

Correlation between Spectral Domain Optical Coherence Tomography Findings and Fluorescein Angiography Patterns in Diabetic Macular Edema

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Objective: To study the relationship between spectral domain optical coherence tomography (SD-OCT) findings and fluorescein angiography (FA) patterns in patients with diabetic macular edema (DME).

Design: Retrospective, observational, cross-sectional study.

Participants: We included 59 eyes from 59 patients with DME that had SD-OCT/scanning laser ophthalmoscope (SLO) and FA performed on the same day. Eyes with macular edema owing to other ocular diseases were excluded.

Methods: The relationship between SD-OCT and FA findings was evaluated by superimposing and aligning the SLO images onto the FA photos. The SLO image of the OPKO/OTI Spectral OCT/SLO (OPKO-OTI, Miami, FL) corresponds with the exact origin and orientation of the SD-OCT scan, which was then correlated with the FA image. Foveal and extrafoveal regions were studied separately. Leakage on FA and pathologic changes on OCT were graded by using standard photographs. Pathologic changes studied in the OCT images included edema and cystic spaces in the inner and outer retina, loss of retinal layers, and foveal cysts.

Main Outcome Measures: Correlation between SD-OCT changes and corresponding FA patterns.

Results: The outer retina was the predominant location of fluid in DME. The severity of the outer retinal edema on OCT was positively correlated with the severity of leakage on FA ($r = 0.735$; $P < 0.001$). Cystic changes in the inner and outer retina were also correlated with the severity of fluorescein leakage ($r = 0.507$ and $P < 0.001$; $r = 0.561$ and $P < 0.001$, respectively). Loss of inner retinal layers on OCT was highly correlated with capillary nonperfusion on FA ($r = 0.953$; $P < 0.001$). Large foveal cysts on SD-OCT corresponded to cystoid leakage patterns on FA.

Conclusions: Pathologic changes on SD-OCT correlated well with FA findings. Loss of inner retinal layers was specifically correlated with capillary nonperfusion and severe ischemia. Judgment of whether management of DME based on fine retinal structural changes influences clinical outcomes must be reserved pending further investigation with prospective trials.

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Diabetic macular edema (DME) is the major vision-threatening retinal complication in nonproliferative diabetic retinopathy (DR).¹ Prompt detection and appropriate management of this condition is essential. Common methods of evaluating DME include slit-lamp biomicroscopy, indirect ophthalmoscopy, and fundus stereophotography.² However, none of these methods provides an objective quantitative measurement of DME.

Optical coherence tomography (OCT) is a noninvasive, noncontact evaluation method that allows quantitative measurements of retinal thickness and volume. It provides cross-sectional images of the retina, which resemble histologic sections seen with light microscopy.^{3–5} Spectral domain OCT (SD-OCT) is the latest generation of the technique and provides images with axial resolution of < 5 microns. It allows identification of individual retinal layers,⁶ and has provided significant clinicopathologic information in several studies of different retinal conditions.^{7–9}

The OPKO/OTI Spectral OCT/SLO combines SD-OCT imaging with confocal scanning laser ophthalmoscope (SLO).¹⁰ The SLO channel provides live real-time images of the retinal surface, which correspond to cross sectional B-scan images in the OCT channel. The simultaneous acquisition of these images using a single light source ensures pixel-to-pixel correspondence between the 2 channels. This allows the precise location of the OCT to be indicated on the corresponding SLO fundus image (Fig 1).

Vascular leakage in DR is the source of increased retinal thickness and, subsequently, DME.¹¹ Fluorescein angiography (FA) provides a useful tool for studying these pathophysiologic changes in patients with DME. Various leakage patterns, such as focal, diffuse, and cystoid, probably indicate different combinations of mechanisms responsible for DME.¹² A few prior studies have attempted to correlate OCT findings and FA patterns to better understand the pathophysiologic changes of DME.^{12–15} However, limita-

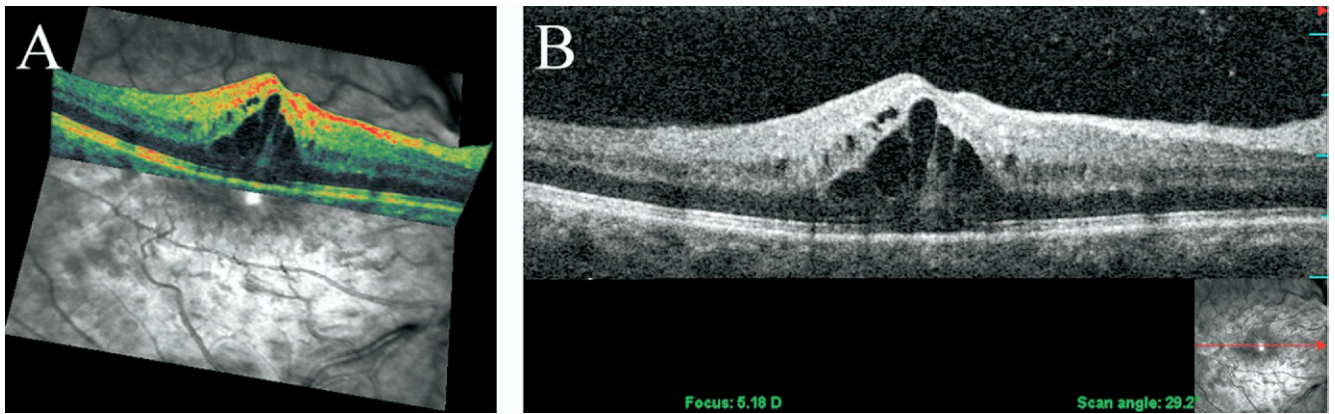


Figure 1. A, Combination of the scanning laser ophthalmoscope (SLO) image and optical coherence tomography (OCT) scan. B, The mark on SLO image (right lower corner) shows the exact location and orientation of the OCT scan.

tions in localization and resolution in older generation imaging devices prevented accurate correlation of pathologic changes between these 2 examinations. The OCT findings could only be compared with the overall FA patterns in a particular macula region.

