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New options for the diagnosis of normal tension glaucoma in the light of Professor V.V. Volkov's concept of its pathogenesis

© Irina L. Simakova, Alfina R. Suleimanova, Natalya. P. Baimuratova

S.M. Kirov Military Medical Academy, Saint Petersburg, Russia

PURPOSE: To measure lamina cribrosa thickness (LCT) and lamina cribrosa depth (LCD), optic nerve subarachnoid space width (ONSASW) in patients with normal tension glaucoma and in healthy individuals and to compare these data with the results of our own pilot study.

MATERIALS AND METHODS: The 1st group included 13 patients (22 eyes) with normal tension glaucoma aged 39 to 88 years (59.8 ± 10.9 years). The 2nd (control) group included 10 healthy people (20 eyes) aged 40 to 59 years (47.9 ± 5.5 years). All subjects underwent structural and functional assessment of the optic nerve head using optical coherent tomograph (OCT) RTVue-100 (Optovue, USA), Humphrey perimeter (HFA II 745i, Germany-USA), and our own modification of Frequency Doubling Technology perimetry. LCT and LCD were measured by OCT RS-3000 Advance (Nidek, Japan). To measure ONSASW we used a cross-sectional image of the optic nerve taken with Magnetic Resonance Imaging (GE Optima MR450w MRI, USA).

RESULTS: Differences in the 1st and 2nd groups between the mean values of LCT (234.14 ± 27.73 and 336.25 ± 21.0 μm, respectively; $p = 0.0000$), LCD (461.8 ± 101.7 and 361.65 ± 58.2 μm, respectively; $p = 0.0004$) and ONSASW (1.371 ± 0.035 and 1.52 ± 0.133 mm, respectively; $p = 0.011$) were statistically significant.

CONCLUSION: Patients with normal tension glaucoma had significantly higher LCD value with significantly lower LCT and ONSASW values compared to healthy individuals, which is comparable with the results of our pilot study, and confirms the importance of these morphometric criteria in normal tension glaucoma diagnosis verification.

Keywords: pathogenesis and diagnosis of normal tension glaucoma; central corneal thickness; lamina cribrosa thickness; lamina cribrosa depth; optic nerve subarachnoid space width.

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Новые возможности диагностики глаукомы нормального давления в свете концепции проф. В.В. Волкова о её патогенезе

© И.Л. Симакова, А.Р. Сулейманова, Н.П. Баймуратова

Военно-медицинская академия им. С.М. Кирова, Санкт-Петербург, Россия

Цель работы — измерить толщину и глубину решётчатой пластинки (ТРП и ГРП) склеры, ширину субарахноидального пространства зрительного нерва (ШСАПЗН) у больных глаукомой нормального давления и здоровых лиц и сравнить эти данные с результатами собственного пилотного исследования.

Материалы и методы. В 1-ю группу включили 13 больных (22 глаза) с глаукомой нормального давления в возрасте от 39 до 88 лет (59,8 ± 10,9 года); 2-ю (контрольную) группу составили 10 здоровых человек (20 глаз) в возрасте от 40 до 59 лет (47,9 ± 5,5 года). Всем испытуемым выполняли структурно-функциональную оценку диска зрительного нерва, используя оптический когерентный томограф RTVue-100 (Optovue, США), периметр Humphrey (HFA II 745i, Германия–США) и собственную модификацию периметрии с удвоением пространственной частоты. ТРП и ГРП измеряли с помощью оптического когерентного томографа RS-3000 Advance (Nidek, Япония). Для измерения ШСАПЗН использовали снимок поперечного среза зрительного нерва, выполненный с помощью аппарата магнитно-резонансной томографии GE Optima MR450w (США).

Результаты. Различия в 1-й и 2-й группах между средними значениями ТРП (234,14 ± 27,73 и 336,25 ± 21,0 мкм соответственно; $p = 0{,}0000$), ГРП (461,8 ± 101,7 и 361,65 ± 58,2 мкм соответственно; $p = 0{,}0004$) и ШСАПЗН (1,371 ± 0,035 и 1,52 ± 0,133 мм соответственно; $p = 0{,}011$) были статистически значимы.

Заключение. Пациенты с глаукомой нормального давления имели достоверно бóльшую величину ГРП при достоверно меньших значениях ТРП и ШСАПЗН по сравнению со здоровыми лицами, что сопоставимо с результатами нашего пилотного исследования и подтверждает значимость этих морфометрических показателей для уточнения диагноза глаукомы нормального давления.

Ключевые слова: патогенез и диагностика глаукомы нормального давления; центральная толщина роговицы; толщина решётчатой пластинки; глубина решётчатой пластинки; ширина субарахноидального пространства зрительного нерва.

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INTRODUCTION

Glaucoma is still one of the leading causes of irreversible blindness globally, ranking first among the causes of vision disability in Russia. Its most worrying clinical form is normal tension glaucoma (NTG): a form that is difficult to diagnose because it develops even with normal intraocular pressure (IOP). NTG was first classified at the end of the 20th century, and, according to contemporary literature, its prevalence in primary open-angle glaucoma is 20%–30% in Europe and ≤50% in Japan. [2, 3]

In the middle of the 20th century, it became known that glaucoma was detected in far from every patient with ocular hypertension [4, 5]. In order to clarify the undefined role of ocular hypertension in the formation of glaucoma, V.V. Volkov turned to experimental studies of cerebrospinal fluid pressure in the optic nerve (ON) to test his own hypothesis about the existence of a transmembrane gradient between intraocular and intraneural (tissue-cerebrospinal fluid) pressure (TMGP), where its impairment may be a key factor in developing glaucoma optic neuropathy (GON). In 1974, under the guidance of Prof. V.V. Volkov, R.I. Korovenkov was the first in the world to experiment on rabbits in order to measure the pressure of the cerebrospinal fluid in the intermembrane spaces of the ON and to confirm the existence of a gradient in the plane of the lamina cribrosa, which acts as a membrane, between the intraocular and tissue-cerebrospinal fluid pressure [6].

20 years later, the results of this experiment were corroborated by Australian scientists from experiments on dogs [7] and by American scientists from data on human spinal punctures [8, 9]. According to these scientists, the gradient (difference) between IOP and tissue-cerebrospinal fluid pressure was 7.4 ± 4.8 and 6.6 ± 3.6 mm Hg, respectively.

