7/29/2023 12:00 am

Imaging, Digital, Angiography Symposium

Evaluation of EZ At-Risk Burden in Automatic Detection of Hydroxychloroquine Retinopathy

- Katherine Talcott, MD
- Gagan Kalra, MD
- Sari Yordi, MD
- Hasan Cetin, MD
- Yavuz Cakir, MD
- Sunil Srivastava, MD
- Justis Ehlers, MD, FASRS

Objective: To assess a novel quantitative biomarker, Ellipsoid Zone (EZ) At-Risk, in patients on hydroxychloroquine (HCQ) therapy with or without retinopathy and compare the measurement of this biomarker in normal eyes using optical coherence tomography (OCT).
Purpose: HCQ retinopathy can cause progressive vision loss even after discontinuation of the medication, so screening is crucial to detect early toxicity. Semi-automated machine learning (ML)-algorithms utilizing clinical history and advanced OCT segmentation have been described in the past for detection of toxicity. A fully automated, novel biomarker has been developed (EZ At-Risk) that can quantitatively measure EZ alterations that may provide an opportunity for automated identification of HCQ toxicity. The purpose of this analysis was to compare the EZ At-Risk burden in eyes with HCQ toxicity to eyes without toxicity.
Methods: This is an IRB-approved, cross-sectional study of 83 patients on HCQ and 44 age-matched normal subjects. SD-OCT images was collected for all patients (one eye per patient) and reviewed by two retina specialists for evidence of HCQ retinopathy. Patients on HCQ with retinopathy were labelled as “toxic” and remaining patients on HCQ as “non-toxic.” An ML-based, fully automatic measurement of percentage of the macular area with EZ At-Risk (i.e., attenuation of the EZ) was performed. Mean percentage area of EZ-At-Risk was compared between “toxic”, “non-toxic”, and the “normal” group.
Results: The mean age of patients on HCQ therapy was 51.6±14.7 years and 49.7±11.3 years for normal subjects. The “toxic” group included 38 patients compared to 45 patients in the “non-toxic” group. The mean EZ At-Risk in the “toxic” group was significantly higher (10.7%) compared to the “non-toxic” group (2.2%; p=0.023). The mean EZ At-Risk in the “toxic” group was also significantly higher than the “normal” group (1.4%; p=0.012). The was no difference between “non-toxic” and “normal” group (p=0.580). Additionally, the percentage area of EZ At-Risk was significantly correlated with HCQ dose based on actual (p=0.016) and ideal body weight (p=0.033) and trended towards significant correlation with cumulative dose (p=0.069).
Conclusion: The novel biomarker EZ-At Risk was significantly higher in patients with evidence of HCQ retinopathy when compared to patients on HCQ without retinopathy and age-matched normal subjects as well as significantly associated with HCQ dose. This novel biomarker should be further evaluated as a potential screening endpoint for patients on HCQ.

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Utility of En Face OCT for the Detection of Clinically Unsuspected Retinal Neovascularization in Patients with Diabetic Retinopathy

- Kotaro Tsuboi, MD
- Mehdi Mazloumi
- Yukun Guo
- Jie Wang
- Christina Flaxel, MD
- Steven Bailey, MD
- David Huang
- Yali Jia
- Thomas Hwang, MD

