Comparison of the sensitivity of the BMO–MRW, GCC, ONH and RNFL methods in the diagnosis and treatment evaluation of juvenile glaucoma
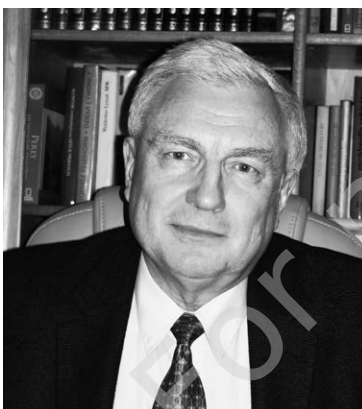
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HIGHLIGHTS

The most sensitive method of the degree of nerve fiber damage in OCT studies in juvenile glaucoma is GCC. BMO-MRW is slightly less sensitive, but may be a valuable diagnostic method in early diagnosis and assessment of the progression of glaucoma lesions.

ABSTRACT

BMO-MRW is a new SOCT parameter that has been introduced in recent years in the diagnosis of glaucomatous damage to optic retinal nerve fibers on the optic disc.

The aim of this study is to compare the sensitivity of this method with other methods used to evaluation of the retinal nerve fibres damage in patients with juvenile glaucoma.

The study was conducted in 20 patients with juvenile glaucoma, aged 5–16 years. In all of them, the degree of retinal nerve fibers damage was measured using BMO-MRW, GCC, ONH and RNFL methods. The examinations were performed every 3 months during a 1.5-year follow-up of these patients. The results of these studies indicate that the most sensitive method of the degree of retinal nerve fibers damage in juvenile glaucoma is GCC and BMO--MRW, the less sensitive RNFL and at least sensitive is the ONH method.

Key words: juvenile glaucoma, BMO-MRW, GCC, ONH, RNFL, comparison of diagnostic sensitivity

INTRODUCTION

Juvenile glaucoma is a type of primary open-angle glaucoma that begins between 3 and 16 years of age. The occurrence of this form of glaucoma is thought to be associated with a mutation in the *MYOC 1q23-q24* gene encoding a protein called myocyline. Myocyline is responsible for changes in the structure of the trabecular meshwork in the iridocorneal angle and its excessive expression may cause an increase in the resistance of the outflow of aqueous liquid from the eye [1]. The prognosis for the preservation of vision is good in this disease if treatment is undertaken at an early stage. Like other forms of glaucoma, juvenile neuropathy is a progressive optic neuropathy characterized by progressive loss of retinal ganglion cells (RGC) [2, 3]. Ganglion cells are in the inner layers of the retina. Their dendrites are located in the inner plexiform layer, nuclei in the ganglion cell layer, and axons in the retinal nerve fiber layer. In OCT studies, the axon, nucleus, and dendrites of the ganglion cell (i.e., the layers of nerve fiber, ganglion cells and the inner plexiform) are referred to as the ganglion cell complex (GCC).

In recent years, our diagnostic capabilities for assessing the degree of glaucoma damage have increased significantly. At the moment, we have the following clinical diagnostic methods:

- standard automated perimetry (SAP)
- short wavelength automated perimetry (SWAP) (blue on yellow)
- frequency doubling technology perimetry (FDT)
- scanning laser polarimetry to measure the thickness of the nerve fiber layer around the optic nerve (GDx)
- assessment of the topography of the optic nerve head (HRT, OCT-ONH)
- assessment of the thickness of the nerve fiber layer around the optic nerve (HRT, OCT-RNFL)
- assessment of the thickness of the macular retinal ganglion cells (ganglion cell complexes) (OCT-GCC)
- pattern electroretinogram (PERG).

However, these methods have different sensitivity and specificity. There are also limitations in their use in patients, e.g., GCC cannot be performed in patients with macular pathology, RNFL in patients with changes around optic disc, and in ONH assessment of the of the optic disc margins could be difficult in patients with myopia, tilted disc syndrome and congenital anomalies etc. The limitations of visual field tests are their subjectivity, long performance time and the fact that most other diagnostic tests show preperimetric changes.

