Comparison of Time- and Spectral-Domain Optical Coherence Tomography in Management of Diabetic Macular Edema

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Purpose. Some clinical trials that proved the benefits of anti-VEGF therapy for diabetic macular edema (DME) based retreatment decisions on visual acuity and time-domain ocular coherence tomography (TD-OCT) central subfield thickness changes since the last treatment. This study assessed the impact of TD-OCT followed by spectral domain (SD)-OCT on as needed treatment decision-making in the management of DME with anti-VEGF medications.

Methods. Patients previously treated for DME with anti-VEGF medications in the Retina Division of the Wilmer Eye Institute, following an institutional review board–approved informed consent process, underwent clinical examination, TD-, and SD-OCT imaging. Their retina specialists recorded whether additional anti-VEGF therapy was recommended and their level of certainty in the decision after performing a clinical examination and reviewing a TD-OCT, and then again after reviewing a SD-OCT.

Results. Data were collected for 129 treatment decision pairs involving 67 eyes from 46 subjects. Nonconcordant decisions occurred in 9 (7%) treatment decision pairs. In 7 of these (5%, 95% confidence interval [CI]: 2%–11%), the addition of SD-OCT changed the retina specialist's decision from not recommending to recommending retreatment. The addition of SD-OCT increased the certainty of the retina specialist in 36% (95% CI: 27%–45%) of all treatment decision pairs.

Conclusions. Spectral-domain OCT does not appear to change the ultimate treatment decision or increase the level of certainty of the retina specialist relative to TD-OCT in most cases of DME under anti-VEGF management in clinical practice. The few nonconcordant decisions appear to trend toward recommending more anti-VEGF therapy following SD-OCT.

Keywords: optical coherence tomography, macular edema, diabetic retinopathy

Diabetic macular edema (DME) is an important cause of preventable blindness. It is estimated that 5.9% and 7.5% of patients with early onset (<30 years of age) and late onset (≥30 years of age) diabetes have clinically significant macular edema.[1] For decades, laser photocoagulation[2] was the treatment of choice for DME, but in recent years, researchers have investigated the use of other therapies, including anti-VEGF agents. Vascular endothelial growth factor is believed to play a critical role in the pathogenesis of diabetic retinopathy and DME by promoting angiogenesis and increasing vascular permeability.[3] Several clinical trials have demonstrated that intravitreal injections of anti-VEGF agents, such as ranibizumab[4–7] (Lucentis; Genentech, Inc., South San Francisco, CA), bevacizumab[8] (Avastin; Genentech, Inc.), and aflibercept[9] (VEGF Trap-Eye; Regeneron Pharmaceuticals, Inc., Tarrytown, NY), safely and effectively reduce vision loss associated with DME and achieve superior clinical outcomes compared with laser photocoagulation. Intravitreal anti-VEGF therapy, with injections repeated as often as every 4 weeks, depending on changes in visual acuity (VA) or central subfield thickness on optical coherence tomography (OCT), is expected to play an increasingly prominent role in the management of DME.

In some of the clinical trials that proved the benefits of anti-VEGF therapy for DME, as needed, or pro re nata (PRN), retreatment decisions were based primarily on changes in VA and changes in central subfield thickness using time-domain OCT (TD-OCT). Time-domain OCT uses interferometry-based technology to generate images with an axial resolution of 10 μm.[10] Spectral-domain OCT (SD-OCT) was developed more recently as a next-generation alternative to TD-OCT. Spectral-domain OCT uses a spectrophotometer and Fourier transformation to generate images with an axial resolution of approximately 5 μm.[11] Spectral-domain OCT also allows automated registration of successive images to evaluate changes in retinal structure over time. Furthermore, SD-OCT affords faster acquisition speeds of A scans, such that numerous B scans can densely sample the area of interest in seconds. Given its technical superiority, and reductions in the manufacturing of TD-OCT, it is likely SD-OCT will gradually take the place of TD-OCT. Consequently, it is critical to understand how this change in OCT imaging modality may impact the management decisions of retina specialists. As SD-OCT provides a more detailed characterization of the retina, this modality may identify more retinal abnormalities that prompt treatment, abnormalities that are not visualized or clearly delineated by

TD-OCT. For patients with AMD, it has been reported that Cirrus SD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) detects subretinal and intraretinal fluid more often than Stratus TD-OCT (Carl Zeiss Meditec, Inc.), thus demonstrating the potential for OCT imaging modality to alter clinical decision making when PRN treatment is administered with OCT guidance.[12]

To our knowledge, no study has compared TD-OCT and SD-OCT in the management of PRN administration of anti-VEGF therapy for DME and determined whether the choice of OCT imaging modality affects the decision to offer treatment. Here, we evaluated the impact of TD-OCT followed by SD-OCT on treatment decision making and report that in select cases, the additional information provided by SD-OCT can increase the certainty and change the treatment decisions of retina specialists managing DME with anti-VEGF.