Objective: Can *en face* OCT detect early neovascularization lesions in diabetic eyes before they are visible with OCTA or clinical examination?
Purpose: To assess the value of *en face* OCT for detecting clinically unsuspected retinal neovascularization (RNV) in patients with nonproliferative diabetic retinopathy (NPDR).
Methods: This retrospective, cross-sectional study included treatment-naïve eyes clinically graded as NPDR in an ongoing prospective OCT angiography (OCTA) study at a tertiary care center. Each patient underwent imaging of one eye with a spectral-domain OCTA (Solix, Optovue), generating a 17′17-mm widefield image by montaging four 9′9-mm scans. Two independent graders examined a combination of *en face* OCT, *en face* OCTA with custom vitreoretinal interface slab, and cross-sectional OCTA to determine the presence of RNV. To measure the membrane area and the flow area of each RNV lesion, the three-dimensional (3D) RNV membrane and RNV flow were constructed by cross-sectional OCT and OCTA scans. We calculated the areas of the RNV membrane and the RNV flow by projecting 3D data into two-dimensional maps (Figure).
Results: Of 63 enrolled eyes, 27 (43%) were clinically graded as severe NPDR, 16 (25%) moderate NPDR, and 20 (32%) mild NPDR. Using the combination of *en face* OCT, *en face* OCTA and cross-sectional OCTA, the graders detected 42 RNV lesions in 12 (19%) eyes, of which 8 (67%) were graded as severe NPDR, 2 (17%) moderate NPDR, and 2 (17%) mild NPDR. The sensitivity of *en face* OCT alone for detecting eyes with RNV was similar to that of *en face* OCTA alone (100% vs. 92%, P = 0.32), while the specificity of *en face* OCT alone was significantly lower than that of *en face* OCTA alone (32% vs. 73%, $p < 0.001$). For detecting individual RNV lesions, the *en face* OCT was 100% sensitive, compared to 67% sensitivity for the *en face* OCTA (P < 0.001). Overall, the mean [SD] membrane area of an RNV lesion on *en face* OCT (0.12 [0.30] mm^2, [95% CI, 0.026 to 0.21]) was larger than the mean flow area by *en face* OCTA (0.027 [0.029] mm^2, [95% CI, 0.018 to 0.036]; $p < 0.001$ by Wilcoxon signed-rank test) by a factor (SD) of 3.4 (2.8) [95% CI, 2.5 to 4.3 times]. The area of RNV lesions that manual grading with *en face* OCTA alone missed was significantly smaller than that of manually detectable RNV (Mean [SD] RNV flow area, 0.015 [0.020] mm^2 vs. 0.16 [0.36] mm^2, $p < 0.001$).
Conclusion: The combination of e*n face* OCT and OCTA can detect clinically occult RNV with high sensitivity. *En face* OCT may provide additional value for detecting these small lesions.

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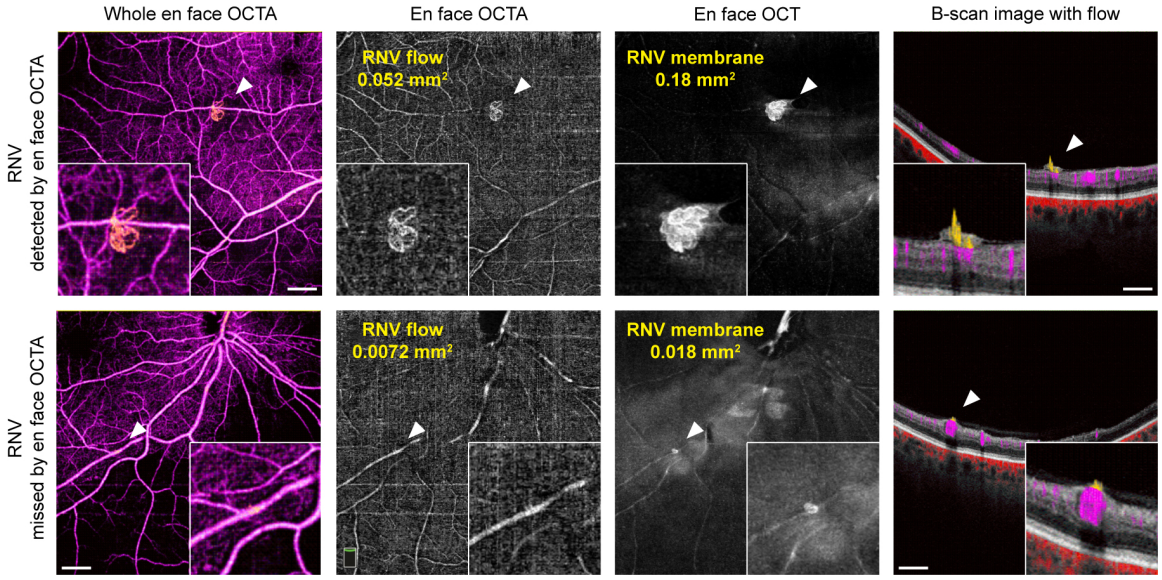

Detected and missed RNV using en face OCTA

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Utility of Outer Retinal Tubulation in Predicting Lesion Growth in Subfoveal and Nonsubfoveal Geographic Atrophy