The present study correlates the SD-OCT and FA findings in DME at exact locations within the lesions.

Patients and Methods

A retrospective chart review was conducted by analyzing the image database of all patients with DR who underwent SD-OCT

and FA examinations on the same day as the clinical examination at the Retina Center of The New York Eye and Ear Infirmary between September 2006 and May 2008. New York Eye and Ear Infirmary Institutional Review Board approval was obtained before performing this retrospective, cross-sectional study. Patients who met the following criteria were included: (1) clinical diagnosis of DME by a retina specialist, regardless of the severity; and (2) having had SD-OCT and FA performed on the same day. The exclusion criteria were: (1) eyes with poor quality OCT scans or FA images, or (2) macular edema caused by other etiologies such as retinal vascular occlusions and postoperative or inflammatory cystoid macular edema. Only 1 eye from each patient was included in this study. In patients with bilateral DME, only the primary study eye on FA examination was analyzed. A total of 59 eyes

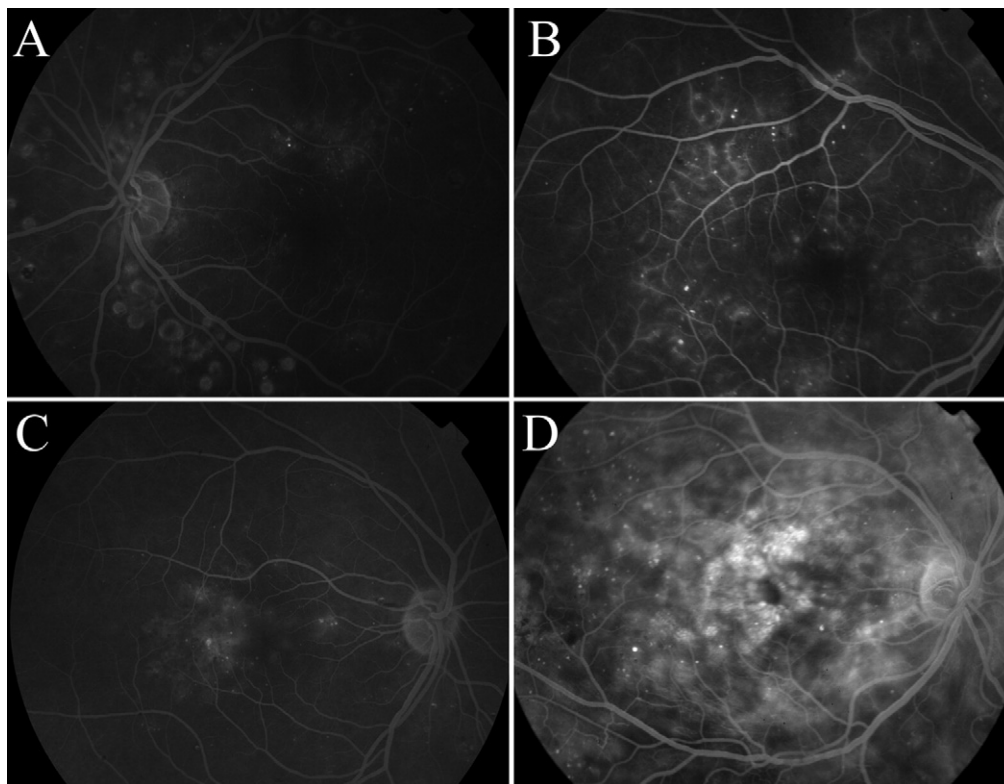


Figure 2. Standard photos with different severities of leakage on fluorescein angiography. A, None or questionable. B, Mild. C, Moderate. D, Severe.

