In Vivo Three-Dimensional Imaging of Neovascular Age-Related Macular Degeneration Using Optical Frequency Domain Imaging at 1050 nm

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PURPOSE. To assess the application of optical frequency domain imaging (OFDI) at 1050 nm for the detection of choroidal neovascularization (CNV) in age-related macular degeneration (AMD) and its response to treatment. Three patients presenting with blurred vision and exudative AMD were imaged before and after anti-VEGF treatment with ranibizumab.

METHODS. The patients were imaged with OFDI, a swept-source–based, high-speed optical coherence tomography (OCT) system developed at the Wellman Center for Photomedicine. A center wavelength of 1050 nm was used that has been demonstrated to provide better imaging of the deeper structures of the retina below the RPE, such as the choroidal vasculature. Three-dimensional data sets were acquired in 2 to 4 seconds.

RESULTS. En face images were compiled from cross-sectional OFDI data and correlated with color fundus photography (CF) and fluorescein angiograms (FAs). Cross-sectional images were coregistered with CF and FA to obtain depth-resolved information about CNV, CNV volume, retinal thickness, subretinal fluid volume and height of neurosensory detachment before and after treatment with ranibizumab. A band of reduced reflectivity below the RPE was identified in all three subjects that corresponded to areas of confirmed and suspected occult CNV on FA. After treatment, this band was reduced in volume in all patients.

CONCLUSIONS. High-speed 3-D OFDI at 1050 nm is a promising technology for imaging the retina and choroid in neovascular AMD. The developed system at 1050 nm provides good contrast for occult (type 1) CNV and may have advantages compared with time domain and current state of the art spectral domain OCT systems (SD-OCT) at 850 nm. (Invest Ophthalmol Vis Sci. 2008;49:4545–4552) DOI:10.1167/iovs.07-1553

Optical coherence tomography (OCT) is a noninvasive, high-resolution technique capable of acquiring cross-sectional images of tissue morphology.1 In ophthalmology, OCT is already a well-established clinical imaging method for the investigation of physiological properties and diseases of the eye.2,3 Until recently, almost all commercially available systems used in retinal OCT imaging were based on first-generation time-domain OCT (TD-OCT) technology,1,2,6 which has limited speed and sensitivity. More recently, spectral, or Fourier domain–based OCT systems (SD/FD-OCT)7 have been developed to overcome limitations prevalent in TD-OCT.8–11 As a result, SD-OCT achieves a 2- to 3-order-of-magnitude increase in sensitivity,12–14 translating to a nearly 100-fold faster imaging method that achieves video rate speeds without sacrificing image quality.11,15,16 Operating at higher speeds permits acquisition of three-dimensional (3-D) data sets11,17,18 and simultaneous ultrahigh speed and ultrahigh resolution.15,16 These improvements accumulatively result in images with more detailed information of the intraretinal layers, including the ganglion cell layer, photoreceptor layer, plexiform layers and nuclear layers.

Because of the design of the spectrometer used in SD-OCT, the effective ranging depth is limited by a depth-dependent sensitivity decay of approximately 6 dB over 1 mm.11 An alternative technique to SD-OCT is optical frequency domain imaging (OFDI).19 In OFDI, a rapidly tuned laser source is used and the spectrally resolved interference fringes are recorded as a function of time in the detection arm of the interferometer. Published results in healthy volunteers have shown that OFDI has better immunity to sensitivity degradation due to lateral and axial eye motion and has an effective ranging depth that is 2 to 2.5 times better then SD-OCT (depth-dependent sensitivity decay of 6 dB over 2 to 2.5 mm).19–21

More important, recent research at a 1050-nm spectral range has demonstrated a better retinal penetration depth,20,22,23 particularly important for detecting retinal abnormalities at or below the retinal pigment epithelium (RPE). A wavelength of 1050 nm has less attenuation from scattering in opaque media, commonly seen in patients with cataract.24 Although the water absorption at 1050 nm is higher than in the 850-nm region, the difference is partially compensated for by the approximately three times higher maximum permissible exposure according to the ANSI standards (1.9 mW at 1050 nm).25

