

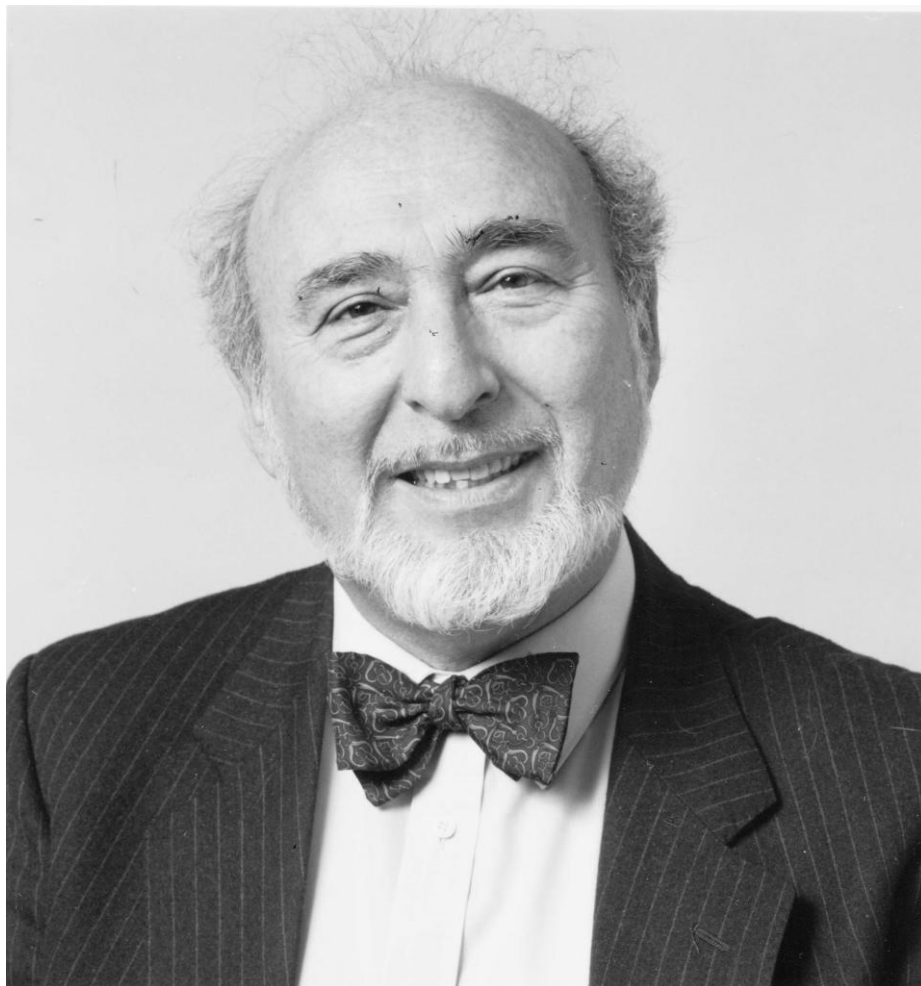
# **“Developments in Visual Science”**

**“Function meets Morphology”**

**9<sup>th</sup> to 11<sup>th</sup> of June, 2010**

**Munich**

***In honour of Professor G. B. Arden’s 80<sup>th</sup> birthday***



# Munich, Bavaria



## Kardinal-Wendel-Haus, Mandlstraße 23 • 80802 München



## **Geoffrey B. ARDEN - CURRICULUM VITAE**

**Born:** April 6th, 1930 in London, England.

**Educated:** Christ's Hospital 1940 - 1947  
University College, London 1948 - 1951  
University College Hospital, London 1951 - 1957

**Degrees:** B.Sc. (1st Class Hons.) 1951  
Ph.D. 1953  
MB.BS. 1957  
FR.C. Ophth 1989

### **Positions Held:**

1957 House Physician, University College Hospital.  
1958 House Surgeon, Whittington Hospital.  
1959 Wernher Fellow of the Royal Society.  
1960 Research Assistant, Institute of Ophthalmology.  
1961 Lecturer, Institute of Ophthalmology.  
1963 Senior Lecturer, Institute of Ophthalmology.  
1966 Reader, University of London.  
1967 Hon. Consultant, Moorfields Eye Hospital. Director, Electrodiagnostic Department.  
1969 Professor, Institute of Ophthalmology, Head, Department of Neurophysiology.  
1970 Department of Visual Science  
1982 Department of Clinical Ophthalmology  
1988 Department of Electrophysiology and Psychophysics

### **Foreign Appointments, Travelling Fellowships etc:**

1959 Maria Andersen Stifteljse (Royal Academy, Sweden).  
1961 Visiting Professor, University of California, San Francisco.  
1968 Visiting Professor, S.U.N.Y., Buffalo.  
1972 Visiting Professor, S.U.N.Y., Buffalo.  
1978 Visiting Professor, N.Y.U. Department of Ophthalmology.  
1984 Visiting Professor, University of Sydney, Department of Ophthalmology  
1985 Visiting Professor, University of Sydney, Department of Ophthalmology  
1992 Visiting Professor, University of Gottingen  
1994 Visiting Professor, University of Amsterdam  
1995 Visiting Professor, City University

### **Honours and Awards:**

1954 F.M.R. Walshe prize, 1954.  
1968 Edridge Green Lecturer.  
1978 Doyne Medal.  
1978 Hon.Member, Hellenic Ophthalmological Society.  
1984 McGaffy Memorial Medalist, University of Sydney.  
1986 Special guest lecture, 90th meeting of the Ophthalmological Society of Japan

1988 Scientific Board, Pakistan RP Society  
1988, Board Member, Int. Soc. Clin. Electrophysiology of Vision  
1989 Mackenzie Lecture and Medal  
1990 Annual Honorary Lecture, Swedish Ophthalmological Society  
1990 Medal, Swedish Academy of Medicine  
1991 Medal Keio University, Yokyo, Japan  
1994; Honorary Member of ISCEV  
2008 Honorary Fellow, Royal College of Ophthalmologists

### **Membership of Societies, etc:**

Royal College of Physicians.  
Royal College of Surgeons.  
Physiological Society.  
Photobiology Society.  
Royal College of Medicine.  
Int.Soc. Clinical Electrophysiology of Vision (ISCEV)  
Association for Research in Vision & Ophthalmology.  
Ophthalmological Society of the United Kingdom.  
Brain Research Association.  
Royal College of Ophthalmology  
Association for Eye Research  
Daltonia  
Jermov (Joint assn of European Professors of Ophthalmology & VisualSciences)

### **Publications in Journals**

1. Arden, G. B. and Weale, R. A. (1953).

"Variations in the latent period of vision." J. Physiol., 122(1): 12P-

and many others

343. G.B. Arden<sup>1</sup>, M. K. Gündüz<sup>2</sup>, A. Kurtenbach<sup>4</sup>, M. Völker<sup>3</sup>, E. Zrenner<sup>4</sup> S.B. Gündüz<sup>5</sup>, Ü. Kamis<sup>2</sup>, B. T. Öztürk<sup>2</sup>, and S. Okudan<sup>2</sup>

"A Preliminary trial to determine whether prevention of dark adaptation affects the course of early diabetic retinopathy", Eye, 2010.

### **Books**

Arden GB (1976). The Retina: neurophysiology. In The Eye Vol.II ed. Davson H. (Academic Press).

Arden GB and Heckenlively J eds. The principles and practice of Clinical Electrophysiology of Vision (1991) Mosby, Yearbook Med pub. Chicago 881 pgs

Arden GB and Heckenlively J eds. The principles and practice of Clinical Electrophysiology of Vision 2<sup>nd</sup> Edition (2006) MIT Press Harvard 1016 pgs.

Geoffrey B. Arden	Professor of Visual Sciences Honorary Fellow of the Royal College of Ophthalmology City University London Northampton Square London EC1V 0HB
Michael Bach	Professor Dr. rer.nat. Head of section funct. Research and Electrophysiology University Freiburg, <b>President of ISCEV</b>
Thomas Berninger	Professor of Ophthalmology University Eye Hospital, Munich
Alan C. Bird	Professor of Ophthalmology, Institute of Ophthalmology Moorfields Eye Hospital, London EC1V 2PD, UK
Kemal Gündüz	Professor, Ophthalmology and Visual Sciences Meram Medical Faculty. Selcuk University. Konya, Turkey
Marko Hawlina	Professor and Chair of Ophthalmology at University of Ljubljana, Slovenia, and President of the Slovenian Society of Ophthalmology
John Heckenlively	Professor, Ophthalmology and Visual Sciences Paul R. Lichter Professor of Ophthalmic Genetics Kellog Eye Center Michigan US
Don Hood	Professor of Psychology, Professor of Ophthalmic Sciences (Ophthalmology), Dept. of Psychology Columbia University
Chris Hogg	Moorfields Eye Hospital, London, UK, Department of Electrophysiology
Graham Holder	Professor, Moorfields Eye Hospital, London, UK Department of Electrophysiology, <b>President of EVER</b>
Anselm Kampik	Professor and Chair of Ophthalmology at University of University Eye Hospital, Munich
Helga Kolb	Professor Emeritus of Ophthalmology and Visual Science at the John Moran Eye Center, University of Utah
Bart Leroy	Professor, Ophthalmology and Visual Sciences Department of Ophthalmology, Ghent University Hospital

Yozo Miyake	Professor, Ophthalmology and Visual Sciences, Department of Ophthalmology, Nagoya University School of Medicine, Nagoya, Japan, <b>former ISCEV President</b>
Sven-Erik Nilsson	Professor, Ophthalmology and Visual Sciences Department of Ophthalmology, Linköping University, Linköping, Sweden, <b>former ISCEV President</b>
Günther Rudolph	Professor of Ophthalmology University Eye Hospital, Munich
Mathias Seeliger	Professor of Ophthalmology, Division of Ocular Neurode- generation Centre for Ophthalmology, Tübingen
Paul Sieving	Professor, Ophthalmology and Visual Sciences Director of the National Eye Institute at the National Institutes of Health (NIH)
Detlev Spiegel	Professor für Augenheilkunde Augsburg/ University Regensburg
Werner Spileers	Full Professor of Ophthalmology Faculty of Medicine, Katholieke Universiteit Leuven
Olaf Strauss	Professor Dr. rer. nat. Experimentelle Ophthalmologie, Klinik und Poliklinik für Augenheilkunde, Universität Regensburg
Dorothy Thompson	Great Ormond Str. London UK Head of Electrophysiology department
Hannes Wildberger	PD, Head of electrophysiology department University Eye Hospital. Zürich, Switzerland
Eberhart Zrenner	Professor of Ophthalmology, Director and Chairman Department for Pathophysiology of Vision and Neuro- Ophthalmology University Eye Hospital of Tübingen <b>former ISCEV President</b>

## **Wednesday 9<sup>th</sup> of June, 2010**

15:00 – 17:30      Registration

17:30 – 17:45      Opening of the meeting

**Anselm Kampik  
Thomas Berninger**

## **Retina (Function and Morphology)**

17:45 – 18:30      Structure of the Retina

**Helga Kolb**

18:30 - 19:15      Genetics and Genterapy

**Paul Sieving**

19:30 -              **Reception in the garden**

**all participants**

## Thursday 10<sup>th</sup> of June, 2010

### Clinical Retina

9:00 - 9:45	What have we learned from focal macular ERG?	<b>Yozo Miyake</b>
9:45 - 10:15	Autofluorescence in retinal diseases	<b>Marko Hawlina</b>
10:15 - 10:45	Morphology and Imaging	<b>Anselm Kampik</b>
10:45 - 11:15	<b>coffee break</b>	
11:15 - 12:00	Clinical Retina: Imaging and Electrophysiology	<b>Bart Leroy</b>
12:00 - 12:30	Diagnostic in retinal diseases	<b>John Heckenlively</b>
12:30 - 13:00	Stimulating degenerating retina with currents: A new field of Clinical Electrophysiology of Vision	<b>Eberhart Zrenner</b>
13:00 - 14:00	<b>Lunch</b>	

