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REVIEW

OPTICAL COHERENCE TOMOGRAPHY IN PROPAEDEUTICS OF EYE DISEASES

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ABSTRACT

The article considers historical. technological. and methodological aspects in optical coherence tomography creation. On the background of a large body of scientific publications the comparative analysis is presented on optical coherence tomography possibilities and the existing methods of ocular fundus pathologies visualization for diagnosis of the most common diseases and changes in retina. choroid and the optic nerve. An attempt was aimed to estimate the diagnostic value of coherence tomography in propaedeutics of mentioned diseases.

According to data available from numerous researchers. optical coherence tomography allows to consider the degree of eye membranes stretching or the level of their stress specifically in persons with myopia. Meanwhile. until present. in a wide scope of clinical practice the research works on optical coherent assessment of fundus-related and some other changes in myopes are very rare. This is especially true in cases of medical examination and management of children. The above-mentioned allowed the author to draw conclusion on optical coherence tomography insufficient use and inefficient application for investigation of eye diseases in children and adolescents.

Keywords: *optical coherence tomography, ocular fundus pathology, retina, choroid.*

Morphological changes of retina and the optic nerve develop in patients much earlier than they can be identified in the survey, which includes modern electrophysiological and physical methods of investigation. Therefore, for early diagnosis of optic tract diseases it is necessary to apply visualization methods allowing to reveal structural disorders in different parts of the visual pathways. Hence, neuroradiological and ultrasound studies, fluorescein and indocyanine green angiography, optical coherence tomography (OCT), laser scanning ophthalmoscopy, digital photo- and video-filming of ocular fundus with various filters are most frequently used in clinical practice. The comparison of data obtained through application of visualization methods and electrophysiological studies in patients with the optic tract pathology allows to widen the insight on pathogenesis of different diseases related to retina and optic nerve and to develop algorithm for their early diagnosis. The OCT is one of the most informative visualization methods applied in the present-day ophthalmology for diagnosis of retina and optic nerve diseases.

The OCT is a diagnostic method that allows cross-sectional *in vivo* imaging of retina, disk of optic nerve and ocular structures in the anterior segment. At OCT, in addition to obtaining high-resolution cross-sectional images of the retina and optic nerve, measurements of retina and nerve fibers layer thickness, as well as those of optic disk parameters are possible using the commercial software available in scanners. Moreover, the characteristics under study might be compared in dynamics and brought to comparison with norm. The software of the third-generation “Stratus optical coherent tomography” (OCT-3) of Carl Zeiss Meditec Inc. (USA) presents data on age-related standards for persons above 18; appropriate data for children and adolescents are lacking.

The OCT method was introduced into clinical practice in 1991; it is based on principles of A. Michelson interferometry [*Jaffe G., Caprioli J., 2004*]. Low-coherence near-infrared range light

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beam emitted by ultra-bright light-emitting diode (LED) is projected onto the retina. The light that passes through retina is reflected by structures that make its layers.

Time delay indicators of light signals reflected by the posterior segment of eye structures are compared with the time delay of signals of the same light beam reflected from the control or reference mirror placed at a specific distance. When light pulses reflected from the retina and the reference mirror are combined in the OCT-3 interferometer, the interference occurs, the parameters of which are recorded and measured by a photodetector.

The path traversed by different reflected signals is measured by varying the distance to the reference mirror, thus allowing to get the required range of time delay values for the control light burst [*Schuman J. et al., 1995*]. This signal is similar to that obtained at A-scan ultrasonography, but light is applied instead of the sound.

