Optical Coherence Tomography in Myopia and Pathologic Myopia

Subjects: Ophthalmology

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Myopia represents a growing and significantly global public health problem, with a prevalence of over two billion people (28.3% of the global population), including 277 million individuals (4.0%) with high myopia. Pathologic myopia is defined by the presence of myopic lesions in the posterior segment of the eye (posterior staphyloma or myopic maculopathy equal to or more serious than diffuse choroidal atrophy). Advances in imaging with optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) technology, including the development of swept source OCT/OCTA, widefield or ultra-widefield systems, have greatly improved the understanding, diagnosis, and treatment of myopia and myopia-related complications.

Keywords: optical coherence tomography (OCT) ; optical coherence tomography angiography (OCTA) ; myopia ; pathologic myopia ; imaging

1. Introduction

Myopia represents a growing and significantly global public health problem, with a prevalence of over two billion people (28.3% of the global population), including 277 million individuals (4.0%) with high myopia [1]. High myopia is defined as a refractive error of −5.00 diopters (D) or worse [2]. Pathologic myopia is defined by the presence of myopic lesions in the posterior segment of the eye (posterior staphyloma or myopic maculopathy equal to or more serious than diffuse choroidal atrophy) [2]. It usually occurs in highly myopic eyes, but can also develop in eyes with low myopia or even in emmetropia. It has been reported that pathologic myopia causes vision impairment or blindness in 0.2–1.5% of the Asian population and is the leading cause of irreversible blindness in China, Japan, and Taiwan [3][4][5][6]. Therefore, myopia and pathologic myopia have become serious threats to vision health worldwide warranting prompt attention [7].

Imaging in myopia has become increasingly important for the early detection, accurate diagnosis, prognostication, and evaluation of treatment for myopia [8]. Optical coherence tomography (OCT), an emerging technology for performing high-resolution cross-sectional imaging, is now the most frequently used tool for ophthalmic imaging. Before the advent of OCT, the pathological changes of the myopic eyes could only be histologically investigated in enucleated eyes. Now, OCT can be applied for imaging characteristic changes in ocular tissue due to myopia [9], from the anterior to posterior segment of the eye, including cornea, anterior chamber, vitreous, retina, optic nerve, choroid and sclera, which has greatly improved the understanding of myopia and pathologic myopia.

More recently, the development of OCT angiography (OCTA) has enabled the production of images of blood flow with unprecedented resolution of all the vascular layers in a rapid, non-invasive manner, which can help detect vascular-related myopia-related macular lesions such as myopic choroidal neovascularization (mCNV) and myopia-associated glaucoma-like optic neuropathy [10][11].

2. Advances in OCT/OCTA Technology

2.1. Time Domain and Spectral Domain OCT

The invention of OCT in 1991 [12] has significantly impacted the entire field of ophthalmology by enabling real-time in vivo subsurface imaging of biological tissue in a non-invasive manner. Since the advent of OCT, there have been extraordinary advances in this imaging technology. The first generation of time-domain OCT (TD-OCT) was limited by low axial resolution (10–15 μm) and longer time for imaging due to limited number of A-scans (400 A-scans/second) [13]. The second generation of spectral domain OCT (SD-OCT) improved axial resolution (3–5 μm) and image acquisition speed (20,000–100,000 A-scans/second) [14]. SD-OCT enables the visualization of retinal microstructures to the same level of detail as histopathology [15]. By changing the imaging acquisition position, enhanced depth imaging (EDI, which allows

imaging of deeper structures such as the choroid and sclera [16]) has been incorporated in commercially available SD-OCT. OCT has become a standard of care in ophthalmology for disease diagnosis, monitoring of progression and treatment response, and advancing the understanding of disease pathogenesis.

2.2. Swept Source OCT

Swept source OCT (SS-OCT) uses a frequency-swept light source and photodetector. The light source is intrinsically more complex and the detectors are able to operate at high speed (200,000 A-scans/second), which allows faster image acquisition and reduces motion artifacts. In addition, SS-OCT employs lasers with a longer wavelength, which can better penetrate through ocular tissues with less sensitivity roll-off, thus increasing imaging depth and improving visualization through dense ocular media, though at the expense of reduced axial resolution (6–8 µm) [17]. Studies have demonstrated that SS-OCT is helpful for imaging the retinochoroidal structures of pathologic myopia and revealing additional pathology along the staphyloma walls not visible using SD-OCT, including incomplete posterior vitreous detachment (PVD) and peripheral retinoschisis [18].

