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Comparison of Spectral Domain OCT Scan Patterns and Clinical Review Strategies in Neovascular Age-related Macular Degeneration

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Abstract

Purpose—To compare various SDOCT scan patterns and review strategies to identify an optimal imaging workflow for neovascular age-related macular degeneration (NVAMD).

Methods—A retrospective consecutive case series was performed in eyes following anti-VEGF therapy for NVAMD with concurrent SDOCT imaging (Zeiss Cirrus), including horizontal/vertical 5-line rasters, and macular cube analysis. For each scan pattern, a single report was independently reviewed in a masked fashion within the clinical image review software, while the cube was reviewed line-by-line in the reader software for the presence of fluid.

Results—One hundred fifty-six reports and 39 cube scans of 39 patients were included. Among all SDOCT scans, 64% (25/39) had definitive fluid and 95% (37/39) had possible fluid. Sensitivities for definite fluid detection for horizontal, combined horizontal/vertical, and horizontal/vertical/map reviews were 68%, 76%, and 88%, respectively. When assessing for possible fluid, sensitivities for detection for horizontal, combined horizontal/vertical, and horizontal/vertical/map reviews were 76%, 92%, and 97%, respectively. Line-by-line review of the cube scan had a sensitivity for definite and possible fluid detection of 96% and 86%, respectively.

Conclusions—Optimizing both clinical accuracy and work-flow are important factors in managing NVAMD. A zero-tolerance strategy with vertical/horizontal raster scans and thickness maps was comparable to line-by-line review of the cube to detect possible fluid.

Keywords

OCT; optical coherence tomography; AMD; age-related macular degeneration; exudation; choroidal neovascularization; intraretinal fluid; subretinal fluid; neovascular AMD; NVAMD; anti-VEGF

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Introduction

Since its introduction in 1991, optical coherence tomography (OCT) has transformed the practice of ophthalmology.¹ More recently, OCT has become a vital diagnostic test in the evaluation of patients with neovascular age-related macular degeneration (NVAMD), serving as the key means of identifying active exudation in the clinic and in national clinical trials.^{2–5} Identification of fluid either within or beneath the retina provides a marker of choroidal neovascular exudation and influences both a clinician's decision to treat and the length of follow up interval.^{6–8}

Despite the ubiquity of OCT in clinical practice, no standardized protocol for scan acquisition or review exists. Systems offer multiple approaches to scan strategy and reviewing images. Most offer over-sampled averaged raster scans that provide reduced scan density of the area of interest, compared to standard volumetric cube scans. The increased sampling density in the cubes provides a line-by-line review with minimal spacing issues for identifying areas of interest. However, these scans are not typically averaged and will frequently have more speckle noise which may limit the visualization of subtle fluid areas that may be seen on an averaged raster scan. Frequently, image reports, such as a PDF file, of the raster scans and cube analysis are published to a review software and reviewed electronically or in print by the clinician in real-time during the patient encounter. In this setting, accuracy, as well as efficiency, of review are clinically relevant, particularly in pro re nata (PRN) and treat-and-extend regimens.

Numerous studies have been published comparing the effectiveness of spectral domain (SD) and time domain (TD) OCT in the management of NVAMD.^{9–12} More recently, the sensitivity of fluid detection with SDOCT raster scans was compared to macular cube review in new patients 1 month following initial anti-VEGF treatment.¹³ Approximately 80% of patients are expected to have fluid 1 month following initiation of anti-VEGF treatment,⁴ while the proportion of patients with fluid on OCT declines significantly over the first 3 months of injections.⁷ At this time point many clinicians adopt a PRN or treat-and-extend regimen that relies on the presence or absence of fluid on OCT to determine if treatment is necessary and adjust the follow up period.^{4,5,7,8} Despite the importance of fluid identification on the OCT, fluid is often missed by the clinician. For example, in the CATT study only 75% of the 6401 patient encounters that had evidence of fluid recognized by the reading center were identified by treating physicians in real-time.⁴ Furthermore, while PRN treatment yields excellent visual acuity results, the CATT study revealed a slight difference in the PRN and monthly arms suggesting under-treatment in some patients on a PRN regimen, highlighting the critical importance of fluid recognition.⁴ Nevertheless, the use of an OCT-guided treatment regimen rather than monthly treatment emphasizes the importance of accurate OCT interpretation. The purpose of this study is to compare various OCT scan patterns and review strategies to identify a clinically relevant “real-world” optimal OCT imaging strategy for NVAMD with a focus on a common time point for treatment decisions (3 months following anti-VEGF therapy).