Methods

This investigation was approved by the Johns Hopkins University School of Medicine institutional review board and adhered to the tenets of the Declaration of Helsinki. All subjects provided oral informed consent before participating in the study. Eligible patients were English speaking and at least 18 years of age, with type 1 or type 2 diabetes, any level of diabetic retinopathy, and a history of intravitreal anti-VEGF treatment for DME. The presence of additional ophthalmologic disease was not an exclusion criterion provided that the study investigator's decision making regarding anti-VEGF retreatment would be based primarily on changes in DME. From July 2011 through October 2011, we enrolled a convenience sample of patients presenting for routine follow-up care with one of four study investigators (SBB, DVD, HSY, NMB) at the Retina Division of the Wilmer Eye Institute (Johns Hopkins University, Baltimore, MD). All study procedures were completed during a single visit, and all study procedures were performed in addition to, and not as a substitute for, routine ophthalmologic care. One or both eyes of each patient could be enrolled in the study. If a patient presented for more than one follow-up visit during the enrollment period, each visit was eligible for enrollment.

After obtaining oral informed consent, patients underwent routine clinical examination, TD-OCT imaging, and SD-OCT imaging during the same visit. No standardized clinical examination was required as a part of the study in order to replicate the standard care methods adopted by the individual clinical practitioners. Study investigators used various examination methods, including slit-lamp biomicroscopy and indirect binocular ophthalmoscopy, as needed and at their discretion. Time-domain OCT imaging was performed using the Stratus OCT (Carl Zeiss Meditec, Inc.). Scans included the six radial sections of the fast macular thickness scan (6-mm diameter, 128 A scans/B scan) and the vertical and horizontal cross-hairs (6-mm length, 512 A scans/B scan). Spectral-domain OCT imaging was performed on either the Cirrus HD-OCT (Carl Zeiss Meditec, Inc.) or the Spectralis SD-OCT (Heidelberg Engineering, Inc., Carlsbad, CA). On the Cirrus HD-OCT, the macular cube 512×128 scan (512 A scans/B scan, 128 B scans, 6 mm $\times$ 6 mm) and the vertical and horizontal high resolution line scans (6 mm, 4096 A scans/B scan) were obtained. With the Spectralis SD-OCT, a macular cube was obtained in high speed mode (768 A scans/B scan) using 49 B scans, 120 μm spacing, $20^\circ \times 20^\circ$, and mean automatic-real time score of 16. Additional vertical and horizontal high resolution line scans (20°, 1536 A scans/B scan) were obtained. All scans were centered relative to the fovea. Because each patient participated in the study during a routine follow-up visit, an OCT was ordered at the conclusion of the last nonstudy visit as part of the patient's standard care, and an OCT instrument had been specified. If the standard care OCT was on either SD-OCT machine, a second research OCT was performed on the TD-OCT. If the standard care OCT was on the TD-OCT, a second research OCT was performed on the Cirrus. In the event that the Cirrus was unavailable, the Spectralis was used. All OCTs were obtained by trained OCT technicians at the Wilmer Eye Institute in the usual manner for routine clinical imaging following pupillary dilation.

For all scans, quantitative measurements were calculated by the automated analysis software, and the center subfield (CSF) thickness, volume, and signal strength were recorded. For each TD-OCT scan, the center point thickness (CPT) and the standard deviation of the CPT were recorded as well. The quality of each OCT scan was determined to be either adequate or inadequate by a single observer (MML). An OCT scan was determined to be of inadequate quality if there were moderate or severe boundary errors, using previously described methods for grading OCT quality,[13,14] if the scan was inappropriately centered, or if an alternate scan protocol was used. All scans were used to guide the treatment decision making of the study investigators, but quantitative measurements from OCT scans of inadequate quality were excluded from summary statistics in Table 3.

