Classification and Guidelines for Widefield Imaging: Recommendations From the International Widefield Imaging Study Group

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OBJECTIVE How should the terms widefield and ultra widefield be defined to be universally applied across all imaging modalies?

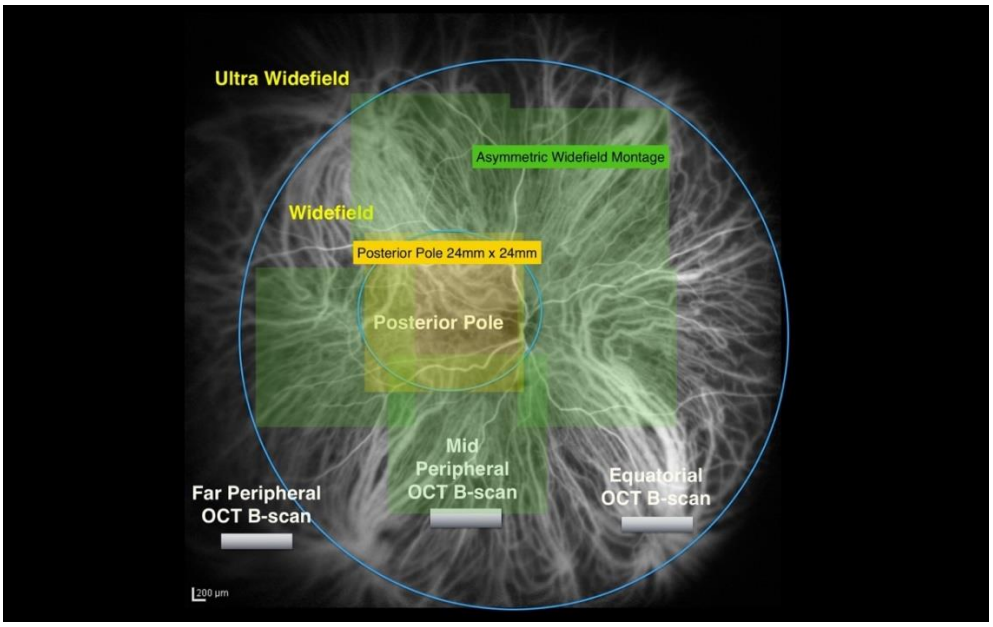
PURPOSE To summarize the results of a consensus meeting aimed at defining terminology for widefield imaging across all retinal imaging modalities and to provide recommendations for the nomenclature used to describe related images.

METHODS Prior to the consensus meeting, set of 7 images acquired with a range of imaging modalities and representing both normal and diseased eyes were circulated to the expert panel for independent assignment of nomenclature to each example. The outputs were assembled and used as the starting point for discussions occurring at a subsequent roundtable meeting. The anatomic location, field of view and perspective provided by each image example was

reviewed. A process of open discussion and negotiation was undertaken until unanimous terminology for widefield imaging was achieved.

RESULTS Across a range of different imaging modalities, the expert panel identified a lack of uniform terminology being used in recent literature to describe widefield images. The panel recommended the term widefield be limited to images depicting retinal anatomy beyond the posterior pole, but posterior to the vortex vein ampulla in all 4 quadrants. The term ultra widefield was recommended to describe images showing retinal anatomy anterior to the vortex vein ampullae in all 4 quadrants. The definitions were recommended over other device-specific terminology.

CONCLUSION A consistent nomenclature for widefield imaging based on normal anatomic landmarks that is applicable to multiple retinal imaging modalities has been proposed by the International Widefield Imaging Study Group. The panel recommends this standardized nomenclature for use in future publications.



A 102^0 asymmetric field of view (shaded green) ICG. The posterior pole (inner blue circle) and the region beyond the posterior pole up to the posterior border of the vortex vein ampulla, are identified as midperiphery. The anatomic region beyond the anterior border of the vortex vein ampulla is identified as the far periphery. A widefield view encompassing the retina up to and including the vortex vein ampullae is delineated by the outer blue circle.

