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Use of OCT Imaging in the Diagnosis and Monitoring of Age Related Macular Degeneration

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1. Introduction

Optical Coherence Tomography (OCT) is a non-invasive, high-resolution imaging technique that has been introduced in the clinical practice at the beginning of the last decade. The first application of this method has been recorded in the field of ophthalmology (Osiac et al., 2011). Retinal diseases such as Age-related Macular Degeneration (AMD), central serous chorio-retinopathy, macular hole, vitreo-macular interface syndrome and diabetic maculopathy have taken advantage of this relatively new imaging method. Among these, AMD is by far, the ocular condition that has benefited the most from the enormous advantages offered by OCT, in terms of diagnosis, response to treatment and monitoring. Future progress in OCT techniques is expected to improve the knowledge in the pathophysiology of this devastating disease. In order to better understand the role of OCT in the management of AMD, a concise review of the physical principles and mathematical equations that sustain this method is provided. The progress in the OCT techniques over the past decade is emphasized, from Time Domain – OCT (TD-OCT) to Spectral Domain – OCT (SD-OCT) and future directions, with implications in the clinical practice. The comparative contribution of TD-OCT and SD-OCT in the different forms of AMD is revealed. The limits of OCT are presented with their possible solutions. After the description of the theoretical data for OCT interpretation, the impact of OCT in the diagnosis is illustrated with examples of various aspects that AMD can display. The role of OCT in the monitoring of AMD is revealed by the response of the wet form of the disease to the anti-VEGF intravitreal injections.

2. OCT imaging in the diagnosis and monitoring of AMD

The development of the retinal imaging was dued to three major events. The first one was represented by the invention of the direct ophthalmoscope by Hermann von Helmholtz in 1851: it opened the field of ocular imaging, by allowing the physicians to examine the retina in vivo. The second one took place in 1961, when Novotny and Davis used fluorescein dye to visualize the retinal circulation, inventing the technique named fluorescein angiography. The third major breakthrough happened in the 1990s, when OCT was invented, providing a

fast, non-invasive, radiation-free examination technique, able to visualize precisely the retinal layers – something done before only on pathology slides. It's easy to understand why OCT has become soon an irreplaceable tool in most of the retina practices (Khaderi et al., 2011).

2.1 Theoretical considerations on OCT

Tomography is based on the reconstruction of cross-sectional images of an object using its projections. The concept of optical coherence tomography (OCT) was developed at Massachusetts Institute of Technology in the early 1990s and the first commercial version of OCT was made available by Carl Zeiss (Jena, Germany) in 1996. OCT is an extension of optical coherence domain reflectometry (OCDR). OCT is a modern noninvasive imaging technique with a high depth resolution, based on low coherence interferometry (LCI), that is able to reconstruct (tomographic) sectional images of the object under study. The first application of LCI in ophthalmology was to measure the eye length. OCT is similar to ultrasound imaging, but as an optical echo technique has much higher resolution. The key benefits of OCT are: live sub-surface images at near-microscopic resolution; instant, direct imaging of tissue morphology; no preparation of the sample or subject; no ionizing radiation. OCT is useful in situations where biopsy can't be performed, where sampling areas with conventional biopsies are likely, and that involve guiding surgical / microsurgical procedures.

The most important advantage of OCT as a diagnostic tool in ophthalmology is the obtain of fast, non-contact images of the ocular structures such as cornea, lens, retina and the optic nerve with depth resolutions better than 3 μm. Thus it is used to obtain a cross section of the retina based on the reflectivity on different layers within the retina, allowing detection of morphologic and micrometric modifications in retinal tissue. The ability to measure thickness of retinal layers has potential for early detection of pathologies and disease diagnosis (Talu et al., 2009).

2.2 OCT methods

OCT is applied by two main methods: Time domain OCT (TD-OCT) and Spectral domain OCT (SD-OCT). Each method has its own advantages and limitations.

TD-OCT produces two-dimensional images of the sample internal structure. In TD-OCT, tissue-reflectance information in depth (an A-scan represents a reflectivity profile in depth) is gradually built up over time by moving a mirror in the reference arm of the interferometer. OCT B-scans (a B-scan represents a cross-section image, a lateral x depth map) are generated by collecting many A-scans (Walther et al., 2011).

SD-OCT can be implemented in two formats, Fourier domain (FD-OCT) and swept source (SS-OCT). SD-OCT units acquire entire A-scans in reflected light at a given point in tissue. Information on depth is transformed from the frequency domain to the time domain, without using a moving reference mirror to obtain complete A-scans. The absence of moving parts allows the image to be acquired rapidly - about 60 times faster than with TD-OCT (Walther et al., 2011). The SD-OCT units allow the improvement of the detection and monitoring of retinal diseases, because these ones have ultra high-speed scan rate, superior

axial and lateral resolution, cross-sectional (2D) scan, 3D raster scanning and a higher imaging sensitivity than the traditional TD-OCT units. The SD-OCT software permits many operations with 3D data compared with traditional TD-OCT. The great number of scans done per time unit also allows SD-OCT systems to generate 3D reconstructions, which can be further manipulated. Visualization of this data in 3D demonstrates subtle pathology not evident with conventional 2D images (Talu et al., 2009).

2.2.1 Time-domain OCT (TD-OCT) or conventional OCT

A superluminiscent diode emits a light beam which is split into two beams: a beam that enters the eye and is reflected back by the ocular media and a beam reflected by a reference mirror. The two beams meet, generating interferences that are intercepted by a light detector (fig. 1). By displacing the reference mirror, different structures, located at various depths, can be analyzed, thus obtaining an A-scan. The transverse scanning of the retina in a predefined axis (horizontal, vertical or oblique) is generating the B-scan of the retina, composed by the A-scan sequences. There are two important specifications concerning the quality of the image obtained: it depends on the number of retinal scans and partly, on the degree of light absorption by various retinal and subretinal structures. The time which is required in order to get the sections is the main determinant of the quality of the signal, justifying the name of Time Domain which is given to this OCT method. Time domain OCT (TD-OCT) is a technique that produces two-dimensional images of the sample internal structure. In standard TD-OCT two different scanning procedures are used in order to obtain an image: a depth scan using time-domain low coherence interferometry and a lateral scan addressing laterally adjacent positions to obtain the location of light scattering bodies in the sample (Talu et al., 2009).

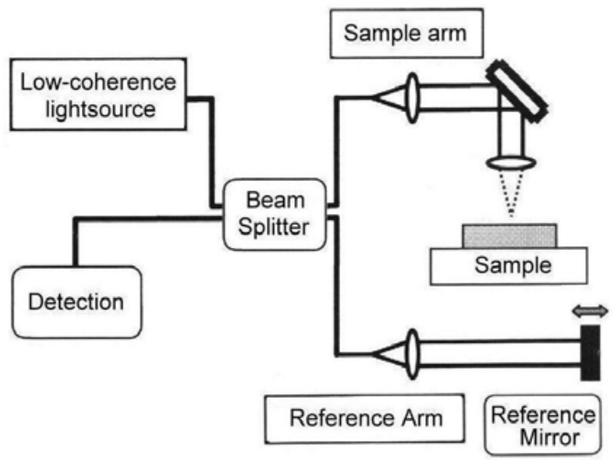

Fig. 1. A simplified schematic of Time domain (TD-OCT)

In TD-OCT, light from the low-coherence light source is divided evenly by the beam splitter. Half the light from the beam splitter is directed toward the sample and half the light toward a moving mirror. Light reflects off the mirror and from within the sample. The light beams reflected back are recombined by the beam splitter and directed into a detector. If the pathlengths match within a coherence length, interference will occur. OCT measures the intensity of interference and uses it to represent back-reflection intensity; the unwanted

background light is suppressed by filtering. The OCT signal contains the oscillating term of the intensity, that is the integral of the contribution of the light reflected back from the biological tissue at all depths. TD-OCT uses light to map the layers within the retina in a cross-sectional image. Each image is made up of a series of A-scans scanned through the depth of the tissue and when aligned side by side, creates a B-scan two dimensional cross-sectional image. Each A-scan is acquired by moving a reference mirror to correspond to each point along the depth of the A-scan, and the signals from the reference arm and from the retina are interfered to determine the signal at that point in the A-scan. A TD-OCT system has two major spatial resolutions: axial and transversal resolution. The axial resolution depends on two laser characteristics: coherence length of the light source and pulse duration. The transversal resolution is determined by the focused spot size of the optical beam. The capability of TD-OCT system to produce images with good quality is characterized by the value of the signal to noise ratio (SNR) (Talu et al., 2009).

