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Clinical Application of Rapid Serial Fourier-Domain Optical Coherence Tomography for Macular Imaging

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Purpose: To introduce and examine the utility of a retinal imaging technique using high-speed optical coherence tomography (OCT) for creating a more complete retinal structural map to aid in the evaluation of patients with macular pathology.

Design: Prospective observational case series.

Participants: Five patients with a variety of macular pathologies.

Methods: Patients were imaged with a Fourier-domain high-speed high-resolution OCT system built at our institution. A sweeping serial OCT B-scan of the macula was acquired to create a detailed retinal structural map. The data were then used to make individual clinical observations.

Results: Rapid serial OCT B-scans produced detailed macular maps for all 5 patients. Diagnoses of imaged patients included macular hole, lamellar macular hole, regressed macular hole or macular microhole, choroidal neovascular membrane (CNV) from age-related macular degeneration, and CNV from presumed ocular histoplasmosis syndrome. Reconstructed B-scans and C-scans are shown for selected patients to illustrate the additional perspectives gained by obtaining a detailed retinal map.

Conclusions: Rapid serial Fourier-domain OCT B-scanning can be used to create a detailed retinal structural map. This technique provides additional information that can be missed on single OCT images and provides an accurate way to image large or complex lesions, and allows B-scan and C-scan reconstructions to be made that provide additional perspectives into retinal structures that may be missed using traditional imaging methods. *Ophthalmology* 2006;113:1425–1431 © 2006 by the American Academy of Ophthalmology.

Optical coherence tomography (OCT) has become an increasingly valuable tool for clinical evaluation of the retina.^{1–3} Traditionally, this has been performed using a commercially available time-domain model (OCT-3, Carl Zeiss, Meditec, Inc., Dublin, CA). Numerous advances in the understanding of retinal diseases are still being made using this model.

One of the main limitations of time-domain OCT, however, is relatively long acquisition times (0.5–1.0 B-scans/second or 400 A-scans/second). This lack of speed allows motion artifacts and thus is problematic in the creation of a detailed retinal map made from several consecutive B-scans. The commercially available OCT system uses only 6 radial B-scans to create a macular map.

Fourier-domain OCT (FD OCT) is an alternative imaging modality that has been developed recently.^{4–7} The advantages of this approach are a factor of 20 to 40 reduction in image acquisition time while maintaining the ultra-high axial image resolution of up to 2 to 3 μm that has been recently achieved by some time-domain OCT models.^{8–11} These improvements permit real-time in vivo imaging with fewer motion artifacts and with resolution approaching histologic-level detail. Several investigations are being carried out to determine whether improving OCT image resolution will lead to useful clinical applications.^{12–15} The clinical application of the improved speed, however, has not yet been fully investigated. A report utilizing this technology to create volumetric representations of retinal lesions has recently been published.¹⁶

In this paper, we describe a technique that can be applied to OCT imaging to produce more detailed retinal maps. It involves performing a rapid sweep of serial OCT B-scans through the macula, analogous to a modern computed tomography scanner. Thus, the entire area of interest can be imaged in a detailed map, compared to traditional methods in which a limited number of cross-sections are used with interpolation to fill in the nonimaged areas. This can be particularly useful for patients with poor fixation, for evaluating smaller lesions that could be missed on a single B-scan, and for evaluating larger, complex lesions that

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cannot be accurately characterized with a limited number of B-scans.

An additional benefit of a detailed retinal structural map is the ability to mathematically reconstruct scans from any desired direction using the data from a single map. B-scans can be reconstructed from a direction different from the scanning direction, and C-scans (en face planes) can also be reconstructed from the same data. This reconstruction approach was first proposed and tested in clinical settings for en face time-domain OCT imaging,^{17,18} in which retinal images were acquired in C-scans; however, to our knowledge, there have been no published reports applying this technique to FD OCT imaging in clinical settings.

In this study of the utility of rapid scanning, FD OCT imaging is examined in selected patients with a variety of macular pathologies.

Materials and Methods

Patients selected for this prospective observational case series were evaluated at the University of California—Davis Medical Center. Prior to imaging, written informed consent was obtained following the Tenets of Helsinki, and with approval of the Office of Human Research Protection of the University of California—Davis School of Medicine. Five patients were selected (Table 1), all having pathology involving the macula.

