Optical Coherence Tomography – Segmentation Performance and Retinal Thickness Measurement Errors

Dessislava Nikolaeva Koleva-Georgieva

Assistant Professor, Department of Ophthalmology, University Hospital 'St George', Plovdiv, Bulgaria

Abstract

Optical coherence tomography (OCT) has become an indispensable tool in the assessment of macular pathology in clinical settings and an integral part of many clinical trials. However, as with any imaging technology, some limitations exist. In this review, the author describes and discusses the various causes that might compromise automated retinal thickness measurements. The segmentation software might perform less accurately in the presence of scan artefacts (e.g. 'out-of-range', mirror, blink and motion artefacts), a low signal:noise ratio, dense media opacities and specific retinal pathological features (e.g. pigment epithelial detachment, subretinal fluid, fibrotic tissue, hard exudates and full-thickness macular holes). The awareness of the clinician and the particular search for, and recognition of, measurement errors would improve the accuracy of OCT interpretation and should be an integral part of OCT scan analysis.

Optical coherence tomography (OCT) was introduced by Huang and colleauges in 1991[1] and became commercially available in 1995. It is a fast, non-invasive, non-contact method that enables *in vivo* visualisation of the retinal and vitreoretinal microstructure on a high-resolution cross-section (2D) or 3D image.[2–5] OCT is also a powerful method for obtaining retinal thickness measurements. Owing to its ability to quantify changes in retinal thickness, OCT has become an indispensable tool for assessing treatment initiation, the response to treatment and the need for retreatment in many retinal diseases. OCT is now an integral part of both retinal clinical practice and many clinical trials. As clinicians are becoming increasingly reliant on OCT retinal thickness measurements, it is important to determine their accuracy.

Several studies have presented good reproducibility of OCT retinal thickness measurements and have shown that it is currently the most precise and reliable instrument for retinal thickness measurements.[6–9] However, all imaging techniques have some limitations and are subject to artefacts. Several studies have uncovered and analysed multiple sources of errors that decrease the accuracy of retinal thickness measurements.[10–12] Over the past few years, increasing evidence has accumulated, based on the concern of many ophthalmologists, of the limitations of current OCT devices and software. Knowledge, anticipation and recognition of image artefacts and erroneous thickness measurements by both OCT technicians and physicians are needed to reduce the influence of such errors on OCT interpretation.

Retinal thickness is defined as the distance between the inner retinal boundary (vitreous–retina interface) and the outer retinal boundary (retina–retinal pigment epithelium interface).[3,13] The automated retinal thickness measurement is based on the ability of the software to detect the inner and outer boundaries based on the change in reflectivity at each of these interfaces. If the software fails to delineate the retinal boundaries correctly (i.e. segmentation break-down), it will result in thickness measurement error. Retinal thickness is displayed on a topographic map and numerical values are given for centre-point thickness, for each of the nine Early Treatment Diabetic Retinopathy Study (ETDRS)-like macular subfields and total macular thickness. Incorrect retinal thickness maps might be the result of segmentation break-down owing to scan artefacts, insufficient image quality or in the presence of specific retinal pathological features, in the case of good-quality scans. Poor patient fixation can also hinder obtaining correct retinal thickness maps.

In this review, the author describes and discusses the various causes that can compromise retinal thickness measurements. The author also stress that the search and recognition of thickness measurement errors should be an integral part of OCT scan analysis.

Scan Artefacts

Several scan artefacts have been described to cause segmentation break-down: 'out-of-range' images, mirror artefacts, and blink and motion artefacts.[10–12,14,15] The out-of-range image artefact appears if the OCT scan is moved out of the scanning range during image acquisition; thus, the OCT image is 'cut' in its upper or lower part. It might also be present if there are pathological high retinal elevations that are out of reach. This artefact can occur more often in highly myopic eyes, whereas in non-myopic eyes, it is usually a result of

poor image acquisition. As the software cannot delineate the true boundaries of the out-of-range retina, an erroneously low thickness is displayed on the retinal thickness map in the corresponding area. The out-of-range image artefact might be present in time-domain (TD) OCT.

