Optical Coherence Tomography Angiography: Imaging in Motion

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1. Introduction
   a. Non-invasive optical coherence tomography (OCT) technology that provides 3D volumetric data regarding retinal and choroidal vasculature and blood flow

2. How optical coherence tomography angiography (OCT-A) works
   a. “Motion contrast”
      i. Motion within tissue creates differing reflectance patterns across time that can be detected when an area is sampled consecutively
      ii. Motion detected by OCT-A is erythrocyte movement in retinal or choroidal blood vessels

3. Analysis and display
   a. Exploration of en-face images (OCT angiograms) provides blood flow information at different depths within the retina and choroid
      i. Superficial inner retina vascular plexus
         1. Includes vasculature within the retinal nerve fiber and ganglion cell layers
         2. Similar to early conventional fluorescein angiography (FA) phases
      ii. Deep inner retinal vascular plexus
         1. Includes vasculature from the border of the inner plexiform layer/inner nuclear layer and the border of the inner nuclear layer/outer plexiform layer
         2. Not visible with conventional FA
      iii. Outer retina vascular plexus
      iv. Choriocapillaris
   b. Co-registration of OCT angiograms with OCT b-scans allows for precise localization of vasculature abnormalities

4. Technology
   a. AngioVue™ (Optovue, Inc.)
      i. First commercially available OCT angiography system
      ii. Available on the RTVue XR Avanti spectral domain OCT
      iii. Not yet approved for sale within the United States
   b. AngioPlex™ (Carl Zeiss Meditec, Inc.)
      i. Cleared by the FDA in September 2015
      ii. Available on the Cirrus 5000 HD-OCT
   c. Spectralis OCT Angiography (Heidelberg Engineering, Heidelberg, Germany)
      i. Still in development

5. Comparison to FA/indocyanine green angiography (ICG)
   a. Advantages
      i. Non-invasive
      ii. Higher resolution
      iii. Avoids injection and dye related risks/side effects
         1. Can be performed even if conventional angiography is not yet indicated
iv. Provides volumetric data with segmentation analysis which allows for depth localization of lesions
v. More precise delineation and measurement of neovascularization due to absence of obscuring leakage
vi. Simultaneous imaging of the retinal and choroidal vascular systems
vii. Rapid acquisition within seconds
viii. Tandem structural and blood flow information
ix. Short-term repeatability possible

b. Limitations
i. Small field of view
   1. Need for montage software
ii. Absence of leakage
   1. Flow information at a fixed point in time
iii. Susceptible to artifacts
   1. Motion
   2. Blink
   3. Shadowing
   a. Large retinal vessels
iv. Poor detection of structures with slow blood flow
   1. Microaneurysms
   2. Fibrotic choroidal neovascularization (CNV)

6. OCT-A in disease
   a. Inner retinal disease
   i. Diabetes
      1. OCT-A illustrates most clinically relevant diabetic vascular changes including enlargement and distortion of the foveal avascular zone (FAZ), microaneurysms, retinal capillary dropout, pruning of arteriolar branches, some forms of intraretinal fluid, vascular loops, intraretinal microvascular abnormalities, neovascularization, and cotton-wool spots that were largely consistent with FA (Matsunaga et al. 2015, Hwang et al. 2015)
      2. Microaneurysms detected by FA appear as focally dilated saccular or fusiform capillaries on OCT-A of the superficial and/or deep capillary plexus. (Ishibazawa et al. 2015)
         a. OCT-A only detects about half of microaneurysms seen with FA (Couturier et al. 2015)
      3. Retinal nonperfused areas visualized by FA appear as lesions with no or sparse capillaries on OCT angiograms. (Ishibazawa et al. 2015)
      4. OCT-A better delineates areas of capillary dropout that are otherwise obscured by fluorescein leakage on FA (Hwang et al. 2015)
      5. The FAZ is significantly enlarged in diabetic eyes compared with healthy eyes, regardless of the presence of retinopathy (Takase et al. 2015, Di et al. 2015)
      6. Eyes with clinically significant macular edema (CSME) have larger FAZ areas than eyes without CSME (Di et al. 2015)
      7. Some areas of focal leakage on FA thought to be microaneurysms may actually be small tufts of neovascularization when evaluated with OCT-A (Hwang et al. 2015)
      8. Can assess changes in retinal blood flow post anti-vascular endothelial growth factor (anti-VEGF) treatment (Ishibazawa et al. 2015)
9. Potential for automated quantification of capillary nonperfusion (Hwang et al. 2016)

