Update On Imaging For AMD

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Agenda

● Discuss the imaging modalities routinely used and their role
● Highlight particular OCT enhancements which aide in the management of AMD patients
● Discuss some of the imaging findings from recent clinical trials

How is AMD Imaged?

- Color Fundus photography
- Fundus Autofluorescence
- Fluorescein Angiography
- ICG Angiography
- OCT
  - Cube scan
  - Enhanced Depth Imaging (EDI)

How: AMD Imaging

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**Color Fundus Photography**

- Role is uncertain except when interpreting FA
- Documenting activity such as hemorrhage may be useful to follow the patient
- Identification of fibrosis usually an exclusion for clinical trials
- Future ‘anti-fibrotic’ therapies may increase the relevance

**Fundus Autofluorescence**

- FAF in AMD mainly used for tracking GA
- Helps explain to patients – Dark is Bad

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**Measuring Geographic Atrophy with RPE Subillumination - Correlation between OCT and FAF**

- Comparison of areas designated as sub-RPE illumination by the CIRRUS HD-OCT versus those designated as Geographic Atrophy on fundus autofluorescence (FAF).

Reference:
Fundus Autofluorescence

- Peripheral FAF findings seen in both neovascular and non neovascular AMD – 68.9% abnormal
- Classification
  - Granular
  - Nummular
  - Mottled

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Fluorescein Angiography - Baseline

- Does fluorescein angiography still have a role in the baseline assessment of a newly diagnosed neovascular AMD patient?

Fluorescein Angiography

- Yes – FA plays a very important role
  - Location may lend itself to PDT or focal laser with cure rate
  - Important to understand if polypoidal, CSR, or other pathology is present
  - Understanding lesion composition may still shape treatment decisions (e.g. occult vs. classic)
**Fluorescein Angiography – Follow-up**

- **Is FA helpful after initiation of therapy?**

**When: Fluorescein Angiography – Follow-up**

- **Yes**
  - Incomplete response to treatment, may be important to re-evaluate other potential pathology.
  - Some clinicians use as a stopping point – if dry on OCT and no leakage on FA, some believe may be a secure point to suspend therapy.

**How: AMD Imaging**

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**Indocyanine Green Angiography**: Does it have a role in AMD?

- Routinely – No
- Select cases – Yes
- At Baseline
  - Looks like neovascular AMD but there are no drusen present
  - In patient population with high incidence of polypoidal or confluent for CSR
- During Follow-up
  - Patient not responding completely to anti-VEGF therapy

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**OCT Treatment Monitoring**
- >90% of patients in US are not treated with monthly dosing
- Most are treated with Treat-and-Extend algorithm
- Both require regular monitoring with OCT
- PRN approach studied and validated in CATT and HARBOR
Improved acquisition times and more data:
Time Domain vs Spectral Domain

**Scanning strategies**
- \(512 \times 6 = 3072\) A-scans
  - (7.7 seconds)
- \(200 \times 200 = 40,000\) A-scans
- \(512 \times 128 = 65,536\) A-scans
- \(4096 \times 5 = 20,480\) A-scans
- Total A-scans = \(126,016\) A-scans
  - (4.7 seconds)

**How is a cube scan made?**

Axial scans (A-scans) make up a B-Scan

**B-scans make up the 3-D dataset or SDOCT cube**

40,000 A-scans in 1.5 seconds

**The benefit of more B-scans**

- An increase in the number of B-scans reduces the variability of measuring the central subfield thickness and macular volume.
Applications for the cube scan

Advanced RPE Analysis

Screen 1

Screen 2
RPS1  Cube scan only, not the picture to the left.
Rishi Singh, 8/21/2013
Measuring Geographic Atrophy with RPE Subillumination - Correlation between OCT and FAF

Comparison of areas designated as sub-RPE illumination by the CIRRUS HD-OCT versus those designated as Geographic Atrophy on fundus autofluorescence (FAF).