Similar to the out-of-range image artefact, but characteristic of spectral-domain (SD)-OCT is the 'mirror' artefact, which has been well described and analysed by Ho and associates.[15] In this type of artefact, the vertically shifted OCT image is flipped onto itself. The flipped mirror image arises from the Fourier transformation used in SD-OCT as it cannot distinguish positive from negative time delays and produces OCT images symmetrically around the 0-delay line. This artefact is present more often in eyes with moderate to high myopia and is associated with a smaller axial measurement range of the OCT instrument. However, it can also be present in poor scan acquisitions, when the OCT image is vertically displaced out of the image frame. It usually results in peripheral breakdown of segmentation and errors in retinal thickness measurements.

The blink and motion artefacts are usually present in TD-OCT. They are uncommon in SD-OCT, as the scanning speed of SD-OCT has been dramatically improved (approximately 100 times faster image acquisition than in TD-OCT). However, in some SD-OCT machines, the volume scans, which are of better image quality, and denser A-scan coverage of the examined area require more time. Thus, blink artefacts are still possible. As these artefacts cause segmentation breakdown because of signal 'dropout', the examiner should repeat the scan to avoid obtaining erroneous retinal thickness maps.
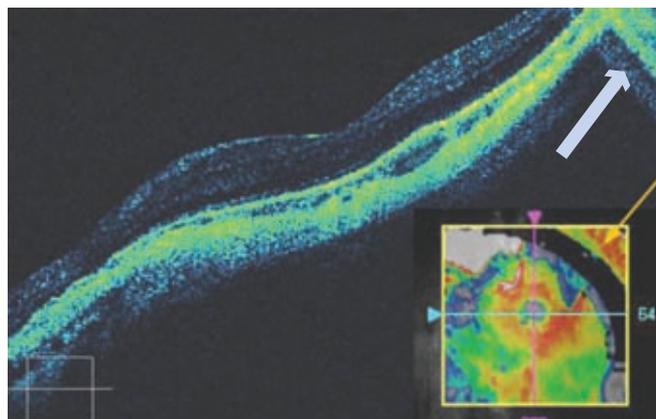
Image Quality

OCT image quality is dependent on the experience of the operator and the clarity of the ocular media. If a scan with very poor quality (i.e. a 'degraded' image artefact) is used for thickness analysis, the automatic measurement result will be doubtful. All OCT devices display the quality parameters of the scan after acquisition (e.g. signal:noise ratio [SNR] and signal strength [SS]). They have proved to be reliable in discriminating poor from acceptable and good scans.[16] Scans with lower SNR have been reported to have more automated retinal thickness measurement errors.[16] Decreased SNR might be to the result of poor scan acquisition (e.g. defocusing and depolarisation).[12] If the image quality is insufficient, the operator can try to improve it by optimising the focus and polarisation before capturing the OCT scan. In other cases, the SNR is not dependent on the operator's skill, but is related to media clarity (cataract, vitreous haemorrhage, etc.). The presence of cortical and posterior subcapsular cataracts has been shown to influence the OCT signal more than do nuclear cataracts.[16]

Therefore, when interpreting retinal thickness maps, the clinician should bear in mind that errors are more frequent in lower SNR scans and in the presence of media opacities. Optimising scan acquisition and obtaining the highest possible SNR could reduce the possibility of automated retinal thickness measurement errors.

Eccentric Fixation

Eccentric fixation can also hinder thickness analysis. In cases with severe macular pathology, poor visual acuity, eccentric or instable fixation, the position of the generated retinal thickness map will be inaccurate with respect to the foveal centre and the ETDRS plot.

The mirror artefact is indicated by a white arrow and the corresponding retinal thickness measurement error by a yellow arrow.