BMO-MRW is the new parameter in OCT tests, which was introduced in 2014 for the diagnosis of glaucoma damage to retinal nerve fibers on the optic nerve disc. The name of this method is an abbreviation of the English name Bruch membrane opening – minimal rim width [4]. In this meth-od, measurements of the thickness of the layer of nerve fibers of the neuro-retinal rim at the border of the opening of the Bruch membrane around the optic disc are made (fig. 1). Imaging the ends of the Bruch membrane allows for a much better determination of the actual of the optic nerve margins than „visible edges" or the optic nerve margins assessed by the apparatus in various diagnostic methods. As mentioned in some diseases (myopia, tilted disc syndrome, congenital anomalies), the clinical margins of the disc are very difficult to determine. The MRW parameter (minimum rim width) is measured as the shortest distance between the end of the Bruch membrane the inner limiting membrane (the surface of the nerve fiber layer) (fig. 2). It is usually a line perpendicular to the surface of the layer of retinal nerve fibers. Measurements are made in radial scans of various meridians of the optic nerve disc.

Clinical studies have shown that BMO-MRW is an objective and valuable diagnostic tool for assessing the degree of damage to the nerve fibers of the retina on the optic nerve disc [5–17]. Many studies have found that BMO-MRW is a more sensitive and specific parameter of the glaucomatous damage to the optic disc than the visual field, ONH and RNFL [5–17].

The aim of this paper is to compare the sensitivity of the BMO-MRW method with other methods used for the assessment of damage to retinal nerve fibers in patients with juvenile glaucoma.

MATERIAL AND METHODS

The study was conducted in 20 patients with juvenile glaucoma aged 5–16 years. In all of them glaucomatous damage was measured using BMO-MRW, GCC, ONH and RNFL methods. The tests were performed every three months during a 1.5-year follow-up of these patients.

BMO-MRW, RNFL AND ONH measurements were performed with the REVO FC apparatus from Optopol (Poland). For BMO-MRW measurements the disc radial mode was used, which performs 16 radial scans of the disc every 22.5°. On obtained scans the thickness of the nerve fiber layer at both ends of the Bruch membrane in each of the 16 radial scans (a total of 32 measurements) were measured. As an abnormal result, it was assessed if the thickness of the nerve fibers was 10% thinner by at least two of the radial scans in comparison to the control group. Since REVO FC does not have a database for evaluating BMO-MRW studies, normal BMO-MRW values were determined in 20 healthy people aged 5–16 years before the start of the study (the only device currently capable of automatic BMO-MRW assessment and comparison to the database is Spectralis from Heidelberg Engineering (Glaucoma Module Premium Edition module).