Case example – RPE elevation analysis

- 63 y/o woman with neovascular AMD
- Decreased vision for 2 months, 20/100

Intravitreal Lucentis Injected

Area: 14.806 mm²
Volume: 7.282 mm³
**Case example – RPE elevation analysis**

Baseline
- VA: 20/100
- 7.242 mm³
- Lucentis #1

1 m s/p L #1
- VA: 20/40
- 2.031 mm³
- Lucentis #2

1 m s/p L #2
- VA: 20/30
- 1.472 mm³
- Lucentis #3

Area: 15 mm² → 13 mm² (-13%)
Volume: 7.2 mm³ → 1.5 mm³ (-79%)

**OCT Artifacts**

- Not uncommon even with SDOCT
- Can affect both quantitative and qualitative interpretations
- Artifacts can result from
  - Software errors
  - Patient factors
  - User errors

**Most common artifacts seen**

- Misalignment
- Blink or motion
- Shadowing
- Software error

**Automatic Fovea Finder**

- OCT software identifies the fovea location automatically by finding the reduced reflectivity below the retina.
### Macula Thickness Report
- Fully automated analysis
- Fovea Finder™ automates ETDRS grid placement
- Layer maps highlight abnormalities

### Case Example – Fovea Finder

**Overlay: ILM - RPE**
**Transparency: 50%**

<table>
<thead>
<tr>
<th>ILM - RPE Cube Average Thickness (µm)</th>
<th>Cube Volume (mm³)</th>
<th>Central Subfield Thickness (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cube 1: 284</td>
<td>10.2</td>
<td>319</td>
</tr>
<tr>
<td>Cube 2: 275</td>
<td>9.9</td>
<td>259</td>
</tr>
</tbody>
</table>

**Fovea Finder OFF**
Central subfield = 319

**Fovea Finder ON**
Central subfield = 259

### Eye Tracking Software
- Allows for improved image acquisition in cases of patient cooperation and eye movement.
- Improves registration capabilities

### Case Example

**Good cooperation**
No Fast Trac

**Patient blinking**
Fast Trac OFF

**Patient blinking**
Fast Trac ON
**EDI-OCT: Imaging the Choroid**

- Enhanced Depth Imaging
  - Improves visualization of the choroid
  - Enhanced understanding of disease pathophysiology
  - Various protocols based on device utilized

**Outer Retinal Tubulation (ORT)**

- Preservation of photoreceptors
- Loss of outer segment interdigitation with RPE
- Disconnect from lateral photoreceptors

**Outer Retinal Tubulation (ORT)**

May not indicate neovascular activity

**Curved C-scan Imaging**
Why does this all matter?

Comparison of AMD Treatments Trials (CATT): Anatomic Results

Supported by Cooperative Agreements from the National Eye Institute, National Institutes of Health, DHHS

Mean Change in Total Retinal Thickness Over Time

OCT of Typical Eye at Baseline
Lucentis Monthly Thinner Than Normal

<table>
<thead>
<tr>
<th></th>
<th>Lucentis Monthly</th>
<th>Avastin Monthly</th>
<th>Lucentis PRN</th>
<th>Avastin PRN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>251u</td>
<td>254u</td>
<td>247u</td>
<td>252u</td>
</tr>
<tr>
<td>Week 52</td>
<td>152u</td>
<td>172u</td>
<td>166u</td>
<td>173u</td>
</tr>
</tbody>
</table>

Percent with No Fluid at 1 Year

- Lucentis Monthly (n=284): 43.7%
- Avastin Monthly (n=265): 26.0%
- Lucentis PRN (n=285): 23.9%
- Avastin PRN (n=271): 19.2%

P < 0.001

Residual Fluid

Small amounts of residual fluid have minimal effect on VA unless intraretinal and in center of fovea

SD-OCT vs TD-OCT

- CATT Year 1 done with TD-OCT
- CATT Year 2 allowed SD-OCT
- Comparative study funded by NEI within CATT — patients had both performed for 4 months
- Surprisingly, SD-OCT did not decrease clinician discrepancy with Reading Center (missed fluid)
Discrepant Treatment?

- Reading Center says fluid: no Rx
- Reading Center says no fluid: yes Rx

Discrepant Treatment

- Lucentis PRN 29%
- Avastin PRN 25%

Conclusions

- Multiple modalities to pick from for imaging AMD
  - Each has their own role
  - Fundus – research, correlating angiography
  - AF – patient education, dry AMD progression
  - FA – Initially and only in cases of poor response
  - ICG – Only in cases of poor response
  - OCT – every visit, still limitations of technology

Conclusions

- Variety of OCT technologies have increased our ability to care for AMD patients
  - Eye Tracking
  - Fovea finder
  - Sub RPE illumination and RPE depression
  - Higher resolution to find fluid and pathology
  - Despite this, outcomes with TDOCT were good.
  - Intraretinal fluid with in the fovea was the biggest predictor of acuity