Age-related macular degeneration (AMD) is one of the leading causes of vision loss in people over age 65 in Western countries.26,27 The gold standard methods for the diagnosis of exudative AMD include color fundus photography (CF) and fluorescein angiography (FA). These methods provide detailed information about the en face location and global dimension of leaking macular abnormalities, but stereo FA and CF images do...
not offer optimal depth information.28 TD-OCT has been compared with FA for the detection of choroidal neovascularization (CNV) in AMD.29 Although the sensitivity of TD-OCT is high, the specificity is not sufficient for it to supplant FA. TD-OCT systems, however, can quantify retinal thickening and subretinal fluid. This has been useful in following the results of treatment of neovascular AMD.30,31 Classic CNV has been visualized with both TD-OCT and SD-OCT.32–34 Small studies have demonstrated regression of classic (presumably type II, or subretinal) CNV with anti-VEGF treatment.34 A recent study by Coscas et al.35 demonstrated that limited or complete RPE detachments could be found in 98% of patients by TD-OCT, often corresponding with areas of occult leakage on FA or ICG. In the images presented in that paper, it is difficult to see Bruch’s membrane. Drexler et al.,36 in a study of a new ultra-high-resolution OCT system, presented one case of occult neovascularization. In their images, Bruch’s membrane could be readily seen.

In this study we present the first application of OFDI at a longer wavelength (1050 nm) for the study of AMD. We hypothesized that the better penetration depth and deeper effective ranging depth of this instrument is particularly important for detecting retinal abnormalities expressed in patients with AMD, such as pigment epithelium detachment (PED) and visualizing occult (type I) CNV below the RPE.

An ultrahigh-speed OFDI system was developed that constituted a nearly twofold speed improvement to 30,000 A-lines/second over the system described in detail in a previous publication regarding the retinal OFDI system.20 Patients underwent CF, FA, TD-OCT (Stratus; Carl Zeiss Meditec, Dublin, CA) and OFDI imaging. After anti-VEGF treatment, OFDI and color fundus photography were repeated. 3-D-OFDI images were coregistered with CF and FA images. Sub-RPE fluid_CNV fluid_volume, retinal thickness, subretinal fluid volume, and the presence of the photoreceptor layer were evaluated before and after anti-VEGF treatment.

MATERIALS AND METHODS

A prototype fiber-based ultrahigh-speed OFDI was developed and used for this study at the Wellman Center for Photomedicine. The OFDI system (Fig. 1) follows the configuration published by Yun et al. and Lee et al. and consists of a swept laser source with a tunable 3-dB bandwidth of 65 nm (Δλ) centered around 1050 nm (λ) (Fig. 2), resulting in a theoretical axial resolution Δl of 7.5 μm, according to Δl = 2 ln(2)k λ 2(πΔλ).37

The measured axial resolution of 11 μm differs from the theoretical value due to a non-Gaussian spectral shape of the light source, imperfect k-space interpolation, and dispersion compensation.38 A 6-dB sensitivity drop was measured over a distance of 2.5 mm (Fig. 2).39 The system operated 12 dB below the theoretical shot noise limit.40 Patients were enrolled after informed consent in accordance with an Institutional Review Board (IRB)/Ethics Committee approved protocol at Massachusetts General Hospital (MGH) and Massachusetts Eye and Ear Infirmary (MEEI) and in compliance with the Declaration of Helsinki. The OFDI system was interfaced with a modified slit lamp, with a power incident on the eye between 0.7 and 1.9 mW, at or below the maximum permissible exposure as defined by the ANSI.41 A fixation spot was provided to stabilize eye motion during measurements. The used scanning protocol consists of a volumetric scan covering a 9 × 8 × 2.5 mm (x, y, z) scanning area around the macula. Each obtained cross-sectional image or frame consisted of 512 or 1024 A-lines, where each A-line contained 512 points in depth. Images were logarithmic gray scale encoded. The A-line rate of the swept source is 32.4 kHz, resulting in an image-acquisition speed of 30 to 60 frames/second, depending on the number of A-lines per image. Patient data sets consisted of 120 to 228 frames/512 A-lines per frame, and 60 to 120 frames/1024 A-lines per frame, corresponding to a 2- to 4-second measurement time per dataset. The choice of presented datasets for a particular patient was made based on the quality of the images in the set.