According to Prof. V.V. Volkov's pathogenesis of glaucoma, GON develops as a result of deflection of the lamina cribrosa or membrane (LC/LM) of the sclera caused by a disturbance of TMGP between intraocular and tissue-cerebrospinal fluid pressure. This explains the possibility of two types of glaucoma development: ocular hypertension glaucoma, which progresses with high IOP, and optic-cerebrospinal fluid hypertension glaucoma, which progresses with normal IOP. The latter's existence was rejected by many scientists. Prof. V.V. Volkov reflected that "...a kind of crisis situation that arose in the understanding of open-angle glaucoma, progressing without obvious ocular hypertension, is based on the trivial habit inherent in all of us to absolutize many quantitative indicators, forgetting about their actual relativity, taking into account the diversity of their defining relationships" [10].

So in the 1970s, under his guidance, his department pioneered the study of the relationship between intraocular, intracranial, and blood pressure levels. In particular, an analysis of a large number of cases showed that glaucoma can progress even if IOP is normal, but this was much more common in patients with arterial hypotension; therefore, blood pressure needed to be taken into account when assessing the normal range of intraocular pressure in the form of individually tolerated IOP [11, 12]. Because the concept of an individual norm, including that for the IOP level, is always broader than the conditional standards for the entire population, in 2001, V.V. Volkov proposed the term "pseudo-normal pressure," and, as a result, the "pseudo-NTG" diagnosis is also used in Russia [10].

Prof. V.V. Volkov's concept on GON pathogenesis contributed to the development of a structural–functional diagnosis approach and open-angle glaucoma classification, which included pseudo-normal pressure that was described in detail in V.V. Volkov's widely known fundamental monographs [10, 12, 13] and was confirmed by the PhD theses of his students [14, 15].

Prof. V.V. Volkov, also states that in the pathogenesis of membranodystrophic glaucoma, the issue is not just TMGP impairment; another extremely important issue are the biomechanical properties of the sclera LC, which worsen because of age-related dystrophic restructuring in the biochemistry of the LC matrix and the surrounding sclera caused by changes in the composition of collagen [13].

Thus, based on the characteristics of GON pathogenesis, V.V. Volkov identified three clinical forms of glaucoma, namely ophthalmic hypertensive, optic-cerebrospinal fluid hypotensive, and membranodystrophic glaucoma.

In current international literature, many authoritative scientists believe that TMGP impairment plays a very important role in the pathogenesis of glaucoma, especially of NTG, referring to the work of V.V. Volkov (1976) [16] as to a primary source [17–19]. It is currently known that arterial hypotension is often detected in patients with NTG and, as a rule, is accompanied by a minor decrease in cerebrospinal fluid pressure. Chinese scientists together with the renowned US scientist Prof. R.N. Weinreb and German Prof. J.B. Jonas, using fat suppressed 3 T magnetic resonance imaging, measured the ON subarachnoid space (SAS) width at distances of 3, 9, and 15 mm behind the eyeball in healthy individuals and in patients with high

and normal pressure glaucoma. SAS was significantly the narrowest at all three measurement points of the eyeball in NTG patients. The authors concluded that there is a direct relationship between the volume of cerebrospinal fluid in the subarachnoid space of the ON and the level of its pressure, which opens up a real possibility of assessing the level of intracranial pressure in a non-invasive way [20].

The advent of modern spectral optical coherence tomographs (OCTs), equipped with an enhanced depth module, enabled to measure the LC parameters, in particular its thickness, which, according to H.-Y.L. Park et al. [21], was 2 times thinner in NTG patients than in healthy individuals, and was significantly thinner than in patients with ocular hypertensive glaucoma. The authors believe that in patients with primary open-angle glaucoma, especially with normal pressure, the LC thickness measurement is comparable in diagnostic value to the retinal nerve fiber layer thickness assessment [21].

Considering the relevance of TMGP assessment in the study of NTG pathogenesis and the emergence of new possibilities for its implementation using modern technologies, in the period from 2017 to 2019, we performed a pilot study to measure the thickness and depth of the LC, as well as the ON SAS width in NTG patients and healthy individuals, and obtained results comparable to the above data from international researchers [1]. But because, in the middle of our study, we relocated of our department and clinic to a new multidisciplinary clinical building of the Academy, which was equipped with more modern equipment, it became necessary to compare the data of the pilot study [1] and the data obtained after the relocation, which we formalized as the initiative scientific research work (R&D) "Development of new morphometric criteria to clarify the pathogenesis and diagnosis of NTG" (deadline 2020–2022) where the co-executors are the departments of X-ray Radiography and Radiology with a course of ultrasound diagnostics and neurosurgery in the Academy. In the pilot study, a Topcon 3D OCT 2000 device (Japan, 2000) and a Siemens Magnetom Symphony 1.5 T MRI device (Germany, 2005) were used to measure the thickness and depth of the LC, the ON SAS width, and in this research work, we used the Nidek OCT RS3000 Advance device (Japan, 2009) and the GE Optima MR450w MRI device (USA, 2012), which differ in technical characteristics.

The work aimed to measure the thickness and depth of the lamina cribrosa (TLC and DLC) of the sclera, the width of the ON SAS in NTG patients and in healthy individuals, and to compare the data with the results of our own pilot study.

MATERIALS AND METHODS

Group 1 included 13 patients (9 women and 4 men, 22 eyes) with NTG; 77% of cases (17 eyes) had the incipient stage of the disease. Their ages ranged from 39 to 88 years (mean age 59.8 ± 10.9 years). All of them had an IOP by Maklakov below 27 mm Hg and arterial hypotension (the maximum BP did not exceed 120/70 mm Hg). Myopia (mean value 2.23 ± 1.26 diopters) was registered in 50% of cases. The inclusion criterion for the study was a confirmed diagnosis of NTG. The study did not include patients with visual acuity below 0.5, ophthalmic or systemic diseases affecting the visual field, and a history of laser refractive surgery.

Group 2 (control) included 10 healthy individuals (6 women and 4 men, 20 eyes) aged 40 to 59 years (mean age 47.9 ± 5.5 years). All studies were performed in accordance to existing international and Russian laws and human biomedical research regulations.

All subjects underwent a complete ophthalmological examination that included a structural and functional assessment of the ON head using the RTVue 100 XR OCT (Optovue, USA), with the determination of the nerve fiber layer thickness and the complex of retinal ganglion cells, as well as standard automated perimetry (HFA II 745i, threshold program "24–2", Germany–USA) and non-standard perimetry with doubling of the spatial frequency in a version of I.L. Simakova et al. [22].

