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High-Definition and 3-dimensional Imaging of Macular Pathologies with High-speed Ultrahigh-Resolution Optical Coherence Tomography

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Abstract

Objective—To assess high-speed ultrahigh-resolution optical coherence tomography (OCT) image resolution, acquisition speed, image quality, and retinal coverage for the visualization of macular pathologies.

Design—Retrospective cross-sectional study.

Participants—Five hundred eighty-eight eyes of 327 patients with various macular pathologies.

Methods—High-speed ultrahigh-resolution OCT images were obtained in 588 eyes of 327 patients with selected macular diseases. Ultrahigh-resolution OCT using Fourier/spectral domain detection achieves ~3- μ m axial image resolutions, acquisition speeds of ~25 000 axial scans per second, and >3 times finer resolution and >50 times higher speed than standard OCT. Three scan protocols were investigated. The first acquires a small number of high-definition images through the fovea. The second acquires a raster series of high-transverse pixel density images. The third acquires 3-dimensional OCT data using a dense raster pattern. Three-dimensional OCT can generate OCT fundus images that enable precise registration of OCT images with the fundus. Using the OCT fundus images, OCT results were correlated with standard ophthalmoscopic examination techniques.

Main Outcome Measures—High-definition macular pathologies.

Results—Macular holes, age-related macular degeneration, epiretinal membranes, diabetic retinopathy, retinal dystrophies, central serous chorioretinopathy, and other pathologies were imaged and correlated with ophthalmic examination, standard OCT, fundus photography, and fluorescein angiography, where applicable. High-speed ultrahigh-resolution OCT generates images of retinal pathologies with improved quality, more comprehensive retinal coverage, and more precise registration than standard OCT. The speed preserves retinal topography, thus enabling the visualization of subtle changes associated with disease. High-definition high-transverse pixel density

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OCT images improve visualization of photoreceptor and pigment epithelial morphology, as well as thin intraretinal and epiretinal structures. Three-dimensional OCT enables comprehensive retinal coverage, reduces sampling errors, and enables assessment of 3-dimensional pathology.

Conclusions— High-definition 3-dimensional imaging using high-speed ultrahigh-resolution OCT improves image quality, retinal coverage, and registration. This new technology has the potential to become a useful tool for elucidating disease pathogenesis and improving disease diagnosis and management.

Optical coherence tomography (OCT) is a medical imaging technology that can perform high-resolution cross-sectional imaging of tissue morphology in situ and in real time. Optical coherence tomography imaging is analogous to ultrasound, except that it uses light rather than sound and measures the echo time delay and magnitude of reflected or backscattered light using low-coherence interferometry. Cross-sectional images are generated by directing an optical beam onto tissue and scanning it in the transverse direction, thus yielding a data set that can be displayed as false-color or grayscale images.¹ Optical coherence tomography can perform optical biopsy by imaging tissue microstructure without the need to excise and process specimens. It is being investigated for numerous medical applications ranging from surgical guidance to cancer diagnosis.²

In ophthalmology, OCT has become a standard diagnostic technique and can provide detailed images and quantitative morphometric information on retinal structure. Cross-sectional and longitudinal studies of a range of diseases, including macular holes, glaucoma, age-related macular degeneration (AMD), macular edema, and diabetic retinopathy, have been performed.^{3–16} The StratusOCT system (Carl Zeiss Meditec, Dublin, CA) is in widespread clinical use and can provide detailed cross-sectional images and quantitative information on retinal pathology. An OCT image with 8- to 10- μm axial resolution and 512 axial scans may be acquired in 1.3 seconds using StratusOCT.¹⁷

More recently, ultrahigh-resolution OCT (UHR OCT) imaging with axial resolutions of 2 to 3 μm has been demonstrated and shown to improve the visualization of retinal morphology^{18,19} and retinal pathology.^{20–24} Improved axial resolution enables better visualization of intraretinal layers such as the photoreceptor layers, ganglion cell layer, and plexiform and nuclear layers. Because small thickness changes or elevations of individual retinal layers may be detected with enhanced resolution, UHR OCT has the potential to provide additional information over standard OCT for elucidating the pathogenesis of macular diseases.^{20–24}

Despite the successful clinical application of OCT technology, there are several limitations. Without using techniques such as eye tracking, the total permissible image acquisition time is limited by subject eye motion, which can cause image artifacts. This limited acquisition time restricts both the number of axial scans per cross-sectional image and the number of cross-sectional images that can be acquired in succession. In standard OCT images, artifacts due to axial eye motion typically are removed using cross-correlation algorithms that automatically align adjacent axial scans. Although these methods do not affect relative measurements such as retinal thickness, they can obscure the true topography of the retina.²⁵ In addition, these algorithms cannot correct for artifacts from transverse eye motion. Transverse eye motion also changes the position of the OCT image on the retina, making registration with fundus features difficult.

Because of these limitations, specialized OCT diagnostic protocols were developed to image and quantitatively assess the macula or peripapillary region.^{4,10,25,26} These OCT diagnostic protocols involve the acquisition of a small set of specified OCT images and do not comprehensively cover the retina. Although high densities of axial scans are desirable to obtain

high-definition OCT images, restrictions in image acquisition time and imaging speed prevent high-definition OCT imaging in many applications. Imaging speeds for UHR OCT are typically 150 to 250 axial scans per second,^{20–24} slower than standard-resolution OCT, so coverage is more restricted and artifacts due to eye motion are more severe.

Recently, dramatic advances in OCT technology have enabled UHR OCT imaging 50 times faster than standard-resolution OCT systems and 100 times faster than previous UHR OCT systems.^{27–30} These techniques are known as Fourier domain or spectral detection, because echo time delays of light are measured by acquiring the interference spectrum of the light signal and taking its Fourier transform.^{31,32} With increased imaging speed, individual images are acquired within a fraction of a second, thereby minimizing motion artifacts. Because motion-correcting cross-correlation algorithms are not required, the images better represent the true topography of the retina.²⁵ In addition, it is possible to use high densities of axial scans to obtain high-definition OCT images, thus improving image quality and visualization of intraretinal layers. Multiple images may be acquired rapidly at different locations or orientations, thereby improving retinal coverage. It also is possible to acquire 3-dimensional OCT data that achieve comprehensive retinal coverage and enable individual OCT images to be registered precisely to fundus features.³³

The purpose of this study is to assess the potential of these recent developments to improve the visualization of retinal pathology relative to standard clinical examination and standard-resolution StratusOCT. The research prototype OCT instrument developed by our group combines UHR OCT with high-speed detection techniques. This instrument achieves a 3.0- to 3.5- μm axial image resolution, ~ 3 times improvement relative to standard 10- μm resolution OCT, and ~ 60 times faster imaging speed than standard StratusOCT. Three scan protocols are investigated in this study. The first acquires a small number of 6-mm high-definition images. The second protocol acquires a series of high-transverse pixel density images in a 6×6 -mm raster pattern. The third protocol acquires 3-dimensional OCT data consisting of closely spaced standard-pixel density images in a 6×6 -mm raster pattern.

