

Spectral –domain optical coherence tomography in patients with congenital nystagmus

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Abstract

- **AIM:** To study macular features in patients with congenital nystagmus and to assess the utility of spectral-domain optical coherence tomography (SD-OCT) in nystagmus.

- **METHODS:** The macular areas of 51 outpatients with congenital nystagmus were examined using SD-OCT. Morphological changes in the retinal layers of the macular area were analysed.

- **RESULTS:** Macular images were successfully obtained with SD-OCT from 50 (98%) patients. Patients with ocular albinism mainly have macular hypoplasia, abnormal foveal depression, and increased foveal thickness with persistence of an inner nuclear layer, an inner plexiform layer, a ganglion cell layer and a nerve fiber layer. Macular morphology similar to albinism was observed in three patients with idiopathic macular hypoplasia. The OCT findings of cone dystrophy included unclear, disrupted or invisible photoreceptor outer segment/inner segment in the fovea; fusion, thickening and uneven reflection of the outer segment/inner segment with external limiting membrane. Some patients with congenital idiopathic nystagmus showed normal macular morphology and structure, and others showed indistinct macular external limiting membrane reflection.

- **CONCLUSION:** SD-OCT is an effective and reliable method to detect the macular morphology of congenital nystagmus patients. This technique has diagnostic value in particular for patients with macular hypoplasia and cone cell dystrophy with no distinct abnormality on funduscopy.

- **KEYWORDS:** optical coherence tomography; congenital nystagmus; macular disease.

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INTRODUCTION

Congenital nystagmus (CN) is an ocular motor disorder characterized by involuntary oscillations of the eyes and an onset before 6 months of age. It is divided into three categories: congenital idiopathic nystagmus (CIN), sensory defect nystagmus and neurogenic nystagmus. Sensory defect nystagmus is associated with visual sensory abnormalities or systemic diseases^[1]. Since macular diseases are important contributors to sensory defect nystagmus, early and accurate diagnosis of macular disorders is very important. Some macular diseases, such as congenital cone dystrophy, can not be easily identified on conventional fundoscopic examinations, so electrophysiological exams, particularly multifocal electroretinogram (mfERG), are important in the diagnosis of macular degeneration. However, the gaze abnormalities in nystagmus patients may affect the accuracy of mfERG results^[2]. And the challenge to keep good fixation throughout a 5-10 minute recording session of ERG is a big hurdle even for adults, not to mention pediatric patients. Optical coherence tomography (OCT) technology allows high-resolution in vivo tomography of the retina, thereby providing a favourable means to study macular diseases^[3]. However, detection is difficult because of the brief nature of a child's gaze. Involuntary eye movement prevents the widespread application of time-domain OCT in the ocular examination of nystagmus patients. With the advance of the new generation spectral-domain OCT (SD-OCT), the scanning speed has been increased by 50 to 100 times through the new spectral domain technology, making three-dimensional retinal imaging possible and increasing the axial resolution to 5µm. Thus, this advanced technique can more accurately display the structure of the retina *in vivo*^[4,5]. SD-OCT has been used to examine patients with congenital nystagmus and can successfully detect the macular morphology in CN^[6]. Previous results have mainly focused on albinism and CIN^[7,8]. OCT findings for other

types of nystagmus require further study. In the present study, we used spectral-domain Topcon OCT for further study on patients who were diagnosed with CN in our hospital, with the results reported as follows.

MATERIALS AND METHODS

Materials Patients who were diagnosed with CN in our hospital and underwent continuous observation from July 2010 to January 2011 were included. All the patients had experienced symptoms since infancy and had undergone a thorough examination of their eyes and afferent visual system that included tests of their monocular and binocular vision, colour vision, refraction, a slit-lamp examination and a fundus examination. Additional tests were also performed, including electroretinography, visual evoked potentials and eye movement examination. Central nervous system imaging including magnetic resonance imaging (MRI) was conducted to exclude the possibility of any central nervous system diseases. Finally, macular OCT examination was conducted. A total of 51 CN patients (35 males, 16 females, 2-46 years of age, average 12.8 years) were included. Of these patients, 22 (43%) were found to have abnormalities in their visual systems, which included cone dystrophy (8 cases), oculocutaneous albinism (OCA, 5 cases), primary macular hypoplasia (3 cases), congenital cataract post-operation (2 cases), myopia (2 cases), and congenital visual nerve atrophy (2 cases); the remaining 29 cases (57%) were CIN. This study was approved by the Southwest Hospital Ethics Committee. Informed consent was obtained from all the patients.