The OCT-3 resolution 10-15 times exceeds the capabilities of standard ultrasound ophthalmic scanners operating in the frequency range of 7-12 *MHz*, and the possibility of high-resolution 20 *MHz* scanners. In optically transparent biological tissues axial resolution of the second-generation scanner OCT-2 was about 15 *μm*, while the cross-sectional resolution was about 20 *μm*. This latter 3-5 times exceeded the resolution of other methods used with similar purposes, in particular, of scanning laser ophthalmoscopy [*Bagga H., Greenfield D., 2004; Monteiro M. et al., 2004*]. Third-generation tomograph "Stratus OCT-3" produced by the same manufacturer has an axial resolution of about 8-10 *μm* [*Smiddy W., 2004*]. Resolution of the image obtained with OCT is mainly determined by the emitter. In commercial scanner models, the ultra-bright LED with emission wavelength of 815-820 *nm* is used as emitter. The ultra-high resolution scanners are equipped with other emitters, for example, titanium-sapphire laser, the use of which allows increasing the axial resolution of the device up to 2-3 *μm*.

In addition to its high resolution, OCT, as compared to other visualization methods applied to study the fundus, has additional advantages: measurements of the retina thickness and retinal nerve fiber layer (RNFL) with the use of OCT are not affected by such parameters as refraction, axial length of the eye, the presence of minor or moderate clouding of the lens nucleus. Such features as non-contact with the tissues in the process of investigation and short duration of scan make the OCT a perfect diagnostic tool for application in children aged 3 years and above [*Schuman J. et al., 1995; Eriksson U. et al., 2004; Hess D. et al., 2005; Mosin I., 2005; Mosin I. et al., 2005a*]. If necessary, in children under 3 years of age or in patients with nystagmus and/or lesions of the central nervous system the OCT can be performed under general anesthesia [*Chen S., Patel C., 2003*].

As indications for OCT under general anesthesia in early childhood S. Chen and C. Patel considered the following states: macular folds, posterior vitreous detachment or persistence of macular subretinal fluid after surgery for retinal detachment in patients with retinopathy of prematurity, those with shaken baby syndrome [*Chen S., Patel C., 2003*].

There is evidence of OCT high information value in various vitreoretinal pathlogy states: macular holes [*Eriksson U. et al., 2004*], cystoid macular edemas of various etiologies [*Ciardella A. et al., 2004; Kang S. et al., 2004*], central serous chorioretinopathy [*Hee M. et al., 1995; Rodin A. et al., 2001*], retinal detachment, macular degeneration, *retinitis pigmentosa* [*Schatz P. et al., 2003*], Best's disease, choroidal neovascularization [*Rudneva M. et al., 2004*; *Hughes E. et al., 2005*], posterior uveitides [*Lieb D. et al., 2004; Kozak I. et al., 2005*], retinal vascular occlusions, myopia, contusion injuries of posterior segment of the eye, and choroidal metastatic tumors, retinoblastomas, choroidal nevuses, melanomas, and osteomas [*Espinoza G. et al., 2004*].

The OCT allows to investigate patients with high myopia [*Mrugacz M. et al., 2004; Sayanagi K. et al., 2005*], as well as the surface topography of the optic disk nerve, to measure its parameters (diameter of the disk, excavation) and the scleral canal: their size and volume, the level of disk prominence, depth of excavation, area of neuroretinal ring, i.e., to quantitatively assess the condition of the nerve fiber layer of the retina in patients with various diseases of the optic nerve – hypoplasia and atrophy of the optic nerve [*Monteiro M. et al., 2003; Mosin I. et al., 2005a;b; 2006*], stagnant disk, glaucomatous neuropathy [*Schuman S. et al., 1995; Hess D. et al., 2005; Medeiros F. et al., 2005*], the expanded excavation syndrome [*Mosin*

I. et al., 2005a;b], the optic nerve disk drusen [*Floyd M. et al., 2005*].

Manipulations of the ophthalmologist during OCT of the retina and optic disk resemble the actions taken while dealing with a fundus camera. The patient is asked to look with the tested eye at the objective, the lens of which is located at a distance of 9 *mm* from the cornea, fixing gaze on the internal green LED. Depending on problems to be solved at study, duration of the medical examination according the specific protocol varies from 1.3 to 12 seconds, during which the patient must hold the view of the fixation stimulus and do not blink.