Materials and Methods

A research prototype OCT system suitable for performing imaging studies in the ophthalmology clinic was developed and is in use at the New England Eye Center. The instrument is a high-speed UHR OCT system using spectral/Fourier domain detection.^{34–36} Spectral/Fourier domain detection operates by first measuring the interference spectrum between backscattered or backreflected light from the tissue and light from a stationary reference arm. The magnitude and echo time delay of the light signal from the tissue is measured by taking the Fourier transform of this interference spectrum. The result is a measurement of the magnitude and echo time delay of light, which is analogous to axial scan measurements in classic OCT, except that mechanical scanning of the interferometer reference arm is not required. Because all light echoes from different axial depths in the sample are measured simultaneously rather than sequentially, it is possible to increase imaging speed dramatically.

The axial (longitudinal) image resolution in OCT is determined by a property of the light source known as the coherence length, which is inversely proportional to the bandwidth ($\Delta\lambda$). The axial resolution is given by the equation $\Delta L = 2\ln(2) \lambda^2 / (\pi \Delta\lambda)$, where λ is the median wavelength of the light source. To improve axial resolution, broad-bandwidth light sources are required. For the clinical imaging results presented in this article, imaging was performed using either a compact femtosecond titanium: sapphire laser with a 3- μm axial resolution³⁷ or a commercially available superluminescent diode source (Broadlighter T40-HP2, Superlum Ltd., Moscow, Russia) with a 3.5- μm axial resolution. Broad-bandwidth superluminescent

diode light sources, similar to the one used in this study, recently have been shown to enable UHR OCT image resolution performance approaching that of femtosecond lasers.^{27–38}

Our research prototype high-speed UHR OCT system has been described in detail in previous publications.^{29–33} This system can acquire up to 25 000 axial scans per second, corresponding to ~49 images (512 axial scans per image) per second. Data processing is required to generate axial scan information from the spectral interference measurement. Real-time display can be performed up to 18 images (512 axial scans per image) per second by using a Pentium IV computer with 3.0-gigahertz clock speed and 1-gigabyte random access memory. This rate is sufficient to provide a flicker-free display and to enable focusing and alignment of the OCT instrument.

Scan Protocols

Three types of scan protocols were investigated in these clinical studies. These protocols were chosen to resemble those used by the commercial StratusOCT, and they take advantage of the enhanced performance provided by high-speed UHR OCT. The first protocol acquires a set of 3 high-definition 6-mm OCT images (8192 axial scans per image) in ~0.3 seconds per image, or a total of ~0.9 seconds. This protocol is especially useful for patients with opaque media or other conditions that result in a low OCT signal. The second protocol acquires 21 high-definition (2048 axial scans per image) images in a raster pattern covering a 6 × 6-mm area of the macula in ~0.07 seconds per image, or a total of ~1.4 seconds. The third protocol acquires 3-dimensional OCT data in a dense raster pattern consisting of 180 images (512 axial scans per image) covering a 6 × 6-mm area in ~4 seconds. The corresponding volume element (voxel) size is 12×33×1.3 μm. Although this scanning protocol is asymmetric, it has the advantage that it yields a series of 180 (512 axial scans per image) OCT images. The 3-dimensional OCT data set may be used for applications such as rendering, OCT fundus image generation, and mapping.³³

The imaging study was performed using our high-speed UHR OCT research prototype system in the ophthalmology clinic of the New England Eye Center of Tufts-New England Medical Center. The study was approved by the institutional review board committees of both the Massachusetts Institute of Technology and Tufts-New England Medical Center. Written informed consent was obtained from all subjects in this study before OCT imaging was performed. The diagnosis of macular pathology was made using standard clinical methods, including fundus examination, fundus photography, and/or fluorescein angiography. Optical coherence tomography imaging was performed on 588 eyes of 327 patients with macular diseases, including macular hole, AMD, epiretinal membrane, diabetic retinopathy, retinal dystrophies, and central serous chorioretinopathy (CSC). Selected cases representing a cross section of macular pathologies are reported here.

Results

Figures 1 to 6 compare high-definition (8192 axial scans per image) UHR OCT images with StratusOCT images. Figure 7 shows selected high-transverse pixel density UHR OCT images (2048 axial scans per image) from a 21-image raster scan. Figures 8 to 11 show OCT fundus images and selected standard-pixel density (512 axial scans per image) UHR OCT images from 3-dimensional OCT data. All UHR OCT images are enlarged in the axial direction to improve visualization of intraretinal layers. No images were corrected for axial eye motion. Arrows showing the OCT scan position are displayed to enable direct comparison with the fundus photograph or fluorescein angiography.

Full-Thickness Macular Hole

Figure 1a shows a fundus photograph of a 68-year-old woman diagnosed with a stage 2 full-thickness macular hole in her right eye according to the Gass classification system.³⁹ Right-eye visual acuity (VA) was 20/400. Both the StratusOCT (Fig 1b) and high-definition UHR OCT (Fig 1c) images clearly show a macular hole and intraretinal cysts, although the cysts are easier to locate relative to the inner retinal layers in the high-definition UHR OCT image. Both OCT images show an increase in signal from the retinal pigment epithelium (RPE) near the hole, most likely due to the absence of scattering and absorption from the inner retina. The StratusOCT image appears wavy due to axial patient eye motion, which is significantly reduced in the high-definition high-speed UHR OCT image. Increased pixel density and improved axial resolution improve visualization of retinal microstructure in the high-speed UHR OCT image, particularly at the level between the photoreceptor inner segment/outer segment (IS/OS) junction and the RPE. Peripheral to the hole, a hyperreflective layer is visualized between the photoreceptor IS/OS junction and the RPE. This layer is labeled *PR OS* for photoreceptor outer segments. As the photoreceptor IS/OS junction becomes disrupted near the edges of the macular hole, this middle layer disappears as well.