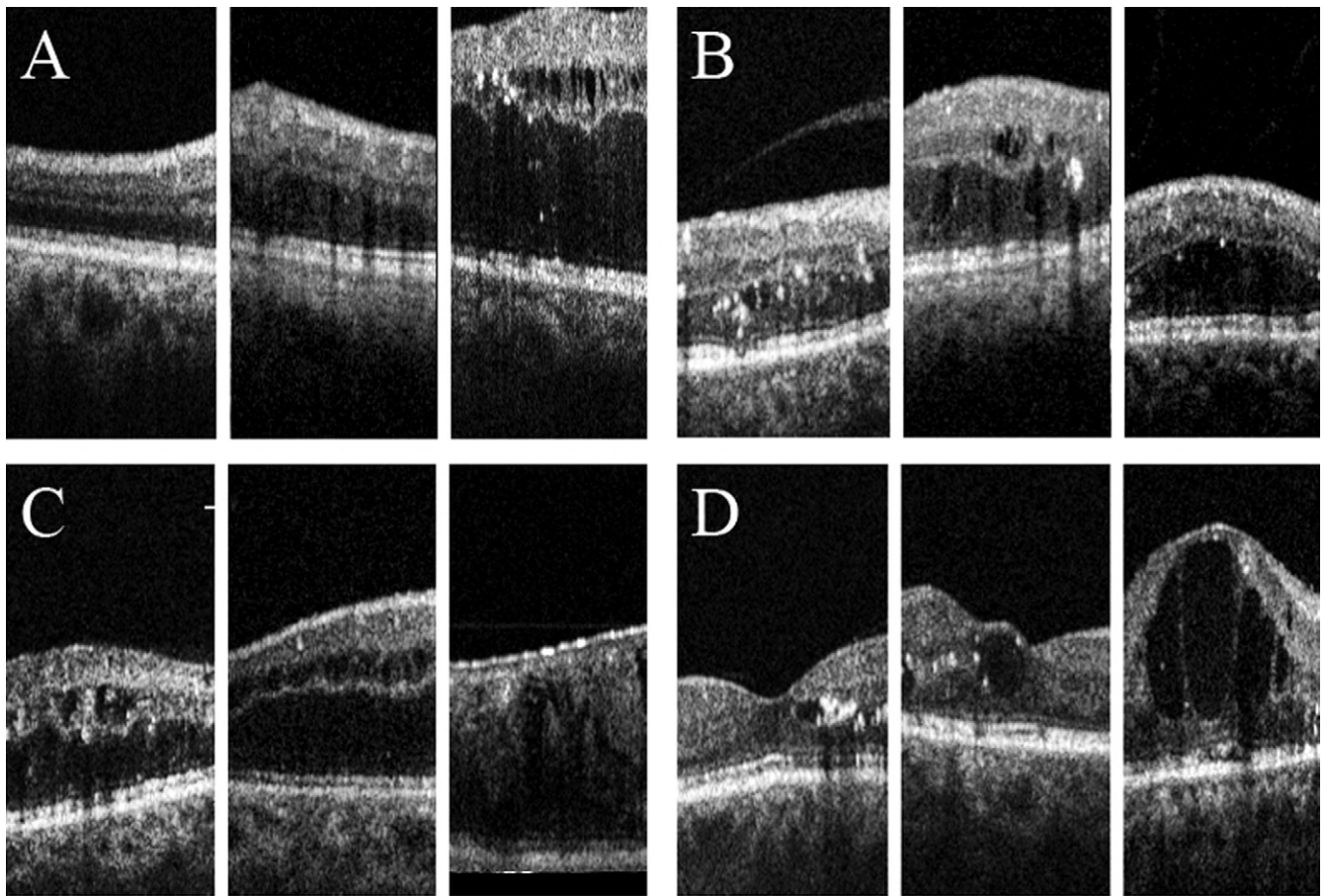


Figure 3. Standard photos with different grades of spectral domain optical coherence tomography pathologic findings. **A**, Outer retina edema severity: mild (1), moderate (2), and severe (3). **B**, Outer retina cystic changes severity: few (1), multiple (2), and diffuse (3). **C**, Inner retina cystic changes severity: few (1), multiple (2), and unable to identify (loss of inner retinal layer; 3). **D**, Size of foveal cysts: small (1), medium (2), and large (3).

from 59 patients were included. Medical records of all eligible patients were reviewed to gather information about age, gender, type of DR (nonproliferative or proliferative) and prior treatments (focal or panretinal photocoagulation).

Procedures

A digital retinal camera system (Topcon TRC 50IX, Topcon Medical Systems Inc., Paramus, NJ) was used for FA examination. One early

or middle phase frame and 1 late phase frame were obtained from each eye. The early/middle phase frame was used to determine the presence of microaneurysms and capillary nonperfusion areas. The late phase frame was used to determine location and severity of leakage. A simplified Early Treatment Diabetic Retinopathy Study classification was used to score the severity of leakage on FA.¹⁶ It was classified into 4 categories by comparing with 4 standard photos: none or questionable, mild, moderate, and severe leakage (Fig 2).

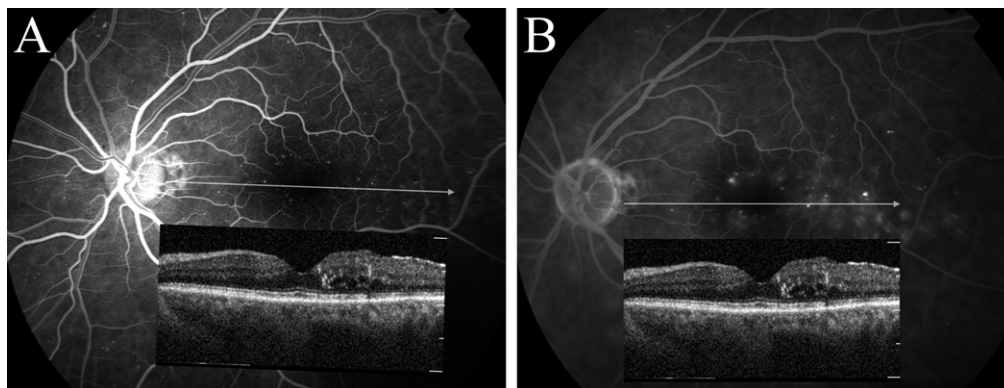


Figure 4. Relationship between spectral domain optical coherence tomography pathologic changes and fluorescein angiography findings of patient 37 on (A) early phase and (B) late phase frames. Cystic changes in the outer plexiform layer correspond to few microaneurysms on the early phase frame and to a focal leakage on the late phase frame.

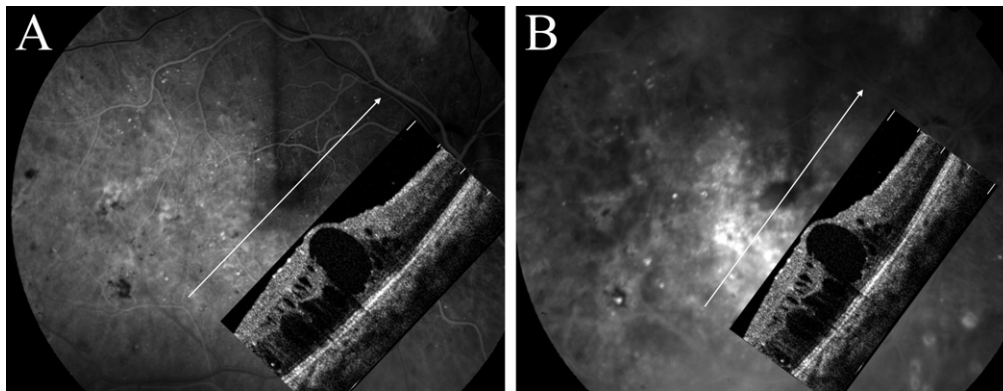


Figure 5. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography (FA) findings of patient 3 on (A) early phase and (B) late phase frames. A large foveal cyst corresponds to a round area of hyperfluorescence at the central fovea since the early phase. Multiple parafoveal cysts correspond to cystoid leakage pattern on FA. Severe extrafoveal leakage is shown in corresponding cross-sectional SD-OCT scan as a diffuse cystic space with severe edema in the outer nuclear layer and multiple cystic changes in the inner nuclear layer.