### Free papers

14:00 - 14:15	Responses to the Argus II retinal prosthesis	<b>Gislin Dagnelie</b>
14:15 - 14:30	Signal to noise ratio of the multifocal VEP	<b>Thomas Meigen</b>
14:30 - 14:45	Chromatic VEPs	<b>Anthony Robson</b>
14:45 - 15:00	Nonorganic visual impairment	<b>Guenther Niemeyer</b>
15:00 - 15:15	Simple tests of chromatic saturation	<b>Hermann Krastel</b>
15:15 - 15:35	Simulation of human colour processing	<b>Frank Siebert</b>
15:35 - 16:00	<b>coffee break</b>	

## **Electrophysiology and Function**

16:00 - 16:45	Function of the pigment epithelium and the retina	<b>Olaf Strauss</b>
16:45 - 17:15	Functional aspects of gene therapy	<b>Mathias Seeliger</b>
17:15 - 17:45	Electrophysiology and imaging in paediatrics	<b>Dorothy Thompson</b>

## **Poster Session**

17:45 - 18:30

Correlation of visual field limits	<b>Peter Ahnelt</b>
Nifedipine alters the light rise of the EOG	<b>Paul Constable</b>
Simulation of responses to FIS	<b>Roland Gemperlein</b>
VEPs in optic disc swelling	<b>Christina Gerth</b>
Age-related changes in the PERG	<b>Anne Kurtenbach</b>
Electrophysiology in neurosensory detachment	<b>Anja Palmowski</b>
How is the object in the vitreous perceived?	<b>Kei Shinoda</b>
Treatment potential of valproic acid	<b>Radouil Tzekov</b>
Retinal topography in retinal degenerations	<b>Inna Zolnikova</b>
Stimulating degenerating retina with currents	<b>Florian Gekeler</b>
	<b>Eberhart Zrenner</b>

19:30

**Bavarian Evening in the garden**

## Friday 11<sup>th</sup> of June, 2010

### Electrophysiology and Imaging

9:00 - 9:30	VEP and Brain	<b>Michael Bach</b>
9:30 - 10:00	PERG, OCT and Autofluorescence	<b>Graham Holder</b>
10:00 - 10:30	OCT and electrophysiology in optic nerve diseases	<b>H. Wildberger</b>
10:30 - 11:00	<b>coffee break</b>	
11:00 - 11:20	Approaching (Sub-) cellular resolution in an in-vivo retinal imaging with ultrahigh resolution optical coherence tomography (UHR).	<b>Peter Ahnelt</b>
11:20 - 11:45	GDx+HRT+ Electrophysiology in glaucoma	<b>Detlev Spiegel</b>
11:45 - 12:00	Topographic mapping of retinal function SLO-mfERG	<b>Günther Rudolph Thomas Berninger</b>
12:00 - 12:30	Comparisons of Local Structural and Functional Damage in Patients with Glaucoma	<b>Don Hood</b>
12:30 - 13:30	<b>Lunch</b>	
13:30 - 13:45	The Arden Effect: A bibliometric analysis of the impact of Geoffrey Arden's research	<b>Pamela Sieving</b>
13:45 - 14:05	Technical developments by Geoffrey Arden	<b>Chris Hogg</b>

### Colour and Psychophysics

14:05 - 14:20	Colour Contrast sensitivity (CCS): Basics	<b>Thomas Berninger</b>
14:20 - 14:40	CCS and Diabetes and glaucoma	<b>Kemal Gündüz</b>
14:40 - 15:00	CCS: Clinical value	<b>Werner Spileers</b>
15:00 - 15:30	<b>coffee break</b>	

### Diabetes and AMD

15:30 - 16:00	A new therapy of diabetic Retinopathy	<b>Geoffrey Arden</b>
16:00 - 16:45	Cell death in geographic atrophy: Function meets morphology	<b>Alan Bird</b>
<b>19:00 -</b>	<b>Gala diner and birthday party</b>	
	55 years of electrophysiology	<b>Sven-Erik Nilsson</b>

Wednesday: 17:45 -18:30

## ***Helga Kolb***

### **STRUCTURE OF THE RETINA**

Helga Kolb, Ophthalmology and Visual Science at the John Moran Eye Center,  
University of Utah

Understanding the organization of the vertebrate retina has been the goal of many talented visual scientists during the past 30 years. With Cajal's (1892) anatomic descriptions of the cell types that constitute the retina in a number of vertebrate species, and with an early understanding of the role of visual purple in photochemistry in combination with psychophysical studies of adaptation and color vision, we had in the sixties the rudiments of an understanding of how the retina might be organized and functioning. To go further, though, we were beginning to need detailed information of neural circuits that underlay these functions. It was the advent of electron microscopy, microelectrode recording techniques, and pharmacology that then allowed us an era of very rapid advancement. The purpose of this presentation is to summarize these recent advances and to describe our present understanding, based primarily on anatomic investigations, of the underlying architecture of four important functional circuits in the vertebrate retina. A naive understanding of the retina emphasizes only the sensory photoreceptors and the ganglion cells; however, it is evident on deeper probing that there are many interneurons packed into the central nuclear layer here (Fig. 1) and the neuropil layers, particularly the inner plexiform layer (IPL), are thick and composed of a tangle of interconnecting neural profiles. The first area of neuropil is the outer plexiform layer (OPL), where connections between rod and cones and vertically running bipolar cells and horizontally oriented horizontal cells occur. The second neuropil of the retina, the IPL, functions as a relay station for the vertical information-carrying nerve cells, the bipolar cells, to connect to ganglion cells. Moreover, a multitude of different varieties of horizontally and vertically directed amacrine cells somehow interact in further networks to influence and integrate the ganglion cell signals. It is only at the culmination of all this neural processing that the message concerning the visual image is transmitted to the brain along the optic nerve. The central question for many of us concerns what kinds of interaction are going on between the cells of the layers of the retina before the visual message is sent to the brain. Clearly, the retina is more than just photoreceptors and ganglion cells, and we need to understand what circuits of neurons are interposed between the photoreceptors and the optic nerve and how they are organized for functional roles.

Wednesday: 18:30 -19:15

## ***Paul Sieving***

### ***GENE, GENETICS, GENOMICS AND GENE THERAPY***

Paul A. Sieving, M.D., Ph.D.  
Bethesda, MD, USA

Over the last two decades, discovery for retinal disease has focused on gene identification. Currently more than 150 disease-causing genes have been identified for retinal dystrophies and diseases. Concurrent attention focused on the pathophysiology of the gene mutations that disrupted cell function and lead to vision loss from cell death. Beyond the single-gene Mendelian traits, genetics is beginning to uncover the basis of complex traits that cause the more common eye diseases such as age-related macular degeneration (AMD), which affects eight million U.S. adults. A common coding variant in the complement factor H gene was identified and shown to account for nearly 40% of the genetic AMD risk. Additional gene discovery has further implicated the complement cascade in AMD etiology and the possible interaction of environmental factors with genetic susceptibility is currently being explored.

The wealth of ophthalmic genetic information has paved the way for the development of interventions such as direct gene therapy, small molecules, neurotrophic factors, nanomedicine and cell-based systems. The recent gene therapy success for Leber congenital amaurosis has solidified proof-of-concept for human gene-based interventions. While we still have substantial clinical and biological research ahead to define how gene variants or mutations cause or contribute to disease phenotypes, the investment in basic research is beginning to pay dividends in medicine and health care. An overview will be given, along with a short description of our work to develop gene therapy for one of these conditions.

Thursday: 9:00 - 9:45

## ***Yozo Miyake***

### **WHAT HAVE WE LEARNED FROM FOCAL MACULAR ERG?**

*Yozo Miyake*, (Aichi Medical University)

During the past 30 years, I have been focusing on focal macular ERG (FMERG) as one of my life works. In 1982, we developed the system with which we can record FMERG showing many components of photopic ERG, including a-wave, b-wave, d-wave, OPs and PHNR under the fundus monitor with infrared TV fundus camera. This system is now still being used, providing many interesting findings of the human macular function, particularly when FMERG is compared with OCT. The unique distribution of macular OPs and the sensitive indicator of macular OPs in some macular diseases are worthy of special mention.

The system can be used for evaluation of macular function in monkey. An example will be shown in a family with autosomal dominant of age-related macular degeneration.

The most exciting discovery using FMERG is "Occult macular dystrophy", which is not a rare disease. Some of them show autosomal dominant heredity, and we found a big family recently in Japan. The future study of occult macular dystrophy will be discussed.

Thursday: 9:45 - 10:15

## ***Marko Hawlina***

### **AUTOFLOURESCENCE IN INHERITED RETINAL DISEASES**

Marko Hawlina, Martina Jarc, Petra Popović, Eva Lenassi, Jelka Brecej  
Eye Hospital, University Medical Centre Ljubljana, Slovenia

Current emphasis on autofluorescence imaging of the retinal pigment epithelium in different retinopathies show distinct patterns which enable identification of the exact location and dynamics of the pathological process. Distinct patterns of autofluorescence have been identified in most prevalent inherited retinal diseases such as retinitis pigmentosa, Best disease, Stargardt disease, cone-dystrophy, cone-rod dystrophy, acromathopsia and others. Comparison of the cross sections of autofluorescence patterns with spectral OCT and functional assessment with microperimetry and electrophysiology reveal exact degree of photoreceptor loss, which is of great help in non-invasive assessment and understanding of the nature and progression of these diseases.

Thursday: 10:15 – 10:45

## ***Anselm Kampik***

### **MORPHOLOGY AND IMAGING IN CLINICAL RETINA**

Anselm Kampik, University Eye Hospital, Munich

Detailed morphology in retinal disorders was largely dependent the examination of autopsy eyes or surgical specimens. Although this remains of high importance new technical advances have opened new imaging techniques in vivo to obtain not only structural details from the diseased retina. These modalities also allow by combining different imaging techniques pathogenetic and perhaps even functional insight in retinal disorders.

The presentation will discuss today's clinically available imaging modalities, which have a high impact on therapeutic decisions. These include wide angle imaging as well as OCT, fluorescein angiography and autofluorescence imaging of the RPE, and ultrasound findings.

Finally, new modalities of functional molecular imaging techniques will give further insight into understanding of retinal diseases, although they are not readily available in clinical use.

Thursday: 11:15 – 12:00

## ***Bart Leroy***

### **CLINICAL RETINA: IMAGING AND ELECTROPHYSIOLOGY**

Bart P Leroy  
Ghent University Hospital & Ghent University, Ghent, Belgium

**Purpose:** to illustrate the importance of electro-oculography (EOG) and imaging as detective tools in the identification of the underlying cause of disease in inherited dystrophies of the retinal pigment epithelium (RPE).

**Methods:** a case presentation format will be used to present data on how the EOG and imaging can assist in identification of the pathogenetic cause of disease in retinal dystrophies.