A state-of-the-art FD OCT system similar to that previously described by Wojtkowski et al⁶ and further improved by Nassif et al⁷ was used to image the 5 patients. This system was constructed and developed at University of California—Davis in collaboration with Duke University.¹⁹ Two superluminescent diodes were used as light sources, SLD1 and SLD2. The measured axial resolution on the retina (defined as full-width-half-maximum of the coherence envelope) was about 6 μm for SLD1 (840@50 nm), and 3.5 μm for SLD2 (890@150 nm). The lateral resolution (defined as full-width-1/e²-diameter of the light spot on the retina) was identical for both light sources (the OCT beam diameter was 2 mm for both light sources in our system). The lateral resolution was calculated (using the OCT beam diameter and a standard eye model) to be in the range of 10 to 15 μm for most of our subjects (excluding those with a high value of aberrations, where lateral resolution could be >15 μm). The B-scans were acquired in 1000 A-scan frames with 100 μsecond exposure time per A-scan, resulting in data acquisition and real-time postprocessing of 9000 scans/second. This results in a 9 frames-per-second display and acquisition speed (compared to approximately 0.5 frames per second for standard OCT). A set of 100 B-scans were acquired for

Figure 1. A, Black-and-white Fourier-domain optical coherence tomography image of normal retina. CL = connecting cilia; GCL = ganglion cell layer; ILM/NFL = internal limiting membrane/nerve fiber layer; INL = inner nuclear layer; IPL = inner plexiform layer; ISL = inner segment layer; OLM = outer limiting membrane; ONL = outer nuclear layer; OPL = outer plexiform layer; OSL = outer segment layer; RPE/BM = retinal pigment epithelium/Bruch's membrane; VM = Verhoeff's membrane. B, Same image displayed in false color.

each patient covering 6×6×2-mm volume of retina (lateral × lateral × depth). Total acquisition time for a single map was 11 seconds. The macular sweep was performed for approximately 1 to 2 minutes until an 11-second window of relatively consistent fixation was acquired.

The B-scan direction was temporal to nasal. Thus, B-scans are swept on different retinal locations from superior to inferior retina. Each consecutive B-scan was translated by 60 μm . The lateral spacing between pixels on B-scans was 6 μm (smaller than actual lateral resolution) and the axial (z) spacing between pixels was equal to 2 μm for 6- μm axial resolution imaging and 1 μm for 3.5- μm axial resolution imaging.

After acquisition of a full set of B-scans, the images were registered for fine axial eye motion artifacts. This was achieved by a partially automated technique, in which custom software automatically found axial shifts between structures on 2 consecutive B-scans. After inspection and manual correction of registration, the B-scans were shifted and rotated to reduce axial shift. No software correction was used for lateral motion artifacts. This registered volume (1000×500×100 pixels) was further used as a reference for a cross-sectional extraction algorithm, which allows reconstruction of any desired B-scans or C-scans from the acquired data.

In this paper, selected images of the maps are shown in black and white. As shown in Figure 1, black-and-white and false-color OCT images are similar in quality under ideal conditions; however, it was felt that, because of the small image sizes shown in print, the black-and-white images would allow better appreciation of details that may be lost if the images were shown in false color. Indeed, several recent papers have claimed improved ability at

Table 1. Summary of Patients Imaged with FD-OCT Mapping

Patient	Age (yrs)	Eye	Diagnosis
1	72	Left	Macular hole
2	79	Right	Lamellar macular hole
3	73	Right	Regressed macular hole
4	78	Left	CNV in AMD
5	30	Left	CNV in POHS

AMD = age-related macular degeneration; CNV = choroidal neovascular membrane; FD-OCT = Fourier-domain optical coherence tomography; POHS = presumed ocular histoplasmosis syndrome.

Figure 2. Full-thickness macular hole. **A**, Selected images from 100 B-scans, horizontal direction showing a full-thickness macular hole (arrowhead). **B**, Selected images from reconstructed B-scans, vertical direction, showing a full-thickness macular hole (arrowhead). **C**, Selected images from reconstructed C-scans (en face slices).

detecting fine OCT structures using black-and-white rather than false-color OCT images.^{20–23}

The labeling of the retinal layers in Figure 1 was presented in a recent publication²⁴; however, there is not a consensus in the literature regarding the accuracy of these labels in the outer retina.