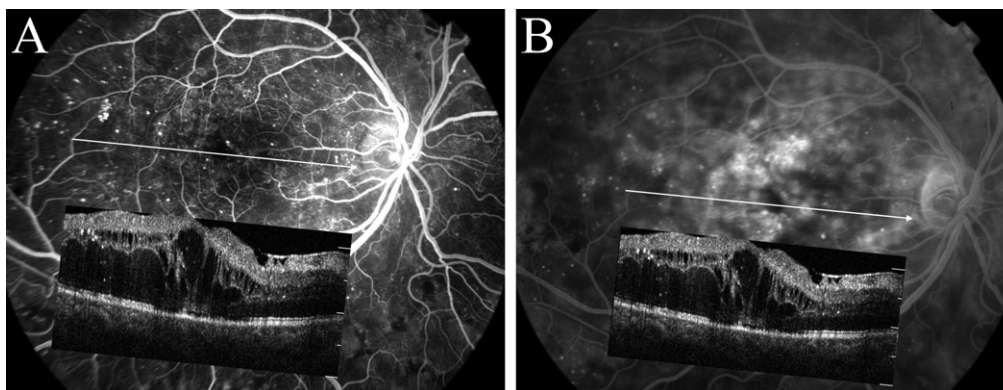


Figure 6. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography (FA) findings of patient 1 on (A) early phase and (B) late phase frames. Several large foveal cysts correspond to a cystoid leakage pattern on FA. The septa between these large foveal cysts are the stretched retinal tissue in the outer plexiform layer. Severe leakage at the extrafoveal region corresponds to a diffuse spongy space in the outer retina and to multiple, small cysts in the inner retinal layer. The increase in thickness in the outer retina is more prominent than in the inner retina.

An SD-OCT device (OPKO/OTI Spectral OCT/SLO) was used to gather both SLO and OCT images. The most characteristic OCT scan was chosen from each eye studied, and then divided into foveal and extrafoveal regions. Foveal and extrafoveal regions were evaluated separately owing to their different anatomical structures. In the extrafoveal region, outer retinal edema and outer and inner retinal cystic spaces were graded according to the

severity of the pathologic changes. The outer retinal edema was graded as none, mild, moderate, or severe. The severity of outer retinal cystic spaces was graded as none, few (≤ 3 cysts), multiple (>3 cysts), and ill-defined (diffuse cystic spaces). The severity of inner retinal cystic spaces was graded as none, few (≤ 3 cysts), multiple (>3 cysts), and unable to classify (due to loss of inner retinal layers). In the foveal area, the cystic spaces were classified

Table 1. Correlation between the Grade of Outer Retinal Edema on Spectral Domain Optical Coherence Tomography and the Severity of Leakage on Fluorescein Angiography

Outer Retinal Edema	Leakage on Fluorescein Angiography				Total
	None	Mild	Moderate	Severe	
None	4	3	0	0	7
Mild	4	7	6	2	19
Moderate	1	0	11	12	24
Severe	0	0	1	8	9

Spearman correlation coefficient $r = 0.735$; $P < 0.001$.

Table 2. Correlation between the Grade of Outer Retina Cystic Changes on Spectral Domain Optical Coherence Tomography and the Severity of Leakage on Fluorescein Angiography

Outer Retinal Cyst	Leakage on Fluorescein Angiography				Total
	None	Mild	Moderate	Severe	
None	3	6	2	1	12
Few (≤ 3)	6	3	9	6	24
Multiple (>3)	0	0	2	3	5
Ill-defined	0	1	5	12	18

Spearman correlation coefficient $r = 0.561$; $P < 0.001$.

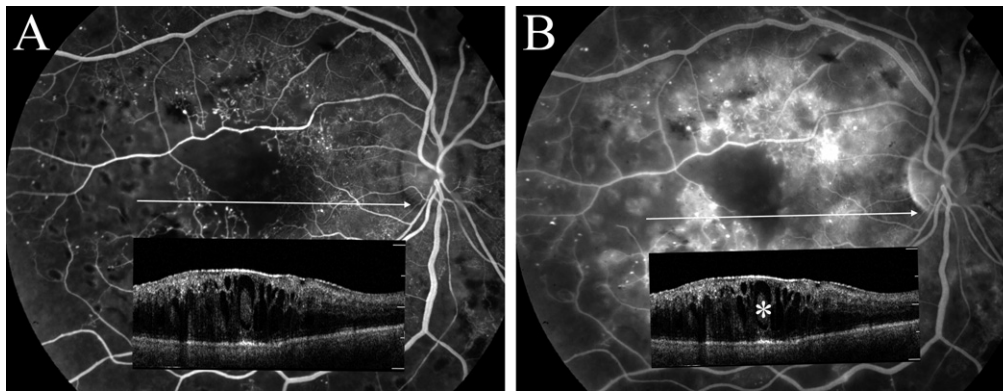


Figure 7. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography (FA) findings of patient 4 on (A) early phase and (B) late phase frames. Areas of capillary nonperfusion on FA correspond to areas with loss of retinal layers and severe edema on SD-OCT. The junction of the inner and outer segments of photoreceptors can be recognized. The different retinal layers can be identified over the area nasal to fovea with relatively better capillary perfusion. The round area of hyperreflectivity in a large foveal cyst (*) is a part of the septum between the cysts.

into 3 grades according to the different sizes: small (the foveal contour was well-preserved), medium (foveal contour was still recognizable), and large (foveal contour was severely distorted). Standard photos for each of the above pathologic findings are shown in Figure 3.

Computer software (Adobe Photoshop 7.0, Adobe Systems Incorporated, San Jose, CA) was used to adjust the transparency of SLO image to allow it to be accurately overlaid and aligned onto the FA photos. Optic disc and retinal vessels were used as landmarks to facilitate the point-to-point registration between the 2 images. The exact scanning location of OCT was transferred from SLO image to FA photos. After marking the scan line on FA, the superimposed SLO image was removed, leaving the scan line on the FA image. Then pathologic changes demonstrated by the SD-OCT could be compared with the FA image based on the location of the scan line.