Therefore, even in the absence of segmentation breakdown, the displayed thickness will be erroneous. Assessing this as a thickness measurement error, Odell and colleagues found that incorrect scan positioning using Cirrus HD-OCT resulted in a central foveal thickness error of 3.18 ± 6.09 μm in normal subjects (maximum 32 μm) and 10.50 ± 19.43 μm in patients with retinal pathology (maximum 104 μm).[17] Campbell et al. used Stratus OCT to analyse how scan decentration would affect central subfield thickness in healthy subjects, and found that a shift of 0.5 mm resulted in foveal thickness measurements that were in error by approximately 45 %.[18]

In TD-OCT, retinal thickness maps are a result of interpolation of the measured thickness in six radial B-scan lines, intersecting in the foveal centre (i.e. the fixation point). Thus, macular thickness is generated from a total of 768 sampled A-scan points (six scan lines × 128 A-scan points, for the most widely used protocol, Fast Macular Thickness Map). The centre-point thickness was found to be less reproducible than was the central foveal subfield thickness,[6,19] especially in patients with severe macular pathology (e.g. neovascular age-related macular degeneration [AMD]). Therefore, in such cases it has been advocated not to use centre-point thickness alone to guide follow-up and retreatment.[19,20] In addition, because of interpolation, small changes in retinal thickness between the six scan lines might be missed and, in cases of inaccurate fixation, the exact rescanning of the same area is doubtful in follow-up examinations.

In SD-OCT, there are several improvements that minimise errors related to eccentric fixation. The generated retinal thickness map is based on thickness measurements of a greater number of A-scan points. For example, in Cirrus HD-OCT, the volume scan comprises 128 B-scans, each having 512 A-scans (128 × 512 = 65,536 A-scan points). Thus interpolation is reduced. The scan acquisition speed is faster than in TD-OCT; thus, ocular saccades have less influence. Some SD-OCT devices have a tracking system that ensures the exact same area is scanned during scan acquisition (i.e. Spectralis OCT). Studies have shown that SD-OCT retinal thickness measurements have higher reproducibility compared with those obtained by TD-OCT.[14,21] However, errors in central subfield thickness owing to improper anchoring of the scan grid to the foveal centre in patients with poor fixation are also present in SD-OCT.[17] SD-OCT devices offer ways to
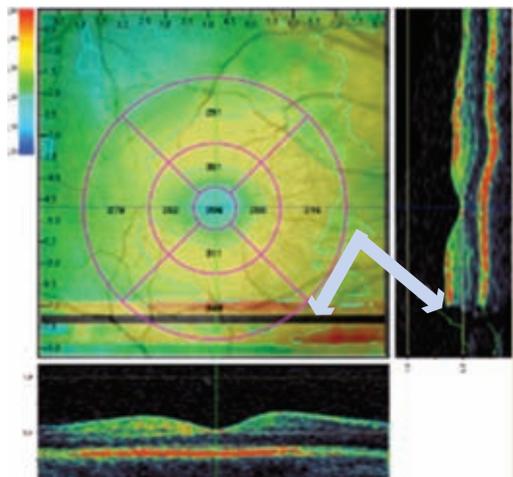
overcome this problem. If eccentric fixation is identified by the OCT operator, the location of the scan grid can be repositioned and centred on the fovea before scan acquisition. Despite this, if an eccentrically fixated scan is saved, the ETDRS map grid can be correctly positioned over the macular centre after image acquisition (either manually or automatically depending on the SD-OCT machine). Thus, if there is no segmentation breakdown (i.e. the automated retinal thickness measurement is correct) with post-acquisition recentreing of the ETDRS map, there will be a correctly displayed reliable retinal thickness measurement. In addition, all SD-OCT devices have the ability to rescan the exact area in separate examinations, thus ensuring precise follow-up.

