Title

Adaptive optics retinal imaging in patients with Stargardt disease

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Purpose

The course of Stargardt disease based on standard clinical retinal imaging has been well described. However, with the integration of adaptive optics imaging into ophthalmology, a better knowledge of Stargardt disease at the cellular level is possible. The aim of the study is to correlate adaptive optics retinal imaging patterns with standard clinical examinations to improve the understanding of the disease, to identify possible early markers and to describe the phenotype at the cellular level.

Setting/Venue

University Eye Hospital, Centre for Ophthalmology, University of Tuebingen, Tuebingen, Germany; Center for Rare Eye Diseases, University of Tuebingen, Tuebingen, Germany

Methods

We observed twenty-two eyes of twenty-two patients (age 34±9, 9 females, 13 males) with a genetically confirmed Stargardt disease at the baseline visit for an interventional trial for Stargardt disease (EudraCT no.: 2018-001496-20) at the site Tuebingen (DE). Patients were examined by the rtx1, an adaptive optics (AO) flood illuminated retinal camera (Imagine Eyes, Orsay, France). A standardized protocol of 17 central images covering approximately 13x13° of the central retina and a composition of 5 single images of the arterioles was used. After the acquisition the wall lumen ratio (WLR) of the arterioles was calculated and the cone mosaic pattern was compared with the findings of the color fundus images, OCT and fundus autofluorescence.

Financial Disclosure

none

Results

The WLR was 0,32±0,09 and tended to be slightly higher in small arteries. In one patient the arterioles were narrowed and in two patients the WLR was slightly increased compared to the other patients and the vessels were mildly tortuous. In all other eyes the appearance of the arterioles was normal. The WLR of retinal arterioles revealed a significant correlation with age (Spearman ρ=0,5221, p=0,0106). In all eyes the AO images correlated well with standard clinical examinations. In 4 eyes we observed clumping of the RPE, and in 4 other eyes in a very advanced stage the choroidal vessels became visible due to severe cell loss, which could also be seen in fundus photography. In 7 eyes a typical ring pattern was visible in the AO images, which could be correlated with the FAF images. In 7 eyes the fundus flavimaculatus could be identified as hyperreflective spots in the AO images. In 2 eyes the retinal pigment epithelium was visible in areas where the EZ and IZ could not be delineated on OCT. However, in many patients the RPE was not visible although EZ and IZ were disrupted.

Conclusions

The images correlated well with routine retinal imaging and have shown that the images can be helpful in assessing cellular changes. Nevertheless, further investigations are needed to clarify, for example, the cause of the retinal pigment epithelium visibility.

Title

Parafoveal Cone Density Change in Retinitis Pigmentosa over Six Months

Purpose

Spectral-domain optical coherence tomography (SD-OCT) is the standard method for evaluating retinal structure in various pathologies, including retinitis pigmentosa (RP). The span and area of the ellipsoid zone (EZ) decline at a rate of approximately 4–10% and up to 13% per year, respectively, in patients with RP. Current SD-OCT devices lack the resolution to visualize individual photoreceptors. Adaptive optics (AO) imaging is an evolving technology enabling in vivo photoreceptor imaging in the clinical setting. Multiple AO retinal cameras have been used to measure cone density (CD) at different retinal eccentricities in healthy individuals and a range of retinal pathologies, including RP. However, longitudinal changes in CD in patients with RP have not been reported previously. We investigated the feasibility and utility of AO flood-illumination ophthalmoscope (FIO) in analysing the cone mosaic and monitoring parafoveal CD in RP.

Setting/Venue

This study was the single-centre prospective observational cohort; a part of the Western Australian Retinal Degeneration study. All examinations were performed between September 2018 and December 2020 at the Lions Eye Institute, Perth, Western Australia, Australia.

