

# SICKLE CELL RETINOPATHY: CORRELATION BETWEEN VISUAL FUNCTION AND VASCULAR STRUCTURE

Giovanna Vieira Moreira, Marcela Pedreira e Ataíde, Mariana Gouveia Bastos Meirelles, Luiz Roisman, Eduardo Novais, Emmerson Badaró Cardoso, Cezar Luz Leitão Guerra, Ricardo Luz Leitão Guerra

## PURPOSE

To determine whether the area, perimeter and circularity of the foveal avascular zone (FAZ) is correlated with an objective evaluation of visual function in patients with sickle cell disease.

## METHODS

A prospective cross-section study was performed from April 2021 to may 2022. The amount of 44 eyes of 25 patients (mean age, 36.4 ± 11.1 years) with sickle cell disease were reviewed.

All the patients underwent visual function measurement through Snellen chart visual acuity test, Regan Low Contrast Sensitivity Letter Charts and visual fixation through microperimetry measurements (ellipse and circularity).

Optical coherence tomography angiography (OCTA) was conducted for measurement of the FAZ area, perimeter and circularity in full thickness retina analysis as well as through segmented superficial and deep capillary plexus. Person's and Spearman's correlation tests were used for statistical analysis

## RESULTS

44 eyes of 25 patients were included. Mean age was 36.4 years, 22 eyes were from the SS genotype and 22 from SC. Non-proliferative retinopathy was found in 24 eyes.

A weak correlation between FAZ perimeter in the superficial capillary plexus and visual acuity was found analysing the total sample of patients with sickle cell retinopathy.

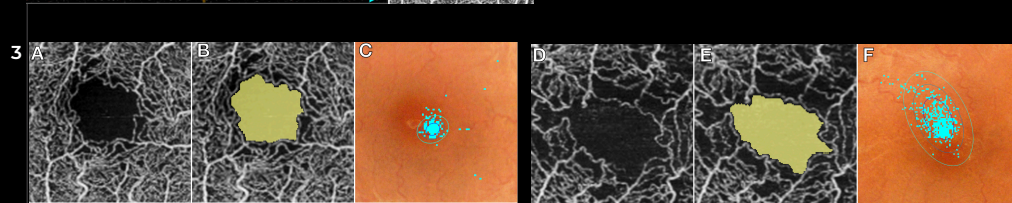
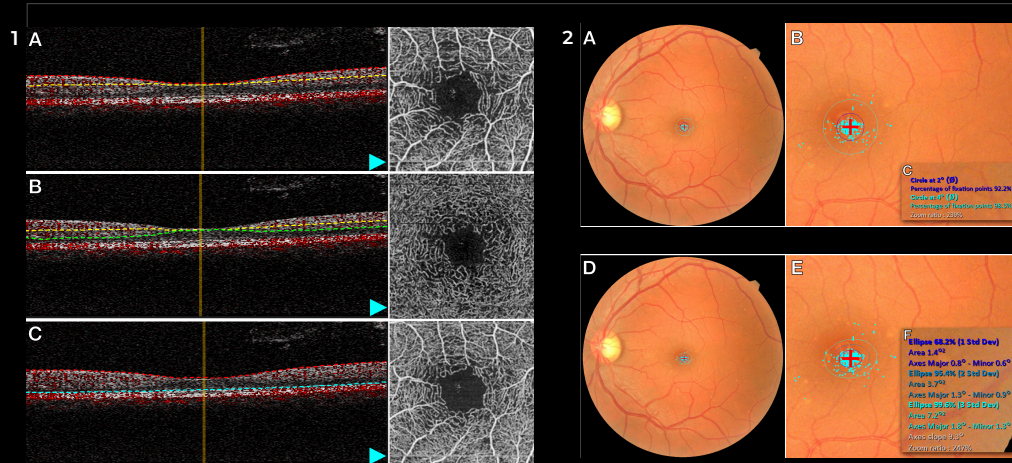
The genotype SC was found to present a moderate negative correlation between the FAZ perimeter in the superficial capillary plexus and visual acuity. Also regarding SC genotype, moderate positive correlation was found between contrast sensitivity and FAZ in full thickness retina angiogram both area and perimeter.

The same interpreted correlation was possible studying area and perimeter of FAZ both in superficial and deep capillary plexus.

Genotype SS showed a moderate, statistically significant correlation between the circularity of the FAZ in the superficial, deep, and entire retinal capillary plexus compared to the bivariate contour ellipse area (BCEA) in the first, second, and third standard deviations.

Circularity in the superficial plexus was moderately correlated with fixation on the 4-degree circle. It has also shown moderate negative correlation with its genotype identification and goldberg staging.

Figures regarding one of the patients are presented here. Tables summing the data in 3 different analysis are available through reading of the QR code ahead.



**FIGURE 1 LEGEND:** Angiogram fields of view and segmentation sayers in one of the patients of the study. On the left each structural OCT B-Scan images and correspondent angiograms on the right. Segmentations regarding superficial (A), deep (B) and full-thickness (internal limiting membrane to Bruch's membrane) (C) plexus, respectively.