The use of first-generation tomographs required pupil dilation to 5 *mm* or more. Third-generation scanner "Stratus OCT-3" allows adequate visualizing structures of the retina in case the pupil diameter makes 3 *mm*. It should be noted that medical mydriasis simplifies scanning, especially in patients with poor fixation or blurred optical media of the eye, by increasing the study-controlled area.

In patients with retinal and optic nerve injuries and low visual acuity scanning the macula is much simpler than scan of optic nerve disk or other parts of the fundus, because mentioned patients are easier to control internal fixation stimulus projected onto the center of foveola or try to keep in mind given direction, for example, to look straight ahead.

At examination of retina and the optic nerve disk using "Stratus OCT-3" scanner the software that provides 19 modes of scanning and 18 image analysis protocols is applied. Depending on the purpose of the study various scan protocols provided by commercial software can be applied.

The most significant feature of the coherence tomograph is the ability to quantify the thickness of retina in the studied area.

The available software can automatically identify the inner layers of the retina along the vitreoretinal surface and the outer layers of the retina along the surface of pigment epithelium, due to the different reflectivity of depicted structures of the retina. Upon the automatic image processing by the specified software, retinal thickness is determined in all six tomograms by measuring the distance between the layers in each evaluation point along the longitudinal axis. The measurement results for each slice are graphically displayed as a curve resembling the profile of the retina. According to results of these measurements, computer software produces maps of the surface reconstruction.

Since upon the use of 6 radial sections the number of points, at which the thickness of retina is measured in the central zone (for example, the fovea), is considerably greater than in the peripheral regions, the accuracy of measurements on retinal thickness in the center of the fovea is higher than in the peripheral areas of macula.

The results of analysis with the use of scan protocols "Retinal Thickness Map" and "Fast Retinal Thickness Map" includes six cross-sectional images of the retina, the color and digital topographic maps of the retina, at which – in addition to the thickness of the retina in the test points – pre-conditioned colors indicate in micrometers the averaged parameters of retinal thickness in 9 sectors. At correct OCT the variability of results on measurements of retina thickness, as a rule, does not exceed 5%. Retinal thickness measurements performed by OCT are sufficiently accurate and well reproducible, even in patients with macular edema [*Hee M. et al., 1998; Ciardella A. et al., 2004*].

The macula measurement function should be used at medical management of patients with retinal pathology: it is possible to determine the changes of macula thickness in dynamics; this latter gives an idea about the course of the disease or allows assessing the effectiveness of treatment.

Thickness of retinal nerve fiber layer is evaluated automatically or manually by measuring the distance between the outer (upper) boundary of the first reflection of the retinal surface and the "bottom" layer of nervous fibers. The RNFL thickness is not uniform in the upper, nasal, the lower and temporal quadrants, and the graphical representation looks like a "double-humped curve".

J.S. Schuman and co-researchers noted that in healthy people RNFL thickness decreases with age [*Schuman S. et al., 1995*]. Due to the software available for OCT-3 scanner the comparative analysis of the results on RNFL thickness measurements is possible in patients over 18 years *versus* the age-related norms. B. Alamouti and J. Funk examined the retinal thickness in 100 healthy individuals at the age from 6 to 79 years, evaluating its average parameters on vertical scans in the area of papillomacular bundle at the temporal edge of the disk [*Alamouti B., Funk J., 2003*]. The average thickness of the retina according to OCT-derived data was 249 *µm*. The authors found that the thickness of retina at this locus decreases on average by 0.53 *µm* per year.

In clinical practice it is expedient to use the scanning and analysis protocols “RNFL Thickness Map” upon examination of patients with suspected glaucoma, neuropathy of various genesis, atrophy or anomalies of the optic nerve for more precise defining the state of the retinal nerve fiber layer. For each eye these protocols allow to create two maps of RNFL thickness in the peripapillary area. The RNFL thickness map is presented in the form of a ring with a fixed outer and inner diameter (2.9 *mm* and 6.8 *mm*) in two versions: the color and digital ones. In a digital map the RNFL thickness is shown in micrometers at eight internal and external sectors of the investigated annular area.