Statistical Analysis

The Spearman correlation coefficient was used to analyze the relationship between the severity of each pathologic OCT findings (outer retina edema, outer and inner retina cystic spaces) and the severity of leakage on FA. The Fisher exact test and the Spearman correlation coefficient were used to determine the correlation be-

tween nonperfusion areas on FA and loss of retinal layers on SD-OCT. A 2-tailed *P* value < 0.05 was considered as statistically significant. All the data were analyzed using SPSS Program Package Version 13.0 (SPSS Inc., Chicago, IL).

Results

We included 59 eyes from 59 patients (29 female and 30 male; mean age, 61.4 years; standard deviation, 9.3). Thirty-eight (64.4%) eyes had nonproliferative and 21 (35.6%) eyes had proliferative DR. Fifteen (25.4%) eyes had received macular focal laser photocoagulation, 9 (15.2%) eyes were treated with panretinal photocoagulation, and 11 (18.6%) eyes had received both treatments. In total, 59 OCT scans were obtained for analysis.

Extrafoveal Outer Retina

At the extrafoveal region, the outer retina was the predominant location of the fluid accumulation in DME. On SD-OCT, cystic or edematous changes of outer retina were noted in 50 (84.7%) eyes. For mild retinal edema on FA, cystic spaces were located only in the outer plexiform layer (Fig 4). However, when the cystic spaces became more pronounced or when they were ill-defined, they

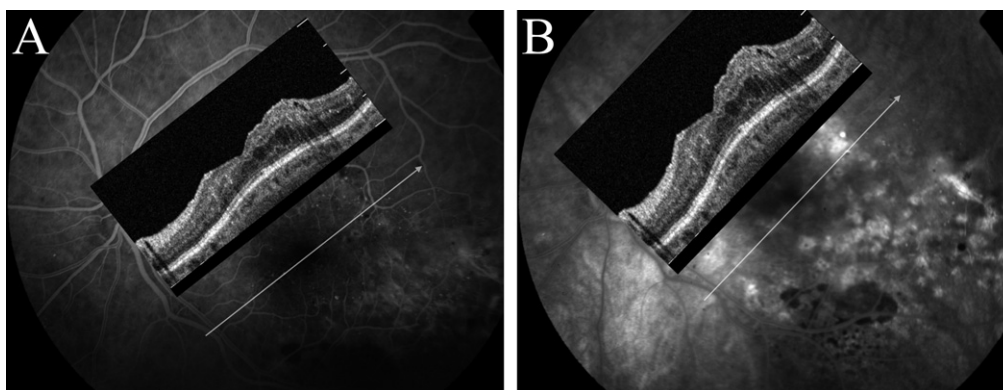


Figure 8. Relationship between spectral domain optical coherence tomography pathologic changes and fluorescein angiography (FA) findings of patient 32 on (A) early phase and (B) late phase frames. Two small cysts can be seen in the ganglion cell layer. Medium foveal cysts correspond to mild cystoid leakage pattern on FA.

Table 3. Correlation between the Grade of Inner Retina Cystic Changes on Spectral Domain Optical Coherence Tomography and the Severity of Leakage on Fluorescein Angiography

Inner Retinal Cyst	Leakage on Fluorescein Angiography				Total
	None	Mild	Moderate	Severe	
None	7	2	7	4	20
Few (≤ 3)	2	8	10	5	25
Multiple (>3)	0	0	0	11	11
Unable to define	0	0	1	2	3

Spearman correlation coefficient $r = 0.507$; $P < 0.001$.

involved both the outer plexiform layer and outer nuclear layer (Figs 5 and 6).

The severity of outer retinal edema on the SD-OCT positively correlated with the severity of leakage on FA ($r = 0.735$; $P < 0.001$; Table 1). The grading of the outer retinal cystic spaces also correlated with the severity of leakage on FA ($r = 0.561$; $P < 0.001$; Table 2). If no cyst or only few cysts (≤ 3) were found, the corresponding fluorescein leakage was more likely to be mild to moderate. If multiple cysts (>3) or ill-defined cystic spaces were noted, the fluorescein leakage were more likely to be severe. Although focal leakage on FA could sometimes be found at the corresponding location of outer retinal cysts (Fig 4), it was highly variable. No significant correlation between the different grade of cystic changes and the source (diffuse or focal) of fluorescein leakage was found.

Extrafoveal Inner Retina

At the extrafoveal region, changes of inner retinal layer on SD-OCT were less prominent than the outer retinal layer in DME. Retinal changes were difficult to evaluate in 3 (5.1%) eyes owing to a loss of inner layers (Fig 7). Cystic spaces were found in 36 (61%) eyes. In 20 (33.9%) eyes, no specific cystic changes were found. The cystic spaces were more commonly located in the inner nuclear layer (35 eyes) than in the ganglion cell or nerve fiber layers (4 eyes; Fig 8).

Different severities of cystic changes in the inner retina correlated with the severity of fluorescein leakage on FA ($r = 0.507$; $P < 0.001$; Table 3). Fluorescein leakage could vary from no leak-

age to severe leakage when the SD-OCT showed no or few cysts. However, multiple cysts always were related to severe leakage on FA (Fig 6). The focal cystic spaces in the inner retina could sometimes be matched with a focal leakage area on FA, but it was highly variable (Fig 9). No significant correlation between the different grades of cystic changes in the inner retina and the source (diffuse or focal) of fluorescein leakage was found.

In addition, there was a positive correlation between the severity of cystic spaces in the inner retina and severity of the outer retinal edema ($r = 0.563$; $P < 0.001$). However, the inner retinal thickness often remained relatively stable even in eyes with severe edema in the outer layers (Fig 6).

