

THE ACCOMMODATION CLUB

8TH MEETING

11th May, 2012

**Jose Berrocal Auditorium
Retter Educational Center
Bascom Palmer Eye Institute
University of Miami**

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Welcome to the Accommodation Club

The Accommodation Club provides a forum for scientists, engineers, clinical practitioners and developers to discuss and foster research into understanding accommodation and the development of systems to restore accommodative function. Our mission is to promote knowledge that leads to the provision of normal vision at all distances to the enormous number of presbyopic and cataract patients around the world.

We invite you to actively participate in this meeting and contribute your latest findings relevant to the study of accommodation, presbyopia and restoration of accommodation during this meeting to further our knowledge in this important area of vision correction.

Jean-Marie Parel, President

Acknowledgements

The Accommodation Club gratefully acknowledges the generous support provided by the Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA, the Brien Holden Vision Institute and the Vision Cooperative Research Centre, Sydney, NSW, Australia. Their provision of the venue, audio-visual support, meeting organisation and catering have greatly enhanced our ability to hold this meeting.

8th Meeting Program Outline

06:45	Registration	
07:45	Introduction & Welcome Welcome from the President Official Address from Chairman of BPEI Meeting "Ground Rules"	<i>Jean-Marie Parel</i> <i>Eduardo Alfonso, Chair BPEI</i> <i>Arthur Ho</i>
	<i>Meeting Chair: Sonia Yoo</i>	
08:00	Session 1: Anatomy & Physiology	<i>Session Moderators: Mary Anne Croft</i> <i>Philippe Sourdille</i>
08:40	Session 2A: Accommodation & Presbyopia	<i>Session Moderators: William Culbertson</i> <i>Paul Kaufman</i>
09:35	Morning Break	
10:00	Session 2B: Accommodation & Presbyopia	<i>Session Moderators: Ron Krueger</i> <i>Fabrice Manns</i>
11:00	Session 3: New Instruments & Techniques	<i>Session Moderators: Thomas Aller</i> <i>Norberto Lopez-Gil</i>
12:15	Lunch Break	
13:45	Session 4: Restoring Accommodation: The Biology	<i>Session Moderators: Sonia Yoo</i> <i>Robert Augusteyn</i>
14:15	Session 5: Restoring Accommodation: Solutions	<i>Session Moderators: Arlene Gwon</i> <i>Arthur Ho</i>
15:00	General Discussions & Closing Remarks	<i>Jean-Marie Parel</i>
15:15	Close	
15:30	Tour of Ophthalmic Biophysics Center, McKnight Building	<i>Hosts: Jean-Marie Parel, Fabrice Manns, Mariela Aguilar</i>

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1: The Lens: Anatomy & Physiology

Moderators: Mary Anne Croft, Philippe Sourdille

1. BIOMETRY OF THE INTERNAL STRUCTURE OF THE HUMAN CRYSTALLINE LENS WITH AGE USING OCT: A PILOT STUDY

Marco Ruggeri, Caro de Freitas, Arthur Ho, Fabrice Manns, Jean-Marie Parel

Purpose: To measure the human crystalline lens nucleus and cortex of subject of different ages with Optical Coherence Tomography (OCT).

Methods: An OCT system with 8µm axial resolution was developed to image the human eye. Images of the anterior segment were acquired on 5 subjects of age 35, 42, 50, 68 and 69 years. The internal structures of the crystalline lens were identified in the images based on the zones of optical discontinuity. The images were processed to extract the thickness of the crystalline lens nucleus and cortex.

Results: The system can detect changes in the thickness of the nucleus and the cortex as the crystalline lens grows with age. Thickness measurements of lens, nucleus and cortex are reported for each subject in function of age.

	Age (Years)				
	35	42	50	68	69
Cortex thickness (mm)	1.32	1.34	1.80	2.17	1.35
Nucleus thickness (mm)	2.78	2.87	2.86	2.90	3.02
Lens thickness (mm)	4.10	4.21	4.66	5.07	4.37

Conclusions: We demonstrated that OCT can perform biometry of the nucleus and the cortex of the human crystalline lens at different ages.

2. EX VIVO MEASUREMENT OF POSTMORTEM TISSUE CHANGES IN THE CRYSTALLINE LENS BY BRILLOUIN SPECTROSCOPY AND CONFOCAL REFLECTANCE MICROSCOPY

Oliver Stachs, Stephen Reiss, Marine Hovakimyan, Rudolf Guthoff, Heinrich Stolz

Purpose: Use of Brillouin spectroscopy enables non-invasive, spatially resolved determination of the rheological properties of crystalline lens tissue. Furthermore the Brillouin shift correlates with the protein concentration inside the lens.

Methods: Extracted porcine lenses were examined ex vivo for up to 25.5 hours to study time-dependent postmortem lens tissue changes using Brillouin spectroscopy and confocal reflectance microscopy.

Results: Measurements on extracted porcine lenses demonstrate that rheological properties depend strongly on time after death. The intensity of the Brillouin signal decreases significantly as early as five hours postmortem. Moreover, the fluctuation of the Brillouin frequency shift inside the lens increases with postmortem time. Images of lens tissue taken with a confocal reflectance microscopy between measurements reveal a degenerative aging process. These tissue changes correlate with results from Brillouin spectroscopy.

Conclusion: It is concluded that only in vivo measurements appropriately reflect the rheological properties of the eye lens and its protein concentration.

3. EFFECT OF ACCOMMODATION ON THE LENS ULTRASTRUCTURE

Rebecca Zoltoski, Elizabeth Wyles, Jennifer Harthan, Jer Kuszak

[Abstract not available]

4. FLUID MOVEMENT IN THE ISOLATED BOVINE LENS

Oscar Candia, Rosana Gerometta

Purpose: We have shown that the mechanical forces of accommodation move fluid in and out of the lens. We now show that the osmotic force, consequence of the lens active ionic transport, can also induce fluid movement but in a different time scale.

Methods: A lens stretching device and a 3-compartment chamber were respectively used for the mechanical and osmotic experiments.

Results: We have determined that 100 µl leaves the lens in less than 200 milliseconds (across an undetermined area) when it is stretched. In contrast, the fluid movement produced by ionic transport follows a circulatory pattern: leaves the equatorial area at a rate of 0.07 µl/min and re-enters the lens at the anterior and posterior areas closing a circulation loop.