Figure 2 shows images from a 65-year-old woman 2 years after the surgical repair of a full-thickness macular hole in her left eye. Left-eye VA had improved to 20/25. Both the StratusOCT image (Fig 2b) and the high-definition UHR OCT image (Fig 2c) depict an epiretinal membrane. The high-definition UHR OCT image enables better visualization of the membrane in the nasal portion of the image. A very small central disruption of the photoreceptor IS/OS junction and OSs in the fovea is visualized in the high-definition UHR OCT image, but not in the StratusOCT image. This apparent disruption is probably not a shadowing artifact, as evidenced by the absence of shadowing in the inner retina above the disruption and the fact that the RPE signal is not reduced below the disruption. This disruption, along with the epiretinal membrane, may explain the patient's slight decrease in VA. Small photoreceptor disruptions visualized by OCT after macular hole repair have been reported previously and may be correlated with decreased VA.⁴⁰ These postoperative photoreceptor structural defects and VA can improve with time.⁴¹

Age-Related Macular Degeneration

Figure 3 shows images from a 73-year-old man with nonexudative AMD. Clinical examination showed multiple macular drusen in both eyes, which had been stable for the past several years (Fig 3a). No neovascularization was noted on examination or fluorescein angiography. At the time of OCT imaging, left-eye VA was 20/40. StratusOCT showed irregularities in the RPE, representing drusen (Fig 3b). However, the visualization of these topographic features is compromised by eye motion artifacts, which can be seen in the slow undulations of RPE and the vitreoretinal interface. The high-definition high-speed UHR OCT image (Fig 3c) better depicts the retinal topography, thus improving the visualization of RPE irregularities. Bruch's membrane (BM) is visible as a thin reflective band under the RPE in this image but not in the StratusOCT image. The high-definition high-speed UHR OCT image clearly shows photoreceptor impairment in areas overlying drusen. Solid material with varying reflectance is present between the RPE and BM. Temporal to the fovea, several small, highly reflective areas are present within this region, possibly corresponding to an early stage of choroidal neovascularization.⁸

Figure 4 shows images from a 77-year-old man with exudative AMD after focal laser treatment in the left eye for a small extrafoveal choroidal neovascularization seen on fluorescein angiography 3 months previously. At the time of laser treatment, left-eye VA was 20/25, whereas at the most recent visit, left-eye VA was 20/40. Fundus examination of the left eye revealed multiple confluent soft drusen and persistent submacular fluid (Fig 4a). StratusOCT

(Fig 4b) and high-definition UHR OCT (Fig 4c) show intraretinal cystic edema in the nuclear layers and loss of foveal contour, as well as diffusive thickening in the highly reflective band corresponding to the RPE. Both images show shadowing caused by neovascular vessels slightly nasal to the fovea. The high-definition UFTR OCT image enables localization of edematous changes to specific layers and clearly shows significant photoreceptor disruption in the foveal region. The RPE irregularities and confluent drusen are clearly visualized, whereas the smooth contour of BM remains intact. The extent of RPE elevation may be assessed by referencing the RPE to the contour defined by BM in the high-definition UFTR OCT image.

Diabetic Retinopathy

Figure 5 shows images from a 37-year-old man diagnosed with proliferative diabetic retinopathy in his right eye with 20/40 right eye VA. Both StratusOCT (Fig 5b) and high-definition UHR OCT (Fig 5c) show hard exudates as highly reflective areas in the intraretinal space. These hard exudates are better visualized in the high-definition UHR OCT image. Small cystic changes, present in the ganglion cell layer and nuclear layers, are also evident. Due to reduced motion artifacts and higher resolution, small distortions in the retinal contour are more evident in the UHR OCT image than in the StratusOCT image. The UHR OCT image also shows a thin epiretinal membrane, which is not visible in the StratusOCT image. A small disruption in the photoreceptor IS/OS junction is also visible.

Retinitis Pigmentosa

Figure 6 (available at <http://aaojournal.org>) shows images from an 18-year-old myopic man (right eye, -3.00 diopters [D]; left eye, -6.75 D) with recently diagnosed retinitis pigmentosa. Testing at an outside institution revealed constricted visual fields and an attenuated, delayed electroretinogram. Visual acuity was 20/25 in both eyes. Fundus examination revealed attenuated vessels and bony spicule RPE changes in the right eye. StratusOCT (Fig 6b) and high-definition UHR OCT (Fig 6c) show thinning of the neurosensory retina and loss of the photoreceptor IS/OS junction. High-definition UHR OCT images more clearly depict the area of photoreceptor degeneration. The photoreceptor IS/OS junction and external limiting membrane are intact at the fovea and are lost extrafoveally as rod concentration increases. Curvature of the posterior pole, due to high myopia, also can be visualized.

Central Serous Chorioretinopathy

Figure 7 shows images from a 44-year-old man diagnosed with CSC in his right eye after experiencing visual blurriness in that eye for the past 1 to 2 weeks. Right-eye VA was 20/25. Fluorescein angiography (Fig 7b) confirmed the diagnosis and revealed hyperfluorescence nasal to the fovea. Selected images from a raster series of 21 images are shown (Fig 7c–g). The high-definition UHR OCT images show that the OSs of the photoreceptors have lifted away from the normal anatomic position due to the accumulated serous fluid. There is a reduced signal from the RPE beneath the serous fluid (Fig 7f), possibly caused by shadowing. The hyperfluorescent spot on the fluorescein angiogram occurs near RPE disruptions in the OCT images (Fig 7d, e). Bruch's membrane can be seen under the RPE disruptions in these images. The series of images enables assessment of the full volume of fluid accumulation. As in the full-thickness macular hole case (Fig 1), this image set shows a middle hyperreflective layer between the photoreceptor IS/OS junction and RPE, which is labeled *PR OS* in Figure 7g. This layer is disrupted in areas of serous fluid accumulation, where the photoreceptor OSs are detached from the RPE. The transition between the anatomically normal region and the serous detachment is marked with a white arrow in Figure 7g. The OSs of the photoreceptors are abnormally long in the area of the retinal detachment.

Figure 8 shows images from a 33-year-old man with resolved CSC in the left eye. The patient had been treated with laser photocoagulation 6 weeks earlier. Left-eye VA remained 20/30

despite resolution of fluid leakage (Fig 8a). Three-dimensional OCT imaging was performed, and an OCT fundus image (Fig 8b) was used to register individual OCT images with the fluorescein angiogram. Individual OCT images from the 3-dimensional OCT data set (Fig 8c–f) show a resolution of the leakage, consistent with clinical examination. Optical coherence tomography also showed a loss in signal from the middle hyperreflective layer between the photoreceptor IS/OS junction and the RPE in the foveal region (Fig 8d, e). This photoreceptor impairment is seen in multiple OCT images from the 3-dimensional OCT data set, and there is no evidence that it is a shadowing artifact from other structures. This photoreceptor impairment may explain the patient's reduced VA.

