



## Short Communication

## Preoperative and postoperative features of macular holes on en face imaging and optical coherence tomography angiography

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## ABSTRACT

**Purpose:** To characterize and quantify the pre- and postoperative foveal structural and functional patterns in full-thickness macular holes.**Methods:** Subjects presenting with a full-thickness macular hole that had pre- and postoperative imaging were included. En face optical coherence tomography (OCT) and OCT angiography (OCTA) was performed. Foveal avascular zone (FAZ) area, macular hole size, number and size of perifoveal cysts were measured.**Results:** Five eyes from 5 patients were included in the study. The hole was closed in all eyes after the initial surgery. OCTA showed enlargement of the FAZ and delineation of the holes within the FAZ. Mean preoperative FAZ area was  $0.41 \pm 0.104 \text{ mm}^2$ . Visual acuity was improved and mean FAZ area was reduced to  $0.27 \pm 0.098 \text{ mm}^2$  postoperatively ( $P < 0.05$ ) with resolution of the macular hole and adjacent cystic areas. En face images of the middle retina showed a range of preoperative cystic patterns surrounding the hole. Smaller holes showed fewer but larger cystic areas and larger holes had more numerous but smaller cystic areas.**Conclusions and Importance:** Quantitative evaluation of vascular and cystic changes following macular hole repair demonstrates the potential for recovery due to neuronal and vascular plasticity. Perifoveal microstructural patterns and their quantitative characteristics may serve as useful anatomic biomarkers for assessment of macular holes.© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

The foveal microstructure of macular holes has been extensively investigated using spectral-domain optical coherence tomography (SD-OCT). Most studies in this regard have utilized cross-sectional imaging analysis of the retinal layers, implicating the external limiting membrane,<sup>1,2</sup> ellipsoid zone,<sup>3,4</sup> interdigitation zone of the photoreceptors,<sup>5</sup> and the photoreceptor outer segment integrity<sup>6</sup> on preoperative visual function and postoperative visual outcome after surgical hole closure.

Recent advancements in image acquisition and processing provide the ability to use en face projections of volumetric data obtained by SD-OCT, allowing for simultaneous assessment of structural and functional (blood flow) information. Such en face

images have recently been used to characterize full-thickness macular holes as well as the perifoveal hyporeflexive intraretinal spaces observed surrounding them. Matet et al.<sup>7</sup> showed a marked concordance between en face OCT images of perifoveal cysts in full-thickness macular holes and histology of flat-mounted retinas, demonstrating the paramount contribution of Müller cells to macular microstructure. How subsequent pars plana vitrectomy and macular surgery affects these cystic areas and the underlying foveal retinal vasculature has not been reported to date.

OCT angiography (OCTA) is a novel imaging platform that utilizes motion contrast to visualize macular microvascular perfusion in a rapid, non-invasive, and depth-resolved fashion. Co-registration of structural en face projections of corresponding retinal layers is also performed with micrometer scale depth resolution. This offers the potential to perform quantitative assessment. New OCTA findings have been reported in a variety of fundus abnormalities.<sup>8–11</sup> The purpose of this report was to characterize and quantify the pre- and postoperative foveal structural and functional patterns in eyes with a full-thickness macular hole.

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## 2. Methods

Institutional review board approval was obtained through the Wills Eye Hospital (Philadelphia, PA) for a retrospective nonconsecutive interventional case series. Research adhered to the tenets of the Declaration of Helsinki and was conducted in accordance with regulations set forth by the Health Insurance Portability and Accountability Act (HIPAA).

### 2.1. Study subjects

Patients presenting with an idiopathic full-thickness macular hole that had pre- and postoperative imaging were included in the study. These eyes had been imaged between March 2015 and September 2015 at the Retina Service of Wills Eye Hospital. Cases with poor image quality, or any other concurrent macular disorder (such as epiretinal membrane, choroidal neovascularization, macular atrophy, macular edema), were excluded. All patients had been evaluated with comprehensive ophthalmologic examination including full medical history, best-corrected visual acuity (BCVA) testing, slit-lamp biomicroscopy, and funduscopy. A standard three-port 23-gauge pars plana vitrectomy, indocyanine green staining, internal limiting membrane peeling, and gas-fluid exchange with SF<sub>6</sub> was performed in all cases.

### 2.2. Imaging

A commercial SD-OCT system (RTVue-XR Avanti, Optovue, Fremont, CA) was used for imaging. All images were acquired over a 3 × 3 mm region centered on the macula with 304 raster B-scans obtained through each dimension.

