OCT Angiography: An Upcoming Tool for Diagnosis and Treatment of Retinal Vascular Diseases

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Abstract

Optical Coherence Tomography (OCT) angiography is an upcoming non-invasive and dyeless imaging modality which depicts retinal microvasculature by processing scans taken repeatedly at the same location, at different points of time using Split-spectrum Amplitude Decorrelation Angiography (SSADA) algorithm. The currently available Optovue AngioVue System uses spectral-domain technology, an 840-nm laser, and SSADA algorithm. The utility of OCT angiography has been described for diagnosis and management of various chorioretinal disorders like Macular telangiectasia, Choroidal Neovascularisation (CNV), secondary to Age-related macular degeneration (ARMD), chronic Central Serous Chorioretinopathy (CSCR) or multifocal chorioiditis, neovascularisation or areas of capillary non-perfusion seen in Diabetic Retinopathy, vascular occlusions, glaucoma and optic disc. It provides fast, 3-dimensional visualization of vascular structures, with the ease of repeated frequent imaging and clearly show extent and morphology of neovascularisation. It is reliable, sensitive and reproducible tool and it can also be used to quantitatively show the course of decrease and re-increase of blood flow in new vessels and changes in the capillary non perfusion areas after treatment in various retinal disorders. However, it has certain limitations. Any movement by the patient causes significant artifact and deterioration of image quality. Projection artifact, where the transit of blood cells in a superficial blood vessel cast flickering shadows on the deeper tissue layer that is indistinguishable from blood flow in deeper layer, is another limitation of this technology making it sometimes difficult to distinguish normal physiological vessels from pathological ones. All neovascular complexes are not visualized because of imprecision in slab segmentation, which requires careful control of depth and thickness of the slab to more precisely identify neovascular membrane. It is an upcoming modality which can help us to diagnose various retinal vascular disorders with ease in the near future. However, improvements in the form of more continuous monitoring of flow, imaging a larger area of fundus and shortening acquisition time can help increase the efficacy and popularity of this modality.

Keywords: OCT Angiography, SSADA algorithm, Macular telangiectasia, CNV, CSCR, Diabetic retinopathy

Introduction

The pathophysiology of various retinal disorders revolves around the abnormalities in the chorioretinal circulation. The retinal circulation can be classified for simplification into the superficial and the deep retinal capillary plexus. Fluorescein Angiography (FA) is the conventional tool for evaluation of the architecture of the retinal blood vessels, blood flow, and leakage from damaged or diseased retinal vessels. However, the radial peripapillary capillary network and deeper retinal capillary plexus are not well visualised by FA. The radial peripapillary capillary network has been studied using histologic techniques and has not been found to correlate with FA images. Similarly, it has been found that FA does not image the deeper capillary plexus well in animal models. This may be attributed to scattering from the deeper layers that obliterates specific image of capillaries. The relative importance of radial peripapillary capillary network lies in diagnosis and management of important blinding diseases like glaucoma and ischemic optic neuropathy. The role of deeper retinal plexus is not as well defined as for the superficial retinal plexus due to lack of advanced experimental tools to define the deeper plexus and its role in abnormalities of the retina.

Optical Coherence Tomography(OCT) angiography is an upcoming noninvasive and dyeless imaging modality which depicts retinal microvasculature by processing scans taken repeatedly at the same location, at different points of time, allowing differentiation of areas with motion signals(i.e. blood flow within a blood vessel) from a static signal(i.e. tissue). This is performed by calculating differences in phase, intensity or combination of the two. OCT angiography or Dyeless angiography is based upon the principle of the Split-spectrum Amplitude Decorrelation Angiography (SSADA) algorithm which allows visualization of both inner and outer retinal vascular plexus and the choriocapillary layer without the need for dye injection. It applies highspeed OCT scanning to detect blood flow by carrying out signal decorrelation between scans and analysing it to differentiate the blood vessels from non vascularized tissue. Four volumetric raster scans, including 2 horizontal fast transverse (x fast) scans and 2 vertical fast transverse (y fast) scans, are taken consecutively in 1 session. The best x fast and y fast scans are selected after correction of the motion artifacts, including residual axial motion and transverse saccadic motion. After processing of the volume scans, the points of decorrelation in the images are calculated. Stationary tissue shows a high...
correlation in imaging characteristics from one frame to the next. Blood flowing through vessels causes a changing reflectance over time and localized areas of low correlation between frames (or conversely a high decorrelation). Thus, compared with stationary areas of the retina, movement of erythrocytes within a vessel generates a decorrelated signal. The spectrum of light source is split into 4 component parts to decrease the noise present in the image; each is used to perform the decorrelation step, and the results of all 4 are averaged. This split spectrum strategy trades axial resolution for decreased noise. After this step, a block of information exists that contains levels of decorrelation that range from 0 to 1. In any given region of tissue, the maximal projection image can be viewed to obtain an image of the blood flow. Because retina is a laminar structure with a corresponding stratification of the blood supply, segmentation of retina in specific layers allows simple en face visualization of corresponding vascular supply for that layer. The currently available Optovue AngioVue System uses spectral domain technology, an 840nm laser, and SSADA algorithm. The 70kHz A scan rate on this device allows a 3 × 3mm OCT angiography volume to be acquired in 3 seconds. The lateral and axial resolutions are both 15 μm; the axial resolution is significantly less than that for Spectral-domain OCT (5 μm) owing to signal averaging. The inner nuclear layer is ordinarily bracketed by a layer of capillaries on either side.45 The inner one is the superficial retinal capillary plexus while the outer one is the deep retinal capillary plexus. The inner capillary layer is taken from the internal limiting membrane and includes the ganglion cell layer and the inner plexiform layer up to the margin of the inner nuclear layer (superficial retinal capillary plexus). The deep vascular plexus extends from the outer border of the inner nuclear layer up to the midpoint of the outer plexiform layer to obtain images of the outer layers of capillaries (Figure 1). The choriocapillaris is imaged within 10μ beneath the Bruch’s membrane.

