

Title

Absolute retinal blood flow in healthy eyes and in eyes with retinal vein occlusion

Purpose

To non-invasively measure retinal venous blood flow (RBF) in healthy subjects and patients with retinal venous occlusion (RVO).

Setting/Venue

The prototype named AO-LDV (Adaptive Optics Laser Doppler Velocimeter), which combines a new absolute laser Doppler velocimeter with an adaptive optics fundus camera (rtx1, Imagine Eyes®, Orsay, France), allows for the measurement of absolute RBF as a function of retinal vessel diameters and simultaneous measurement of red blood cell velocity.

Methods

A total of 15 healthy subjects and six RVO patients were included. For healthy subjects, all the retinal veins in one eye were measured to obtain the total RBF. For RVO patients, only the temporal veins were measured in both eyes.

Financial Disclosure

Bayer : financial support of this study

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Results

In healthy subjects, the total RBF was 37.8 ± 6.8 $\mu\text{l}/\text{min}$. Our results suggest an inversely proportional relationship between total RBF and intra-ocular pressure ($r = -0.57$) or central subretinal thickness ($r = -0.48$). No significant relationship was found between total RBF and systolic blood pressure, diastolic blood pressure, ocular perfusion pressure, heart rate, or hematocrit. In RVO patients, a decrease in RBF was noted in occluded veins compared with the contralateral healthy eye.

Conclusions

The new AO-LDV prototype allowed RBF to be measured in healthy and RVO patients. The main limitation at this time is the parallax phenomenon, which could be avoided using the optical path of the rtx1 for the LDV part of the system. The prototype was improved with a fixation system for both eyes and a laser projection system to reduce the parallax phenomenon.

Title

High resolution imaging of normal and pathological retinal pigment epithelium (RPE) using a transscleral illumination adaptive optics camera

Purpose

Retinal pigment epithelium (RPE) cell mosaic can be resolved in the living retina using an adaptive optics (AO) system with transscleral illumination (TSI), as recently shown by Laforet et al. The combination of autofluorescence imaging with adaptive optics scanning laser ophthalmoscopy (AF-AOSLO) has also led in the past to the precise imaging of the RPE mosaic, as reported by our group (K. Grieve et al). The present study evaluates the RPE cells mosaic in the normal retina and other clinical features such as pigment clumps in patients with age related macular degeneration (AMD) and Stargardt disease, using with a commercially available flood-illumination AO retinal camera modified by the addition of TSI, and compared with AF-AOSLO images.

Setting/Venue

Patients were recruited and examined at the clinical investigation center 1423 in the National Quinze-Vingts Ophthalmology Hospital, Paris in France. The procedures used in this study conformed to the tenets of the Declaration of Helsinki, and they were approved by our local ethics committee. A written informed consent was obtained from each subject.

Methods

An infrared LED projector was attached to an AO retinal camera (rtx1-e, Imagine Eyes, France) in order to illuminate the retina with an 850 nm beam focused at the pars plana. This system illumination is composed of two led arrays illuminating the retina through the sclera on both sides of the pupil. The system complied with ANSI regulations. The oblique trans illumination of the posterior retina leads to the generation of phase images that could show the boundaries of the RPE cells. These images were averaged using customized ImageJ software. Infrared AF AOSLO images were registered to TSI images. For AMD and Stargardt disease cases, conventional multi-imaging, including infrared scanning laser ophthalmoscopy (IR SLO), IRAF SLO, SD-OCT (Spectralis), AO-SLO (PSI, USA), AO fundus camera was performed.

Financial Disclosure

Christophe RONDEAU is employee of Imagine eyes

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Results

We have currently imaged 3 normal subjects, aged between 28 and 56 years, 3 AMD patients and a Stargardt disease patient. In three normal eyes, circular cell-like structures with dark centers surrounded by brighter rings were visible in almost all images. At eccentricities beyond 5 degrees, cell-like structures were visible in the entire field of images. Cell density ranged between 4.4×10^3 and 6.2×10^3 cell/mm² across subjects, which showed good correlation with AF AOSLO results and lie within the ranges reported in the literature. In AMD and Stargardt eyes, pigment clumps were visible in the pathological area with a high contrast.