In all subjects, TLC and DLC were measured using the OCT RS-3000 Advance (Nidek, Japan) in an enhanced depth imaging mode, using the DISC RADIAL protocol and calculating the average value of these parameters from three consecutive measurements. DLC (posterior LC displacement) was defined as the perpendicular straight line drawn between the center of this line and the front surface of the LC (a–b). TLC was defined as the segment between the anterior and posterior surfaces of the LC in its central part (c–d) (Fig. 1, 2). To measure the LC parameters, a line connecting the end points of the Bruch's membrane was used as a base plane. The same OCT device was used to measure the central thickness of the cornea using a nozzle for the anterior segment of the eye. It was additionally measured using a Pentacam HR device (Oculus, Germany).

In our pilot study, a 3D-OCT 2000 OCT instrument (Topcon, Japan) was used to measure the TLC and DLC. In this work, the LC parameters were measured using the modern OCT Nidek RS-3000 Advance that has a higher scanning speed (53,000 A-scans per second) and a higher optical resolution, giving better images of the anterior

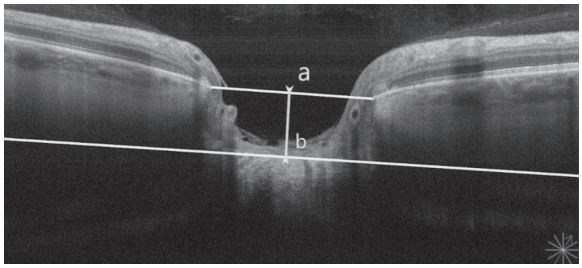

Fig. 1. Lamina cribrosa depth measurement (a–b) by EDI (Enhanced Depth Imaging) mode of Nidek RS-3000 Advance
Рис. 1. Измерение глубины решётчатой пластинки (a–b) с помощью оптического когерентного томографа Nidek RS-3000 Advance в режиме увеличенной глубины изображения (EDI)

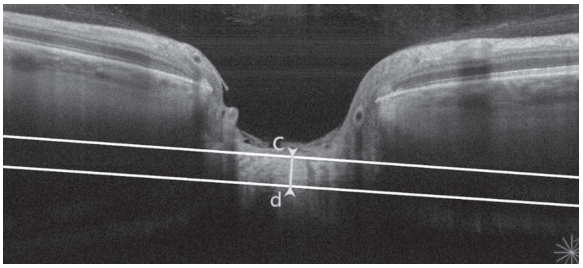

Fig. 2. Lamina cribrosa thickness measurement (c–d) by EDI (Enhanced Depth Imaging) mode of Nidek RS-3000 Advance
Рис. 2. Измерение толщины решётчатой пластинки (c–d) с помощью оптического когерентного томографа Nidek RS-3000 Advance в режиме увеличенной глубины изображения (EDI)

Table 1. Comparison of the technical characteristics of OCT devices
Таблица 1. Сравнение технических характеристик оптических когерентных томографов

Specifications	Nidek RS 3000 Advance (Japan, 2009)	Topcon 3D-OCT 2000 (Japan, 2000)
A-scans per second	53,000	27,000
B-scan	512 A-scans	512 A-scans
Optical resolution	4 μm	5–6 μm
Image extended depth mod-ule (EDI)	Yes	Yes

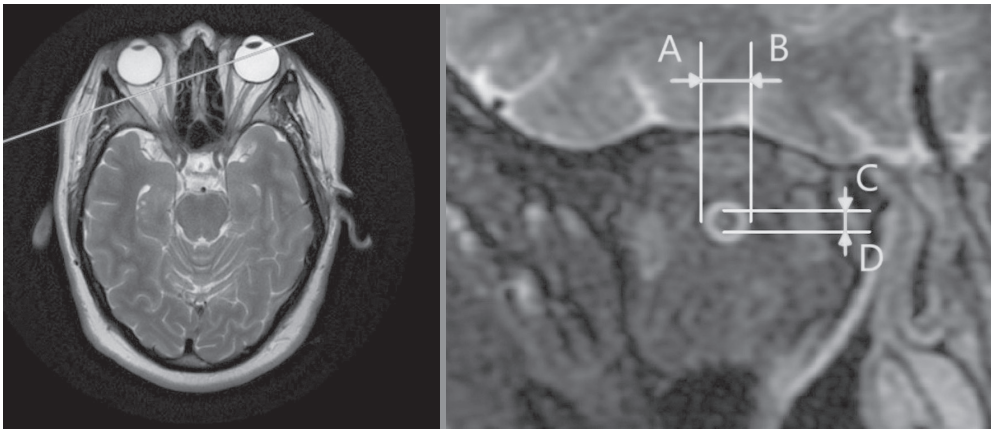

Fig. 3. Cross-sectional image of the optic nerve (right) taken 3 mm behind the eye using MRI. A–B – is the diameter of the optic nerve with its sheaths; C–D – is the diameter of the optic nerve without its sheaths
Рис. 3. Изображение поперечного среза зрительного нерва (справа), выполненного в 3 мм за глазным яблоком, с помощью магнитно-резонансного томографа. A–B — диаметр зрительного нерва с оболочками; C–D — диаметр зрительного нерва без его оболочек

and the posterior surface of the scleral LC through reducing the number of artifacts (Table 1).

To assess the SAS width, we used a snapshot of the transverse section of the ON made 3 mm behind the eyeball using a GE Optima MR450w magnetic resonance tomograph (GE, USA) with a magnetic field induction of 1.5 T (Figure 3). The study was performed using a head coil where the patient's head was immobilized with special cushions. The patients fixed their gaze on their own through a mark applied to a magnetic coil, which enabled to reduce eye mobility and obtain more contrasting images. Before the study of the ON, a standard protocol for scanning the structures of the brain in the axial and sagittal planes was performed, without an inter-slice interval. Standard scan images were required for the correct positioning and direction of the ON slices. A targeted study of ON was performed in the oblique coronal plane in the fat suppression mode. On the obtained images of the cross section of the ON, the width of the SAS was determined as half the difference between the average diameter of the MR image of the ON slice with its sheath (A–B) and the average diameter of the MR image of the ON slice without its sheath (C–D). Measurements were performed using the RadiAnt Dicom Viewer software for X-ray images.