HUMAN RESEARCH No: Study does not involve

Rapid Array Capture Technology for Fundus Imaging

- Tushar M. Ranchod, MD

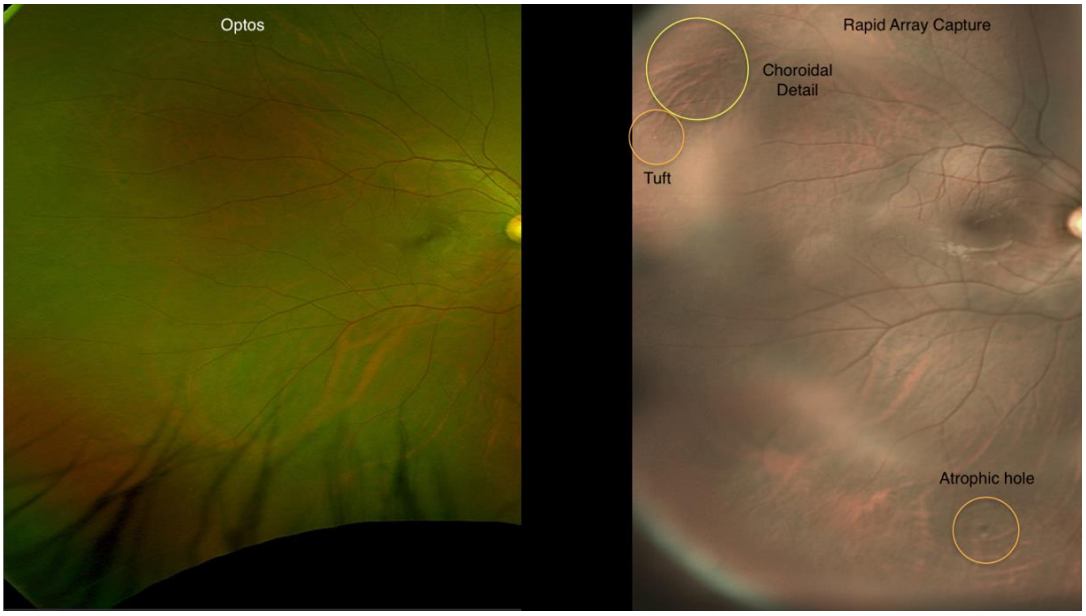
OBJECTIVE Rapid Array Capture (RAC) Technology is able to acquire true color 180 degree images of the retina and choroid

PURPOSE The purpose of this study is to demonstrate an unprecedented level of retinal and choroidal imaging detail combined with an ultrawidefield view using a novel and small-scale fundus imaging optical design.

METHODS This proof of concept study prospectively imaged human eyes with a prototype handheld device. The device captured an array of images in less than 500 ms and generated a composite image for review.

RESULTS The RAC technology was able to acquire 180 degree true color fundus images that identified peripheral retinal and choroidal details not see in images taken with existing ultrawidefield devices. The RAC technology was able to fit into a compact, hand-held form factor.

CONCLUSION The RAC technology enables ultrawidefield true color fundus imaging with a level of retinal and choroidal detail not imaged with current diagnostic devices. The RAC technology also enables UWF imaging in a form factor that is dramatically smaller than current UWF diagnostic devices.



The same eye imaged using an Optos California (left) and a Rapid Array Capture (RAC) prototype (right). Subtle clinical features (labeled orange circles) are visible in the RAC image but not in the Optos image. Choroidal detail (yellow circle) is also more prominent in the RAC image.

HUMAN RESEARCH Yes: Approved by institutional review board

Longitudinal Panretinal Leakage Index Assessment in Proliferative Diabetic Retinopathy Treated With Aflibercept From the RECOVERY Study

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OBJECTIVE To determine if leakage index on ultra-widefield fluorescein angiography (UWFA) improves following intravitreal aflibercept (IAI) treatment in eyes with proliferative diabetic retinopathy (PDR).

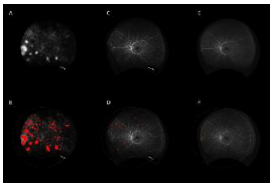
PURPOSE To assess the longitudinal change in panretinal leakage index on UWFA in eyes with PDR following intravitreal aflibercept (IAI) in the RECOVERY Study (NCT02863354).

METHODS Forty subjects with PDR without vitreous hemorrhage or panretinal photocoagulation were randomized (1:1 ratio) into 2 treatment arms. The 2q4 group received 2 mg IAI every 4 weeks, the 2q12 group received 2 mg IAI every 12 weeks. UWFA was performed at baseline, 24 weeks, and 48 weeks. Quantitative UWFA was performed using a semi-automated analysis platform. Panretinal leakage index was calculated as the percentage of

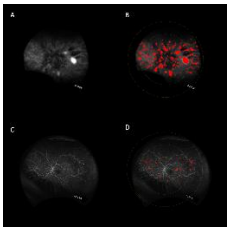
leaking retinal area defined as leakage area(s) divided by analyzable retinal area. Two independent masked expert readers reviewed and manually corrected any segmentation errors. Longitudinal change within each group and comparative assessment between groups was evaluated.

