CONTRIBUTION OF OPTICAL COHERENCE TOMOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF DIABETIC RETINOPATHY

MIHAELA FLORESCU[1], ADRIANA STĂNILĂ[2]

[1]Dr. Stănilă Medical Centre, [2]"Lucian Blaga" University of Sibiu

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Abstract: *Purpose of the paper: is to present the major contribution optical coherence tomography has now in the evaluation of patients with diabetic retinopathy and thus, the contribution of this method to establish the optimal therapeutic management in these patients. Methods: We have studied 63 patients with diabetic retinopathy at different stages of development, in whom OCT was performed. The patients who received laser treatment, intravitreal injection were re-examined one month later and depending on the OCT appearance, we decided upon the treatment to follow, which was individualized for each patient. Results and Discussion: Tomography elements encountered in the patients with diabetic retinopathy taken in the study were: macular edema / cystoid macular edema, hard exudates, serous detachment of the neuroephitelium, preretinal membrane, vitreo-macular traction, lamellar hole. In macular edema, we observed increased retinal thickness with or without deletion of foveal depression and hiporeflectivity of the optical signal from the external retinal layers. Clinically, early diagnosis of diabetic macular edema with optical coherence tomography would lead to early laser intervention, resulting in a stagnation of progression and even an improvement in visual acuity in some patients with diabetic retinopathy. Conclusions: OCT allows diagnosing and identifying the morphological characteristics of macular edema. OCT is useful in monitoring the response after therapy: quantification of retinal thickness, achieving the foveal central volume and retinal maps, helping monitoring the effects of therapy (laser, intravitreal injections with triamcinolone acetonide and / or anti-VEGF factor). OCT is the ideal method for tracking diabetic macular edema.*

Cuvinte cheie: *tomografie in coerenţă optică*
retinopatie diabetică
edem macular

Rezumat: *Scopul lucrării: Este de a prezenta contribuţia majoră pe care o are în prezent tomografia în coerenţă optică în evaluarea pacienţilor cu retinopatie diabetică şi, implicit, aportul acestei metode la stabilirea conduitei terapeutice optime în cazul acestor pacienţi. Material şi metodă: Am luat în studiu 63 de pacienţi cu retinopatie diabetică în diverse stadii de evoluţie, la care s-a efectuat OCT. Pacienţii care au beneficiat de tratament (laser, injecţii intravitreene) au fost reexaminaţi la o lună şi, în funcţie de aspectul OCT, am decis tratamentul de urmat, individualizat pentru fiecare pacient. Rezultate şi discuţii: Elementele tomografice întâlnite la pacienţii cu retinopatie diabetică luaţi în studiu au fost următoarele: edem macular/edem macular cistoid, exudate dure, decolare seroasă de neuroepiteliu, membrană preretiniană, tracţiune vitreo-maculară, gaură lamelară. În edemul macular am observat creşterea grosimii retiniene cu sau fără ştergerea depresiunii foveale şi hiporeflectivitatea semnalului optic de la nivelul straturilor retiniene externe. Din perspectiva clinică, diagnosticul precoce al edemului macular diabetic cu ajutorul tomografiei în coerenţă optică ar duce la o intervenţie laser timpurie, rezultând astfel o stagnare a progresiei şi chiar o îmbunătăţire a acuităţii vizuale la o parte din pacienţii cu retinopatie diabetică. Concluzii: OCT permite diagnosticarea şi identificarea caracteristicilor morfologice ale edemului macular. OCT este util în monitorizarea răspunsului după terapie: cuantificarea grosimii retiniene, realizarea volumului central foveal şi a hărţilor retiniene, ajută la monitorizarea efectelor terapiei (laser, injecţii intravitreene cu Triamcinolon acetonid şi/sau factor anti-VEGF). OCT este metoda ideală pentru urmărirea edemului macular diabetic.*

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder, characterized by hyperglycemia with severe variations thereof, secondary to decreased endogenous insulin efficiency.(1,4,5,6,9,12) Diabetic retinopathy (DR) is a microvascular complication of diabetes and the leading cause of blindness in the working population in most industrialized countries.(2,7,8,10,13,22)

