



Imaging and Quantifying Surviving Photoreceptors within Areas of Geographic Atrophy in Patients with Age-related Macular Degeneration



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Purpose

To measure the presence and density of cones in areas of geographic atrophy using an adaptive optics scanning laser ophthalmoscope (AOSLO).

Background

- ❑ Age-related macular degeneration (AMD) is a leading cause of vision loss in Americans 65 yr and older.¹
- ❑ Visually significant age-related macular degeneration is estimated to increase from 1.75 million Americans in 2000 to 2.95 million in the year 2020.²
- ❑ Clinical management depends on AMD staging: Prevention of AMD progression is targeted through AREDS supplementation and lifestyle.^{3,4} Neovascular AMD is treated with anti-VEGF intra-vitreous injections.⁵
- ❑ Currently, there are no approved therapeutics for geographic atrophy.
- ❑ Depression rates among AMD patients with vision loss of 20/60 or worse in the better seeing eye are double that of a similar demographic. The percentage of depression 32.5% in this population with vision loss is comparable to those with life threatening chronic illness.⁶
- ❑ Patient education remains important including: UV protection, smoking cessation, home Amsler grid use, healthy diets, active lifestyle, low vision rehabilitation, and access to support groups.⁴

Methods

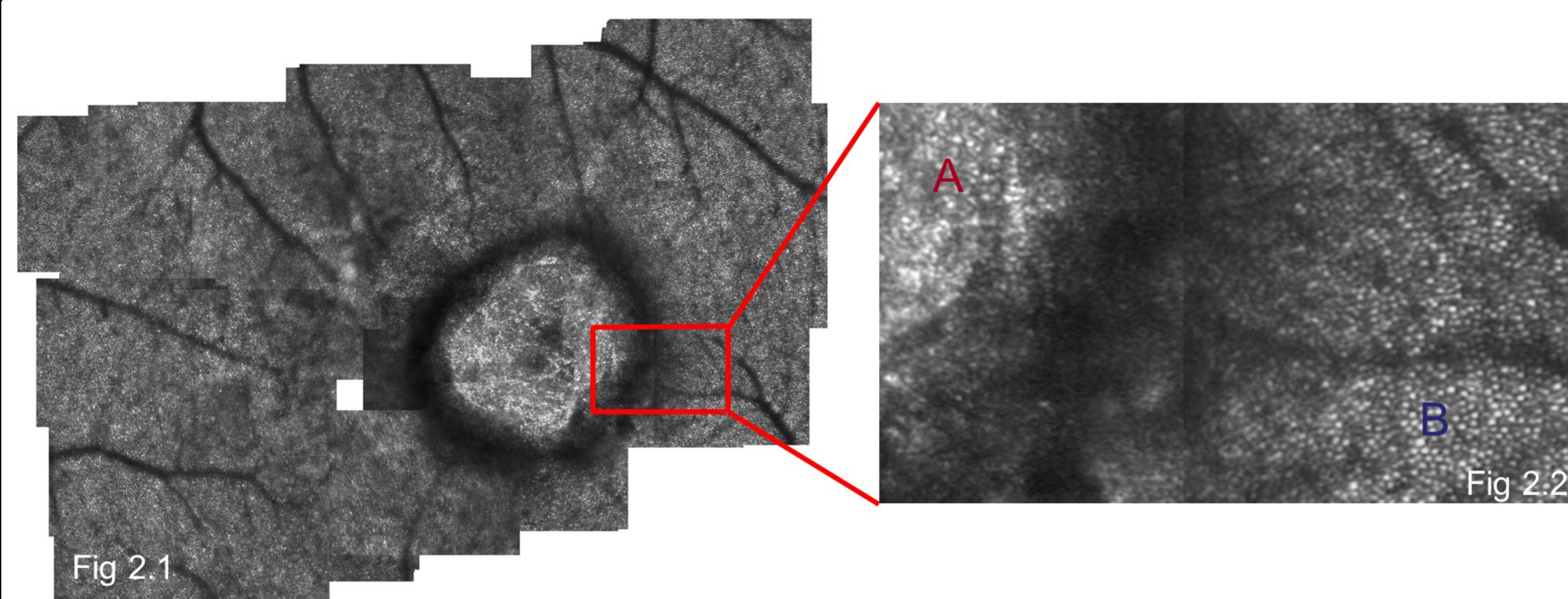
- ❑ An adaptive optics scanning laser ophthalmoscope has laser scanning to improve contrast, plus adaptive optics to correct for higher order aberrations, which allows for resolution at the cellular level.
- ❑ Five patients with geographic atrophy (GA) and a visual acuity of 20/40 or better in the tested eye were prospectively enrolled.
- ❑ GDx, SD OCT, and AOSLO images were taken of the study eye mapping out the area of GA.
- ❑ AOSLO images were processed with retinal landmarks given from OCT and GDx images.
- ❑ Cone density was quantified for areas of atrophy and an adjacent area outside the atrophy.