RESULTS Forty eyes of 40 subjects were included with a mean age of 48±12.1 years. Nineteen (47.5%) subjects were female and 21 (52.5%) were male. The mean number of injections was 11±1.7 in the 2q4 arm and 4±0.4 in the 2q12 arm. The median baseline panretinal leakage index in the 2q4 and 2q12 groups was 5.1% and 4.3%, respectively ($p = 0.22$). At week 24 and week 52, the 2q4 group had significantly improved to 1.1% (-79%, $p < 0.0001$). At week 24, the 2q12 group improved but not significantly to 3.4% (-21%, $p = 0.47$); but at week 52, the leakage index had improved significantly to 1.4% (-68%, $p = 0.02$). The 2q4 group resulted in lower leakage indices compared to the 2q12 group at 24 weeks (1.1% vs 3.4%, respectively; $p = 0.008$), but by week 52 the leakage indices were similar between the 2q4 and 2q12 groups (1.1% vs 1.4%, respectively; $p = 0.34$).

CONCLUSION IAI resulted in dramatic reductions in panretinal leakage index in eyes with PDR. 2q4 dosing provided more rapid reduction in leakage index compared to 2q12 dosing. Future research will focus on the impact of leakage index dynamics on outcomes and its potential as a quantitative biomarker for treatment indication/disease activity.



Representative case demonstrating leakage on ultrawidefield angiography: at baseline (A) with leakage overlay (B), at 6-months (C) with leakage overlay (D), and at 12 months (E) with leakage overlay (F). Disc centered concentric rings seen in B,D,F outline the regions where leakage was defined.



Representative case demonstrating leakage on ultrawidefield angiography: at baseline (A) with leakage overlay (B), and at 6-months (C) with leakage overlay (D). Disc centered concentric rings seen in B,D outline the regions where leakage was defined.

HUMAN RESEARCH Yes: Approved by institutional review board

Longitudinal Ellipsoid Zone Mapping on Spectral Domain OCT in Eyes With Hydroxychloroquine Use to Evaluate for Subclinical Outer Retinal Alterations

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OBJECTIVE Can a semi-automated ellipsoid zone mapping platform be used to detect longitudinal changes on spectral domain OCT that may precede clinical hydroxychloroquine toxicity?

PURPOSE Loss of ellipsoid zone (EZ) integrity on optical coherence tomography (OCT) is a hallmark feature of hydroxychloroquine (HCQ) toxicity but early alterations can be subtle. The purpose of this study is to evaluate longitudinal changes on OCT that may precede clinical HCQ toxicity using a semi-automated EZ mapping platform.

METHODS This study was an IRB-approved retrospective image analysis of patients currently taking HCQ who had OCTs at two time points. Patients with concurrent macular disease were excluded. The two macular cube scans were exported and analyzed in the EZ mapping platform. Seven outer retinal parameters were utilized to evaluate for subtle alterations over time: mean parafoveal (central 2-mm) ONL-EZ thickness/volume, mean parafoveal EZ-RPE thickness/volume, en face percentage of EZ total attenuation (EZ thickness = 0µm), en face EZ attenuation (EZ thickness < 20µm). Outputs were compared between scans using paired t-tests.

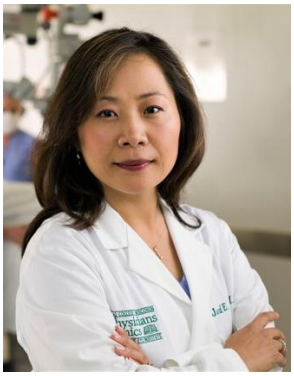
RESULTS Four hundred one eyes of 401 subjects were included. Mean age was 57.6±0.2 years, mean daily HCQ dose was 367.1±72.6 mg, and mean HCQ dose based on actual body weight was 4.9±1.8 mg/kg. At time of the first OCT, mean duration of HCQ use was 5.8±3.9 years and cumulative HCQ dose was 2.1±1.5 grams. Mean time between the two OCT time points was

3.1±0.9 years. There was a significant increase in en face EZ attenuation from the first OCT (1.4±5.6%) to the second OCT (1.8±6.3%; p=0.01). The increase in EZ loss significantly correlated with age (p=0.04), drug duration (p=0.004), and cumulative dose (p=0.002), but not daily dose (p=0.24) or dose based on actual body weight (p=0.11). There was also an increase in en face EZ total attenuation between the 2 OCTs (0.9±5.0% vs 1.1±5.3%) but this was non-significant (p=0.08). There was no significant longitudinal change in mean parafoveal (central 2-mm) ONL-EZ thickness/volumes or parafoveal EZ-RPE thickness/volumes (all p>0.09).

CONCLUSION Longitudinal assessment of outer retinal integrity revealed a significant increase in EZ attenuation which correlated with age, cumulative dose, and duration on drug. Additional research is needed to further validate these subclinical progressive changes and their impact on identification of HCQ toxicity.