Diabetic maculopathy may be present at any stage of diabetic retinopathy.(8,14,15,16,24) Retinal thickness measurement by using OCT is used to diagnose macular edema, most commonly in patients with DR.(3,11,22,17)

OCT (optical coherence tomography) is a modern imaging, objective, fast, non-invasive and non-contact technique, which allows to obtain detailed information about the structure of the retina. Within the examination, we can observe different longitudinal optical sections of the retina, facilitated by

[1]Corresponding author: Mihaela Florescu, B-dul V. Milea, Bl. 3, Sc A, Ap. 7, Sibiu, România, E-mail: mihaela.florescu@yahoo.com, Tel: +40740 205405
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the differences of optical reflectivity existing both at the internal limit and external one of the neurosensory retina.(3)

PURPOSE

The paper aims at highlighting specific information obtained by OCT, the morphological changes in all layers of the retina, especially the retinal and foveal thickness, the most important parameter followed in edematous exudative maculopathy. We analyzed the contribution of optical coherence tomography in the evaluation of patients with diabetic retinopathy and implicitly, the contribution of this method to establish the optimal therapeutic management in these patients.

METHODS

A number of 124 eyes from 63 patients (39 women and 24 men) diagnosed with diabetic retinopathy, with / without macular edema were analyzed using optical coherence tomography. The patients were examined through OCT, pre and post treatment in selected cases to determine the effectiveness of laser photocoagulation and intravitreal injections with triamcinolone acetonide and / or anti-VEGF agents.

Previously the tomographic examination, we made eye examinations that included visual acuity determination with correction, anterior and posterior pole biomicroscopy, tonometry and pictures of the retina.

The patients were explained that retinal optical coherence tomography is a noninvasive method, like ultrasound and uses a light source. Pupil dilation was required only in certain cases and for a clearer view of the retinal area that was to be scanned.

To achieve tomography scans, there has been used the Cirrus HD-OCT-Zeiss within the Dr. Stănilă Medical Centre, Sibiu. It uses the advanced imaging of the optical coherence technology and spectral range. Spectral domain devices acquire data 70 times faster (27000 vs 400 A scans / second) and better axial resolution in tissue (5 mm vs 10 mm), compared to the first OCT generation - time domain.

In terms of acquisition protocols, we used the macular Cube and 5 laser Lines.

"Macular Cube 512x128" (figure no. 1 and figure no. 2) provides quantitative information by acquiring data from a 6 mm square area by scanning 128 horizontal lines, each consisting of 512 scans type A. Each HD cross scan is made up of 1024 scans type A. In cube analysis, an automated algorithm is used, specifying the internal limiting membrane and the retinal pigment epithelium. These layers are used as the basis for the measurements of macula thickness and macular volume.

Selecting macular thickness provides the following information: location of the fovea, fundus image with overlaid scanned cube and coloured grid map of the retinal thickness with the 9 ETDRS areas (Early Treatment Diabetic Retinopahy Study), normative data on the thickness of the retina, the measurements table with the average thickness and the average volume, thickness 3D colour map, 3D map of the internal limiting membrane and the pigment epithelium. ETDRS grid map shows the average thickness of the retina in 9 sectors and is composed of three concentric circles with a diameter of 1 mm, 3 mm and 6 mm, divided in upper areas, temporal, nasal and lower, with the exception of the central circle whose radius measures 500 µm.