**Results:** EOG in combination with imaging and electroretinography is not only able to identify cases of Best vitelliform macular dystrophy (BVMD), but also provided the basis for the recent identification of mutations in the *BEST1* gene as the cause of disease in autosomal dominant vitreo-retino-choroidopathy (ADVIRC) and autosomal recessive bestrophinopathy (ARB).

**Conclusions:** identification of mutations in the *BEST1* gene as the cause of disease in ADVIRC and ARB, in addition to BVMD, were guided by results of the EOG and imaging. Consequently, the EOG is again confirmed as an essential tool for identification of RPE-related disease in the electrophysiologists detective arsenal.

Thursday: 12:00 – 12:30

## ***John Heckenlively***

### **DIAGNOSTIC ELECTROPHYSIOLOGY**

John R Heckenlively, Kellogg Eye Center, University of Michigan Ann Arbor, Michigan USA

There are many powerful features from employing electrophysiologic testing. Testing often confirms diagnoses in patients with minimal clinical findings, and can be used to objectively follow patients. The tests themselves often point to specific layers or cell types of the retina, or parts of the visual pathway in which the disease is having the maximal effect, and in many cases, the standardized approach to testing, often points to specific diagnoses, or at least categories of disease. Electroretinography in particular has been extensively utilized in research to document and understand the many retinal dystrophies and degenerations. Derivatives of standard electroretinography have evolved which more specifically address macular function (e.g. mfERG), or central inner retinal function (pattern ERG). Non-invasive morphological imaging techniques also have advanced in the last decade, so that autofluorescence imaging and optical coherent tomography have assume prominent roles in diagnostic testing or functional assessment, often complementing the electrophysiology and psychophysical testing. The expansion of testing now available gives a much broader understanding of a patients' disease processes than would have been possible compared to the simple ERG of 20 years ago.

Two disease groups, Occult Foveal Dystrophy and Autoimmune retinopathy, which have been enhanced by the expanded testing evaluations now available, will be discussed.

**Occult foveal dystrophy** (Occult macular dystrophy) was first described and concept developed by Professor Yozo Miyake. While dominant pedigrees have been identified, most patients who meet the diagnostic criteria are sporadic occurrences. These formerly normal patients present with sudden loss of central vision, normal full field ERGs, and focally abnormal multifocal ERGs. Inspection of the maculae shows no discernible changes. The initial OCT is often normal, and later may progress to show foveal atrophy. A few cases may show later diminution of the full field ERG. Currently the causes of this disorder are unknown, and it is difficult to explain given the anatomy of the fovea what pathologic events are occurring. Possible explanation would be mitochondrial mutations affecting the foveal function only, anti-retinal antibodies to the fovea.

**Autoimmune retinopathy** (AIR) is a complex group of disorders whose patients have in common that they have circulating antiretinal antibodies at higher levels than normal, and most (>70 %) have family histories of other family members with

autoimmune disorders. The disease may present as a paraneoplastic event or may occur secondary to head trauma, as a secondary feature of a retinal degeneration, or idiopathic. AIR was first identified by Keltner, Ross, and Thirkill as an autoimmune reaction to recoverin a 23kD protein in the visual transduction cascade, which appears to be a potent antigen in susceptible individuals. They found that patients with cancer associated retinopathy (CAR syndrome) had antibodies to this protein, and later studies showed that the antibodies were pathologic.

Subsequently, other patients with autoimmune retinopathy have shown antibodies to a variety of antigenic retinal proteins including: 30kD carbonic anhydrase, 35kD transducins- $\beta$ , 36kD aldolase C, 46kD  $\alpha$ -enolase, 46kD aldolase A, 48kD arrestin, 65 kD heat shock protein-70, 78kD TULP-1, 141 kD Intra- retinal binding protein and others. Much of the variability found in AIR patients is dependent on the mixtures of anti-retinal antibodies that the patients have and how long they have had them. Patients with strong family histories of autoimmune disorders often have more severe AIR. Other paraneoplastic disorders have been identified ranging from rare conditions such as lymphoma and tetratomas, to melanoma associated retinopathy, and a new related putative AIR group, naevus associated retinopathy. A majority of MAR cases have had anti-aldolase antibodies along with anti-recoverin and  $\alpha$ -enolase.

Electroretinographic testing is particularly helpful in making the AIR diagnosis in this group of retinopathies. Patients present with symptoms similar to RP, though with symptoms of much shorter duration. On clinical examinations the patients usually demonstrate no pigment deposits in the retina, although the visual field is typically abnormal with contraction or large scotomatous areas. A very abnormal ERG is found confirming that a retinopathy is present, and in conjunction with the other findings has a high correlation with the diagnosis of AIR or AZOOR.

Thursday: 12:30 - 13:00

## ***Eberhart Zrenner***

### **STIMULATING DEGENERATING RETINA WITH CURRENTS: A NEW FIELD OF CLINICAL ELECTROPHYSIOLOGY OF VISION**

Eberhart Zrenner, Florian Gekeler  
Center for Ophthalmology, University of Tübingen, Germany

**Purpose:** To explore the effect of electrical stimulation on restoring functions of the eye:

1. by using subretinal electrode arrays to provide images to blind patients
2. by using global electrical stimulation for improvement of remnant visual function on the basis of the hypothesis that this may liberate neurotrophic factors, as indicated in preclinical experiments.

#### **Methods:**

Ad 1. Electronic microphotodiode arrays (MPDAs) with 1500 amplifiers and electrodes were implanted subretinally in 11 RP-patients;

Ad 2. The effect of 6 sessions of transcorneal stimulation (30 min, weekly) was assessed in 24 RP-patients (either 150%, or 66% of psychophysical threshold, in comparison to sham-stimulation, n=8 each).

#### **Results:**

1. MPDAs allow previously blind patients to detect and name unknown objects, decipher words, discern 7 shades of grey and move freely towards persons.
2. Regular transcorneal stimulation showed a clear tendency to improve visual acuity, area of visual field and electrical phosphene threshold in stimulated patients vs. sham

**Conclusion:** New electrophysiological tools allow improvement of vision in various stages of retinal degeneration, including blindness.

**Acknowledgement:** We are grateful to study physicians Drs. Bruckmann, Naycheva, Stingl, Röck, Wilhelm and Wilke, to surgeons Drs. Besch, Bartz-Schmidt and Sachs and support from Federal

Thursday: 14:00 -14:15

## ***Gislin Dagnelie***

### **VISUAL FUNCTION WITHOUT PHOTORECEPTORS: NONINVASIVE RECORDING OF RETINAL AND FUNCTIONAL RESPONSES TO THE ARGUS™ II RETINAL PROSTHESIS**

Gislin Dagnelie, Chris Stronks, Argus™ II Study Group  
Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD, USA

**Purpose:** Several dozen groups around the world are engaged in the pursuit of functional visual prostheses for patients blind from degenerative diseases or other adventitious causes. Among several groups that have brought retinal implants into early clinical studies. Second Sight Medical Products and its 10 clinical partners have collected by far the largest body of clinical data, studying 30 recipients of the Argus™ II implant in Europe and the US, for up to three years. Five of these implant recipients participate in regular tests at our center. Despite the volume of functional results very little is known about the fundamental response of the degenerated human retina to electrical stimulation.

**Methods:** We have recently embarked on a study of the ERG and VEP evoked by activation of the Argus™ II electrode array. Argus™ II implant wearers are fitted with DTL corneal electrodes and/or Ag-AgCl scalp electrodes for standard electrophysiological recordings. Using the Espion clinical electrophysiology system, continuous epochs of raw ERG and EEG signal are recorded, while the Argus™ II implant is being stimulated by its laboratory control system. The stimulation artifact serves as the trigger for post-hoc signal analysis and is sufficiently short to allow recovery of the subsequent retinal response. Until now, only synchronous multi-electrode stimulation has been performed, but we anticipate that multifocal stimulation of individual electrodes with standard m-sequence techniques will be possible.

**Results:** Preliminary analysis of ERG recordings shows that stimulus artifacts with amplitudes of several mV and trace contaminations by nearby power sources can be effectively removed, and that the residual signal is clean enough to allow responses in the range of 10-100 nV to be recovered, using standard off-line averaging and filtering techniques. Within the next few months we expect to be able to compare responses to multi-electrode stimulation across the five Argus™ II recipients at our center, and correlate the findings with differences in visual function and performance among these individuals.

**Conclusion:** Standard electrophysiology techniques can be employed to study the activity of the degenerated retina, and provide insights into function of the severely degenerated retina.

Supported by NIH grant R21EY019991 and Second Sight Medical Products

Thursday: 14:15-14:30

## ***Thomas Meigen***

### **INCLUSION OF HIGHER ORDER KERNELS INCREASES THE SIGNAL-TO-NOISE RATIO OF MULTIFOCAL VEP RECORDINGS.**

Thomas Meigen, Philipp Müller  
Univ.-Augenklinik Würzburg, Germany

**Purpose:** Higher order kernel responses to pseudorandom m-sequence stimulation reflect nonlinearities of the visual system. So far, second and third order responses have been studied mainly in multifocal ERG recordings to flash stimuli. The purpose of the current study was to investigate whether (a) higher orders are present in multifocal VEP (mfVEP) recordings, and (b) whether these responses can be used to increase the signal-to-noise ratio of mfVEPs.

**Methods:** MfVEPs to dartboard stimuli with 6 wedge-shaped fields were recorded in 15 normal subjects with 3 different derivations (Oz – Fpz, and 2 bipolar occipital derivations). Within the stimulus fields eccentrically scaled checkerboard patterns were modulated with pattern reversal (PR) or pattern onset (PO) stimulation mode. The speed of the stimulation was varied between 1, 2, and 4 monitor frames per m-step. The length of the m-sequence was adjusted to yield an identical recording duration for all conditions. The signal strength was derived from a multifocal power function (MPF) which consisted in a summation of the squared mfVEP traces from all 6 fields.

**Results:** (1) Significant higher order mfVEP kernels were found up to the third order. (2) By slowing down the stimulation rate the MPF signal-to-noise ratio increased mainly for the earliest component below 130 ms. (3) A similar increase of the MPF amplitude and signal-to-noise ratio could be achieved by linear combination of all significant kernels up to the third order.

**Conclusions:** Although a slowing of the stimulation rate leads to fewer visual stimulations within the same time interval, the signal-to-noise ratio of the resulting mfVEP responses is increased significantly. A similar effect can be achieved by the inclusion of higher order kernels as the analysis is focussed on parts of the m-sequence cycle with fewer stimulations. The increased signal-to-noise ratio may help to improve functional testing of the retino-cortical pathway with mfVEPs.

Thursday: 14:30-14:45

## ***Anthony G. Robson***

### **OPTIMIZATION OF CHROMATIC VEPS USING LARGE MULTIPLE ANNULAR ISOLUMINANT STIMULI**

Robson AG<sup>1,2</sup> and Parry NRA<sup>3,4</sup>

Moorfields Eye Hospital, London, EC1V 2PD.<sup>1</sup> Institute of Ophthalmology, London, EC1V 9EL.<sup>2</sup> Vision Science Centre, Manchester Royal Eye Hospital, Manchester M13 9WH.<sup>3</sup> Faculty of Medicine, University of Manchester.<sup>4</sup>

**Purpose:** To optimize the koniocellular selectivity of large chromatic gratings using multiple annular isoluminant stimuli.