FIGURE 1

Bruch membrane margins in the SOCT study. A. Bruch membrane margins marked with yellow arrows. B. Measurement of the width of the Bruch membrane opening (red line).
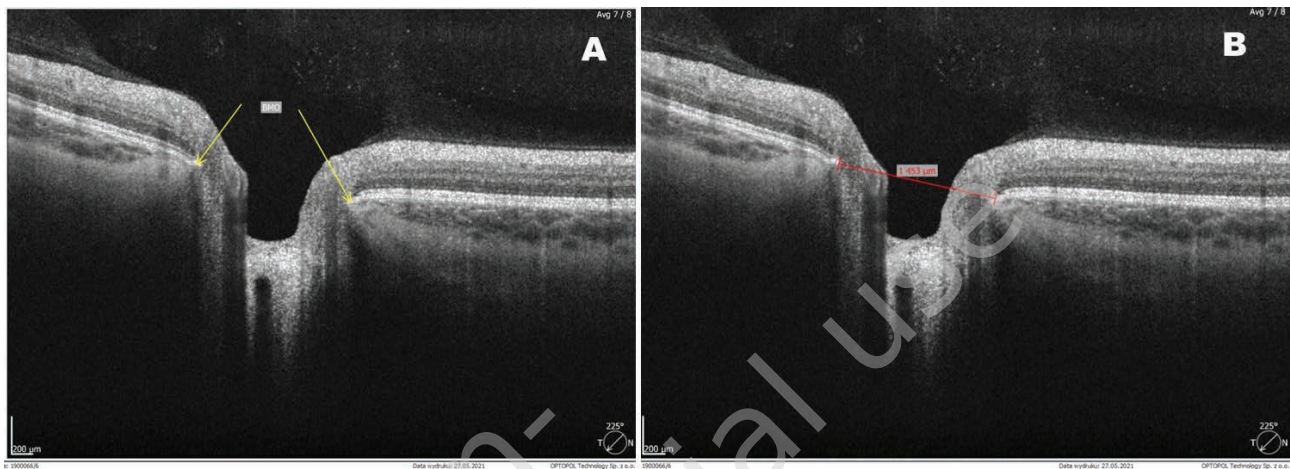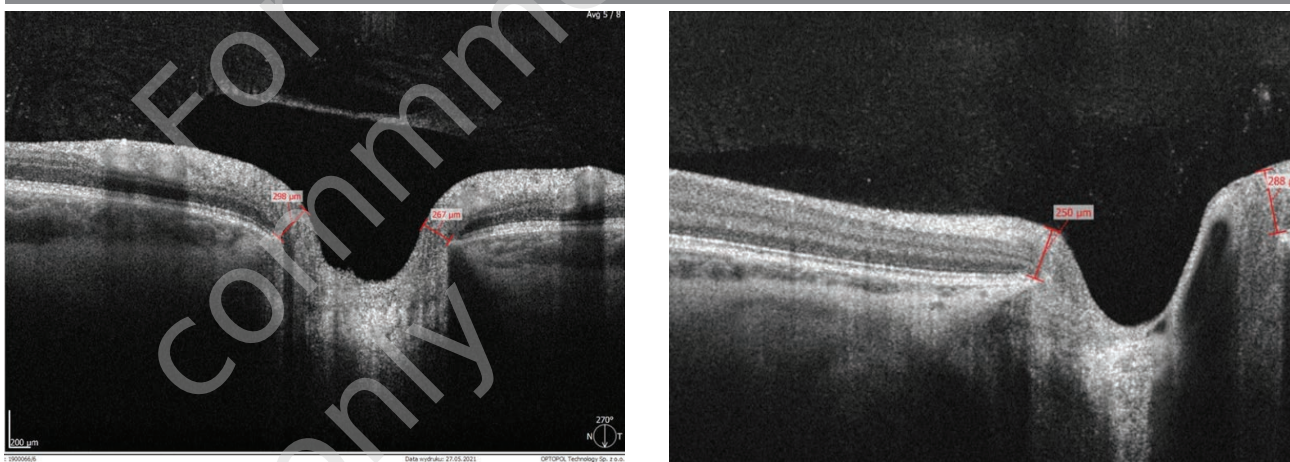

FIGURE 2

Measurement of the thickness of the layer of nerve fibers on the optic nerve disc by the BMO-MRW method in patients with juvenile glaucoma.

The GCC was performed with Optovue's iVue due to its possibility to evaluate FLV and GLV coefficients. The GCC study evaluated the following coefficients: ganglion cell thickness in the upper and lower hemispheres, FLV and GLV. An incorrect result was assessed if at least one of them was abnormal.

To assess the results of the tests and assess the progression of changes in the GCC, RNFL and ONH studies, automatic diagnostic tools were used in the equipment of the REVO FC and iVUE devices.

Since the above methods evaluate the different anatomical structures of the retina and nerve II (tab. 1) and there is no single reference method to which the results can be compared (such as Goldmann tonometry in intraocular pres-

sure measurements) the following methods were used to assess the sensitivity of the diagnostic methods studied:

- assessment of the nerve fiber damage in various methods at the beginning of the observation period (the bigger the damage so probably the more sensitive is the method)
- evaluation of the progression of changes over time of 1.5 years of follow-up in various tests (the greater progression so probably the more sensitive is the method)
- comparison of nerve fiber thickness in μm (BMO-MRW, and RNFL GCC) and neuro-retinal rim surface (mm^2) during 1.5 years of observation (for statistical analysis Statistica program was used).