Methods

Cleveland Clinic Institutional Review Board approval was obtained. A retrospective consecutive case series was carried out to identify patients with NVAMD (362.52) and concurrent SDOCT imaging with horizontal 5-line rasters (4096 A scans per B Scan), vertical 5-line rasters, and macular cube analysis (512 A scans x 112 B scans) (Cirrus, Carl Zeiss Meditec, Dublin, CA) who were undergoing anti-VEGF therapy. Only the month 4 encounter was analyzed in the study. Specifically, patients were included who presented with a new diagnosis of NVAMD were treated with monthly anti-VEGF therapy for 3 consecutive months, and then on the 4th month (3–6 weeks after their 3rd consecutive injection) evaluated with SDOCT with all of the above parameters. This time point was selected as a common time point where anti-VEGF therapy may be discontinued if fluid has resolved and/or the treatment interval may be extended. If both eyes were affected only the right eye was included in the analysis. Patients with any other diagnosis that could contribute to intra- or subretinal fluid, such as diabetic retinopathy, macular telangiectasia, retinal vein occlusion, pathologic myopia, central serous chorioretinopathy, vitreomacular traction were excluded from study.

A single published report was reviewed for each of the horizontal and vertical rasters, the macular thickness map, and macular thickness change analysis (Figure 1) with clinical image review software (Zeiss Forum). These reports were not altered (e.g., image switching) from the original report published by the ophthalmic photographer for clinical assessment on the day the patient presented. The macular cube was reviewed line-by-line in the Cirrus reader software. Each of the reports was assessed for the presence or absence of “definite exudation” as defined by unequivocal intra- or subretinal fluid (Figure 2A–B). In addition to unequivocal fluid, images were also scored for any possible fluid to assume a “zero-tolerance strategy” for any potential fluid present (Figure 3A–B). The line-by-line scans were reviewed for identical variables with Cirrus reader software for the macular cube. There were 2 experienced graders (RJC, JIM) who reviewed the images independently and in a masked fashion; any disagreement was resolved by a 3rd independent grader (JPE).

For analysis of the macular thickness maps and change analysis, three thresholds were predefined as “disease activity”: (1) any area of thickness greater than 400 microns on the macular thickness analysis report (Figure 4), (2) an increase of 10 microns on any of the sub-areas measured by the macular change analysis report (Figure 5), and (3) any evidence of definite exudation on the representative single horizontal and vertical raster presented on the macular thickness analysis report. These thresholds were based on the authors’ clinical experience that would reflect potential true clinical change. For the change analysis maps, the 10 micron change was selected as it is 2–3 times the resolution of the Cirrus device and potentially represented real change. For the overall thickness map, the 400 micron level was also selected for similar reasons based on ease of recognition on the thickness map and the likelihood of representing true clinical change. The gold standard for both unequivocal and the zero-tolerance strategy were the sum total findings of all B-scan patterns (e.g., fluid on any scan).

Results

Five hundred fourteen encounters from 43 patients were identified based on the diagnosis of NVAMD and reviewed for potential inclusion in the study. One hundred fifty-six reports and 39 cube scans of 39 patients were included in the study based on the inclusion criteria. These 39 eyes were identified with a new diagnosis of NVAMD treated for 3 consecutive months with intravitreal anti-VEGF injections and had SDOCT evaluation one month following the last injection. Of the 39 eyes, 25 eyes (64%) had definitive fluid on any scan and 37 eyes (96%) had possible fluid. Review of only the horizontal raster report demonstrated definite fluid in 44% (17/39) and possible fluid in 72% (28/39), corresponding to sensitivities of 68% (17/25) and 76% (28/37), respectively. Review of the vertical raster report demonstrated definite fluid in 38% (15/39) and possible fluid in 82% (32/39), for sensitivities of 60% (15/25) and 86% (32/37), respectively. Combining both horizontal and vertical reports revealed definite fluid in 49% (19/32) of eyes and possible fluid in 87% (34/39) of eyes, yielding sensitivities of 76% (19/25) and 92% (34/37), respectively. By comparison, the line-by-line review of the cube revealed definite fluid in 62% (24 out of 39 eyes), for a sensitivity of 96% (24/25). For a zero tolerance strategy, the cube demonstrated possible fluid in 82% (32/39), for a sensitivity of 86% (32/37).