**Methods:** Blue/Green (B/G) gratings were generated within a circular stimulus (diameter 1.2 degrees) and within 7 concentric annular fields (maximum diameter 18 degrees) on a colour monitor. Each annulus was modulated along a tritan axis as determined using a minimum distinct border criterion. Isoluminance was determined for each annulus according to minimum flicker photometry, allowing generation of a large B/G grating that was isoluminant over the whole of the 18-degree stimulus area. The optimised B/G field was used to probe koniocellular function using 2Hz onset-offset VEPs and psychophysically-determined temporal tuning characteristics.

**Results:** Onset VEPs to achromatic and to standard 18-degree B/G fields were dominated by positive components. Large B/G gratings comprising of multiple isoluminant annuli elicited large chromatic-specific onset VEPs of negative polarity. Temporal tuning characteristics to achromatic stimuli were band-pass and to multiple annular isoluminant stimuli were low-pass, in keeping with the low temporal resolution of the koniocellular system.

**Conclusions:** Multiple annular isoluminant gratings may be used to optimise the koniocellular selectivity and amplitude of chromatic onset VEPs.

**Acknowledgements:** Foundation Fighting Blindness (AGR)

Thursday, 14:45 – 15:00

## ***Guenter Niemeyer***

### **NONORGANIC VISUAL IMPAIRMENT: FUNCTION FAILS TO MATCH STRUCTURE (?)**

Guenter Niemeyer and Daniel Barthelmes  
Deptm. of Ophthalmology, University Hospital Zuerich/Switzerland

**Purpose:** To show the role of electrophysiology in nonorganic visual disorder (dissociative, functional, or conversion disorder, visual conversion syndrome, hysterical amblyopia) and to examine the contemporary understanding .

**Methods:** Retrospective study of 20 patients. mean age 18yrs, 14 female and 10 male. Primarily Ganzfeld ERG recording (ISCEV standard) in addition to ophthalmologic examination. Consulting with colleagues from a psychiatric outpatient institution.

**Results:** The ERGs of 20 patients recorded over a period of 10 years revealed normal amplitudes and timing of rod-driven, mixed responses and cone-driven ERGs. Visual field defects and reduced visual acuity were the typical clinical symptoms. Psychological or emotional conflict situations were often detected. Retrospective psychiatric evaluation can be applied by interview and by a specific questionnaire.

**Conclusion:** Individual informing about the diagnosis and possibly advising by the ophthalmologist of patients or their parents with unexplained visual loss remains a challenge. It usually requires communication with a psychiatrist/psychologist, occasionally resulting in long term treatment, is required to unveil the underlying causes for thenonorganic visual loss. Functional magnetic resonance imaging of the cerebral response to visual stimulation points in a new direction. (D. J. WERRING et al, Psychological Medicine, 2004, 34, 583–589)

Thursday, 15:00 -15:15

## ***Hermann Krastel***

### **SIMPLE TESTS OF CHROMATIC SATURATION AND CHROMATIC ACUITY IN CLINICAL PRACTICE**

Hermann Krastel (1), Gerold Kolling (2), Sven Beutelspacher (1)

(1) Dept. of Ophthalmology, University Medical Center Mannheim, Germany

(2) Dept. of Ophthalmology, University of Heidelberg, Germany

**Purpose:** To apply simple tests of chromatic acuity and chromatic saturation in limited conditions of examination

#### **Methods comprise:**

- i) A series of plates containing optotypes of graded colour contrast to examine the center of the visual field
- ii) The Kolling plate, consisting of a rectangular pattern of four red dots to observe suprathreshold chromatic saturation within the four quadrants of the visual field
- iii) Modified Velhagen plates to assess chromatic acuity in the visual field center

#### **Results:**

- i) Graded colour contrast plates are suited to show reduced colour contrast sensitivity in dystrophic retinal disease, e.g. RP, or in CAR;
- ii) Kolling plate results point to hemifield type or nerve fibre bundle defects in AION, in chiasmal impairment, and in lesions of the visual pathways;
- iii) Chromatic acuity as evaluated by modified Velhagen plates is useful in screening for axial opticopathies due to e.g. Ethambutol, tobacco & alcohol, and inflammatory affections.

**Conclusion:** These simple tests are useful tools in clinical diagnosis in particular, if conditions of examination are limited (severely diseased patients, or even bedside exam).

Thursday: 15:15 -15:35

## ***Frank Siebert***

### **SIMULATION OF HUMAN COLOR PROCESSING MECHANISM USING AN AMPLITUDE PHASE VECTOR MODELL**

Roland Gemperlein, Frank Siebert, Ludwig Maximilian University, Munich

**Purpose:** To reveal the interaction of color processing mechanism in the human retina.

**Methods:** Using a Michelson Interferometer and a broadband Xenon lightsource a spectral modulated stimulus (Fourier Interferometric Stimulation, FIS) is generated. Retinal response is recorded by a cornea electrode and response amplitude and response phase is calculated by fourier transformation. A modell based on amplitude phase vector addition was set up to simulate retinal response.

**Results:** The response for a wide range of different measurement parameters, e.g. frequency, luminance and colour can be simulated using 5 independend subsystems with different spectral sensitivities and temporal response properties.

**Conclusion:** Retinal response to FIS is composed of 5 subsystems (3 with single source input, 2 with antagonistic input of 2 sources) which interact according to vector addition manner.

Thursday: 16:00 -16:45

## ***Olaf Strauss***

### **FUNCTION OF THE PIGMENT EPITHELIUM AND THE RETINA**

Olaf Strauss, University Eye Hospital, Regensburg, Germany

The retinal pigment epithelium (RPE) is a monolayer of pigmented cells which faces with its apical membrane the light-sensitive outer-segments of the photoreceptors and with its basolateral side the bloodstream of the choroid. The RPE form a part of the blood/retina barrier and interacts closely with the photoreceptors. In this interaction the RPE forms a functional unit with the photoreceptors: mutations in genes expressed in the RPE can lead to primary photoreceptor degeneration and vice versa. In this interaction the RPE fulfills a lot of different tasks: absorption of light, secretion, transepithelial transport of water, ions or nutrients, phagocytosis of photoreceptor outer segments and recycling of all-trans retinal in the visual cycle. Alterations of one these functions are known to lead to different forms of retinal degenerations. Thus the understanding of the regulation of these tasks is of great importance to understand the patho-mechanisms leading to retinal degeneration. An important regulatory mechanism for these tasks is a change in intracellular free  $Ca^{2+}$ . For this purpose the RPE expresses a large number of different  $Ca^{2+}$  transporting molecules: voltage-dependent  $Ca^{2+}$  channels, heat-sensitive TRPV channels or constitutive active TRPC channels. Regulation of these ion channels leads to changes in cell function. Regulation of voltage-dependent channels leads to either change in secretory activity or phagocytosis. Bestrophin-1, the product of the gene which can lead to Best's macular dystrophy, strongly intervenes with  $Ca^{2+}$  homeostasis by modulation of voltage-dependent  $Ca^{2+}$  channels and release from cytosolic  $Ca^{2+}$  stores.  $Ca^{2+}$ -dependent mechanisms also regulate transport of water which driven by a transepithelial transport of  $Cl^-$ . Since these regulatory mechanisms involve the flux of ions they also are involved in the generation of RPE dependent signals in the ERG or EOG. The c-wave of the ERG is generated by a large apical membrane conductance for  $K^+$  whereas the light-peak in the EOG depend on the activity of bestrophin-1 and L-type  $Ca^{2+}$  channels in the basolateral membrane of the RPE. A disturbed regulation of L-type channels in RPE cells is involved in a changed secretion rate of VEGF leading to choroidal neovascularisation. Changes in the function of bestrophin-1 leads to altered L-type channel activity and thus to a decreased light-peak in the patient's EOG. The disturbed  $Ca^{2+}$  channel regulation by bestrophin-1 probably changes phagocytic activity of RPE cells. Activation of heat-sensitive TRPV2 channels would probably provide a base for beneficial effects in the treatment of retinal degeneration using laser treatment.

Thursday: 16:45-17:15

## ***Mathias Seeliger***

### **FUNCTIONAL ASPECTS OF GENE THERAPY**

Mathias W. Seeliger Division of Ocular Neurodegeneration, Institute for Ophthalmic Research, Department of Ophthalmology, Eberhard-Karls-University of Tuebingen, Germany

Several lines of promising therapeutic approaches for retinal degenerations have been developed in the immediate past years, but so far none has made such an impact as gene therapy.

In particular, the successful restoration of function using mainly recombinant adeno-associated viral vectors (rAAV) but also lentiviral vectors (LV) has been demonstrated in animal models, and has now led to human clinical trials.

The functional rescue of vision requires an adequate assessment at different sites along the visual pathway. Here, the focus is on electroretinography (ERG), *the* functional test in the clinical and experimental follow-up of retinal degenerations.

As the current treatment options commonly lead to areas of different functionality, it may require novel concepts and/or techniques to take care of the topographic differences, particularly with respect to potential alterations of regular retinal behavior.

This presentation addresses some of the issues associated with the assessment and the monitoring of therapeutic success, which eventually may become equally important to the diagnostic use in hereditary retinal degenerations in the future .

Thursday: 17:15 – 17:45

## ***Dorothy Thompson***

### **ELECTROPHYSIOLOGY AND IMAGING IN PAEDIATRICS**

Dorothy Thompson, Great Ormon Str. London UK

Young children, perhaps uniquely, benefit from a combination of all aspects of visual electrophysiology assessment - from retinal to cortex. Often the presenting sign of not looking and smiling at 'Mum' occurs in isolation, without any helpful diagnostic clues in fundus, family history or general health. It's this detective, diagnostic part of electrophysiology which has become all the more powerful when associated with imaging techniques and our increased understanding of genetics. Yet children are ungratefully indifferent to our burgeoning sophistication, they are great levellers and demand robust science.

Even today I use some of the data from my PhD on PERG which Neville Drasdo and I gathered with Prof Arden. Understanding the linear relationship between PERG amplitude and contrast was key to using the MTF to analyse PERG generators. Now it's key when coupled with pVEPs to investigate functional overlay and malingering. The PERG's n95 is valuable in distinguishing optic nerve from retinal disease in our young kidney patients. Today routine retinal imaging with micron resolution will directly quantify the loss of the RNFL and allow us to directly explore structure function correlations with n95 and indeed the ERG b-wave.

During my talk I hope to show the valuable role of visual electrophysiology in children as practised at Great Ormond Street Hospital for Children London, UK, for both routine and more unusual cases, together with some of the imaging techniques that are becoming clinically available.

## ***Poster session***

Thursday: 17:45 -18:30

### ***Peter K. Ahnelt***

#### **CORRELATION OF VISUAL FIELD LIMITS WITH HUMAN AND MAMMALIAN RETINAL FACIAL TOPOGRAPHIES BY VIRTUAL PERIMETRIC MODELING**

Peter K. Ahnelt (1), Carl Glittenberg (2), Mohamed Abdel Keream (1), Christian Schubert (1), Bence Viola (3),  
1) Dept. Physiology, Med. Univ. Vienna; 2) L. Boltzmann Inst. of Retinology, Vienna;  
3) Dept. Anthropology, Univ. Vienna, Austria.

**Purpose:** Establish a virtual perimetric system to study the variation of anatomical constraints on visual field limits in humans and mammals.

**Methods:** Virtual masks were obtained from human subjects taxidermy specimens and the masks' pupils were aligned to the center of a virtual perimetric dome (radius = 50 m) developed with Cinema 4D. For human subjects, the optimum positions of virtual floodlights (180°) along the mask's pupillary axis were identified by maximum congruence to related Goldmann visual field limits. This allowed to demarcate the unobstructed rays at a) the perimetric surface, and b) on a virtual ground floor related to eye level as well as to c) „paint“ facial elements obstructing the light path. The same procedures were then applied to primate and canine models.