TABLE 1

What anatomical structures of the retina and optic nerve are evaluated by the different methods of evaluation of glaucoma damage.

| Method	Anatomical structure
BMO-MRW	thickness of retinal nerve fibers at the border of the opening of the Bruch's membrane on the optic disc
GCC	thickness of the ganglion cell complex in the macula
RNFL	the thickness of the nerve fiber layer around the optic nerve
ONH	disc topography (optic disc cupping, width and surface of the neuro-retinal rim)
Visual field	assessment of the functions of the entire visual path

BMO-MRW – Bruch membrane opening – minimal rim width; GCC – ganglion cell complex; ONH – optic nerve head; RNFL – retinal nerve fiber layer.

RESULTS

In all patients, during the three-monthly examinations, there was no increased intraocular pressure as well as changes in the anterior and posterior segments of the eye. Norma values of BMO-MRW obtained during measurements in healthy people is presented in table 2. Nerve fibers were the thickest superior and inferior parts off the disc, and the thinnest temporal, which results from the fact that the temporal part of the disc is formed only by fibers from macula, and the superior and inferior parts by the superior and inferior fibers as well as the temporal fibers, surrounding the macula.

TABLE 2

BMO-MRW thickness in healthy children.
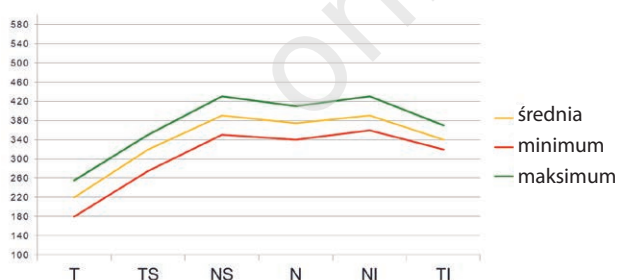
N – nasal part of the disc; NI – inferonasal part of the disc, NS – superonasal part of the disc, T – temporal part of the disc; TI – inferotemporal part of the disc; TS – superotemporal part of the disc.

The results of studies in patients with juvenile glaucoma are presented in tables 3 and 4.

TABLE 3

Percent of patients who had nerve fiber damage at the beginning and after 1.5 years of follow-up (progression of changes over time).

	BMO-MRW	GCC	RNFL	ONH
At the beginning of the observation period	10%	15%	5%	5%
After 1.5 years	15%	25%	10%	5%

BMO-MRW – Bruch membrane opening – minimal rim width; GCC – ganglion cell complex; ONH – optic nerve head; RNFL – retinal nerve fiber layer.

TABLE 4

Changes of BMO-MRW, GCC, RNFL AND ONH after 1.5 years of follow-up of patients.
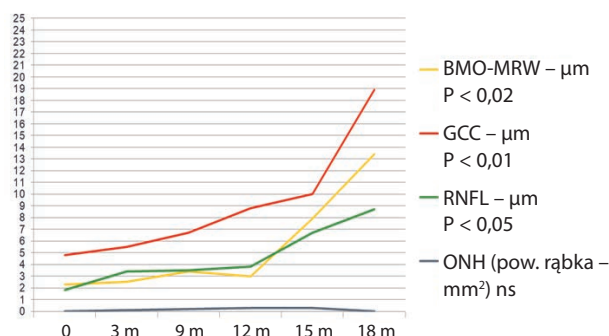
BMO-RMW – Bruch membrane opening – minimal rim width; GCC – ganglion cell complex; ns – statistically insignificant; ONH – optic nerve head; P – significance of changes; RNFL – retinal nerve fiber layer.

In 20 patients with juvenile glaucoma at the time of the first study, abnormal results were found in the GCC study in 15%, BMO-MRW in 10%, and in the RNFL and ONH studies in 5% of patients (tab. 2). After 1.5 years of follow-up, abnormal results were found in 25% of patients and GCC studies, 15% in BMO-MRW, 10% RNFL, and in the ONH study the results were identical. The degree of glaucoma damage in the studied group of patients was not considerable.

A comparison of nerve fiber thickness (RNFL and BMO--MRW) and ganglion cell complexes (GCC) and neuro--retinal rim surface (ONH) showed the largest changes in the GCC study, slightly smaller in BMO-MRW, and the smallest in the RNFL study. These changes were statistically significant at different levels of significance (tab. 4). However, no significant changes of the surface of the neuro-retinal rim were found in the ONH study.