2.3. OCT Angiography

Established on the basic principles of OCT, OCTA can achieve non-invasive, depth-resolved, and refined imaging of the choroid and retina microstructures. The concept of imaging vasculature through OCT and Doppler shift formed the basis for OCTA as OCT scanning speeds improved dramatically [19]. OCTA generates images through calculating differences in phase, amplitude, or both between sequential OCT scans at the same spot, known as a decorrelation signal, which is yielded by moving architecture. For example, the movement of blood cells within retinal blood vessels yield a decorrelation signal, allowing OCTA images to highlight retinal microvasculature [20]. In addition, quantitative OCTA analysis of chorioretinal microvasculature, such as blood vessel density, tortuosity, and caliber, etc., have been established for objective description and explanation of clinical outcomes [21].

2.4. Widefield OCT

The introduction of widefield and ultra-widefield phenotypes represent one of the most important recent advances of OCT/OCTA. Ultra-widefield SS-OCT has been reported to scan a field of view up to 100° of the retina [22], thus enabling the detection of wide staphyloma as well as estimation of ocular curvature [23][24]. Ultra-widefield OCT is extremely useful for imaging peripheral retinal lesions in high myopia, some of which had not been previously imaged. The advent of widefield and ultra-widefield OCTA has greatly expanded the field of view of 50–80° of the retina and have been employed for the detection and treatment of various chorioretinal diseases [20][25].

2.5. Polarization Sensitive OCT

Polarization sensitive OCT (PS-OCT) bears added advantages owing to the fact that several ocular tissues can change the polarization state of light, creating an extra contrast channel and providing quantitative information, which has shown to be useful for both anterior and posterior segment imaging, including the evaluation of trabecular meshwork, retinal nerve fiber layer (RNFL) and macular lesions [26]. PS-OCT has shown potential utility in evaluating myopia-related pathologic changes. For example, PS-OCT successfully demonstrated the structure of collagen fibers of the retinal nerve fibers, sclera, and Henle's fiber layer [27]. In addition, PS-OCT was used to assess melanin distribution at the retinal pigment epithelium (RPE) in high myopia patients and showed decreased depolarization at the RPE [28].

3. OCT and OCTA for the Assessment of Ocular Structures in Myopes

3.1. Anterior Segment

Anterior segment OCT (AS-OCT) imaging is increasingly influencing clinical practice. AS-OCT can be used to assess modest anterior segment morphological changes, such as slight reductions in the accommodation response of ocular biometric elements elicited by atropine eye drops, which are used for childhood myopia control [29]. AS-OCT is also useful in the pre-operative, intra-operative, and post-operative evaluations of corneal refractive surgery candidates [30]. Ultra-high-resolution OCT can effectively detect subclinical keratoconus [31][32], an important part of pre-operative screening for refractive surgery. High-resolution AS-OCT is useful for the measurements of corneal thickness, corneal keratometry, flap thickness or displacements after laser in situ keratomileusis (LASIK) [33][34]. The curvatures of the stromal layers can also be measured to visualize the reconstruction of the stroma and epithelium after photorefractive keratectomy (PRK) [35]. For example, using ultra-high-resolution AS-OCT, corneal epithelial hyperplasia after PRK was found to be associated with preoperative myopic error and ablation zone diameter [36]. In addition, AS-OCT has an important role in determining the

pre-operative ocular biometrics of implantable collamer lenses (ICL) implantation for myopes [37], which provides reliable basis for the optimization of ICL sizing [38]. The important safety postoperative parameter known as the lens vault, which is the distance between the anterior surface of the crystalline lens and the posterior surface of the ICL [39], can also be measured using AS-OCT [40]. Moreover, AS-OCT has been used to investigate the development and risk factors for intraocular lens (IOL) tilt and decentration in high myopes [41]. Extra precautionary measures should be taken before implanting multifocal or toric IOL in such eyes.