**Results:** For humans, the resulting virtual contours concur with large-stimulus isopters and display the limiting roles of the nasal ridge, as well as the relatively extended ventral and temporal limits. In contrast, the facial design of chimpanzees and baboons obstructs significant portions of the ventro-medial foreground putting them at risk during bipedal locomotion. For a canid model, virtual perimetry demonstrates good accordance with its retinal visual streak organization: a small binocular central area accompanied by a far-reaching monocular temporal zone.

**Conclusion:** The virtual perimeter is able to delineate monocular and binocular visual field extensions and its projection on a virtual floor or other virtually (re-) constructed spaces. This allows assessment of intra- and interspecific variability in perceptive space as well as differentiation of peripheral visual field impairments from anatomical constraints.

***Paul Constable***

**NIFEDIPINE ALTERS THE LIGHT-RISE OF THE ELECTRO-OCULOGRAM IN MAN**

Paul Constable, Seema Rauniar  
City University, Department of Optometry, London UK

**Purpose:** Animal studies have demonstrated a reduction in the light-rise of the electro-oculogram (EOG) following L-type calcium channel inhibition. The principal aim was to use nifedipine, a specific, L-type calcium channel inhibitor to determine its effects on the light-rise of the EOG in healthy participants.

**Methods:** The EOG was recorded in 14 participants before and after a 10 mg oral dose of fast acting nifedipine. Heart rate was also measured during the recordings and the Arden index and time to peak of the EOGs before and after nifedipine compared. The mean  $\pm$  SEM oral dose was 142  $\pm$  26  $\mu$ g/kg.

**Results:** The light-rise of the EOG was significantly reduced in 57% of participants by 16.0  $\pm$  4.8% ( $p=0.006$ ) whilst in the remaining 43% of participants the light-rise increased by 12.2  $\pm$  2.2% ( $p=0.006$ ). There was no significant differences in the time to peak of the light-rise in those that showed an increase ( $p=0.4$ ) or a decrease ( $p=0.6$ ) in the EOG after nifedipine. Heart rate increased significantly after nifedipine ( $p=0.025$ ) in the group overall as well as those that showed an increased light-rise ( $p=0.012$ ). The heart rate in participants whose light-rise fell did not change ( $p=0.278$ ).

**Conclusions:** The L-type calcium channel is responsible for altering intracellular calcium in the RPE in man. Inhibiting this channel alters the amplitude of the light-rise of the EOG. The EOG may provide a useful clinical tool for assessing RPE-photoreceptor function in patients using L-type calcium channel inhibitors for ischemic retinal disease such as glaucoma.

## ***Roland Gemperlein***

### **SIMULATION OF RESPONSES TO FIS (FOURIER INTERFEROMETRIC STIMULATION) USING A VECTOR MODELL**

Roland Gemperlein, Frank Siebert, Ludwig Maximilian University, Munich

**Purpose:** To describe the effect of FIS on different structures in the human retina.

**Methods:** Using a Michelson Interferometer and a broadband Xenon light source a spectral modulated stimulus (Fourier Interferometric Stimulation, FIS) is generated. Retinal response is recorded by a cornea electrode and response amplitude and response phase is calculated by fourier transformation. A model based on amplitude phase vector addition was set up to simulate retinal response.

**Results:** The response for a wide range of different measurement parameters, e.g. frequency, luminance and colour can be simulated using 5 independent subsystems with different spectral sensitivities and temporal response properties.

**Conclusion:** Retinal response to FIS is composed of 5 subsystems (3 with single source input, 2 with antagonistic input of 2 sources) which interact according to vector addition manner.

**Christina Gerth**

## **THE ROLE OF VISUAL EVOKED POTENTIALS IN THE DIFFERENTIAL DIAGNOSIS OF OPTIC DISC SWELLING**

Gerth C, Tech, S, Guthoff R  
University of Rostock, Department of Ophthalmology, Germany

**Purpose:** To investigate visual evoked potentials (VEP) as a diagnostic tool to differentiate between inflammatory, vascular and others causes of optic disc swelling. **Methods:** Analysis of pattern reversal VEP P100 amplitude and latency in respect to final diagnosis. **Study design:** retrospective chart review. **Inclusion criteria:** uni- or bilateral optic disc swelling, examination period 1/2009- 12/2009.

**Results:** VEPs were recorded in a total of 21 patients with optic disc swelling with initially unknown etiology in one (n= 18) or both eyes (n=3). Snellen visual acuity ranged between 0.05 and 1.25. Diagnosis of optic disc swelling were: anterior ischemic optic neuropathy (AION) 7/21, optic neuritis (ON) 4/21, thyroid orbitopathy n=3, buried optic nerve head drusen=2, retinitis n=2, branch vein occlusion n=1, sinus venous thrombosis n=1, pseudotumor orbitae n=1. VEP responses were within normal limits in 7/21. Abnormal P100 amplitude and latency were found in 7/21 and significant amplitude reduction but normal latency in 3/21. Pattern VEPs from the affected eye were not recordable in 4/21. VEPs were abnormal in all patients with ON but only in 4/7 with AION. VEP responses were more severe affected in the NNO group compared with the AION group. Reduced visual acuity was associated with abnormal VEPs in the AION group.

**Conclusion:** Optic disc swelling can be associated with normal or abnormal VEP responses. Severe VEP response disruption point more to inflammatory than to vascular cause of optic disc swelling.

## **Anne Kurtenbach**

### **AGE-RELATED CHANGES IN THE PATTERN ERG: A COMPARISON OF MULTIFOCAL AND FULL-FIELD RECORDINGS**

Anne Kurtenbach, Nicola Ballerina, Andre Messias, Tobias Röck, Eberhard Zrenner  
Centre for Ophthalmology, Institute for Ophthalmic Research, University of Tübingen,  
Germany

**Purpose:** To compare multifocal recordings of the pattern-ERG with those of full-field recordings in normal subjects and to investigate alterations that occur with age in both measures.

**Methods:** One eye of 59 subjects, aged between 12 and 69 years, was examined and results grouped according to decade of life. DTL electrodes were used for all recordings. Multifocal pattern ERGs were obtained with the Veris 4.9.1 system (EDI) with a stimulus of 19 hexagons, grouped into 3 rings, which stimulated the central 20 deg of the retina. One run of approx. 7 min was performed. The luminance of the black-white pattern was 2 cd/m<sup>2</sup> and 102cd/m<sup>2</sup>, respectively. The Espion E<sup>2</sup> System (Diagnosys) was used for recording full-field pattern ERGs, with checkerboards of 2 spatial frequencies (0.8 deg and 0.25 deg) at 90.5% contrast and alternating at 4 Hz. The results of two runs, each of 128 sweeps, were averaged.

**Results:** The multifocal PERG recordings generally show decreases in mean amplitude for both positive and negative components with age, but are significantly largest in the 20-30 year-old group for all rings. The ratio of amplitudes between rings (ring 1/ring2 and ring 1/ring3) remains constant with age. There is tendency for delayed implicit times in the older eye which was significant between the oldest and youngest groups for the first negative component in ring 1 and the positive component in rings 2 and 3. Full-field pattern ERGs similarly have the largest amplitudes in the 20-30 year old group although the difference to other age groups is not significant, with a non-significant trend towards delays in latency with age for both check sizes.

**Conclusion:** Full-field and multifocal pattern ERG responses are comparable for all age groups tested. The finding that the highest amplitudes are not found in the youngest age group of subjects indicates that there may be a relatively slow maturation of inner retinal function.

## **Anja Palmowski-Wolfe**

### **ELECTROPHYSIOLOGICAL FINDING IN A CHILD WITH NEUROSENSORY DETACHMENT DUE TO AN OPTIC PIT**

Anja Palmowski-Wolfe, Margarita Todorova  
University Eye Hospital Basel

We report on an 8 year old with an optic pit OS, who was referred for evaluation of anisometropic amblyopia. His cycloplegic Refraction was: OD + 1.75 -0.5 A130, OS: + 3.5. On examination his best corrected visual acuity was OD: 1.0, OS: 0.5. His left eye only achieved a near acuity of 0.25.

On examination of the left eye, a light reflex, close to the vascular arcades raised the suspicion of a detachment of the neurosensory retina which was confirmed on OCT. Occlusion treatment for amblyopia was recommended. On follow up 3 months later, the 'subretinal cavity' was markedly improved on ophthalmoscopy and OCT. Distance acuity also improved to 0.8, near acuity to 0.6.

At this point in time electrophysiology was performed. Pattern VEP showed normal amplitudes OU but increased latencies OS. Amplitudes and latencies of the scotopic and photopic ERG were within the normal range OU. The EOG was normal OD but slightly pathologic OS (AQ 2.2, 2.6), suggesting some minor secondary (?) impairment of the RPE.

A multifocal ERG (mfERG) was performed according to ISCEV guidelines (VERIS, FMS III stimulator, DTL electrode, Lmx 200cd, Lmin <1cd). The first and second order mfERG was normal OD. In the left eye, good response waveforms were present at all eccentricities in both, first and second order, responses. In the first order response, amplitudes were markedly reduced in the central 30°. Latencies were slightly increased in a paracentral ring around the fovea. In the second order response, amplitudes were again markedly reduced and latencies prolonged in the left eye. Interestingly the perifoveal responses seemed to be affected most. In summary, good mfERG responses could be elicited from a child with a central detachment of the neurosensory retina even after several months of detachment. Both first and second order responses were affected, showing decreased amplitudes and increased latencies, especially in a parafoveal area. In contrast to the OCT which is very helpful to assess the extent of the neurosensory detachment, mfERG offers an additional tool for follow up of retinal function in this disorder. This may be especially important in children, where surgical intervention is rendered difficult due to the strong connection between vitreous and retina. Thus follow up seems a valid option in children. Better understanding of the predictive value of functional tests are needed in order not to miss the time-point where intervention becomes necessary.

## ***Kei Shinoda***

### **HOW IS THE OBJECT IN THE VITREOUS CAVITY PERCEIVED?**

Kei Shinoda<sup>1,2</sup>, Makoto Inoue<sup>2,3</sup>, Eiko Sugisaka<sup>2</sup>, Soiti Matsumoto<sup>1</sup>, Atsushi Mizota<sup>1</sup>, Masatoshi Furushima<sup>4</sup>, Yozo Miyake<sup>5</sup>.

<sup>1</sup>Department of Ophthalmology, Teikyo University School of Medicine, Tokyo, Japan

<sup>2</sup>Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan

<sup>3</sup>Kyorin Eye Center, Kyorin University School of Medicine, Tokyo, Japan

<sup>4</sup>Furushima Eye Clinic, Oita, Japan

<sup>5</sup>Department of Ophthalmology, Aichi Medical University, Aichi, Japan

**Purpose:** To investigate how patients perceive object in the vitreous cavity.

**Methods:** An interview about their visual sensations during surgery was conducted with the patient who underwent vitrectomy under retrobulbar anesthesia during and within 3 hours after vitrectomy. Several individual patients drew their visual experiences onto the fundus photograph. We analyzed the relationship between those visual perceptions and surgical procedures; i.e. core vitrectomy, triamcinolone acetonide injection, membrane peeling, and fluid/air exchange. In addition, a 74-year-old woman with an intravitreally luxated intraocular lens (IOL) in the right eye made drawings showing what she saw with the right eye. We compared the fundus picture showing the luxated IOL with patient's sketch and description.