At OCT in patients with cystic macular edema of various etiologies (diabetic retinopathy, uveitis, vascular occlusions, etc.) the following changes are usually determined: diffuse thickening of the neurosensory retina, its cystic changes in the form of hyporeflective different sized spaces, subfoveolar fluid accumulation defined as the subretinal area, in which there is no return (echo) signal. These changes occur both separately and in combination with each other.

Vitreoretinal interactions might play an important role in the pathogenesis of macular edema. D. Gaucher and co-workers revealed perifoveolar posterior vitreous detachment in diabetic patients with cystic macular edema [*Gaucher D. et al., 2005*]. At the same time, in diabetes patients of the similar age but without macular changes the perifoveolar vitreous detachment was detected only in 30.6% of eyes.

“Volumetric OCT” allows to evaluate retinal thickness and macular volume in patients with macular edema and to compare these parameters in dynamics. It is especially useful to compare these parameters for assessment of conservative [*Ciardella A. et al., 2004*] or surgical treatment efficacy and determination of the optimal time for medical intervention.

The OCT allows detecting vitreoretinal tractions, not detectable by biomicroscopy with three-mirror lens. Vitreoretinal tractions appear at the tomogram as thin hyper-reflective little strands connecting the cortical structures of the vitreous body and the inner surface of the retina. In patients with diabetic macular edema the “taut hyaloid” syndrome is often observed, at which vitreomacular tractions are combined with the thickening of the retina and submacular fluid retention.

For scanning the eyes of patients with suspected macular hole the same scan protocols are used as for the evaluation of patients with cystic macular edema. In the last decade differential diagnosis of cystic macular edema and full-thickness macular holes acquires the particular importance due to the achievements of vitreoretinal surgery and the possibility for successful rehabilitation of patients with macular ruptures and cystic macular edema.

There are differences in pathogenesis of these diseases. Macular pseudo-ruptures are characterized by the following changes: at the fovea a small diameter hole is determined with the vertical steeply thickened edges; the thickness of retina at the center of the fovea is normal or slightly increased, in perifoveal zone at a distance of 750 µ*m* from the center of fovea the retina thickness is much greater than normal; in most cases the epiretinal membrane is revealed, partially peeled from the underlying retina or connected to the edges of the rupture. At lamellar ruptures uneven thinning of the fovea is observed as a notch, moderate thickening of the retina in perifoveolar area, the presence of a gap between the outer and inner layers of the retina.

On the tomogram a macular hole appears as the central defect of all retinal layers combined with a thickening of the neuroepithelium at the edges. Within the thickened neuroepithelium at the edges of the defect multiple hyporeflective cystic cavities are frequently determined.

The OCT allows to investigate the causes of some insufficiently known complications developing after surgical treatment of macular breaks. J. Chung and R. Spaide described a rare complication of surgical intervention for macular rupture, including vitrectomy, removal of the posterior boundary membrane and silicone oil tamponade, which was removed in 2 months post-surgery [*Chung J., Spaide R., 2003*]. Six months later, upon the OCT vacuoles (silicone oil droplets) were revealed in the middle layers of retina in the macula.

It is believed that after the successful surgical intervention on macular holes the results of OCT allow to predict improved vision in the long term. As a criterion that allows to expect the possible improvement of vision, the presence of uneven high-reflective line above the layer of retinal pigment epithelium and corresponding to photoreceptors layer on tomogram in the postoperative period is considered.

At the OCT in patients with idiopathic central serous chorioretinopathy violations of the foveal contour, cystic and atrophic changes in the macula are revealed. J.A. Montero and J.M. Ruiz-Moreno used the third-generation scanner to investigate 39 eyes of 36 patients with idiopathic central serous chorioretinopathy [*Montero J., Ruiz-Moreno J., 2005*]. In 92% of eyes (15 eyes with acute, 11 with relapsed, 10-with chronic forms of the disease) they determined detachment of the neuroepithelium in the affected area. In 90% of eyes under the detachment of the neuroepithelium in the projection of “filtration points” detected by fluorescein angiography there were found one or two protrusions emanating from the pigment epithelium.