Retinal and Vitreoretinal Pathology

The described scan artefacts (out-of-range, mirror, blink and motion) and low SNR can cause segmentation breakdown and errors in retinal thickness measurements. However, there are cases of retinal boundary misidentification in the absence of such artefacts. In these cases, the presence of retinal pathology might confuse the software in the correct placement of retinal boundaries.[11] Full-thickness macular holes and neovascular AMD were found to be associated with a higher percentage of thickness measurement errors than were cases with macular oedema.[10,11,22] Domalpally et al. showed that the highest frequency of errors occurred with ADM (54.981 %), followed by retinal vein occlusion (23.9 %) and diabetic macular oedema (16.3 %).[22] Ray et al. reported errors in 70 % of eyes with neovascular AMD and, in 86 % of these, they were related to photodynamic therapy.[10] In neovascular AMD, Patel et al. detected segmentation errors in 90 % of eyes examined and, in 74 %, the error was significant (affecting the central 1mm subfield).[20] Krebs and colleagues reported segmentation failure in 69.2 % of cases for Stratus TD-OCT and in 25 % for Cirrus HD-OCT.[23]

The presence of morphological features, such as subretinal fluid, neovascular membrane, pigment epithelium detachment and fibrous scar tissue, can confuse the segmentation software so that it incorrectly delineates the outer retinal boundary.[10,11,23] In cases of macular oedema (diabetic retinopathy, retinal vein occlusion, etc.), the presence of hard exudates can cause segmentation breakdown. To a lesser extent, the

presence of epiretinal membrane or a highly reflective posterior hyaloid can provoke inner retinal boundary misidentification. If low SNR or significant media opacities are present, there might be incorrect identification of the inner boundary. Incorrect delineation of retinal boundaries by the segmentation software results in automated retinal thickness measurement errors and erroneous thickness maps displays. The presence of the above-mentioned pathomorphological features could alert the clinician to the possibility of errors. Particular searches and recognition of measurement errors could improve the accuracy of OCT interpretation and prevent false conclusions.

Comparison of Different Optical Coherence Tomography Devices

Several studies have compared the performance of TD-OCT and different SD-OCT devices in their accuracy of segmentation.[14,23,24] The results show significantly lower rates of segmentation breakdown and measurement errors in SD-OCT (Cirrus HD-OCT, Spectral OCT/SLO, RTVue 100 OCT and Topcon 3D-OCT) compared with TD-OCT (Stratus OCT).

Ho and associates found the following incidence of any artefacts: Stratus TD-OCT – 73.8 %; Cirrus HD-OCT Macular Cube 128 × 512 – 68.5 %; RTVue MM6 – 88.9 %; and Topcon 3D – 90.6 %; and the presence of clinically significant error in central subfield thickness (>11 μm) was: Stratus TD-OCT – 45.2 %; Cirrus HD-OCT Macular Cube 128 × 512 – 11.1 %; RTVue MM6 – 24.1 %; and Topcon 3D – 20.4 %.[14] Therefore, Cirrus HD-OCT exhibited the lowest rate of any artefacts and clinically significant improper foveal thickness measurements, whereas Stratus TD-OCT had the highest rate of clinically significant improper foveal thickness.

Forte et al. found scan artefacts in 35 % of eyes examined with Stratus TD-OCT and in 21.7 % of eyes examined with Spectral OCT/SLO.[24] Krebs and colleagues also reported better performance of the segmentation algorithm of Cirrus HD-OCT compared with Stratus OCT in cases with neovascular AMD.[23]

These data show better performance of SD-OCT compared with TD-OCT. This is attributable to the improvements in SD-OCT technology, including higher resolution, faster scan acquisition, raster volume scanning with considerably greater number of A-scanned points, and better quality of the segmentation software. Even though improvements have been made, and the error rate in automated retinal thickness measurements has decreased, the clinician still needs to be cautious in interpreting OCT scans as errors can still occur.

Possible Ways to Overcome Retinal Thickness Measurement Errors

To reduce the possibility of obtaining OCT scans with erroneous retinal thickness maps, the examiner should be aware of, and make attempts to avoid, image acquisition artefacts, such as out-of-range, mirror and blink artefacts, and obtain the highest quality scan possible (i.e. with the highest possible SNR). Before image capture, the best possible scan focus, polarisation and centreing should be done. Improvement in SD-OCT instruments in terms of enlarging the axial imaging depth (over 2 mm) could reduce the incidence of mirror artefacts and the related improper retinal thickness measurements.[15] It has been stated that axial length should also be taken in consideration as differences in axial length and ocular magnification might also affect the accuracy of retinal thickness maps.[17] Odell