Recently, studies have shown that anterior segment OCTA is able to non-invasively measure functional vascular parameters that may assist the evaluation of ocular surface diseases [42]. Future studies are necessary to explore its potential applications in myopia-related diseases.

3.2. Vitreous

OCT technology has significantly improved the imaging of vitreous structure with advancements in depth of view [43]. Recently, the combination of ultra-widefield OCT and 3D imaging has shown to be very useful in visualizing the complex structure of the posterior vitreous [44]. The posterior precortical vitreous pocket (PPVP) is defined as the liquefied lacuna anterior to the macular and is physiologically present in some adults [45]. Using SS-OCT, PPVPs have found to be larger in highly myopic eyes, which may indicate earlier vitreous liquefaction that may induce partial or complete PVD in these patients [46]. Recently, a higher incidence of asymmetrical PVD was found in high myopia, and correlated with posterior protrusion of the sclera of the highly myopic eye, which suggests that myopic macular retinoschisis and myopic traction maculopathy (MTM) may be induced by vitreous traction spanning a wider distance in these eyes [47]. In addition, SD-OCT has also been used to confirm PVD in myopic eyes, which is associated with structural and functional abnormalities such as vision-degrading myodesopsia [48].

3.3. Retina

High myopia and pathologic myopia are featured by excessive elongation of the eyeball that can lead to a series of retinal complications including retinoschisis, lacquer cracks, myopic maculopathy, and myopic macular hole (MH) [49]. OCT can be used to qualitatively and quantitatively evaluate the chorioretinal structures in high myopes [50]. Using SD-OCT, a correlation was found between the degree of myopia and the change of retinal thickness. With the increase in myopia, the foveal thickness increased while the inner/outer macular thickness decreased [51]. In addition, the morphology of Bruch's membrane defects visualized by SS-OCT were consistent with prior histopathology studies in high myopia [52][53], which were characterized by a lack of Bruch's membrane, choriocapillaris, photoreceptors, and RPE [53]. It is important to visualize and image the pathological features in the peripheral retina for the diagnosis and evaluation of pathology in the area [54]. Ultra-widefield OCT imaging of the retinal periphery is feasible with commercially-available devices which provide detailed anatomic information of the peripheral retina [55]. Advances in ultra-widefield OCT technology address many challenges and allow new findings of the structure and function in high myopes. For example, ultra-widefield OCT can visualize the staphylomatous contour of highly myopic eyes, generating detailed imaging of the vitreoretinal interface and progressive lesions of MTM [56].

Above all, it is important to consider the magnification correction for the accurate interpretation of OCTA-derived parameters in myopia, since ocular magnification can affect the outcomes of chorioretinal blood flow quantification with OCTA [57]. Retinal perfusion has been found to be associated with chorioretinal atrophy, mCNV, and lacquer crack formation in myopic eyes [58][59]. Studies using SD-OCTA have reported disparity in correlated changes to the deep versus superficial retinal circulations, indicating that retinal circulations can be affected by high myopia. SS-OCTA can be used to quantitatively assess the retinal microvasculature and choriocapillaris in myopes [60]. Compared with low and moderate myopia, vessel density of the superficial capillary plexus was lower, and impairment of the choriocapillaris in the macular area was more severe in the high myopia group [60]. Widefield SS-OCTA can generate detailed images of the chorioretinal microvasculature in a large field of view, with which researchers found that decreases in microvasculature and structural changes were correlated with myopia [61].

3.4. Choroid

The choroid plays an important role in the pathological alterations of myopia and myopia-related complications [62]. It has been demonstrated that the extreme thinning of the choroid can cause decreased choroidal perfusion, which may induce the development of mCNV and myopic macular degeneration (MMD) [63]. Using SD-OCT, choroidal thickness has been identified to be associated with axial length and visual outcomes in high myopes [64][65]. SS-OCT has the advantage of generating high-resolution images of the choroid and the choroid–scleral interface [66]. Using SS-OCT, researchers found that choroidal thinning actually developed before retinal thinning occurred during myopia progression; myopia shift was