2.2.2 Spectral-domain OCT (SD-OCT)

The development of the SD-OCT is originating in the Fourier mathematical equation (1807) that can sum a periodic function into a series of sinusoidal functions. When applied to the OCT, the Fourier transformation replaces the sequential measurement of the reflected beam (by moving a mirror in front of the reference beam), with the simultaneous measurement of the light reflection. Subsequently, the image resolution in SD-OCT is 1 μm, as compared to 10 μm in TD-OCT. The practical impact of this improvement in resolution is the early detection of small cystic changes associated with the wet form of AMD. The early diagnosis is followed by the early treatment and the better preservation of the visual function. In SD-OCT, a spectrometer is used in order to analyze simultaneously all the frequencies. Therefore, all echoes of light from the various layers of the retina can be measured simultaneously, making the image acquisition much more rapid: SD-OCT is 50 times faster than the conventional TD-OCT and 100 times faster than the first ultrahigh-resolution OCT (UHR-OCT). The axial depth depends mainly on the bandwidth of the light source. With UHR-OCT, the resolution is 2 – 3 μ (the standard is of 10 μ). This ultrahigh resolution is comparable with the one obtained in histopathology, which makes possible the earlier diagnosis in AMD, better guidance of treatment and improvement of knowledge in the pathogenesis of this disease (Coscas et al., 2009).

Given the possibility to simultaneously get images in various planes, the 3D reconstruction is possible with SD-OCT, allowing the obtaining of hundreds of high-resolution images per second. The reduction of the examination time considerably decreases the artifacts related to patient movements. The SD-OCT images have proven to be clearer and with higher quality as compared to the ones obtained by the successive TD-OCT systems (OCT1, OCT3, stratus). The SD-OCT systems are continuously improving, by adding complementary functions: fundus photography, angiography, microperimetry. The 3D evaluation permits the accurate measurement of the macula (total volume) in various conditions (edema, fluid, drusen, CNV) with implications in the follow up and treatment of AMD (Luviano et al., 2009). The ultra-high resolution images obtained by SD-OCT allow a better differentiation between the retinal and subretinal layers. Further research has led to another significant improvement in resolution and speed: the novel frequency-domain OCT devices (FD-OCT), which are not yet available for widespread use. The difference between SD-OCT and FD-OCT resides in

the light source. As explained above, the SD-OCT devices use a broadband light source and a spectrometer, generating readout rates of 40 kHz. FD-OCT utilizes a wavelength-swept laser source, which allows the obtaining of repetition rates as high as 370 kHz. The clinical potential of FD-OCTs is vast, given to their wide fields of view: for instance, they reach the coronary arteries and esophageal epithelium (Khaderi et al., 2011).

Feature	TD-OCT	SD-OCT
Basis	An interferometer measures **sequentially** the echo delay time of light that is reflected by the retinal microstructures.	The Fourier transformation allows the **simultaneous** measurement of the light reflection with a spectrometer
Modality of sampling	It samples one point at the time	It samples all the points simultaneously 60 times faster than TD-OCT
Scanned area	6 radial scans, 20 µ wide and 6 mm long (the area between the 6 scans is not imaged)	65.000 scans in a 6-mm area, without excluding areas
Rate of acquisition	400 scans/second	20.000 – 40.000 scans/second
Result	Two-dimensional images of the sample internal structure	3D reconstruction possible
Image resolution and quality	10 µ	1 µ, clearer

Table 1. Comparison of TD-OCT vs. SD-OCT

2.3 Clinical applications of OCT in AMD

The antero-posterior sections on OCT reveal the succession of the retinal layers and of the Retinal Pigmented Epithelium (RPE), as well as the presence of any spaces between these layers. The information offered by OCT is detailed, simple and easily interpretable.

2.3.1 Basis of OCT interpretation

The OCT signs in AMD are extremely valuable for the ophthalmologist.

Retinal thickening (the thickness of the retina is measured between the internal limiting membrane and the RPE) is determined by the exudation from the choroidal new vessels.

The occult Choroidal Neovascularization (CNV) is revealed by the constant presence of the elevation or detachment of the RPE band. Frequently, the occult CNV is suggested by various alteration of the RPE: irregularities, fragmentation, thickening, thinning.

The subretinal fluid appears as diffuse infiltration or as the constitution of cystic spaces in the macular area.

The classic CNV is translated on OCT as hyper-reflective zones adjacent to or away from the RPE. They must be differentiated from other hyper-reflective structures: fibrous tissue, exudate, pigment, pseudo-vitelliform material.

Other signs of prognostic value can be visualized at the level of the outer retinal layers (outer nuclear layer and external limiting membrane): hyper-reflective spots and areas of densification. They prove the progression of the disease (Coscas et al., 2009).

2.3.2 Technological parameters

Axial resolution (depth) refers to the capability to measure the morphological architecture of each retinal layer.

The depth of penetration depends mainly on two parameters: the optical properties of the tissues and the imaging wavelength that is used. Studies are conducted in order to find a possibility to visualize the choroid.

Transverse resolution of the image could reach a level allowing to distinguish cells.

The sensitivity of detection is a measure of the ease to obtain good quality OCT images in case of ocular media opacities.

The data acquisition time settles the number of transverse pixels of the OCT image.

Image contrast is an additional parameter meant to improve the visualization of various structures.

Functional extensions of OCT have the purpose to offer an optical biopsy of the retina, simultaneously with functional and metabolic data on its activity (Coscas et al., 2009).

2.3.3 Macula

The most frequent application of OCT in retinal disease is the measurement and monitoring of the retinal thickness.

The TD - OCT system (Stratus) gives a macular thickness map which is calculated from 6 radial B-scans crossing at the fovea. By interpolating data from these scans, the average macular thickness is calculated in 9 subfields centered on the fovea. Similarly, the total macular volume is obtained.

The SD-OCT provides images with much higher resolution. Given the differences between the measurements with the two types of OCT (TD and SD), algorithms are necessary in order to establish correlations between them.

Various studies compared the retinal thickness measured with TD-OCT and SD-OCT. For instance, the comparative measurements of the retinal thickness performed with Cirrus HD-OCT and Stratus TD-OCT in healthy individuals revealed that the average retinal thickness measured with SD-OCT has been significantly higher as with TD-OCT: 60 μm thicker (Kakinoki et al., 2009). This is explained by the difference in defining the retinal thickness between the two machines. In TD-OCT, the outer segments of the photoreceptors are not differentiated from the RPE, thus being excluded from the retinal thickness evaluation. The

high resolution scans obtained in SD-OCT allows the separation of the outer photoreceptor segments from the RPE and subsequently, their inclusion in the calculation of the retinal thickness (Coscas et al., 2009).