Extrafoveal Loss of Retinal Layers

A loss of retinal layers was detected in 14 (23.7%) eyes. The ability to distinguish individual retinal layers using SD-OCT was lost in these cases. Destruction of layers was more prominent in the inner retina. The junction of inner and outer segments of the photoreceptors often remained identifiable, although it became irregular once severe retinal edema developed (Fig 9). Loss of retinal layers could be present either with (Figs 7 and 10) or without outer retinal edema (Fig 11) on SD-OCT. Capillary non-perfusion over the corresponding area was present in 13 of 14 eyes. One eye presented with diffuse laser scars (Fig 12). Loss of retinal layers on SD-OCT corresponded with capillary nonperfusion areas on FA with a high degree of correlation (Spearman correlation coefficient $r = 0.953$; Fisher exact test $P < 0.001$).

Foveal Cystic Changes

Cystic spaces in the fovea were found in 43 (72.9%) eyes. Among 16 eyes without them, 5 eyes presented mild increased foveal thickness and 3 eyes showed loss of outer nuclear layers (Fig 12).

The size of cysts was moderately correlated to the different patterns of leakage ($r = 0.401$; $P = 0.002$; Table 4). If small or medium cysts were found on SD-OCT, the leakage on FA showed as either mild or focal, or as a cystoid pattern. If the OCT showed large foveal cysts, it was more likely to correspond with cystoid leakage on FA. It was difficult to determine the number of cysts in an eye because it depends on the locations or orientations of the OCT scan (Fig 13).

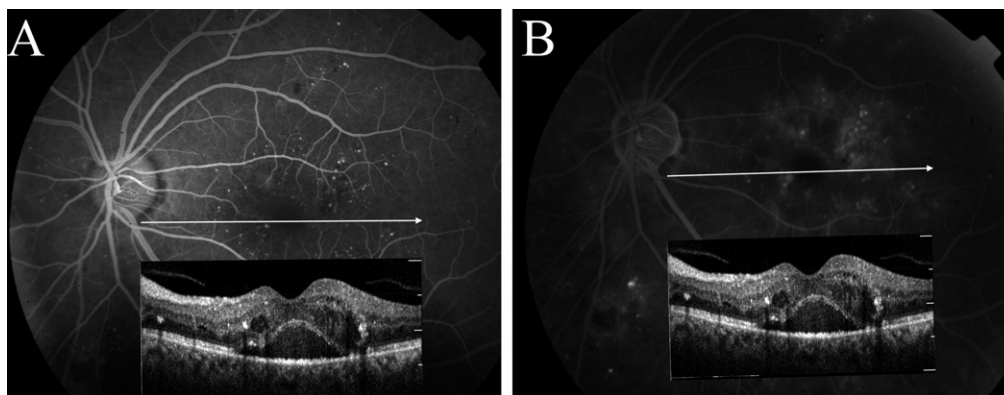


Figure 9. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography (FA) findings of patient 21 on (A) early phase and (B) late phase frames. The small foveal detachment does not correspond with any specific pattern on FA. A cyst in the outer plexiform layer can be matched with a focal leakage on FA from an inferonasal microaneurysm. Hard exudates show as highly reflective objects that shadow deeper layers on the SD-OCT.

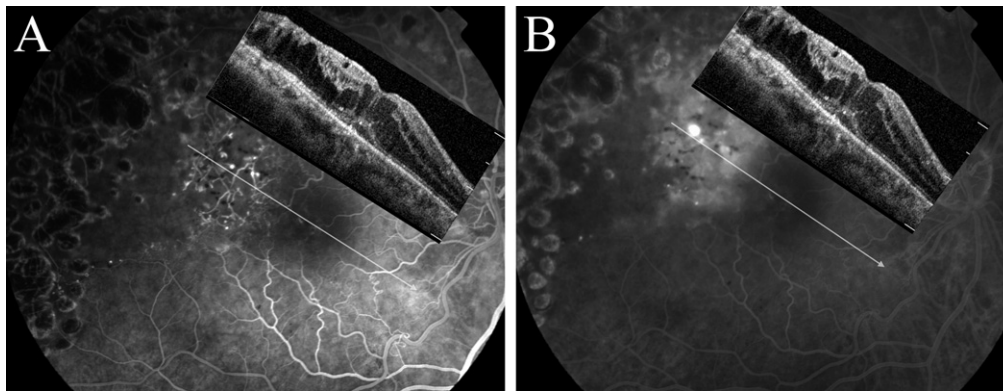


Figure 10. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography findings of patient 40 on (A) early phase and (B) late phase frames. The superotemporal area of capillary nonperfusion corresponds with the loss of retinal layers and severe edema on SD-OCT. The junction of the inner and outer segments of photoreceptors remains recognizable. Individual retinal layers can be identified in the inferonasal area to the fovea, which demonstrates better capillary perfusion.

Foveal Detachments

Foveal detachments were found in 11 (18.6%) eyes. No consistently specific fluorescein leakage or pooling pattern was noted on FA in cases where these small, serous detachments were demonstrated by the SD-OCT. Hence, no correlation between foveal detachment and leakage on FA was found (Fig 8). Moreover, foveal serous detachments were not associated with any specific foveal cystic changes. Among 11 eyes with foveal serous detachment, 2 eyes had no foveal cysts, 3 had small cysts, 2 had medium cysts, and 4 had large cysts.

Hard Exudates

Hard exudates appeared on OCT as highly reflective objects that shadowed the layers beneath it (Figs 8 and 12). They could be found in the foveal or extrafoveal regions. Their most common locations were the outer plexiform and outer nuclear layers. They were not easily identified on FA, except in cases with very severe exudation causing local fluorescence blockage.

Discussion

In this study, OCT and corresponding SLO scans of eyes with DME were acquired simultaneously using a SD-OCT/SLO

device. The SLO images were superimposed and aligned on corresponding FA photos using a photography editing software, and the OCT scan location was transferred to the corresponding location on the FA. This permitted direct correlation of pathologic lesions on the OCT with fluorescence patterns on FA. The OCT enabled us to evaluate structural changes on different retinal layers, and the FA provided information about hemodynamic and vascular changes of the inner retina. When evaluated together, the 2 imaging modalities provided a more comprehensive picture of the pathophysiologic mechanisms of DME.