Results

- ❑ All areas of geographic atrophy had cones, not just at the border of atrophy, but well within the center (Figure 2.1).
- ❑ Density was decreased compared with adjacent non-atrophic retina, but areas within the atrophic region had at least 10,000 cones/mm² for all eyes imaged.

Subject	Atrophic cone density Cones/mm ²	Adjacent cone Density Cones/mm ²
1	10178	12656
2	14720	19449
3	10023	13675
4	13633	19118
5	16886	17046

Figure 1: Table comparing each subject's cone density in atrophic vs adjacent non-atrophic retina.



Figures 2.1-2.2: Figure 2.1 is an AOSLO image of a well circumscribed area of geographic atrophy surrounded by non-atrophic retina in subject 2. Figure 2.2 is the same patient AOSLO image enlarged to enable appreciation of individual cones, pinpoint hyper-reflectance. 'A' represents cones in atrophic retina, and 'B' represents cones in non-atrophic retina.

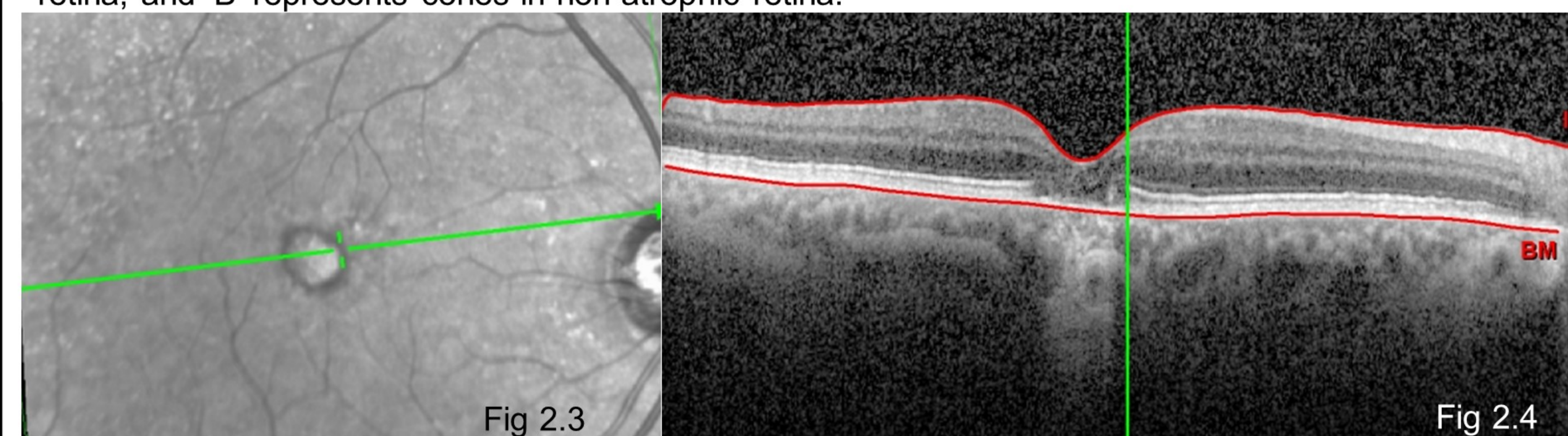
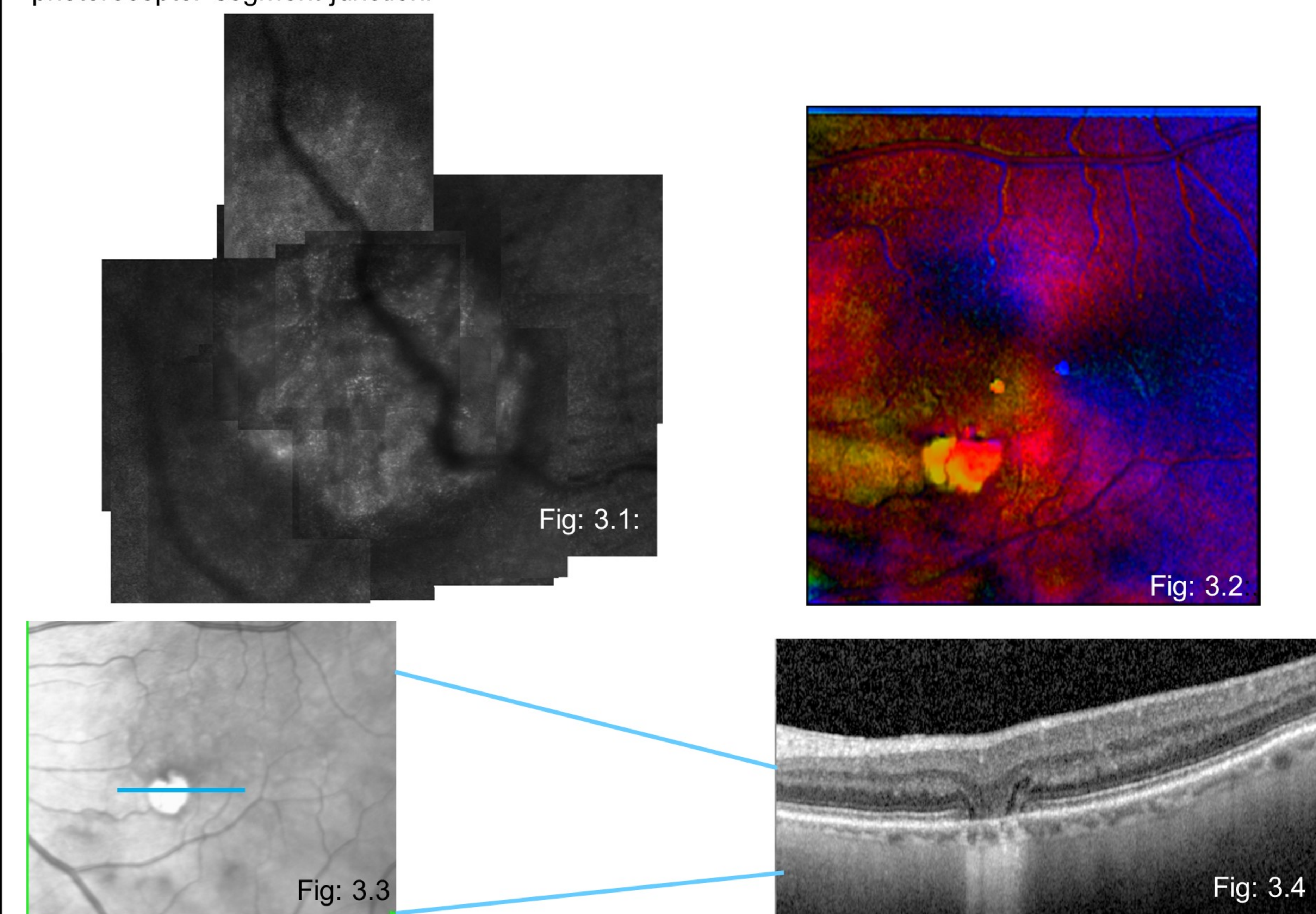


