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CLINICAL INVESTIGATION

Sectoral Thinning of the Retina After Branch Retinal Artery Occlusion

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Abstract

Purpose: We studied the temporal aspects of retinal thickness in eyes with branch retinal artery occlusion (BRAO) to demonstrate the retinal thinning process subsequent to the acute stage of the disease.

Methods: We studied the retinal thickness map obtained with optical coherence tomography (OCT) in nine eyes of nine patients with BRAO. Central foveal thickness and average retinal thickness in the superior or inferior sectors of the inner macula (IM) and outer macula (OM) were measured several times after the onset of BRAO.

Results: All follow-up data combined from the eyes with the occluded branch artery on the same vertical side showed a common pattern of decrease in the retinal thickness in the affected superior or inferior sectors of the IM and OM, which was described by an exponential decay curve, whereas few changes were seen in central foveal thickness. The fitting of the reducing retinal thickness curves to an exponential decay curve led to the final estimated thickness in the affected sectors of 60% that of the control.

Conclusion: The initially thickened retina in the vertical sectors of the macula in eyes with BRAO decreases exponentially to a final thickness of 60% of that the normal retina. **Jpn J Ophthalmol** 2009;53:494–500 © Japanese Ophthalmological Society 2009

Keywords: branch retinal artery occlusion, exponential decay curve, foveal thickness, optical coherence tomography, retinal thickness

Introduction

Patients with branch retinal artery occlusion (BRAO) complaining of unilateral upper or lower field defect[1,2] show cloudy swelling in the affected area—usually in the upper or lower half of the posterior pole of the retina—with clear contrast against its vertical counterpart showing normal retinal color. Optical coherence tomography (OCT) demonstrates localized hyper-reflectivity of the inner retinal layers and increased retinal thickness in this acute stage of BRAO.[3] Several months later, despite little recovery of field defects, the whitish color of the affected retina fades to show a normal appearance, obscuring the color contrast with the adjacent normal retina and making it difficult to diagnose the previous BRAO in an ophthalmoscopic examination. However, the findings on OCT examination at this late stage of the disease are remarkable for revealing marked thinning of the retina in the affected vertical half of the macula.[3] The thickening immediately after the onset of the disease and the thinning that occurs several months later in the affected retina both result in an asymmetric contour of the retinal surface in a vertical cross section of the OCT image, which is characteristic of BRAO. Unfortunately, the temporal aspects of the retinal thickness change from early thickening to later thinning have not been precisely demonstrated.

The difference in retinal thickness in the macular area could be more precisely evaluated by a retinal thickness map made by using volumetric OCT.[4] In the present study, therefore, we examined the temporal aspects of the retinal thickness in the affected area in eyes with BRAO using a retinal thickness map.

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Methods

Subjects

We studied nine eyes of nine patients with unilateral BRAO from whom one or more OCT images were obtained with an OCT scanner (Stratus OCT; Humphrey-Zeiss Instruments, San Leandro, CA, USA) between August 2003 and June 2008. All patients had been initially examined at the Yamanashi University Hospital within 10 days of the onset of visual symptoms and were diagnosed as having BRAO on the basis of the typical ophthalmoscopic appearance: demarcated white ischemic swelling in the affected retina and delayed arterial perfusion revealed by fluorescein fundus angiography. We included in the study only those patients with BRAO affecting the superior or inferior temporal branch of the central retinal artery, in which the milky white retina was demarcated by a horizontal line across the fovea. We excluded those with BRAO affecting a tributary artery perfusing a small retinal area without affecting half of the macular area and those with other ocular diseases, including diabetic retinopathy or glaucoma. In three patients, the onset of BRAO occurred prior to August 2003, and the first OCT study was performed between 320 and 1800 days thereafter. In the remaining six patients, four or more OCT examinations were performed, including at ≤10 days and at ≥6 months after onset. The patients consisted of four men and five women between 54 and 79 years old (62 ± 8 years). Their clinical data are shown in Table 1. No treatments other than ocular massage had been provided.[5]

The patients' OCT data were compared with the results from 60 normal control eyes. These were either one eye each from healthy controls or the contralateral eye of patients with unilateral fundus diseases, including retinal vein occlusion and retinal artery occlusion. The average age of this control group was 63 ± 9 years.