found to be independently correlated with central fovea choroidal thinning and axial length [67], indicating the value of SS-OCT to clarify the critical roles of choroid and retina during myopia progression. In addition, choroidal thinning was also found to be correlated to MMD [68], and topographic variations were identified in 3D maps of choroidal thickness [69]. Another important choroidal feature is peripapillary intrachoroidal cavitation, usually located inferior to the optic nerve in highly myopic eyes [70]. Contrary to the traditional hypothesis that intrachoroidal cavitation was an elevation of the retina and RPE, studies using EDI SD-OCT and SS-OCT reported that it could also develop sparing the alteration of the retina and RPE through posterior scleral bowing [70]. In addition, intrachoroidal cavitation was identified in 4.9% of highly myopic eyes, of which 71% were associated with glaucomatous visual field defects [71]. Nevertheless, the underlying pathogenesis of intrachoroidal cavitation development and its association with visual field defects remains unelucidated.

OCTA has also been used to explore the choriocapillaris in myopic eyes [60][72][73][74]. Researchers developed a novel segmentation technique based on OCTA to assess different choroidal layers' thickness and vasculature, which may serve as new biomarkers to study myopia-related complications [73]. In addition, studies showed more severe choriocapillaris flow defects in high myopia, even in those with mild fundus changes, in both standard scans and quantitative mapping [60][72], which worsened with increasing severity of myopic maculopathy [74]. More specifically, quantitative OCTA measurements of the chorioretinal microvasculature in high myopes demonstrated that decreased retinal perfusion was related with axial length elongation [75]. Using SS-OCTA, studies showed that retinal perfusion and choriocapillaris flow decreased with worsening severity of MMD, indicating that both the retinal and choriocapillaris vasculature are affected in eyes with MMD [76]. More recently, studies using SS-OCTA to measure retinal perfusion density demonstrated that macular sensitivity was associated with deep retinal perfusion density, indicating a vasculature-function correlation in MMD development [77].

4. OCT and OCTA for the Assessment of Pathology in High Myopes

4.1. Myopic Maculopathy

Myopic maculopathy is defined as "macular alterations induced by high myopia, in which an excessive axial length and/or posterior staphyloma is the main common factor but not the only factor" [78]. The META-PM classification is based solely on fundus photographs showing only the atrophic alterations of myopic maculopathy [79]. However, macular alterations include atrophic changes in addition to neovascular alteration, traction-induced changes, and dome-shaped macula (DSM), which can only be visualized and diagnosed with OCT. Therefore, an OCT-based classification system has been proposed [80]. Using SS-OCT, the cut-off value of 56.5 μm for the nasal choroidal thickness can predict peripapillary diffuse choroidal atrophy from the tessellation, and the cut-off value of 62 μm at subfoveal can predict the macular diffuse choroidal atrophy. During progression from macular diffuse choroidal atrophy to patchy atrophy, other factors besides choroidal thinning, including defect of Bruch's membrane may also be involved [80].

Recently, researchers have proposed another new classification system of myopic maculopathy based on the three key factors—Atrophy, Traction, and Neovascularization, which is known as the ATN classification system [79]. It keeps the original META-PM classification as the atrophy classification; adds the tractional component including five stages of inner or/and outer foveoschisis, foveal detachment, macular hole, and retinal detachment; three plus signs in the META-PM classification are included as neovascular components [79].

4.2. Dome-Shaped Macula (DSM)

DSM has been better depicted and visualized with the advancement of OCT technology that has allowed acquisition of high-resolution images of the macula area [81]. According to the primary orientation of the macula based on OCT images, three different types of DSM have been recorded: round dome (20%), vertical oval-shaped dome (18%), and horizontal oval-shaped dome (62%) [81][82]. Studies using 3D OCT macular reconstruction and 3D MRI have confirmed these findings since the conventional OCT equipment has a restricted scan length and may not achieve comprehensive evaluation [83][84]. Using SS-OCT, one study demonstrated a correlation between Bruch's membrane defects and the occurrence of DSM in high myopia [52]. In addition, using ultra-widefield SS-OCT, a recent study reported that DSMs develop independently from staphyloma, and tend to form in eyes with a substantial enlargement of the posterior fundus and should be regarded as scleral curvature deformation [23].

4.3. Optic Nerve

Several studies have reported the myopia-related complications in the optic nerve and peripapillary area, such as peripapillary atrophy (PPA) enlargement [85], tilted and rotated discs [86][87], scleral thinning, and abnormality between the macular and the optic nerve head [88], which have been found to be accountable for the predisposition to glaucoma.