For each study eye, study investigators recorded whether treatment with additional anti-VEGF medication was recommended (yes or no) and their level of certainty in their decision (very confident: >90% confident; somewhat confident: 75%–89% confident; neither confident nor unconfident: 26%–74% confident; somewhat unconfident: 11%–25% confident; very unconfident: <10% confident), first after reviewing the patient's medical record, performing the clinical examination, and reviewing a TD-OCT, and then again after reviewing a SD-OCT. Any one-step change in this scale of certainty after viewing the SD-OCT was considered to be an increase or decrease in certainty level. Typically, the treating ophthalmologists followed the retreatment regimen used by the Diabetic Retinopathy Clinical Research Network.[4] If any additional imaging, such as fluorescein angiography or fundus photography, was performed during the study visit as a part of the patient's routine follow-up care, these images were reviewed by the study investigator prior to recording the first set of responses. There were 15 study visits during which fundus photography was performed, 41 study visits during which fundus photography and fluorescein angiography were performed, and 73 study visits during which no additional imaging was performed.

Patient characteristics, including age at time of enrollment, age at initial diagnosis of diabetes, race, gender, level of diabetic retinopathy, history of laser treatment for DME and any panretinal photocoagulation (PRP), phakic status, most recent glycated hemoglobin (HbA1c), and VA with habitual correction at the study visit and at the most recent visit prior to the study visit were recorded from the patient's medical record. Data for age at initial diagnosis of diabetes, race, gender, and most recent HbA1c were reported by the patient. Level of diabetic retinopathy was characterized as either nonproliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) by the managing retina specialist. Visual acuity with habitual correction was determined using a standard Early Treatment Diabetic Retinopathy Study (ETDRS) chart. Any fields for which data were unavailable in the patient's medical record were omitted from analyses. All calculations were performed using R statistical software v2.13.0 (The R Foundation for Statistical Computing, Vienna, Austria).

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Table 1. Characteristics of Study Participants

Gender, *n* (%)	
Women	22 (48)
Men	24 (52)
Race, *n* (%)	
Caucasian	35 (76)
Black	8 (17)
Asian	1 (2)
Other	2 (4)
Type of diabetes, *n* (%)	
Early onset (≤30 y)	5 (11)
Late onset (>30 y)	24 (52)
Unknown	17 (37)
Number of study eye(s), *n* (%)	
1	25 (54)
2	21 (46)
Age, y*	68 ± 10 (45, 87)
Age diabetes diagnosis, y, *n* = 29*	46 ± 14 (20, 71)
Glycated hemoglobin, *n* = 26*	7.3 ± 1.0 (5.2, 9.3)

* Mean ± SD (min, max).

Results

During the enrollment period, 49 unique patients participated in the study at least once. Clinical examination, TD-OCT, and SD-OCT data were collected to guide 147 treatment decisions involving 70 eyes from 49 patients. In 18 treatment decisions, data could not be included in this study due to technical difficulties with the OCT viewing software (*n* = 16), OCT images obtained for the incorrect eye (*n* = 1), and inadvertent viewing of the SD-OCT image by the study investigator before viewing the TD-OCT image (*n* = 1). Ultimately, data were collected for 129 treatment decision making pairs involving 67 eyes from 46 participants. Study participant characteristics are summarized in Tables 1, 2, and 3.

Treatment decision making results are summarized in Tables 4 and 5. In the 129 treatment decision pairs, treatment with additional anti-VEGF was recommended in 65% of visits after viewing the TD-OCT and 69% of visits after viewing the SD-OCT. Additional anti-VEGF was recommended in 63% of visits when Cirrus was used as the SD-OCT modality, compared with 81% of visits when Spectralis was used (Pearson's χ^2 test, $P = 0.07$). Nonconcordant decisions occurred in nine (7%) treatment decision pairs (exact binomial test, 95% confidence interval [CI]: 3%–13%). In seven of these nine, or 5% (95% CI: 2%–11%) of all treatment decision pairs, the addition of SD-OCT changed the retina specialist's decision from not recommending to recommending treatment. For four of the nine nonconcordant decision pairs, additional imaging was performed during the study visit as a part of the patient's routine care. For two visits, fundus photography was performed, and for two visits, fundus photography and fluorescein angiography were performed. The nine nonconcordant decision pairs were from nine unique patients.

When additional anti-VEGF treatment ultimately was not recommended, the certainty of the retina specialist increased in 48% of visits after viewing the SD-OCT. The certainty of the

Table 2. Characteristics of Study Eyes

Antivascular endothelial growth factor agent at last administration, *n* (%)	
Ranibizumab	54 (81)
Bevacizumab	13 (19)
Number of study visits, *n* (%)	
1	27 (40)
2	23 (34)
3	12 (18)
4	5 (8)
Level of diabetic retinopathy, *n* (%)	
Nonproliferative diabetic retinopathy	47 (70)
Proliferative diabetic retinopathy	20 (30)
Phakic status, *n* (%)	
Phakic	35 (52)
Not phakic	32 (48)
Previous therapies, *n* (%)	
Laser for diabetic macular edema	37 (55)
Panretinal photocoagulation	20 (30)