Different retinal structures at foveal and extrafoveal areas were studied separately. In the extrafoveal area, severity of the outer retinal edema along with the outer and inner retinal cystic changes on OCT was positively correlated with severity of leakage on FA. Cystic spaces were more commonly found in the outer retina. Otani and Kishi¹³ studied 59 eyes with DME by OCT and stated that cystoid macular edema was located mainly in the outer retinal layers. At that time, they did not have the advantage of a combined SD-OCT/SLO device, and they were not able to distinguish which of the retinal layers were involved in the edema or accurately localize the relationship of OCT findings to the leakage on FA. The present study shows that

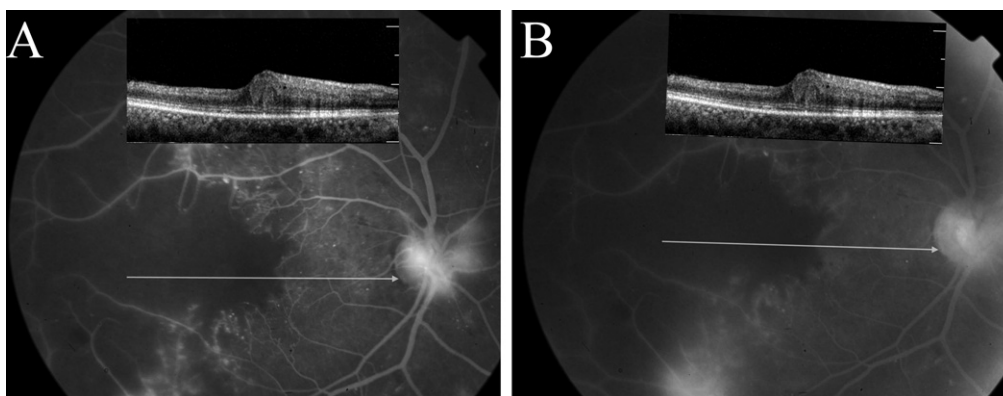


Figure 11. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography findings of patient 24 on (A) middle phase and (B) late phase frames. The temporal area of capillary nonperfusion corresponds with the loss of retinal layers and no edema on SD-OCT. The junction of the inner and outer segments of photoreceptors seems to be well preserved generally.

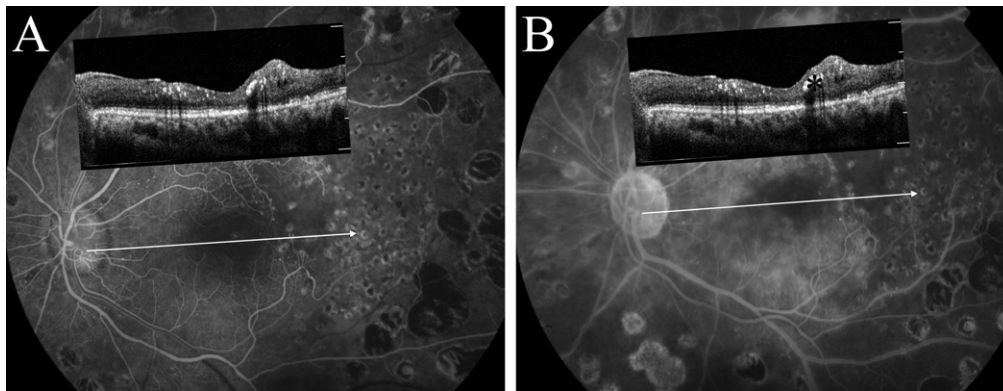


Figure 12. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography (FA) findings of patient 7 on (A) early phase and (B) late phase frames. Macular ischemia is indicated by the enlargement of the foveal avascular zone with capillary dropout around the fovea. It corresponds with the loss of outer nuclear layer on SD-OCT. The capillary nonperfusion and laser scars over the temporal macula correspond with the loss of layers and lack of edema on SD-OCT. The junction of the inner and outer segments of photoreceptors is disrupted over the location of the laser scars. Exudates present as hyperreflective objects that cast a shadow (*) onto deeper layers of the SD-OCT, but are generally not visible on FA.

mild leakage can be associated with cystic spaces in any of the outer nuclear, outer plexiform, inner nuclear, or even ganglion cell layers. These findings are compatible with prior histopathologic reports. Tso¹⁷ reviewed the histopathologic features in 35 human eyes with cystoid macular edema and found that cystic spaces were located not only in the outer plexiform layer, but also in the inner plexiform and nuclear layers, and even in the ganglion cell layer. In the present study, when the fluorescein leakage was more profound, the cystic or edematous changes on SD-OCT were more likely to expand toward the outer nuclear layer. As the severity of edema and number of cysts in the outer nuclear layer increased, the corresponding fluorescein leakage also increased. In severe cases, these cysts could be confluent and become a diffuse, spongy space. According to previous histopathologic reports in autopsy eyes with retinal edema, retinal swelling initiates the intracytoplasmic swelling of Müller cells.^{18,19} The outer plexiform layer or Henle fiber layer is markedly swollen in macular edema. If it persists, some data suggest that liquefaction necrosis of the Müller cells and adjacent neural cells leads to the formation of cystic cavities. These cavities may present as the spongy space seen on OCT in this study. In the inner nuclear layer, the cystic spaces also increased with the leakage, but this finding was less common than in the outer nuclear layer.

Table 4. Correlation between the Grade of Foveal Cystic Changes on Spectral Domain Optical Coherence Tomography and the Pattern of Leakage on Fluorescein Angiography

Foveal Cyst	Leakage on Fluorescein Angiography				Total
	None	Mild/Focal	Cystoid	Diffuse	
None	6	4	4	2	16
Small	0	9	5	1	15
Medium	0	2	8	0	7
Large	0	3	17	1	21

Spearman correlation coefficient $r = 0.401$; $P = .002$.