**FIGURE 2 LEGEND:** Fixation test in the MP-3 microperimeter analyzed through dots in one of the patients. Each of the blue dots represents the retinal area gazing the center of the target at a certain time, therefore, the cloud of dots identifies the retinal area involved in fixating a target stimulus. Analysis of the 2° and 4° circles in (A) and (B). Analysis of the percentage of dots inside and outside the ellipse area (C) and (D).

**FIGURE 3 LEGEND:** FAZ measurements of two of the patients through OCT angiograms and respective microperimetric recordings in the fixation test. Patient 1: A) Area measuring 0.38 mm<sup>2</sup>, B) Perimeter with measure of 2.75mm and circularity 0.64. C) Area of the analysis point ellipse measuring 0.4 mm<sup>2</sup>. Patient 2: D) Area measuring 0.48mm<sup>2</sup>, E) Perimeter with measure of 3.39mm and circularity 0.52, F) Area of the analysis point ellipse measuring 3,8 mm<sup>2</sup>



**QR CODE FOR VISUALIZATION OF CORRESPONDING TABLES** Analysis of demographic population (TABLE 1), data comparing the total population (TABLE 2) and data regarding comparison between SS and SC genotypes (TABLE 3)

## DISCUSSION

Snellen letter test evaluation is useful for visual acuity measure although it lacks providing all the possible information regarding perception of spatial vision. Acting as an important complement in such assessment contrast sensitivity measures the ability to see details at low contrast levels and is shown to be considerable representative of visual functions.<sup>1,2</sup>

Fixation stability relies on the precision of eye fixation when one fixates intently on a stimulus for a certain period of time and it has been shown that correlates with slow reading speed.<sup>3,4</sup>

As opposed to subjective assessment to visual function, OCTA is used to assess retinal vascular structure.<sup>5</sup>

Athwart the decorrelation signal of the OCTA, in which differences in the backscattered OCT signal between sequential OCT B-scans construct a map of blood flow. Hence, enables the acquisition of volumetric angiographic information, which leads to visualization of each individual vascular plexus and segment the inner retina, outer retina, choriocapillaris, or other area of interest.<sup>5,6</sup>

Sickle cell retinopathy (SCR) is characterized by retinal vascular changes occurring due to such consequences of SCD. Under hypoxia, erythrocytes become sickle-shaped, causing vaso-occlusive complications that may occur in the peripheral retina or in the macula.<sup>7,8,9</sup> Secondary angiogenesis due to retinal ischemia can cause peripheral neovascularization so called proliferative SCR.<sup>8,10</sup>

Such high rates of maculopathy detected by OCTA were explained by the capability of OCTA to detect both superficial and DCP lack of perfusion even before retinal thinning onset revealing its undoubtedly major importance in patients with this disease.<sup>9</sup>

To the best of our knowledge, this is the first study to compare OCTA findings and fixation test. Our results supports FAZ circularity as a possible biomarker for estimating visual function and fixation stability in the SCD population. Nevertheless, future studies are needed to evaluate such applicability in other populations

## REFERENCES

1. Strain A, Carlson W. Relationship of contrast sensitivity measured using quick contrast sensitivity function with other visual functions in a low vision population. *Invest Ophthalmol Vis Sci*. 2011;52(10):6165-6170. doi:10.1167/2011.0071
2. Patel E. Contrast sensitivity function and image discrimination. 2001.
3. Liu H, Hattar K, Muehlestein M, et al. Fixation Stability Measurements Using Two Types of Microperimetry Devices. *Trans Am Ophthalmol Soc*. 2015; 4:3.
4. Crossland MD, Culham LL, Rubin GS. Fixation stability and reading speed in patients with newly developed macular disease?
5. de Carlo TE, Romano A, Willard NK, et al. A review of optical coherence tomography angiography (OCTA). *International Journal of Retina and Vitreous*. 1. Epub ahead of print July 2018; DOI: 10.1186/s12918-018-0005-8
6. Schwartz DM, Finger J, Kim DY, et al. Phase-variance optical coherence tomography: A technique for noninvasive angiography. *Ophthalmology*. 2016; 121:180-187.
7. Gouveia Bastos Meirelles M, de Araujo H, et al. CORRELATION OF MULTIMODAL IMAGING IN SICKLE CELL RETINOPATHY
8. Braxatoro R, Martins TT, Campos SB, et al. MACULAR AND PERIPHERAL SPECTRAL-DOMAIN OPTICAL COHERENCE TOMOGRAPHY CHANGES IN SICKLE CELL RETINOPATHY
9. Leitão Guerra RL, Leitão Guerra CL, Barros MC, et al. Sickle cell retinopathy: What we now understand using optical coherence tomography angiography. A systematic review. *Blood Reviews*. 2019; 35: 101-112.
10. DETECTION AND MONITORING OF SICKLE CELL RETINOPATHY USING ULTRA-WIDE-FIELD COLOR PHOTOGRAPHY AND FLUORESCIN ANGIOGRAPHY