The images shown are constructed after correct wavelength mapping and dispersion compensation. The first step in data processing was to compensate for patient motion artifact during measurement time. To reconstruct properly an en face image or a 3-D topography from the data set, we used a published automated 2-D cross-correlation program to align frames in both the lateral and axial directions (Mujat M, et al. IOVS 2006;47:ARVO E-Abstract 3538).42 En face images were reconstructed by integrating the gray-level intensity over depth for each A-line on all frames. The individual frames were coregistered with the en face image and the locations of the individual frames were indicated on the en face image. The cross-sectional images correspond to the Movies, compiled of all frames of the 3-D data set (all Movies are online at http://www.iovs.org/cgi/content/full/49/10/4545/DC1).

Along with the OFDI images, FA and CF images were obtained for each patient. The locations of the presented individual OFDI cross-sectional images were indicated on the FA and fundus photographs after coregistering with the OCT en face images by overlaying the images (Photoshop CS; Adobe Systems, San Jose, CA) and finding the optimal alignment of blood vessels.

Distinct structures visible in the OFDI image datasets can be identified, and the 3-D topography was reconstructed by using a combination of commercially available software (Amira; Mercury Computer Systems Inc., Chelmsford, MA) interfaced with open-source C++ algorithms (Insight Registration and Segmentation Toolkit; Kitware Inc., Clifton Park, NY).43 The subretinal fluid and retinal edema volumes were segmented by using a semiautomated 3-D algorithm to propagate a contour within the volume of interest, while stopping at the prominent edges. The volume bounded by the RPE band and Bruch’s membrane was segmented on each 2-D frame individually by using a seed voxel-initiated, connected-threshold algorithm and was propagated within specified boundary limits. In the final step, the 3-D reconstruction was achieved by interpolating the segmentation sequentially between each 2-D frame. This defined all the points in 3-D space, which were then connected and the surface topography displayed. The volume of the 3-D topography was calculated by determining the number of voxels and volume per voxel within the segmentation. Each segmentation was repeated five times with different seed voxels to characterize the segmented volume reproducibility. The rendered 3-D objects were included in the en face images for optimal correlation with FA and color fundus images.

RESULTS

Patient 1

Patient 1 was a 70-year-old man with a history of mild nonproliferative diabetic retinopathy, cataract extraction with intraoc-
ular lens implantation in the right eye, and previously non-
neovascular AMD who presented with a chief complaint of
increasingly blurred vision in the right eye. Visual acuity with
spectacle correction in the right eye measured 20/50 by
ETDRS (Early Treatment Diabetic Retinopathy Study) chart.
Comprehensive examination including fundus biomicros-
copy, FA, and OCT imaging (Stratus; Carl Zeiss Meditec) of
the macula revealed CNV in the affected eye. OFDI was then
obtained, followed by nine total treatments with intravitre-
ous ranibizumab (Genentech, Inc., San Francisco, CA) over
the ensuing 10 months. Repeat imaging by OFDI was per-
formed immediately before the ninth injection, at which
time the visual acuity in the affected eye measured 20/32-1
by ETDRS chart.

**Pretreatment.** Figures 3A–C, 3E show the color fundus
photograph, FA at 36 seconds, FA at 6 minutes 38 seconds, and
the en face OFDI image computed from 120 OFDI cross-
sectional images. The en face image was used to locate the
OFDI images in the color fundus and FA photographs. The
late-phase FA showed leakage in two distinct locations (indi-
cated by white circles). The FA appearance suggested occult
CNV. OFDI scans taken at these locations showed a distinct