ii. Retinal venous occlusive disease

1. OCT-A demonstrates most clinically relevant findings in acute and chronic retinal venous and is consistent with FA findings of impaired vascular perfusion, retinal atrophy, vascular dilation, shunt vessels, and some forms of intraretinal edema (Kashani et al. 2015)
2. May be superior to FA for detection of nonperfusion and deep capillary telangiectasias in eyes with branch retinal vein occlusion (BRVO) (Suzuki et al. 2016)
3. Retinal capillary network abnormalities within the superficial and deep capillary plexuses are present in nearly all patients with RVO with the deep capillary plexus typically being more severely affected (Coscas et al. 2016)
4. Intraretinal cystoid spaces are more likely to be observed with OCT-A than SD OCT or FA in eyes with RVO (Coscas et al. 2016)
5. Non-perfused gray areas visualized with FA are more frequently associated with abnormalities of the deep capillary plexus than the superficial plexus in eyes with RVO (Coscas et al. 2016)
6. OCT angiography facilitates depth localization of microaneurysms, collaterals, and capillary telangiectasias in eyes with BRVO (Suzuki et al. 2016)

iii. Retinal arterial occlusive disease

1. OCT-A reveals decreased perfusion in both the superficial and deep retinal capillary plexuses corresponding to areas of delayed dye perfusion on FA in eyes with branch retinal artery occlusion (BRAO) and central retinal artery occlusion (CRAO) (Bonini et al. 2015)
2. OCT-A may be more sensitive for precisely characterizing macular ischemia and monitoring vascular flow changes in eyes with BRAO and CRAO (Bonini et al. 2015, de Castro-Abeger et al. 2015)
3. Demonstrates prompt reperfusion in eyes with CRAO following paracentesis (Bhanushali et al. 2016)

b. Outer retinal disease

i. Non-exudative age-related macular degeneration (AMD)

1. OCT-A demonstrates decreased superficial and deep plexus vessel densities in eyes with non-exudative AMD compared to normals (Toto et al. 2016)
2. Focal areas of decreased choriocapillaris signal underlying many drusen can be visualized with OCT-A (de Carlo et al. 2015)
3. OCT-A reveals significant choriocapillaris flow impairment within regions of geographic atrophy that typically extends beyond the borders of the geographic zone (Choi et al. 2015, de Carlo et al. 2015)

ii. Exudative age-related macular degeneration (AMD)

1. OCT-A provides quantitative information regarding CNV flow and area (Jia et al. 2014)
2. OCT-A demonstrates CNV location and size comparable to FA but provides more distinct vascular network patterns that are less obscured by subretinal hemorrhage (Jia et al. 2014)
3. Areas of decreased choroidal flow are often found adjacent to CNV (Jia et al. 2014)
4. There is a high level of correspondence between different CNV patterns identified on OCT-A and treatment decisions established using conventional multimodal imaging including FA, ICG, and OCT (Coscas et al. 2015)

5. Palejwala et al. evaluated eyes with drusen, pigmentary changes, and CNV in the fellow eye and found that 6% had type 1 CNV lesions that were not associated with leakage on FA or fluid on conventional OCT (Palejwala et al. 2015)

6. Potential for an automated algorithm for CNV area detection (Liu et al. 2015)

7. OCT-A may be a useful tool for monitoring and quantifying the response of CNV to anti-VEGF treatment (Muakkassa et al. 2015, Coscas et al. 2015, Marques et al. 2016)
   a. Often demonstrates decreases in CNV linear dimension and area (Muakkassa et al. 2015)

8. Glaucoma
   i. Visible attenuation of the optic disc vasculature in eyes with glaucoma (Jia et al. 2014)
   ii. Disc Flow index
      1. 25% reduction in glaucomatous eyes (Jia et al. 2014)
      2. Significantly correlated with severity of glaucoma, visual field mean deviation and pattern standard deviation, RNFL, and GCC thickness in glaucomatous eyes (Jia et al. 2014, Wang et al. 2015)
      3. May be useful for differentiating glaucomatous and normal eyes (Jia et al. 2014, Wang et al. 2015)
   iii. Peripapillary vessel density
      1. Significantly decreased in glaucomatous eyes compared to normal (Liu et al. 2015)
      2. Highly correlated with visual field pattern standard deviation (Liu et al. 2015)

7. Conclusion

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