface ablation. Although the latter scars may differ from those after HSV, both conditions may in part result from recipient BL damage and an abnormal epithelial-stromal interaction. Hence, it would be preferable to position a donor BL graft in its 'anatomical' position, that is,



directly under the epithelium and onto the recipient's stroma (or damaged BL). Our first experience showed that a BL onlay graft significantly reduces the density of a HSV scar, similar to those after excimer laser surface ablation.

Another group of patients that is difficult to manage with any surgical technique currently available to corneal surgeons, are those who suffer from diurnal fluctuation in visual acuity owing to continuous corneal contour changes and associated variability in refractive error. Within a first series of eyes decades after eight (or more) incision radial keratotomy, Bowman layer onlay transplantation was found to be effective to reduce the fluctuation in visual acuity to acceptable levels. When presbyopia kicks in, these patients may experience growing difficulties and seem satisfied when their refractive error is better stabilized.

Pre- (A) and postoperative (B) topography images of an eye that underwent Bowman layer onlay transplantation for diurnal fluctuation in visual acuity 20 years after eight-incision radial keratotomy. Notice the corneal steepening effect induced by the graft on the difference map (C). The subjective complaints were reduced to acceptable levels within the first month after surgery.







# NIIOS-USA Cornea Evening in Boston and NIIOS Cornea Evening in Amsterdam (preceding 2020 ASCRS and 2020 ESCRS)

Friday May 15th 2020; 7-10 p.m. - The State Room, 60 State Str. 33rd Floor, Boston MA 02109 Friday October 2nd 2020; 7-10 p.m. - Rode Hoed, Keizersgracht 102, 1015CV Amsterdam

Twice a year NIIOS organizes a 'NIIOS Cornea Evening'. In 2020 the meetings will be held in Boston (preceding the ASCRS) and in Amsterdam (preceding the ESCRS). The latest topics in the field of corneal surgery are again on the agenda: DMEK for cases with complex pathology, the latest tips and tricks in eye banking including Quarter-DMEK, the outcomes of 'descemet-stripping only', the first experience with Bowman layer onlay transplantation performed for HSV corneal scars and in eyes after radial keratotomy, and an e-device for self-biomicroscopy.

Invited speakers include: Dr. Ula Jurkunas, Dr. Kathryn Colby, Prof. Shigeru Kinoshita, Dr. Mark Terry and Dr. Sadeer Hannush, and of course NIIOS staff and fellows. Free entry tickets are available through info@niios.com or www.niios.com/CorneaEvening. For Boston, please apply before April 6, 2020: for security reasons all visitors must be registered in advance.

Half of the NIIOS' staff and former clinical and research fellows just before the NIIOS Cornea Evening in Paris, while the other half was stuck somewhere due to the perpetuous strike of the French public transportation



## Dr. Melles gives Tilanus lecture on 'Democrasillity'

## Every 10 years, an award is assigned by 'The Society for Physics & Medicine & Surgery'

For an audience other than ophthalmologists, Dr. Melles focused on 'democrasillity' in medical R&D: more often than not, mainstream opinions may lead away from effective treatments, since nature simply has her own, unintelligible agenda. If extrapolated to daily life, could our democratic mindset undermine our societies, because mainstream opinion diverts from addressing the root cause of the current social polarization? In fact, could the social division be a symptom of a 'new disease entity', resulting from being forced to continuously choose between globalistic and nationalistic conveniences, fueled by the internet? Full lecture text available at www.niios.com or dekort@niios.com

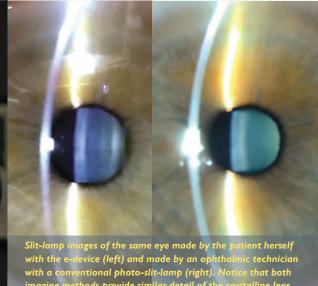


## E-device for slit-lamp selfimaging by patient, developed in collaboration with UCSD/CMRR

Patient self-imaging may potentially reduce examination time and allow for remote eye exams

To digitally image the eye through a conventional slitlamp, various smart phone devices have been developed that can be mounted on the slit-lamp oculars. So far, all these devices require an ophthalmic professional to perform the actual imaging, while the patient only has a passive role in the process.

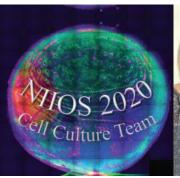
An e-device that would enable patients to perform biomicroscopic self-imaging may have several potential benefits, especially when combined with internet connectivity. First, remote slit-lamp examinations may allow for more efficient clinical follow-up, especially if combined with other functionalities, so that patients would no longer need to visit the clinic for follow-up visits. Second, remote biomicroscopy would allow for quick screenings in various settings, for example in remote areas or to enable a second opinion at a more specialized center. Third, the use of an e-device at home may allow for more frequent screenings and therefore more data points, which may potentially improve the level of care provided, especially when the data points could be processed with artificial intelligence applications.