In another recent study, it has been shown an increased measurement in retinal thickness of 65 – 70 μm as measured by Spectralis OCT compared with Stratus OCT which corresponds to the inclusion of the outer segment-RPE-Bruch's membrane complex by Spectralis OCT (Grover et al., 2010). Other studies proved the superiority of SD-OCT versus TD-OCT in quantifying the retinal thickness and evaluating the activity of the CNV membranes in wet AMD (Sayanagi et al, 2009; Mylonas et al, 2009). The differences between the macular thickness and volume measured with TD-OCT and SD-SLO (Scanning Laser Ophthalmoscopy)/OCT have been evaluated in eyes with macular edema and in normal eyes. The SD-SLO/OCT produced fewer artefacts than Stratus TD-OCT in normal and oedematous retina. Retinal thickness measured with SD-SLO/OCT has been significantly higher than retinal thickness obtained with TD-OCT. Therefore, it is advisable to follow the patient with the same OCT device, otherwise a correcting value of 1.1 should be considered when extrapolating the values from TD-OCT to SD-OCT. Retinal volume measurements were strongly reproducible and could be used to compare examinations with Stratus TD-OCT and SD-SLO/OCT (Forte et al., 2009).

The interchangeability of retinal thickness measurements resulting from different protocols of Spectralis OCT (which combines the OCT with the confocal laser ophthalmoscopy) has been evaluated in healthy eyes. It showed good protocol interchangeability for all tested protocols, which is important as it allows the selection of a more rapid and simpler protocol, especially in less cooperative patients. Higher number of measurements might influence negatively the results due to corneal dryness and loss of attentiveness (Wenner et al., 2011).

2.3.4 The segmentation of the retinal layers

TD-OCT can measure the thickness of the entire retina (from the vitreo-retinal interface to the RPE), but the only structure that can be isolated and measured individually is the nerve fiber layer. The TD-OCT conventional software does not allow the measurement of the structures that are external to the RPE: Pigment Epithelial Detachments (PED), CNV. Because the evolution in time of the subretinal space is extremely important for the monitoring and decision making in AMD, they are measured with custom programs or manually.

SD-OCT, by facilitating the image segmentation, makes it possible to individualize certain layers of the retina: plexiform layer, subretinal space, subretinal pigment epithelial space. The segmentation of the retina into two components (neurosensory and subretinal space) is also a promising option for the follow up of AMD (Coscas et al., 2009).

2.3.5 Drusen

The evaluation of drusen is important for the prediction of AMD risk for progression, despite the differences in agreement between observers. Whereas with TD-OCT the imaging of drusen is limited because of artifacts, the SD-OCT is capable to provide its detailed structure, thanks to the segmentation techniques. The internal structure of the drusen, that can now be specified, seems to be an indirect indicator of the complement-related activity which is associated with the risk of progression. However, this observation needs to be

validated by clinical studies. The possibility to precisely measure the drusen volume with the support of the computer-assisted techniques offers a very useful tool to monitor the disease and to assess the risk of AMD progression (Coscas et al., 2009).

2.3.6 Choroidal neovascularization

Conventional TD-OCT represents a reference moment in the retinal imaging by having made it possible to: quantify the retinal response to CNV (macular edema, subretinal fluid); establish a correlation between the morphological (cystoid macular edema) and functional (visual acuity) parameters and between the OCT measurements and the response to treatment; visualize the fibro-vascular membranes in the subretinal and sub-RPE space.

The advantages of SD-OCT are represented by: the possibility to generate 3D images of the fibro-vascular complexes and to correlate them with fluorescein angiography and microperimetry; the easier detection of small PED, CNV and subretinal fluid. These advantages are particularly important for the identification of the chorio-retinal anastomoses and for the management of higher precision clinical studies (Coscas et al., 2009).

2.3.7 Geographic atrophy

Areas of geographic atrophy are evaluated in clinical studies by color photographs and autofluorescence. In TD-OCT, the RPE atrophy can be revealed by the increased choroidal hyper-reflectivity. In SD-OCT, the improved transverse resolution differentiates more clearly the limits between the normal and abnormal RPE and the segmentation techniques allow the correlations of the RPE changes with the photoreceptor layer (Coscas et al., 2009).

2.3.8 Therapeutical impact of OCT

Besides its contribution in the diagnosis of AMD, OCT examination is extremely useful in establishing the indication of the modern treatments in wet AMD (intravitreal injections with anti-VEGF agents) and in the monitoring of the response to treatment. The clinical experience has set up an algorithm of follow-up and treatment, although the number of injections is not yet established. However, it seems that the recurrence rate decreases with time (Coscas et al., 2009).

2.3.9 Limits of OCT

OCT cannot precisely describe a CNV network, nor can it define its nature: active or pre-fibrotic. Therefore, the OCT scan must be interpreted in correlation with the fundus photography, direction of scan and ideally, the angiography (Coscas et al., 2009).

Another limitation of OCT is revealed in evaluating the extension of the geographic atrophy (GA). In a recent study, the GA areas identified in SLO scans were significantly larger than the ones detected on the OCT maps. Spectralis OCT showed significantly more mild and severe segmentation errors than 3D and Cirrus OCT. Taking into account the fact that GA is a frequent form of AMD, this limitation should be resolved in order to identify and document RPE loss in a realistic manner (Schutze et al., 2011).

2.3.10 Future developments of OCT

One of the most recent innovations is the possibility to deliver simultaneously data offered by various examination methods: OCT, red-free photography, autofluorescence,

angiography, SLO, Eye -Tracking systems, microperimetry (Marschall et al., 2011). The use of various wavelengths would create the possibility to penetrate deeper and examine the choroid. The improvement of the possibilities to process the 3D images will allow the more detailed and precise evaluation of a certain structure (Coscas et al., 2009).

2.4 Personal experience with OCT imaging in the diagnosis and monitoring of AMD

The contribution of OCT in the daily practice is illustrated by several examples of various AMD modifications.

2.4.1 Fourier Domain-OCT (FD-OCT) in the diagnosis of AMD

FD-OCT imaging was performed with a Topcon 3D OCT-1000 instrument (TOPCON, Japan, model 2007) that uses a monochromatic light source of 840 nm wave length. The Topcon 3D OCT-1000 combines FD-OCT system with a color non-mydriatic retinal camera.

In fig. 2a appears the image of a normal fundus, showing the optic nerve head, the macular region and the retinal vessels (arteries and veins). Fig. 2b displays the 2D FD-OCT image of the macula, showing (from the surface to the deep layers): the foveolar depression, the neurosensory retina and the RPE (the red layer). Fig. 2c illustrates the 3D FD-OCT image of the macula, revealing the architecture of the normal macular region, tridimensionally - a true "live biopsy" of the tissues. The tissues with high reflectivity appear more red on the OCT. For instance, on the normal OCT, the RPE band has the highest reflectivity (red color).

