Adaptive Optics and OCTA:
Update on Retinal Imaging

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- Advisory Board
  - Alimera Science, Allergan, Bayer, Novartis
- Research Equipment
  - Optos, Notal Vision

- None related to this presentation
- Device for research use only and not yet FDA approved
What is OCT Angiography?

- A non invasive way of performing retinal angiography without the use of extraneous dyes
- Done using newer generation OCT machines
- Takes 3-4 secs per eye
OCTA: How is it done?

Speed

Resolution
Depth Resolved Microvasculature

Total
Superficial
Intermediate
Deep
Choriocapillaris

3x3mm
Pressing Questions

- Where is OCTA clinically useful? What does it do better than what we have now?
  - Does it add to information from standard imaging modalities
  - Does it allow for better follow up
  - Does it drive better treatment options
  - Does it improve prognosis
  - What are the cost and time implications
Disease Modalities

- Diabetic retinopathy
- Choroidal neovascularization
  - Exudative AMD
  - Non-exudative AMD
- Other retinal vascular disease
OCTA in Diabetic Retinopathy
OCTA in Diabetic Retinopathy
Vessel Density

**RETINAL VASCULAR PERFUSION DENSITY MAPPING USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN NORMALS AND DIABETIC RETINOPATHY PATIENTS**

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Fig. 1. An en face OCTA of a normal subject demonstrating the visualization of the (A) superficial retinal plexus, (B) the deep retinal plexus, and (C) the choroidplexus. Skeletonized vessel maps, vascular perfusion maps (VPMs), and an overlay of the OCTA and VPMs (far right) are also included for each layer. Using these density maps, a CPD is calculated for each microvascular layer. The corresponding CPD values for the layers show an 0.197, 0.235, and 0.334, respectively. The increased perfusion in the choroidplexus compared with the superficial retinal plexus can be appreciated quantitatively with flow index and qualitatively with the color perfusion maps.
Vision Limiting Macular Ischemia
OCTA in PDR

- Identify NV
- Follow NV for regression
- Follow NV for re-growth
Disease Modalities

- Diabetic retinopathy
- Choroidal neovascularization
- Other retinal vascular disease
OCTA of CNV: Type 1

Flow under PED
OCTA of CNV: Type 3

OCTA: Sensitivity and Specificity

- Investigated CNV qualities on OCTA

- Sensitivity and specificity of CNV detection by OCTA using FA as the gold standard:
  - Sensitivity = 4/8 (50%)
  - Specificity = 20/22 (91%)

- Sensitivity 70-100% in type 1 CNV

OCTA: Size of Lesion

CNV 1 Week Post-Injection

CNV 3 Weeks Post-Injection
CHARACTERIZING THE EFFECT OF ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY ON TREATMENT-NAIVE CHOROIDAL NEOVASCULARIZATION USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

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Purpose: To use optical coherence tomography angiography (OCTA) to characterize the effects of anti-VEGF injections on treatment-naive choroidal neovascularization (CNV).

Methods: From August 2014 to May 2015, treatment-naive eyes with CNV were scanned using a prototype OCTA system on a commercially available SD-OCT device (Optovue Inc, Fremont, CA). Optical coherence tomography angiography scans were obtained before anti-VEGF injection and at follow-up visits. The CNV area and greatest linear dimension (GLD) were measured along with the maximum retinal pigment epithelial detachment (RPED) height. Changes in subretinal and/or intraretinal fluid were also assessed.

Results: Six eyes of six patients with treatment-naive CNV were included. Diagnoses included neovascular age-related macular degeneration, idiopathic polypoidal choroidal vasculopathy, CNV secondary to central serous chorioretinopathy and multifocal choroiditis, and macular telangiectasia Type 2 with subfoveal neovascularization. After treatment, all patients with fluid on OCT initially showed a decrease in the amount of fluid. Five of six patients demonstrated decreases in CNV GLD and area with an average reduction of 20.6% and 29.8%, respectively.

Conclusions: Both CNV greatest linear dimension and area measured using OCTA decreased after anti-VEGF treatment in most patients. Optical coherence tomography angiography may be a useful tool for monitoring and quantifying the response of CNV to treatment.