The study was approved by the Ethics Committee of the University of Yamanashi and conformed to the tenets of the World Medical Association Declaration of Helsinki. Informed consent was obtained from each of the patients and control participants after they were provided with sufficient information regarding the procedures to be used.

OCT Measurements

Volumetric OCT was performed using the Fast Macular Thickness Map (FMTM) protocol of the Stratus OCT. The macula was scanned along six radiating scan lines centered at the fovea and with a scan length of 6 mm. The patients were instructed to fixate on the inner fixation target. All OCT images along the six scan lines were examined to confirm central fixation and that a proper tracing was drawn at the front border of the sensory retina and at the retinal pigment epithelium line.

The FMTM results provided a false color image of the retinal thickness map along with the central foveal thickness, which was the averaged retinal thickness at the center of each cross-sectional image along the six radial scans,[4] and the averaged retinal thickness (ART) in nine separate regions in the macula, including four sectors in the inner macula (IM), 0.5–1.5 mm from the fovea, and four sectors in the outer macula (OM), 1.5–3 mm from the fovea. In the present study, we evaluated the central foveal thickness and ART of both the superior and inferior sectors of the IM and OM.

The relationship between retinal thickness and days after onset was fitted to an exponential decay curve using KaleidaGraph software (Version 4.0; Synergy Software, Reading, PA, USA).[6]

The statistical analysis was performed using SPSS software (version 17.0; SPSS Japan, Tokyo, Japan).

Results

Temporal Profile of Retinal Thickness in Each Case

Figure 1 shows a color fundus photograph of case 9 taken 8 days after the onset of BRAO and serial records of the

Table 1. Characteristics of nine eyes in nine patients with branch retinal artery occlusion and final data for best-corrected visual acuity, averaged retinal thickness in affected inner or outer macular sectors, and central foveal thickness

Case/Age/ Sex/RL	Affected branch of retinal artery	HT	DM	Days between onset and OCT testing	BCVA at final visit	Final ART in the affected IM sector	Final ART in the affected OM sector	Final central foveal thickness
1/54/F/L	Inferior	+	–	2, 26, 54, 117, 194, 278	2.0	188 (70%)	151 (68%)	167 (102%)
2/62/F/L	Superior	+	–	1645, 2016	0.3	158 (58%)	131 (56%)	140 (85%)
3/65/M/L	Superior	+	–	1867	0.4	137 (51%)	140 (59%)	122 (74%)
4/55/F/R	Inferior	+	–	326, 410, 508	0.9	151 (56%)	116 (52%)	213 (130%)
5/60/F/R	Superior	+	–	1, 24, 115, 199, 297	1.2	214 (79%)	143 (61%)	169 (103%)
6/79/M/L	Inferior	–	–	1, 8, 36, 86, 162, 253, 337, 428, 519	1.2	140 (52%)	127 (57%)	153 (93%)
7/68/M/L	Inferior	–	–	8, 26, 46, 95, 354	0.7	158 (59%)	124 (56%)	183 (112%)
8/55/F/L	Inferior	–	–	1, 51, 156, 254	0.8	180 (67%)	126 (57%)	208 (127%)
9/57/M/R	Superior	+	–	8, 20, 57, 120, 379, 470	0.5	124 (46%)	121 (51%)	143 (87%)

Percentage of the measured thickness compared with the normal control is given in parentheses.

HT, hypertension; DM, diabetes mellitus; BCVA, best-corrected visual acuity; ART, averaged retinal thickness; IM, inner macula; OM, outer macula.