Figure no. 1. Macular cube, macula thickness

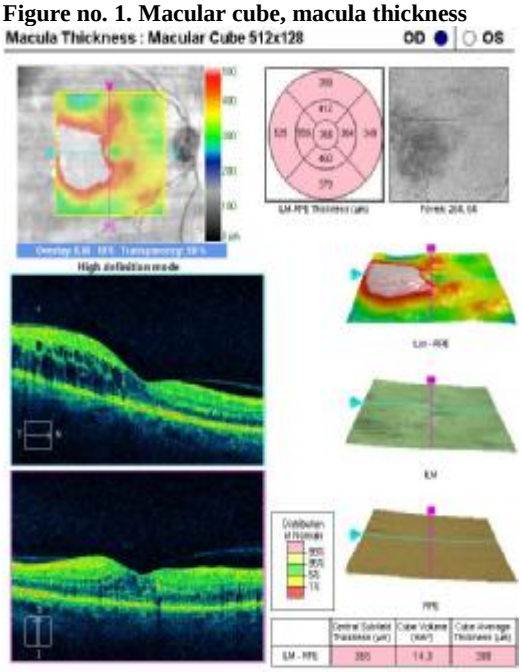
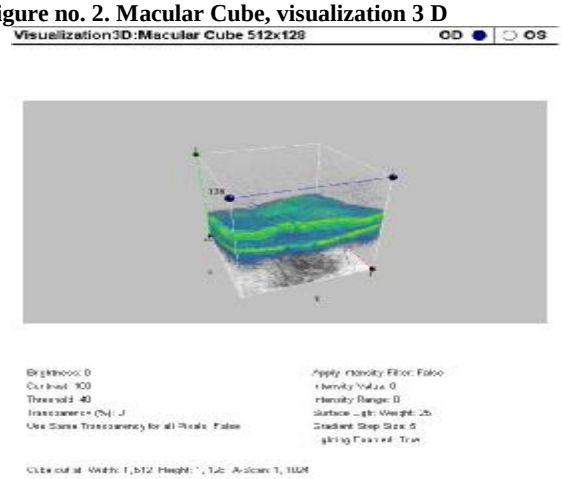
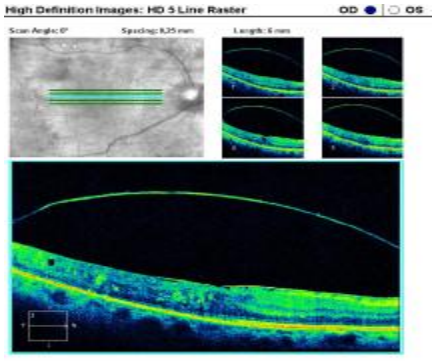


Figure no. 2. Macular Cube, visualization 3 D



"5 raster lines" (figure no. 3) shows us a qualitative morphological analysis with high resolution (HD) of the retinal images. Five parallel lines are scanned, of equal length, with adjustable rotation and spacing. This type of scanning has the highest resolution, each line consisting of 4096 A scans. Lines length can be selected at 3, 6, 9 mm. Usually, the horizontal lines of 6 mm length are used, separated by spaces of 0.5 mm.

Figure no. 3. OCT image, 5 Line Raster



RESULTS

Tomographic elements found in the patients with diabetic retinopathy in the study were:

- Macular edema / cystoid macular edema - 44 patients
- Hard exudates - 32 patients
- Detachment of serous neuroepithelium - 8 patients
- Preretinal membrane -5 patients
- Vitreo-macular traction - 3 patients
- Lamellar hole- 1 patient
- Associated changes were reported in most studied patients.

Central macular thickness exceeded 200 μm in a number of 79 eyes. Diabetic Macular Edema was evidenced through OCT in the following forms: diffuse macular thickening, presence of nonreflective cystic spaces of various sizes, subretinal fluid accumulation.

At present, the laser is the "gold standard" for the therapy of diabetic retinopathy and diabetic macular edema, particularly. The patients who have experienced changes in macular received laser treatment: focal for a "leakage" located around a microaneurysm and "grid" in the presence of diffuse macular edema. In selected cases, fluorescein angiography was performed prior to photocoagulation therapy, the only investigation able to identify hypoxic retinal territories and that can properly guide the laser treatment.

Case 1: Patient, P.F., 56 years old, in both eyes middle non-proliferative diabetic retinopathy, left eye-focal maculopathy (figure no. 4) ETDRS grid map (figure no. 5) shows a macula thickness of the temporal subcamp at 6 mm of 288 μm.