Results

Case 1

A 72-year-old male presented to the retina clinic complaining of distortion in the central vision in his left eye for several months. The clinical examination was consistent with a stage 2 full-thickness macular hole. A serial FD OCT scan is shown in Figure 2A. The scans identify the macular hole as well as the surrounding intraretinal edema and structural retinal changes. Several reconstructed OCT images are shown as well, which allow visualization of the macular hole from various perspectives (Fig 2B, C).

Case 2

A 70-year-old white female presented to the retina clinic for a second opinion regarding a “macular cyst.” On clinical fundus examination, a macular lesion was seen that was suggestive of a macular hole. An FD OCT macular scan was performed, which revealed a lamellar macular hole (Fig 3A). Several eccentric images could have been misinterpreted as cystic macular edema if viewed alone. A reconstructed B-scan was generated that was perpendicular to original B-scans (Fig 3B). This image provides

another perspective of the lamellar macular hole. In addition, a disturbance in the outer retina was identified in an area adjacent to the lamellar macular hole, an unusual finding that has not been previously described. This retinal structural change did not correlate with any lesion seen on clinical examination or fluorescein angiogram.

Case 3

A 65-year-old white female presented with a complaint of a persistent scotoma. On examination, a lesion was identified suggestive of a small macular hole with an overlying operculum. An FD OCT macular scan was performed (Fig 4), revealing a subtle outer retinal lesion. Such a lesion appears consistent with previous reports of either a spontaneously regressed macular hole²⁵ or a macular microhole.²⁶

Case 4

A 70-year-old white male presented to the retina clinic complaining of metamorphopsia and decreased vision. On clinical evaluation with fluorescein angiography, he was found to have a classic extrafoveal choroidal neovascular membrane (CNV; Fig 5A). Serial B-scans were acquired by FD OCT (Fig 5B, D). A reconstructed C-scan was created, providing another perspective of this larger, more complex lesion (Fig 5C). Subretinal fluid is seen surrounding a highly reflective primarily subretinal pigment epithelium lesion. In addition, surrounding the lesion, the C-scan shows a less reflective halo that appears to be a subretinal process corresponding to the dark halo seen on the angiogram (arrowhead).

Figure 3. A, Lamellar macular hole. Selected images from 100 B-scans, horizontal direction, showing outer retinal structural changes (arrowhead). B, Selected image of reconstructed B-scan, perpendicular direction.

Case 5

A 30-year-old white female presented with decreased vision in her right eye. She had been previously treated with thermal laser for CNV secondary to ocular histoplasmosis. On evaluation, she was determined to have recurrent CNV (Fig 6A). An FD OCT map was obtained and a C-scan was generated to characterize the neovascular complex (Fig 6B). An abnormal subretinal process is seen that extends beyond the angiographic lesion (Fig 6B1–B3). At that time, the significance of this OCT finding was unknown. The patient underwent photodynamic therapy, and another fluorescein angiogram was

performed at her 3-month follow-up visit (Fig 6C). The angiogram demonstrated progression of her CNV in a configuration that appears to correspond to the lesion seen on the OCT map 3 months prior. Unfortunately, the patient chose not to be reimaged with FD OCT.

Discussion

These cases illustrate the possibility of creating a detailed and accurate retinal structural map using high-speed FD

Figure 4. Regressed macular hole. Selected images from 100 B-scans showing an operculum (arrowhead) and an outer retinal defect in photoreceptor layers (arrow).

Figure 5. Choroidal neovascular membrane (CNV) in age-related macular degeneration. Selected images from 100 B-scans. **A**, Fluorescein angiogram showing extrafoveal classic CNV. **B**, Enlarged image of B-scan through CNV. **C**, Reconstructed C-scan through CNV with surrounding subretinal fluid. The arrowhead in A–C points to the hypofluorescent border of CNV, possible unrecognized CNV component. **D**, Montage of selected images from a single sweeping optical coherence tomography (OCT) scan showing hypofluorescent angiographic halo (arrowhead) and corresponding subretinal OCT structure.