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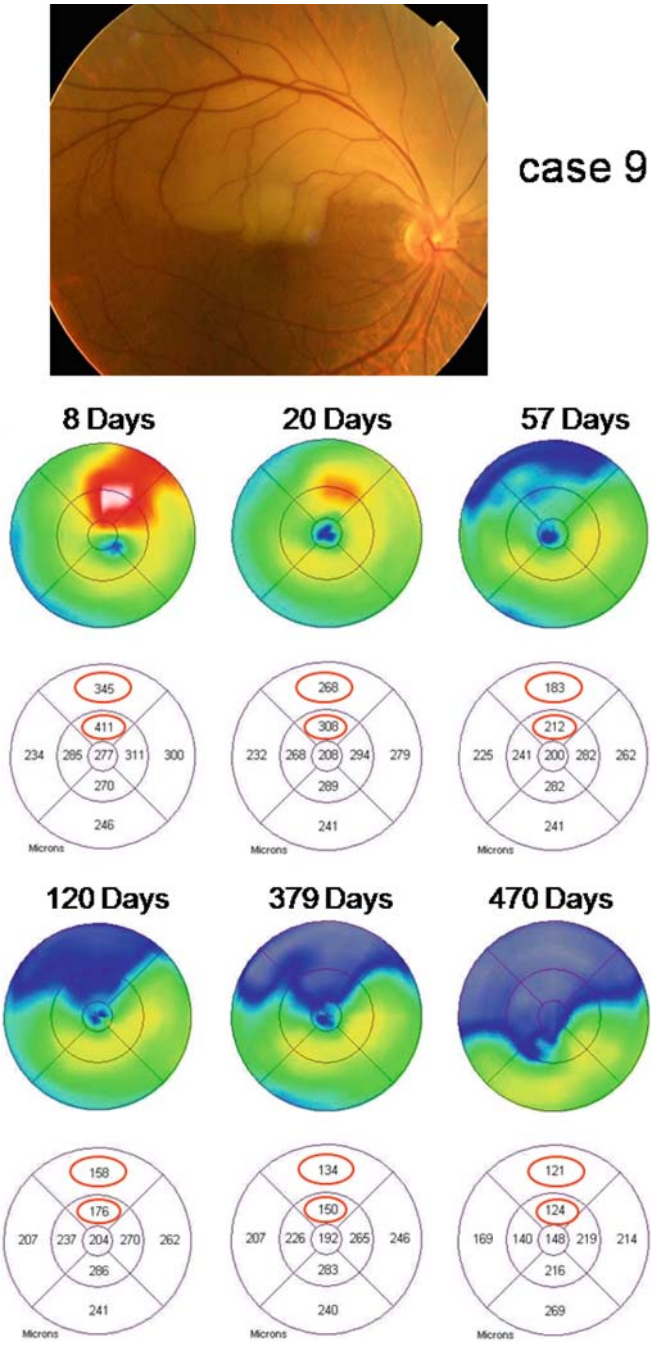

Figure 1. Fundus photograph and serial retinal thickness map of case 9. (*Top*) A color photograph of case 9 taken 8 days after occlusion of the superior temporal branch of the retinal artery shows white swelling in the superior half of the posterior pole of the retina, which is supplied by the occluded arterial branch. (*Bottom*) Serial retinal thickness maps and their numerical displays showing the average retinal thickness (ART) in the nine areas within the 6-mm-diameter circle, along with the indicated days after onset.

retinal thickness map during the subsequent follow-up period of 1.5 years. The retinal thickness map shows a gradual color change from red or white, indicating a thickened retina, to blue, indicating thinning, in the superior sectors of the IM and OM. In the numeric display shown beneath each retinal thickness map, the figures highlighted with red circles indicate the ART in the superior sectors of the IM and OM, which decreased gradually from 411 μm and 345 μm at 8 days after onset to 124 μm and 121 μm, respectively, at the time of the final record.

In Fig. 2, the temporal profiles of central foveal thickness and ART in the superior and inferior sectors of the IM and OM during the follow-up period are shown, along with those of five other cases for which four or more retinal thickness map measurements were obtained, including at ≤10 days and at ≥180 days after onset.

In cases 5 and 9, in which the superior branch of the retinal artery was occluded, retinal thickness in the superior sectors of the IM and OM decreased exponentially during the follow-up period, whereas central foveal thickness and retinal thickness in the inferior sectors of the IM and OM appeared almost unchanged throughout the follow-up period.

In cases 1, 6, 7, and 8, in which the inferior branch retinal artery was occluded, retinal thickness in the inferior sectors decreased exponentially during the follow-up period, whereas central foveal thickness and retinal thickness in superior sectors appeared unchanged throughout the follow-up period.