Conclusion: These results show that the lens capsule is freely permeable to water, and fluid can leave and enter the lens driven by the forces of accommodation and ion transport. The ionic-driven movement provides support to the Mathias FCM. It is interesting to note that fluid movement in the lens may occur simultaneously in two different domains and time scale.

5. LENS VOLUME MEASUREMENTS DURING ACCOMMODATION IN A LENS STRETCHER

Fabrice Manns, Lauren Marussich, Bianca Maceo, Derek Nankivil, Esdras Arrieta Quintero, Arthur Ho, Jean-Marie Parel

Purpose: To determine if the lens volume changes during accommodation in a lens stretcher (EVAS II).

Methods: The cross-sectional shape of 20 hamadryas baboon lenses (1.8–21 years) and 32 cynomolgus monkey lenses (1.4–13.7 years) was imaged during simulated accommodation in a lens stretcher, using Optical Coherence Tomography (OCT). The lens contour was extracted from the OCT images using semi-automatic segmentation. The lens contour was derived from the segmented lens boundary by using the pixel coordinates of the boundary (Method 1) and by using a cosine-series fit (Method 2). The lens volume was calculated from the lens contour assuming rotational symmetry. An error analysis on a cynomolgus monkey lens was used to determine the effect of image distortions due to refraction of the OCT beam and other measurement errors.

Results: On average (±SD) the change in volume with accommodation (stretched to unstretched states) was -0.1±2.6% with Method 1 and -1.0±2.4% with Method 2 for the monkey lenses; +1.0±3.5% with Method 1 and +0.1±2.7% with Method 2 for the baboon lenses. The error analysis shows that OCT distortions produce a 3.6 mm³ (2.0%) and

3.3 mm³ (1.8%) overestimation of the lens volume in the stretched and unstretched states, respectively. This error corresponds to a 0.3 mm³ (0.2%) overestimation of the volume change.

Conclusions: Within the precision of our measurements, there was no change in lens volume with accommodation. Reliable estimates of changes in lens volume require measurements with high resolution and highly accurate models of lens contour.

2A: Accommodation & Presbyopia

Moderators: William Culbertson, Paul Kaufman

6. THE VITREOUS MEMBRANE (ANTERIOR HYALOID) BENDS POSTERIORLY IN PROPORTION TO ACCOMMODATIVE AMPLITUDE AND LENS THICKENING

Mary Ann Croft, Jared McDonald, Alexander Katz, Timothy Nork, Paul Kaufman

Purpose: Determine vitreous membrane/anterior hyaloid (AH) configuration in relationship to the lens and ciliary body during accommodation.

Methods: Accommodation induced by midbrain electrical stimulation was measured by coincidence refractometry in 4 rhesus monkeys (ages 7-25). Visualization of intravitreal structures was enhanced by a 50µl intravitreal injection of triamcinolone. The AH configuration, ciliary muscle and zonular attachments were imaged by ultrasound. **Results:** The AH bends posteriorly and the cleft between the AH and the lens/pars plicata increases with accommodative lens thickening and accommodative amplitude. The posterior peripheral vitreous and the vitreous membrane adjacent to the vitreous zonule are all pulled forward via the vitreous zonule during ciliary muscle contraction. The AH cleft width was ~0.3 mm narrower in the resting older eye compared to the young eye.

Conclusions: The vitreous/AH may play a role in accommodation but perhaps not as previously theorized. These findings may relate to accommodating IOL function.

7. CHANGE IN GRADIENT INDEX OF CYNOMOLGUS MONKEY LENSES WITH SIMULATED ACCOMMODATION

Judith Birkenfeld, Alberto de Castro, Bianca Maceo, Esdras Arrieta, Fabrice Manns, Jean-Marie Parel, Susana Marcos

Background: Purpose of this study was to investigate the change of the Gradient refractive Index (GRIN) with accommodation, and the relative impact of shape changes and GRIN to power and spherical aberration changes.

Methods: GRIN was estimated from experimental data using an optimization method (de Castro OE 2010) in ex vivo lenses of cynomolgus monkeys at various states of simulated accommodation (EVAS II). Change between nucleus and surface refractive index was modeled with a power function. Spherical aberration and power were estimated for the reconstructed GRIN and a homogeneous index

Results: Lens surface radii of curvatures and asphericities decreased with increasing accommodation as well as the

average refractive index. The GRIN was found to be more concentrated in the surface in the unaccommodated state.

Conclusions: Both shape and GRIN distribution contributed to the change in lens power and shift of the spherical aberration toward negative values with accommodation.

8. ARE MONKEYS GOOD MODELS FOR STUDYING PRESBYOPIA?

Robert Augusteyn

Purpose: Monkeys are commonly used as models for exploring the mechanisms of human presbyopia formation, on the assumption that the mechanisms are the same. The validity of this assumption will be examined.

Methods: In vitro data on age-related changes in lens properties were collected for human and several other primates. These were compared using logistic and allometric analyses.

Results: Human lens growth is biphasic, asymptotic before birth and linear thereafter, generating the distinct nucleus and cortex. Lens growth in other species is asymptotic only. Human lens shape changes in a unique and complex manner. From birth to the teens, thickness decreases while diameter increases. Around the time of sexual maturation, diameter growth slows while thickness starts to increase. In monkeys, lens thickness decreases while diameter increases throughout life.

Conclusions: There are substantial differences in the growth of human and other primate lenses which produce lenses of different shapes and properties at different ages. This suggests there may be differences in the way accommodation is achieved.

9. THE INDUCED CORNEAL ASTIGMATISM AT PRESBYOPIA.

Lydia Mineeva, Vladimir Strakhov

purpose – studying of presbyopia clinic and of the reasons of temporary eyesight aggravation of presbyopes at shifting glance from short to long distance after prolonged work at short distance.

Materials and methods – 58 patients of 40-70 years old with emmetropic refraction and different stages of presbyopia without concomitant eye pathology. All patients were being held with the “testing with intensive reading” during 40 min, including reading in uncomfortable conditions of insufficient presbyopia correction.

Results and discussion – after short distance reading the aggravation of a far eye sighting and asthenopia symptoms were discovered. During the “testing with intensive reading” the increasing of a direct corneal astigmatism (an average of 0,75±0,09 diopters) was determined which was clinically significant. After reading the appeared induced astigmatism was kept for 22,8 min in average and that allowed to fix the change of cornea configuration by means of keratopography and ophthalmometry.