Figure 6. A, Late-phase fluorescein angiogram of a recurrent choroidal neovascular membrane (CNV) (red arrowheads) in presumed ocular histoplasmosis syndrome after thermal laser. B, C-scan (en face) image demonstrating lesion seen on angiogram (red arrowheads), additional unspecified subretinal structure (blue arrowheads), and surrounding subretinal fluid. B1, B-scan of CNV (red arrowhead) and adjacent subretinal lesion (blue arrowhead). B2, B-scan showing broad extent of unspecified subretinal lesion. B3, B-scan showing surrounding subretinal fluid. C, Fluorescein angiogram at 3-month follow-up visit showing progression of CNV, possibly correlating with subretinal lesion identified 3 months earlier on optical coherence tomography.

OCT. The map is created from 100 consecutive B-scans made possible by the rapid imaging speed of the system, which also limits motion artifacts. Once the map is obtained, the data can then be viewed and manipulated in different ways, allowing the clinician to view dynamically the individual B-scans that make up the map.

Cases 1 and 2 illustrate the use of this technique to image macular holes. Using current technology, information in areas distal to the center of pathology could be overlooked because of the limited number of scans performed by conventional OCT imaging. In this technique, the entire region is mapped and areas of interest can be identified and closely examined, with freedom to inspect the surrounding areas distal to the obvious area of interest. The ability to scan the entire macular area may lead to a greater understanding of the pathogenesis of macular holes and lamellar macular holes; even a subtle area of vitreomacular interface abnormality in an unexpected area would not be overlooked.

Case 3 demonstrates the possibility of finding small defects on the retinal map that could be missed with current OCT imaging techniques. Smaller lesions such as these may prove especially challenging to locate in a patient with poor fixation. The technique we present may prove especially useful in this scenario because the high-speed FD OCT can rapidly create a complete macular structural map. The higher resolution images also allow more precise localization within the retinal layers. The images obtained in this case appear to correlate with standard OCT images of spontaneously regressed macular holes or macular microholes. Because the clinical history suggests the latter, this would represent the first high-resolution images of this entity.

Cases 4 and 5 illustrate possible applications of FD OCT mapping to cases of choroidal neovascularization. The

highly detailed macular map provides a unique opportunity to perform *in vivo* histology of the entire membrane complex. In the clinical setting, a choroidal neovascular complex is classified, characterized, and localized based on its appearance on a fluorescein angiogram; however, its accuracy in determining the localization (type 1, type 2, or combined) is uncertain. Recent reports suggest that angiographic features alone might not be sufficient to make this determination.²⁷ In addition, case 5 raises the question of whether fluorescein angiogram is adequate for determining the full extent of the CNV complex. Incomplete localization of the CNV by fluorescein angiography may, in part, explain some treatment failures. These cases illustrate the potential for FD OCT to accomplish these tasks, which may aid in selecting which patients would benefit most from submacular surgery versus other therapeutic interventions. Improved localization of CNV may also improve treatment outcomes of photodynamic therapy or thermal laser.

An additional benefit to having a detailed dataset is the ability to create reconstructed B-scans or C-scans. Although the resolution of these images is decreased, they can still provide additional perspectives that could be useful in the analysis of various lesions. Similarly, this detailed map could be used to calculate more accurate volumetric data regarding the macula. Current OCT systems rely heavily on interpolation to calculate macular thickness maps, which may be subject to error and variability in measurements. The new technique of detailed macular mapping would avoid such problems. This could be used to measure macular edema in an extremely precise and accurate manner, which would aid in evaluating the various treatments for this condition.

This, to our knowledge, is the first report of macular pathology mapping using FD OCT. Recently, a report was

published that showed the use of FD OCT to create volumetric representations of various macular lesions, which is an extension of the technique we have illustrated in this article.¹⁶ Other reports have been published which demonstrate similar mapping techniques using time-domain OCT.^{17,18,28} In those time-domain models, however, the map was created from a series of C-scans, a potential weakness of which is that most clinicians rely on B-scans for evaluation of the retina. Therefore, high-quality B-scans are more desirable than C-scans. Because these time-domain models do not acquire B-scans, they would have to be reconstructed from C-scans, potentially limiting the image quality. Further evaluation of these tools will demonstrate whether these potential limitations can be overcome in a clinical setting.

In conclusion, a rapid-sweep serial OCT B-scan based on the FD model can be used to create a detailed retinal structural map. The map provides additional information that can be missed on single scans, provides an accurate way to image large or complex lesions, and can be helpful in imaging smaller lesions especially in the patient with poor fixation. In addition, this may prove to be a useful research tool to examine more closely a variety of macular diseases.

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