The best-corrected visual acuity (BCVA), ART of the affected sectors in the IM and OM, and central foveal thickness at the final visit of each patient, relative to the normal control values, are presented in Table 1. The means ± SD of the ART in the superior and inferior sectors of the IM in the control eyes were 271 ± 12 μm and 269 ± 12 μm, and in those of the OM they were 236 ± 13 μm and 223 ± 12 μm, respectively. The mean ± SD of the central foveal thickness was 164 ± 17 μm.

Overall Pattern of Thinning in the Affected Sectors of the Macula

All ART data of the affected superior sectors in the IM and OM were combined to generate a scatterplot against follow-up days for cases 2, 3, 5, and 9, in which the superior branch retinal artery was occluded (Fig. 3, top). Data from cases 2 and 3 contributed only to the follow-up period more than 1600 days after onset. The ART data in the affected sectors of the IM and OM were well approximated by an exponential decay curve with final values of 170 and 142 μm, that is, 63% and 60% of the normal ART value in the corresponding sectors. The time constants of the exponential decay curves of the ART in the IM and OM sectors were 42 and 31 days, respectively.

All ART data of the affected inferior sectors in the IM and OM for cases 1, 4, 6, 7, and 8 were similarly combined to generate a scatterplot against follow-up days (Fig. 3, middle). In each of the fitted exponential decay curves for the ART of the inferior sectors in the IM and OM, the final respective values were 161 and 133 μm, representing 60% and 60% of the normal ART value in the corresponding sectors. The time constants of the exponential decay curves