Conclusions – The temporary loss of far vision with presbyopes after the visual proximity for near vision is the result of the appeared direct corneal astigmatism due to the strengthening of the internal rectus muscles tonus under convergence and pressing effect of eyelids at blinking. We explain this effect by the involuntal decreasing of cor-

neal scleral elasticity (due to the age) of presbyopia eye which delays restoring of corneal sphericity after the cessation of reading.

10. IS RETINAL IMAGE QUALITY MAXIMUM DURING ACCOMMODATION?

Larry Thibos, Jesson Martin, Tao Liu, David Diaz-Muñoz, Arthur Bradley, Norberto Lopez-Gil

Purpose: Our goal was to test the physiological hypothesis that the purpose of accommodation is to improve retinal image quality sufficiently to perform a visual task. This hypothesis predicts that, despite changes in aberrations and pupil size, accommodative error is negligible when the task is to read very small letters.

Methods: Wavefront aberrations were measured for 10 young adult eyes when viewing monocularly the smallest resolvable letters on an acuity chart at variable distance. A control condition used phenylephrine to inhibit pupil constriction during accommodation. Retinal image quality was computed from the aberration data using unbiased scalar metrics (Martin et al. (2011) Vis. Res. 51:1932). Accommodative error is the difference between target vergence and the computed target vergence that would have maximized image quality.

Results: For most subjects, with or without phenylephrine, image quality was maximum and accommodative error was negligible when acuity was better than 20/20. Retinal image quality was sub-optimal in subjects with acuity worse than 20/20 due to a tendency to under-accommodate for all target vergences.

Conclusion: Reading fine text requires accurate accommodation that maximizes retinal image quality. Wavefront aberrometry confirms that most subjects can achieve this optimum state during monocular vision.

2B: Accommodation & Presbyopia

Moderators: Ron Krueger, Fabrice Manns

11. IN SEARCH OF GULLSTRAND'S INTRACAPSULAR ACCOMMODATION

Norberto López-Gil, Elvira Pérez-Jiménez

Purpose: A century ago Allvar Gullstrand proposed an intracapsular accommodation mechanism based in the concept that the change of the lens power during accommodation is larger in the case of supposing the lens formed by two different refractive indexes (cortex and nucleus) than the case of a homogenous lens.

Methods: We computed paraxial and non-paraxial intracapsular accommodation of the original six-surfaces model proposed by Gullstrand and a model eye from built in base of precise actual data of the lens surfaces and nucleus changes during accommodation.

Results: Gullstrand's model eye presented an intracapsular accommodation of 4.6 D while the actual model eye does not present such type of accommodation but the opposite (-2.7 D).

Conclusions: Gullstrand proposed a much larger change of the anterior radius of the lens nucleus during accommodation than the change observed using actual techniques, which explains why intracapsular accommodation appears

in the Gullstrand's model eye, but not in the real human eye.

12. EFFECT OF ANTERIOR ZONULES TRANSECTION USING A FINITE ELEMENT MODEL

Hooman Mohammad Pour, Sangarapillai Kanapathipillai, Fabrice Manns, Arthur Ho

Introduction: The discovery of trans-hyaloid zonules and findings on the role of posterior zonules and the hyaloid membrane renewed interest in understanding the role of these hitherto lesser-studied components of the accommodation system. One recent attempt (Bernal et al, 2009) to investigate the role of the zonules compared ex vivo accommodative response in a lens-stretcher before and following transection of the anterior zonules. In the present study, we developed an initial attempt to model the effect of zonules transection on the opto-mechanical response of the lens using finite element (FE) analysis. The results were first compared against published results. We then used the model to predict the effect of posterior zonules transection.

Methods: An axisymmetric FE model based on the geometry from Erickson et al (2011, ARVO) was constructed using ANSYS (desktop version 13). The model included the following modifications: use of literature values for material properties; inclusion of a capsule; and adoption of a 6:3:1 zonules ratios (Burd et al, 2002). The FE model was radially stretched to simulate dis-accommodation up to a maximum of 0.76 mm displacement of the ciliary body. To model partial zonules transection, the anterior or posterior zonular bundle was deleted from the model and the stretching simulation repeated. At each step (up to 8 steps) of stretch, ciliary load, ciliary ring half-diameter, lens half-diameter and lens thickness were outputted.

Results: A load of 87.6 mN was required to change the lens half-diameter by 0.6 mm in the intact lens. When the anterior zonules were removed, the required load increased to 116.3 mN (33% increase; which compares reasonably well with Bernal et al). The model predicts that posterior zonules transection has a lesser effect, requiring only 97.1 mN (11% increase) to produce the same lens diameter change.

Conclusions: While absolute values for load and dimensional changes require refinements to match actual ex vivo lens stretching results, the FE model qualitatively agrees with ex vivo lens stretching results. It is predicted that posterior zonules play a lesser role than the anterior zonules.

13. COMPUTER-ANIMATED MODEL OF ACCOMMODATION AND THEORY OF RECIPROCAL ZONULAR ACTION

Daniel Goldberg

Model: A computer-animated model of the structures of accommodation is presented based on new understanding of the anatomy of the zonular apparatus integrated with current understanding of the mechanism of accommodation. Recent studies (Bernal, Parel, Manns IOVS 2006, and Lutjen-Drecoll, Kaufman, Wasielewski, Ting-Li, Croft IOVS 2010) have demonstrated 3 components of the vitreous zonule (anterior, intermediate, and posterior) in addition to the pars plana zonule. Utilizing model-based reasoning, it is shown that the posterior zonules attach to and provide traction to the anterior vitreous membrane and Weiger's liga-

ment. This model supports the concept that the ciliary body/zonule/anterior hyaloid complex contributes to the changes in the posterior lens capsule during accommodation, supporting an extralenticular component to accommodation and demonstrating an alternative to the "vitreous support" theories. There is a reciprocal action of the anterior zonules and the posterior zonules. During ciliary body contraction, the anterior zonules lose tension while the posterior zonules stretch and exert force on the posterior lens capsule playing a role in shaping the posterior lens thickness and curvature. During ciliary body relaxation, the posterior zonules lose tension as the lens flattens and is pulled back by the increasing tension of the anterior zonules.