Figure 3: Retinal Thickness Measurement Errors Owing to Segmentation Break-down
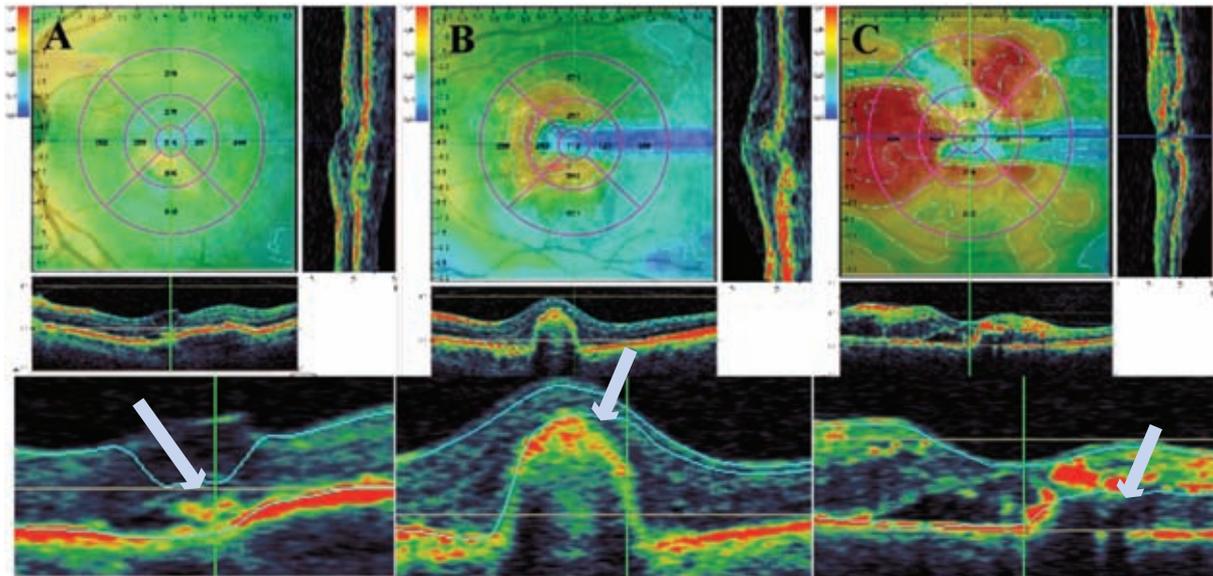
Retinal thickness measurement errors due to a segmentation break-down are indicated by a white arrow. A: low signal:noise ratio scan; B: pigment epithelial detachment in an eye with neovascular age-related macular degeneration; C: hard exudates in an eye with diabetic macular oedema. The scans were obtained by Spectral OCT/SLO.

and colleagues advocate correcting the nominal scan length for differences in ocular axial length to obtain correct thickness maps and also to correct measurements in the lateral dimension (size of macular hole, geographic atrophy, druse, etc.).[17]

In cases of eccentric fixation and poor visual acuity, the operator can improve scan placement by manually shifting the scan grid and centreing it on the foveal pit. If an off-centre retinal thickness map is still an issue, the examiner can reposition the ETDRS grid over the fovea after image acquisition to obtain a more accurate thickness map.

Although all these measures can improve the quality of the scan and reduce the possibility of errors by avoiding artefacts, segmentation errors might still occur. As mentioned above, such errors might be the result of software algorithm failure in the presence of retinal or vitreoretinal pathology. In the presence of neovascular membrane, pigment epithelial detachment, subretinal fluid, fibrous tissue and hard exudates, the clinician should be aware and evaluate the positioning of the inner and outer boundary lines by the segmentation software. Thus, when detecting improper segmentation and the presence of automated retinal thickness measurement error, one should be cautious in interpreting the outcome and the resulting decision-making.