Demonstrating the structural abnormalities in the optic nerve and surrounding area may aid in elucidating the underlying etiology of myopia-associated glaucoma-like optic neuropathy and detecting high-risk eyes of developing glaucoma.

It was reported that a higher incidence of glaucoma in axial high myopia is due to the disc enlargement in axial myopia, instead of the elongated axial length [89]. In most high myopes, an OCT scan provides enough information to diagnose glaucomatous optic neuropathy accurately [90]. SS-OCT can be a helpful method to visualize peripapillary morphologic characteristics in high myopia. The peripapillary area is frequently reported to be inferotemporal tilted in highly myopic eyes using SS-OCT [91]. Deeper staphyloma, thinner choroid, and larger area of PPA were found to be associated with greater tilt [91]. Recently, researchers published a public dataset of SD-OCT images of optic disc tilt in myopia, aiming to develop new findings between optic disc tilt and pathologic myopia [92]. Study using high-resolution SS-OCT suggested that eyes with sudden alterations to the sclera have greater visual field defects than those without, and the angle of scleral bending was correlated with the thickness of retinal nerve fiber layer and visual field defect in high myopes [88]. In addition, there was a correlation between tilted disc ratio measured by SS-OCT and retinal perfusion measured by SD-OCTA in high myopia [93]. Choroidal thinning of the macular area was correlated with optic disc tilt degree and increased PPA area, and macular choroidal microvasculature changes were also correlated with increased PPA area [94].

OCTA measurements of calculated indices such as average macular vessel density ratio have proved to be helpful for diagnosing glaucoma in high myopic eyes [95]. Primary open-angle glaucoma eyes with high myopia had a higher rate of decrease in macular vessel density in the deep capillary plexuses than those without high myopia, which may provide new clues to the longitudinal effects of high myopia in retinal microvasculature [96]. Using OCTA, topographic differences on choroidal microvasculature and superficial radial peripapillary capillary were identified in PPA subzones, indicating there may be a microcirculatory deficiency in PPA beta zone in myopia [97]. Choroidal microvascular dropout observed by OCTA were found in highly myopic glaucoma eyes and were topographically associated with the region of visual field defects, which may facilitate diagnosis of glaucoma in high myopia [98]. In addition, a study found that the widefield SS-OCTA vascular density map showed good diagnostic ability for the detection of glaucomatous alterations in high myopes, which was stronger than traditional imaging methods such as OCT or red-free fundus photography [99].

4.4. Sclera and Posterior Staphyloma

The sclera plays an important role in the development of myopia and the related retinal complications through its biochemical and biomechanical properties. OCT can be helpful in the investigation of the sclera, revealing subtle abnormalities in posterior staphyloma, and allows identification of the spatial relationship between the protruded sclera and morphology of the retinal and choroidal layers [100]. In particular, SS-OCT is now able to generate high-resolution images of the entire sclera in one single scan with even more refined architectural study.

The abnormalities found in the shape and thickness of the sclera in myopic eyes have led to some new perceptions into the pathophysiology of myopia. For example, it is reported that the choroid and sclera are thinner in myopic eyes than in normal eyes, and the subfoveal scleral thickness were reported to be associated with refractive error, choroidal and retinal thickness, and age [101]. Using SS-OCT and 3D MRI, researchers studied the morphology of the sclera in highly myopic eyes to understand the pathogenesis of myopic retinochoroidal lesions [100]. Irregular curvature of the inner sclera, which may cause abnormal stress of retinal RNFL and vitreomacular interface, was reported to be related to higher incidence of myopic maculopathy including MTM, mCNV, and chorioretinal atrophy [100]. The subfoveal scleral thickness measured by SS-OCT was comparable with that by histological studies and EDI SD-OCT [64][100][102]. The central scleral thickness measured by SS-OCT was found to be negatively correlated with axial length and age in high myopes [103]. In addition, a dome-shaped macula may be attributed to relative thickening of the macular sclera within staphyloma, which may cause RPE detachment [103]. It is speculated that the dome shape can act as a macular buckle, possibly alleviating the traditional forces over the fovea [104].

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