- Srinivas Sai Kondapalli, MD
- Kensington Hatcher
- Mark Burch
- Birva Shah

Objective: Is the presence of an outer retinal tubulation associated with slower geographic atrophy growth rates regardless of lesion location?
Purpose: Outer retinal tubulation (ORT) is a known optical coherence tomography (OCT) biomarker in age-related macular degeneration (AMD) with unclear clinical value. The aim of this analysis is to examine the relationship between ORT and GA lesion growth. The predictive value of an ORT in subfoveal and nonsubfoveal lesions on GA growth rates was investigated with data from the FILLY trial, a Phase 2 clinical study investigating the C3 and C3b inhibitor pegcetacoplan in GA secondary to AMD.
Methods: This retrospective, longitudinal cohort analysis included eyes randomized to the sham arm of the FILLY trial. Lesions were characterized as subfoveal or nonsubfoveal based on distance from the atrophy junction to the center point of the fovea, with ≥1 µm defining nonsubfoveal. In both groups, a baseline Spectralis OCT was used to determine presence or absence of a fully formed ORT. At least one post- baseline fundus autofluorescence (FAF) GA lesion measurement was also required. The analysis included descriptive summaries of the change in GA lesion size (mm^2) as measured by FAF over 18 months.
Results: Sixty-two eyes were enrolled: 35 (56.5%) were subfoveal, 27 (43.5%) were nonsubfoveal. Of the subfoveal lesions, 9 (25.7%) had ORTs and of the nonsubfoveal lesions, 6 (22.2%) had ORTs.

Patients with a subfoveal lesion and ORT present had a mean change in baseline GA lesion area of 2.55mm^2 (SE: 0.33; 95% CI: 1.76–3.34) and a mean percentage change from baseline of 27.42% at Month 18.

Patients with a subfoveal lesion but no ORT present had a mean change in baseline GA lesion area of 2.71 mm^2 (SE: 0.41; 95% CI: 1.85–3.56) and a mean percentage change from baseline of 34.65%.

Patients with a nonsubfoveal lesion and ORT present had a mean change in baseline GA lesion area of 2.92 mm^2 (SE: 0.75; 95% CI: 0.99–4.84) and a mean percentage change from baseline of 47.66% at Month 18.

Patients with a nonsubfoveal lesion but no ORT present had a mean change in baseline GA lesion area of 4.10 mm^2 (SE: 0.64; 95% CI: 2.75–5.45) and a mean percentage change from baseline of 60.53%.
Conclusion: Presence of ORTs was associated with slower GA lesion growth over 18 months in subfoveal and nonsubfoveal lesions. Incidence of ORTs at baseline was similar between subfoveal and nonsubfoveal lesions. These results warrant consideration as clinicians assess progression risk in patients with GA. Further evaluation of this relationship in a larger population is warranted.

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Home OCT and Artificial Intelligence in Neovascular AMD

- Miguel Busquets, MD, FACS

Objective: To characterize Home OCT-derived fluid trajectories and effect of treatment timing in nAMD patients undergoing standard of care therapy.

Purpose: To investigate the characteristics of artificial intelligence-derived fluid volume trajectories in nAMD patients using Home OCT by evaluating fluid dynamics during the **reactivation to time of treatment** and **treatment to response** intervals, and to analyze the impact of treatment delay on the response to treatment.

Methods: Daily monitoring by the Notal Vision Home OCT (NVHO) and automatic AI-driven fluid quantification produces longitudinal fluid volume trajectories that depict the disease dynamics over the phases of reactivation, treatment, and response. In this study, phases of the fluid volume trajectory were manually annotated, resulting in 35 reactivations and 48 responses from 54 patients and 57 eyes. The mean and standard deviation of the time gap between the beginning of the reactivation and the time of treatment, as well as the mean and standard deviation of response duration, were calculated. In addition, the mean fluid increase and reduction rates were calculated for reactivations and responses respectively. Furthermore, all 35 reactivation episodes were divided into those with treatment within a week from reactivation vs those with treatment delay of more than one week. The differences between these populations were evaluated via mean fluid volume at treatment time, mean time to fluid resolution, and the mean fluid exposure over the course of the response to treatment represented by the AUC (area under the curve) response.

Results: The mean (SD) reactivation phase duration was 12 (10) days with a mean (SD) fluid increase rate of 12 (18) nL/day . The mean (SD) response phase duration was 11 (8) days with a mean (SD) fluid reduction rate of 8 (9) nL/day . When dividing the events according to treatment timing [measured as $\leq$1 week or >1 week since beginning of reactivation phase], the groups had a significant difference in mean volume at treatment [36 versus 139 nanoliters ($p<0.003$)], as well as in mean time to fluid resolution [4.7 versus 13.6 days ($p<0.02$)]. The mean AUC was 76 and 769 nL-days ($p<10^{-4}$) for treatment timing $\leq$1 week and >1 week, respectively.