Table 2. Comparison of the technical characteristics of MRI devices
Таблица 2. Сравнение технических характеристик магнитно-резонансных томографов

Specifications	GE Optima MR450w (USA, 2012)	Siemens Magnetom Symphony (Germany, 2005)
Magnetic field induction	1,5 T	1,5 T
Aspects of scanning of the optic nerve, fat suppression	More uniform and pronounced	Additional implementation
T2-WI protocol (thin-slice gradi-ent version)	Slice thickness 1 mm	Slice thickness 1 mm
Scan time	15 min	20–25 min

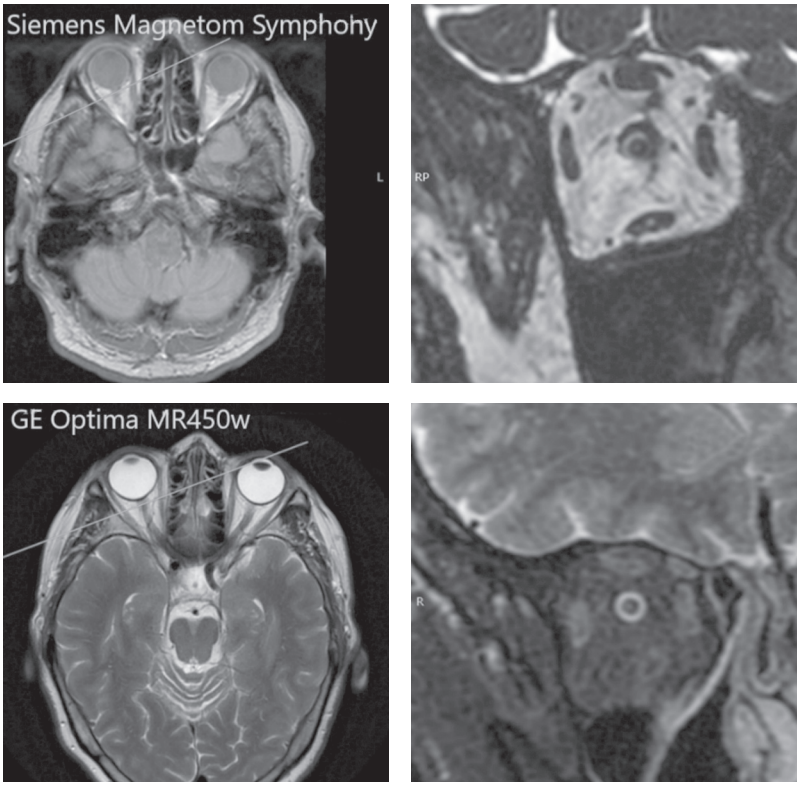

Fig. 4. Comparison of cross-sectional slices of the optic nerve obtained with MRI Siemens Magnetom Symphony and MRI GE Optima MR450w
Рис. 4. Сравнение изображений поперечных срезов зрительного нерва, полученных при помощи магнитно-резонансных томографов Siemens Magnetom Symphony и GE Optima MR450w

In this study, we used a more modern magnetic resonance imager GE Optima MR450w (USA) with a magnetic field induction of 1.5 T, which enables us to obtain T2 IDEAL pulse sequences with a slice thickness of 1 mm without inter-slice spacing (Table 2).

The IDEAL T2 pulse train suppresses chemical shift artifacts in images of hard-to-reach anatomical structures such as eye sockets. When using this program, 4 different contrast images are generated per one data collection (water, adipose tissue in phase and antiphase). Reliable uniform suppression of the signal from adipose tissue enables to more clearly visualize the perineural cerebrospinal fluid spaces of the ON against the hypointense intraorbital adipose tissue and to avoid repeated fat suppressed scanning. Thus, the T2 IDEAL pulse sequence in the study protocol turned out to be preferable because it enabled us to replace the 3D CISS and turbo-spin-echo with fat suppression sequences that we used in our previous study on a Siemens Magnetom Symphony tomograph, which reduced high-quality imaging scan time (Fig. 4).

RESULTS AND DISCUSSION

In this research (Table 3), as well as according to the results of our pilot study, the difference between the average values of the central corneal thickness in NTG patients and healthy individuals turned out to

be insignificant. However, a statistically significant (p = 0.000) difference was revealed between the mean values of TLC in NTG patients (234.14 ± 27.73 μm) and healthy individuals (336.25 ± 21.0 μm), which is comparable with the findings of our pilot study (217.60 ± 36.92 and 345.86 ± 33.29 μm, respectively, p = 0.000), as well as to the international literature data. In particular, H.-Y.L. Park et al. [21], using spectral-domain OCT (SD-OCT, Germany) equipped with an enhanced depth imaging module to measure TLC in NTG patients and healthy subjects, also registered a significant difference between these parameters (175.11 ± 22.60 and 348.14 ± 23.41 μm, respectively, p < 0.001).

According to our data (Table 3), the average DLC in NTG patients (461.8 ± 101.7 μm) was significantly larger (p = 0.0004) than in the control group (361.65 ± 58.2 μm), which was also comparable with the results of our pilot study (435.0 ± 86.31 and 367.31 ± 87.0, respectively, p = 0.014) and international authors [23–25].

In their work, S. Cakmak et al. [26] measured DLC in healthy individuals and in patients with pseudoexfoliative glaucoma using SD-OCT and swept-source OCT (SS-OCT). According to their findings, DLC was 392.2 ± 82.9 μm (SD-OCT) and 393.2 ± 73.8 μm (SS-OCT) in the control group, and 437.2 ± 125.1 μm (SD-OCT) and 451.1 ± 121.1 μm (SS-OCT) in the glaucoma group. J.R. Vianna et al. [27] believe that the deeper location of the scleral LC is the same characteristic aspect as the thinning of the retinal nerve fiber layer in primary open-angle glaucoma.

According to the results of electron microscopic examination, it became clear that the ON SAS of humans (the space between the arachnoid and the layers of the pia mater) is not a homogeneous homotypic space of an anatomically simple structure filled with cerebrospinal fluid, but it comprises complex systems of arachnoid trabeculae and septa that separate the subarachnoid fissure. This structure of SAS, on the one hand, prevents the subarachnoid space from collapsing at a sharp decrease in cerebrospinal fluid pressure; on the other hand, it does not allow this cavity of the arachnoid-dural sac to significantly expand at a sharp increase in intracranial pressure [28].