Figure 9 (available at <http://aaojournal.org>) shows images from the right eye of the patient with resolved CSC in the left eye in Figure 8. The right eye was normal on examination, but a small hyperfluorescent spot was apparent on the fluorescein angiogram (Fig 9a). Three-dimensional OCT images superior to the fovea (Fig 9c–f) show a small elevation of the RPE that corresponds to the location of the hyperfluorescence on the fluorescein angiogram. The OCT fundus image (Fig 9b) enables the precise registration of the RPE detachment seen in the cross-sectional images with the location of the hyperfluorescence on the fluorescein angiogram. This RPE detachment is also visible on the OCT fundus image as a region of reduced signal (Fig 9b). Bruch's membrane may be visible under the RPE elevation (Fig 9d). Visualization is aided by the high resolution and absence of motion artifacts that might obscure subtle topographic changes.

Epiretinal Membrane with Pseudohole

Figure 10 (available at <http://aaojournal.org>) shows images from a 41-year-old Caucasian woman who presented to the eye clinic for follow-up examination of vitreomacular traction syndrome and epiretinal membrane with pseudohole in the right eye (Fig 10a), initially diagnosed 2 years earlier. Visual acuity was 20/20 in the right eye and had remained stable since diagnosis. The 3-dimensional OCT fundus image (Fig 10b) and cross-sectional images (Fig 10c, d) show an epiretinal membrane. Irregularities of the retinal surface caused by the epiretinal membrane are visualized without motion artifacts.

Figure 10 also shows a fundus photograph (Fig 10e), OCT fundus image (Fig 10f), and 3-dimensional OCT cross-sectional images (Fig 10g, h) of the same eye taken 4.5 months later. Using the OCT fundus images (Fig 10b, f), it is possible to register the position of OCT images between visits so that the images in Figure 10g, h are in the same location as in Figure 10c, d. Differences between the image sets are due to variations in alignment of the OCT instrument through the patient's pupil. Consequently, the posterior hyaloid membrane is more visible in the second set of images (Fig 10g, h). Otherwise, the image sets are similar and show no change in pathology, consistent with the clinical examination.

Stargardt's Disease

Figure 11 shows images from a 25-year-old man with Stargardt's disease diagnosed via ophthalmic examination and fluorescein angiography 4 years earlier. Visual acuity was stable, at 20/60 (right eye) and 20/100 (left eye). Fundus examination revealed yellow flecks in the maculae of both eyes (Fig 11 a). A 3-dimensional OCT fundus image (Fig 11b) and cross-sectional OCT images (Fig 11c–f) are shown. In the peripheral macula, all retinal layers appear relatively normal. Closer to the fovea, the outer nuclear layer (ONL) starts to thin, and is accompanied by disruption of the photoreceptor IS/OS junction. Figure 11d shows marked thinning of the ONL and an abnormal hyperreflective region in the outer retina that extends from the outer plexiform layer to the RPE. At the fovea, the photoreceptor OSs appear atrophied, resulting in increased penetration and an increased signal from the RPE, as shown in Figure 11e. The ONL thickness is marked with bars extrafoveally and near the fovea (Fig

11e). The loss of the normal retinal contour is shown in Figure 11f, where small undulations of the retinal surface are clearly visualized.

Discussion

High-speed UHR OCT has several advantages, including improved image quality, preservation of retinal topography, improved retinal coverage, and registration of the image set to fundus features. High-speed imaging can increase the number of transverse pixels per image to yield high-definition images and can increase the number of acquired images to improve retinal coverage. The increased speed enables several novel imaging protocols. Clinical data from 3 imaging protocols are presented here. The first protocol acquires a small number of high-definition, very high-pixel density images at a fixed location on the retina. The second protocol acquires a greater number of high-definition images in a raster pattern on the retina. Finally, the third protocol acquires 3-dimensional OCT data in a dense raster pattern consisting of standard-transverse pixel density images. Three-dimensional OCT achieves comprehensive coverage of the retina and may be used to generate OCT fundus images.

Preservation of Retinal Topography

Using high-speed UHR OCT, images with 512, 2048, and 8192 axial scans can be acquired in approximately 20, 70, and 300 milliseconds, respectively. The shortened image acquisition time relative to standard OCT minimizes motion artifacts and avoids the need for motion-correcting algorithms, which distort retinal topography.²⁵ The contours of features such as the RPE, BM, vitreoretinal interface, posterior hyaloid, and epiretinal membranes are visualized in high-speed UHR OCT images. The accurate representation of retinal topography can improve the assessment of structural changes caused by epiretinal membranes (Figs 2, 10 [the latter available at <http://aaojournal.org>]), serous fluid accumulation and loss of the normal retinal contour in CSC (Fig 7), RPE elevations in dry AMD (Fig 3) and wet AMD (Fig 4), and subtle detachments of the RPE from BM (Fig 9d [available at <http://aaojournal.org>]).

Improved Image Quality

High-definition UHR imaging of pathology improves image quality and discrimination of intraretinal layers. Epiretinal membranes can be discriminated from the retina more clearly (Figs 2, 5). Clear visualization of BM under RPE detachments or disruptions (Figs 4, 7, 9d [the last available at <http://aaojournal.org>]) is possible. In addition, small exudates in diabetic retinopathy are differentiated readily from normal retinal architecture (Fig 5). Small photoreceptor impairments are visible in cases such as repaired macular holes (Fig 2), diabetic retinopathy (Fig 5), and resolved CSC (Fig 8). In the case of retinitis pigmentosa (Fig 6 [available at <http://aaojournal.org>]), the extent of photoreceptor loss is visualized clearly in the fovea and peripherally. Finally, Figure 2 shows that an extremely small abnormality in the photoreceptor signal after macular hole repair is visualized with high-speed UHR OCT images. The high-definition imaging protocol samples across a $\sim 30\text{-}\mu\text{m}$ disruption with approximately 40 axial scans, whereas standard imaging protocols would sample across the same disruption ~ 3 times. The increase in transverse pixel sampling density enables the clear distinction between this small retinal disruption and normal variations in image intensity.