Conclusion: Longitudinal fluid volume trajectories from automatic at-home patient monitoring open a window to previously unseen retinal fluid dynamics. Here, the relevant time constants for a standard-care nAMD patient undergoing treatment were evaluated. The results suggest that timely treatment improves the response and reduces fluid exposure. Remote patient monitoring may allow personalized treatment for better clinical outcomes.

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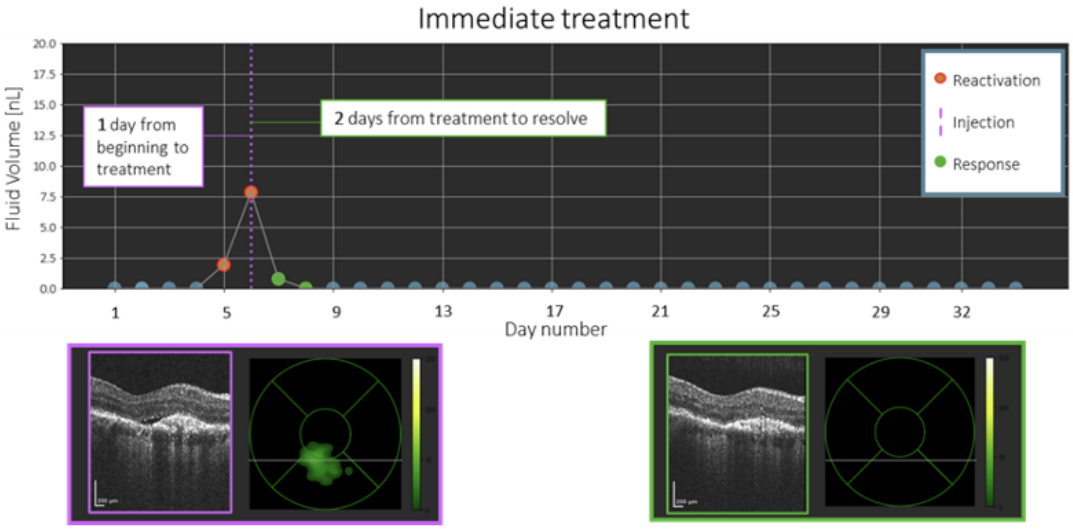

Figure 1: Prompt treatment resulting in rapid fluid resolution.

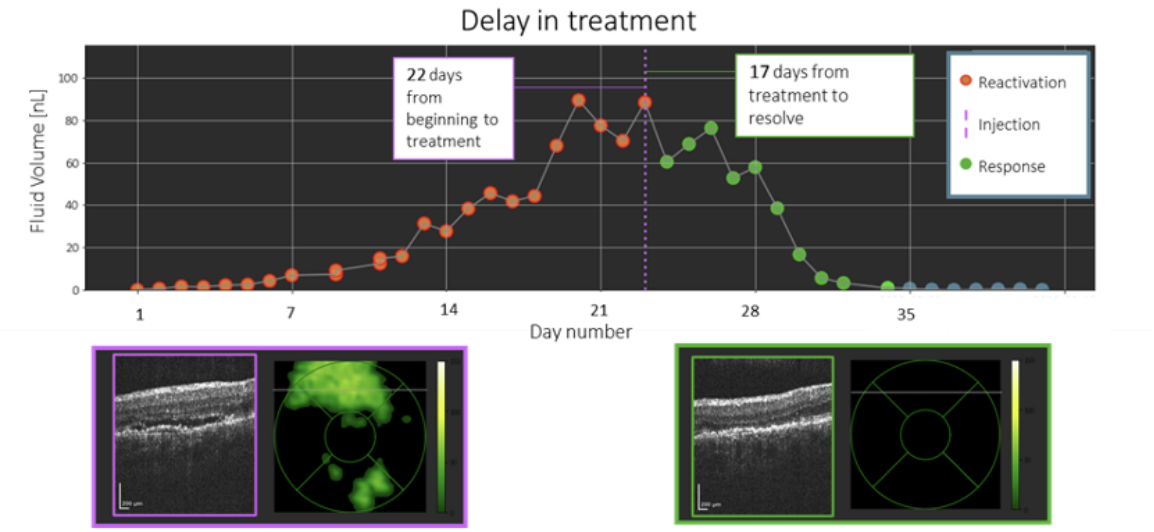

Figure 2: Delayed treatment with resulting lag in fluid resolution.