**Results:** Patients perceived highly accurate details including the movements and color of the intravitreal objects during each surgical procedure. The patients' description and drawings appeared to arise mainly from the shadows cast by the intravitreal objects. The drawing and description by the 74-year-old woman were precisely the shape and colors of the encapsulated IOL with its loops.

**Conclusions:** The perception was obtained probably not through the normal optics of the eye. There is an undetermined mechanism that focuses intravitreal objects on the retina that does not use the optics of the eye.

## ***Radouil Tzekov***

### **TREATMENT POTENTIAL OF VALPROIC ACID IN AGE-RELATED MACULAR DEGENERATION AND RETINITIS PIGMENTOSA**

Radouil Tzekov<sup>1</sup>, Christine Clemson<sup>2</sup>, Jenna Chechi<sup>1</sup>, Mark Krebs<sup>3</sup>, Shalesh Kaushal<sup>1</sup>

1 - Ophthalmology, UMASS Medical School, Worcester, MA

2 - Office of Research, UMASS Medical School, Worcester, MA

3 - Ophthalmology, UF, Gainesville, FL

**Purpose:** Valproic Acid (VPA) is an FDA approved drug. Our lab has established this drug that exerts a unique set of biological activities on the retina including mitigating RPE and photoreceptor cell loss from oxidative stress or alternative complement pathway activation, improving fluid transport across the RPE and downregulating inflammatory/proangiogenic cytokines produced in the retina. The purpose of this retrospective analysis was to examine the efficacy and safety of VPA in patients with Retinitis Pigmentosa (RP) and age-related macular degeneration (ARMD).

**Methods:** A retrospective chart review of patients diagnosed with RP and ARMD and treated off-label with VPA (500 or 750 mg/day) was conducted. 15 ARMD patients (28 eyes) and 7 RP patients (13 eyes) met all inclusion and exclusion criteria. The patients were followed up for an average period of 22.7 weeks (ARMD) and 16 weeks (RP). Best –corrected visual acuity (BCVA) values were converted to logMAR and analyzed. In RP patients, visual fields (VF) for each eye were defined using digitized Goldmann Kinetic Perimetry tracings. OCT was performed in patients with wet ARMD.

**Results:** In ARMD patients, the average change in BCVA at the time of follow-up for all eyes was an improvement of -0.071 logMAR ( $\pm 0.25$ ) units, equivalent to 0.7 lines ( $\pm 2.5$  lines). BCVA improved in 12 eyes, remained unchanged in 11 eyes and worsened in 5 eyes. However, in patients taking 750 mg/day of VPA, BCVA improved in 11 eyes (61.1%), was unchanged in seven eyes (38.9%) and did not worsen in any eyes. Eleven patients (73.3%) reported subjective improvement in visual perception. For wet ARMD eyes for which central retinal thickness was measured (n=9), 6 eyes (67%) improved. In RP patients, the visual fields of 5 of 7 patients increased with treatment and in one case, the improvement was confirmed at two time points (23 and 27 weeks). Of the 13 eyes examined, 9 eyes had increased visual field (69%), 2 eyes (15%) had decreased visual field and 2 eyes (15%) experienced no change. Assuming typical loss in VF area without treatment, this increase in VF was statistically significant ( $p < .02$ ). An average decrease in logMAR scores was seen in the 13 RP eyes, which was significant ( $p < .02$ ) assuming no loss in acuity without treatment. In both groups, side effects were mild and well tolerated.

**Conclusion:** Off-label treatment with 750mg/day VPA improved BCVA and subjective visual perception in patients with both dry and wet ARMD. Additionally, central retinal thickness decreased in the majority of wet ARMD eyes. Similarly, in patients with RP, BCVA improved in the majority of the patients and an enlargement in visual field area was found. This study served as the basis for the design of randomized, placebo-controlled clinical trials for RP, wet and dry AMD

**Inna Zolnikova**

## **RETINAL TOPOGRAPHY AND BIOELECTRICAL ACTIVITY OF THE CENTRAL RETINA IN HEREDITARY RETINAL DEGENERATIONS.**

Inna Zolnikova, Irina Egorova, Elena Viadro, Elena Rogatina  
Moscow Helmholtz Research Institute of Eye Diseases, Moscow, Russian Federation

Hereditary retinal diseases include the number of retinal degenerations and dysfunctions, which involve central retina. Visual acuity, commonly used indicator of foveal dysfunction, is nowadays a screening procedure. Electroretinographic methods and visualization techniques provide finer detail of macular function and structure assessment.

**Purpose:** to receive the evidence of structural and functional correlations in Best and Stargardt disease.

**Methods:** standard ophthalmic examination was extended by the set of electroretinographic methods which included macular chromatic ERG (M-ERG), pattern ERG (MBN, Russia), and multifocal ERG (mf-ERG) (Roland Consult, Germany). Optical coherence tomography (OCT) was performed with Stratus OCT, Carl Zeiss Meditec (USA). The topography of contrast sensitivity was assessed by the sensomotor reaction time (SMRT) to contrast stimuli darker and lighter than background. We compared morphometric parameters of macula from standard OCT with electrogenesis of the central retina in eyes of patients with Stargardt disease (n=22), Best disease (n=22). Statistical analysis included Pearson correlation analyses and Mann-Witney tests.

**Results:** In Stargardt disease high correlations were observed between the averaged amplitude of P1 component of the mf-ERG from central three rings in a 103 hexagonal stimuli and total macular volume (TMV,  $r=0,94$ ,  $p<0,001$ ), and the amplitude of b-wave of M-ERG and TMV ( $r=0,89$ ,  $p<0,001$ ). TMV is an additional parameter to central foveal thickness which was found to be reduced in patients with Stargardt's disease ( $p<0,001$ ). In Best disease (Arden's ratio 91 - 126 %) central foveal thickness positively correlates with P1 retinal response density of the mf-ERG in the central hexagon ( $r=0,73$ ,  $p<0,01$ ). Statistical analyses of data revealed a high inverse correlation between the stage of Best disease and retinal response density in the central hexagon ( $r=-0,8$ ,  $p<0,05$ ) and paracentral ring in the area 2,3-8 degrees ( $r=-0,78$ ,  $p<0,05$ ), between the stage of disease and the amplitude of b-wave of M-ERG to red stimulus ( $r=-0,8$ ,  $p<0,05$ ). Achromatic contrast sensitivity in Best disease in 1 degree from fixation point is also in agreement with retinal response density of mf-ERG from the central hexagon, demonstrating significant correlation between P1 response density of mf-ERG and SMRT to contrast stimuli lighter than background ( $r=-0,75$ ,  $p<0,05$ ).

**Conclusions:** In Best disease foveal atrophy of retinal layers progress parallel to the reduction of P1 retinal response density. Although bioelectric activity of the central retina do not demonstrate direct correspondence with fundus changes, the association exist between retinal response density and contrast sensitivity with the stages of the disease. In Stargardt disease retinal response from the central retina diminishes proportionally with macular tissue volume.

## ***Florian Gekeler and Eberhart Zrenner***

### **STIMULATING DEGENERATING RETINA WITH CURRENTS: A NEW FIELD OF CLINICAL ELECTROPHYSIOLOGY OF VISION**

Eberhart Zrenner, Florian Gekeler  
Center for Ophthalmology, University of Tübingen, Germany

**Purpose:** To explore the effect of electrical stimulation on restoring functions of the eye:

1. by using subretinal electrode arrays to provide images to blind patients
2. by using global electrical stimulation for improvement of remnant visual function on the basis of the hypothesis that this may liberate neurotrophic factors, as indicated in preclinical experiments.

#### **Methods:**

Ad 1. Electronic microphotodiode arrays (MPDAs) with 1500 amplifiers and electrodes were implanted subretinally in 11 RP-patients;

Ad 2. The effect of 6 sessions of transcorneal stimulation (30 min, weekly) was assessed in 24 RP-patients (either 150%, or 66% of psychophysical threshold, in comparison to sham-stimulation, n=8 each).

#### **Results:**

1. MPDAs allow previously blind patients to detect and name unknown objects, decipher words, discern 7 shades of grey and move freely towards persons.
2. Regular transcorneal stimulation showed a clear tendency to improve visual acuity, area of visual field and electrical phosphene threshold in stimulated patients vs. sham

**Conclusion:** New electrophysiological tools allow improvement of vision in various stages of retinal degeneration, including blindness.

**Acknowledgement:** We are grateful to study physicians Drs. Bruckmann, Naycheva, Stingl, Röck, Wilhelm and Wilke, to surgeons Drs. Besch, Bartz-Schmidt and Sachs and support from Federal

Friday: 9:00 - 9:30

## ***Michael Bach***

### **VEP AND BRAIN**

Michael Bach

Section Visual Function/Electrophysiology, University Eye Hospital, Freiburg, Germany.

Talking about VEP and brain feels like carrying coals to Newcastle when considering Prof. Arden's contributions to the field and the friends who have gathered here for his festschrift. I will first touch on the history of visual evoked potentials. While VEPs do offer an exciting tap on the brain, it is easily submerged in the entire "factory noise". However, with appropriate stimuli it is possible to isolate specific functions. I will demonstrate such applications progressing from flash over pattern (reversal vs. on/off), colour, motion, texture segregation to perceptual phenomena, namely the double flash illusion (Arden, 2003) and multistable perception (e.g., the Necker cube). The main weight will be on basic research findings, with some crossover to clinical applications. Much is history, but recent findings, for instance in the field of multistable perception, demonstrate that visual evoked potentials are alive and kicking in face of the exciting new imaging advances.

Friday: 9:30 – 10:00

## ***Graham Holder***

### **PATTEN ERG, AUTOFLUORESCENCE AND OCT**

Graham E Holder  
Moorfields Eye Hospital and Institute of Ophthalmology, London.

The pattern ERG (PERG) has been established for many years as an effective objective test of macular and retinal ganglion cell dysfunction. More recently, fundus autofluorescence imaging (FAF) and optical coherence tomography (OCT) have enabled new insights into the structural changes that can occur, and, particularly for FAF, it has been the correlation with electrophysiology that has enabled the significance of some of the imaging abnormalities to be determined.

The presentation will review some of the changes in FAF and OCT that can occur in rod-cone dystrophy, autosomal recessive bestrophinopathy, Stargardt-fundus flavimaculatus and other disorders, demonstrating how optimal assessment of such patients involves taking the functional electrophysiological data and the imaging data in conjunction.

Friday: 10:00-10:30

## ***Hannes Wildberger***

### **OCT AND ELECTROPHYSIOLOGY IN OPTIC NERVE DISEASES**

Hannes Wildberger, University Eye Hospital, Zürich, Switzerland

**Background:** Diagnostic decisions differentiating between retinopathies and optic neuropathies in absence of observable disc pallor or retinal changes were formerly mostly dependent on electrophysiology. The VEP demonstrated interruption of the visual pathway at different levels, the mfERG disclosed dysfunction at the outer retina. That situation is dramatically changed by OCT in terms of improved and easy available diagnostic information. Structure and function go now hand in hand since 3-dimensional images are obtainable. The frequency domain OCT (fdOCT) offers: a) qualitative estimation of local structural changes; b) quantitative measurement of total retinal, foveolar and axonal thickness with statistical evaluation; c) the highest information gain is obtained by layer-by-layer analysis with measurement of individual retinal layers from the outer retina (photoreceptors) to the inner retina (ganglion cell layer).