Using this volumetric information, the retinal layers were automatically segmented between the internal limiting membrane (ILM) and the retinal pigment epithelium. Built-in software offset settings (version 2015.100.0.35) were used for this purpose. The boundaries for superficial network were from 3 μm below the ILM to 15 μm below the inner plexiform layer (IPL). The deep capillary network boundaries extended from 15 to 70 μm below the IPL. The split-spectrum amplitude-decorrelation angiography (SSADA) algorithm was used to generate flow information by computing inter-B-scan decorrelation from two consecutive raster B-scans performed at each location. En face structural and OCTA images were co-registered between the segmentation lines.

### 2.3. Image processing

Calculation of foveal avascular zone (FAZ) area was performed on the superficial retinal OCTA slab using the non-flow function of the imaging software (Fig. 1A and B). Quantification of cystic areas was performed semi-automatically from structural en face images acquired from the deep retinal slab. The public domain ImageJ software, version 1.49 (National Institutes of Health, Bethesda, MD) was used for this purpose. Following conversion to 8-bit grayscale images, hyporeflexive spaces were identified via the auto threshold v1.15 function using the “minimum thresholding” method. The identified areas were then highlighted on the original image and “particle analysis” was used to calculate the number of hyporeflexive spaces and their area (Fig. 1C and D). In order to reduce noise, an area of greater than 0.001 mm<sup>2</sup> was set as the threshold for inclusion in particle analysis calculations. SPSS, Version 20 (SPSS, Inc., Chicago, IL) was used for statistical analysis. Significance level was set at  $P < 0.05$  for performing comparisons.

## 3. Results

Five eyes from 5 patients presenting with a full-thickness macular hole were included in the study. The hole was closed in all eyes after the initial surgery as demonstrated by structural volumetric scans (Fig. 2). En face structural imaging demonstrated hyporeflexive areas corresponding to the hole and surrounding cystic areas that were best visualized on the deep retinal slab obtained just below the inner plexiform layer. Co-registered OCTA images showed enlargement of the FAZ and flow void in the areas with cystic changes. These cystic areas could clearly be delineated due to lack of the background noise that was otherwise present in the non-flow areas of the OCTA images (Fig. 3). Postoperative imaging was performed at a mean of 70 (range 56–91) days following surgery. Comparing pre- and postoperative images showed resolution of the cystic structures along with a decrease in superficial and deep FAZ size demonstrating preserved macular blood flow (Fig. 4).

The baseline, clinical, and imaging characteristics of the patients are presented in Fig. 5. OCTA images of the superficial vascular network showed enlargement of the FAZ and delineation of the holes within the FAZ. Mean preoperative FAZ area was  $0.41 \pm 0.104$  mm<sup>2</sup>. Visual acuity was improved and FAZ area was reduced to  $0.27 \pm 0.098$  mm<sup>2</sup> postoperatively in all cases ( $P < 0.05$ ) with resolution of the macular hole and adjacent cystic areas. En face images of the middle retina showed the preoperative cystic areas surrounding the hole in all cases. These appeared as different patterns ranging from larger, regular, and well-defined radial cystic areas with a petaloid or “grapefruit” configuration (Patient 1) to smaller, more dispersed cystic areas with a “sponge-like” appearance (Patient 5). The cross-sectional areas of the macular hole, cumulative area of the cystic spaces, and number of cystic areas appearing on the deep retinal slab were calculated using the automated algorithm previously described. Fig. 5 demonstrates increasing hole area from patient 1 through 5. As such, smaller holes showed fewer but larger cystic areas and larger holes had more numerous but smaller cystic areas.

## 4. Discussion

Evolving technologies such as en face OCT and adaptive optics have helped expand our understanding of the foveal ultrastructural changes that occur during macular hole formation and following surgery, as well as the impact of these changes on functional vision. With its improved acquisition speed and sensitivity, SD-OCT allows for three-dimensional (3D) imaging of the macular area. This form of volumetric imaging is clinically useful both for the physician and also for patient education. Previous studies on 3D imaging have demonstrated the ability to visualize intraretinal microstructures in consecutive orthogonal cross-sectional and sectioned volume images.<sup>12</sup> This enables for much more precise and minute observations of structural changes associated with macular holes than conventional OCT imaging. Furthermore, the volumetric data obtained allows for comprehensive measurement of retinal layer thickness. Novel image processing algorithms such as SSADA also enable simultaneous characterization of blood flow using OCTA.

Using OCTA, we demonstrated enlargement of the FAZ in eyes with full-thickness macular hole prior to surgical intervention. OCTA has recently been shown to measure FAZ area in healthy subjects in a reproducible and reliable manner,<sup>13,14</sup> especially when obtained at the level of the superficial vascular network.<sup>14</sup> We found that the mean FAZ area in our patients was larger compared to prior studies with healthy individuals, which showed mean

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