Table 3. Parameters for Treatment Decisions

Time since most recent injection, *n* (%)	
14–30 d	30 (23)
31–60 d	50 (39)
61–90 d	23 (18)
>90 d	26 (20)
Time since most recent visit, *n* (%)	
7–30 d	42 (33)
31–60 d	66 (51)
61–90 d	9 (7)
>90 d	12 (9)
Anti-VEGF treatment during most recent visit prior to study visit, *n* (%)	86 (67)
Visual acuity at study visit, *n* (%)	
20/20 or better	14 (11)
20/25–20/40	55 (43)
20/50–20/80	42 (33)
20/100–20/250	18 (14)
CSF thickness at study visit, TD-OCT*	
mean ± SD	291 ± 109
median (25th, 75th quartile)	263 (209, 335)
CSF thickness at study visit, Cirrus*	
mean ± SD	299 ± 79
median (25th, 75th quartile)	278 (244, 326)
CSF thickness at study visit, Heidelberg*	
mean ± SD	400 ± 135
median (25th, 75th quartile)	384 (286, 494)
Volume at study visit, TD-OCT†	
mean ± SD	7.6 ± 1.8
median (25th, 75th quartile)	7.0 (6.6, 8.3)
Volume at study visit, Cirrus†	
mean ± SD	10.1 ± 1.0
median (25th, 75th quartile)	10.1 (9.6, 10.5)
Volume at study visit, Heidelberg†	
mean ± SD	9.9 ± 2.3
median (25th, 75th quartile)	9.3 (8.5, 10.6)

* Cannot be graded in 24 TD-OCT, 14 Cirrus, and 11 Heidelberg OCT images due to boundary line placement, decentration, or use of an alternate scan protocol.

† Cannot be graded in 30 TD-OCT, 31 Cirrus, and 19 Heidelberg OCT images due to boundary line placement, decentration, or use of an alternate scan protocol.

Table 4. Treatment Decisions From Study Visits

	Cirrus, SD		Spectralis, SD		All SD	
	Yes	No	Yes	No	Yes	No
TD-OCT						
Yes	48 (55%)	2 (2%)	34 (81%)	0 (0%)	82 (64%)	2 (2%)
No	7 (8%)	30 (35%)	0 (0%)	8 (19%)	7 (5%)	38 (30%)

retina specialist increased in only 30% of visits when additional anti-VEGF was ultimately recommended (Pearson's χ^2 test, $P = 0.09$). Overall, the addition of SD-OCT increased the certainty of the retina specialist in 36% of all treatment decision pairs (exact binomial test, 95% CI: 27%–45%).

Representative OCT images from nonconcordant decision pairs are shown in Figures 1 and 2. Cirrus was the SD-OCT instrument for all nine nonconcordant decision pairs. Optical coherence tomography findings and impressions were described by the managing retina specialists, either verbally or in writing, during the study visits. Figure 1 includes images from the seven nonconcordant decision pairs in which the retina specialist's decision changed from not recommending to recommending additional anti-VEGF treatment. In 1A and 1C, cystoid abnormalities were seen on TD-OCT, but the extent and severity of these abnormalities were more apparent on Cirrus. In 1B, 1E, and 1G, juxtafoveal fluid was seen on both TD-OCT and Cirrus, but cystoid abnormalities in the central subfield were only observed on Cirrus. In 1D, intraretinal fluid was visualized on both TD-OCT and Cirrus, but the extent of subretinal fluid was more apparent and substantial on Cirrus. In 1F, no fluid was seen on either TD-OCT or Cirrus. Comparing the Cirrus from the study visit with the Cirrus from the most recent previous visit 3 months prior demonstrated resolution of cystoid abnormalities and thinning in the superior parafoveal region (Fig. 3), suggesting continued improvement with anti-VEGF therapy, which motivated this investigator to continue treatment until improvement plateaued. Figure 2 shows representative OCT images from the two nonconcordant decision pairs in which the decision changed from recommending to not recommending additional anti-VEGF treatment. In both Figures 2A and 2B, cystoid abnormalities were observed on TD-OCT. On Cirrus, comparison with the most recent previous study more clearly demonstrated that the edema had remained stable. For Figure 2A, the patient's most recent ranibizumab injection was 3 months prior to the image in this figure. For Figure 2B, the patient received both ranibizumab and laser photocoagulation 1 month prior to the image in this figure.