Improved Coverage of the Retina

Another advantage of high-speed UHR OCT is improved retinal coverage. Two protocols covering a $6\times 6\text{-mm}$ square region of the retina were described. The first acquired 21 high-definition images with 2048 axial scans per image in 1.4 seconds, which is comparable to the time required for a single StratusOCT image. The vertical distance between consecutive images in the raster is $<300\text{ }\mu\text{m}$. In contrast, the StratusOCT macular mapping protocol of 6 scans through the fovea yields $\sim 1.6\text{-mm}$ spacing between images at a 3-mm radius from the fovea.

Therefore, new raster scan protocols have the potential to detect small focal changes in the parafoveal region that are not detectable by standard OCT imaging protocols. Using this protocol, fluid accumulation associated with acute CSC (Fig 7) is visualized in multiple high-transverse pixel density cross-sectional images. Quantitative measurements of the total volume of subretinal fluid can be used to detect small changes over time, thus providing information that can assist in the management of CSC and other diseases.

The 3-dimensional OCT imaging protocol achieves comprehensive retinal coverage, taking measurements on a 6×6-mm area with a spacing of 12×33 μm between axial scans. The large set of cross-sectional images can be useful for tracking pathologies in 3 dimensions or for detecting small focal pathologies. Figure 8, resolved CSC, shows that 3-dimensional OCT data enables the detection and assessment of photoreceptor OS changes. In addition, the parafoveal images may reveal small or subtle changes, such as the RPE detachment shown in Figure 9d (available at <http://aaojournal.org>). These types of changes can be missed with standard OCT scanning protocols that sparsely sample the parafoveal region. Figure 10 (available at <http://aaojournal.org>) illustrates the importance of retinal coverage. Optical coherence tomography scans through the fovea suggest a cystic structure (Fig 10c, g), whereas other images reveal that the pathology is a pseudohole (Fig 10d, h). Finally, the 3-dimensional OCT images in Figure 11 suggest the potential to map photoreceptor loss and ONL thinning in retinal dystrophies such as Stargardt's disease.

Registration of Optical Coherence Tomography Images

An additional advantage of 3-dimensional OCT is that it can be used to create an OCT fundus image directly that shows features such as the macula, optic disc, and blood vessels. Because this OCT fundus image is created by axial integration of the 3-dimensional OCT data set, each cross-sectional OCT image is registered precisely to the fundus image. The OCT fundus image enables direct comparison of OCT findings with those from clinical examination, such as fundus photographs or fluorescein angiography. Correlation of the OCT fundus images with the fluorescein angiogram in Figure 9 (available at <http://aaojournal.org>) shows that RPE detachments visualized with OCT correspond to the areas of hyperfluorescence. The OCT fundus image also may be used to register precisely 3-dimensional OCT data taken at different time points, as shown in Figure 10 (available at <http://aaojournal.org>). Differences in alignment between imaging sessions may cause slight differences in curvature or tilt between corresponding OCT images. These effects can be minimized by a skilled operator. Optical coherence tomography fundus image registration promises to improve the precision of longitudinal tracking and to enable the tracking of subtle or focal pathologic changes.

Three-dimensional Optical Coherence Tomography Data

Three-dimensional optical coherence tomography may be performed using any OCT scanning protocol that achieves high sampling density in all 3 dimensions. The 3-dimensional OCT data presented here consist of 180 images with 512 axial scans (transverse pixels) each, for a total of 92 160 axial scans. Each axial scan has 1024 pixels, so the total data set has $180 \times 512 \times 1024$ volume elements (voxels). An asymmetric raster protocol with different horizontal and vertical sampling intervals was chosen so that a series of OCT images were obtained in one direction. The 512 axial scan images have transverse pixel density comparable to that of StratusOCT images. Currently, it takes approximately 4 seconds to acquire 3-dimensional OCT data of a 6 × 6-mm region of the retina. It is also possible to acquire 3-dimensional OCT data in a symmetric raster pattern with 300×300 axial scans in approximately the same time as that used for the aforementioned protocol; however, the quality of cross-sectional images would be reduced. The image acquisition time can be reduced either by reducing the number of transverse pixels acquired or by reducing the area that is scanned. For example, comparable

3-dimensional OCT data from a 4×4 -mm area can be acquired more than 2 times faster than from a 6×6 -mm area.

Three-dimensional OCT data also may be used to segment, measure, and map intraretinal layer thicknesses.³³ Although previous work on UHR OCT has shown the potential for quantitative morphometric measurements,¹⁹ advances in speed have the potential to improve the coverage and reproducibility of these measurements, as well as to enable the precise registration of morphometric information across multiple imaging sessions.

Comment on Interpretation of Layers

Although this work focuses on the clinical utility of high-speed UHR OCT images, it is appropriate to comment on the interpretation of the highly reflective bands visible in UHR OCT images in the region corresponding to the photoreceptors and RPE-choriocapillaris-BM complex. This has remained a topic of controversy, and comparisons of UHR OCT with pig and monkey retinal histology have been performed to investigate this question.^{42,43} We have based our interpretations of pathologic changes in these reflective bands upon corresponding clinical diagnosis and comparison to known retinal histopathology. High-speed UHR OCT imaging enables the visualization of a third, highly back-scattering band between the RPE and photoreceptor IS/OS junction. Although this band is also visible in conventional UHR OCT images, visualization of this layer is dramatically improved in high-speed UHR OCT images where the retinal topography is preserved. In the case of acute CSC (Fig 7), the middle band appears to be elevated from the RPE, suggesting that it corresponds to part of the photoreceptor OSs and that it is separated from the RPE by fluid accumulation. The reduction in scattering from the middle layer in the region of serous fluid accumulation may be accounted for by the fact that the photoreceptor OSs are not in their normal anatomical position. Adjacent to the serous detachment, the middle band appears highly reflecting, indicating normal photoreceptor OS structure and positioning relative to the RPE.

The results of this work have shown that high-speed UHR OCT can visualize small morphological changes, and a definitive interpretation of these changes will require further clinical and, possibly, histological studies. However, based on the analysis of high-speed UHR OCT images of pathologies such as acute CSC, there is strong evidence to support the identification of this middle reflective layer as part of the photoreceptor OSs.

