Fundus Autofluorescence: Applications for Clinical Practice

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Fundus Autofluorescence
- Sutton: no financial disclosures
- Bedwell: no financial disclosures

History of fundus imaging
- Direct Ophthalmoscope
  - Helmholz in 1850
- Indirect Ophthalmoscope
  - Ruette in 1852

Fundus photography
- Jackson and Weber in 1886
- Camera was fixed to the patients head
- Exposure time of 2.5 MINUTES!

Indirect Ophthalmoscope

Fundus Photography
- 1959: electronic flash tube, black and white film
- 1980's: digital retinal imaging
- Color segmentation / multispectral imaging (Annidis, etc.)
  - 25% R, 25% B, 50% G
  - Blue: superficial NFL
  - Green: retina / vessels
  - Red: choroid / RPE
IVFA
- 1961 by Novotny and Alvis
- Indocyanine green angiography in the 1990’s
- Statistically very safe, but invasive with extremely small chance of significant complications
- Common “nuisance” complications

OCT
- 1991 James Fujimoto at MIT
- Original research instrument 400 A-scans / sec
- Current 3D-OCT 27,000 A-scans / sec
- Current Swept Source-OCT 249,000 A-scans / sec

First commercial OCT company in 1992: Advanced Ophthalmic Devices
- Sold on August 27th of 1993 to Humphrey—Now Carl Zeiss Meditech
- First commercial OCT from them in 1996

- By 2008, Zeiss had sold 10,000 OCT’s
- Now, there are 8 companies that manufacture OCT’s commercially
- Zeiss, Heidelberg, Optovue, Topcon best known.

OCT
- Heidelberg, Zeiss, Optos, Others
- Gaining traction over about the last 15 years or so
- Recently becoming more integrated into clinical practice, with applications in multiple disease states

Adaptive Optics (Images courtesy of Dr. Steve Burns)
- Can be performed with a confocal Scanning Laser Ophthalmoscope (CSLO): example...Heidelberg Spectralis
- Or with an FAF Camera: example Zeiss, others
- CSLO: uses a low energy laser and averages up to 30 scans
- FAF camera uses a single, ‘VERY’ bright flash (300 watts second), yielding a single image
FAF
- Images are entirely based upon the presence of lipofuscin in the RPE
- In the eye, a byproduct of photoreceptor outer segment phagocytosis
- Accumulates in the RPE with age and certain diseases
- Also accumulates in other tissues and organs with age or disease (brain, liver, heart)
- Lipofuscin autofluoresces in the 300nm-600nm wavelength range, which is very close to visible light (400nm-700nm), so visible light can excite an emission
- Valuable diagnostic and monitoring tool in an ever increasing list of ocular conditions
- Can show damage well before it is visible to examination or in regular photos

FAF interpretation
- Sick or stressed RPE hyperfluoresces as does any other accumulation of lipofuscin
- Dead, absent, or hypertrophic RPE hypo fluorsces
- The optic nerve head, blood vessels, and fovea are always hypo fluorescent (dark)
- Normal fundi are diffusely, mildly hyper fluorescent and grainy

Conditions in which FAF is useful
- AMD
- ICSC (central serous retinopathy)
- Fluorescein toxicity
- Nevus / melanomas, choroidal lesions
- Glaucoma
- ONH Drusen
- Macular / retinal dystrophies

FAF: AMD
- Useful in detecting reticular pseudo drusen, drusenoid formation, and extent of geographic RPE loss
- Very common for FAF to reveal RPE loss / stress that is not as visible or even not visible at all to examination or color photography.
- Study performed to compare the phenotypic FAF AMD appearance in various patients to the color photographs
- Fundus Auto fluorescence in Age-Related Macular Degeneration Study (FAM Study)

FAF AMD
- Eight different FAF phenotypes identified based upon appearance at the junctional zone
- Most had little to no correlation with the color photo appearance
- Authors concluded that FAF revealed damage not yet visible to observation
- Normal
- Minimal change
- Focal increase
- Patchy
- Linear pattern
- Lacelike pattern
- Reticular pattern
- Speckled pattern

AMD FAF
- Very interesting finding that the rate of progression of geographic atrophy is most dependent upon the FAF pattern at the junctional zone.
- Hyperfluorescence at the junctional zone is a bad sign
- Hypo fluorescence / normal fluorescence portends slow progression
- Hyperfluorescence that is......
- Focal = slow progression
- Banded = rapid progression
- Diffuse = rapid progression
- More predictive of progression that any other factor studied
ICSC FAF