Case # 1

- 58-year-old Asian man followed for dry AMD
  - OD 20/50
  - OS 20/70+2
Neovascular ‘Dry’ AMD

Optical Coherence Tomography Angiography of Asymptomatic Neovascularization in Intermediate Age-Related Macular Degeneration

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Objective: To determine whether angiography with swept-source (SS) optical coherence tomography (OCTA) identifies subclinical type 1 neovascularization in asymptomatic eyes with intermediate age-related macular degeneration (AMD). Design: Prospective, observational, consecutive case series.

Participants: Patients with asymptomatic AMD in one eye and neovascular age-related macular degeneration (AMD) in their fellow eye.

Methods: The patients underwent SS OCT angiography (OCTA), fluorescein angiography (FA), and indocyanine green angiography (ICGA), and the images from these 3 angiographic techniques were compared.

Main Outcome Measures: Identification of subclinical type 1 neovascularization with SS OCTA in asymptomatic eyes with AMD.

Results: Eleven consecutive patients with AMD in one eye and neovascular AMD in their fellow eye were imaged with FA, ICGA, and SS OCTA between August 2014 and September 2015. Clinical examination of the 11 eyes revealed drusen and pigmentary abnormalities in the central macula and no evidence of macular fluid on routine OCT imaging. Ten of the 11 eyes had no evidence of leakage on FA and 1 eye had questionable fluorescein leakage. Indocyanine green angiography revealed the presence of central macular plaques in 3 of the 11 asymptomatic eyes with AMD, and SS OCTA revealed unambiguous type 1 neovascularization corresponding to the plaques in all 3 eyes. Optical coherence tomography angiography did not identify neovascularization in the remaining 8 eyes.

Conclusions: Swept-source OCTA identified type 1 neovascularization corresponding to ICGA plaques in asymptomatic eyes with AMD. The ability of OCTA to provide noninvasive, fast, detailed, depth-resolved identification of neovascular and non-neovascular lesions in eyes with AMD suggests the need for a new classification system that distinguishes between neovascular and non-neovascular AMD. Ophthalmology 2016;113:7–11 © 2016 by the American Academy of Ophthalmology.
Disease Modalities

- Choroidal neovascularization
- Diabetic retinopathy
- Other retinal vascular disease
BRVO on OCTA

FA

OCTA Wide-Field Montage
Clinical Utility of OCTA

- Multidimensional imaging modality
  - OCTA provides all the information that you would get in a regular OCT, AND provides cross-registered vascular information

- Depth Resolved
  - Can separate out the superficial from the deep layers of vasculature

- Non-Invasive and Fast
  - Repeat at multiple visits and to closely monitor patients
  - Acquisition times are 3-4s per eye.
  - Total time in room is 10 mins

- OCTA is becoming a staple of retinal clinical practice in the diagnosis and management of AMD, DR and Retinal Vascular Disease
Adaptive Optics
Adaptive Optics

- Technology used to improve the performance of optical systems by reducing the effect of wave front distortions
- Corrects aberrations in lens and cornea that distort wavefront
Components of Adaptive Optics

Wavefront Sensor

Lenslet array

CCD array

Controller

Wavefront Corrector

\[ \Delta x_i \]
Components of Adaptive Optics

Wavefront Sensor
- Lenslet array
- CCD array

Controller
- \( \Delta x_i \)

Wavefront Corrector
How does it work?

Courtesy of Geunyoung Yoon
Retinal Images

No AO correction

AO correction
## Resolutions of Adaptive Optics Retinal Cameras

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<th>Resolution</th>
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<tr>
<td>AO-fundus camera</td>
<td>Lateral: 2 μm  Axial: 60 μm</td>
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<tr>
<td>AO-confocal SLO</td>
<td>Lateral: 2 μm  Axial: 20 μm</td>
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<tr>
<td>AO-SD OCT</td>
<td>Lateral: 2 μm  Axial: 3 μm</td>
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AOSLO montage overlaid on fundus photo

Cone mosaic 1° from foveal center

Courtesy: Mina Chung, MD
Create a montage from many locations

Cone Density Profile
Cone-rod dystrophy
AOSLO montage overlaid on fundus photograph of a patient with MacTel: 10° from fovea

Courtesy: Hongxin Song, MD PhD and Mina Chung MD
Rod Image @ 10 degree

Histology

In vivo Image

Foveal Cones

Scale bar: 10μm

Cone Reflectance Variation Over Time

“Twinkle Twinkle Little Cones”