### NIIOS NEWSLETTER March 2020









### Advanced keratoplasty wetlab courses in Rotterdam, The Netherlands

Bowman layer transplantation for advanced keratoconus & Descemet membrane endothelial keratoplasty (DMEK)

Beginner DMEK courses are scheduled on a Tuesday & Wednesday. On Tuesday, the course participants join live surgery sessions; on Wednesday, various techniques are practiced during educational wetlab sessions and patient demonstrations are given. Bowman layer wetlabs and Advanced DMEK courses are given on Thursdays.

Further information and applications: dekort@niios.com Level: Corneal fellows and surgeons

Beginner **DMEK** surgical course: March 10/11, 2020

Bowman layer surgical course: March 12, 2020

Beginner **DMEK** surgical course: June 9/10, 2020

Advanced **DMEK** surgical course: June 11, 2018

Beginner **DMEK** surgical course: September 29/30, 2020

Bowman layer surgical course: October 1, 2020

Beginner **DMEK** surgical course: November 24/25, 2020

Advanced **DMEK** surgical course: November 26, 2020





## Melles Research Fund thanks 2019 sponsors

R&D costs increase exponentially due to expanding research on NIIOS' techniques

In 2019, MRF received € 130,335.= in donations for the NIIOS R&D program. If you are interested yourself in financially supporting MRF and NIIOS R&D, to enable the continued development of NIIOS' surgical techniques, please contact Christa de Kort via info@niios.com

## Global interest in corneal endothelial cell culture and cell modification techniques

Research into potential treatment of Fuchs endothelial dystrophy with endothelial cell culture and modification techniques

In Fuchs endothelial dystrophy, corneal edema and 'guttae' result in lower visual acuity, reduced contrast sensitivity and degradation of visual quality even in early disease stages.

Patients with mild Fuchs dystrophy are usually managed conservatively with hypertonic saline eye drops, while in more advanced stages, keratoplasty is the main therapeutic option. Over the last two decades, there has been a shift in transplantation procedures for endothelial disease from penetrating keratoplasty (PKP) to small incision procedures such as Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK). Selective replacement of diseased corneal endothelium by a healthy graft allows for restoration of the endothelial pump activity and corneal transparency, while reducing the risk of graft rejection and allowing for a faster visual recovery.

A global survey of corneal transplants performed in 116 different countries in 2012 showed that Fuchs dystrophy was the leading indication (39%) for corneal grafting. Interestingly, this survey also highlighted the worldwide corneal graft shortage, since about 50% of patients may not have access to keratoplasty. Hence, researchers are trying to find new ways to more efficiently use the available donor tissue pool. As such, our R&D team at NIIOS is currently working on new surgical techniques using smaller grafts (Hemi-DMEK, Quarter-DMEK) allowing for transplantation of tissue to several patients from only one donor cornea.

In addition, alternative concepts are being investigated, such as Descemet Stripping Only, which entails removal of the diseased Descemet membrane with its guttae, but without transplanting tissue. In Descemet Membrane Transfer a decellularized Descemet membrane is grafted. The idea is that in the absence of diseased host tissue, the central corneal endothelium may regenerate via migration from healthy peripheral endothelial stem cells. More severe cases of Fuchs dystrophy may not be eligible for such approaches, so that surgical or non surgical concepts such as Descemet Membrane Endothelial Transfer (a free floating graft in the host anterior chamber which might enable repopulation of the denuded host stroma with donor cells) or cell-based therapies are of scientific interest. Cell therapy modalities would require engineered endothelium positioned onto the posterior corneal surface to replace the host endothelial cell layer either by injection directly into the host anterior chamber of the eye, or via a synthetic or biological carrier.

Diagrammatic representation of the past, current and potential future treatment methods for Fuchs endothelial  $\textit{dystrophy}. \ PK = \textit{Perforating keratoplasty}; \ DSEK/DSAEK = \textit{Descemet stripping (automated) endothelial}$  $keratoplasty; DMEK = Descemet\ membrane\ endothelial\ keratoplasty; Q-DMEK = Quarter\ DMEK; DSO = Constraints and Constraints and Constraints are constraints and Constraints and Constraints and Constraints are constraints and Constraints and Constraints and Constraints are constraints and Constraint$ Descemet stripping only; DWEK = Descemet stripping without endothelial keratoplasty

## Therapies for Fuchs Dystrophy **Experimental Therapie** Current Developing Therap DSAEK DSO DMET DMEK Cell Therapy DMT