In summary, high-speed UHR OCT enables an increase in acquisition speed of ~60 times relative to the StratusOCT and ~3 times finer axial resolution. Although UHR OCT imaging has been demonstrated to improve visualization of tissue microstructure and small changes in the photoreceptors and RPE, high-speed detection promises to enable numerous advances that will help to realize the full potential of OCT. The quality of cross-sectional images may be improved by increasing the number of transverse pixels in each image to yield high-definition images. This, combined with the absence of motion artifacts, improves visualization of morphology and topography in cross-sectional images and should improve the performance of segmentation algorithms designed to quantify intraretinal layer thicknesses or other retinal parameters. In addition, high-speed acquisition enables improved coverage of the retina, thus allowing the assessment of changes associated with retinal disease to be performed in 3 dimensions. Finally, the en face OCT fundus image created from 3-dimensional OCT data enables precise registration of each cross-sectional OCT image to features on the fundus. Together, these improvements have the potential to improve the diagnosis and monitoring of disease progression and to improve understanding of retinal disease pathogenesis.

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References

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science* 1991;254:1178–81. [PubMed: 1957169]
2. Fujimoto JG. Optical coherence tomography for ultrahigh resolution in vivo imaging. *Nat Biotechnol* 2003;21:1361–7. [PubMed: 14595364]
3. Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. *Arch Ophthalmol* 1995;113:325–32. [PubMed: 7887846]
4. Hee MR, Puliafito CA, Wong C, et al. Quantitative assessment of macular edema with optical coherence tomography. *Arch Ophthalmol* 1995;113:1019–29. [PubMed: 7639652]
5. Hee MR, Puliafito CA, Wong C, et al. Optical coherence tomography of macular holes. *Ophthalmology* 1995;102:748–56. [PubMed: 7777274]
6. Hee MR, Puliafito CA, Wong C, et al. Optical coherence tomography of central serous chorioretinopathy. *Am J Ophthalmol* 1995;120:65–74. [PubMed: 7611331]
7. Puliafito CA, Hee MR, Lin CP, et al. Imaging of macular diseases with optical coherence tomography. *Ophthalmology* 1995;102:217–29. [PubMed: 7862410]
8. Hee MR, Bauman CR, Puliafito CA, et al. Optical coherence tomography of age-related macular degeneration and choroidal neovascularization. *Ophthalmology* 1996;103:1260–70. [PubMed: 8764797]
9. Schuman JS, Hee MR, Arya AV, et al. Optical coherence tomography: a new tool for glaucoma diagnosis. *Curr Opin Ophthalmol* 1995;6:89–95. [PubMed: 10150863]
10. Schuman JS, Hee MR, Puliafito CA, et al. Quantification of nerve fiber layer thickness in normal and glaucomatous eyes using optical coherence tomography. *Arch Ophthalmol* 1995;113:586–96. [PubMed: 7748128]
11. Gaudric A, Haouchine B, Massin P, et al. Macular hole formation: new data provided by optical coherence tomography. *Arch Ophthalmol* 1999;117:744–51. [PubMed: 10369584]
12. Chauhan DS, Antcliff RJ, Rai PA, et al. Papillofoveal traction in macular hole formation: the role of optical coherence tomography. *Arch Ophthalmol* 2000;118:32–8. [PubMed: 10636411]
13. Massin P, Allouch C, Haouchine B, et al. Optical coherence tomography of idiopathic macular epiretinal membranes before and after surgery. *Am J Ophthalmol* 2000;130:732–9. [PubMed: 11124291]
14. Massin P, Haouchine B, Gaudric A. Macular traction detachment and diabetic edema associated with posterior hyaloidal traction [letter]. *Am J Ophthalmol* 2001;132:599–600. [PubMed: 11678135]
15. Spaide RF, Wong D, Fisher Y, Goldbaum M. Correlation of vitreous attachment and foveal deformation in early macular hole states. *Am J Ophthalmol* 2002;133:226–9. [PubMed: 11812426]
16. Sánchez-Tocino H, Alvarez-Vidal A, Maldonado MJ, et al. Retinal thickness study with optical coherence tomography in patients with diabetes. *Invest Ophthalmol Vis Sci* 2002;43:1588–94. [PubMed: 11980878]
17. Fujimoto, JG.; Huang, D.; Hee, MR., et al. Physical properties of optical coherence tomography. In: Schuman, JS.; Puliafito, CA.; Fujimoto, JG., editors. *Optical Coherence Tomography of Ocular Diseases*. 2. Thorofare, NJ: SLACK Inc; 2004. p. 677-88.
18. Drexler W, Morgner U, Kartner FX, et al. In vivo ultrahigh-resolution optical coherence tomography. *Opt Lett* 1999;24:1221–3.
19. Drexler W, Morgner U, Ghanta RK, et al. Ultrahigh-resolution ophthalmic optical coherence tomography. *Nat Med* 2001;7:502–7. [PubMed: 11283681]
20. Drexler W, Sattmann H, Hermann B, et al. Enhanced visualization of macular pathology with the use of ultrahigh-resolution optical coherence tomography. *Arch Ophthalmol* 2003;121:695–706. [PubMed: 12742848]