Rod Reflectance Variation Over Time

R.F. Cooper, A.M. Dubis, A. Pavaskar, J. Rha, A. Dubra and J. Carroll

Retinal Pigment Epithelial Cell Mosaic

Nerve Fiber Layer
Glaucoma

62 y.o. female

Glaucoma

D.H. Scoles, Y.N. Sulai, A.D. Manguikian, S. Shareef and A. Dubra

2012 ARVO Abstract 53:6957

500 μm
Optic Nerve Imaging: Lamina Cribrosa

Courtesy: Imagine Eyes
Vascular Imaging and Perfusion Maps:

50 µm
Foveal Perfusion Map: Normal Subject
Without Fluorescein Dye

Scale bar: 100 µm
Despite macular hole (MH) closure following pars plana vitrectomy (PPV) surgery, vision loss or metamorphopsia may persist.
Despite macular hole (MH) closure following pars plana vitrectomy (PPV) surgery, vision loss or metamorphopsia may persist.
SD-OCT studies have shown that mild outer segment changes are common in the early post-operative course.
Macular Hole Closure

- What is going on at the photoreceptor layer at the fovea following surgery?
- Why are there differences in VA even when MH is closed?
Case 1: 3 months post-op
VA 20/50-2
Case 1: 3 months post-op VA
20/50^-2
Case 1: 3 months post-op VA 20/50−2
Case 1: 3 months post-op VA 20/50^{-2}

17 months post-op VA 20/30^{-2}
Case 1: 3 months post-op VA 20/50-²

17 months post-op VA 20/30-²
Case 2: 3 months post-op
VA 20/80
Case 2: 3 months post-op
VA 20/80
Case 2: 3 months post-op
VA 20/80

12 months post-op
VA 20/30
- Significant photoreceptor disruption appears to exist following MH closure
- Remodeling of the foveal cone mosaic can continue following surgery, perhaps accounting for the delayed post-operative VA improvements
“Dark Cones”

Cones present but not wave-guiding

Cones are absent
AO SLO Imaging of Photoreceptors

Visualization of cone structure with confocal AOSLO relies on IS/OS alignment and intact outer segment structure

AO SLO Imaging of Photoreceptors

Visualization of cone structure with confocal AOSLO relies on IS/OS alignment and intact outer segment structure

Scoles D, et al., In vivo imaging of human cone photoreceptor inner segments, IOVS 2014;6;55(7):4244-51
Split Detector AOSLO

- Captures the non-confocal light and divides it spatially
- Creates good contrast for structures that scatter light
  - Blood vessels
  - Rounded pole of photoreceptor inner segments

Confocal AO

Split detector AO

Scoles et al. (submitted)
Variable Foveal Cone Structure in *Achromatopsia*

**CNGB3**
c.1148 delC: p.Thr383fs
c.983T>A: p.Met328Lys

**CNGB3**
c.1148 delC: p.Thr383fs
c.1255G>T: p.Glu419stop
Achromatopsia (ACHM)

Autosomal recessive; ≈1 in 33,000 incidence

- Caused by defects in CNGA3, CNGB3, GNAT2, PDE6C, PDE6H, or ATF6
- Affected individuals are thought to have no cone function (though see Nishiguchi, et al., 2005)
- Photophobia, reduced acuity, nystagmus
- Histological data concerning remnant cone structure is variable, ranging from normal numbers in the fovea (Falls et al., 1965) to reduced numbers throughout (Larsen, 1921)
Variable Foveal Cone Structure in Achromatopsia

**CNGB3**
c.1148 delC: p.Thr383fs
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c.1255G>T: p.Glu419stop
Recent success in retinal gene therapy
May be possible to restore cone function in some retinal disorders

“…identifying and then targeting retinal locations with retained photoreceptors will be a prerequisite for successful gene therapy in humans…” Jacobson et al. (2005)
Why is AO needed?

- Necessary to detect photoreceptor loss early
- Assist in selection of candidates for therapies
- Earlier detection of treatment effect
AO Imaging

- Assist in better understanding of photoreceptor structure and vessels
- Allow assessment of the therapeutic potential and outcomes in patients with retinal disorders