Clinical research with the rtx1[™] Adaptive Optics retinal camera

Summary of published results in inherited retinal diseases

Inherited retinal diseases (IRDs) cause severe visual loss in over 2 million patients worldwide. The last two decades have been marked by accelerated progress in the development of therapies for IRDs¹. Over the same period of time, advances in adaptive optics technology have enabled imaging the retina at a scale where individual cells are visible.

Clinical studies using the rtx1 Adaptive Optics Retina Camera in IRDs have resulted in several new findings:

- rtx1 images enabled quantifying the mosaic of cone photoreceptor cells using morphological metrics*. In groups of healthy volunteers, cone cell density findings were consistent with previous histological data in the parafoveal region of the retina^{2,3}
- The rtx1 was used to investigate different types of IRDs and revealed microscopic retinal changes in every pathology under study³⁻²³
- Publications reported abnormalities in the parafoveal cone mosaic such as reduced cone visibility³⁻⁷, disorganized mosaic⁸⁻¹⁴, and reduced cell density^{3,5,8,10-20}. Reduced cone density in the center of the fovea was also found in two studies^{7,10}
- Outer retinal tubules²⁰, crystal deposits^{20,21}, microcysts²², and retinal folds²³ were visible in rtx1 images with a higher level of detail than in conventional imaging.
- Such microscopic signs of pathology could be detected even in patients with relatively good visual acuity^{3,10,17} as well as cases with almost normal findings from examinations with color fundus imaging, auto-fluorescence imaging, optical coherence tomography or electroretinography^{3,8,9,15,17,22}
- In macular dystrophies, follow-up imaging with the rtx1 enabled tracking the same group of cells over time with micrometer precision^{6,17}

?? The quantitative assessment of photoreceptor survival or loss, based on analysis of adaptive optics retinal images, was valuable to monitor disease progression at a cellular level.

Ziccardi et al., American Journal of Opthalmology, 2015

Occult Macular Dystrophy	Retinitis Pigmentosa
Stargardt	Usher Syndrome
Achromatopsia	Macular Telangiectasia type 2
Peripheral Cone Dystrophy	Bestrophinopathy
Cone Dystrophy	Bietti's Crystalline Dystrophy
Choroideremia	Autosomal Dominant Optic Atrophy
Choroidal Dystrophy	X-linked Retinoschisis

Inherited retinal diseases investigated with the rtx1.

?? Adaptive optics fundus imaging is particularly suited for exploration of the healthy and dystrophic retinal structures, including photoreceptor detection and counting.

Prof. José Sahel, University of Pittsburg Medical School, USA



Peripheral cone dystrophy





Case of peripheral cone dystrophy with abnormal cone mosaics at $600\mu m$ (H) and $450\mu m$ (I) from the fovea. Credit: Ito et al. 2015

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99 Adaptive optics imaging technology has revolutionized our understanding of structural changes in retinal disease

Gale et al. Retinal Degenerative Diseases, 2015



Abnormal cone mosaics and reduced cone density in Usher syndrome caused by CEP250 mutation. Credit: Kubota et al. 2018

99 we have seen that significant photoreceptor loss occurs before the development of visual symptoms Palejwala et al. *Retina*, 2016