Figure no. 4. Patient, P.F., Retinal photography of left eye

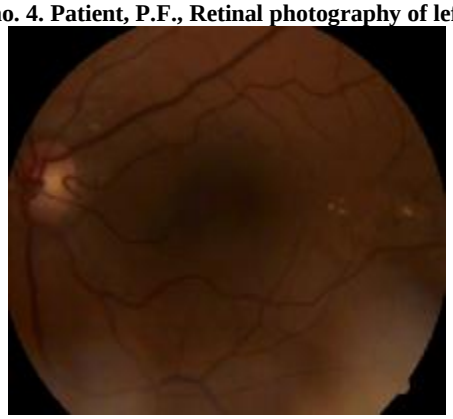
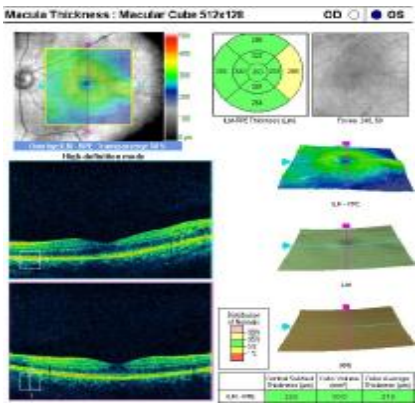


Figure no. 5. Patient, P.F., OCT aspect – left eye



Case 2: Patient, M. M., 64 years old, in both eyes, middle non-proliferative diabetic retinopathy, maculopathy in both eyes, left eye > right eye. Focal laser photocoagulation was performed in the right eye and intravitreal injection with triamcinolone acetonide (between 2 mg in 0.05 ml and 4 mg in 0.1 ml solution) in the left eye. Comparative OCT examination shows: right eye (figure no. 6), reduced macular thickness, especially in temporal subfields of 3 mm and central (from 289 μm - 385 μm to 258 μm - 345 μm); left eye (figure no. 7) serous detachment of the neuroepithelium, macula thickness decreased, especially in the central subfield (from 526 μm to 419 μm). Periodically, we measured the intraocular pressure (in this case, it was in the normal range).

Figure no. 6. Patient, M. M., OCT right eye

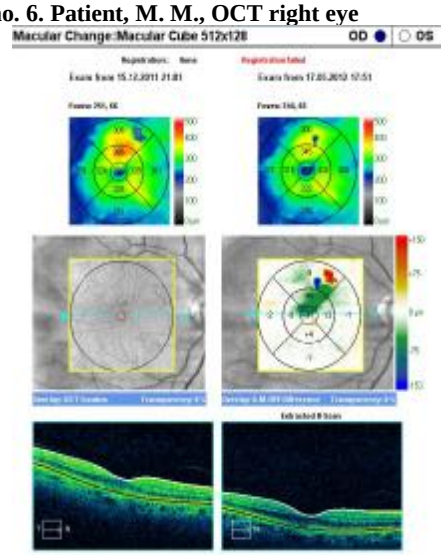
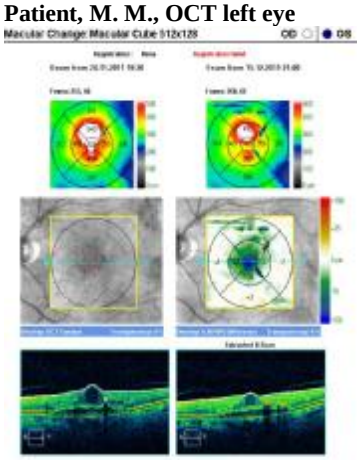


Figure no. 7. Patient, M. M., OCT left eye



Case 3: Patient, B.I., 60 years old, in both eyes middle non-proliferative diabetic retinopathy, right eye diffuse maculopathy. ETDRS grid map (figure no. 8) shows a macular thickness of the central macular subfield of 716 μm. 3 months later, after a series of 3 intravitreal injections with triamcinolone acetonide, one every 1 month, macula thickness of the central macular subfield decreased to 258 μm.

Case 4: Patient, M. L., 61 years old, in both eyes middle non-proliferative diabetic retinopathy, left eye diffuse maculopathy. ETDRS grid map (figure no. 9) shows a macula thickness of the central macular subfield of 669 μm. 1 month after the intravitreal injection combined with triamcinolone acetonide and bevacizumab (1.25 mg in 0.05 ml solution),

macula thickness of the central macular subfield decreased to 598 μm.