**Figure 3.** Patient 1. **Pretreatment:**
(A) CF image, (B) FA 36 seconds, (C) 
FA 6.38 m, (E) OFDI en face recon-
struction; red lines: cross-sections
E.I–III (see Movie 1). **Posttreatment:**
(D) color fundus, (F) OFDI en face
reconstruction; red lines: cross-sec-
tions F.I–III (see Movie 2). Features 
are: A, drusen; B, blood clot; C, sub-
retinal fluid; D, RPE detachment; E, 
cystic changes; F, weak scattering in
photoreceptors; G, strong scattering
in photoreceptors; H, presumed sub-
RPE CNV; I, strong scattering from
photoreceptors in the periphery of
the subretinal fluid.
feature corresponding to the location of leakage interpreted as possible occult CNV in Figure 3E.II (feature H). The image in Figure 3E.II (feature F) also showed reduced scattering in the photoreceptor layer at the location of largest subretinal fluid thickness. In the periphery of the subretinal fluid volume, a substantial increase in scattering by the photoreceptors was observed (Fig. 3E.II, feature G). Figure 3E.III shows a scan of the periphery of the subretinal fluid with strong scattering by the photoreceptors over the full width of the subretinal fluid. The location and extension of the subretinal fluid volume (Fig. 3E, green) corresponded to the slight yellow discoloration in the fundus image (Fig. 3A, white arrows). Other observable features were drusen, blood, subretinal fluid, RPE detachment, and cystic changes. OCT showed thickening and cystic change of the neurosensory retina, subretinal fluid, highly scattering subretinal material consistent with blood, irregularity of the RPE, and a serous RPE detachment (see the Supplementary Document).

Posttreatment. The patient was studied again 10 months later, after eight ranibizumab injections. Figures 3D and 3F show the color fundus photograph and the en face OFDI image from 114 OFDI cross-sectional images. The OFDI data were obtained from the same region as the pretreatment scan was taken, and an obvious change in subretinal fluid and RPE detachment volume was visible in the cross-sectional images (Figs. 3E.I–III). The resultant en face with topography overlay showed clearly the almost complete absence of this area. The posttreatment en face image the presumed CNV was still present at the location of leakage interpreted as possible occult CNV in Figure 3E.II (feature B). These bands may be due to atrophy of the RPE, particularly below the fovea. The late-phase FA showed diffuse hyperfluorescence that probably represents leakage from occult CNV. The OFDI scans showed a membrane suspected as CNV below the RPE at all four locations of the cross-sectional images (Figs. 4E.I–IV, feature B). Other features that were observed are pigmentation (Figs. 4E.I–III, feature A), cystic changes, such as edema (Figs. 4E.II, 4E.III, feature C), a highly scattering structure compatible with type II CNV (Figs. 4E.II, 4E.III, features D), a potential breach of the RPE (Fig. 4E.III, feature E), and subretinal fluid (Fig. 4E.IV, feature F). OCT demonstrated thickening and cystic change of the neurosensory retina, highly scattering intraretinal material corresponding to pigment, a small area of subretinal fluid, and irregularity of the RPE (see the Supplementary Document).

Posttreatment. The patient was studied again 9 months later, after 4 ranibizumab injections. Figures 4D and 4F show the CF photograph and the en face OFDI image from 114 OFDI cross-sectional images. The OFDI posttreatment en face image showed a change in scattering (Fig. 4F), whereas in the pretreatment en face image the presumed CNV was still present at this location (Fig. 4E). The corresponding cross-sectional images showed bands of increased scattering where CNV leakage was previously detected—particularly visible in Figure 4E.IV, feature B. These bands may be due to atrophy of the RPE, which was evident on the color fundus photograph. The posttreatment dataset showed, besides the reduction of subretinal elevation and subretinal cysts, a reduction of the CNV volume by a mean of 73% ± 3.9% (see Table 1 and the Supplementary Document).