The map analyses provided useful surrogates for fluid. The macular change analysis showed a focal area of increased thickness greater than 10 microns in 31% (12/39) corresponding to areas of exudation. The macular thickness analysis report showed a focal area of thickness greater than 400 microns in 46% (18/39). The macular thickness analysis report horizontal and vertical rasters demonstrated definite fluid in 49% (19/39), a sensitivity of 76% (19/25). Reviewing the single page macular thickness analysis report demonstrates at least possible fluid in 62% (24/39), a sensitivity of 65% (24/37). Reviewing the horizontal and vertical raster reports as well as map reports and change analysis, definite fluid was demonstrated in 56% (22/39) and possible fluid in 92% (36/39), corresponding to sensitivities of 88% (22/25) and 97% (36/37), respectively.

Discussion

Previous studies have reported improved identification of intra- and subretinal fluid with SDOCT over TDOCT in patients with neovascular AMD.^{9,10,12} SDOCT based macular map analyses have also been shown to be more accurate than those obtained with TDOCT.¹¹ Until recently however, little was known about the rates of fluid detection with different SDOCT acquisition and review patterns. One report compared 5 -line SD-OCT raster reports to line-by-line cube review in 79 patients at one month after initiation of anti-VEGF therapy.¹³ Of the 63 patients with fluid on line-by-line cube review, 62 had fluid on at least the 5 or 20-line raster report, leading the authors to conclude that raster scans have a similar sensitivity to the cube for fluid detection. In contrast, another recent report that compared 9 mm horizontal 5-line rasters with a 6 x 6 mm volumetric cube found that line-by-line review of the cube was more sensitive in identifying fluid than rasters in patients with treatment resistant NVAMD.¹² Our study examined the “real-world” comparison of raster and macular thickness reports reviewed on a clinical image review software platform to the line-by-line review of the macular cube with the reader software similar to what would occur in practice.

A combination of different scan patterns reviewed as published reports demonstrated a similar sensitivity for fluid detection compared to line-by-line review of the macular cube.

Numerous differences in study design between the present study and its contemporaries may help to explain the differing results. First, this study defined different thresholds of fluid detection, creating a distinction between definite fluid and possible or suspected fluid. For definite exudation, the 5-line horizontal raster report found fluid in 17 eyes and the 5-line vertical raster report found fluid in 15 eyes whereas line-by-line review of the cube demonstrated definite fluid in 24 eyes. De Niro et al utilized a 9-mm 5-line raster pattern rather than the 6-mm, which inherently would increase the sampling results. By comparison, in this study the horizontal raster report identified possible fluid in 28 patients, while the vertical raster report and cube both identified possible fluid in 32 patients. This is more in agreement with De Niro. As neither previous report reviewed images for suspected fluid, it is possible that our threshold for definite fluid detection may differ from previous studies. Based on the timing and/or patient populations, both previous reports have a higher pre-test probability of fluid appearance on SDOCT. As the presence of fluid decreases with additional treatment of naïve choroidal neovascular membranes, so too will the probability of detecting fluid with any modality.⁷ De Niro et al evaluated patients after a single treatment, a time period with a greater probability of detecting fluid on any scan.¹³ Major et al evaluated patients with recalcitrant fluid on OCT despite an average of 28 preceding anti-VEGF injections; in this population too, there is an expectedly higher probability of fluid presence.¹² Both of the previous studies utilized reader software to review the raster scans in a line-by-line fashion, rather than a single published report as was performed in this study.

There is less known about the utility of segmentation volumetric analysis reports, such as the macular thickness analysis report. A comparison of a radial raster pattern to the fast macular thickness map volumetric analysis on the Stratus TDOCT device found significantly fewer segmentation errors and more accurate retinal thickness measurements with the radial raster pattern in patients with NVAMD.¹⁴ However, with the transition from TDOCT to SDOCT, the frequency of segmentation errors has decreased and the reproducibility of retinal thickness measurements increased, allowing for greater utilization of macular map analysis generated by volumetric or cube acquisition patterns.¹¹ A small study which included 8 patients with NVAMD found no significant difference in SDOCT retinal thickness measurements between a radial raster pattern and macular map.¹⁵ In the present study the single page macular thickness report, when reviewed for definite exudation on the single horizontal and vertical rasters and for possible exudative activity as defined by a focal area of greater than 400 microns on the map representation, provides a surprising wealth of information. Reviewing only the single horizontal and vertical rasters on the macular thickness analysis report identifies definite exudation in 19 patients, similar to the 19 patients identified with reviewing both the horizontal raster report and vertical raster report. While analyzing the macular map for any focal areas of thickness greater than 400 microns only identifies 18 patients with possible exudation, combining this review technique with the included horizontal raster and vertical raster yields 24 eyes with possible fluid that may be considered for anti-VEGF therapy, equaling that of line-by-line review of the cube for definite fluid. The signal-to-noise ratio of raster scans exceeds that of volumetric scans whereas volumetric scans provide imaging over a greater sampling density of the retina in

comparison to raster scans. With improved signal to noise ratio, the visualization of subtle pathology on the raster scans exceeds that of a single cube b-scan. This higher resolution scanning pattern may better identify areas of suspected intra- or subretinal fluid than volumetric analysis. In the current study, the raster scans identified 3 patients with suspected fluid that were not identified by line-by-line cube review; by comparison, line-by-line cube review identified a single patient not identified by the rasters.