- ICSC: related to steroids/cortisol, either by taking steroids or endogenously elevating steroids through stress
- Type A personalities
- Also linked to sleep apnea

ICSC FAF

- Focal RPE damage/PED with secondary neurosensory retinal detachment
- Metamorphopsia, decreased vision
- Recurrent and often multifocal
- Observation typically
- Topical NSAIDs, laser PDT

AMD FAF: 2012 TO 2015

AMD FAF: 2012 TO 2015

FAF paints a completely different picture than fundoscopy/color photography
- RPE damage and death, “troughing”
- Much greater multifocality
Plaquenil toxicity first occurs in a ring shaped area surrounding the center of the fovea and can be imaged before easily visible to fundoscopy by several means:

- Multifocal ERG
- SD-OCT
- IVFA
- FAF
Plaquenil FAF

Chen et al. Clinical Ophthalmology 2010:4 p. 1151

Bull’s Eye IVFA

Can FAF help to distinguish choroidal nevi from choroidal melanomas? Maybe.
Typically we look for things like diameter, thickness / height, symptoms, subretinal fluid, proximity to the ONH, and lipofuscin.
Choroidal lesions FAF: Nevus or Melanoma?

- On FAF........
- Nevi tend to show patchy but distinct areas of hyperfluorescence
- Melanomas tend to show patchy or diffuse hyperfluorescence with less distinct borders, typically covering at least 50% of the lesion

FAF choroidal lesions: CHRPE

- Glaucoma patients and even patients with ocular hypertension exhibit increased hyperfluorescence of the peripapillary RPE adjoining PPA
- May be correlated with the severity of the disease
- Due to increased lipofuscin accumulation in this area

FAF ONH Drusen

- FAF can image ONH drusen
- SLO FAF does this well, camera based FAF not as well.
- Very good with visible drusen (when you don't need it), marginal with buried drusen (when confirmation is useful)

FAF glaucoma

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FAF ONH Drusen: B-Scan

- FAF can image ONH drusen
- SLO FAF does this well, camera based FAF not as well.
- Very good with visible drusen (when you don't need it), marginal with buried drusen (when confirmation is useful)
FAF PDR with NVE

White dot syndromes FAF
- AMMAPE:
  - Early / acute: hypo
  - Late: hyper
- MEWDS
  - Early/acute: hyper
  - Late: returns to normal
- Multifocal choroiditis
  - Early/acute: hypo of spots > 125 microns
  - Late: Hypo of all spots

White dot syndromes FAF
- Serpiginous Choroiditis
  - Early / acute: hyper
  - Late: Hypo
- Birdshot
  - Early/acute: hypo
  - Late: Returns to normal?

Retinal Dystrophies
- Causes lipofuscin build up in the RPE
- Utility of FAF:
  - Aid in proper diagnosis
  - Earlier diagnosis
  - Examine family members at risk to diagnosis before clinically visible changes
  - Track progression over time

Vitelliform Dystrophy

Vitelliform Dystrophy - FAF
Best’s Vitelliform Dystrophy

Atrophic Stage

Adult Vitelliform vs. Best’s

<table>
<thead>
<tr>
<th>Feature</th>
<th>AOFVD</th>
<th>Best’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>30-50 yrs</td>
<td>3-15 yrs</td>
</tr>
<tr>
<td>Size of lesion</td>
<td>1/3 - ½ DD</td>
<td>½ - 3 DD</td>
</tr>
<tr>
<td>Progression of vision loss</td>
<td>Slow</td>
<td>Variable</td>
</tr>
<tr>
<td>EOG</td>
<td>Normal or slightly subnormal</td>
<td>Severely subnormal</td>
</tr>
<tr>
<td>OCT findings</td>
<td>Dome-shaped clump of hyper-reflective material</td>
<td>Variable, typically with subretinal fluid</td>
</tr>
<tr>
<td>Inheritance pattern</td>
<td>Autosomal Dominant</td>
<td>Autosomal Dominant</td>
</tr>
</tbody>
</table>

Butterfly (Pattern Dystrophy)

Pattern Dystrophy - FAF

Fundus Flavimaculatus

Fundus Flavimaculatus - FAF
Stargardt’s disease

OCT in Stargardt’s Disease

- Thickening and increased hyper reflectivity of the ELM early in disease
- Occurs prior to photoreceptor atrophy
- Could use SD OCT and FAF for early diagnosis
Retinitis Pigmentosa

Central Areolar Choroidal Dystrophy

FAF useful in monitoring stage and functional loss

Boon et al

CACD

CACD FAF