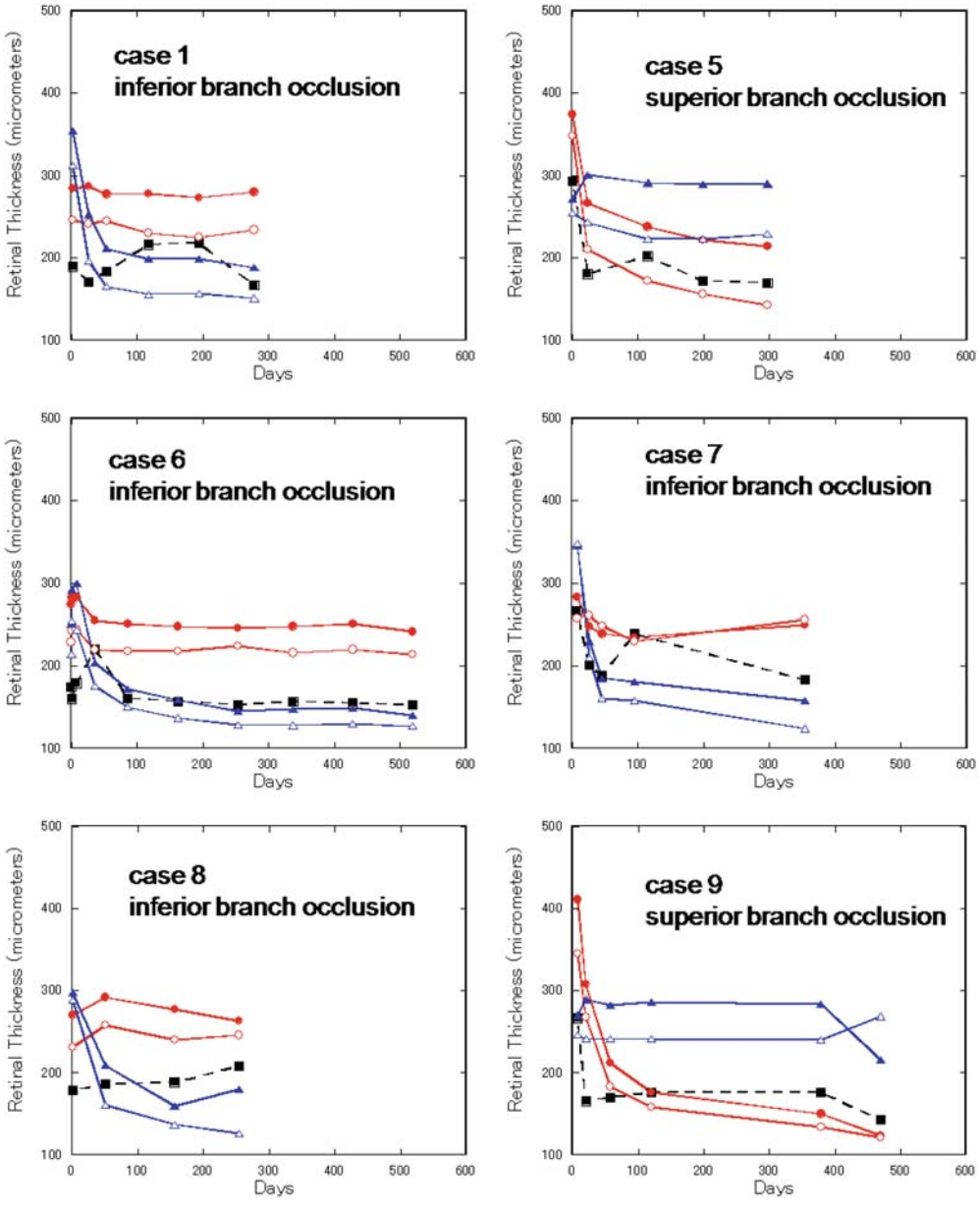

Figure 2. Temporal profile of the retinal thickness consisting of the central foveal thickness and ART of the superior and inferior sectors in the inner macula (IM) and outer macula (OM). Only cases 1, 5, 6, 7, 8, and 9, in which four or more optical coherence tomography scans were performed, including at ≥10 days and at ≤6 months after onset are presented. ■, central foveal thickness; ●, ART of the superior IM; ○, ART of the superior OM; ▲, ART of the inferior IM; △, ART of the inferior OM.

of the ART in the IM and OM sectors were 43 days and 38 days, respectively.

A scatterplot was also generated of all central foveal thickness data against follow-up days (Fig. 3, bottom). Central foveal thickness appeared to be independent of the number of days between the onset of BRAO and the follow-up examination, except for a few days after onset.

Discussion

In the present study, we demonstrated gradual thinning of the initially thickened retina in the affected sectors in the macula of eyes with BRAO. Such retinal thinning was previously suggested by several reports on a small number of patients with BRAO;[3,7] however, these studies did not report temporal aspects of the thinning of the affected retina. In the present study, we quantitatively analyzed retinal thickness map data to demonstrate that retinal thickness in the affected sectors of the IM and OM is reduced in a common temporal pattern.

Since the retinal arteries perfuse the inner two-thirds of the neural retina, retinal thickness changes are expected to develop in the inner retinal layers. Histopathologic investigations have already demonstrated that the inner retinal layers in eyes with retinal artery occlusion show swelling due to diffuse edema in the early stage and shrinkage and thinning due to neural cell loss without gliosis in the late stage, and that fewer changes are observed in the deeper retinal layers.[8,9]