A three-dimensional (3D) SD-OCT (OCT-1000 MARKII, TOPCON Corporation) was used for OCT examination. Patients were examined in the sitting position and a light emitting diode internal fixation target was used. The scanning mode included linear scan or 3D scan. Linear scan used following parameters: 6mm scan line length with 1 024 A scans, 2.3 mm detection depth with an axial resolution of 5 μ m. For the 3D scan protocol, OCT images were acquired from the top to the bottom with a scanning speed of 27 000 A scans per second. The scan covered a 6.0mm \times 6.0mm area centered around the fovea with 128 horizontal scan lines with 512 pixels. Each A scan had a detection depth of 2.3mm. All OCT examinations were performed by the same physician (CS).

RESULTS

A boy with oculocutaneous albinism (OCA) was not cooperative for OCT imaging. Clear OCT images of the macular were successfully obtained from 50 patients (98%). It was primarily observed in OCA patients that normal foveal depression (Figure 1) disappeared or became shallower. Foveal region was thicker than normal (the mean

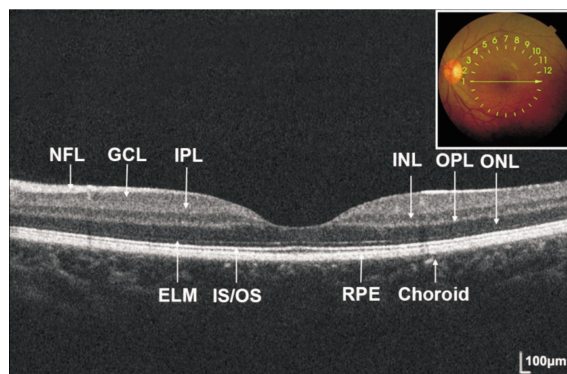


Figure 1 SD-OCT image in a normal subject

central retinal thickness was 273 \pm 43 μ m for our patients, and is 222 \pm 23 μ m^[9] for normal subjects with OCT-1000), with the preservation of inner nuclear, inner plexiform, ganglion cell and nerve fiber layers (Figure 2A, B). Three patients with primary macular hypoplasia without apparent albinism also had macular hypoplasia (Figure 2C), with no normal foveal depression but preservation of the inner nuclear, inner plexiform, ganglion cell and nerve fiber layers, and dim reflection of the external limiting membrane (ELM). The macular area in cone dystrophy showed following main features in OCT: thinning of the outer nuclear layer (ONL), vague photoreceptor outer segment (OS) / inner segment (IS) and indistinct ELM boundary (Figure 3A), scattered or discontinuous OS/IS and ELM reflection (Figure 3B), or fusion, thickening and uneven reflection of the OS/IS with ELM and thinning of the ONL (Figure 3C). Some patients with CIN had essentially normal retinal morphology in macular area (Figure 4A), but others had a sparse or no reflection of ELM (Figure 4B).

DISCUSSION

OCT technology is a non-contact, non-invasive, quantitative imaging modality developed in the 1990s, which makes it possible to obtain *in vivo* images of the internal fine structures of biological tissue. Topcon 3D OCT-1000 was adopted to perform OCT in patients with the following examination parameters: high-speed scanning, high resolution, and high-density three-dimensional scanning. This type of OCT greatly improves the efficiency of scanning and can be used to successfully scan the majority of patients with nystagmus, yielding clear images^[10-12]. With un-dilated pupils, there is less light into the fundi and it's difficult to track the pupils in nystagmus, which results in low quality of the image. So it's better to exam the patient under the condition of mydriasis. For scanning mode, linear scanning was initially adopted, but in a small number of patients, it was not possible to obtain an image through the macular area. For this group of patients, we switched approaches to obtain a macular image after 3D scanning.