Patient 3 Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with visual distortion and decreased acuity in the right eye. Visual acuity in this eye measured 20/320-1 by ETDRS chart, and examination findings by fundus biomicroscopy, FA, and OCT were consistent with CNV. Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with new-onset vision loss and distortion in the right eye. Visual acuity in this eye measured 20/200-2 without correction by ETDRS chart. Results with examination with fundus biomicroscopy, FA, and OCT were consistent with CNV in the affected eye. OFDI was then performed, followed by monthly intravitreous injections with ranibizumab for a total of four treatments. After treatment, visual acuity of the right eye stabilized at 20/50, and there was a marked reduction in CNV-associated exudative changes, as seen on fundus biomicroscopy and confirmed by OCT. The patient persisted at this level, and treatment was withheld during a 6-month period of close observation, at the conclusion of which OFDI imaging was repeated.

### Table 1. Pre- and Posttreatment Segmentation Volumes of CNV, Subretinal Fluid and Retina Edema for Patients 1–3

<table>
<thead>
<tr>
<th>Patient Scan</th>
<th>Choroidal Neovascularization</th>
<th>Subretinal Fluid</th>
<th>Retinal Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Pretreatment</td>
<td>0.238 ± 0.0107</td>
<td>0.961 ± 0.0294</td>
</tr>
<tr>
<td></td>
<td>Posttreatment</td>
<td>0.127 ± 0.0139</td>
<td>0.00314 ± 0.000171</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Pretreatment</td>
<td>0.231 ± 0.0182</td>
<td>0.0620 ± 0.00740</td>
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<tr>
<td></td>
<td>Posttreatment</td>
<td>0.0617 ± 0.00493</td>
<td>0</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Pretreatment</td>
<td>0.479 ± 0.00742</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Posttreatment</td>
<td>0.277 ± 0.0149</td>
<td>N/A</td>
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</table>

**Pre- and Posttreatment Segmentation Volumes of CNV, Subretinal Fluid and Retina Edema for Patients 1–3**

**Mean Segmentation Volumes (mm³)**

**Patient 1**

**Pretreatment.** Figures 4A–C, 4E show the CF image, FA at 35 seconds, FA at 2 minutes 58 seconds, and the en face OCT image computed from 60 OFDI cross-sectional images. Figure 4A shows a small area of subretinal blood (white circle). There are many areas of focal hyperpigmentation. Lighter areas represent atrophy of the RPE, particularly below the fovea. The late-phase FA showed diffuse hyperfluorescence that probably represents leakage from occult CNV. The OFDI scans showed a membrane suspected as CNV below the RPE at all four locations of the cross-sectional images (Figs. 4E.I–IV, feature B). Other features that were observed are pigmentation (Figs. 4E.I–III, feature A), cystic changes, such as edema (Figs. 4E.II, 4E.III, feature C), a highly scattering structure compatible with type II CNV (Figs. 4E.II, 4E.III, features D), a potential breach of the RPE (Fig. 4E.III, feature E), and subretinal fluid (Fig. 4E.IV, feature F). OCT demonstrated thickening and cystic change of the neurosensory retina, highly scattering intraretinal material corresponding to pigment, a small area of subretinal fluid, and irregularity of the RPE (see the Supplementary Document).

**Posttreatment.** The patient was studied again 9 months later, after 4 ranibizumab injections. Figures 4D and 4F show the CF photograph and the en face OFDI image from 114 OFDI cross-sectional images. The OFDI posttreatment en face image showed a change in scattering (Fig. 4F), whereas in the pretreatment en face image the presumed CNV was still present at this location (Fig. 4E). The corresponding cross-sectional images showed bands of increased scattering where CNV leakage was previously detected—particularly visible in Figure 4E.IV, feature B. These bands may be due to atrophy of the RPE, which was evident on the color fundus photograph. The posttreatment dataset showed, besides the reduction of subretinal elevation and subretinal cysts, a reduction of the CNV volume by a mean of 73% ± 3.9% (see Table 1 and the Supplementary Document).