14. ACCOMMODATION STATUS UNDER GENERAL ANESTHESIA WITH AND WITHOUT CYCLOPLEGIA IN PEDIATRIC POPULATION

Mukesh Taneja, Veerendranath Pesala, Bhuvaneshwari Ganesan, Virender Sangwan

Purpose: To determine accommodation status under general anesthesia with and without cycloplegia in pediatric population

Material & Methods: Ten eyes of 10 pediatric patients undergoing unilateral ocular surgery in the contra lateral eye under general anesthesia were included in the study. 6 patients in group I underwent cycloplegic refraction while under anesthesia with cyclopentolate (IA) and later without anesthesia (IB). 4 patients in group II underwent refraction under anesthesia with phenylephrine (IIA) and later without anesthesia (IIB).

Results: Group IA showed a mean refraction of 0.917 D (SD=1.158) and IB showed 0.667 D (SD= 0.983). The difference between the two groups was not statistically significant (P value= 0.695).

Group IIA showed a mean refraction of 2.00 D (SD= 0.842) and IIB showed 1.25 D (SD= 0.935). The difference between the two groups was not statistically significant (P value= 0.278).

Conclusion: General anesthesia appears to be causing partial relaxation of accommodation which does not eliminate the need for cycloplegia for accurate refraction under anesthesia

15. ACCOMMODATIVE STATUS IN CHILDREN WITH CEREBRAL PALSY

JayaRajini Vasanth, Namita Jacob, Krishnakumar R, Viswanathan S

Purpose: To examine the visual functions and accommodative status in children with cerebral palsy.

Methods: 145 children with cerebral palsy were assessed for the study. We assessed their visual functions and accommodative status. Visual acuity was assessed using LEA paddles and LEA symbols depending upon the age, cooperation and cognitive ability of the child. Visual fields were assessed by using LEA flicker wand. Hirschberg test and cover test procedures were done to identify the squint of the children. The technique of Mohindra near retinoscopy was done to find the static refractive status of the children. Accommodation was measured using MEM and NOTT dynamic retinoscopy technique. The values were compared with the age matched normal values.

Results: The standard deviation of the age was 4.479, 20.50% of children had near normal vision, 30.50% had moderate low vision, 44% had severe low vision and 5% had profound low vision. The Squint was present in 69.40% of the kids and absent in 30.60% of the children. Among those who had squint Nystagmus was present in 5.90%. The accommodative status was assessed by MEM and NOTT dynamic retinoscopy. The results are analyzed using a Mann-Whitney Wilcoxon on test.

Conclusion: This ongoing study shows that most of the cerebral palsy kids have lag of accommodation and hence the refractive error was corrected accordingly considering their binocular status. Both MEM and Nott dynamic retinoscopy techniques showed lag of accommodation.

3: New Instruments & Techniques

Moderators: Thomas Aller, Norberto Lopez-Gil

16. INVESTIGATING THE ACCOMMODATIVE RESPONSE WITH A NATURAL-VIEW WAVEFRONT SENSOR

Len Zheleznyak, Geunyoung Yoon

Purpose: To measure through-focus visual performance simultaneously with the near triad (wavefront, vergence, pupil miosis) under binocular, natural-viewing conditions.

Methods: The system consists of a custom Shack-Hartmann wavefront sensor, a binocular pupil camera and a visual stimulus for vision testing. The subject viewed a microdisplay for vision testing with both eyes through a large dichroic beam splitter (10 x 13 cm). The microdisplay was mounted to a translational rail, allowing for a range of object distances (0.25 to 3 D). The wavefront sensor (980nm) and binocular pupil camera were located below the beam splitter and did not obstruct the subject's field of view. The wavefront sensor and binocular pupil camera were synchronized, such that simultaneous data was collected in real time (10Hz) during vision testing. The system was verified by measuring a young, normal subject viewing the stimulus at object distances of 0.25, 1.5 and 2.5 D.

Results: Significant changes in optical power, pupil size and interpupillary distance was observed. For far, intermediate and near object distances, the subject's defocus was 0.22±0.14, 1.11±0.15 and 2.70±0.16 D, respectively. Pupil size in both eyes was 6.4±0.0, 5.5±0.2 and 3.6±0.1 mm, respectively. Intrapupillary distance was 68.0±0.0, 67.6±0.1 and 66.2±0.1 mm, respectively.

Conclusions: The proposed device is an important tool for understanding the mechanism of accommodation under binocular, natural viewing conditions.

17. AN IMAGE CONVOLUTION BASED RETINAL IMAGE QUALITY METRIC FOR PREDICTING THROUGH-FOCUS VISUAL PERFORMANCE FOR PRESBYOPIC CORRECTION

Scott MacRae, Len Zheleznyak, Ramkumar Sabesan, Geunyoung Yoon

Purpose: To investigate the effectiveness of an image convolution based retinal image quality metric (RIQ) for predicting monocular through-focus visual performance with presbyopic corrections.

Methods: To estimate monocular through-focus visual quality, RIQ was calculated using correlation coefficient of convolved images. The correlation coefficient symbolizes the likeness between a reference image (aberration free) and a convolved image (aberrated). To assess the performance of the metric, an adaptive optics vision simulator was used to measure monocular through-focus high contrast visual acuity in cycloplegic subjects under various aberration conditions (Zernike primary spherical aberration). The log of the visual Strehl ratio (logVSOTF) was computed for comparison. A 4mm pupil was used for all theoretical simulations and visual performance measures.

Results: Through-focus high contrast visual acuity was well predicted using the correlation coefficient RIQ metric for all presbyopic corrections (R²=0.74). The logVSOTF was reliable RIQ metrics for diffraction-limited monocular through-focus visual performance (R²=0.85), however, predictability was reduced in the presence of spherical aberration (R²=0.46).

Conclusions: The image convolution based metric reliably predicts monocular visual performance in the presence of spherical aberration and large amounts of defocus. This is a useful tool for the design of ophthalmic lenses for presbyopia.