Manual remeasurements are advocated by many authors. For Stratus TD-OCT, there are built-in callipers for point-to-point measurements, which are sufficient if one wants to obtain a correct thickness map. Sadda and colleagues proposed the use of software termed 'OCTOR', designed by Doheny Image Reading Center (DIRC) engineers to allow manual delineation of retinal boundaries.[25] After proper placement of the inner and outer retinal boundaries on all exported six B-scans from the Fast Macular Thickness Map scan protocol, the software generates a correct retinal thickness map. The measurements produced by OCTOR software are validated and, in the absence of errors, showed high intergrade agreeability and were highly correlated with automated Stratus measurements.[25] In SD-OCT machines, there is a built-in system for manual delineation of retinal

Figure 4: Incorrect Delineation of the Inner Retinal Boundary in the Presence of a Thick and Taut Posterior Hyaloid in an Eye with Diabetic Macular Oedema
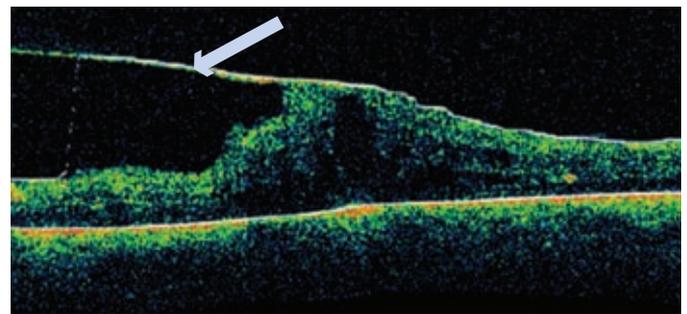
The inner retinal boundary is indicated by a white arrow. The scan was obtained by time-domain Stratus OCT.

boundaries. Thus, the clinician has the ability to correct thickness measurements manually for each B-scan in cases of automated error. However, if one needs a thickness map, one should perform manual delineation of retinal boundaries on all B-scans that comprise the volume data set (128 B-scans or 200 B-scans for the volume scan in Cirrus HD-OCT). This would be time consuming and not feasible in clinical settings; it also remains subjective. Frequently, in cases of neovascular AMD, neovascular tissue, fibrotic tissue and the retinal pigment epithelium form a highly reflective complex and even experienced examiners cannot identify and delineate the posterior retinal boundary without any doubt. Improved methods to segment retinal layers correctly or to compensate for errors will be of great value and are currently anticipated.

Sadda and colleagues described an updated version of the OCTOR software that allows analysis of SD-OCT data sets ('3D-OCTOR').[26] They also analysed the impact of B-scan density on retinal thickness measurements in eyes with retinal disease. The authors concluded that B-scan density reduction of up to 32 horizontal B-scans (for Cirrus HD-OCT 128 x 512 scan protocol) results in only a minimal change in the calculated retinal thickness measurements. Therefore, scan density

reduction could be a less time-consuming way to obtain correct retinal thickness maps if manual remeasurement is needed. It might also be useful for OCT examination of patients with neovascular AMD in clinical trials. Still, the authors raise the concern that less-dense scan patterns might reduce image quality and might be insufficient for the analysis and quantification of some pathological features, such as small pigment epithelial detachments, druse and others. The authors recommend considering more dense scans for qualitative assessment and less dense scans for obtaining retinal thickness maps, particularly when manual correction is expected to be necessary. However, manual segmentation is subjective and still time-consuming.

A team of researchers, comprising Cabrera Fernandez, Salinas, DeBuc, Somfai and Puliafito, have developed a computer-aided grading methodology for OCT retinal image analysis (OCTRIMA).[27–31] It integrates a denoising and edge enhancement technique along with a new segmentation algorithm. The OCTRIMA software provides better automatic segmentation results and also incorporates a semiautomatic and manual segmentation correction tool. Compared with free-hand corrections, it is a less time-consuming method to correct retinal thickness measurement errors. It was designed to analyse TD-OCT Stratus-derived images, but has also been applied to segmental retinal layers from images derived from SD-OCT and ultra-high resolution OCT devices. The OCTRIMA also offers segmentation, and measures and displays topographic maps of each cellular layer. This methodology was validated and proved to be highly reproducible, repeatable and reliable for retinal thickness measurements in healthy eyes (total retina and all intraretinal layers, except the outer segment–retinal pigment epithelium junction). The OCTRIMA total retinal and intraretinal layer analysis of Stratus OCT-derived images was found to be highly correspondent to SD-OCT (RTVue 100) segmentation analysis. However,

the absolute numerical thickness values need to be compensated with a correction factor (because of the differences in the segmentation of the posterior retinal boundary) between TD-OCT and different SD-OCT machines.