In addition, OCT allowed to more accurately determine the disease activity, and the degree of pigment epithelium atrophy did not affect the results. The authors concluded that OCT is more informative than the fluorescein angiography for the diagnosis of central serous chorioretinopathy. Given the non-invasive and highly informative features of OCT, the authors consider its application in the management of patients with central serous chorioretinopathy preferable and safer than the use of fluorescein angiography.

In the early stage of choroidal neovascularization single ruptures are identified in the layer of choriocapillaris, Bruch’s membrane and the retinal pigment epithelium, fusiform high-reflective formation at the level of these structures with clear boundaries.

In clinical practice, to select the optimal treatment strategy it is necessary to differentiate the “classical” (subretinal), and “hidden” (formed under the pigment epithelium) forms of choroidal neovascularization. E.N. Hughes and associates examined patients with acute choroidal neovascularization using the third-generation scanner and found that OCT can effectively differentiate these forms of the disease [*Hughes E. et al., 2005*].

In patients with anomalies of the optic nerve the concentric scanning around the optic disk is generally used. In glaucoma, a decrease in average peripapillary thickness of the nerve fiber layer is observed; the affection is revealed in all quadrants, however, at the initial stage thinning is predominantly detected in lower quadrant (according to supra-nasal visual field defect of sight). Some studies indicate that reducing the thickness of the nerve fiber layer in the lower quadrant of the peripapillary region is typical for ocular hypertension as well.

At OCT in patients with optic nerve hypoplasia it is possible to determine the diameter of the optic nerve, RNFL thickness and the thickness of the retina in the macula [*Mosin I., 2005*]. The OCT plays an important role in identification of segmental hypoplasia of the optic nerve. In addition, OCT allows to diagnose subclinical hypoplasia of the optic nerve in patients with minor visual impairments and almost normal ophthalmoscopic picture.

There is a theory that diameter of scleral canal plays an important role in the origin of the optic disk drusen. M. Floyd and co-workers used OCT to examine diameter of the scleral canal in 38 eyes of patients with drusen, 12 fellow eyes without drusen at them, 34 eyes of their first-degree relatives without drusen, and 26 eyes of healthy subjects of the same age [*Floyd M. et al., 2005*]. The average area of the scleral canal in these groups made 2.520 mm^2, 1.836 mm^2, 2.067 mm^2 and 1.832 mm^2, respectively. Scleral canal area in the eyes of patients with drusen and their unaffected relatives was significantly higher than in the eyes of healthy subjects and fellow eyes of patients with drusen. The authors concluded that dimensions of the scleral canal do not make an etiologic factor in the pathogenesis of drusen.

The OCT-3 has a high sensitivity in the study of patients with congestive disk: even with a slight decrease in the level of intracranial pressure in patients with benign intracranial hypertension (e.g., a few hours after the ventricular or lumbar puncture) one can detect a positive dynamics of these parameters.

Thus, the method of OCT provides unique information about the anatomy of the investigated structure of the retina at the microscopic level. The method is non-contact; the procedure is safe and painless. The capabilities of modern optical coherence tomographs allow to build three-dimensional models of the studied area of the retina, thickness maps, to obtain objective evaluation of the dynamics. This latter provides entirely new possibilities in the diagnosis and treatment of the retina. At the same time, as follows from the above, until present the reliable standards for OCT examinations of ocular fundus in children and adolescents (0 – 18 years) are lacking; to some extent this latter unreasonably restricts the use of OCT in pediatric ophthalmic practice. Obviously, this direction is relevant for further OCT studies: in particular, in the aspect of early diagnosis setting on some widespread eye pathologies in children.

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