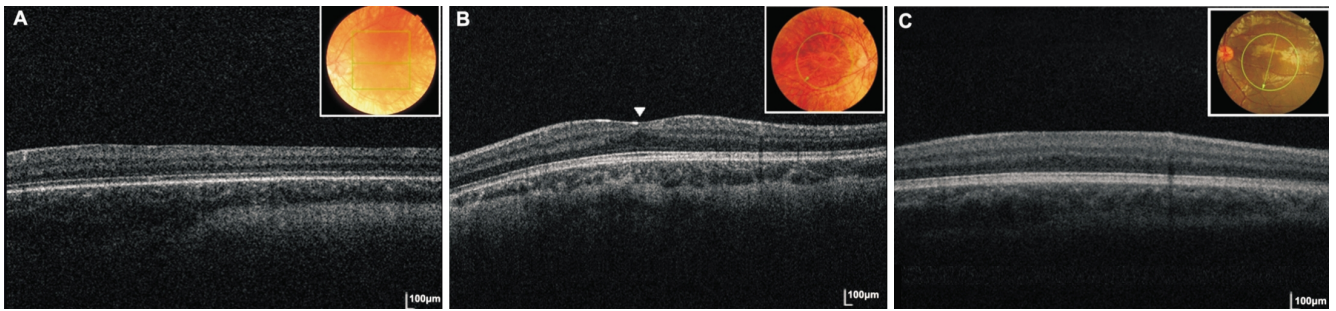


Figure 2 SD-OCT image A: Macular hypoplasia and foveal plana in OCA; B: Slight foveal differentiation (white arrow), increased foveal thickness, preservation of the inner nuclear, inner plexiform, ganglion cell and nerve fiber layers; C: Primary macular hypoplasia. Fovea pit was missing, whereas the inner nuclear, inner plexiform, ganglion cell and nerve fiber layers were present

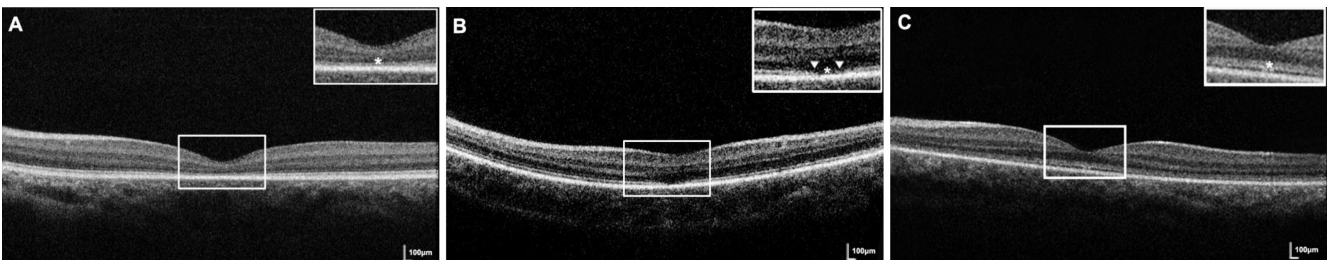


Figure 3 SD-OCT manifestation in macular area of cone dystrophy A: Thinning of ONL, vague OS/IS and indistinct ELM boundary (white asterisk); B: Disruption of OS/IS in macula (white asterisk); C: Fusion, thickening and uneven reflection of the OS/IS with ELM (white asterisk)

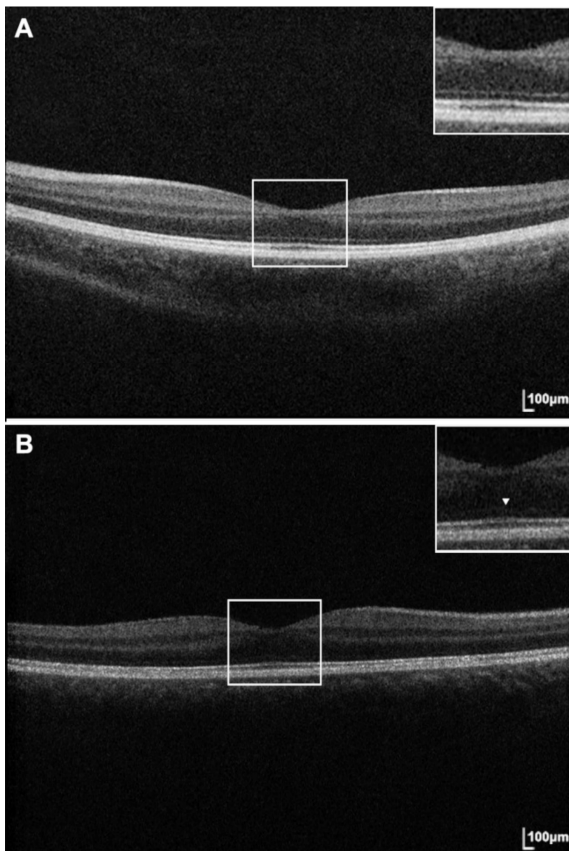


Figure 4 SD-OCT image in CIN A: Normal macular structure; B: Sparse ELM reflection (white arrow)