In addition, the OCTRIMA software incorporates a method for reporting changes in retinal thickness and thus offers objective monitoring of disease progression or response to treatment in the follow-up. These recently developed, sophisticated and accurate software packages for the manual or automatic correction of errors in retinal thickness measurements offer the clinician a more accurate and precise diagnostic assessment and follow-up of patients with error-prone diseases (e.g. AMD).

Conclusion

OCT is currently the most precise, reliable and objective method for obtaining automated retinal thickness measurements. However, some limitations exist. The segmentation software might perform less accurately in the presence of scan artefacts, low SNR and specific retinal pathological features. Improved scan acquisition for the best possible image quality might improve the segmentation performance in some cases. Owing to improvements in SD-OCT technology, the error rate has been reduced. However, inaccurate automated retinal thickness measurements often still occur with current SD-OCT. The awareness of the clinician and particular searches for, and recognition of, measurement errors would improve the accuracy of OCT interpretation and should be an integral part of an OCT scan assessment. Manual or automated error correction by the use of additional software (3D-OCTOR or OCTRIMA) might be a strategy for dealing with errors when a more precise and sophisticated approach is needed. ∎

1. Huang D, Swanson EA, Lin CP, et al., Optical coherence tomography, *Science*, 1991;254(5035):1178–81.
2. Hee MR, Izatt JA, Swanson EA, et al., Optical coherence tomography of the human retina, *Arch Ophthalmol*, 1995;113(3):325–32.
3. Schuman JS, Puliafito CA, Fujimoto JG, Interpretation of the retinal image. In: Schuman JS, Puliafito CA, Fujimoto JG, *Optical Coherence Tomography of Ocular Diseases* (2nd edn), Thorofare, NJ, USA: SLACK Inc. 2004;21–57.
4. Podoleanu AG, Optical coherence tomography, *Br J Radiol*, 2005;78(935):976–88.
5. Wojtkowski M, Leitgeb R, Kowalczyk A, et al., In vivo human retinal imaging by Fourier domain optical coherence tomography, *J Biomed Opt*, 2002;7(3):457–63.
6. Diabetic Retinopathy Clinical Research Network, Krzystolik MG, Strauber SF, et al., Reproducibility of macular thickness and volume using Zeiss optical coherence tomography in patients with diabetic macular edema, *Ophthalmology*, 2007;114(8):1520–5.
7. Massin P, Vicaut E, Haouchine B, et al., Reproducibility of retinal mapping using optical coherence tomography, *Arch Ophthalmol*, 2001;119(8):1135–42.
8. Browning DJ, Interobserver variability in optical coherence tomography for macular edema, *Am J Ophthalmol*, 2004;137(6):1116–7.
9. Paunescu LA, Schuman JS, Price LL, et al., Reproducibility of nerve fiber thickness, macular thickness, and optic nerve head measurements using StratusOCT, *Invest Ophthalmol Vis Sci*, 2004;45(6):1716–24.
10. Ray R, Stinnett SS and Jaffe GJ, Evaluation of image artefact produced by optical coherence tomography of retinal pathology, *Am J Ophthalmol*, 2005;139(1):18–29.
11. Sadda RS, Wu Z, Walsh AC, et al., Errors in retinal thickness measurements obtained by optical coherence tomography, *Ophthalmology*, 2006;113(2):285–93.
12. Somfai GM, Salinas HM, Puliafito CA and Fernandez DC, Evaluation of potential image acquisition pitfalls during