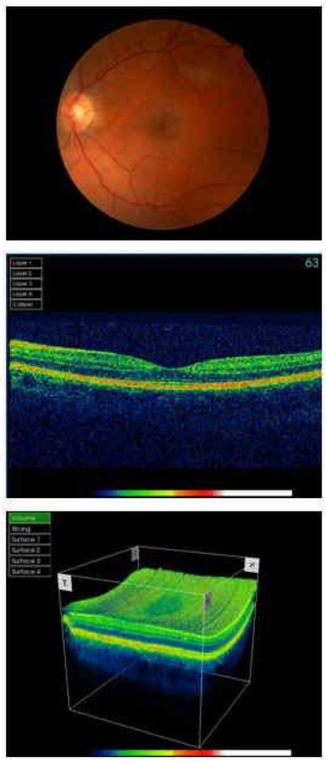

Fig. 2. The normal macula: a) ocular fundus; b) 2D scan; c) 3D scan (courtesy of Dr. F. Balta, Eye Hospital, Bucharest, Romania)

In fig. 3a, the ophthalmoscopic aspect of a wet form of AMD is illustrated: subfoveal neovascular membrane, elevating the retina, on average 1,5 disc diameters in surface. Fig. 3b depicts the 2D FD-OCT image of the macula in wet AMD: elevation of the macular retina, the space under the neurosensory retina is occupied by an irregular, opaque structure; the retinal pigmented epithelium is thickened. The 3D FD-OCT image of the macula in wet AMD (fig. 3c) offers a tridimensional view: elevation of the macular retina, better depiction of the retinal topography, thus improving the visualization of RPE irregularities. The advantage of FD-OCT in AMD is revealed by the fact that because it more densely samples the macula, it will be more likely to diagnose the presence of fluid in its nascent stages, meaning treatment can be introduced early and before it causes limitations to vision. FD-OCT can also capture macular hemorrhaging. While TD-OCT would also theoretically show fluid and blood at the macula, it would not be able to depict with the same accuracy at what retinal layer the buildup occurs.

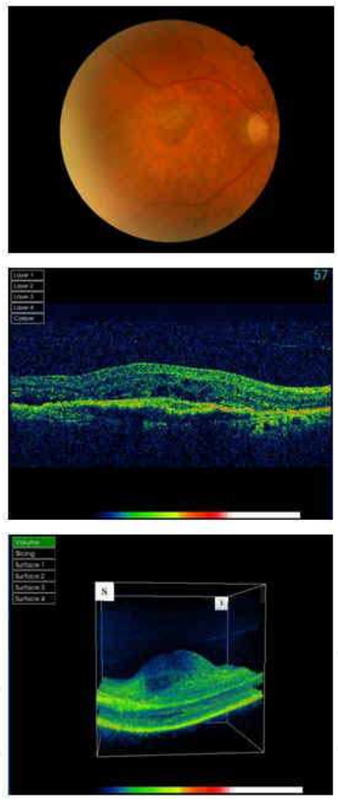

Fig. 3. Age-related macular degeneration: a) ocular fundus; b) 2D scan; c) 3D scan (courtesy of Dr. F. Balta, Eye Hospital, Bucharest, Romania)

2.4.2 Cirrus High Definition-OCT (HD-OCT) in the diagnosis of AMD

Cirrus HD-OCT (Carl Zeiss Meditec) provides detailed maps and quantifies the retinal thickness and volume.The 5-line raster, with over 4.000 A-scans per line, offers such high definition images that differences in fluid are identifiable, thus helping to indicate the specific disease process. The representation of the macula is useful for layer identification, segmentation, and the quantitative and qualitative analysis.

RPE detachment is characterized by the accumulation of fluid between the highly reflective RPE (red line) and the moderately reflective choriocapillaris. Blister-like elevation of the retina and RPE are evident on the OCT image. Figures 4 and 5 depict the PEDs: the red line representing the RPE is irregular and present focal elevations. Fig. 4 also shows the fluid accumulation in the retina in a region adjacent to the RPE detachment.

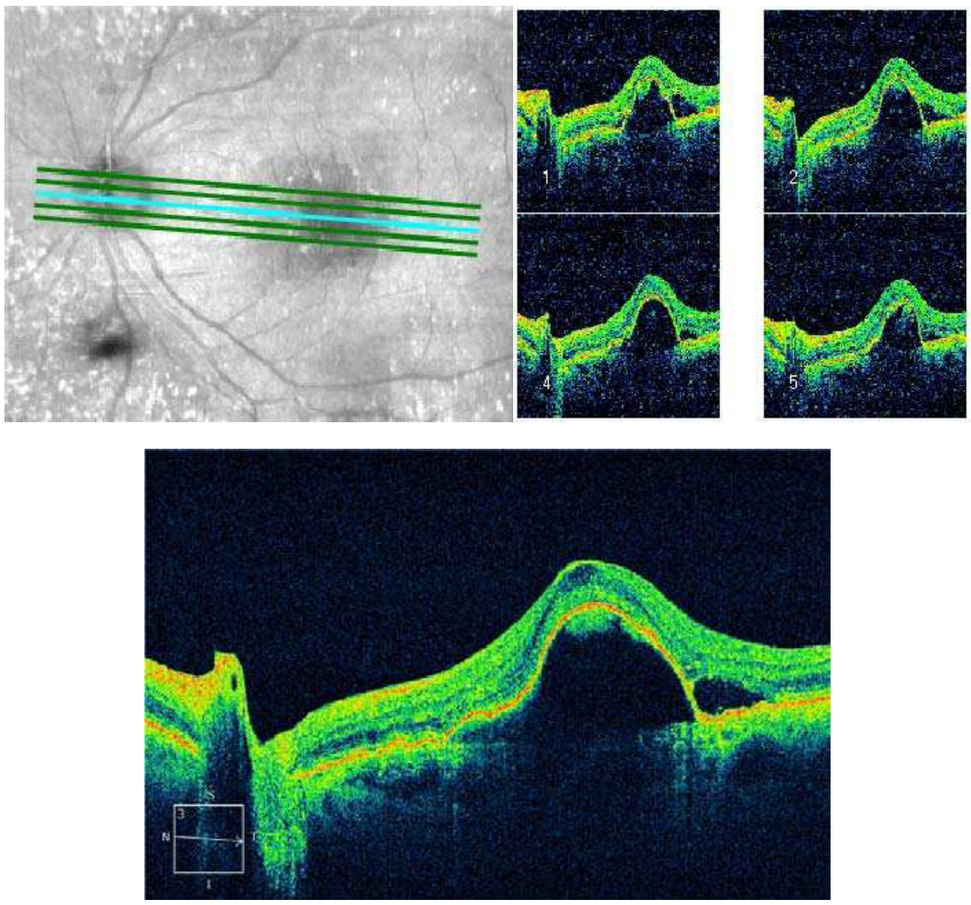

Fig. 4. HD-5 line raster: Drusen and PEDs
(courtesy of Dr. H. Shah, Midland, Texas, USA)

Occult CNV is a term given to a specific „blothcy" appearance on the angiogram. The occult CNV in fig. 6 is suggested by the irregularities and thickening of the RPE layer and the CME appears like small, cystic spaces within the macula. In the figure above, the occult CNV is not accompanied by PED, therefore it is cathegorized as type 2 occult CNV. The type 1 occult CNV associates PEDs and is also named vascularized PED. The occult CNV might be an early phase of the classic CNV and therefore its identification is important for the early diagnosis of the wet AMD.

When the choroidal new vessels that have grown under the macula are seen on the angiogram, this condition is named classic CNV. The classic CNV appears on OCT as a hyper-reflective structure that elevates the RPE. This aspect is easily demonstrated in fig. 7, 8, and 9.

