Contemporary Use of OCT Technology

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I. Introduction to Optical Coherence Tomography (OCT)

1. Principles of the technique
    - Imaging by sections through the use of superposition of wave (wave = light)
    - Allows visualization of tissue structure on the micron scale in situ and in real time
    - Imaging depth is affected by optical attenuation which in turn depends on tissue scattering and tissue absorption (up to 2 -3 mm in most tissues)

2. Time Domain-OCT vs Spectral Domain-OCT
    - More resolution in SD-OCT

3. Anatomy of retina as seen on SD-OCT:
    - Inner limiting membrane (ILM)
    - Nerve fibre layer (NFL) – axons of ganglion cells
    - Ganglion cell layer (GCL) – nuclei of ganglion cells
    - Inner plexiform layer (IPL) – dendrites of the ganglion cells & their synapse w/ bipolar cells
    - Inner nuclear layer (INL) – nuclei of bipolar cells
    - Outer plexiform layer (OPL) – projections of photoreceptors ending and their synapses with bipolar cells
    - Outer nuclear layer (ONL) – cell bodies of photoreceptors
    - External limiting membrane (ELM)
    - Photoreceptor Integrity Line (PIL) - Presence or loss in foveal area is predictive of visual fn
    - Retinal pigment epithelium (RPE)
    - Choroid (choriocapillaris)
    - Sclera

II. Clinical entities

A. White/Yellow Lesions

1. Drusen
   - Yellow/white accumulations of extracellular material (fatty deposits) that build up between Bruch's membrane and the retinal pigment epithelium
   - OCT: can be seen as hyper-reflective material below the RPE causing the latter to undulate

2. Cotton Wool Spots
   - White spots caused by retinal nerve fiber layer micro-infarcts
   - OCT: can be seen as hyper-reflective, fuzzy lesions at the level of the NFL

3. Exudates
   - Yellow lipid residues of serous leakage from damaged deep capillaries
   - OCT: appears as hyper-reflective spots around the OPL/INL

4. Vitelliform
   - Lipofuscin deposition as a result of a macular dystrophy
   - OCT: appears as a coalesced hyper-reflective mound above the RPE
   - Stages
     - Stage I - Previtelliform (normal or subtle RPE changes)
     - Stage II - Vitelliform (classic "egg-yolk" lesion)
     - Stage III - Pseudohypopyon (layering of lipofuscin, mostly concentrated inferiorly)
     - Stage IV - Vitelliruptive ("scrambled egg" appearance)
     - Stage V - Atrophic (central RPE and retinal atrophy)
     - Stage VI - CNV (occurs in about 20% of patients) - may be visualized on OCTA

B. Red lesions

1. Hemorrhagic Detachment of RPE vs Serous Detachment of RPE (PED)
   - Heme = hyper-reflective
   - Fluid = Hypo-reflective

2. Intraretinal dot/blot hemes
   - Deeper retinal hemorrhages, blood usually accumulates in the OPL or INL
   - OCT: hyper-reflective spots

3. Subretinal Hemorrhage
   - Circular shape ophthalmoscopically
   - OCT: hyper-reflectivity under the sensory retina

4. Pre-retinal/Subhyaloid Hemorrhage
   - Boat-shaped
   - OCT: hyper-reflectivity either at the level of subhyaloid space between posterior vitreous face and retina or under internal limiting membrane

C. Vitreoretinal Interface

1. Posterior Vitreous Detachment
2. VMT
   - Incomplete vitreous detachment with persistently adherent vitreous exerting tractional pull on the macula and resulting in morphological alterations
3. VMA
   - Perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphological features
4. Epiretinal Membrane
   - Fibrocellular tissue that proliferates on the surface of the internal limiting membrane
   - Highly reflective on OCT
   - May cause retinal wrinkling and/or thickening

5. Macular Hole (MH)
    - Full thickness retinal defect from the internal limiting membrane to the outer segment of the photoreceptor layer
    - Stages
        - Stage 1A - Impending MH
        - Stage 1B - Impending MH, or outer MH
        - Stage 2 - Full thickness MH w/ incompletely detached operculum
        - Stage 3 - Full thickness MH w/ complete detachment of operculum
        - Stage 4 - Stage 3 + Weiss ring (complete PVD)

D. Miscellaneous Choroidal/Retinal Lesions

1. Subretinal Fluid
    - OCT: Hypo-reflectivity under the sensory retina
    - Eg, CSCR, Retinal Detachment

2. CNVM
    - Choroidal Neovascular Membrane
    - OCT: thickening or disruption of the RPE-choriocapillaris complex (type 2 CNVM)
    - Other findings include retinal edema/hemorrhages
    - See below