**Methods:** The retinal layers, mainly the complex of retinal ganglion cell layer and of inner plexiform layer (RGL+IPL), were identified according to Hood et al (IOVS 2009). In an array with fixed coordinates 5 positions were chosen in the foveal area and 8 positions in the near periphery. The retinal layers were measured manually. A group of normal subjects provided normal thickness values at each position. The results were electrophysiologically confirmed using VEP, mfVEP and mfERG.

**Results:** The complex of RGL+IPL is precisely measurable and allows differentiating between a) isolated involvement of the visual field centre (papillomacular bundle), b) diffuse optic neuropathies and c) focal defects of the near-periphery (glaucoma, NAION).

**Conclusions:** Analysis of the RGL+IPL is a sensitive method to demonstrate structural intraretinal deficits even in mild stages of neural disease. The observed thinning of the ganglion cell layer correlates directly with the severity of a (chronic) optic nerve disease. Moreover measurement of all retinal layers differentiates optic neuropathies from disorders affecting the outer retina.

Friday: 11:00 -11:20

## **Peter Ahnelt**

### **APPROACHING (SUB-) CELLULAR RESOLUTION IN IN-VIVO RETINAL IMAGING WITH ULTRAHIGH RESOLUTION OPTICAL COHERENCE TOMOGRAPHY (UHR)**

Peter K. **Ahnelt**<sup>1</sup>, Elisabeth **Anger**<sup>1</sup>, Martin **Glösmann**<sup>1</sup>, Renate **Pflug**<sup>1</sup>, Enrique J. **Fernández**<sup>2,3,4</sup>, Boris **Hermann**<sup>2,4</sup>, Boris **Povazay**<sup>2,4</sup>, Angelika **Unterhuber**<sup>2,4</sup>, Harald **Sattmann**<sup>4</sup>, Kostadinka **Bizheva**<sup>4</sup>, Wolfgang **Drexler**<sup>2,4</sup>

<sup>1</sup>Center for Physiology and Pharmacology, Vienna University of Medicine, Austria; <sup>2</sup>Biomedical Imaging Group, Department of Optometry and Vision Sciences, Cardiff University, Wales, UK;

<sup>3</sup>Laboratorio de Óptica, Departamento de Física, Universidad de Murcia, 30071 Murcia, Spain;

<sup>4</sup>Center of Biomedical Engineering and Physics, Vienna University of Medicine, Austria.

**Purpose:** In-vivo imaging of retinal structures has been a long standing goal of vision science. Optical coherence tomography (OCT) is one of the recently established ophthalmic-imaging techniques.

**Methods:** We have approached identification of retinal sublayers and their stimulus related alteration by correlation of ultra-high resolution (UHR) OCT of human eyes and in vitro preparations of model species including pig [1], rhesus monkey [2] and rabbit [3] with corresponding histologies. In a further step, correcting for wavefront aberrations in the optical path between the imaging camera and the retina, adaptive optics (AO) is providing further improvements for cellular-level resolution [4].

For polychromatic light sources, as used for OCT, a further cause of image degradation is chromatic aberration. When applying pancorrection by introducing a specifically designed lens and an AO mirror system in combination with UHR OCT-imaging resolution approaches 2  $\mu\text{m}$ .

**Results:** This resolution allows for visualization of the fine texture of retinal sublayers and, strikingly, resolving outer and inner segments, even myoids from ellipsoids, has become possible in the parafoveal zone.

**Conclusions:** These improvements will allow assessment of the state of photoreceptor and intraretinal elements [5] for both, ophthalmologic diagnostics as well as for experimental conditions, including genetically engineered photoreceptor degenerations.

1. Glösmann M, Hermann B, Schubert C, Sattmann H, Ahnelt PK, et al. Histologic correlation of pig retina radial stratification with ultrahigh-resolution optical coherence tomography; 2003 Apr. pp. 1696-1703.
2. Anger EM, Unterhuber A, Hermann B, Sattmann H, Schubert C, et al. (2004) Ultrahigh resolution optical coherence tomography of the monkey fovea. Identification of retinal sublayers by correlation with semithin histology sections. *Experimental Eye Research* 78: 1117-1125.
3. Bizheva K, Pflug R, Hermann B, Povazay B, Sattmann H, et al. (2006) Optophysiology: Depth-resolved probing of retinal physiology with functional ultrahigh-resolution optical coherence tomography. *Proceedings of the National Academy of Sciences of the United States of America* 103: 5066-5071.
4. Fernandez EJ, Povazay B, Hermann B, Unterhuber A, Sattmann H, et al. (2005) Three-dimensional adaptive optics ultrahigh-resolution optical coherence tomography using a liquid crystal spatial light modulator. *Vision Research* 45: 3432-3444.
5. Torti C, Povazay B, Hofer B, Unterhuber A, Carroll J, et al. (2009) Adaptive optics optical coherence tomography at 120,000 depth scans/s for non-invasive cellular phenotyping of the living human retina. *Optics Express* 17: 19382-19400.

Friday: 11:20 –11:45

## ***Detlev Spiegel***

### **GDx + HRT + ELECTROPHYSIOLOGY IN GLAUCOMA**

Detlev Spiegel, Augsburg and University Eye Hospital Regensburg

Glaucoma is a major cause of visual impairment characterized by structural changes of the optic nerve head and retinal nerve fiber layer, resulting in ganglion cell loss. The primary clinical goal in patient with glaucoma is firstly to diagnose the disease early and secondly to prevent further damage by adequate treatment of the risk factor: the IOP. Objective diagnostic tools as GDx and HRT on the level of morphology and electrophysiology for functional testing have been implemented in our focus of managing the disease. While the morphologic tools (GDx and HRT) have been improved in the past and broaden our clinical management of the disease in terms of diagnosis and treatment at the present, the electrophysiology functional tests detected scientific information which may lead us to new concepts and treatment regarding the glaucomatous disease in future.

Friday: 11:45-12:00

## ***Günther Rudolph***

### **TOPOGRAPHIC MAPPING OF RETINAL FUNCTION (SLO-MFERG)**

Rudolph G., Berninger Th.  
Eye Hospital, Ludwig-Maximilians-University Munich. Germany

The scanning laser ophthalmoscope can be used for multifocal electroretinography (mfERG) measurements under simultaneous fundus monitoring. The mfERG device is combined with a scanning laser ophthalmoscope (SLO), which is used both as a stimulus and trigger unit as well as a fundus monitoring system. Imaging of the fundus is given by using an infrared laser (780nm). The stimulus matrix consists of 61 hexagonal elements, covering 24° of the posterior pole.

The SLO-mfERG is a feasible technique to investigate macular function under simultaneous control of fixation. A main advantage could be that control of fixation can be used in order to obtain reliable results correlating with the fundus abnormalities. Further investigations and development of diagnostic devices have to be performed in order to overcome the problem of fixation instability.

Friday: 12:00-12:30

## ***Don Hood***

### **COMPARISONS OF LOCAL STRUCTURAL AND FUNCTIONAL DAMAGE IN PATIENTS WITH GLAUCOMA**

Don Hood, Dept. of Psychology Columbia University

Using frequency domain OCT and static automated perimetry, it is now possible to compare local changes in retinal structure to local changes in behavioral sensitivity. This talk will largely focus on 3 recent studies that relate local changes in the inner retina to visual field losses in sensitivity due to glaucoma. The first study focuses on the nature of glaucomatous damage in the macular. We show that the damage to the retinal nerve fiber layer is often an arcuate, which may or may not appear as an arcuate on the visual field. In the second study, we introduce a manual segmentation technique and demonstrate that local retinal ganglion cell layer loss can be quantified in patients with glaucoma. Finally, the third study explores the relationship between local retinal ganglion cell loss and local changes in the visual field.

Friday: 13:30- 13:45

## ***Pamela Sieving***

### **THE ARDEN EFFECT: A BIBLIOMETRIC ANALYSIS OF THE IMPACT OF GEOFFREY ARDEN'S RESEARCH**

Pamela C. Sieving, National Institutes of Health, USA

**Purpose:** To examine the impact of Arden's research using bibliometric methods and tools.

**Methods:** Databases which track citations, including Web of Science, Scopus, PsycINFO, and Google Scholar, were searched to identify citations to Geoffrey Arden's publications.

**Results:** Results were analyzed to determine most-cited material and patterns of citations, including subjects of citing journals, country of residence of citing authors, and implications for clinical care.

**Conclusions:** Bibliometric data demonstrate that Arden's publications have been widely cited in a broad range of biomedical and clinical journals, but have also had an impact on engineering, physics, psychology, veterinary science, aviation science, public health.

Friday: 13:45 -14:05

## ***CHRIS HOGG***

### **TECHNICAL DEVELOPMENTS BY GEOFFREY ARDEN**

Chris Hogg

Moorfields Eye Hospital

During a long and ongoing scientific career, Professor Arden has introduced many technical developments into the field of visual science.

Whilst a number of these innovations have been solutions to immediate problems, others have and still are having a significant effect on clinical practice.

A selection of these developments in both psychophysics and electrophysiology will be described, and their impact discussed.

Friday: 14:05-14:20

## ***Thomas Berninger***

### **COLOUR CONTRAST SENSITIVITY (CCS): BASICS**

Thomas Berninger, University Eye Hospital, Munich

Our world is full of colours. Nevertheless, not all people are able to see the colours in the same way. At least 8% of the male population has a colour vision defect mainly in the red-and-green axis. Already at the beginning of the 20th century - after severe railway accidents - it was recognized that the disclosure of these defective colour vision is of great importance. In 1920 Nagel developed the Anomaloskop which is still today the goldstandard for the diagnosis of inherited colour vision defects. While we are able to detect inherited colour vision defects quite easily we did not have very useful techniques at hand to detect acquired colour vision defects which very often effects the blue-and-yellow axis. Up to recent years only a few colour tests were available to detect acquired colour vision defects (Velhagen, Panel-D-15. FM-100 etc.). They are all at most semi-quantitative and for example the FM 100 is very tedious for both the patients and the examiners.

Only with the development of computer graphics it became possible to develop a monitor-steered colour test device which allows a quick and reproducible and quantitative colour examination. This talk will give a short introduction of the so-called Colour-Contrast-Sensitivity (CCS) test which was designed by Geoffrey Arden.

Friday: 14:20 -14:40

## ***Kemal Gündüz***

### **COLOUR CONTRAST SENSITIVITY: DIABETES & MACULOPATHY**

M. Kemal Gündüz,  
Ophthalmology and Visual Sciences,  
Meram Medical Faculty Selcuk University. Konya, Turkey

A computer driven test of colour vision using monitors enables a rapid testing of colour discrimination at any site in the CIE colour space possible with TV phosphors and along any chromaticity vector without any associated change in luminance. The coloured images to be discriminated can be chosen as letters, spatially filtered in a variety of ways. The system is proven to be very sensitive and colour contrast sensitivity and subtle colour vision defects can be detected.

DR is the most common microvascular complication in diabetes which can lead to severe visual loss. In diabetes, alterations in retinal function occur such as abnormal dark adaptation, abnormalities in ERG and in PERG, sensitivity losses in S-cone-pathway (abnormal contrast sensitivity and colour vision).

The attenuation in colour contrast sensitivity is correlated with the severity of DR and the assessment of colour vision may be more sensitive than ERG in the detection of early visual dysfunction. Changes in tritan thresholds are seen very early. In patients with more severe retinopathy, protan thresholds are also raised. Especially the central CCS seems to correlate to the degree of retinopathy.

