

Fundus Auto Fluorescence and high resolution OCT technology for novel detection of Vision Threatening Disease.

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A. Lipofuscin (LF)

- a. Accumulates in post-mitotic neurons
- b. Seen with aging, severe malnutrition, chronic disease of neurons, cardiac myocytes, skeletal muscle cells, liver cells, etc..
- c. Photoreceptors (PR), Retinal Pigment Epithelium (RPE) Degradation, toxins
 - i. PR outer segments (OS)
 - ii. RPE
 - 1. toxin removal
 - 2. byproducts of the visual cycle accumulates as LF granules
- d. Retinal health assessment
 - i. Age, Ocular pathology = LF accumulation seen at the level of the RPE
- e. Lipofuscin cellular toxicity in age and ocular disease
 - i. LF accumulation effects:
 - 1. Loss of cellular cytoplasmic space
 - 2. Loss of cellular function
 - 3. Photosensitizing irreversible damage
 - 4. Apoptosis
 - ii. Macular degeneration, lipofuscinopathies (Best's, Stargardt's, macular dystrophy), Glaucoma, and other retinal and vascular pathology
- f. Visual Function and LF
 - i. LF measured through Autofluorescence (AF) correlates to change in functional vision
 - 1. AMD
 - a. Early AMD
 - b. Micro- Perimetry
 - 2. RP
 - 3. Macular translocation surgery
 - 4. Diabetic Retinopathy (DR) in pan retinal photocoagulation (PRP)

B. Fundus Auto Fluorescence (FAF)

- a. Lipofuscin Fluorophores are quantifiable
 - b. In vivo LF imaging
 - i. LF excitation range: 300 – 600 nm
 - 1. Visible light range: 400 – 700 nm
 - 2. Visible light can be used to excite LF
 - ii. LF emission range: 480 – 800 nm
 - 1. Maximal: 600 – 640 nm
 - c. FAF signal/ image
 - i. Low, weak signal compared to other fluorescent imaging (fluorescein angiography)
 - ii. Requires digital image processing
 - 1. enhancement, electronic noise reduction
 - iii. Benefits include
 - 1. Non-invasive nature, quick acquisition, & specific study of the RPE cell layer in isolation
 - d. FAF instruments, specifications, review.
 - i. No Standardization between manufacturers or within instruments = differing FAF results.
 - 1. Laser power, detector sensitivity, correction of refractive errors, image processing steps, media opacities (presence of cataracts), camera axial orientation & corneal vertex, etc.
 - ii. Fundus Spectrophotometer
 - 1. Research labs, small field of view
 - iii. Confocal Scanning Laser Ophthalmoscope (cSLO)
 - 1. High contrast, processed image, multiple scans
 - 2. E.g., Heidelberg
 - iv. Fundus Camera
 - 1. Lower contrast, single image, real time result, larger field of view
 - 2. E.g., Canon CX-1
- C. FAF Imaging: Anterior Segment
- a. Sclera – pterygium and pinguecula
 - b. Aging Lens fluorophores
 - i. Can interfere with posterior pole AF imaging.
- D. FAF Imaging: Posterior pole
- a. Hypofluorescence
 - i. Absence of RPE/ LF and/ or when AF emission is blocked.
 - b. Hyperfluorescence

- i. Presence of LF or other AF material.
 - ii. Signal intensity is related to concentration of LF or AF material present.
- E. Interpretation of the FAF image including gray scale variances
 - a. Healthy Eye
 - i. Hypofluorescent Structures: absence of RPE/ LF and when AF emission is blocked
 - 1. E.g., optic nerve head, blood vessels, fovea
 - ii. Hyperfluorescent Structures: Presence of LF is in all ages is normal, appears as an overall, diffuse low-grade hyperfluorescent signal throughout the posterior pole, gradually diminishes towards fovea
 - b. Unhealthy Eye
 - i. Classification of FAF Pattern in Early and Geographic Atrophy Age related Macular Degeneration, Fundus Auto Fluorescence in Age-Related Macular Degeneration (FAM) Study group
- F. High resolution Optical Coherence Tomography (HR-OCT): Interpretation
 - a. High resolution
 - i. measured in tissue microns
 - ii. More resolving power, more visibility, more detail of retinal layers
 - 1. Inner segment (IS) and outer segment (OS) junction line of the PR
 - b. Scanning the retina: differences between a 3 mm scan and a 12 mm scan
 - c. Scanning the optic nerve head
 - i. Assisted software programs in the measurements of Cup/Disc and Rim to Disk in determining the Disk Damage Likelihood System (DDLs)
 - ii. Optic Nerve Analysis
 - d. Mydriatic and non-mydriatic use of the HR-OCT
 - i. Advantages of non-mydriatic use
 - 1. Community-based ocular health screenings, triage, and telemedicine protocol.
 - ii. Limitations of non-mydriatic
 - 1. small pupil aperture, ocular media opacity, fixation/ cooperation, etc.
 - e. Scanning beyond the posterior pole (requires pupillary dilation)
 - f. Time Domain vs. Spectral Domain
 - i. Importance of identifying good normative studies when selecting OCT technology
- G. Clinical relevance of Imaging Technology
 - a. Tracking temporal changes
 - i. OCT image registration pattern

- ii. Color/ FAF fundus image overlay
 - b. Internal software measuring tools
 - i. Linear, 2D surface, and 3D volume OCT scans
 - c. Integration of advanced posterior pole imaging technology in ocular disease evaluation
 - i. Color imaging software-assisted Technology
 - 1. Red, Green, Blue (RGB) filter.
 - a. Blue channel (wavelength 490 nm): nerve fiber layer.
 - b. Green channel (530 to 550 nm): retinal structures including arteries, veins, hemorrhages, exudates versus drusen.
 - c. Red channel (610 nm): choroidal vasculature, RPE changes, nevi vs. choroidal melanoma, drusen and AMD changes.
 - 2. Emboss filter
 - a. Positive or negative stereo image with dimensional elevation or depression from a single fundus-camera image
 - ii. Image registration pattern, software driven fade-in/ fade-out retinal imaging overlay.
- H. Case study presentation
- a. Age Related Macular Degeneration (stages: Early, mid and late)
 - b. Geographic atrophy (stages: Early, mid and late)
 - i. Tracking GA: Non Invasive (Color fundus photography, FAF) vs. Invasive techniques (FA)
 - 1. Color fundus photography vs. FAF
 - a. Area measurements, Growth rates and Estimates of foveal involvement have demonstrated differences between color and FAF imagery.
 - c. Lipofuscinopathies
 - d. Diabetic Retinopathy (stages: Early, mid and late)
 - e. Glaucoma (stages: Early, mid and late)
 - i. Including OCT protocols
 - f. Tracking patients on Plaquenil
 - i. Protocol which includes OCT or FAF or mfERG
 - g. Lupus
 - h. Alzheimer's (study of Retinal A/V and NFL)
 - i. Other known and unknown pathology detected with FAF and OCT, otherwise UNDETECTED with routine color fundus photography.