Clinical research with the **rtx1™** Adaptive Optics Retinal Camera

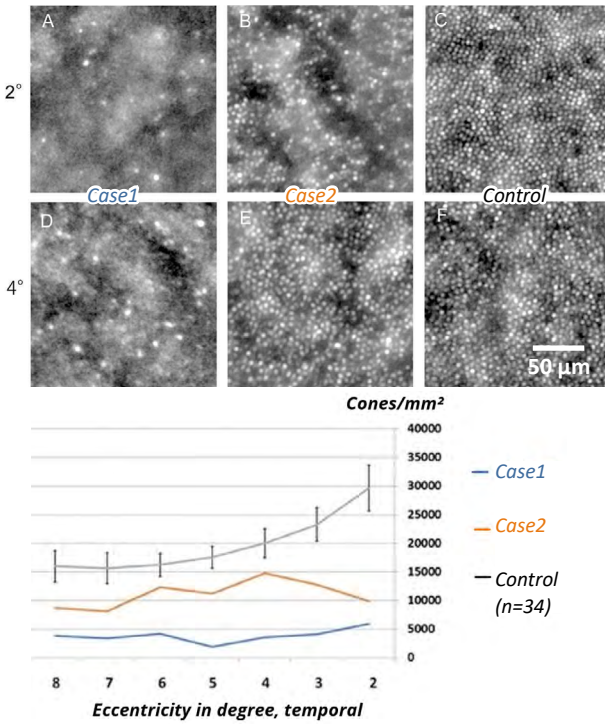
Summary of published results in **Inherited Retinal Diseases**

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

13 teams of ophthalmologists have carried out 29 studies using the rtx1 to investigate IRDs. They published the following findings:

- **Phenotype information**
  In all the investigated IRDs, the rtx1 revealed microscopic signs of pathology that were invisible with conventional imaging techniques[2–29]. rtx1 publications reported observations of 5 different patterns of abnormality in the cone cell mosaic[2–5,7–12,15–23] as well as 5 additional types of alterations in other retinal structures[5,24,26–29] (see table).
- **Cell quantification**
  The rtx1 has enabled the analysis of quantitative metrics of the cone mosaic[2–17,20–26,30]. In images acquired in healthy volunteers, parafoveal cone density measured with the rtx1 was consistent with previous histological and AO-SLO data[2,12,25,30]. In almost all IRDs under study[2–4,6–17,20–24,26], the rtx1 revealed significant reductions in cone density, even when photoreceptor abnormalities were barely visible in OCT images[7,13,21]. Moreover, several rtx1 studies reported reduced cone density in patients who had normal fundus images[10–14,21] and/or normal visual function[7,10–13,16,23].
- **Assessing microscopic progressions and therapy effects**
  Several longitudinal investigations in IRDs have analyzed follow-up images captured with the rtx1[5,6,10,15,16,18,29]. In Stargardt[16], OMD[10] and incomplete achromatopsia[15], these images enabled tracking the same groups of cells over time. In retinitis pigmentosa, the rtx1 allowed the detection of microscopic disease progressions in patients whose visual acuity remained stable between visits[5,6]. In LCA, rtx1 images revealed improvements in the central cone mosaic from 5 weeks after gene therapy[18].

> *Adaptive optics imaging technology has revolutionized our understanding of structural changes in retinal diseases*
>
> Gale et al. *Retinal Degenerative Diseases*, 2015



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

> *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

		RP	OMD	Choroidal dystrophy	Achromatopsia	Stargardt	LCA	Cone dystrophy (CD)	Peripheral CD	Usher	MacTel type 2	Bestrophinopathy	Choroideremia	Bietti	ADOA	X-linked retinoschisis
		2–7	8–11	12,13	14,15	16,17	18	19	20	21	22	23	24	25,26	27	28
Cone mosaic alterations	Cone disappearance	●		●	●	●	●				●		●			
	↘ Blurred areas			●							●					
	Disorganized cone pattern	●	●				●	●	●	●		●				
	↘ Starry-night pattern		●													
	Distinct foveal cones	●	●		●	●						●				
	Hyporeflective parafoveal cones											●				
	Distinct RPE cell pattern	●	●			●			●							
Other alterations	Borders of lesions	●											●		●	
	Pigmented clumps	●											●			
	Outer retinal tubules													●		
	Crystal deposits													●		
	Retinal folds															●

Phenotype information obtained ↗ from rtx1 images in different IRDs

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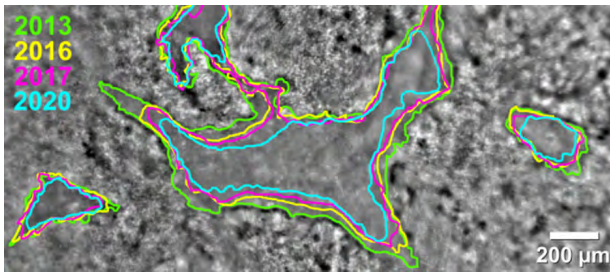
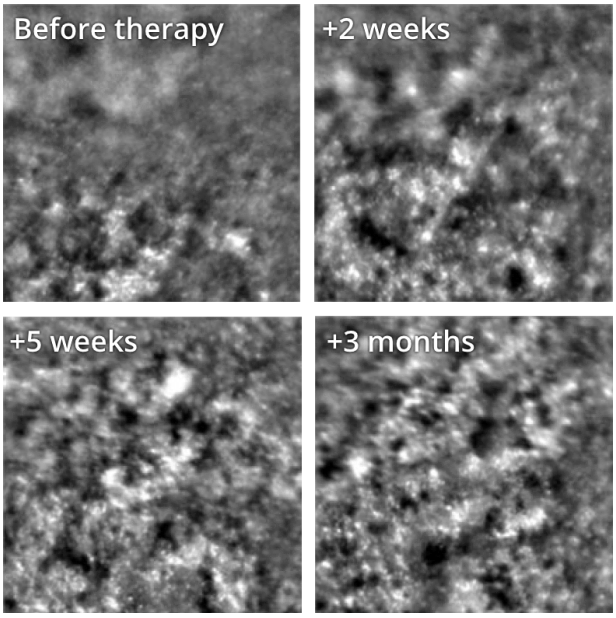
> *The application of AO in IRDs has progressed from exploring disease genotype-phenotype correlations, to longitudinal assessment of disease progression using cellular metrics as potential trial endpoints.*
>
> Gill et al., *Nature*, 2019



Progression of late-stage RP: borders of surviving cone areas overlaid on the baseline image. Credit: Nagoya University Hospital, 2020

> *It is a sensitive modality to detect photoreceptor changes over time even if visual acuity does not change much as it did in our patient.*
>
> Kortuem et al., *Acta Ophthalmologica*, 2021



Follow-up after gene therapy in LCA: restoration of central cone photoreceptors from 5 weeks after treatment. Credit: Kortuem et al. 2021

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