Conclusions

The implementation of TSI on an AO camera allowed visualization and quantification of the RPE mosaic in healthy subjects. The RPE images taken by TSI and AF AO-SLO were similar in shape and density. In pathological eyes, pigment clumps are electively detected with a high contrast. TSI could thus be a valuable addition to a conventional trans-pupillary flood-illumination AO camera, not only for seeing the RPE cells, but also for detecting clinical features such as pigment clumps.

Title

High-resolution adaptive optics retinal imaging analysis of patients with autosomal dominant retinitis pigmentosa caused by HK1 mutation

Purpose

The hexokinase 1 (HK1) gene encodes one of the four human hexokinases that play essential roles in glucose metabolism. Recently, several cases of E847K mutation in the HK1 gene were reported to cause inherited retinal dystrophy. The purpose of this study was to identify the phenotypical characteristics of patients with a recurrent E847K mutation in the HK1 gene.

Setting/Venue

All subjects were recruited and examined at a university hospital, the Nippon Medical School Chiba Hokusoh hospital in Japan. The procedures used in this study conformed to the tenets of the Declaration of Helsinki, and they were approved by the Institutional Review Board of the Nippon Medical School. A signed written informed consent was obtained from the patient and family members after the nature and possible consequences of the study were explained.

Methods

Three generations of one family with autosomal dominant retinitis pigmentosa were examined. Whole exome sequencing was performed on the DNA. The ophthalmological examinations included measurements of the best-corrected visual acuity (BCVA), slit-lamp bio-microscopy, ophthalmoscopy, Goldman kinetic perimetry, fundus photography, fundus auto-fluorescence imaging (FAF) with short-wavelength excitation, spectral domain optical coherence tomography (SD-OCT), full-field electroretinography (ERG), and multifocal ERGs (mfERGs). The ERGs were recorded using the extended testing protocol conforming to the International Society for Clinical Electrophysiology of Vision protocol (ISCEV). Fundus imaging by an adaptive optics fundus camera was used to obtain high-resolution photoreceptor images, and cone densities of the families were compared to that of normal eyes of healthy subjects.

Financial Disclosure

Kiyoko GOCHO (spouse) : imagine eyes

Presenter

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Fundus examination of the proband showed degeneration of the mid-peripheral retina, and SD-OCT images showed an absence of the ellipsoid zone (EZ) and interdigitation zone (IZ) in the parafovea and more peripherally. SD-OCT images of the mother of the proband showed an absence of the EZ and IZ, and fundus autofluorescence images showed hypo-autofluorescence surrounding the macular region. One daughter of the proband had only mild night blindness, however, the density of the cone photo-receptors was reduced in the parafoveal region. Whole exome sequencing identified a heterozygous variant, E847K, in the HK1 gene. This variant was found to co-segregate with the disease in three family members.

Conclusions

Fundus, FAF, and OCT imaging revealed that the areas of photoreceptor degeneration were mainly in the parafovea to mid-peripheral region. High-resolution retinal imaging by AO revealed that the cone photoreceptor densities were significantly reduced in the parafoveal area at the age of 20 years, though fundus examinations showed only slight abnormalities without functional visual defects at this age. High-resolution retinal imaging analysis, such as that by AO and FAF analysis would be helpful in identifying patients with HK1-retinopathy caused by an E847K mutation. AO examination in between the different generations might be helpful to understand the prognosis and progression of the diseases.

Title

In vivo assessment of associations between photoreceptors structure and macular perfusion in type 1 diabetes

Purpose

To explore the potential relationships between macular vascular network and different adaptive optics (AO) metrics in patients with type 1 diabetes mellitus with no or early signs of non proliferative diabetic retinopathy (NPDR).