**Patient 3**

Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with visual distortion and decreased acuity in the right eye. Visual acuity in this eye measured 20/320-1 by ETDRS chart, and examination findings by fundus biomicroscopy, FA, and OCT were consistent with CNV. Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with new-onset vision loss and distortion in the right eye. Visual acuity in this eye measured 20/200-2 without correction by ETDRS chart. Results with examination with fundus biomicroscopy, FA, and OCT were consistent with CNV. Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with new-onset vision loss and distortion in the right eye. Visual acuity in this eye measured 20/200-2 without correction by ETDRS chart. Results with examination with fundus biomicroscopy, FA, and OCT were consistent with CNV. Patient 3 was a 72-year-old man with history of mild nuclear sclerotic cataracts and non-neovascular AMD who presented with new-onset vision loss and distortion in the right eye. Visual acuity in this eye measured 20/200-2 without correction by ETDRS chart. Results with examination with fundus biomicroscopy, FA, and OCT were consistent with CNV.
face OFDI image from 228 OFDI cross-sectional images. The early-phase FA (Fig. 5B) showed the presence of obvious but probably occult CNV indicated by the arrows. The CNV in both FA images appeared as an oval-shaped diffuse fluorescence. This shape and location was confirmed by OFDI cross-sectional scans taken in this area (Figs. 5E.I–III, feature C), and the rendered 3-D volume, showing the presumed CNV in red (Fig. 5E). The cross-sectional images and 3-D rendering also showed the existence of cystic edema in purple (Figs. 5E.II, E5.III, feature D), above the presumed CNV. It is notable that the existence of the cystic edema was not visible in both FA images and the CF image, but the OFDI cross-sectional images showed these abnormalities clearly. A large area of retinal edema, also in purple (Figs. 5E.I–III, feature A), was also visualized, but due to limitations in scanning range, this area was not completely covered, and therefore a partial volume was calculated. Hard exudates were visible in all the cross-sectional images and appeared as individual strong scattering accumulations in the retina. OCT showed severe retinal thickening and cystic change and marked RPE irregularity (see the Supplementary Document).

**Posttreatment.** The patient was studied again 4 months later after 4 ranibizumab injections. Figures 5D and 5F show the CF photograph and the en face OFDI image from 114 OFDI cross-sectional images. The first obvious change visualized in the cross-sectional images (Figs. 5F.I–III) was the absence of retinal edema, which was greatly reduced compared with the first data set (Figs. 5E.I–III). The signal-to-noise ratio (SNR) in the second data set, compared with the first one was also improved, resulting in cross-sectional images with more detail. The presumed CNV area, however, did not qualitatively appear to be reduced after the treatment, but the volume was reduced by a mean of 42% ± 3.3% (see Table 1 and the Supplementary Document).

**DISCUSSION**

High-speed OFDI at 1050 nm is a promising technology for imaging the retina and choroid in AMD. The developed system provides a large effective depth range (up to 2.5 mm in air), and previous work suggests that a center wavelength at 1050 nm provides better penetration below the RPE than does the 850-nm wavelength.20,22 This method could eventually result in a better detection and quantification of sub-RPE changes, particularly in exudative AMD. The sub-RPE changes in exudative AMD demonstrated in our cases, as well as those previously reported, could represent type I CNV, sub-RPE fluid, or both. The images showed good definition of the choroidal vasculature, except in the areas of substantial subretinal blood accumulation. Three-dimensional imaging and rendering gave valuable additional volumetric information on CNV, subretinal...
fluid, and retinal edema. The low variability in the repeated volume measurements suggests good reproducibility of the segmentation techniques. The resultant en face images demonstrated excellent correlation with CF and FA images. Comparisons of the pre- and postvolumetric datasets showed interesting changes after treatment and made it possible to determine the effectiveness of treatment in the future. CNV thickness maps and corresponding 3-D reconstructions have been compared for both pre- and posttreatment scans and are shown in the Supplementary Document.