The utility of OCT angiography has been described for diagnosis and management of various choriotinal disorders like Macular telangiectasia, Choroidal Neovascularisation (CNV), secondary to Age related macular degeneration (AMD), chronic Central serous Chorioretinopathy (CSCR) or multifocal choroiditis, neovascularisation or areas of capillary non perfusion seen in Diabetic Retinopathy, vascular occlusions, glaucoma and optic disc disorders.

Role of OCT Angiography in Macular Telangiectasia

The retinal vascular abnormalities seen in Macular Telangiectasia Type 2 (Mac Tel 2) or Idiopathic Juxtafoveal Telangiectasia Type 2 includes ectatic vessels with hyperfluorescence in the involved regions on FA, right-angled venules, proliferation of vessels in outer retina and subretinal space and obliteration of foveal avascular zone. The histologic examination conducted by various studies showed abnormally dilated vessels in deeper plexus of retinal vasculature with focal vascular invasion to inner border of outer nuclear layer.67. OCT angiographic study of eyes with MacTel 2 by Spaide et al8 showed some loss of capillary density in the inner vascular plexus. The deep retinal plexus showed dilation and telangiectasia in the early stage of the disease, with vascular invasion into the outer retina (Figure 2 & 3), with vessels in the outer plexus showing a more widespread thinning in caliber and density in advanced disease. This may be followed by development of subretinal neovascularisation. The vascular invasion to normally avascular outer plexiform layer / outer nuclear layers is beneath areas of prominent retinal vascular leakage seen on FA. More advanced cases of MacTel 2 have increased loss of the perifoveal capillaries of inner plexus, more prominent decrease in imaged outer plexus, and invasion of deeper layers and subretinal space with new vessels. OCT angiography has an important role in identifying CNV in a case of retinal telangiectasia.

Role of OCT Angiography in CNV

Neovascular ARMD has been defined on OCT as Type 1 (originating from choroid and present beneath Retinal Pigment Epithelium [RPE]), Type 2 (originating from choroid and present above RPE) and Type 3 or Retinal Angiomatous Proliferation (RAP) lesion (originating from deeper retinal capillary plexus and present intraretinally). Because of the occult nature of type 1 membranes and their location under the RPE, it is difficult to visualize the microvascular complex using conventional angiography or spectral domain OCT. Monitoring the response to anti-
Vascular Endothelial Growth Factor (VEGF) therapy is usually done by assessment of reduction in RPE detachment and resolution of intraretinal and subretinal fluid as seen in Spectral domain OCT. OCT angiography can often visualize specific choriocapillaris loss and the highly organized microvascular complex which are usually seen beneath the retinal exudation. In its chronic stage, this vascular complex matures with a main central trunk and large branching vessels. The main central trunk may have a different structure than the surrounding finer plexus and may be more prevalent in older lesions and more resistant to anti-VEGF therapy. Occult pathological vessels cannot be adequately visualized on conventional angiography. OCT angiography also helps to assess the response of culprit vessels to anti-VEGF therapy and better assess efficacy of the treatment in terms of change in area and density of vessels in the microvascular complex before and after the treatment. Leakage and pooling of dye in a Pigment Epithelial Detachment (PED) usually obscures the underlying CNV, which can be seen clearly on OCT angiography. CNV is more common in certain eyes with CSCR, such as those who have undergone laser photocoagulation older patients with CSCR, and eyes that feature diffuse RPE loss. Features that can be seen in both chronic CSCR with and without CNV include RPE detachment, subretinal fluid, intraretinal fluid, cystoid macular degeneration, retinal atrophy, and diffuse irregular hyperfluorescence on FA or ICG angiography. Thus, CNV complicating chronic CSCR is difficult to diagnose using conventional angiography. OCT Angiography can help delineate the two disease process in such cases. The characteristic picture of the CNV on OCT angiography will show outer retinal

Figure 2: OCT angiographic image; (2a) Superficial retinal capillary layer shows increased vessel tortuosity; (2b) Telangiectatic vessels lying in the deep retinal capillary layer; (2c) Fluorescein angiographic image shows leakage temporal to fovea.