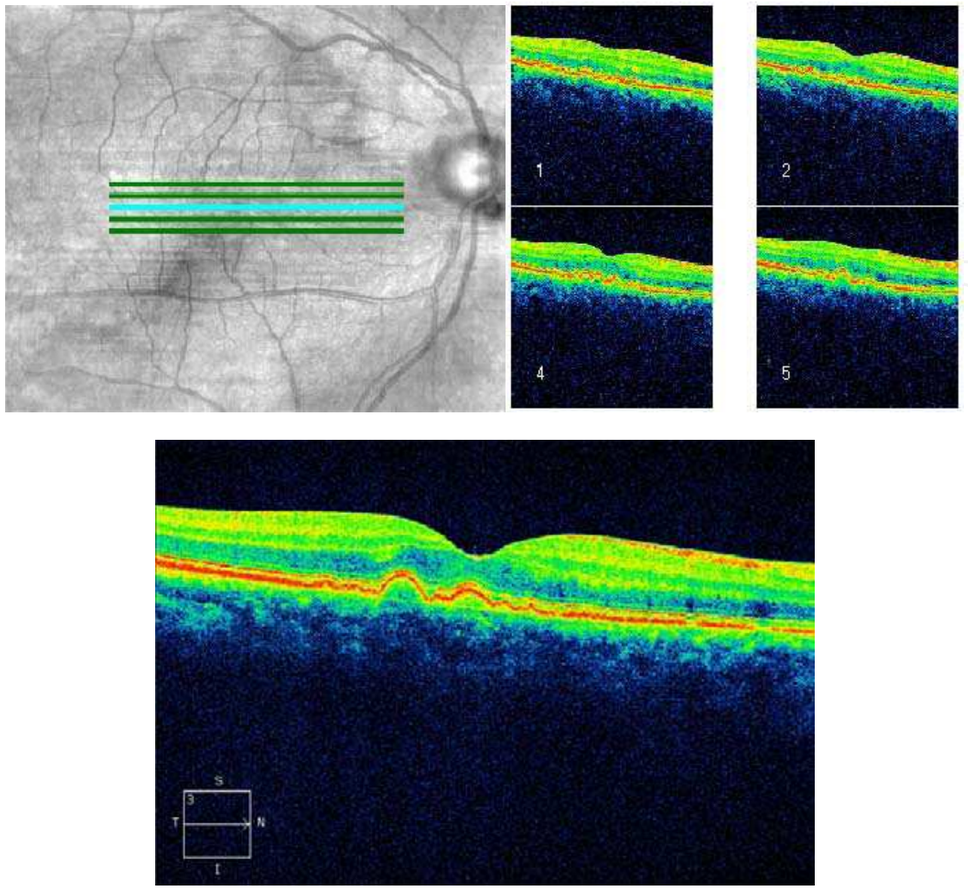

Fig. 5. HD-5 line raster: PEDs (courtesy of Dr. H. Shah, Midland, Texas, USA)

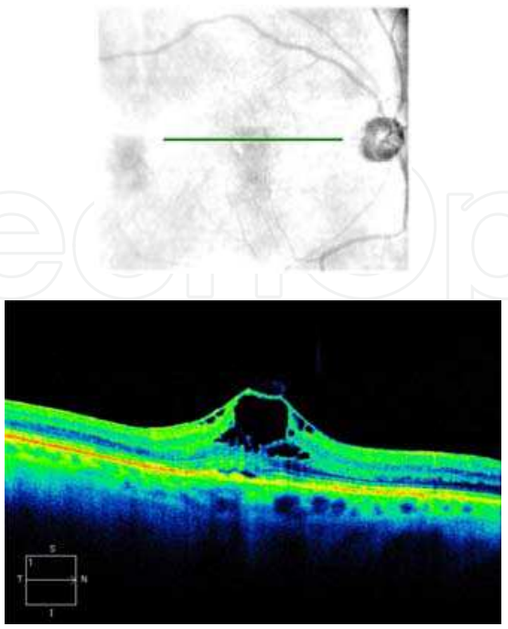

Fig. 6. Occult CNV with CME (courtesy of Dr. H. Shah, Midland, Texas, USA)

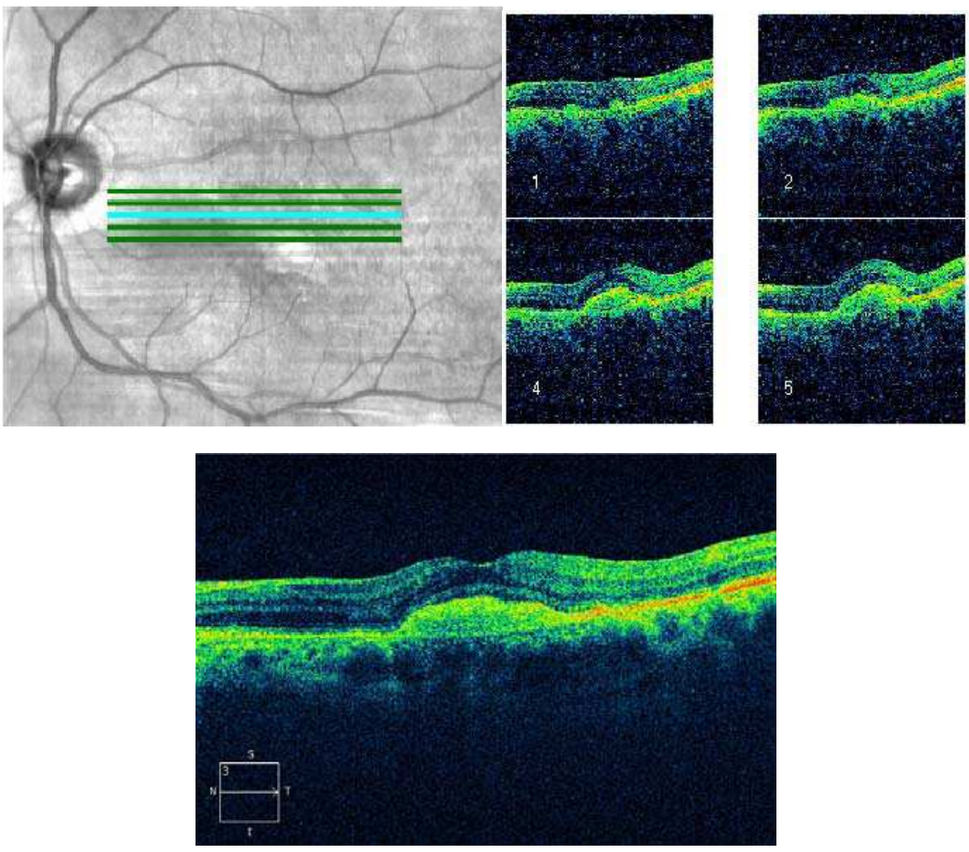

Fig. 7. HD-5 line raster: Classic CNV (courtesy of Dr. H. Shah, Midland, Texas, USA)

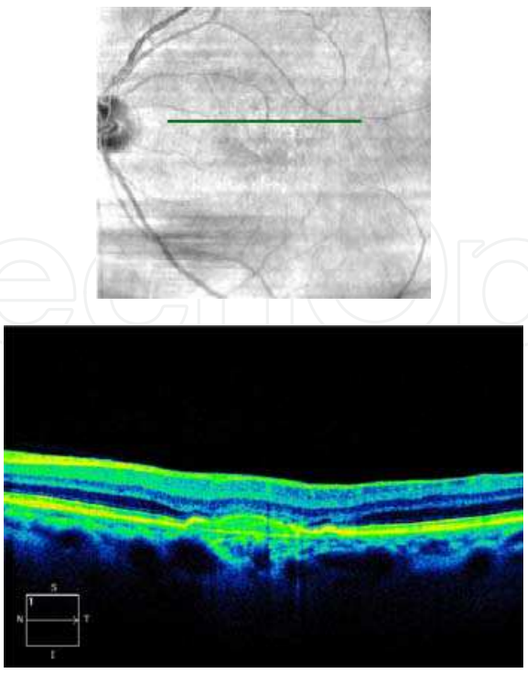

Fig. 8. Classic CNV (courtesy of Dr. H. Shah, Midland, Texas, USA)