optical coherence tomography and their influence on retinal image segmentation, *J Biomed Opt*, 2007;12(4):041209.
13. Hee MR, Puliafito CA, Duker JS, et al., Topography of diabetic macular edema with optical coherence tomography, *Ophthalmology*, 1998;105(2):360–70.
14. Ho J, Sull AC, Vuong LN, et al., Assessment of artefacts and reproducibility across spectral- and time-domain optical coherence tomography, *Ophthalmology*, 2009;116(10):1960–70.
15. Ho J, Castro DPE, Castro LC, et al., Clinical assessment of mirror artefacts in spectral-domain optical coherence tomography, *Invest Ophthalmol Vis Sci*, 2010;51(7):3714–20.
16. van Velthoven MEJ, van der Linden MH, de Smet MD, et al., Influence of cataract on optical coherence tomography image quality and retinal thickness, *Br J Ophthalmol*, 2006;90(10):1259–62.
17. Odell D, Dubis AM, Lever JF, et al., Assessing errors inherent in OCT-derived macular thickness maps, *J Ophthalmol*, 2011;2011:692574.
18. Campbell RJ, Coupland SG, Buhrmaann RR, Kertes PJ, Effect of eccentric and inconsistent fixation on retinal optical coherence tomography measures, *Arch Ophthalmol*, 2007;125(5):624–7.
19. Patel PJ, Chen FK, Ikeji F, et al., Repeatability of Stratus optical coherence tomography measures in neovascular age-related macular degeneration, *Invest Ophthalmol Vis Sci*, 2008;49(3):1084–8.
20. Patel PJ, Chen FK, da Cruz L, Tufail A, Segmentation error in Stratus optical coherence tomography for neovascular age-related macular degeneration, *Invest Ophthalmol Vis Sci*, 2009;50(1):399–404.
21. Leung CK, Cheung CY, Weinreb RN, et al., Comparison of macular thickness measurements between time domain and spectral domain optical coherence tomography, *Invest Ophthalmol Vis Sci*, 2008;49(11):4893–7.
22. Domalpally A, Danis RP, Zhang B, et al., Quality issues in interpretation of optical coherence tomograms in macular diseases, *Retina*, 2009;29(6):775–81.

23. Krebs I, Falkner-Radler C, Hagen S, et al., Quality of the threshold algorithm in age-related macular degeneration: Stratus versus Cirrus OCT, *Invest Ophthalmol Vis Sci*, 2009;50(3):995–1000.
24. Forte R, Cennamo GL, Finelli ML and de Crecchio G, Comparison of time domain Stratus OCT and spectral domain SLO/OCT for assessment of macular thickness and volume, *Eye*, 2009;23(11):2071–8.
25. Sadda SR, Joeres S, Wu Z, et al., Error correction and quantitative subanalysis of optical coherence tomography data using computer-assisted grading, *Invest Ophthalmol Vis Sci*, 2007;48(2):839–48.
26. Sadda SR, Keane PA, Ouyang Y, et al., Impact of scanning density on measurements from spectral domain optical coherence tomography, *Invest Ophthalmol Vis Sci*, 2010;51(2):1071–8.
27. Fernandez DC, Delineating fluid-filled region boundaries in optical coherence tomography images of the retina, *IEEE Trans Med Imaging*, 2005;24(8):929–45.
28. Fernandez DC, Salinas HM, Puliafito CA, Automated detection of retinal layer structures on optical coherence tomography images, *Opt Express*, 2005;13(25):10200–16.
29. DeBuc DC, Somfai GM, Ranganathan S, et al., Reliability and reproducibility of macular segmentation using a custom-built OCT retinal image analysis software, *J Biomed Opt*, 2009;14(6):064023.
30. DeBuc DC, Salinas HM, Ranganathan S, et al., Improving image segmentation performance and quantitative analysis via a computer-aided grading methodology for optical coherence tomography retinal image analysis, *J Biomed Opt*, 2009;15(4):046015.
31. Tatrai E, Ranganathan S, Ferencz M, et al., Comparison of retinal thickness by Fourier-domain optical coherence tomography and OCT retinal image analysis software segmentation analysis derived from Stratus optical coherence tomography images, *J Biomed Opt*, 2011;16(5):056004.