In Patient 1, the cross-sectional images were coregistered with the CF and FA images before and after treatment. The locations in the pretreatment dataset with CNV are showing small well-defined structures beneath the RPE layer, and the RPE layer itself shows a significant increase in contrast in the image (Fig. 3E.I). Other striking features in the Figure 3E cross-sectional images are the existence of cystic changes, drusen, blood clots, RPE detachment, and a large subretinal fluid pool. This fluid pool appears in a large part of the scanned area, and in Figure 3E.II the changes in the photoreceptor layer, which is located above the fluid pool, are clearly visualized. We hypothesize that the reduced scattering at the point of highest elevation of the subretinal fluid is a signature of the absence of the photoreceptors or their outer segments in Figure 3E.II, feature F, due to prolonged separation from the RPE, whereas the strong scattering in the periphery (Fig. 3E.II, feature G) indicates the presence of the photoreceptor layer. The scattering between the RPE and Bruch's membrane could represent CNV and/or fluid. The segmentation of this structure for patient 1 included the entire area of RPE elevation (i.e., the volume of the RPE detachment and the region between the RPE and Bruch's below the hemorrhage, by extrapolating the extension of Bruch's membrane). The volumetric amount of subretinal fluid and presumed CNV and/or fluid was calculated from the 3-D rendering of the segmentation. The posttreatment data set showed dramatic change in elevation suggesting re-reduction of subretinal fluid and blood. The apparent CNV and/or fluid volume was reduced by a mean of 46% ± 7.8% (see Table 1 and the Supplementary Document).

In patient 2, the cross-sectional images were coregistered with the CF and FA images before and after treatment. In the pretreatment dataset, the OFDI scans showed a membrane suspected to be CNV between the RPE and Bruch's membrane at different locations of the cross-sectional images. The cross-sectional images showed disrupted RPE layers at the suspected CNV locations. The appearances of pigment accumulations were also clearly visible in all the images. A highly scattering structure compatible with type II CNV is observed in Figures 4E.II and 4E.III. In Figure 4E.III, a possible breakthrough of the RPE and cystic changes are observed, and in Figure 4E.IV subtle subretinal fluid is visible. The volume for the retinal edema, the subretinal fluid, and CNV was calculated from the 3-D rendering of the segmentations. The posttreatment dataset showed, besides the reduction of subretinal elevation and subretinal...
cysts, a reduction of the CNV volume by a mean of 73% ± 3.9% (see Table 1 and the Supplementary Document). A dark band was visible in the cross-sectional images and the en face image, indicating change in scattering at the location where CNV had been detected. We believe this band was due to overlying atrophy of the RPE.

Patient 3 had exudative AMD with obvious, though occult CNV. Correlation of OFDI images with CF and FA at the suspected areas showed changes between the RPE band and Bruch’s membrane that correspond to occult CNV. The cross-sectional images of the pretreatment dataset consisted of 512 A-lines and therefore had a noisier appearance, which can also be partly due to poor focusing of the eye lens in this patient. The rendered 3-D volume of this dataset showed a large, oval, presumed area of CNV, with good correlation with the oval-shaped diffuse fluorescence in the FA images (Figs. 5E.I–III, feature C). The large cystic edema compartment was visible only in the cross-sectional images and the rendered en face 3-D volume (Figs. 5E.II, 5E.III, feature D). This limitation was also the case for the retinal edema (Fig. 5E.I–III, feature A). Furthermore, the scanned area did not completely cover the area of retinal edema due to the limitations of the hardware in the slit lamp. The different volumes could be calculated for the retinal edema and the presumed CNV area. Again the posttreatment dataset showed a marked change in subretinal elevation. The retinal edema had completely disappeared. The presumed CNV was still visible, covering approximately the same area, but had decreased in volume by a mean of 42% ± 3.3% (see Table 1 and the Supplementary Document).

The changes demonstrated between the RPE band and Bruch’s membrane could represent fluid or type I CNV, or both. We doubt that they represent hemorrhage, given the lack of characteristic color on fundus photographs. The variable extent of regression of these volumes after anti-VEGF treatment, in contrast to the virtually complete resolution of retinal edema and subretinal fluid, suggests that at least some of the volume represents type I CNV.

In conclusion, we demonstrated high-speed 3-D imaging of exudative AMD with occult CNV before and after treatment, using OFDI at 1050 nm. We believe that these images demonstrate occult, type I CNV below the RPE. This relatively new OCT technology in combination with the wavelength in the 1-μm region can have a valuable contribution to early AMD research and as a follow-up treatment-imaging tool.

References