Figure no. 8. Patient, B.I., OCT right eye

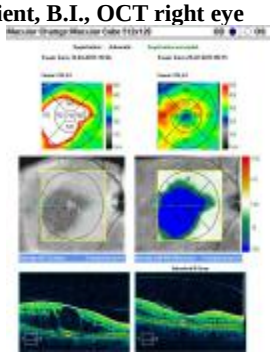
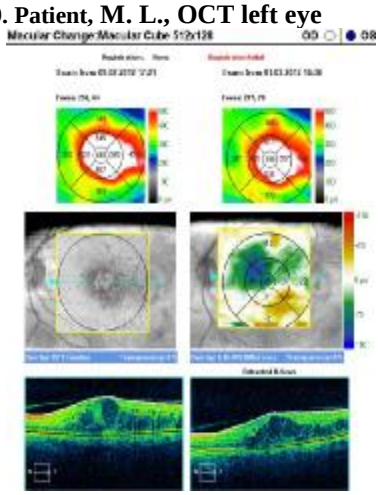


Figure no. 9. Patient, M. L., OCT left eye



DISCUSSIONS

In macular edema, we observed increased retinal thickness with or without deletion of the foveal depression. This should be correlated with changes in reflectivity in the retinal layers, such as the emergence of the nonreflective fluid cystic spaces or decrease of the reflectivity at the level of the external external retinal layers (due to the attenuation of the optical signal that enters and is reflected at this level). In ETDRS, the presence of cystoid changes did not eliminate the benefit of laser photocoagulation in reducing the risk of moderate vision loss.(21.34)

The hard exudates were identified as hiperreflective points with posterior shadow cone localized at the level of the outer plexiform layer.(31)

In the cystoid macular edema, we recognized the presence of fluid cystic spaces of various sizes, nonreflective, usually with the deletion of the foveal depression.

The epiretinial membranes appeared on OCT as hiperreflective preretinal bands of varying thickness, adhering to the internal retinal layers or separated from these ones by black fluid, nonreflective spaces.(36)

In foveal retinal detachment, posterior hyaloid was attached only at the fovea whose outline appeared deformed.(32)

Lamellar hole formed by breaking a serous cystic space presented debris of the broken inner wall, and in the vicinity, we noticed other 5 nonreflective cystic spaces of varying sizes.

When macular edema is present, OCT can detect changes of at least 36 μm in the fovea and 55 μm in parafoveal areas below 744 μm in thickness, so we have to consider that macular edema may itself directly influence the accuracy of measurement in extrafoveal areas.(30)

Currently, macular edema occurring in diabetic retinopathy with intra-and / or sub-retinal fluid accumulation is treated with triamcinolone acetonide (between 2 mg in 0.05 ml and 4 mg in 0.1 ml) combined with bevacizumab (1.25 mg in 0.05 ml solution) in selected cases.(18,25,26)

When administering triamcinolone acetonide, the period measurements of intraocular pressure is necessary due to the risk of secondary glaucoma occurence.(11,20,27,29,35) We found that in some cases, macular edema is significantly reduced or even it disappears on the second day after the intravitreal administration.

We usually check up one month later, and depending on the OCT aspect, the doctor decides upon the therapy to follow, individualized for each patient.

OCT establishes the indications for the surgical treatment - pars plana vitrectomy. Cystoid macular edema secondary to foveal traction and hyaloids membrane thickening or stretching did not benefit from laser photocoagulation and it represents an indication for vitrectomy.(19,28,30)

Clinically, the early diagnosis of diabetic macular edema with optical coherence tomography leads to early laser intervention, resulting in a stagnation of progression and even an improvement in visual acuity in some patients with diabetic retinopathy.(23,33,37)

CONCLUSIONS

OCT allows real-time diagnosis of the morphological characteristics by simultaneously viewing the transverse tomography section and the position of the eye structure.

Due to large differences in reflectivity and well defined contrasts from the posterior and anterior edge of the retina, retinal thickness is a parameter easy to follow, due to the topographic mapping protocol that provides objective information.

Cystic and traction macular edema forms can be easily diagnosed using the OCT that contributes to the understanding of the anatomy of macular edema and of the intraretinal lesions.

OCT is useful in monitoring the response after therapy, quantification of retinal thickness, achieving the central foveal volume and retinal maps, helping in the objective assessment of the imaging aspect before and after the treatment.

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