21. Ko TH, Fujimoto JG, Duker JS, et al. Comparison of ultrahigh- and standard-resolution optical coherence tomography for imaging macular hole pathology and repair. *Ophthalmology* 2004;111:2033–43. [PubMed: 15522369]
22. Wollstein G, Paunescu LA, Ko TH, et al. Ultrahigh-resolution optical coherence tomography in glaucoma. *Ophthalmology* 2005;112:229–37. [PubMed: 15691556]
23. Ergun E, Hermann B, Wirtitsch M, et al. Assessment of central visual function in Stargardt's disease/fundus flavimaculatus with ultrahigh-resolution optical coherence tomography. *Invest Ophthalmol Vis Sci* 2005;46:310–6. [PubMed: 15623790]
24. Ko TH, Fujimoto JG, Schuman JS, et al. Comparison of ultrahigh and standard resolution optical coherence tomography for imaging of macular pathology. *Ophthalmology* 2005;112:1922–1922.e15. [PubMed: 16183127]
25. Swanson EA, Izatt JA, Hee MR, et al. In-vivo retinal imaging by optical coherence tomography. *Opt Lett* 1993;18:1864–6.
26. Hee MR, Puliafito CA, Duker JS, et al. Topography of diabetic macular edema with optical coherence tomography. *Ophthalmology* 1998;105:360–70. [PubMed: 9479300]
27. Cense, B.; Nassif, NA.; Chen, TC., et al. Ultrahigh-resolution highspeed retinal imaging using spectral-domain optical coherence tomography; *Opt Express* [serial online]. 2004 [Accessed June 14, 2004]. p. 2435-47. Available at: <http://www.opticsexpress.org/ViewMedia.cfm?id=80150&seq=0>
28. Leitgeb, RA.; Drexler, W.; Unterhuber, A., et al. Ultrahigh resolution Fourier domain optical coherence tomography; *Opt Express* [serial online]. 2004 [Accessed August 15, 2004]. p. 2156-65. Available at: <http://www.opticsexpress.org/abstract.cfm?id=79930>
29. Wojtkowski, M.; Srinivasan, VJ.; Ko, TH., et al. Ultrahigh-resolution, high-speed, Fourier domain optical coherence tomography and methods for dispersion compensation; *Opt Express* [serial online]. 2004 [Accessed July 4, 2004]. p. 2404-22. Available at: <http://www.opticsexpress.org/abstract.cfm?id=80147>
30. Wojtkowski M, Bajraszewski T, Gorczynska I, et al. Ophthalmic imaging by spectral optical coherence tomography. *Am J Ophthalmol* 2004;138:412–9. [PubMed: 15364223]
31. Fercher AF, Hitzenberger CK, Kamp G, Elzaiat SY. Measurement of intraocular distances by backscattering spectral interferometry. *Opt Commun* 1995;117:43–8.
32. Hausler G, Lindner MW. Coherence radar" and "spectral radar"—new tools for dermatological diagnosis. *J Biomed Opt* 1998;3:21–31.
33. Wojtkowski M, Srinivasan VJ, Fujimoto JG, et al. Three-dimensional retinal imaging with high-speed, ultrahigh-resolution, optical coherence tomography. *Ophthalmology* 2005;112:1734–46. [PubMed: 16140383]
34. Leitgeb, R.; Hitzenberger, CK.; Fercher, A. Performance of Fourier domain vs. time domain optical coherence tomography; *Opt Express* [serial online]. 2003 [Accessed January 26, 2004]. p. 889-94. Available at: <http://www.opticsexpress.org/abstract.cfm?id=71990>
35. de Boer JF, Cense B, Park BH, et al. Improved signal-to-noise ratio in spectral-domain compared with time-domain optical coherence tomography. *Opt Lett* 2003;28:2067–9. [PubMed: 14587817]
36. Choma, M.; Sarunic, M.; Yang, C.; Izatt, J. Sensitivity advantage of swept source and Fourier domain optical coherence tomography; *Opt Express* [serial online]. 2003 [Accessed January 25, 2004]. p. 2183-9. Available at: <http://www.opticsexpress.org/abstract.cfm?id=7878>
37. Kowalevicz AM Jr, Schibli TR, Kartner FX, Fujimoto JG. Ultralow-threshold Kerr-lens mode-locked TiAl(2)O(3) laser. *Opt Lett* 2002;27:2037–9.
38. Ko, T.; Adler, D.; Fujimoto, J., et al. Ultrahigh resolution optical coherence tomography imaging with a broadband superluminescent diode light source; *Opt Express* [serial online]. 2004 [Accessed January 3, 2005]. p. 2112-9. Available at: <http://www.opticsexpress.org/abstract.cfm?id=79925>
39. Gass JD. Idiopathic senile macular hole: its early stages and pathogenesis. *Arch Ophthalmol* 1988;106:629–39. [PubMed: 3358729]
40. Kitaya N, Hikichi T, Kagokawa H, et al. Irregularity of photoreceptor layer after successful macular hole surgery prevents visual acuity improvement. *Am J Ophthalmol* 2004;138:308–10. [PubMed: 15289151]

41. Moshfeghi AA, Flynn HW Jr, Elner SG, et al. Persistent outer retinal defect after successful macular hole repair. *Am J Ophthalmol* 2005;139:183–4. [PubMed: 15652846]
42. Gloesmann M, Hermann B, Schubert C, et al. Histologic correlation of pig retina radial stratification with ultrahigh-resolution optical coherence tomography. *Invest Ophthalmol Vis Sci* 2003;44:1696–703. [PubMed: 12657611]
43. Anger EM, Unterhuber A, Hermann B, et al. Ultrahigh resolution optical coherence tomography of the monkey fovea: identification of retinal sublayers by correlation with semithin histology sections. *Exp Eye Res* 2004;78:1117–25. [PubMed: 15109918]

Figure 1.

a. A 68-year-old woman diagnosed with a stage 2 full-thickness macular hole in her right eye (OD). Both the StratusOCT image (**b**) and high-definition, 8192–transverse pixel, high-speed ultrahigh-resolution optical coherence tomography (OCT) image (**c**) clearly show a macular hole and intraretinal cysts. The high-definition OCT image enables better visualization of cystic changes and photoreceptor impairment. ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; IS/OS = photoreceptor inner segment/outer segment junction; NFL = nerve fiber layer; ONL = outer nuclear layer; OPL = outer plexiform layer; PR OS = photoreceptor outer segments; RPE = retinal pigment epithelium.

Figure 2.

a. A 65-year-old woman 2 years after surgical repair of a full-thickness macular hole in her left eye (OS). Left-eye visual acuity (VA) improved to 20/25. Both the StratusOCT image (**b**) and high-definition, 8192–transverse pixel, high-speed ultrahigh-resolution optical coherence tomography (OCT) image (**c**) show an epiretinal membrane (yellow arrows). The high-definition OCT image shows a small photoreceptor disruption (white arrow) that may account for the 20/25 VA. ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; IS/OS = photoreceptor inner segment/outer segment junction; NFL = nerve fiber layer; ONL = outer nuclear layer; OPL = outer plexiform layer; PR OS = photoreceptor outer segments; RPE = retinal pigment epithelium.

Figure 3.

a. A 73-year-old man with nonexudative age-related macular degeneration. Clinical examination showed multiple macular drusen in both eyes, which had been stable for the past several years, **b.** StratusOCT showed irregularities in the retinal pigment epithelium (RPE), representing drusen. **c.** The high-definition, 8192-transverse pixel, high-speed ultrahigh-resolution optical coherence tomography image better reveals the true topography of the retina, thereby improving the visualization of RPE irregularities. Bruch's membrane (BM) is clearly visible and labeled. Regions of high reflectivity between BM and the RPE are evident in the temporal region of the image (white arrows) and may represent an early stage of neovascularization. ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; NFL = nerve fiber layer; OS = left eye; ONL = outer nuclear layer; OPL = outer plexiform layer.

Figure 4.

