Developing Treatments for Dry Age-related Macular Degeneration – Workshop

Anatomical Endpoints

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• Research Support through my University from National Eye Institute, Genentech, Bioptigen, The Hartwell Foundation, Research to Prevent Blindness, The Arnold and Mabel Beckman Foundation
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• Patents pending in image processing and OCT

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Recording Anatomical endpoints

- **GA:** a sharply demarcated area of apparent absence of RPE, with visible choroidal vessels

  Sarks SH. Br J Ophthalmol 1976
  Sarks JP et al Eye 1988
  AREDS Report #26 Arch Ophthalmol 2009

- **Histopathology/biopsy:**
  - Not feasible

- **In vivo imaging:**
  - Retinal photographs
    - Multi-spectral imaging, visible and infrared
    - Wide field imaging
  - Fluorescein angiography
  - Fundus autofluorescence
  - Optical Coherence Tomography
Imaging Anatomical endpoints

• Different methods
  – Often complementary
  – Strengths and weaknesses

• Extract qualitative and quantitative data extraction

• Involvement of foveal center as endpoint

• Influence of history or genotype
• Classical endpoint
• Used in multiple trials
• Impact of cataract on image

Sunness et al IOVS 1999
Sunness et al Ophthalmol 1999
Sunness et al Ophthalmol 2007
Fluorescein Angiography

- Requires Intravenous injection
- Useful in examination for leakage

Mid AV phase
Late
- **Blue**
  - Excitation at 488 nm: optically pumped solid-state laser
  - Emission 500 – 700 nm with a barrier filter

- **Green**
  - Excitation at 514 nm
  - Wolf-Schnurrbusch IOVS 2011

- **Infrared**
  - Excitation at 787 nm
  - Keilhauer and Delori IOVS 2006
Quantitative assessment of GA
Wide-field autofluorescence
GA with drusen regression
Foveal Center

- Difficult to assess on CFP
  - Sunness et al IOVS 1999
  - Sunness et al Ophthalmol 1999
  - Sunness et al Ophthalmol 2007

- Blue light FAF

- Green light FAF does not have a dark central spot
  - Wolf-Schnurrbusch et al IOVS 2011

- Near IR FAF, bright macula
Optical coherence tomography-based
Retinal and choroidal morphology in GA

Loss of:
• Outer plexiform layer
• Henle’s fiber layer
• Photoreceptor nuclei
• External limiting membrane
• Ellipsoid zone (inner segment)
• Interdigitation zone
• Retinal pigment epithelium

Gain of:
• Reflectance signal into choroid and sclera

Outer Retinal Tubulation (ORT)

Reticular drusen
Optical coherence tomography
Segmentation of critical layers
• SDOCT to measure GA
  – Yehoshua et al IOVS 2013
  – Simader C et al AJO 2014
- Quantitative assessment of drusen volumes and atrophy over time

**OCT findings precede atrophy**

Nathoo et al AJO 2014
Folgar et al ARVO 2013
Wu Z et al Ophthalmol 2014
GA on OCT versus Autofluorescence

- SDOCT vs FAF
  - Sayegh et al Ophthalmol 2011
  - Hu et al IOVS 2013
  - Simader C et al AJO 2014
On OCT imaging:

hyporeflective drusen in eyes with GA

Leuschen et al *Ophthalmology* 2013
On OCT imaging: Hyporeflective wedge-shaped retinal bands precede GA

Wu Z et al Ophthalmology 2014
Vitelliform lesion resulting in GA

85 yo F
Geographic Atrophy in the antiVEGF era

Comparisons of AMD Treatments Trials
Comparisons of AMD Treatments Trials
Geographic Atrophy in the antiVEGF era

Baseline

Year 1

Year 2
Anatomic endpoints from imaging
Imaging Anatomical endpoints

- Different methods
  - Often complementary
  - Strengths and weaknesses
- Extract qualitative and quantitative data extraction
- Involvement of foveal center as endpoint
- Influence of history or genotype
- Different if the endpoint is onset of atrophy or progression of atrophy