According to the results of our study (Table 3), the average value of the ON SAS width in patients with NTG (1.371 ± 0.035 mm) turned out to be significantly less (p = 0.011) than in healthy individuals (1.52 ± 0.133 mm), which corresponds to the results of our pilot studies (1.27 ± 0.13 and 1.44 ± 0.19 mm, respectively, p = 0.004) and international literature. Thus, in our sample, all NTG patients had low blood pressure, which coincides with the experience of J.H. Lee et al. [29], who believed that arterial hypotension, which is often detected in NTG patients, is usually accompanied by a minor decrease in cerebrospinal pressure, which results in a decrease in the filling of ON SAS with the cerebrospinal fluid, which leads to a narrowing of this space. N. Wang et al. [20] using an MRI device with a high magnetic field induction (Signa HDxt 3.0 T, USA) in the fat suppression mode measured the ON SAS width at distances of 3, 9, and 15 mm behind the eyeball in NTG patients and healthy individuals. SAS was significantly (p = 0.003) the narrowest at all three points of measurement of the eyeball in NTG patients. For example, at 3 mm behind the eyeball, the indicator of the ON SAS width, according to these authors, was 0.67 ± 0.16 mm in NTG, and 0.87 ± 0.15 mm in healthy subjects [20].

Table 3. Results obtained in the study groups

Таблица 3. Полученные результаты в исследуемых группах

Indicator	1 Group 1, NTG patients, R&D/PS	Group 2 (control), healthy individu-als, R&D/PS	Significance of differences (p), R&D/PS
Central corneal thickness, μm	538.1 ± 35.9 / 543.26 ± 31.52	556.4 ± 24.7 / 557.50 ± 24.92	0.06 / 0.101
Lamina cribrosa thickness, μm	234.14 ± 27.73 / 217.60 ± 36.92	336.25 ± 21.0 / 345.86 ± 33.29	0.000 / 0.000
Lamina cribrosa depth, μm	461.8 ± 101.7 / 435.0 ± 86.31	361.65 ± 58.2 / 367.31 ± 87.0	0.0004 / 0.014
Optic nerve subarachnoid space width, mm	1.371 ± 0.035 / 1.27 ± 0.13	1.52 ± 0.133 / 1.44±0.19	0.011 / 0.004

Note. NTG – normal tension glaucoma, R&D – research work, PS – pilot study.

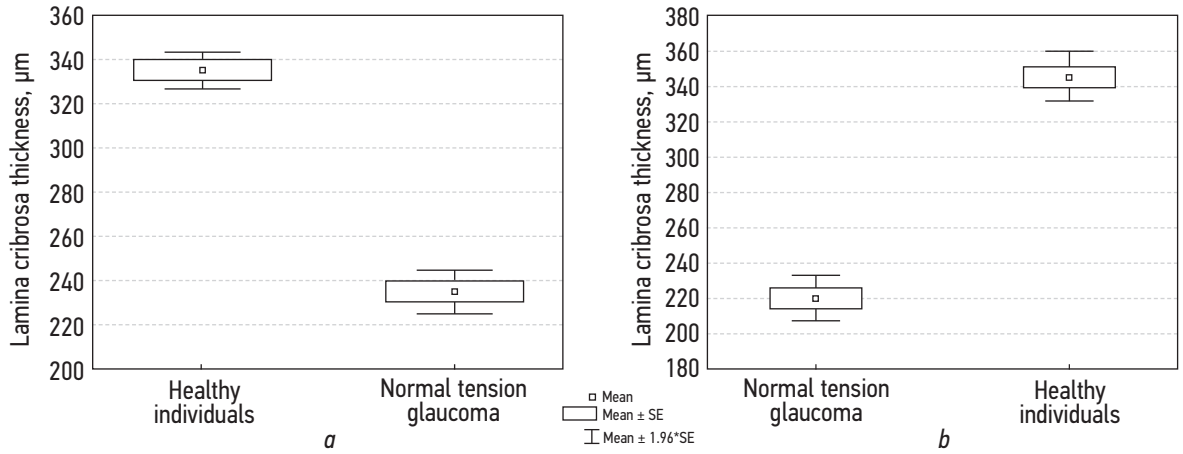

Fig. 5. Average LCT values by the spectral OCT data in the enhanced depth imaging (EDI) mode in research work (*a*) and pilot study (*b*) in two groups (with 95% confidence intervals)

Рис. 5. Средние значения толщины решётчатой пластинки по данным спектральных оптических-когерентных томографов в режиме увеличенной глубины изображения (EDI) при выполнении научно-исследовательской работы (*a*) и пилотного исследования (*b*) в двух группах (с указанием 95 % доверительных интервалов)

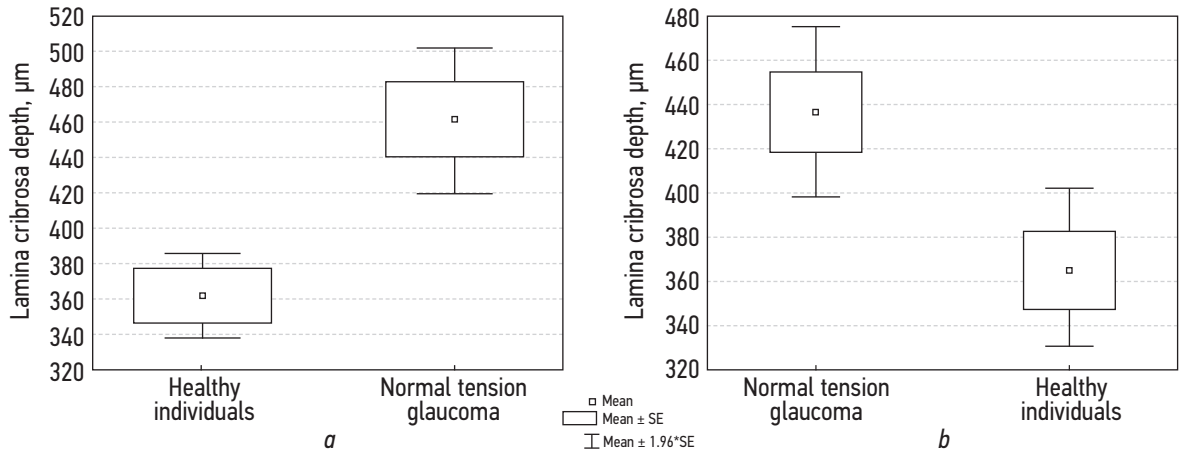

Fig. 6. Average LCD values by the 3D OCT data in the enhanced depth imaging (EDI) mode in research work (*a*) and pilot study (*b*) in two groups (with 95% confidence intervals)