E. Dark Lesions

1. Choroidal Nevus
    - Benign melanocytic lesion of the posterior uvea
    - OCT: a gradual transition between the hyper-reflective inner choroid and hyporeflective outer choroid is usually seen
2. CHRPE
    - Congenital hypertrophy of the RPE.
    - Hypertrophy = Increase in size of cells
    - OCT: thickened and irregular RPE/Thinning of overlying retina
    - Lacunae = absence of RPE

3. RPE hyperplasia
    - Hyperplasia = increase in number of cells
    - OCT: pigment clumps scattered in many different layers of the neurosensory retina

G. ONH

1. ONH drusen
    - An elevated optic nerve head with a “lumpy-bumpy” internal optic nerve contour and a more abrupt taper of the hypo-reflective space located between the sensory retina and the retinal pigment epithelium

2. Disc Edema
    - An elevated optic nerve head with a smooth internal contour and an increased hypo-reflective space located between the sensory retina and the retinal pigment epithelium (lazy V pattern)

III. Glaucoma screening and monitoring progression

1. Glaucoma is a multifactorial optic neuropathy characterized by a loss of retinal ganglion cells with subsequent loss of retinal nerve fiber ultimately resulting in visual impairment.

2. The Ganglion Cell Complex (GCC) is comprised of 3 layers:
   (1) Nerve Fiber Layer (ganglion cell axons)
   (2) Ganglion Cell Layer (ganglion cell bodies)
   (3) Inner plexiform layer (ganglion cell dendrites)

3. The GCC (all 3 layers) becomes thinner as ganglion cells die

4. It is measured in the macular area because the macula has over 50% of all retinal ganglion so it is the ideal region to detect early loss or mild changes over time

5. GCC vs RNFL: RNFL distribution depends on individual anatomy whereas GCC complex appears regular and elliptical for most normals

5. 3 different maps in the analysis:
   (1) Thickness Map: Maps “Raw Data”
      - Thicker = Warmer Color
      - Thinner = Colder Color
      - No GCC at the fovea (black color)
      - Thicker GCC perifoveally in normal eyes
   (2) Deviation Map: Maps percent loss from normal
      - Comparison to a normative database (calculated at each pixel of the map)
      - Blue shades = ~20-30% loss
      - Grey-Black shades = 50% loss or greater
   (3) Significance Map: Maps stastical significance of change from normal
      - Green = Within normal range
      - Yellow = Borderline
      - Red = Outside of normal limits

IV. Plaquenil Screening (2016 Guidelines)

A. What are we screening for?

1. Plaquenil retinopathy:
    a) Pathophysiology
        (1) Lysosomal function of RPE affected
        (2) Phagocytosis of outer segments affected
        (3) Increased lipufuscin
        (4) All of this leads to PR an RPE damage, usually in the perifoveal area first
        (5) Leads to Bull's Eye maculopathy
2. Point of irreversible damage after which cessation of drug still leads to bull's eye maculopathy and legal blindness
3. Early toxicity (before point of irreversible damage is reached):
    a) Before fundus changes are visible

B. How often should we monitor the patient?

1. Low-risk patients
    a) Annual screening within first 5 years after starting drug, then yearly
2. High-risk patients
    a) Annual screening directly after starting drug

C. Risk Factors

1. Major
    a) Daily dosage
        (1) > 5.0 mg/kg REAL weight
    b) Duration of Use (relative to daily dose)
        (1) > 5yrs, assuming no other risk factors
    c) Renal disease
    d) Concomitant use (Tamoxifen)
    e) Pre-existing macular disease
2. Minor
    a) Age
    b) Liver disease
    c) Genetic factors

D. **What tests should we perform according to the new guidelines?**

1. Primary Tests: Ideally Both
    a) Automated VF appropriate to Race (white on white)
        (1) Non-Asian: 10-2
        (2) Asian: 24-2 or 10-2
    b) <u>SD-OCT (Sinkhole Effect)</u>
        (1) <u>Thinning of ONL</u>
        (2) <u>Disruption/Discontinuation of IS/OS junction line</u>
2. Other Objective Tests (as needed or available)
    a) FAF
        (1) Increased hyperfluorescence/hypofluorescence
    b) mfERG
        (1) Decreased pericentral amplitude of P wave

VI. Visualization of the choroid

1. Why do we need to visualize the choroid?

a) Choroid plays a vital role in pathophysiology of many conditions
    a) AMD
    b) CSCR
    c) Choroidal Melanoma (Source of most common intra-ocular tumors)