Discussion

Since the introduction of SD-OCT, which offers faster imaging speed, higher resolution images, and improved registration of longitudinal scans with three-dimensional visualization of the retinal layers, ophthalmologists have had more information to guide clinical management decisions than previously available on TD-OCT alone. Studies have also demonstrated that SD-OCT may be more sensitive for detecting retinal changes associated with AMD,[12,15,16] glaucoma,[17] uveitis,[18] and toxoplasma retinochoroiditis.[19] Although technical differences between various OCT instruments have been well characterized, the impact of OCT modality on clinical decision making and management has not been fully evaluated. In this study, we report the impact of TD-OCT followed by SD-OCT on clinical decision making in the management of anti-VEGF therapy in eyes with DME.

The design of this study allowed for documentation of retina specialists' treatment decision making in their customary clinical setting. One potential limitation of this design is that independent evaluation of the images by masked evaluators might have permitted comparison of the pathological features in TD-OCT and SD-OCT images that might have led to different rates of agreement. However, this type of comparison would have its limitations by being performed in an artificial environment in which first-hand clinical exam findings could not have been integrated realistically into the treatment decision. Since the goal of the study was to compare treatment decisions with TD-OCT followed by SD-OCT in the clinic setting across multiple patients and across multiple physicians, the methods did not include additional comparisons by masked graders of the OCT. Because decision making in the management of anti-VEGF for DME relies on clinical exam findings, such as patient symptoms, VA findings, and ophthalmoscope findings, in addition to OCT findings, expert grading of the OCT outside of the clinic environment would not have allowed us to achieve our aim, which was to evaluate clinical decision making in a realistic environment. For this reason, it was necessary for retina specialists to evaluate the TD-OCT and

Table 5. Treatment Certainty From Study Visits by Treatment Recommendation

	Increased	No Change	Decreased
Treatment certainty after viewing SD-OCT image: yes, $n = 89$			
TD-OCT then Cirrus, SD	21 (38%)	34 (62%)	0 (0%)
TD-OCT then Spectralis, SD	6 (18%)	28 (82%)	0 (0%)
Total	27 (30%)	62 (70%)	0 (0%)
Treatment certainty after viewing SD-OCT image: no, $n = 40$			
TD-OCT then Cirrus, SD	14 (44%)	17 (53%)	1 (3%)
TD-OCT then Spectralis, SD	5 (63%)	3 (38%)	0 (0%)
Total	19 (48%)	20 (50%)	1 (3%)
Treatment certainty after viewing SD-OCT image: all, $n = 129$			
TD-OCT then Cirrus, SD	35 (40%)	51 (59%)	1 (1%)
TD-OCT then Spectralis, SD	11 (26%)	31 (74%)	0 (0%)
Total	46 (36%)	82 (64%)	1 (1%)