18. THE SALZBURG READING DESK (SRD) AS A TOOL FOR QUANTIFYING THE RESULTS OF MULTIFOCAL IOLS AND PRESBYOPIC SURGERY

Guenther Grabner, A.Dexl

The focus of interest in refractive surgery has, in recent years, clearly shifted towards the correction of presbyopia. The sheer number of potential patients who might seek spectacle- and contact-lens-free permanent correction certainly is a great stimulus for clinical research and many extraocular and intraocular procedures have been introduced into the clinical practice without any single one yet gaining acceptance as the final solution for the perfect correction of presbyopia. Over the last several years the IOL-research group at the University Eye Clinic in Salzburg has devoted concentrated efforts to develop a system that allows for the precise assessment and quantification of several aspects of reading with the use of a system called "Salzburg Reading Desk" (SRD) which is based on principles published by Radner (2) and adding an automatic computerized system of distance measurement as shown in previous publications (3,4). In this presentation the main features of the SRD will be presented as applicable to the assessment of reading parameters following the implantation of different multifocal IOL's.

In a study performed at two surgical centers (Vissum-Instituto de Oftalmológico de Alicante, Spain, and the University Eye Clinic, PMU, Salzburg, Austria) a total of 304 eyes (152 patients) were implanted with Acri.Smart 48S monofocal, Acrysof Restor SN6AD3 apodized multifocal, Acri.LISA 366D diffractive multifocal or Rezoom multifocal IOL's following bilateral phaco-emulsification. Bilateral reading performance was measured with and without near correction preoperatively and postoperatively using the SRD with the Spanish and German language tables. All groups had a significantly improved UDVA and CDVA postoperatively with the apodized and diffractive MF groups showing a significantly better uncorrected reading acuity and smallest print size than the monofocal and refractive multifocal

groups at all time points. The maximum corrected reading speed at 1 month was statistically significantly better in the diffractive MF group than in the other groups ($P > 0.03$, Mann-Whitney test). During the postoperative follow-up there was a statistically significant improvement in maximum corrected reading speed in the monofocal, apodized MF and refractive MF groups ($P > 0.01$, Wilcoxon Test).

Measurement of reading speed and smallest print size provides more information about near functional vision than near visual acuity measurement alone. Conventional charts assess RVA alone, and these first results indicate that for the evaluation of reading performance under standardized conditions at least four parameters should be evaluated: reading acuity, reading speed, reading distance and smallest print size. This is also important for studies that wish to compare other types of surgical corrections for presbyopia. In this regard the SRD will prove to be a useful instrument as shown with newer refractive devices, such as the KAMRA intracorneal inlay (Dexl A. et al., JCRS 2011).

19. THREE-DIMENSIONAL OCT-BASED BIOMETRY IN EYES IMPLANTED WITH AIOLS UNDER DIFFERENT ACCOMMODATIVE DEMANDS

Susana Marcos, Sergio Ortiz, Pablo Pérez-Merino, Judith Birkenfeld, Sonia Durán, Ignacio Jiménez-Alfaro

Background: We provided full 3-D biometry in eyes implanted with the single-element Crystalens Accommodative-Intraocular lens (AIOL) applying newly developed distortion correction and image processing tools in OCT.

Methods: A custom developed sOCT was used to image the anterior segment (cornea and crystalline lens/IOL) in patients implanted with AIOLs. Images were automatically merged, using the peripheral corneal region and iris for registration. Denoising volume clustering, edge detection and segmentation algorithms, and distortion correction were developed and applied. Patients were imaged before and after surgery under relaxed accommodation and 2.5-D of accommodative effort. 3-D 4-surface real-eye models were obtained. Biometrical parameters such as A-IOL location with respect to the pre-operative lens, and A-IOL displacement as a function of accommodation were estimated.

Results: The A-IOL center fell 100 μ m behind the pre-op natural lens equator. With accommodation, lenses moved from 400 μ m from the cornea (opposite to expected shift) to 180 μ m towards the cornea.

Conclusions: Quantitative full 3-D sOCT is a powerful tool to assess performance of AIOLs.

20. INVESTIGATING PRESBYOPIC CORRECTIONS WITH ADAPTIVE OPTICS

Geunyoung Yoon, Len Zheleznyak, Ramkumar Sabesan

Purpose: To investigate the application of adaptive optics (AO) in presbyopic corrections in a model eye and human studies measuring through-focus visual performance and stereoacuity.

Methods: An AO vision simulator has been incorporated into an IOL metrology system and applied to vision testing studies of multifocal corrections and modified monovision. With AO, it is possible to induce arbitrary corneal aberrations onto a model eye, enabling the study of the impact of corneal aberrations on through-focus image quality of pres-

byopia-correcting IOLs. In addition, the AO vision simulator has been used to study the effect of spherical aberrations on through-focus visual performance for monocular and binocular presbyopic corrections, such as modified monovision. Visual performance measures in these paradigms include through-focus visual acuity, contrast sensitivity and stereoacuity. Furthermore, measures of visual performance in presbyopic corrections allow for the study of image quality metrics.

Results: The AO-IOL metrology system has shown that diffractive multifocal IOLs are more sensitive to corneal astigmatism than monofocal IOLs. In human studies, combinations of higher order spherical aberrations have been shown to improve through-focus visual performance and depth of focus. In addition, modified monovision has been shown to improve through-focus visual acuity, binocular summation in contrast sensitivity and stereoacuity, as compared to traditional monovision.

Conclusion: Adaptive optics is a powerful tool for the investigation of presbyopic corrections, both in vitro and in vivo.

21. OPHTHALMIC OPTICAL SAFETY STANDARDS UPDATE

David Sliney

Ophthalmic research, diagnostic and surgical procedures often requires high levels of ultraviolet, visible or infrared radiation to attain efficacy. Questions then arise as to what levels are acceptable for the cornea, iris, lens and retina. Although safe exposure levels for optical radiation exist for occupational and general public exposure, adjustments have to be made to these limits for ophthalmic patient exposure to account for the possibilities of pupil dilation, stabilization of the retinal image, Maxwellian view, etc. These factors are treated for lasers in ANSI Z136.1, para. 8.3 and in ISO 15004-2 for all ophthalmic instruments. Laser exposure limits are changing in several international standards this year, and will relax limits for large-area, pulsed, retinal exposures. An improved treatment of thermal loading of the cornea and retina are expected for the international standard, ISO 15004-2.

22. NEW COMPACT ACCOMMODOMETER TO MEASURE ACCOMMODATION AMPLITUDE AS A BIOMARKER

Kazuo Tsubota, Takeshi Ide, Kazuno Negishi, Takefumi Yamaguchi, Shuya Hara, Ikuko Toda

Purpose: To evaluate a newly designed compact accommodometer (CA) and compare this with a conventional accommodometer for measuring accommodation as a biomarker for aging and lifestyle.