HUMAN RESEARCH Yes: Approved by institutional review board

Performance and Usability of a Self-Operated Home Optical Coherence Tomography (OCT) System: NOTAL-OCT V2.5 (NO V2.5)



- Judy E. Kim, MD
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- David R. Lally, MD
- Oren Tomkins-Netzer, MD

OBJECTIVE To evaluate performance of self-operated home OCT device in retinal fluid detection, by comparing with commercial OCT devices and in patient usability.

PURPOSE Home OCT device has the potential to reduce treatment burden of frequent office visits for patients to be assessed while allowing timely detection of disease worsening during treatments in many of the retinal conditions. We evaluated a novel self-operated home OCT device, by comparing fluid detection ability with commercial OCT devices and by patient usability.

METHODS Consecutive eyes with either intermediate or neovascular age-related macular degeneration (nAMD) and VA ≥ 20/400 from 2 clinics were included. Demographic and ophthalmic history, and VA were collected. Non-dilated subjects were imaged by a commercial OCT (Zeiss Cirrus or Heidelberg Spectralis). After a 1-minute tutorial, subjects self-operated the Notal Home OCT (NO V2.5) to capture OCT images of their own eyes. Initial sessions were video recorded to obtain ergonomic data and patient training. 3x3mm NO V2.5 images from the central 10 degrees of the macula were compared, by an ophthalmologist, to the commercial OCT reference images for presence of intra and/or subretinal fluid.

RESULTS 89 eyes from 48 subjects were enrolled (22 male; 26 female), with a mean age of 78 years (median, 80.5 years; range, 54-92 years). 7 eyes from 7 subjects were excluded due to VA <20/400. Mean VA was 20/40 (median, 20/40; range, 20/16-20/200). 45/48 (94%) subjects and 84/89 (97%) eyes were successfully imaged with both the commercial OCT and the NO V2.5. Among 5 eyes that could not be imaged, 4 eyes were from 3 patients who could not self-operate the NO V2.5 due to decreased cognitive ability preventing task understanding, and 1 eye was due to a NO V2.5 system failure. The sensitivity and specificity of the NO V2.5 for detecting fluid were 91% and 100% respectively when compared to the commercial OCTs.

	Commercial OCTs (Fluid Positive)	**Commercial OCTs (Fluid Negative)**	**Total Eyes**
NOTAL-OCT V2.5 (Fluid Positive)	**43**	**0**	**43**
NOTAL-OCT V2.5 (Fluid Negative)	**4**	**37**	**41**
Total	**47**	**37**	**84**
	Sensitivity = 91%	**Specificity =100%**	

CONCLUSION 94% of the patients were able to self-operate the NO V2.5 and capture gradable image of their macula. Therefore, it appears user-friendly. NO V2.5 comparison to commercial OCT demonstrated excellent sensitivity and specificity. This user-friendly OCT system, designed for self-operation at-home use, has a potential to obtain images comparable to those from commercial OCTs.

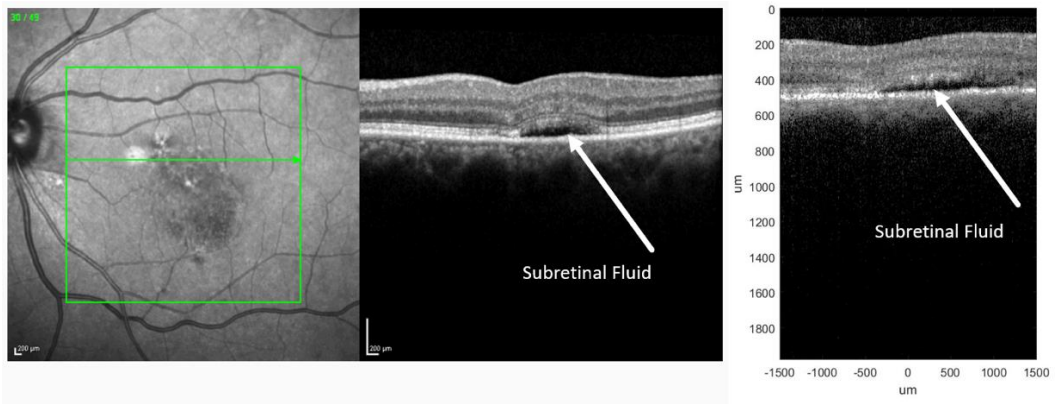

Figure 1: A small pocket of subretinal fluid is evident in images captured by Heidelberg Spectralis and NOTAL-OCT V2.5

HUMAN RESEARCH Yes: Approved by institutional review board