Рис. 6. Средние значения глубины решётчатой пластинки по данным 3D-OCT в режиме увеличенной глубины изображения (EDI) при выполнении научно-исследовательской работы (*a*) и пилотного исследования (*b*) в двух группах (с указанием 95 % доверительных интервалов)

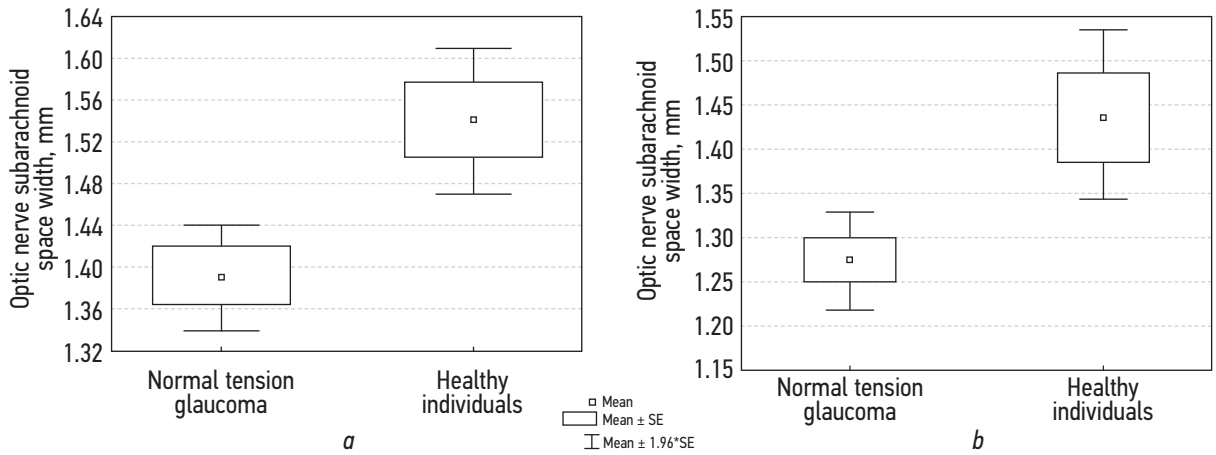

Fig. 7. Average ONSASW values by the MRI data in research work (*a*) and pilot study (*b*) in two groups (with 95% confidence intervals)

Рис. 7. Средние значения ширины субарахноидального пространства зрительного нерва по данным магнитно-резонансной томографии при выполнении научно-исследовательской работы (*a*) и пилотного исследования (*b*) в двух группах (с указанием 95 % доверительных интервалов)

To assess the value of new morphometric indicators in glaucoma diagnosis, we used the parametric Student's test to assess the significance of the difference between the mean values of these indicators obtained in NTG patient and in healthy individuals. According to Figs. 5–7, for the groups 1 and 2, the confidence interval of the mean values of TLC, DLC, and the ON SAS does not overlap according to the research data and according to the results of our pilot study. It follows from these morphometric parameters that eyes with NTG differ with high confidence from healthy eyes.

CONCLUSION

According to the results of both our works, the pilot study and the present one, performed within the framework of the research work at the department, despite the use of different spectral OCT devices and MRI devices, similar morphometric parameters were obtained when assessing the state of the scleral LC and ON SAS in the group of NTG patients and in the control group of healthy individuals. With NTG, the LC thickness was significantly less at a greater depth of its location compared with healthy individuals, which may explain the occurrence of LC deflection and the development of GON at a normal IOP level. In addition, in NTG patients, the ON SAS width of 3 mm behind the eye was also significantly less than in healthy individuals, which, along with their existing arterial hypotension, may indicate a lowered cerebrospinal pressure and, consequently, an increased transmembrane pressure gradient resulting in GON at a normal IOP level.

Thus, in the NTG pathogenesis, the deterioration of biomechanical properties of the membrane itself due to the thinner LC of the sclera and the impairment of TMGP are both important. Therefore, the measurement of the thickness and depth of the LC, as well as the ON SAS width is important in the diagnosis of NTG.

ADDITIONAL INFORMATION

Conflict of interest. The authors declare no conflict of interest.

REFERENCES

1. Volkov VV, Simakova IL, Kulikov AN, et al. New morphometric criteria in the study of pathogenesis of normal-tension glaucoma. *Vestnik Oftal'mologii*. 2020;136(2):49–55. (In Russ.) DOI: 10.17116/oftalma202013602149

2. Hong C, Hong SW, Park CK, et al. Profiles and clinical characteristics of newly diagnosed glaucoma in urban Korea: a multicenter study. *Korean J Ophthalmol*. 2020;34(5):353–360. DOI: 10.3341/kjo.2020.0033

3. Killer HE, Pircher A. Normal tension glaucoma: review of current understanding and mechanisms of the pathogenesis. *Eye*. 2018;32(5):924–930. DOI: 10.1038/s41433-018-0042-2

4. Van Beuningen E, Fischer W. Methodical notes on tonographic and gonioscopy. *Klin. Monatsbl Augenh.* 1956;129(5):202–210. (In German)

5. Duke-Elder SD. *System of ophthalmology vol.11: diseases of the lens and vitreous; glaucoma and hypotony*. London: Henry Kimpton Publisher; 1969.

6. Volkov VV, Korovenkov RI. Ob urovne davleniya zhidkosti v mezhobolochechnykh prostranstvakh zritel'nogo nerva krolika. *Fiziologicheskii zhurnal SSSR im. I.M. Sechenova.* 1974;(61)93–196. (In Russ.)

7. Morgan WH. The influence of cerebrospinal fluid pressure on the lamina cribrosa tissue pressure gradient. *Investig Ophthalmol Vis Sci.* 1995;36(6):1163–1172.

8. Berdahl JP, Fautsch MP, Stinnett SS. Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: a case–control study. *Investig Ophthalmol Vis Sci.* 2008;49(12):5412–5418. DOI: 10.1167/iovs.08-2228

9. Ren R, Jonas JB, Tian G, et al. Cerebrospinal Fluid Pressure in Glaucoma. *Ophthalmology*. 2010;117(2):259–266. DOI:10.1016/j.ophtha.2009.06.058

10. Volkov VV. *Glaukoma pri psevdonormal'nom davlenii*. Moscow; 2001. (In Russ.)

11. Volkov VV, Romova TYa. Obshchaya arterial'naya gipotenziya i glaukomatoznyi protsess v glazu. Vserossiiskoe obshchestvo oftal'mologov: materialy konferentsii. Ordzhonikidze. 1970:37–39. (In Russ.)