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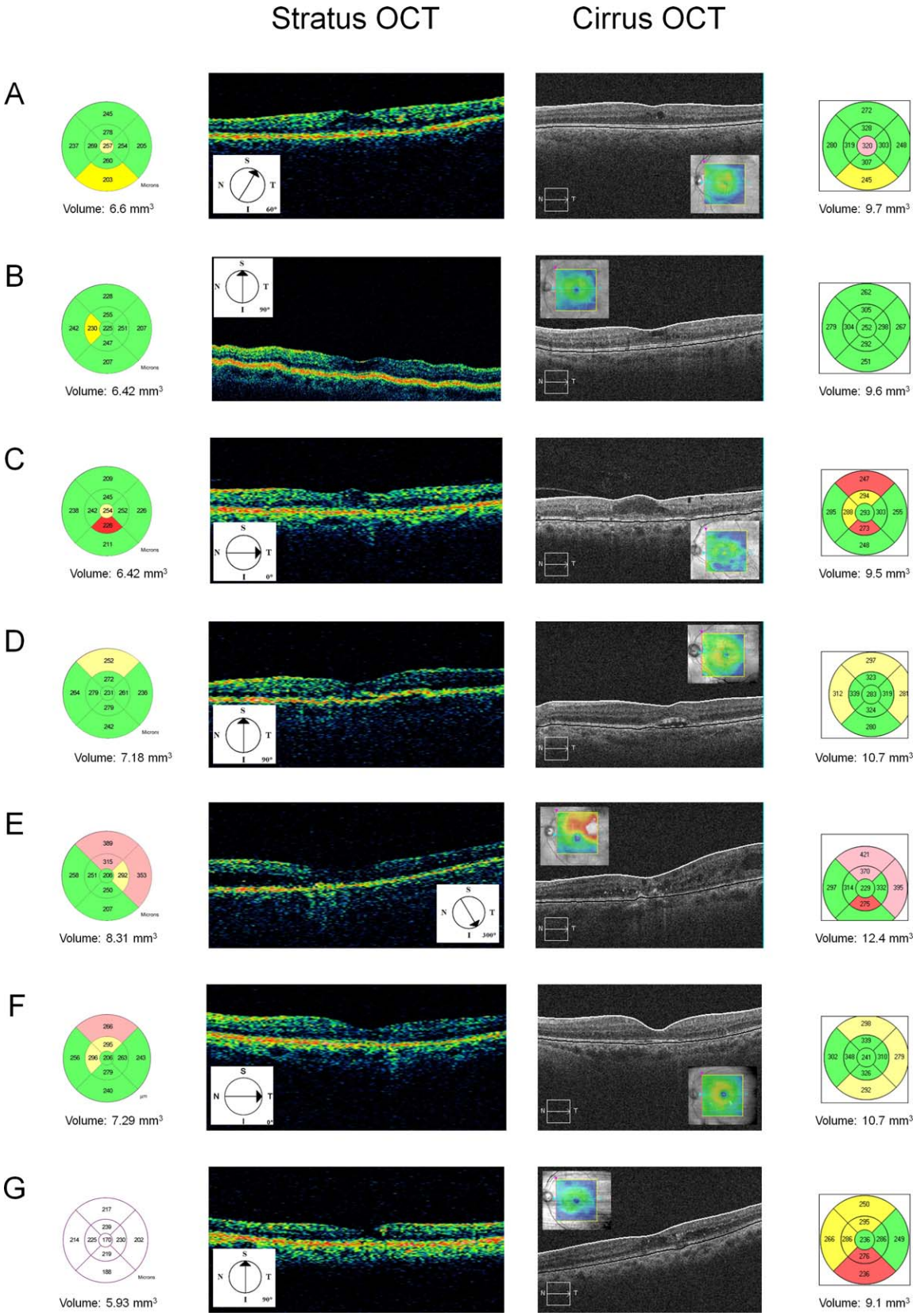

Figure 1. Nonconcordant treatment decision pairs: no treatment to treatment. (**A**) Questionable cystoid abnormalities superotemporally on TD-OCT. Cirrus shows relative loss of the foveal depression and parafoveal cystoid abnormalities. (**B**) Time-domain OCT fast macular scan shows no interstitial fluid (image not shown). On vertical high resolution cross hair, cyst present in immediate juxtafoveal region superiorly. On Cirrus, cysts temporally are more easily appreciated. Cyst immediately beneath the fovea extending inferotemporally not fully appreciated on TD-OCT. (**C**) On TD-OCT, cystoid abnormalities with thickening in central subfield, but questionable whether edema had worsened relative to previous visit. On Cirrus, extent of fluid more apparent and substantial. (**D**) Intraretinal fluid seen on both TD-OCT and Cirrus. Extent of subretinal fluid more

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apparent and substantial on Cirrus. (**E**) Juxtafoveal fluid seen superiorly on both TD-OCT and Cirrus. Cystoid abnormalities in central subfield only observed on Cirrus. (**F**) On TD-OCT, normal foveal depression with no evidence of interstitial fluid. Cirrus shows thinning and absence of cysts in temporal parafoveal region, which were seen in multiple images from previous visit. (**G**) Questionable small cystoid abnormality in superior parafoveal region on TD-OCT. Cirrus shows interstitial fluid in juxtafoveal area temporally and nasally and beneath the fovea.

SD-OCT images sequentially during routine clinic visits. Given the technical superiority of SD-OCT, retinal features that can be visualized on TD-OCT may be expected to be similarly, or more clearly, visualized on SD-OCT. Therefore, our study design, in which TD-OCT evaluation was followed by SD-OCT evaluation, allowed for an accurate assessment of the impact of the additional information afforded by SD-OCT on clinical decision making.

Because study eligibility was not limited with respect to VA, level of diabetic retinopathy, media opacity, or the presence of other ophthalmologic diseases, provided that DME was the primary pathology determining the need for additional anti-VEGF therapy, our study population presumably represented a broad spectrum of DME patients. Another limitation of the study, however, is that participants were mostly Caucasian and Black, while other ethnic groups were poorly represented. All OCTs also were collected in the usual manner for routine clinical imaging, without added requirements for image quality. Although quantitative measurements of CSF thickness and volume were excluded from analyses for 19% and 31%, respectively, of all OCTs due to boundary errors, decentration, or use of an alternate scan protocol, all OCT images were otherwise judged adequate to visualize retinal morphology and guide clinical decision making.