Methods: Accommodative amplitude was measured using 2 different accommodometers in 114 patients. We obtained the data of the near point and accommodation amplitude. Subsequently, we employed smoking habit as an example of lifestyle-related factor to evaluate its effect on the accommodative power.

Results: In the first study, the subjects were 60 eyes of 60 males, and 54 eyes of 54 females, mean age of 43.8 \pm 12.9 years (range, 18 to 58). There was a significant correlation between the two devices ($r^2 = 0.65$). Measuring accommo-

dation by CA was significantly faster than by conventional modality (190.9 \pm 58.1 seconds for CA and 371.8 \pm 123.6 seconds for D'ACOMO, $p < 0.0001$, paired t test). In the second part of the study, we found a significant correlation between age and accommodative amplitude both in smokers and non-smokers (statistical data). The accommodative amplitude of the smoker group was significantly lower than that of the non-smoker group ($P < 0.001$).

Conclusions: CA may work as an alternative and convenient method in place of the conventional accommodometer for measuring accommodative amplitude as an aging biomarker. Lifestyle factors can affect the magnitude of accommodation, which can be measured by CA.

4: Restoring Accommodation: Biology

Moderators: Sonia Yoo, Robert Augusteyn

23. OPINION: LEC & PCO ... WHERE ARE WE?

Jean-Marie Parel

Purpose: To summarize the methods utilised to prevent "secondary cataracts", and the opacification and contraction of the capsular bag. **Methods:** 40 years of experimentation at the Ophthalmic Biophysics Center that includes: mechanical, cryogenic, hyperthermia, antiproliferative, hypotonic, photodynamic, antifibrotic treatments and the use of sodium hyaluronate to modulate proliferation, as well as literature results will be presented.

Results: In the rabbit and non-human primate model, the safest treatment only slowed down LEC proliferation. Clinically, the only method to stop this phenomenon has been to establish a mechanical barrier to block LEC from migrating but this requires tailor-made annular implants that expand the lens capsule at the equator and reduces the potential for full restoration of accommodation.

Conclusion: In addition to capsular opacification, LEC proliferation engenders capsule fibrosis and thus, a change in the capsule's ability to contract during accommodation results and in time, methods and devices designed to restore accommodation will fail. Ad Hoc intensive research to harness LEC propensity to proliferate is necessary to maintain restored accommodation.

24. A POTENTIAL ROLE FOR ZEB FAMILY TRANSCRIPTION FACTORS IN THE REGULATION OF POSTERIOR CAPSULAR OPACIFICATION

Melinda K. Duncan, Abby Grabitz-Manthey, Yan Wang, Jennifer Remington-Taube, Alisha Yallowitz

Purpose: Posterior capsular opacification (PCO) is a side effect of cataract surgery and is regulated in part by TGF β activation. Zeb proteins are transcription factors that regulate epithelial-mesenchymal transition in other systems. This work examines Zeb expression during PCO progression.

Methods: Zeb expression following cataract surgery was evaluated by immunohistochemistry and compared to that of known markers of both "fibrotic" and "pearl type" PCO.

Results: Zeb2 is expressed in the lens and is essential for lens fiber cell formation. During PCO development, Zeb2 is expressed in cells undergoing both EMT and lens fiber cell differentiation. In contrast, Zeb1 protein is only detected occasionally in the adult lens epithelium. However, Zeb1

expression is robustly induced coincident with α SMA in the mouse lens following extracapsular fiber cell removal.

Conclusion: These data indicate that Zeb2 is important for normal lens structure while Zeb1 is more likely to be important for PCO progression.

25. CAN THE TOPICAL ALDOSE REDUCTASE INHIBITOR KINOSTATTM CLINICALLY PREVENT CATARACTS IN DIABETICS?

Peter F. Kador

Purpose: Cataract formation is the leading need for cataract surgery in diabetic dogs with 75% of dogs developing cataracts within the first year of diagnosed diabetes. Moreover, the strong development of PCOs in dogs that cannot be treated with laser capsulotomy makes surgery less than satisfactory. Daily topical administration of KinostatTM has prevented the onset and progression of cataracts in diabetic dogs for a period of up to 4 years. For FDA approval, this compound is currently undergoing a masked multi-centered placebo controlled clinical trial for efficacy. Can this drug also prevent cataracts in human diabetics?

Experimental / Results: While ophthalmologists are quick to conclude that aldose reductase activity in the human lens is negligible, the data says otherwise. Similarities between dog and human lenses include: 1) similar specific activity levels of aldose reductase 2) similar distribution of aldose reductase in the lens 3) both lenses can convert glucose to sorbitol and galactose to galactitol, 4) activity of aldose reductase activity decreases with age and is induced by diabetes and 5) similar cataracts are induced in both diabetics and galactosemics.

Conclusion: Topical administration of KinostatTM reduces possible systemic effects associated with this class of drugs. Aldose reductase clearly initiates cataracts in infants and young children and topical administration of KinostatTM could reduce their need for cataract surgery. A similar argument for diabetic cataracts in adults can also be made, however, a clinical trial in adults would be difficult to conduct since the time frame of cataract development has not been established.

5: Restoring Accommodation: Solutions

Moderators: Arlene Gwon, Arthur Ho

26. ACTUATOR CONCEPTS FOR THE OPTICS OF A MECHATRONIC ACCOMMODATION IMPLANT

Thomas Martin, Ulrike Gengenbach, Helmut Guth, Georg Bretthauer, Rudolf Guthoff

Purpose: A mechatronic microsystem implanted into the capsular bag is a novel approach to restore the accommodative function. The main components of such an Artificial Accommodation System are a sensor to detect the accommodation demand, optics of variable refractive power for an accommodation range of at least 3 dpt, a microcontroller, energy supply for at least 24 hours of autonomous operation without recharge, a communication device and a bio-compatible and hermetic encapsulation. For change of refractive power optical systems based on axial or lateral lens shifts have previously been shown to be suitable. In both cases a lens shift has to be generated by an actuator which is the focus of this contribution.

Methods: The approach used in this work is based on a piezoelectric bender and a silicon linkage with a planar compliant mechanism. Piezoelectric actuators feature high dynamics, energy efficiency, reliability, and durability proven on an industrial level. The silicon linkage realizes mechanical amplification of the bender's output displacement. The compliant mechanism of the linkage also ensures suspension as well as synchronization of the lenses in case of the lateral-shift optics. Finite element analysis (FEA) was applied to verify and optimize the design of the linkages. For the axial-shift optics linkages have been fabricated on a scale of 1.5:1. Their kinematic performance was characterized by measurements.