Methods

Patients with RP and healthy controls were evaluated for eligibility for AO imaging. Exclusion criteria included visual acuity (VA) worse than 20/40, poor fixation, history of ocular disease or surgery, significant cataract or other media opacity, nystagmus, cystoid macular oedema, epiretinal membrane and history of using systemic medications with known photoreceptor toxicity. All patients and controls underwent a complete ophthalmic examination with right eye SD-OCT and AO-FIO imaging using a commercial AO retinal camera (rtx1, Imagine Eyes, Orsay, France). Nasal and temporal boundaries of the EZ were marked on the foveal-centred SD-OCT scan and used to measure residual EZ span. Commercial analysis software (AODetect version 3.0, Imagine Eyes, Orsay, France) was used for cone segmentation and measurement of CD at 2° temporal from the foveal centre using regions of interest selected from four partially overlapping tiles. Coefficient of repeatability (CoR) was calculated using partially overlapping images taken at the same session. For each case, the highest CD value from one of the four tiles was used for statistical analysis. All patients were followed for 6 months and measurements were performed on the same location using the same protocol. CD and CoR were reported in angular (cells/deg2) and metric (cells/mm2) units.

Financial Disclosure

None

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Results

Eight patients and 10 age-matched healthy controls were enrolled. There was no significant difference between the control and patient groups in baseline age (p=0.72), spherical equivalent (p=0.99) and axial length (p=0.60). CoR of CD using the same session overlapping tiles was 530 cells/deg2 (6307 cells/mm2) in the control group and 659 cells/deg2 (8364 cells/mm2) in the patient group. Mean baseline CD in the control and patient groups was 2094 cells/deg2 (24732 cells/mm2) and 1750 cells/deg2 (21689 cells/mm2), respectively (p=0.09 and 0.28 for the angular and metric values, respectively). Mean CD declined by 198 cells/deg2 or -11.3% (2356 cells/mm2 or -10.9%) at 6 months follow up in the patient group (p=0.01 for both angular and metric values). EZ span was beyond the SD-OCT imaging field (30°) in two patients. Baseline and follow up residual EZ span of the remaining 6 patients was 3189 µm and 3065 µm, respectively, which was not statistically significant (-3.9%, p=0.08). CD declined by -8.4% and -25.9% in the two patients with greater than 30° EZ span. Mean baseline and follow-up logMAR best-corrected VA in the patient group were 0.08 (0.12) and 0.03 (0.13), respectively (p=0.08).

Conclusions

There was 15% difference in baseline parafoveal CD between the patient and control groups, irrespective of EZ span. Although not statistically significant, this finding suggests further investigation is warranted in exploring the potential use of AO imaging in early stage RP. Significant decline in CD at 6 months despite a stable EZ span suggests that the parafoveal CD may be more sensitive than EZ span for detecting RP progression. CoR using partially overlapping tiles was greater than previous reports, suggesting potential errors in using overlapping tiles and performing CD analysis on montage images. Our results support further studies are required to explore the reliability and short-term test-retest variability of CD measurements in larger patient samples with longer follow up durations.

Euretina 2021 Virtual Abstracts

Type Poster

Title

Short term morphological rescue of the fovea after gene therapy with voretigene neparvovec

Purpose

Leber congenital amaurosis type 2 (LCA2) and early-onset severe retinal dystrophy (EOSRD) are linked to visual impairment with nyctalopia and visual acuity reduction in early childhood. In 2017, the first gene therapy voretigene neparvovec (LuxturnaTM) for patients with LCA and EOSRD cause by bi-allelic mutations in the RPE65 gene has been approved. Here we report on an example of short-term change in the foveal morphology after functionally successful gene therapy with voretigene neparvovec in a 15-year old patient.

Setting/Venue

Departement of Ophthalmology, University of Tübingen, Germany

Methods

The clinical examinations included best corrected visual acuity (BCVA), spectral domain optical coherence tomography (OCT) and adaptive optics retinal imaging.