A 77-year-old man with exudative age-related macular degeneration after focal laser treatment in the left eye (OS) for a small extrafoveal choroidal neovascularization seen on fluorescein angiography 3 months previously, **a**, Fundus examination of the left eye revealed multiple confluent soft drusen and persistent submacular fluid. StratusOCT (**b**) and high-definition, 8192–transverse pixel, high-speed ultrahigh-resolution optical coherence tomography (**c**) showed intraretinal cystic edema and loss of the foveal contour, as well as diffuse thickening of the retinal pigment epithelium (RPE). The high-definition image improves visualization of cystic changes and shows a thin reflective band that likely corresponds to Bruch’s membrane (BM). Neovascular vessels slightly nasal to the fovea (white arrows) cause shadowing of deeper structures. INL = inner nuclear layer; IPL = inner plexiform layer; IS/OS = photoreceptor inner segment/outer segment junction; NFL = nerve fiber layer; ONL = outer nuclear layer; OPL = outer plexiform layer; PR OS = photoreceptor outer segments.

Figure 5.

a. A 37-year-old man diagnosed with proliferative diabetic retinopathy in his right eye (OD). Both StratusOCT (**b**) and high-definition, 8192–transverse pixel, high-speed ultrahigh-resolution optical coherence tomography (OCT) (**c**) show hard exudates as highly reflective areas visualized in the intraretinal space (white arrows). Photoreceptor changes (yellow arrow) and an epiretinal membrane (red arrow) are visualized in the high-definition OCT image. ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; IS/OS = photoreceptor inner segment/outer segment junction; NFL = nerve fiber layer; ONL = outer nuclear layer; OPL = outer plexiform layer; PR OS = photoreceptor outer segments; RPE = retinal pigment epithelium.

Figure 6.

a. An 18-year-old myopic man with recently diagnosed retinitis pigmentosa. Testing at an outside institution revealed constricted visual fields and an attenuated, delayed electroretinogram. Fundus examination revealed attenuated vessels and bony spicule retinal pigment epithelium (RPE) changes. StratusOCT (**b**) and high-definition, 8192-transverse pixel, ultrahigh-resolution optical coherence tomography (**c**) show thinning of the neurosensory retina and loss of the photoreceptor inner segment/outer segment junction (IS/OS) extrafoveally. The distance between the IS/OS and RPE decreases away from the center of the image, and the highly scattering middle layer disappears, thus indicating degeneration of the photoreceptors. The curvature of the retina in the image is most likely due to the patient's myopia. ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; NFL = nerve fiber layer; OD = right eye; ONL = outer nuclear layer; OPL = outer plexiform layer; PR OS = photoreceptor outer segments.

Figure 7.

a, A 44-year-old man diagnosed with central serous chorioretinopathy in his right eye after experiencing visual blurriness in that eye for the past 1 to 2 weeks, **b**, Fluorescein angiography confirmed the diagnosis and revealed a hotspot nasal to the fovea. **c–g**, Selected images from a high-definition raster series with 21 images of 2048 axial scans each are shown. The hyperfluorescent spot on the fluorescein angiogram (**b**) corresponds to retinal pigment epithelium (RPE) disruptions in the optical coherence tomography images (**d, e**; white arrows). The photoreceptor outer segments have lifted away from their normal anatomic position due to the accumulated serous fluid. There is reduced signal from the RPE beneath the serous fluid (**f**, white arrows), possibly caused by shadowing. The photoreceptor inner segment/outer segment junction (IS/OS) and the photoreceptor outer segment band (PR OS) are disrupted in areas of serous fluid accumulation, where the outer segments are detached from the RPE. The transition between the anatomically normal region and the elevated photoreceptor region is marked with a white arrow (**g**). ELM = external limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; NFL = nerve fiber layer; ONL = outer nuclear layer; OPL = outer plexiform layer.

Figure 8.

A 33-year-old man with resolved central serous chorioretinopathy in the left eye (OS), **a**, Fluorescein angiography demonstrated resolution of fluid leakage. Three-dimensional optical coherence tomography (OCT) imaging with 180 images of 512 axial scans each was performed at that time, **b**, An OCT fundus image was used for registration of cross-sectional images with the fluorescein angiogram. **c–f**, Three-dimensional OCT images showed a resolution of the leakage seen previously, consistent with the clinical examination. They also showed a reduction of scattering from the middle band between the photoreceptor inner segment/outer segment junction (IS/OS) and the retinal pigment epithelium in the foveal region (white arrows).

Figure 9. Right eye (OD) of a patient with resolved central serous chorioretinopathy in the left eye in Figure 8. **a**, The right eye was normal on examination, but a small hyperfluorescent spot was apparent on a fluorescein angiogram. **b**, An optical coherence tomography (OCT) fundus image with white lines indicating the locations of selected 3-dimensional OCT cross-sectional images is shown. **c–f**, In the 3-dimensional OCT raster image set, images superior to the fovea show a small elevation of the retinal pigment epithelium (RPE) (white arrows) that corresponds to the location of the hyperfluorescent spot seen on the fluorescein angiogram. The OCT fundus image enables the precise identification of the RPE elevation seen in the cross-sectional images with the location of the hyperfluorescence on the fluorescein angiogram.

Figure 10.

a, A 41-year-old Caucasian woman who presented to the eye clinic for follow-up examination of vitreomacular traction syndrome and epiretinal membrane with pseudohole in the right eye (OD). The optical coherence tomography (OCT) fundus image (**b**) and 3-dimensional OCT cross-sectional images (**c, d**) show an epiretinal membrane and irregularities of the retinal surface caused by the epiretinal membrane (white arrows). A fundus photograph (**e**), OCT fundus image (**f**), and 3-dimensional OCT cross-sectional images (**g, h**) of the same eye taken 4–5 months later. By registration of the features seen on the more recent OCT fundus image (**f**) with the prior OCT fundus image (**b**), it is possible to register cross-sectional images with those from prior visits directly.

Figure 11.

A 25-year-old man with Stargardt's disease, **a**, Fundus examination revealed yellow flecks in the maculae of both eyes. A 3-dimensional optical coherence tomography (OCT) fundus image (**b**) and cross-sectional images from the 3-dimensional OCT set (**c–f**) are shown. An abnormal hyperreflective region in the outer retina that extends from the outer plexiform layer to the retinal pigment epithelium is visualized (**d**, white arrow). In the peripheral macula, all retinal layers appear relatively normal. Closer to the fovea, the outer nuclear layer (ONL) starts to thin, accompanied by disruption of the photoreceptor inner segment/outer segment junction (**e**, white arrow). The ONL thickness is marked with bars both extrafoveally and near the fovea (**e**). Small undulations of the retinal surface are seen near the fovea (**f**, white arrow). OS = left eye.