Results: Two compact actuator solutions were elaborated for an axial-shift optics and a lateral-shift optics. They are virtually friction-free and designed for high durability. Axial and lateral lens displacements of about 300 μ m are achieved facilitating an enhanced optical power range of 4.6 dpt for postoperative refractive compensation. The actuator design ensures a safe failure state in which the implant is equivalent to a conventional IOL. The linkages fabricated from wear-free single-crystal silicon were measured to have an unloaded displacement amplification ratio of 18.1 (SD = 0.80, n = 5) which is in excellent agreement with the ratio of 18.1 calculated by FEA. These results indicate sufficient displacement amplification of the novel compliant mechanisms to generate the required lens shifts.

Conclusions: Two actuator solutions were developed aiming to demonstrate feasibility of an essential component of a mechatronic implant for restoration of the accommodative function of the human eye.

27. FOUR YEAR FOLLOW-UP OF PATIENTS IMPLANTED WITH AN INTRACORNEAL INLAY FOR THE CORRECTION OF EMMETROPIC PRESBYOPIA
Guenther Grabner, T Rückl, A Dextl, O Seyeddain, W Riha, M Hohensinn

Purpose: To assess the safety and efficacy of a small-aperture optic device for the treatment of presbyopia in emmetropic presbyopes.

Methods: The Kamra inlay, formerly the AcuFocus ACI corneal inlay (AcuFocus, Irvine, CA), is an ultrathin microporated, opaque artificial aperture (3.8 mm outer diameter and 1.6 mm inner diameter) made of highly biocompatible polyvinylidene fluoride (PVDF). A randomized pattern of minute holes allows nutritional flow through the implant to the anterior stroma. Following creation of a superior-hinged flap in the non-dominant eye, a Kamra inlay was centered on the stroma based on the first Purkinje reflex in 32 emmetropic patients with a mean age of 51.20 ± 2.2 years. Manifest refraction and visual acuity at three years postoperative are reported here. Four year data will be presented at the meeting.

Results: In the implanted eye, mean spherical equivalent shifted from 0.19 ± 0.22 D preop to 0.08 ± 0.68 D at 3 years. Mean UNVA improved from J7/J8 to J1 at 3 years. Mean UIVA went from 20/40 preop to 20/25 at 3 years. Mean UDVA decreased slightly from 20/16 to 20/20 at 3 years. At 3 years, all eyes achieved UDVA of 20/32 or better. Mean binocular UDVA was 20/16. There were no explants. Two inlays had to be recentered due to initial misplacement. During the follow up period, no irritation, inflammatory reactions, or changes in corneal appearance were observed.

Conclusion: The Kamra corneal inlay improves near and intermediate vision without severe loss of distance visual acuity in emmetropic presbyopes by increasing the depth of field, based on the small aperture optics concept.

28. ULTRASHORT PULSE LASER PHOTODISRUPTION OF THE CRYSTALLINE LENS FOR ACCOMMODATION RESTORATION: IS IT SAFE?

Ronald Krueger, Harvey Uy, Jared McDonald, Keith Edwards

Purpose: We wish to demonstrate that ultrashort pulse lasers can be used to treat the crystalline lens without forming a focal, progressive or vision threatening cataract.

Methods: An Nd:Vanadate picosecond laser (10 ps) with prototype delivery system was used. Primates: 11 rhesus monkey eyes were prospectively treated at the University of Wisconsin (25-45 μ J/pulse and 2.0-11.3M pulses/lens). Analysis of lens clarity and fundus imaging was assessed postop for up to 4.5 years (5 eyes). Humans: 80 patients (ages 44 to 60 years, NS grade 0-2) were prospectively treated in one eye at the Asian Eye Institute in the Philippines (energy 10 μ J/pulse and 0.45 to 1.45M pulses/lens). Analysis of lens clarity, change in visual acuity (BCVA) and subjective symptoms was performed at 1 month, prior to elective lens extraction.

Results: Bubbles were immediately seen with resolution within the first 24 or 48 hours. Afterwards, the laser pattern could be seen with faint, non-coalescing pinpoint microopacity in both primate and human eyes. Primates: Long-term follow-up of up to 4 ½ years showed no focal or progressive cataract, except 2 eyes with pre-existing cataract. Humans: A mean loss of 7 letters of BCVA was seen, mostly among the central treatments. >70% of subjects reported acceptable or better distance vision and no or mild symptoms with central sparing (0.75 and 1.0 mm radius), while the majority without sparing (0 and 0.5 mm radius) reported poor or severe vision and symptoms.

Conclusions: Focal, progressive and vision threatening cataracts can be avoided by lowering the laser energy, avoiding prior cataract and sparing the center of the lens.

29. WILL FEMTOSECOND LASER MODIFICATION CREATE A LENS OXYGEN SINK FROM LENS FLEXURE AND ADDING CHANNELS TO FACILITATE IONIC/FLUID FLOW?

Raymond Myers

Introduction: A femtosecond laser modifies lens tissue in the intact eye. Flexural changes have been demonstrated and adding channels and networks are being proposed to improve ionic flow.

Methods: A literature review suggests favorable physical characteristics including inert, encapsulated tissue and a recyclable glutathione redox cycle that protects lens tissue against flexural changes and light scatter until age related barriers occur as early as age 30.

Results: Lens tissue is a layered crystalline structure that loses transparency regionally as it develops physiological barriers from a cascading reduction in lens movement and increase in light scatter.

Conclusions: Increasing flexure and adding microchannels and networks may reestablish glutathione reductase ions into deeper tissues and create a lens oxygen sink or reservoir for removal of oxygen ions from the lens and ocular fluids. Possible benefits may be cataract retardation and prevention of other eye diseases benefitting from fewer oxygen ions in the ocular fluids.

30. ZONULAR CAPTURE HAPTIC

Paul Beer, Paul Kaufman, Mary Ann Croft, Alex Katz, Greg Heatley, Jarred McDonald

Purpose: To test the novel concept of harnessing and transmitting zonular forces with a Zonular Capture Haptic (ZCH), as a first stage for an "out of the bag" accommodative-disaccommodative IOL system.