Therefore, 3D scanning is a more effective approach for macular scanning in the context of nystagmus. Due to the

short time window for OCT image acquisition, the older children and adults are easily to get successful imaging.

The results showed that the primary manifestation of ocular albinism nystagmus is macular hypoplasia, as demonstrated by the absence of normal fovea depression and thicker than normal foveal thickness, which was identical to the manifestation of albinism in the fundus [7]. Macular morphology is different with the severity of albinism because OCA gene mutations can cause phenotypic variation. Ophthalmologists should, therefore, include this diagnosis in differential for patients with minimal or atypical ocular findings of albinism, such as apparently isolated foveal hypoplasia [13]. Notably, in three patients with idiopathic macular hypoplasia, no significant manifestation of ocular albinism was found, but OCT examination revealed a macular manifestation similar to that observed in albinism. Macular hypoplasia can be easily missed during the routine eye examination in patients with such diseases and even yields essentially normal results upon electrophysiological examination and it is often diagnosed as CIN. OCT examination can easily detect these diseases. Of course, we cannot absolutely exclude the possibility that these patients had atypical albinism. A genetic examination should be conducted if possible for accurate diagnosis.

High-resolution 3D OCT can capture the detailed structure of internal segments of the photoreceptor layer: OS/IS [14]. SD-OCT has been applied to research on retinal thinning in occult macular dystrophy. Some studies showed some

patients with occult macular dystrophy have reduced foveal thickness with thinning of the ONL and others considered as retinal thinning maybe caused by changes of the internal and external segments of photoreceptor cells^[2]. We also observed that in patients diagnosed with cone dystrophy based on electrophysiological examination, regions that appeared abnormal upon OCT were centralised in the photoreceptor layer of the macular, with primary manifestations as scattered or discontinuous OS/IS and ELM reflection. In one patient, the reflection of the OS/IS and the ELM was fused, thickened and uneven. In addition, there were also some cases with significant thinning of the ONL. These show that OCT results differ among patients with cone dystrophy, probably due to different types of cone dystrophy, which are related to various disease aetiologies as well as differences in the site of onset, disease duration and degree of damage. Therefore, using 3D-OCT does not only reveal morphological changes in the photoreceptor layer but also helps in the diagnosis of cone dystrophy and the monitoring of disease progression.

OCT examination revealed that the macular morphology of some CIN patients was normal, which is consistent with previous reports^[6]. However, we found many patients with sparse reflectivity of the ELM. In some cases, this structure was defective or even absent. The difference between normal individuals and those with CIN may result from early development of the eye in the patients with nystagmus. Unstable eye movement also has an impact on the development of the visual system, so even if there is no inherent organic macular degeneration, abnormalities may still exist in macular structures because of acquired developmental effects. Previous studies have suggested that the ELM provides a barrier function. It was reported that the ELM and the photoreceptor cell are closely related, and a genetic defect leading to damage to the ELM can also be found with shortened photoreceptor inner and outer segments^[15]. Recent studies have also shown that ELM status may be more useful than OS/IS status in evaluation of retinal morphology and function in patients with age-related macular degeneration^[16]. Whether changes in the ELM structure are related to CIN and it's possible function still need further study.

There are some limitations of our study, which include lack of blood sampling or genetic testing. Our research focuses on morphological observations and does not include statistical analysis of various layers of the retina in comparison to age-matched normal controls. In conclusion, compared with ERG, SD-OCT is easier to perform. And the technique is conducive to a better and more accurate

understanding of the features of macular diseases. Therefore, SD-OCT provides a new method for the clinical diagnosis of CN to determine whether the cause of nystagmus is related to macular disease.

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