12. Volkov VV, Sukhinina LB, Ustinova EI. *Glaukoma, preglaukoma, oftal'mogipertenziya*. Leningrad; 1985. (In Russ.)

13. Volkov VV. *Glaukoma otkrytougol'naya*. Moscow; 2008. (In Russ.)

14. Zhuravlev AI. Disk zritel'nogo nerva i zritel'nye funktsii v otsenke glaukomatoznogo protsessa. [dissertation]. Leningrad; 1986. (In Russ.)

15. Simakova IL. Videogramma i disk zritel'nogo nerva pri raznykh stadiyakh otkrytougol'noi glaukomy i v otsenke effektivnosti ee operativnogo (khirurgicheskogo i lazernogo) lecheniya. [dissertation]. Saint Petersburg; 1997. (In Russ.)

16. Volkov VV. Sushchestvennyi element glaukomatoznogo protsessa, ne uchityvaemyi v klinicheskoi praktike. *Oftal'mologicheskii Zhurnal.* 1976. № 7. C. 500–504. (In Russ.)

17. Jonas JB. Role of cerebrospinal fluid pressure in the pathogenesis of glaucoma. *Acta Ophthalmologica*. 2011;89(6):505–514. DOI: 10.1111/j.1755–3768.2010.01915.x

18. Ren R, Wang N, Zhang X, et al. Trans-lamina cribrosa pressure difference correlated with neuroretinal rim area in glaucoma. *Graefes Arch Clin Exp Ophthalmol.* 2011;249(7):1057–1063. DOI: 10.1007/s00417-011-1657-1

19. Jóhannesson G, Eklund A, Lindén C. Intracranial and Intraocular Pressure at the Lamina Cribrosa: Gradient Effects. *Curr Neurol Neurosci Rep.* 2018;18(5):25–35. DOI: 10.1007/s11910-018-0831-9

20. Wang N, Xie X, Yang D, et al. Orbital Cerebrospinal Fluid Space in Glaucoma: The Beijing Intracranial and Intraocular

Pressure (iCOP) Study. *Ophthalmology*. 2012;119(10):2065–2073. DOI: 10.1016/j.ophtha.2012.03.054
21. Park H-YL, Jeon SH, Park CK. Enhanced depth imaging detects lamina cribrosa thickness differences in normal tension glaucoma and primary Open-angle glaucoma. *Ophthalmology*. 2012;119(1): 10–20. DOI: 10.1016/j.ophtha.2011.07.033
22. Simakova IL, Volkov VV, Boiko EV. The results of developed method of frequency-doubling technology (FDT) perimetry in comparison with the results of the original FDT-perimetry. *Glaucoma*. 2010;(1):5–11. (In Russ.)
23. Kim M, Bojikian KD, Slabaugh MA, et al. Lamina depth and thickness correlate with glaucoma severity. *Indian J Ophthalmol*. 2016;64(5):358–363. DOI: 10.4103/0301-4738.185594
24. Li L, Bian A, Cheng G, et al. Posterior displacement of the lamina cribrosa in normal-tension and high-tension glaucoma. *Acta Ophthalmologica*. 2016;94(6):492–500. DOI: 10.1111/aos.13012
25. Lee SH, Kim TW, Lee EJ, et al. Diagnostic Power of Lamina Cribrosa Depth and Curvature in Glaucoma. *Investig Ophthalmol Vis Sci*. 2017;58(2):755–762. DOI: 10.1167/iovs.16-20802
26. Cakmak S, Altan C, Topcu H, et al. Comparison of the Lamina Cribrosa Measurements Obtained by Spectral-Domain and Swept-Source Optical Coherence Tomography. *Curr Eye Res*. 2019;44(9):968–974. DOI: 10.1080/02713683.2019.1604971
27. Vianna JR, Lanoe VR, Quach J, et al. Serial changes in lamina cribrosa depth and neuroretinal parameters in glaucoma. *Ophthalmology*. 2017;124(9):1392–1402. DOI: 10.1016/j.ophtha.2017.03.048
28. Morozov VI, Yakovlev AA. Zabolevaniya zritel'nogo puti: klinika, diagnostika, lechenie. Moscow; 2010. (In Russ.)
29. Lee JH, Lee HK, Kim JK, et al. CSF Flow Quantification of the Cerebral Aqueduct in Normal Volunteers Using Phase Contrast Cine MR Imaging. Korean J Radiol. 2004;5(2):81–86. DOI: 10.3348/kjr.2004.5.2.81