The thickness of the inner retina was relatively preserved, even with multiple cysts in the inner nuclear layer.

The finding that loss of retinal layers corresponded to areas of capillary nonperfusion on FA with a high degree of correlation was among the most striking observations we noted. Loss of retinal layers was a specific OCT sign predictive of capillary nonperfusion, with the exception of retinas with cicatricial areas of diffuse scarring owing to fibrosis or laser scars. To distinguish between these 2 causes of retinal layer loss, the photoreceptor layer's appearance could be useful. The hyperreflective layer that identifies the inner/outer segment junction seems to be preserved in SD-OCT images with capillary nonperfusion, whereas this line is typically lost in areas of diffuse fibrotic laser scars. Similar findings were also noticed in other DME eyes that were not included in this study because they were the secondary eyes during the FA examination. Retinal thickness and severity of retinal edema in areas of capillary nonperfusion was highly variable (ranging from none to severe edema), making it impossible to determine the presence of capillary nonperfusion on the basis of retinal thickness alone. Because capillary nonperfusion and ischemic maculopathy are important predictors of poor functional outcomes,^{20–22} SD-OCT structural changes as well as macular thickness need to be evaluated when managing patients with DME or evaluating interventional prospective studies.

Clinicopathologic studies of capillary nonperfusion or ischemic changes owing to retinal vein occlusion have demonstrated inner ischemic atrophy with loss of inner plexiform and inner nuclear layers.^{23–25} Although the mechanisms of capillary nonperfusion in DR and retinal vein occlusion are different, both exhibit compromised retinal circulation, leading to the premise that loss of retinal layers in DR may also be due to inner ischemic atrophy. This observation is supported by the finding that the junction of inner and outer segments of photoreceptors in the outer retina is preserved in nonperfused areas.

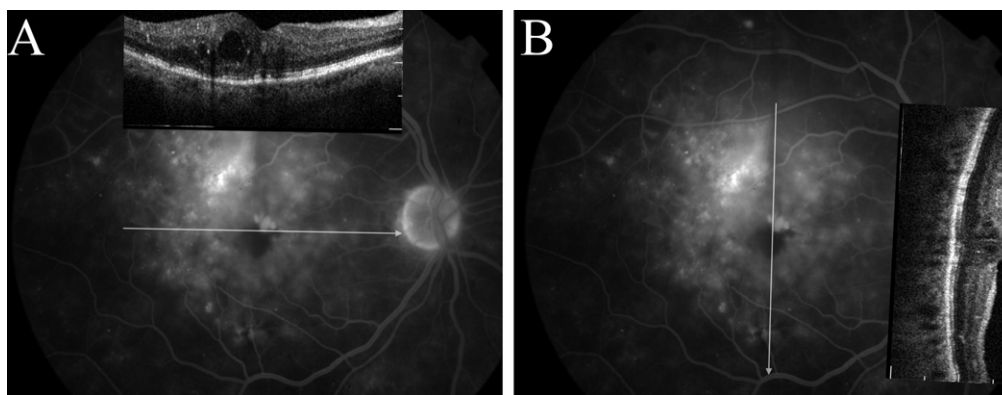


Figure 13. Relationship between spectral domain optical coherence tomography (SD-OCT) pathologic changes and fluorescein angiography findings of patient 23 on late phase frames (A) and (B). The number of cysts varies according to the orientation of the SD-OCT scan.

Almost all recent studies in DME used quantitative OCT parameters (such as retinal thickness or macular volume) as indicators of treatment response and visual outcome.^{26–28} These studies did not take into consideration retinal structural changes (such as loss of retinal layers) in their evaluation, and this may explain why functional changes and visual outcomes were not always consistent with macular thickness. Gibran et al²⁹ evaluated the effectiveness of intravitreal triamcinolone for managing DME and found that eyes with high reflectivity of inner retinal layers on OCT achieved greater visual acuities. From the result of our study, this finding may indicate the absence of capillary nonperfusion, and could explain the better visual outcome in these patients.

The severity of foveal cystic spaces on SD-OCT correlated with specific patterns on FA. Large foveal cysts were more likely to have cystoid leakage pattern on FA, whereas small and medium cysts had mild focal or cystoid leakage pattern on FA. The number of cysts was not a good indicator for the pattern of leakage on FA because it could vary depending on the orientation of the OCT scan.

The mechanism for the formation of cystoid macular edema could be deduced by observing the different severities of foveal cysts. It begins with a small cystic space in the outer plexiform layer, which on FA is seen as diffuse leakage and leakage from adjacent microaneurysms. The size of the cysts increases as the leakage becomes more severe, and the outer plexiform layer is pushed outward, leading to the foveal contour loss. The septa between cysts are the compressed or stretched neural tissue from the outer plexiform layer (Fig 6). Occasionally, single large cysts are seen if only 1 side of the fovea is involved. When the size of the cyst increases, it pushes the outer plexiform layer toward the opposite side of the fovea, giving the appearance of a cyst at the center of the fovea.

Another peculiar finding was that 11 (18.6%) eyes showed foveal detachments on the SD-OCT examination that could not be characterized as any specific pattern on FA. Most of them (9/11 eyes) were also accompanied with foveal cystic changes. This might contribute to some unexplainable visual deterioration on these patients.

In summary, we found that pathologic changes on SD-OCT correspond with a substantial degree of correlation

with specific patterns on FA. Most notably, loss of retinal layers on SD-OCT was characterized as a specific predictive sign of capillary nonperfusion and severe ischemia. Because ischemic maculopathy is an important predictor of poor functional outcome, we believe that structural changes, as well as the macula perfusion status and the central retinal thickness, should be analyzed when evaluating a patient with DME. Judgment of whether management of DME based on fine retinal structural changes influences clinical outcomes must be reserved pending further investigation with prospective trials.

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