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 IRDs[1]. Over the same period of time, advances in adaptive optics technology have enabled imaging the retina at a scale where individual cells are visible.

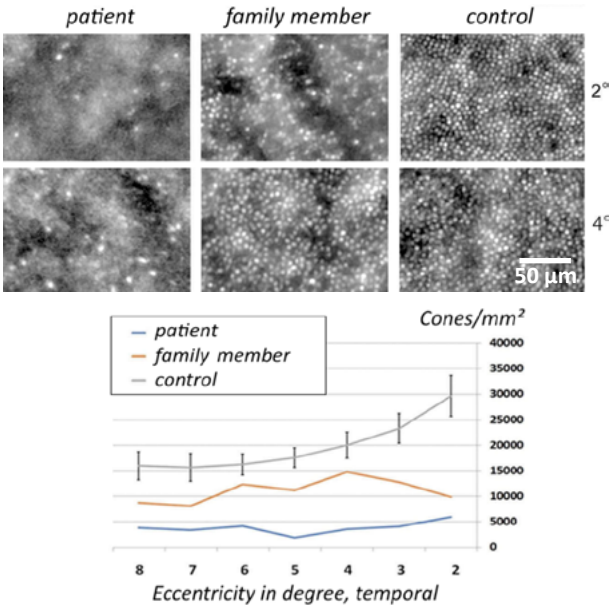
Clinical studies using the rtx1 Adaptive Optics Retinal Camera in IRDs have resulted in the following findings:

- The rtx1 has enabled quantifying the mosaic of cone photoreceptor cells using several metrics: cell density, inter-cell spacing, mosaic regularity and spacing dispersion[2–24]
- In groups of healthy volunteers, cone cell density findings were consistent with previous histological data in the parafoveal region of the retina[2–5]
- The rtx1 has been used to investigate 14 different types of IRDs (see list) and revealed microscopic retinal alterations in every pathology under study[3–28]
- rtx1 publications reported abnormalities in the parafoveal cone mosaic, such as:
  - reduced cone visibility[3,6–9,21,24]
  - disorganized mosaic[4,10–15,25]
  - reduced cell density[3,4,6–8,10–20,22–24]
  - reduced cell spacing dispersion[5]

  Reduced cone density in the center of the fovea was also reported by two studies[9,11]
- Outer retinal tubules[22], crystal deposits[22,26], microcysts[27], retinal folds[28] and borders of preserved photoreceptor areas[21] were visible in rtx1 images with a higher level of detail, in comparison with conventional imaging techniques.
- Such microscopic signs of pathology could be detected even in patients with relatively good visual acuity[3,11,18,24] as well as cases with almost normal findings from examinations with color fundus imaging, auto-fluorescence imaging, optical coherence tomography or electroretinography[3,10,16,18,24,25,27]
- Follow-up examinations with the rtx1 enabled tracking the same cells over time[8,18,23]. In retinitis pigmentosa (RP), longitudinal studies detected photoreceptor losses in patients even when visual acuity remained stable[21,23]

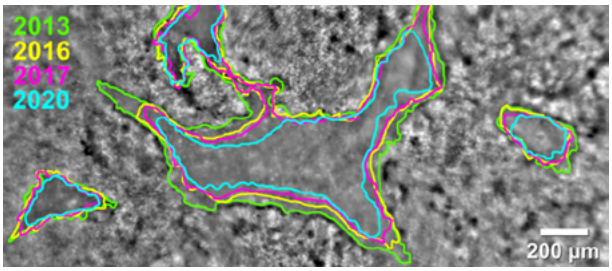
Retinitis Pigmentosa	Occult Macular Dystrophy
Usher Syndrome	Choroideremia
Achromatopsia, Color Deficiency	Stargardt
Cone Dystrophy	Macular Telangiectasia type 2
Peripheral Cone Dystrophy	Bietti's Crystalline Dystrophy
Bestrophinopathy	Autosomal Dominant Optic Atrophy
Choroidal Dystrophy	X-linked Retinoschisis

Inherited retinal diseases investigated with the rtx1.



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

> *The application of AO in IRDs has progressed from exploring disease genotype-phenotype correlations, to longitudinal assessment of disease progression using cellular metrics as potential trial endpoints.*
>
> Gill et al., *Nature*, 2019



Progression of late-stage RP: borders of surviving cone areas overlaid on the baseline image. Credit: Nagoya University Hospital

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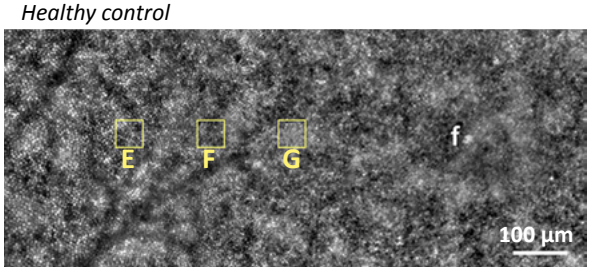
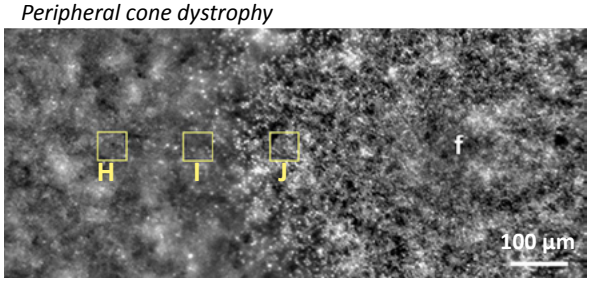
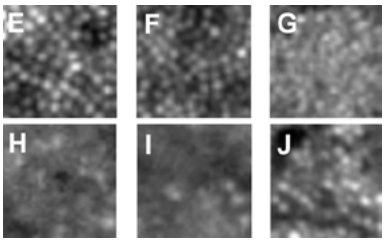
> *Adaptive optics fundus imaging is particularly suited for exploration of the healthy and dystrophic retinal structures, including photoreceptor detection and counting.*
>
> Prof. José Sahel, University of Pittsburg Medical School, USA

Healthy control



Peripheral cone dystrophy





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

> *AO detected a decrease of cone density over 2 years in RP patients. However, visual acuity, foveal sensitivity, and photoreceptor thickness were not changed over the 2 years.*
>
> Ueda-Consolvo et al. *Graefes Arch Clin Exp Ophthalmol,* 2019

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