СПИСОК ЛИТЕРАТУРЫ

1. Волков В.В., Симакова И.Л., Куликов А.Н., и др. Новые морфометрические критерии в изучении патогенеза глаукомы нормального давления // Вестник офтальмологии. 2020. Т. 136. № 2. С. 49–55. DOI: 10.17116/oftalma202013602149
2. Hong C., Hong S.W., Park C.K., et al. Profiles and clinical characteristics of newly diagnosed glaucoma in urban Korea: a multicenter study // Korean J Ophthalmol. 2020. Vol. 34, No. 5. P. 353–360. DOI: 10.3341/kjo.2020.0033
3. Killer H.E., Pircher A. Normal tension glaucoma: review of current understanding and mechanisms of the pathogenesis // Eye. 2018. Vol. 32, No. 5. P. 924–930. DOI: 10.1038/s41433-018-0042-2
4. Van Beuningen E., Fischer W. Methodische hinweise zur tonographic und gonioskopie // Klin. Monatsbl Augenh. 1956. Vol. 129, No. 5. P. 202–210.
5. Duke-Elder S.D. System of ophthalmology vol.11: diseases of the lens and vitreous; glaucoma and hypotony. London: Henry Kimpton Publisher, 1969.
6. Волков В.В., Коровенков Р.И. Об уровне давления жидкости в межоболочечных пространствах зрительного нерва кролика // Физиологический журнал СССР им. И.М. Сеченова. 1974. № 61. С. 93–196.
7. Morgan W.H. The influence of cerebrospinal fluid pressure on the lamina cribrosa tissue pressure gradient // Investig Ophthalmol Vis Sci. 1995. Vol. 36, No. 6. P. 1163–1172.
8. Berdahl J.P., Fautsch M.P., Stinnett S.S. Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: a case-control study // Investig Ophthalmol Vis Sci. 2008. Vol. 49, No. 12. P. 5412–5418. DOI: 10.1167/iovs.08-2228
9. Ren R., Jonas J.B., Tian, G., et al. Cerebrospinal Fluid Pressure in Glaucoma // Ophthalmology. 2010. Vol. 117, No. 2. P. 259–266. DOI: 10.1016/j.ophtha.2009.06.058
10. Волков В.В. Глаукома при псевдонормальном давлении. М., 2001.
11. Волков В.В., Ромова Т.Я. Общая артериальная гипотензия и глаукоматозный процесс в глазу // Всероссийское общество офтальмологов: материалы конференции. Орджоникидзе. 1970. С. 37–39.
12. Волков В.В., Сухинина Л.Б., Устинова Е.И. Глаукома, преглаукома, офтальмогипертензия. Л., 1985.
13. Волков В.В. Глаукома открытоугольная. М., 2008.
14. Журавлев А.И. Диск зрительного нерва и зрительные функции в оценке глаукоматозного процесса: дис. ... канд. мед. наук. Л., 1986.
15. Симакова И.Л. Видеограмма и диск зрительного нерва при разных стадиях открытоугольной глаукомы и в оценке эффективности ее оперативного (хирургического и лазерного) лечения: дис. ... канд. мед. наук. СПб., 1997.
16. Волков В.В. Существенный элемент глаукоматозного процесса, не учитываемый в клинической практике // Офтальмологический журнал. 1976. № 7. С. 500–504.
17. Jonas J.B. Role of cerebrospinal fluid pressure in the pathogenesis of glaucoma // Acta Ophthalmologica. 2011. Vol. 89, No. 6. P. 505–514. DOI: 10.1111/j.1755-3768.2010.01915.x
18. Ren R., Wang N., Zhang X., et al. Trans-lamina cribrosa pressure difference correlated with neuroretinal rim area in glaucoma // Graefes Arch Clin Exp Ophthalmol. 2011. Vol. 249, No. 7. P. 1057–1063. DOI: 10.1007/s00417-011-1657-1
19. Jóhannesson G., Eklund A., Lindén C. Intracranial and Intraocular Pressure at the Lamina Cribrosa: Gradient Effects // Curr Neurol Neurosci Rep. 2018. Vol. 18, No. 5. P. 25–35. DOI: 10.1007/s11910-018-0831-9
20. Wang N., Xie X., Yang D., et al. Orbital Cerebrospinal Fluid Space in Glaucoma: The Beijing Intracranial and Intraocular Pressure (iCOP) Study // Ophthalmology. 2012. Vol. 119, No. 10. P. 2065–2073. DOI: 10.1016/j.ophtha.2012.03.054
21. Park H.-Y.L., Jeon S.H., Park C.K. Enhanced depth imaging detects lamina cribrosa thickness differences in normal tension glaucoma and primary Open-angle glaucoma // Ophthalmology. 2012. Vol. 119, No. 1. P. 10–20. DOI: 10.1016/j.ophtha.2011.07.033
22. Симакова И.Л., Волков В.В., Бойко Э.В. Сравнение результатов разработанного метода периметрии с удвоенной пространственной частотой и оригинального метода FDT-периметрии // Глаукома. 2010. № 1. С. 5–11.
23. Kim M., Bojikian K.D., Slabaugh M.A., et al. Lamina depth and thickness correlate with glaucoma severity // Indian J Ophthalmol. 2016. Vol. 64, No. 5. P. 358–363. DOI: 10.4103/0301-4738.185594
24. Li L., Bian A., Cheng G., et al. Posterior displacement of the lamina cribrosa in normal-tension and high-tension glau-

coma // Acta Ophthalmologica. 2016. Vol. 94, No. 6. P. 492–500. DOI: 10.1111/aos.13012

25. Lee S.H., Kim T.W., Lee E.J., et al. Diagnostic Power of Lamina Cribrosa Depth and Curvature in Glaucoma // Investig Ophthalmol Vis Sci. 2017. Vol. 58, No. 2. P. 755–762. DOI: 10.1167/iovs.16-20802

26. Cakmak S., Altan C., Topcu H., et al. Comparison of the Lamina Cribrosa Measurements Obtained by Spectral-Domain and Swept-Source Optical Coherence Tomography // Curr Eye Res. 2019. Vol. 44, No. 9. P. 968–974. DOI: 10.1080/02713683.2019.1604971

27. Vianna J.R., Lanoe V.R., Quach J., et al. Serial changes in lamina cribrosa depth and neuroretinal parameters in glaucoma // Ophthalmology. 2017. Vol. 124, No. 9. P. 1392–1402. DOI: 10.1016/j.ophtha.2017.03.048

28. Морозов В.И., Яковлев А.А. Заболевания зрительного пути: клиника, диагностика, лечение. М., 2010.

29. Lee J.H., Lee H.K., Kim J.K., et al. CSF Flow Quantification of the Cerebral Aqueduct in Normal Volunteers Using Phase Contrast Cine MR Imaging // Korean J Radiol. 2004. Vol. 5, No. 2. P. 81–86. DOI: 10.3348/kjr.2004.5.2.81

AUTHORS' INFO

***Irina L. Simakova,** MD, Dr. Sci. (Med.);
address: 21 Botkinskaya st., Saint Petersburg, 194044, Russia;
ORCID: https://orcid.org/0000-0001-8389-0421;
eLibrary SPIN: 3422-5512; SCOPUS: 7003824052;
e-mail: irina.l.simakova@gmail.com

Alfina R. Suleimanova, ophthalmologist;
ORCID: https://orcid.org/0000-0003-1893-8075;
e-mail: alfinkamuse1@gmail.com

Natalya P. Baimuratova, roentgenologist;
ORCID: https://orcid.org/0000-0001-5383-6440;
e-mail: skynait@yandex.ru

ОБ АВТОРАХ

***Ирина Леонидовна Симакова,** д-р мед. наук;
адрес: Россия, 194044, Санкт-Петербург, ул. Боткинская, д. 21;
ORCID: https://orcid.org/0000-0001-8389-0421;
eLibrary SPIN: 3422-5512; SCOPUS: 7003824052;
e-mail: irina.l.simakova@gmail.com

Альфина Рауфовна Сулейманова, врач-офтальмолог;
ORCID: https://orcid.org/0000-0003-1893-8075;
e-mail: alfinkamuse1@gmail.com

Наталья Павловна Баймуратова, врач-рентгенолог;
ORCID: https://orcid.org/0000-0001-5383-6440;
e-mail: skynait@yandex.ru