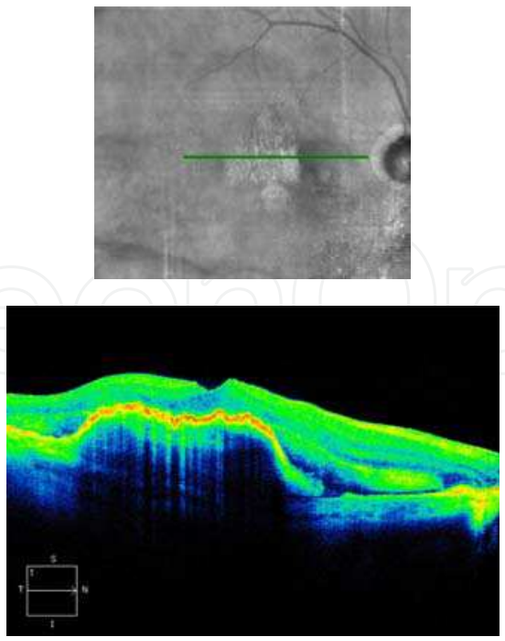

Fig. 9. Classic CNV (courtesy of Dr. H. Shah, Midland, Texas, USA)

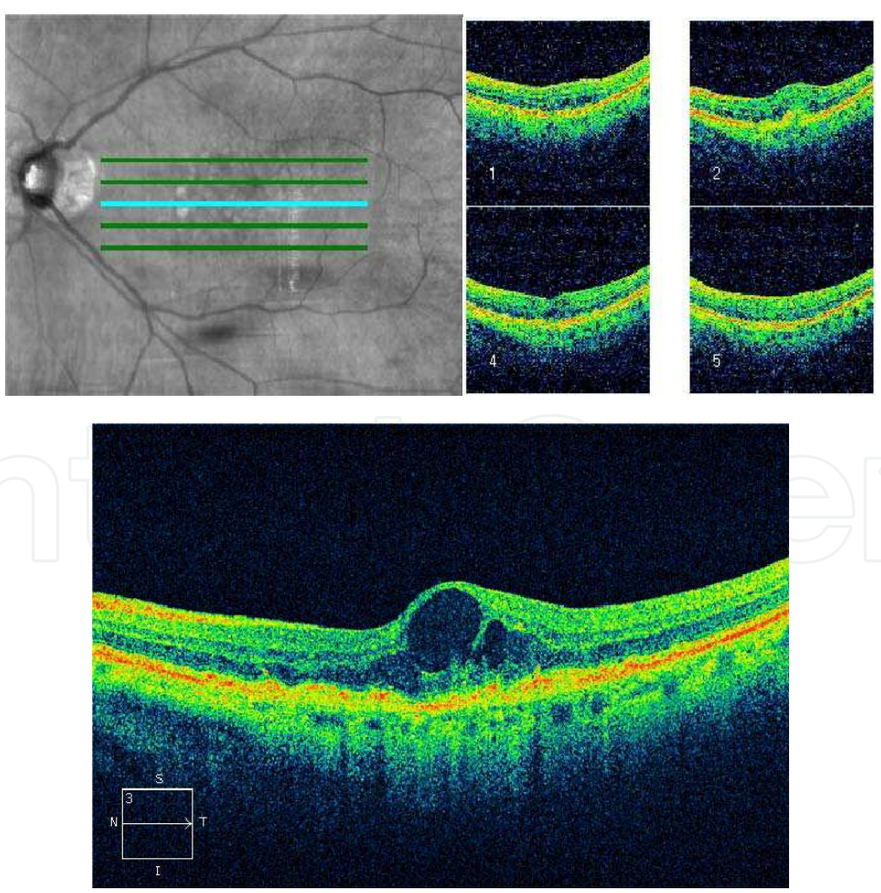

Fig. 10. HD-5 line raster: Wet AMD (courtesy of Dr. H. Shah, Midland, Texas, USA)

In fig. 10 the RPE appears irregular and thickened (suggesting an occult CNV) and under the RPE line there is a hyper-reflective structure slightly elevating the RPE on line 2 of the raster (classic CNV). On the same line, the RPE line appears interrupted. The structure of the neurosensory retina is disorganized by the cystic fluid accumulation within the retinal layers.

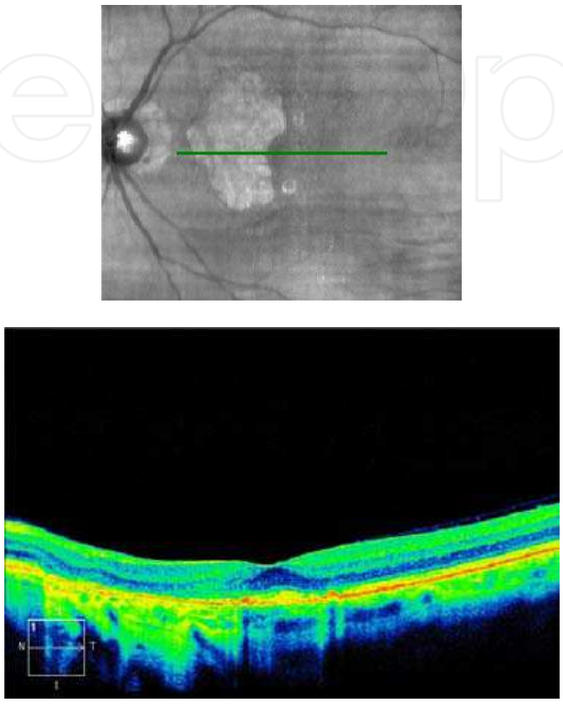

Fig. 11. Choroidal atrophy (courtesy of Dr. H. Shah, Midland, Texas, USA)

Geographic atrophy is the end stage of the dry AMD. The reflectivity of the RPE and underlying choroid is increased (fig. 11). There have been defined spectral-domain OCT patterns that are correlated with a higher risk of atrophy's extension: the irregular margin of the lesion on OCT is significantly associated with increased fundus autofluorescence and a higher risk of progression. The smooth margin of the lesion has been significantly associated with normal fundus autofluorescence and a lower risk of atrophy's progression (Brar M. et al., 2009). In our example (fig. 11), the margins of the choroidal atrophy appear pretty irregular. We can speculate that because it reveals structural changes, the spectral – domain OCT is a better predictor for geographic atrophy's extension, as compared to fundus autofluorescence, but this hasn't been proved yet.

2.4.3 TD-OCT (Stratus) in monitoring AMD

The TD-OCT imaging was performed using a Stratus OCT 2006 commercial instrument (Carl Zeiss Meditec, Dublin, California, USA). The Stratus TD-OCT provides real-time cross-sectional images and quantitative analysis of retinal features to optimize the diagnosis and monitoring of retinal disease and for enhanced pre-and post-therapy assessment. Sensor captures 1 image at a time

In figure 12, the comparation of the macular thickness before and 3 months after Bevacizumab injection revealed no significant modification, which led us to stop the anti-VEGF intravitreal injections.