Figure 3: OCT angiographic image of the other eye of the same patient as in figure 2, showing 3b) tuft of new vessels which seem to originate in the outer retinal layer going up till the (3a) deep retinal capillary plexus; (3c) Fluorescein angiographic image showing diffuse leakage in the area of vascular change suggestive of CNVM.
vascular network corresponding to the area of staining on FA, along with focal areas of reduced choriocapillaris flow which usually correlate with regions of hypofluorescence on ICGA (Figure 4 & 5). The retinal circulation will be normal. Also, response to Anti VEGF can be monitored by OCT Angiography assessing change in morphology of the vascular complex. Early diagnosis of CNV or its recurrence following treatment, will help in preserving the vision by early intervention.

Figure 4: Angiographic images showing tuft of new vessels at the outer retina and choroidal level (depicted by arrow head), suggestive of CNVM. The area of abnormal vessels is well defined and can be used to see the response to treatment by regression of these vessels.

Figure 5: FA images (5a) and ICG angiography (5b) of same patient showing window defects and area leakage inferonasal to fovea ICG angiography shows leakage inferonasal to fovea persisting till late phase.

Role of OCT Angiography in Diabetic Retinopathy

Study evaluating OCT Angiographic picture in Diabetic Retinopathy by Akihiro et al18 described microaneurysms as dilated saccular or fusiform capillaries. Majority of microaneurysms were seen to be located in the inner nuclear layer and its inner/outer borders (i.e. deep plexus) in a histologic study19 and in a clinicopathologic study using OCT.20 Hyperfluorescent dots observed on FA may not always represent microaneurysms but instead may represent focal leakage from impaired retinal capillaries. Conversely, the pinpoint spots observed by OCT angiography and not by FA may simply be capillary ends or vertically oriented capillaries. The extent of retinal nonperfusion, visualized as noflow or sparsecapillary areas, can be evaluated differently in each layer using OCT angiography. The edge of nonperfused areas is fuzzy in FA; however, OCT angiograms can clearly visualize the border between sparsecapillary areas and dense capillary areas (Figure 6). The foveal avascular zone is enlarged in deep retinal vascular plexus in Figure 6b, although the significance of the same has not been described in literature. According to Akihiro et al18, the measured non perfused area in superficial plexus was found to be slightly larger than that in deep plexus. OCT angiography, which is unaffected by fluorescein leakage and visualizes the blood flow inside vessels, can clearly show the extent and morphology of the neovascularisation. OCT angiography can also be used to quantitatively show the course of decrease and reincrease of blood flow in new vessels and changes in the capillary non perfusion areas after treatment. This makes OCT angiography the tool of choice in pregnancy and renal patients, where FA needs to be avoided.

Advantages of OCT Angiography

FA involves injection of a dye, which has a small probability of serious complications but a common incidence of minor adverse effects, such as nausea and hives. FA provides flow information in that speed of filling can be roughly compared in patients, physiologic information concerning health of vessels and integrity of blood retinal barrier can be assessed by looking for leakage with larger field of view. A useful fluorescein angiographic frame can be obtained in a fraction of a second. The advantages of OCT angiography is
Figure 6: OCT angiography showing; (6a) Intact foveal avascular zone at superficial retinal plexus; (6b) Foveal avascular zone appear to be enlarged in deep retinal plexus dilated fusiform capillaries and pin point spots suggestive of microaneurysm are also seen in deep retinal vascular plexus in a patient with diabetic retinopathy; (6c) Corresponding FA images of the same patient where margins of the foveal avascular zone are not clearly seen.

Limitations of OCT Angiography
Limitations of OCT angiography are still considerable and further refinements of technology will certainly improve applicability of this novel technology in clinical practice. As SSADA technology detects blood flow and movement, any movement by the patient will cause significant artifact.
and deterioration of image quality. Projection artifact, where the transit of blood cells in a superficial blood vessel cast flickering shadows on the deeper tissue layer that is indistinguishable from blood flow in deeper layer, is another limitation of this technology making it sometimes difficult to distinguish normal physiological vessels from pathological ones. The normal vessels surrounding the RPE detachment may appear as tuft of abnormal vessels (Figure 7). This appearance occurs due to reflectance of light through the normal retinal vessels oriented vertically over the PED (due to height of the detachment). The software does provide a ‘remove artifacts’ function, which can subtract projection artifact from superficial vessels, but which also causes some loss of signal of pathological blood vessels. All neovascular complexes are not visualized because of imprecision in slab segmentation, which requires careful control of depth and thickness of the slab to more precisely identify neovascular membrane. In addition, some neovascular complexes may not be visualized because of resolution limitations of technology, which will not detect low flow vascular lesions (example- polyps and very fine vessels such as in Type 3 CNV). Therefore, the attenuation seen in the finer capillaries of lesions might be due to very slow blood. OCT angiography images do not show leakage, dye pooling and capillaries of lesions might be due to very slow blood. OCT angiography is of value for the diagnosis of chronic central serous retinopathy. A Prospective Pilot Study. American Journal of Ophthalmology 2015; 160:35-41.

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