2. Enhanced Depth Imaging - OCT (EDI-OCT)

a) SD-OCT used closer to the eye
b) Creates an inverted image
c) Allows visualization of the choroid with more details, even in the presence of overlying retinal pathology
    a) Choroid-Sclera Junction Line becomes visible, which allows choroidal thickness measurement
    b) Increased signal from choroid
d) Subfoveal normal thickness
    a) 287 ± 76 μm (Spectralis)
    b) 272 ± 81 μm (Cirrus)
    c) There is a decrease of about 1.56 μm per year with age
e) Choroidal disease may be related to choroidal thickness changes
    a) Thicker (Pachychoroid Spectrum)
        a) CSCR
        b) Polypoidal Choroidal Vasculopathy
    b) Thinner
        a) Neovascular AMD
        b) Dry AMD
        c) Proliferative Diabetic Retinopathy
        d) Diabetic Macular Edema
        e) Retinitis Pigmentosa
        f) Glaucoma

3. High Myopia

a) Choroidal thinning

1. Choriocapillaris thinning
2. Focal Lack of vessel
3. Correlates with axial length
    1. 12.7 μm / 10 years
    2. 8.7 μm / 1 D myopia

b) Choroidal thickness may be a predictive factor for visual acuity as the choroid is the source of O2 and nutrient supply for the retina

4. Choroidal Melanomas

a) Prognostic Importance of tumor size

1. 5-year mortality after enucleation
    1. Small Melanomas: 16%
    2. Medium Melanomas: 32%
    3. Large Melanomas: 53%
2. Early detection when tumor is small (≤ 3mm thickness) is important

b) Choroidal Melanomas vs Nevi tend to have more:

1. Ophthalmoscopically:
    1. Increased Tumor Thickness
    2. Subretinal fluid
    3. Subretinal Lipofuscin Deposition
    4. RPE atrophy
2. On OCT:
    1. Shaggy photoreceptors
    2. Loss of external limiting membrane
    3. Loss of IS-OS junction
    4. Irregularity in IPL
    5. Intraretinal edema
    6. Irregularity of GCL
    7. Larger Thickness
    8. Compression of the choriocapillaris

I. OCTA

1. Imaging principle
    1. Motion contrast between consecutive scans
2. Printout Analysis
    1. Segmentations: standard vs customized
3. Artifacts
    1. Motion Artifacts
        1. Any movement = blood flow = vessel
        2. Fixation losses/patient movement
        3. Fine tissue
    2. Shadow Artifacts
        1. Large more superficial vessels produce ghost images in deeper layers
    3. Slowest Detectable Flow
        1. Determined by the time between two sequential OCT b-scans
        2. Eg, microaneurysms, fibrotic CNVMs
    4. Obscuration
        1. No signal reaching tissue = no detected movement
        2. Blinks
        3. Overlying lesion eg, hemorrhages

4. Applications
    1. CNVM
        1. Different types
            1. Type 1 = CNVM below the RPE (occult)
            2. Type 2 = CNVM passes through the RPE (classic)
            3. Type 3 = NVM within the neurosensory retina (Retinal Angiomatous Proliferation (RAP))
        2. Different morphologies
            1. Lacy wheel or Sea fan = small filamentous vessels forming anastomoses
            2. Medusa = vessels associated with a central trunk
        3. Sensitivity
        4. OCTA allows monitoring morphological response to treatment
    2. Diabetic Retinopathy
        1. Microaneurysms
        2. Capillary dropout / decreased perfusion
        3. Foveal Avascular Zone (FAZ) enlargement / remodeling
    3. Sickle Cell Retinopathy
        1. Temporal macular thinning on structural OCT correlating with temporal area of avascularity on OCTA
    4. Retinal Neovascularization
        1. VRI segmentation = Vitreoretinal Interface
        2. Eg, Diabetic retinopathy, retinal vein occlusions

5. Polypoidal Choroidal Vasculopathy (PCV)
    1. Main DDX with AMD
        1. Adult Caribbean, Asian, or African American
        2. Higher, more frequent serous retinal detachment, less intraretinal edema
    2. Gold standard for diagnosis = Indocyanine Angiography (ICGA)
        1. Polypoidal lesions with or without branching networks
    3. Funduscopically: Recurrent serosanguinous RPE detachments
    4. Structural OCT:
        1. Double layer sign = branching vascular network
        2. Highly peaked RPE detachments
    5. Visualization of the PCV complex on OCTA:
        1. Customized segmentation important
        2. Using segmentation of the choriocapillaris, the branching vascular network will appear as a hyper-flow lesion whereas the polypoidal lesion will demonstrate lower flow