Setting/Venue

observational cross-sectional study

Methods

Consecutive DM1 patients with no or early signs of NPDR and healthy age matched control subjects were enrolled at the Department of Ophthalmology of IRCCS-Fondazione Bietti, Rome. All patients and controls were imaged by using AO retinal camera (rtx1; Imagine Eyes, Orsay, France) and PLEX Elite 9000 OCT angiography (OCTA, Carl Zeiss Meditec Inc., Dublin, CA, USA). The main AO outcome measures to evaluate cone mosaic characteristics were: i) Cone density (CD), ii) linear dispersion index (LDi), and iii) heterogeneity packing index (HPI). The main OCTA outcome measures were: i) SCP perfusion (PD) and vessel length densities (VLD) (ii) DCP PD and VLD (iii) SCP and DCP vessel diameter index (VDI) (iv) the CC flow deficit (FD).

Financial Disclosure

none

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The multiple regression analysis revealed that the NPDR group was characterized by a close relationship between cone metrics and CC FD. Notably, there was a positive relationship between FD and LDi ($P = .035$). On the contrary, a negative relationship was found between FD with both the CD ($P = .042$) and the HPI ($P = .017$). The OCTA parameters for retinal circulation, including PD and VLD, displayed a significant negative correlation with CD. In the analysis investigating the parafoveal subfields, the NPDR temporal sector was characterized by a higher negative correlation between AO metrics and OCTA variables.

Conclusions

In conclusion, using a combination of SS-OCTA and AO, our study assessed the relationship between macular perfusion (both retinal and choroidal) and AO metrics in patients with DM1 diabetes. In particular, in NPDR eyes photoreceptor damage was strongly associated with choriocapillaris insufficiency even in the early stage of the disease.

Title

Comparing measurements of vascular diameter using adaptive optics imaging and conventional fundus imaging

Purpose

To compare retinal vascular diameter measurements taken from standard fundus images and adaptive optics (AO) images.

Setting/Venue

Prospective comparative study.

Methods

We analyzed retinal images of 20 healthy participants with 45-degree fundusoscopic color photographs (CR-2 Canon fundus camera, Canon™) and adaptive optics (AO) fundus images (rtx1 camera, Imagine Eyes®). Diameters were measured using three software applications: the VAMPIRE® (Vessel Assessment and Measurement Platform for Images of the REtina) Annotation Tool, IVAN (Interactive Vessel ANalyzer) for fundusoscopic color photographs, and AO_Detect_Artery™ for AO images.

Financial Disclosure

Imagine eyes for Nicolas CHATEAU

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For the arterial diameters, the mean difference between AO_Detect_Artery™ and IVAN measurements was 9.1 μm (-27.4–9.2 μm , $p=0.005$) with a significant correlation between measurements ($r=0.79$). The mean difference between the AO_Detect_Artery™ and VAMPIRE™ Annotation Tool measurements was 3.8 μm (-34.4–26.8 μm , $p=0.16$) with a weak correlation between measurements ($r=0.12$). For the venous diameters, the mean difference between the AO_Detect_Artery™ and IVAN measurements was 3.9 μm (-40.9–41.9 μm , $p=0.35$) with a strong correlation between measurements ($r=0.83$). The mean difference between the AO_Detect_Artery™ and VAMPIRE™ Annotation Tool measurements was 0.4 μm (-17.44–25.3 μm , $p=0.91$), and the correlation was moderate ($r=0.41$).

Conclusions

Taking AO imaging as a reference, we found that the VAMPIRE Annotation Tool, an entirely manual software, provides accurate measurements of the arterial and venular diameters, but the correlation is weak. By contrast, IVAN, a semi-automatic software tool, has slightly higher differences in measurements compared with AO imaging, but the correlation is stronger.