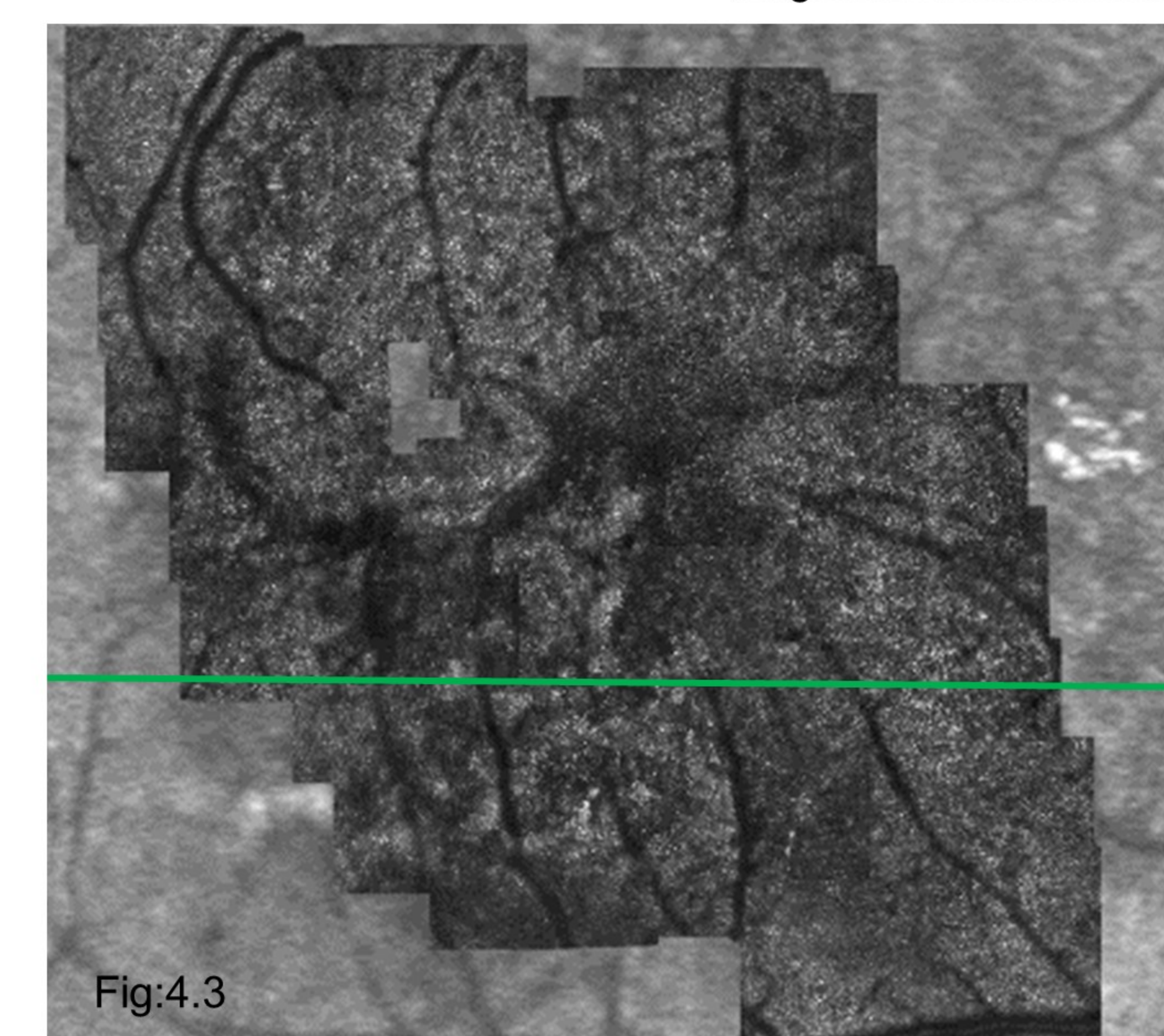
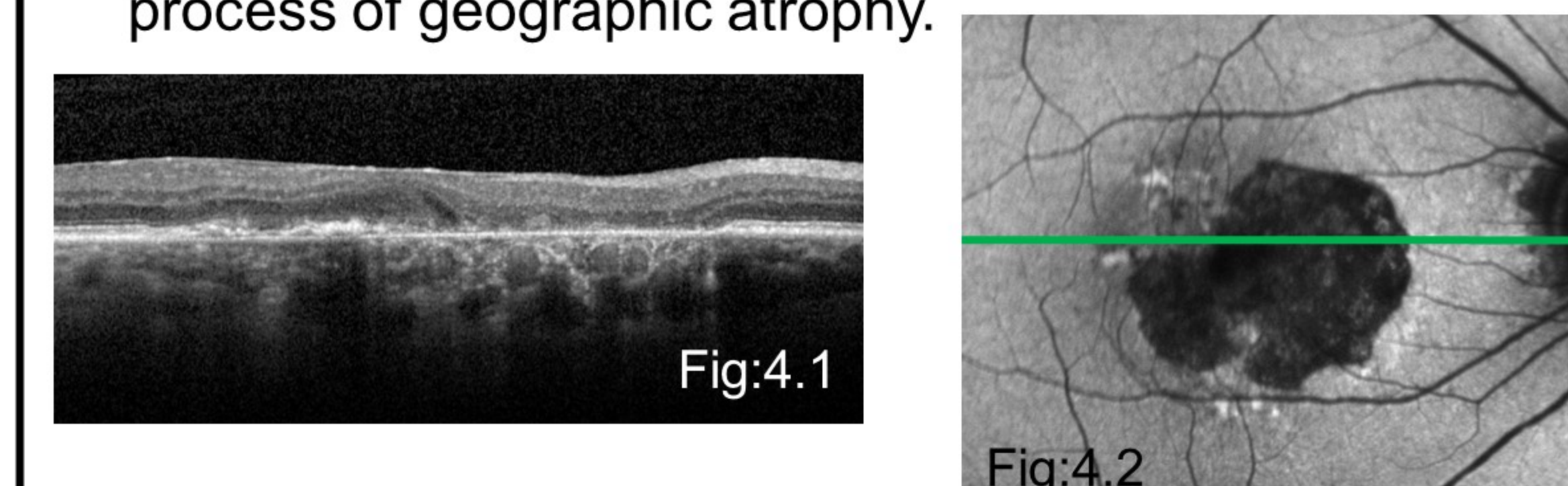
Figure 2.3-2.4: Figure 2.3 is an IR image of subject 2. Figure 2.4 shows the cross sectional OCT image typically used in clinic. Here you can observe the geographic atrophy and loss of the inner and outer photoreceptor segment junction.



Figures 3.1-3.4: Figure 3.1 is the AOSLO image demonstrating a focal area of geographic atrophy surrounded by non-atrophic retina in subject 1. Figure 3.2 is the GDx image where the atrophy can be appreciated as well as the macular bowtie. Figures 3.3 and 3.4 are the IR image and cross sectional OCT images respectively.

Conclusions

- ❑ Cones are surviving in areas of geographic atrophy, at least early in the disease process while acuity remains at a high functioning level.
- ❑ Remarkably, AOSLO demonstrates cones surviving in areas devoid of RPE and choriocapillaris support. This is contrary to the OCT images we typically interpret clinically showing a missing inner and outer photoreceptor segment junction.
- ❑ Knowing that there are cones within geographic atrophy, researchers can begin to investigate methods to preserve remaining cone function, or revive cones with shortened outer segments to provide a halt to the process of geographic atrophy.



Figures 4.1 – 4.3: Figure 4.1 is the cross sectional OCT through an area of geographic atrophy from subject 5. Figure 4.2 is the auto-fluorescent photo that demonstrates the area of geographic atrophy and surrounding pigment changes. Figure 4.3 is the en face AOSLO image, demonstrating cone appearance through the same location (green lines) in Figures 4.1 and 4.2.

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