All the alterations in retinal function suggest that in the course of diabetes, the retina is abnormal, and the abnormalities are those associated with mild lack of oxygen. Although the mechanism of altered colour vision is unknown, there is evidence that reduced retinal oxygen saturation is associated with impaired colour vision in diabetics.

Key words: Diabetes, maculopathy, colour contrast sensitivity.

Friday: 14:40 -15:00

## ***Werner Spileers***

### **COLOUR CONTRAST THRESHOLDS IN OPHTHALMOLOGICAL PRACTICE**

Werner Spileers, University Hospitals Leuven, Belgium

Isoluminant central and periheral colour contrast threshold measurements (*Arden et al., 1988*) are useful in clinical ophthalmological practice.

Central thresholds are routinely measured along a protan and tritan axis. The test is simple and quick to perform in a routine clinical setting and investigates visual function in optic neuropathies, macular diseases. The tritan threshold is unaffected by congenital red-green colour deficiency (*Devos et al., 1996*).

The original peripheral "ring" test (*Falcao-Reis et al., 1990; Yu et al., 1991*) was later on modified into a "quadrant" test, measuring colour contrast thresholds at 12.5 ° eccentricity in four quadrants of the visual field. The "quadrant" test was shown to be more sensitive in the detection of functional loss in incipient glaucoma (*Devos et al., 1995*)

Friday: 15:30 – 16:00

## ***Geoffrey Arden***

### **A NEW VIEW OF DIABETIC RETINOPATHY: FUNCTION MEETS MORPHOLOGY**

G.B. Arden and S. Sivaprasad, City University, London, Northampton Square,  
London EC1V 0HB

**Background:** In diabetics, where oxygen transport to the retina is slightly reduced, and metabolic requirements enhanced through hyperglycaemia, the extra oxygen demand of retinal rods in darkness cannot be met, and the resulting hypoxia causes loss of rod sensitivity. It seemed possible that this was related to the peculiar susceptibility of retinal capillaries to damage that characterises diabetic retinopathy (DR). A link between hypoxia and vessel damage is the upregulation of VEGF, known to occur in diabetic retina. The evidence for this hypothesis is reviewed and some problems with alternative explanations of the pathogenesis of DR are highlighted. If rod-induced hypoxia contributes to the development of DR, then the damage must accelerate during periods of dark adaptation. But urban man only dark-adapts during sleep, and a critical test of the hypothesis is to determine whether the progress of DR is slowed by prevention of complete dark adaptation. We have now conducted clinical trials to determine whether this prediction is correct.

**Methods:** Patients slept with continuous illumination of one closed lid sufficient to light adapt the rods by 4 log units. We used chemiluminescent (“glowpatches”) in a Phase I trial, and blue green illumination from light emitting diodes in a Phase II trial. In the phase I trial, type 1 diabetic patients with mild background DR were followed for 3-12 months. In the Phase II trial, 40 patients with stage 1 DME were followed for 6 months.

**Results:** In the Phase I trial: patients tolerated this intervention well and suffered no sleep disturbance or any adverse effect. 9 out of 10 showed a decrease in the area of microaneurysms and dot haemorrhages, and an increase in Tritan colour contrast sensitivity ( $p=0.01$ ). In the Phase II trial: macular cysts visualised by OCT vanished after 3 months, central macular volume decreased ( $p=0.0003$ ), microperimetry sensitivity increased ( $p=0.01$ ) and achromatic and tritan contrast sensitivity increased ( $p<<0.01$ ).

**Conclusions:** These patients’ retinal changes were slight or otherwise did not permit lasering or intravitreal injections. However rapid and dramatic improvement of morphology and function occurred in light-treated eyes while fellow eyes deteriorated, providing “proof of principle”. Since the technique is non-invasive, does not require medical intervention and is inexpensive, it could be of general use in people with diabetes and could reduce the incidence of retinopathy.

Friday: 16:00 – 16:45

## ***Alan Bird***

### **CELL DEATH IN GEOGRAPHIC ATROPHY: FUNCTION MEETS MORPHOLOGY**

Alan Bird, Institute of Ophthalmology, Moorfields Eye Hospital, London, UK

Geographic atrophy (GA) of the retinal pigment epithelium (RPE) is a term used by Gass to designate one form of late age-related macular disease (AMD).<sup>1</sup> It is a major cause of visual loss in Western communities, although, with few exceptions, less common than choroidal neovascularization.<sup>2-4</sup> Concepts as to the pathological processes leading to GA are incompletely understood, and sequence of events has been debated for some years. On the basis of histological studies, Hogan took the view that the target cell of disease was the photoreceptor cell and that cell loss was consequent upon RPE dysfunction.<sup>5</sup> Sarks and co-workers undertook meticulous morphological studies on donor eyes and supported this view.<sup>6,7</sup>

Clinical studies using autofluorescence have supported these general conclusions. The observation that GA is preceded by excess autofluorescence implies that that accumulation of lipofuscin in the retinal pigment epithelium (RPE) is intrinsic to the evolution of GA.<sup>8,9</sup>

High quality imaging using OCT implies that in the area of GA there is complete or almost complete loss of photoreceptor cells.<sup>11,12</sup> The alternatives that RPE may be absent, or thinned and depigmented could be distinguished one from the other. Beyond the edge of GA the RPE may or may not be hyper-autofluorescent. In areas of abnormal autofluorescence, the images were interpreted as implying that the outer nuclear layer may be thinner than normal, but there was great variation from one patient to another. In those cases with homogeneous autofluorescence beyond the edge of atrophy, there tended to be an abrupt transition from normal outer nuclear thickness, and therefore photoreceptor cell population. In these cases, some change in the bands, interpreted as being derived from the outer limiting membrane and inner/outer segment junction, were recorded beyond the edge of the GA. This suggested that there may be abnormalities of the inner and outer segments in ophthalmoscopically normal retina. The reliability of autofluorescence as an indicator of integrity of the photoreceptor cells is not reported in either of these two studies. In addition the relative frequency of normal and abnormal outer nuclear layer beyond the margin of atrophy is not documented. However both indicate that there may be major loss of photoreceptor cells in retina that may appear normal by ophthalmoscopy.

Functional testing also gives some clues as to the state of the outer retina in AMD. In early disease slow acquisition of fluorescence on fluorescein angiography is seen in about 25% of eyes.<sup>13</sup> In such cases there is consistent loss of scotopic function by as much as 3.5 log units whereas photopic function is normal or near normal. In addition loss of sensitivity has been recorded over areas of abnormal autofluorescence.<sup>14</sup> Whether these losses are due to cell death or cell dysfunction is unknown. In an attempt establish the extent of cell loss in cases of GA we examined 38 pairs of donor eyes in which GA had been documented clinically.

In the area of GA there was no RPE and the outer retina was reduced to scattered cone nuclei with no outer or inner segment. Beyond the edge of GA in 4 eyes there was a sharp transition to an outer retina that was intact with several rows of photoreceptor nuclei with outer and inner segments. In the remaining eyes there was major loss of photoreceptor cells to one row of cones for up to 1,400 from the edge with some inner segments but no outer segments. The state of the outer retina did not correspond with age changes in the RPE.

It was concluded that:

1. Photoreceptor cells are the target cell of disease.
2. The area of GA as assessed clinically does not indicate accurately the state of the outer retina.
3. The sensory loss measured in early AMD is due in part or completely to photoreceptor cell death
4. That autofluorescence is not a reliable indicator of the state of the outer retina.

### **References:**

1. Gass JDM. *Drusen and disciform macular detachment and degeneration. Arch Ophthalmol* 1973;90:206-17
2. Sarks SH. *Drusen patterns predisposing to geographic atrophy of the retinal pigment epithelium. Aust J Ophthalmol* 1982;10:91-7.
3. Maguire P, Vine AK. *Geographic atrophy of the retinal pigment epithelium. Am J Ophthalmol.* 1986;102:621-79.
4. Jonasson F, Arnarsson A, Sasaki H, Peto T, Sasaki K, Bird AC. *The prevalence of age-related maculopathy in Iceland: Reykjavik eye study. Arch Ophthalmol* 2003;121:379-85.
5. Hogan MJ. *Role of the retinal pigment epithelium in macular disease. Trans Amer Acad Ophthalmol Otolaryngol.* 1972;76:64-80.
6. Sarks SH. *Ageing and degeneration in the macular region: a clinico-pathological study. Br J Ophthalmol.* 1976;60:324-341.
7. Sarks JP, Sarks SH, Killingsworth MC. *Evolution of geographic atrophy of the retinal pigment epithelium. Eye* 1988; 2:552-77.
8. von Ruckmann A, Fitzke FF, Bird AC. *Fundus autofluorescence in age-related disease imaged with a scanning laser ophthalmoscope. Invest Ophthalmol Vis Sci* 1997; 38:478-86
9. Holz FG, Bellmann C, Margaritidis M, Schutt F, Volker V. *Patterns of increased autofluorescence in the junctional zone of geographic atrophy of the retinal pigment epithelium associated with age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol.* 1999; 237:145-52
10. Green WR, Key SN 3rd. *Senile macular degeneration: a histopathologic study. Trans Am Ophthalmol Soc.* 1977;75:180-254.
11. Wolf-Schnurrbusch UE, Enzmann V, Brinkmann CK, Wolf S. *Morphologic changes in patients with geographic atrophy assessed with a novel spectral OCT-SLO combination. Invest Ophthalmol Vis Sci.* 2008;49:3095-9.
12. Fleckenstein M, Charbel Issa P, Helb HM, Schmitz-Valckenberg S, Finger RP, Scholl HP, Loeffler KU, Holz FG. *High-resolution spectral domain-OCT imaging in geographic atrophy associated with age-related macular degeneration. Invest Ophthalmol Vis Sci.* 2008;49:4137-44

## **Accompanying person's programme**

**Thursday: start 10:00 outside Kardinal-Wendel-Haus**

### **“Literature and Art in Old Schwabing”**

A two hour walk through Schwabing with Dr. Heiserer

**Friday: start 10:00 outside Kardinal-Wendel-Haus**

### **“The Munich Residenz”**

A guided tour through the old King's palace with Mrs. Korten

**Thursday: 19<sup>th</sup> of June**

Starts 19:30

## **Bavarian Evening**



With the “Oberlandstreicher”, a group of six young musicians

Bavarian music, food and beverages

**Friday, 11<sup>th</sup> of June**

**Gala dinner in honour of G. B. Arden's 80<sup>th</sup> birthday**

19:00-19:30      Champagne toast to Geoffrey Arden  
19:30-20:00      Hors-d'oeuvre  
20:00 -20:15      "55 years of electrophysiology" by S.-E. Nilsson  
20:15- 20:45      Main course  
20:45-21:15      "gefilte fish"  
21:15-21:45      Dessert  
21:45-              "gefilte fish"



Tobias Schwartz

Andrea Giani

Roman Chowdhury

Vlad Cojocaru

Joe Rappaport

**We thank all our sponsors:**

- 1. Deutsche Forschungsgemeinschaft**
- 2. Chibret Pharmazeutische GmbH**
- 3. Heidelberg Engineering GmbH**
- 4. Novartis Pharma GmbH**
- 5. OmniVision® GmbH**
- 6. Pharm-Allergan GmbH**
- 7. Roland Consult Stasche & Finger GmbH**
- 8. Santen GmbH**
  
- 9. Tourist Office Munich**