In the management of DME with anti-VEGF therapy, there appears to be generally good agreement between treatment decisions guided by TD-OCT and SD-OCT imaging modalities. In the majority of all treatment decision pairs, the addition of SD-OCT did not change the ultimate treatment decision or increase the level of certainty of the retina specialist. However, in 7% of instances, the addition of SD-OCT changed the ultimate treatment decision, and in 36% of instances, the addition of SD-OCT increased the certainty of the retina specialist, demonstrating that in this study population, OCT imaging modality had a measurable, though limited, impact on clinical decision making. Since the SD-OCT was evaluated after the TD-OCT, this design biases toward overestimating the impact of SD-OCT on changes in confidence level. Even in this context, an increase in the level of confidence of the retina specialist was detected only in a minority of instances.

The majority of nonconcordant decisions tended toward recommending more anti-VEGF treatment after viewing the SD-OCT. In these instances, the presence or severity of abnormalities warranting retreatment was often more apparent on SD-OCT than on TD-OCT. This finding is consistent with previous reports describing the greater sensitivity of SD-OCT for detecting retinal pathology. Spatial registration of SD-OCT images from the study visit to the most recent previous visit also facilitates visualization of changes in retinal morphology and was occasionally a factor that led to a change in the ultimate treatment decision. For both of the decision pairs in which treatment was recommended based on the TD-OCT, but not on the SD-OCT, longitudinal comparison facilitated by the automated registration software of the SD-OCT demonstrated that the edema was stable; therefore, the clinician was comfortable recommending observation. For one nonconcordant decision pair in which treatment was ultimately recommended, longitudinal comparison demonstrated improvement following the most recent anti-VEGF injection and led to the decision to offer additional therapy to potentially dry the retina further.

Although we note that Cirrus was the SD-OCT modality for all nonconcordant decision pairs in this study, additional investigation would be needed to characterize treatment decision making differences between Cirrus and Spectralis due to the limited size of this study population and the

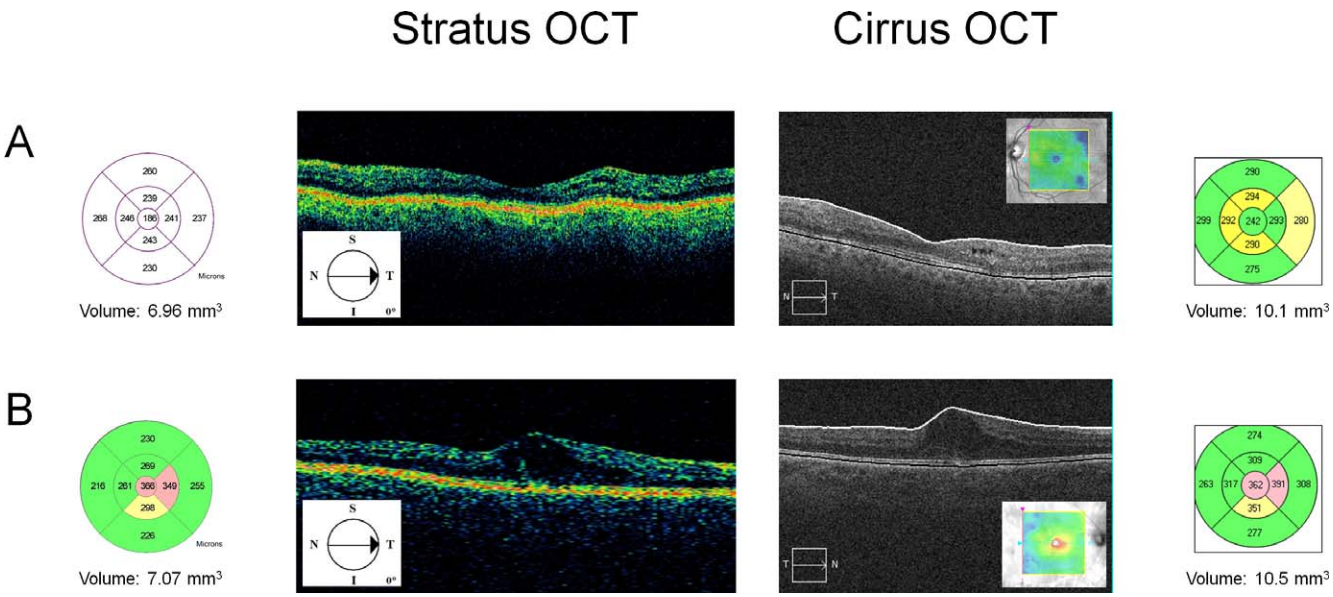

Figure 2. Nonconcordant treatment decision pairs: treatment to no treatment. (**A**) Mild cystoid abnormalities in temporal parafoveal region on TD-OCT. Cirrus shows small cystoid abnormality temporally with normal foveal depression in the absence of thickening. (**B**) Time-domain OCT and Cirrus show large cystoid abnormality in central subfield with loss of normal foveal depression. On Cirrus, comparison with most recent previous study showed that while retinal thickening persisted, fluid was judged to be stable and not to warrant resumption of anti-VEGF therapy unless worsening was noted.