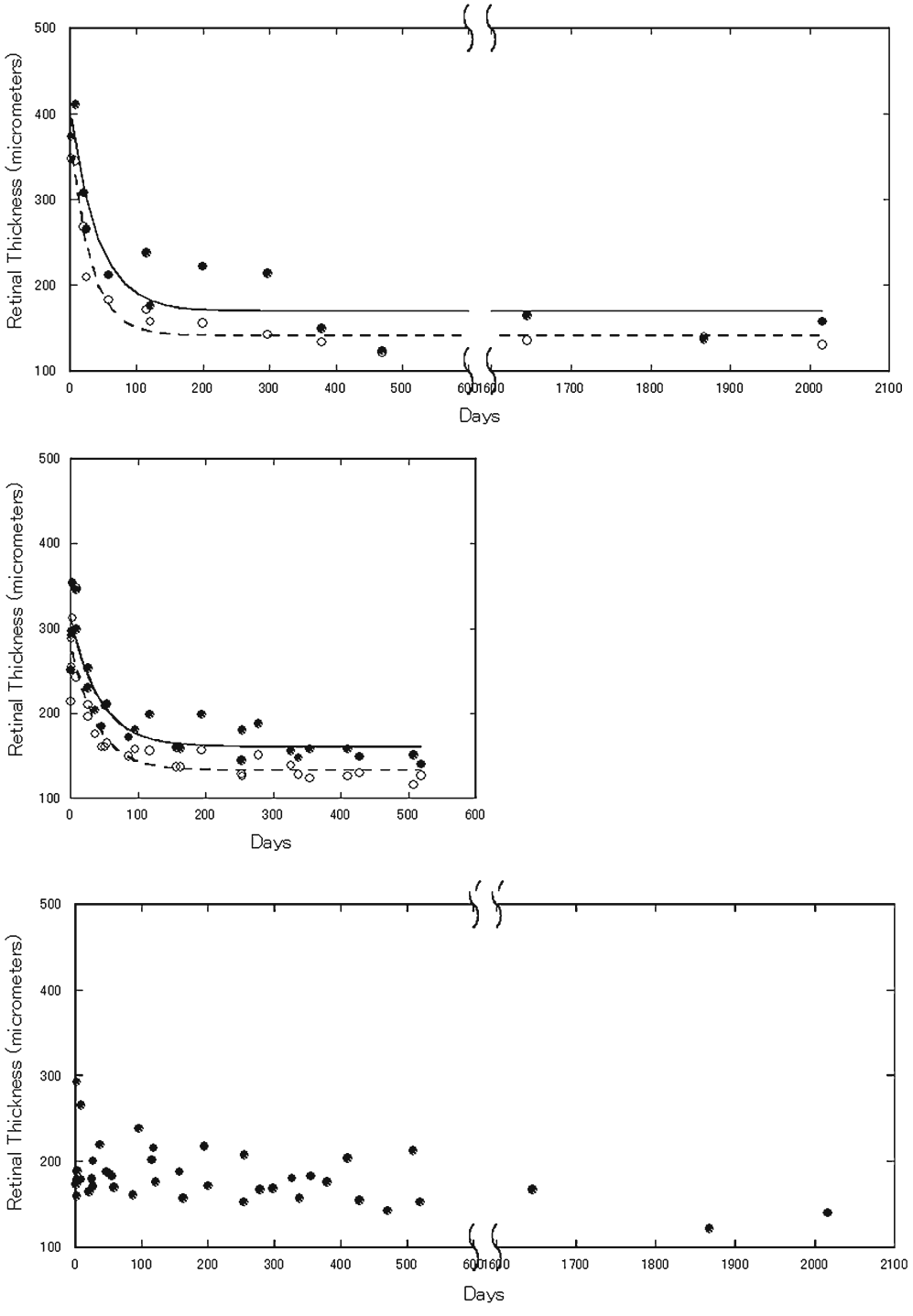

Figure 3. Retinal thickness change after the onset of branch retinal artery occlusion. (*Top*) All ART data for the superior sectors of the IM (●) and OM (○) are plotted against days after onset for cases 2, 3, 5, and 9, in which the superior branch of the retinal artery was occluded. (*Middle*) All ART data for the inferior sectors of the IM (●) and OM (○) are plotted against days after onset for cases 1, 4, 6, 7, and 8, in which the inferior branch of retinal artery was occluded. (*Bottom*) All central foveal thickness data for all nine cases are plotted against days after onset.

Sectors of the IM, from 0.5 to 1.5 mm from the center of the fovea, correspond roughly to the parafoveal area, which is from 0.75 to 1.25 mm from the center of the fovea and where the inner retina is thickest in a normal retina.[10] The ART of the sectors in the IM is expected to show the greatest thickness changes during the follow-up period for BRAO. Despite this being a retrospective study, we successfully demonstrated the gradual thinning of the retina in the affected sectors of the IM along with those of the OM (Figs. 2 and 3).

In contrast to the progressive retinal thinning in the affected sectors of the IM and OM, retinal thickness changes in the center of the fovea were unremarkable. The central fovea within a 0.35-mm-diameter circle lacks an inner retinal layer, and the retina within a 0.5-mm-diameter circle is a capillary-free zone. Therefore, the very center of the fovea

is not expected to be influenced by ischemic damage resulting from occlusion of the retinal arteries supplying the inner retina, which may explain the minimal changes in central foveal thickness in this study.