Financial Disclosure

none

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Results

During follow-up over a period of three months after the treatment an improvement of the photoreceptor structure could be observed in OCT, with a clear demarcation of the external limiting membrane and changes in the photoreceptor mosaic on adaptive optics retinal imaging. These morphological rescue parameters correlated in part with the improvement in foveal mediated vision after the treatment and adaptive optics imaging. Although the visual acuity improved only slightly at month 3, objective central cone evaluation with chromatic pupil campimetry showed an increase in the central function. In daily life, the patient reported her visional experience after the treatment as ‘brighter’.

Conclusions

Rapid changes in the photoreceptor morphology after successful gene therapy in patients with LCA/EORD can be quantifiable on individual level.

Euretina 2021 Virtual Abstracts

Type Poster

Title

Adaptive optics ophthalmoscopy in retinitis pigmentosa: typical patterns

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Purpose

Due to advances in optics, electronics and computation, morphological changes of the photoreceptor mosaic can be made visible by adaptive optics ophthalmoscopy (AOO). Retinitis pigmentosa (RP) is a degenerative retinal disease that affects primarily the rod photoreceptors followed by the loss of cone receptors. This paper aims to present typical findings in RP with the adaptive optics flood illumination retinal camera rtx1.

Setting/Venue

Departement of Ophthalmology, University of Tübingen, Germany

Methods

174 patients with syndromic or non-syndromic RP were examined with the commercially available adaptive optics flood illumination retinal camera rtx1 and spectral domain optical coherence tomography (OCT) and fundus autofluorescence (FAF) imaging at the Center for Ophthalmology, University of Tuebingen. AOO patterns were studied in the context of multimodal retinal imaging.

Financial Disclosure

None

Results

Five different patterns in RP could be observed: 1) unspecific atrophy, 2) central visibility of cones, 3) “puffy” cones, 4) the “cheetah” pattern, and 5) atrophic pigment clumping. These patterns in AOO correlated with findings on OCT and FAF imaging. We hypothesize that these patterns represent specific stages of photoreceptor degeneration in RP.

Conclusions

AOO provides an additional dimension to high-resolution retinal imaging in RP, enabling to determine patterns of retinal degeneration. Future evaluation of cone photoreceptor mosaic using AAO imaging is warranted to determine changes on an even more microscopical level, e.g. photoreceptor integrity.

Euretina 2021 Virtual Abstracts

Type Poster

Title

Adaptive optics study of retinal vessels in patients affected by pseudoxantoma elasticum

Purpose

The aim is to study retinal vessels in vivo through adaptive optics flood illumination ophthalmoscopy imaging (FIAO) in PXE patients.

Setting/Venue

University of Florence

Methods

PXE patients were recruited at Careggi Hospital (Regional Reference Center for Hereditary Retinal Dystrophies). All patients underwent complete ophthalmological examination and FIAO (rtx1; Image Eyes, Orsay, France). Adaptive optics montage imaging was done along the superior-temporal retinal vascular arcade. Wall lumen ratio (WLR) and cross-sectional area of the vascular wall (WCSA) were calculated on the basis of retinal arteriolar wall thickness (VW), lumen diameter (LD) and vessel diameter (VD) assessed by rtx1 Adaptive Optics retinal camera.

Financial Disclosure

No financial relations

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Results

Mean arteriolar WLR is 0,21 (0,16-0,24) and mean arteriolar WCSA is 3908 (2958-5630). Arteriolar mean VW is 10,4 (9,3-11,9), mean LD 103,9 (84,8-128,4) and mean TD 125,54 (108,9-121,4). Mean venular WLR is 0,07 (0,05-0,1) and mean venular WCSA is 2593 (1713-3498). Venular mean VW is 4,18 (1,7-5,4), mean LD 145,24 (139,8-149,1) and mean TD 156,1 (151-159,9).

Conclusions

Our study firstly presented quantitative retinal vessels parameters using FIAO; we did not detect qualitative alterations of retinal vessels due to calcium deposits in our Pxe patients.