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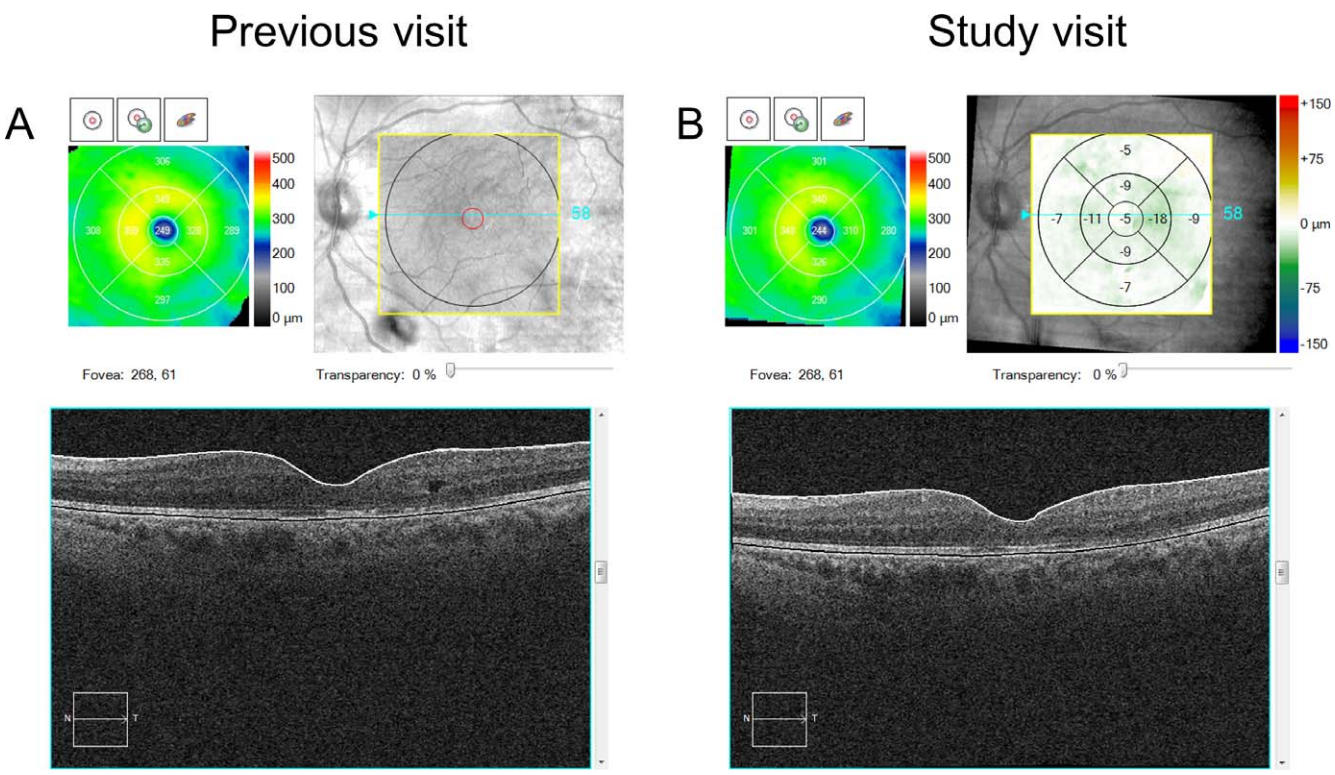

Figure 3. Improvement demonstrated by spatial registration of sequential Cirrus images. (**A**) Cirrus image from most recent previous visit and (**B**) Cirrus image from study visit for patient in Figure 1F. Comparison demonstrates thinning and resolution of perifoveal cystoid abnormalities.

predominant use of Cirrus as compared with Spectralis among our study eyes. Further studies are also needed to identify specific clinical factors that may be associated with non-concordant treatment decisions. Spectral-domain OCT may lead to an increase in the number of additional anti-VEGF treatments for some patients, but it is unknown whether this would lead to a clinically relevant difference in VA outcomes.

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