Only measurements obtained within 10 days of onset for cases 5, 7, and 9 exceeded 250 μm (393, 266, and 266 μm at 1, 8, and 8 days after onset, respectively). The central foveal thickness immediately after onset may have been influenced by swelling in the ischemic parafoveal retina. The final measurements in cases 2 and 3 showed some thinning (140 and 122 μm at 2000 and 1800 days after onset, respectively). Central foveal thickness several years after the onset of BRAO may exhibit thinning due to ischemic changes in the adjacent area. Excluding these data, the relationship between central foveal thickness and the timing from 10 to 500 days after onset for all follow-up data (Fig. 3) was not significant ($P = 0.147$, $n = 31$). The final central foveal thickness in all nine patients was between 74% and 130% that of the controls.

We studied the central foveal thickness, which is the simple mean of the retinal thickness at the center of the fovea, instead of the ART in the central circle with a radius of 0.5 mm, because the Stratus OCT software calculates ART in the central circle by averaging all points on six radial lines within the circle, which results in averaging of data of unevenly distributed points in the area with a bias toward the very center of the circle. The retinal thickness data for the very center of the circle included six repeated measurements of the ART in the central circle with a radius of 0.5 mm.

Regarding the progressive thinning of the affected retina in eyes with occlusion of the retinal artery, the retinal thickness changes were previously studied 1 day, 1 month, and 4 months after onset in five eyes with central retinal artery occlusion.[11] In that study, the retinal thickness decreased rapidly within 1 month of onset and slowed down thereafter at 1° nasal and temporal to the fovea.

In the present study, thickness data were collected more frequently to show the precise profile of retinal thinning and demonstrated that the retinal thinning was well approximated by an exponential decay curve from each tracing of ART in the affected sectors in the IM and OM in six cases (Fig. 2).

The approximation of the curve in Fig. 3 based upon a data set including different data sample sizes from each case might result in a bias reflecting the relative contribution of each case to the results. Nevertheless, the data were well-fitted by an exponential decay curve, suggesting that the time course of retinal thinning in the affected sectors in the IM and OM might be identical among the patients, independent of their individual clinical characteristics, including age, sex, and disease severity.

The affected sectors in the IM and OM, which correspond roughly to the parafoveal and perifoveal retinal areas, respectively, reach a final thickness of approximately 60% of that of the normal retina (Fig. 3). The time constants of the four exponential decay curves of the IM and OM of both the superior and inferior macula were similar between 32 and 45 days, suggesting that the thickness of the thinning retina reaches a constant level by several months after onset. In fact, the percentage of the final retinal thickness in the IM and OM sectors in all nine of the participant eyes measured between 254 and 2016 days after onset compared with that of the normal controls (shown in parentheses in Table 1) was independent of the number of days after onset ($P = 0.308$, IM; $P = 0.897$, OM).

Unfortunately, the present study does not provide precise data for the retinal thickening immediately after onset. From clinical experience, the peak of the retinal thickening may appear within several days of onset. To study the thickness changes during the acute phase of BRAO, it will be necessary to conduct a prospective study with daily OCT recordings in patients with BRAO.

We studied the total thickness of the neural retina, irrespective of its layers because of the limited resolution of Stratus OCT. Another investigation should address detection of the possibly selective thinning of the inner retina using Fourier domain OCT,[12] which is superior for visualization and analysis of the internal structure of the neural retina.

The results of the present study are applicable to clinical practice. In eyes with visual field defect but few findings on ophthalmoscopic examination, as is seen in eyes with BRAO at several months after onset, diagnosis may be difficult. The differential diagnosis includes the chronic stage of ischemic optic neuropathy, glaucoma, and retinal diseases such as acute zonal occult outer retinopathy. If the OCT retinal thickness map of the affected retina demonstrates sectoral thinning to as little as 60% that of the normal retina, BRAO might have developed in the previous several months.

In conclusion, we demonstrated an exponential decrease in the thickness of the affected retina in eyes with BRAO. Over the course of several months, the retinal thickness reached a constant level at about 60% that of the normal retina in the parafoveal and perifoveal areas.

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