DISCUSSION

The results of this study indicate that the sensitivity of different methods for assessing retinal nerve cell damage in juvenile glaucoma is different. The most sensitive method are GCC and BMO-MRW, the less sensitive RNFL and the least sensitive is the ONH method. These results are confirmed by the results of published works by other authors. These publications concerned other forms of glaucoma (open-angle glaucoma in adults), but their results probably also apply to juvenile glaucoma. Studies by many authors have shown that changes in BMO-MRW occur earlier than changes in RNFL in patients with open-angle glaucoma [6, 8, 10–13]. In other clinical studies, it has been found that the results of the assessment of the thickness of the layer of retinal nerve fibers with BMO-MRW and RNFL are comparable in patients with glaucoma [7, 15, 16] and in healthy subjects [17]. It has also been shown that BMO-MRW assesses the condition of the optic nerve better than ONH in patients with glaucoma and in healthy patients [11].

Changes in the thickness of nerve fibers in the BMO-MRW in patient with open-angle glaucoma occur earlier than changes in the field of vision. Park and others found that the first changes in the visual field occur in patients if there is 26% loss of nerve fibers in BMO-MRW measurements [5]. Mizumoto and others also observed that changes in BMO--MRW parameters occur earlier than changes in the field of vision [12].

In the available literature, no publications on the use of the BMO-MRW method in juvenile glaucoma and the comparison of GCC and BMO-MRW sensitivity in glaucoma were found. Therefore, the aim of the study is to compare the sensitivity of the BMO-MRW method with other methods used for the evaluation of damage of the retinal nerve fibers in patients with juvenile glaucoma. Studies have shown that GCC and BMO-MRW are the most sensitive methods, less sensitive is RNFL, while the ONH method is the least. These results are consistent with the results of the author's previous study, which compared the sensitivity of GCC, RNFL and ONH methods in the diagnosis and evaluation of the progression of juvenile glaucoma [18]. What are the reasons why GCCs were the most sensitive in evaluation of the degree of ganglion cell damage? The results of the recently published histopathological studies have shown that in, the first damage in glaucoma is the disappearance of dendrites of ganglion cells [3] and GCC is the only method in which the thickness of dendrites layer is measured.

During follow-up there was no increased intraocular pressure in the observed patients. Despite this, in some of them progression was observed in OCT examinations. This speaks in favor of noncompliance with glaucoma therapy in some of patients [19].

BMO-MRW may be a valuable method in assessing the progression of glaucoma damage in juvenile glaucoma. This examination will be used primarily in patients with macular (GCC is then unreliable) or peripapillary changes (myopia, tilted disc syndrome, congenital disc anomalies etc., which then can change the results of the RNFL measurements). Therefore, BMO-MRW can be a valuable complementary method to assess the progression of ganglion cell damage in glaucoma in situations where the use of other OCT methods is limited.

It should be noted, however, that limitation of this study is fact that the SOCT equipment that was used for BMO--MRW measurements does not currently have the possibility of automatic calculation of BMO-MRW results and its comparison to the normative database (the only such apparatus is currently Spectralis from Heidelberg Engineering). Therefore, it was necessary to create the own database to evaluate the results. The patients included to the study were not with advanced glaucoma. Therefore, the results could be different in the case of advanced glaucoma.

It should also be noted that the results obtained with SOCT devices from different companies may differ slightly from each other. There are some technical differences between the devices, other software is used to evaluate the measured parameters and there are different normative database used for evaluation of the measured parameters. OCT methods used to assess glaucoma damage (BMO-MRW, GCC, ONH and RNFL) evaluate the different anatomical structures of the retina and optic nerve and therefore their results may vary. Therefore, it the same method and OCT device should be used for the assessment of glaucoma progression in a given patient.

CONCLUSION

It should be stated that:
1. The results of these studies indicate that the most sensitive method of evaluation of the degree of the retinal nerve fibers damage in juvenile glaucoma is GCC, slightly less sensitive BMO-MRW, less sensitive RNFL, and the least sensitive is the ONH method.
2. BMO-MRW should be the valuable diagnostic method in the early diagnosis and evaluation of the progression of glaucoma lesions in juvenile glaucoma.

Figures: from author's own materials.

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