The present study sought to identify efficient and accurate methods of obtaining and reviewing SDOCT images in patients with NVAMD through an assessment of one “real-world” practice of image review. The efficiency of clinical practice depends on many variables. Time for scan acquisition, ability to cooperate with scan protocol, distance from scanner to exam room, time to print published images, and the distance to OCT reading station all directly influence the efficiency of image review. Optimizing office flow and utilizing remote access reader software or published reports (ideally within exam rooms or in a central station between exam rooms) are some options to increase clinical throughput. The scan protocol and the capabilities of a reader software platform, as well as the individual clinician’s style influence the accuracy of image interpretation. Defining an OCT acquisition and review protocol that maximizes the rapid detection of subtle signs of active NVAMD has the ability to not only influence clinical efficiency, but also influence patient outcomes.

There are noteworthy limitations to the present study including its retrospective design and sample size. Any study evaluating the sensitivity of fluid detection of different OCT devices and scan patterns is lacking a clear gold standard of what defines “true” fluid. For this study, we defined both definitive fluid and possible fluid to help facilitate consistent interpretation. This study sought to examine comparative review strategies in a “real-world” clinical environment to better define strategies that provide the clinician with decision-making information regarding treatment and follow-up. Time variables for reviewing the various reports and line-by-line review were not available to truly define “clinical efficiency” differences in this study; likewise, the time required to obtain various scan protocols depends on patient and photographer and was not studied.

Ultimately, each clinician will define his or her own threshold for fluid identification on OCT in patients with NVAMD. The clinical utility, both in terms of accuracy and efficiency, of an image acquisition and review strategy will depend on each individual clinician’s preference and practice pattern. However, it appears that published reports, including raster scans and thickness analysis provide the clinician with important information that nearly mirrors the line-by-line cube review in this study. Further study with different SDOCT devices and time studies will be needed to identify the most efficient and accurate means of imaging patients with neovascular AMD to determine therapy and follow-up intervals. As many physicians continue to individually tailor treatment regimens to patients through “as-needed” or “treat-and-extend” approaches, the critical importance of fluid detection and avoidance of undertreatment is underscored by recent NVAMD clinical trials.^{4,5} Optimizing clinical accuracy and efficiency of image review will continue to be vital to patient outcomes and satisfaction.

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Summary Statement

Multiple OCT review strategies are compared to assess sensitivity of detection of disease activity in NVAMD. Compiling multiple scan patterns (e.g., vertical and horizontal rasters) and analyses (e.g., macular thickness map) provides similar detection to line-by-line review of the macular cube.

Figure 1. Compilation of spectral domain optical coherence tomography (SDOCT) reports reviewed as presented in the clinical image review software package. (A) SDOCT macular thickness map with focal area of thickening > 400 microns and intraretinal fluid present on the B-scans. (B) Macular change analysis with focal area of increased thickening of > 10 microns. (C) Horizontal 5-Line raster report with definitive fluid in windows 4 and 5. (D) Vertical 5-Line raster report with definitive fluid present in windows 1, 2, and 4.

Figure 2. Representative spectral domain optical coherence tomography (SDOCT) raster scans exhibiting definitive exudation. (A) Definitive intraretinal fluid is present on the SDOCT scan (white arrows). (B) Definitive subretinal fluid (white asterisk) is visualized on the SDOCT scan.

Figure 3. Representative spectral domain optical coherence tomography (SDOCT) raster scans exhibiting possible exudation. (A) Possible intraretinal fluid is present on the SDOCT scan (white arrowhead). (B) Possible subretinal fluid (white arrow) is visualized on the SDOCT scan.

Figure 4. Representative spectral domain optical coherence tomography macula thickness map revealing areas of thickening > 400 microns and definitive fluid on the B-scan windows.

Figure 5.
Representative spectral domain optical coherence tomography macular change analysis with focal area of increased thickening of > 10 microns.