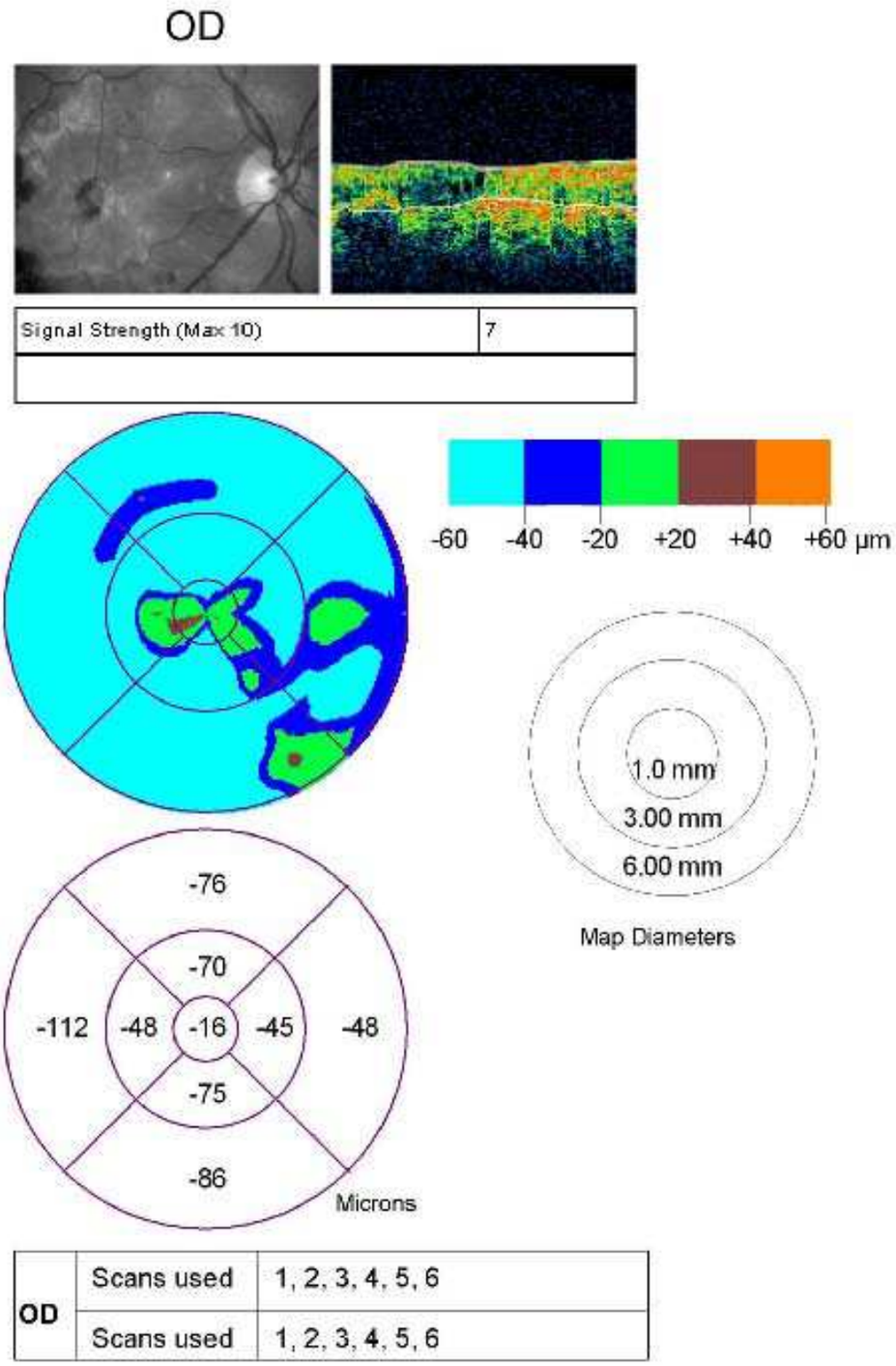

Fig. 12. RTM: comparation of the macular thickness before and 3 months after Bevacizumab injection (courtesy of dr. H. Demea, Review Centre, Cluj-Napoca, Romania)

The next case (figure 13) showed a slight improvement in the right eye, 3 months after 3 Bevacizumab injections. The fibrotic nature of the submacular tissue in the left eye kept us from performing the anti-VEGF intravitreal injections.

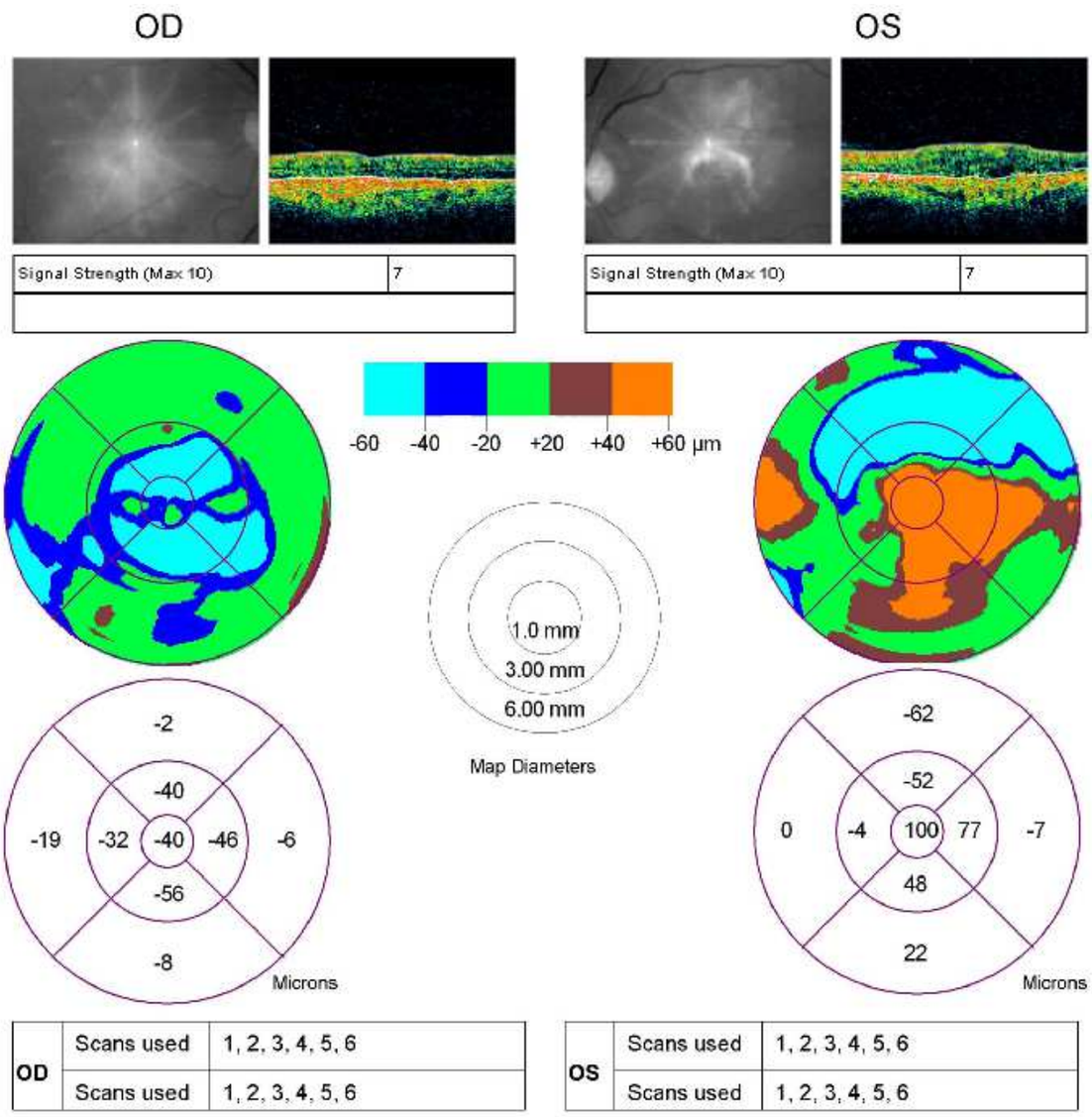

Fig. 13. RTM: comparation of the macular thickness before and 3 months after Bevacizumab injection (courtesy of dr. H. Demea, Review Centre, Cluj-Napoca, Romania)

Figure 14 illustrates the decrease of the macular thickness 3 months after 3 Bevacizumab injections.