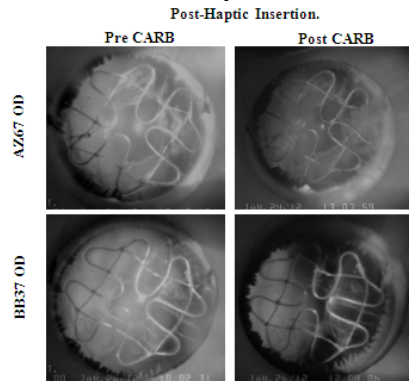


Figure 2. Plano perfusion lens images 56 days post-haptic insertion in the unaccommodated and accommodated states. Both animals have ciliary processes that overlap the lens in the unaccommodated and accommodated state.

Methods: A Zonular Capture Haptic prototype was implanted in one surgically aniridic eye of two rhesus monkeys (*Macaca mulatta*). A second haptic activation surgery was completed 5 weeks later. 56 days post implantation, haptic function was assessed with goniovideography, ultrasound biomicroscopy and a plano perfusion lens. Supramaximal accommodation was induced by pharmacological stimulation with 40% carbachol.

Results: Prior to haptic implantation, supramaximal accommodation induced a decrease in the diameter of the ciliary ring and capsular bag by 1.87mm and 0.99 mm respectively. Post implantation ciliary ring diameter reduced by 1.38 ± 0.085 mm, capsular bag diameter by 1.62 ± 0.1 mm, and the haptic itself by 1.06 ± 0.57 mm.

Conclusions: Both Zonular Capture Haptics were secure at 56 days post implantation and responded appropriately to zonular tension during pharmacologically induced accommodation. ZCH is a promising novel approach and warrants additional investigation.

31. INJECTABLE INTRAOCULAR LENS EXCHANGE IN THE RABBIT MODEL

Arlene Gwon

Purpose: In standard cataract surgery with IOL implantation, it often becomes necessary to explant the original IOL and replace it with an alternative IOL. The current study evaluated the feasibility of injectable silicone polymer lens

exchange with a silicone polymer or a foldable hydrophobic acrylic IOL in New Zealand white rabbits.

Methods: Endocapsular lens extraction was performed through a 2 mm capsulorrhexis in both eyes of 4 New Zealand white rabbits. Following removal of the lens, a silicone plug was inserted into the capsule bag and maneuvered behind the anterior capsulotomy. Hyaluronic acid (HA) was injected prior to refilling the capsule bag with a silicone polymer. At 3 months postoperative, the injectable polymer was extracted through the original 2 mm capsulorrhexis. In 3 eyes a collagen patch was inserted and another injectable silicone polymer was injected into the capsule bag. In 5 eyes, the capsulorrhexis was enlarged to approximately 6 mm and a hydrophobic acrylic IOL was implanted in the capsule bag.

Results: After 3 to 6 months in the eye, the clear silicone polymer was readily explanted through a 2 mm capsulorrhexis by simple aspiration with 10 cc syringe and a small 90g cannula. The silicone gel was noted to be gooey (glue like), sticky, stringy and required slightly more force to aspirate than required for the initial injection.

Re-implantation of an injectable Silicone polymer or a hydrophobic acrylic IOL was associated with slightly more inflammation than seen in the primary surgery. Most inflammatory signs resolved by 3 weeks, which is slightly longer than the primary surgery. Persistent posterior synechiae was similar to that seen with standard IOL surgery in rabbits.

Conclusion: Injectable lens removal was readily accomplished by simple aspiration and successfully replaced with either an injectable silicone polymer or foldable hydrophobic acrylic IOL in NZ white rabbits.

32. A SYNTHETIC ACCOMMODATION APPARATUS: POTENTIAL USE IN ACCOMMODATION RESEARCH

Andres Bernal

Background: Accommodation research has relied heavily on animal model tissue or human donor tissue to perform ex-vivo testing and research on accommodation mechanics. Biological tissue properties are subject to variation, depending on factors like postmortem time, age/ health of the donor, storage conditions, and individual anatomical variations amongst others. This introduces variables that are sometimes very difficult to account for during accommodation simulation experiments and analysis. A synthetic model of the accommodation apparatus would provide an available, consistent and customizable structure that could be replicated and used to perform ex-vivo research experiments, or calibration of research equipment such as lens stretchers. Thus, the objective is to create an artificial anterior segment with properties that mimic ex-vivo tissues and thus giving reproducible results.

Methods: Design of a simplified geometrical model of the human eye accommodation apparatus was done using Solid Works. Tissue characteristics were obtained from the literature. 3-D printing using "digital materials" having customizable characteristics were used.

Results: Prototypes of the anterior segment that comprise a portion of the sclera, a zonular region and a lens consisting of a lens capsule and a removable cortex was fabricated. Using an operation microscope, experimental exam

and cataract surgery were performed on the model by a surgeon.

Conclusion: Reproducible artificial anterior segment models of human and animal eyes with variable tissue characteristics can be made and refined for use in accommodation research.

33. FOLLOWING UP ON ANATOMICAL PREREQUISITES FOR ACCOMMODATION: THE OPEN BAG CONCEPT

Philippe Sourdille

Purpose: Keeping the whole capsular bag transparent by permanently separating both capsules and keeping the anterior capsule away from the IOL optic.

Methods: The Concept 360 (Cornéal, 2000) IOL has six angulated (10°) haptics coming into contact at the capsular bag equator, keeping the anterior capsule away from the IOL optic. From the initial design, derived a second IOL: Le Ring (Cornéal-Croma laboratoires) with an adaptable circular ring attached to the IOL. The Concept 360 was experimented on post mortem eyes (Miyake Apple views) and clinically tested thereafter. Le Ring was tested on post mortem eyes to control adaptability to different capsular bags diameters and separation of both capsules.

Results: the incidence of YAG capsulotomy (Concept 360) at 5 years was inferior to 4% and the anterior capsule, distant from the IOL optic was totally transparent in 90% of cases. Le Ring demonstrated experimental (Miyake-Apple views and OCT) capsular diameter adaptability, posterior capsule immediate contact, and anterior capsule away from the IOL optic.

Conclusion: The open bag concept is feasible and efficient. Since our initial work three new models confirm the study: Visiogen AMO Synchrony IOL, Anew Optics IOL, Capsular Adhesion Prevention Ring (CAPR, Nagamoto).

The Accommodation Club



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