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References

- Sahel, J.-A. et al. Clinical Characteristics and Current Therapies for Inherited Retinal Degenerations. *Cold Spring Harbor Perspectives in Medicine* 5:a017111 (2015).
- Legras, R. et al. Distribution of Cone Density, Spacing and Arrangement in Adult Healthy Retinas with Adaptive Optics Flood Illumination. *PLOS ONE* 13, e0191141 (2018).
- Gocho, K. et al. High-Resolution Adaptive Optics Retinal Image Analysis at Early Stage Central Areolar Choroidal Dystrophy With PRPH2 Mutation. Ophthalmic Surgery, Lasers and Imaging Retina 47, 1115–1126 (2016).
- Gale, M. J. et al. Interpretation of Flood-Illuminated Adaptive Optics Images in Subjects with Retinitis Pigmentosa. in *Retinal Degenerative Diseases* 854, 291–297 (Springer International Publishing, 2015).
- Jacob, J. et al. Cone Density Loss on Adaptive Optics in Early Macular Telangiectasia Type 2. *Retina* 36, 545–551 (2016).
- Palejwala, N. V. et al. Insights into Autosomal Dominant Stargardt-Like Macular Dystrophy Through Multimodality Diagnostic Imaging. *Retina* 36, 119–130 (2016).
- Pang, C. E. et al. New Insights Into Stargardt Disease With Multimodal Imaging. Ophthalmic Surgery, Lasers and Imaging Retina 46, 257–261 (2015).
- Kubota, D. et al. CEP250 Mutations Associated with Mild Cone-Rod Dystrophy and Sensorineural Hearing Loss in a Japanese Family. *Ophthalmic Genetics* (2018). doi:10.1080/13816810.2018.1466338
- Kominami, A. et al. Case of Cone Dystrophy with Normal Fundus Appearance Associated with Biallelic POC1B Variants. *Ophthalmic Genetics* (2017). doi:1 0.1080/13816810.2017.1408846
- Nakanishi, A. et al. Changes of Cone Photoreceptor Mosaic in Autosomal Recessive Bestrophinopathy. *Retina* (2018). doi:10.1097/ IAE.00000000002363
- Ito, N. et al. Multimodal Imaging of a Case of Peripheral Cone Dystrophy. Documenta Ophthalmologica 130, 241–251 (2015).
- Kikuchi, S. et al. Cone Dystrophy in Patient with Homozygous RP1L1 Mutation. *BioMed Research International*, Article ID 545243, 13 pages (2015).
- Nakanishi, A. et al. Pathologic Changes of Cone Photoreceptors in Eyes With Occult Macular Dystrophy. *Investigative Opthalmology & Visual Science* 56, 7243-7249 (2015).
- Dessalces, E. et al. Early-Onset Foveal Involvement in Retinitis Punctata Albescens With Mutations in RLBP1. JAMA Ophthalmology 131, 1314-1323 (2013).
- Forte, R. et al. Multimodal Imaging of Posterior Polar Annular Choroidal Dystrophy. *Retinal Cases & Brief Reports* (2016). doi:10.1097/ ICB.000000000000400
- Ueno, S. et al. In Vivo Imaging of a Cone Mosaic in a Patient with Achromatopsia Associated with a Gnat2 Variant. *Japanese Journal of Ophthalmology* 61, 92–98 (2016).
- Ziccardi, L. et al. Multimodal Approach to Monitoring and Investigating Cone Structure and Function in an Inherited Macular Dystrophy. *American Journal of Ophthalmology* 160, 301-312.e6 (2015).
- Tojo, N. et al. Analysis of Macular Cone Photoreceptors in a Case of Occult Macular Dystrophy. *Clinical Ophthalmology* 7, 859–864 (2013).
- Nabholz, N. et al. Clinical Evaluation and Cone Alterations in Choroideremia. Ophthalmology 123, 1830–1832 (2016).
- Battu, R. et al. Adaptive Optics Imaging of the Outer Retinal Tubules in Bietti's Crystalline Dystrophy. *Eye* 30, 705–712 (2016).
- Gocho, K. et al. High-Resolution Imaging of Patients with Bietti Crystalline Dystrophy with CYP4V2 Mutation. *Journal of Ophthalmology*, Article ID 283603, 12 pages (2014).
- Gocho, K. et al. High-Resolution En Face Images of Microcystic Macular Edema in Patients with Autosomal Dominant Optic Atrophy. *BioMed Research International*, Article ID 676803, 12 pages (2013).
- Akeo, K. et al. Detailed Morphological Changes of Foveoschisis in Patient with X-Linked Retinoschisis Detected by SD-OCT and Adaptive Optics Fundus Camera. *Case Reports in Ophthalmological Medicine*, Article ID 432782, 8 pages (2015).

(*) Quantifications based on adaptive optics retinal images have not been approved for clinical use.

The rtx1 is an approved medical device in the European Union (device class 2a) and in Japan. In the USA, the rtx1 has not received FDA clearance. It is an investigational device and requires Institutional Review Board (IRB) oversight for use in any research application. Further information is provided in the user's documentation.