In all the cases with favorable outcome, the most spectacular improvement, both in vision and in the anatomical aspect, has been obtained after the first injection. The better results are directly correlated with the early stage of the disease. Even if the vision has not changed

from the quantitative point of view, all the patients with a better anatomical aspect of the macula on OCT have also experienced a significant improvement in the quality of vision, translated by the diminishing of the central scotoma, both in surface and in density (Talu et al., 2010).

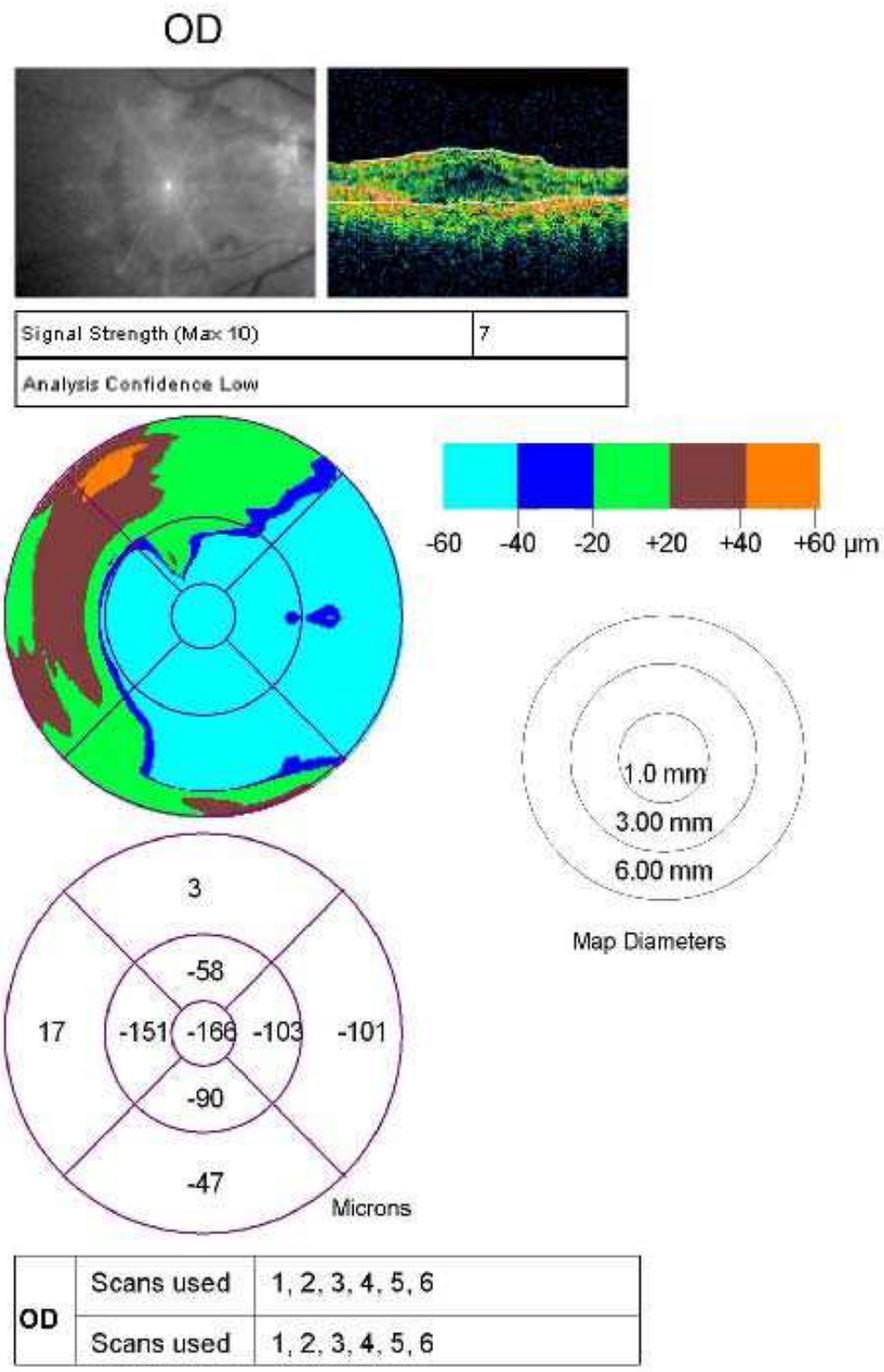

Fig. 14. RTM: comparison of the macular thickness before and 3 months after Bevacizumab injection (courtesy of dr. H. Demea, Review Centre, Cluj-Napoca, Romania)

3. Conclusion

The invention of OCT in the 1990s is a major breakthrough in ocular imaging, as it represents a fast, non-invasive, radiation-free examination technique, able to visualize precisely the retinal layers – something done before only on pathology slides. The information offered by OCT is detailed, simple and easily interpretable. AMD is by far, the ocular condition that has benefited the most from the enormous advantages offered by OCT, in terms of diagnosis, response to treatment and monitoring. OCT is applied by two main methods: Time domain OCT (TD-OCT) and Spectral domain OCT (SD-OCT). TD-OCT produces two-dimensional images of the sample internal structure. SD-OCT can be implemented in two formats, Fourier domain (FD-OCT) and swept source (SS-OCT). The image is acquired rapidly - about 60 times faster than with TD-OCT. The image resolution in SD-OCT is 1 μm, as compared to 10 μm in TD-OCT. The practical impact of this improvement in resolution is the early detection of small cystic changes associated with the wet form of AMD. The great number of scans done per second allows SD-OCT systems to generate 3D reconstructions, which can be further manipulated. Visualization of these data in 3D demonstrates subtle pathology that are not evident with conventional 2D images. The most frequent application of OCT in retinal disease is the measurement and monitoring of the retinal thickness. The TD - OCT system (Stratus) gives a macular thickness map which is calculated from 6 radial B-scans crossing at the fovea. By interpolating data from these scans, the average macular thickness is calculated in 9 subfields centered on the fovea. Similarly, the total macular volume is obtained. The SD-OCT provides images with much higher resolution. Given the differences between the measurements with the two types of OCT (TD and SD), algorithms are necessary in order to establish correlations between them. Besides its contribution in the diagnosis of AMD, OCT examination is extremely useful in establishing the indication of the modern treatments in wet AMD (intravitreal injections with anti-VEGF agents) and in the monitoring of the response to treatment. Ideally, the OCT scan must be interpreted in correlation with the fundus photography, direction of scan and ideally, the angiography. Despite the obvious advantages offered by OCT at the present moment, there is still room for future developments and improvement.

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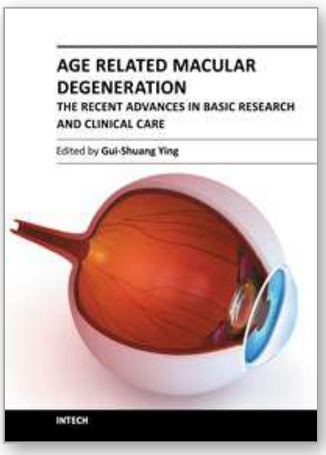

Age Related Macular Degeneration - The Recent Advances in Basic Research and Clinical Care

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Age-related Macular Degeneration (AMD) is the leading cause of vision loss and blindness in the developed countries. In the past decade, great progress has been made in understanding the pathobiology and genetics of this blinding disease, as well as in finding new therapies for its treatment. These include the discovery of several genes that are associated with the risk of AMD, new anti-VEGF treatments for wet AMD and new imaging techniques to diagnose and monitor the AMD. All chapters in this book were contributed by outstanding research scientists and clinicians in the area of AMD. I hope this timely book will provide the basic scientists and clinicians with an opportunity to learn about the recent advances in the field of AMD.

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