PHOTODYNAMIC THERAPY FOR CILIARY BODY MELANOMA: EXPERIENCE WITH AN ISOLATED TRANSSCLERAL APPROACH

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Abstract

Ciliary body melanoma (CBM) accounts for up to 20% of uveal melanoma cases and presents challenges for organ-preserving treatment due to its peripheral location and proximity to critical ocular structures. This study presents the first clinical results evaluating the efficacy and safety of isolated transscleral photodynamic therapy (TSPDT) with a chlorin e6 photosensitizer in 7 patients with CBM. The procedure was performed using an «ALOD-01» laser system (λ=662 nm) and standardized irradiation parameters (energy density 519.5 J/cm^2, accounting for power loss during scleral transmission). The mean follow-up period was 19.0±5.9 months and demonstrated high local tumor control: complete regression was achieved in 4 patients, and partial regression in 3 patients. A statistically significant reduction in tumor height (from 4.69±2.58 mm to 1.36±1.14 mm; p=0.0062) and basal diameter (from 8.54±3.56 mm to 6.65±3.70 mm; p=0.016) was accompanied by a pronounced vasculo-occlusive effect, manifested as complete tumor avascularity in the majority of patients according to ultrasound with color Doppler Imaging (CDI). Echodenstitometry recorded a statistically significant decrease in mean acoustic density from 35.53±1.26 dB to 28.97±0.83 dB (p=0.0002), which may indicate tumor tissue destruction. No intra– or postoperative complications were recorded throughout the observation period, and a trend towards stable visual acuity was noted. The obtained data suggest that TSPDT is a promising minimally invasive organ-preserving method for treating CBM, requiring further investigation to define its role as either a standalone or combined therapy.

Keywords: uveal melanoma, ciliary body melanoma, choroidal melanoma, ophthalmic oncology, photodynamic therapy, chlorin e6, transscleral photodynamic therapy, photosensitizer.

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ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ ПРИ МЕЛАНОМЕ ЦИЛИАРНОГО ТЕЛА: ОПЫТ ИЗОЛИРОВАННОГО ТРАНССКЛЕРАЛЬНОГО ПОДХОДА

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Резюме

Меланома цилиарного тела (МЦТ) составляет до 20% случаев увеальной меланомы и представляет сложности для органосохранного лечения ввиду периферической локализации и близости к критическим структурам глаза. В настоящем исследовании представлены первые клинические результаты оценки эффективности и безопасности изолированной транссклеральной фотодинамической терапии (ТСФДТ) с фотосенсибилизатором (ФС) хлорин е6 у 7 пациентов с МЦТ. Процедура выполнена с использованием лазерной установки «АЛОД-01» (λ=662 нм) и унифицированных параметров воздействия (плотность энергии 519,5 Дж/см^2 с учетом потерь мощности при прохождении излучения через склеру). Динамическое наблюдение в среднем в течение 19,0±5,9 мес показало высокий локальный контроль над опухолью: полный регресс был достигнут у 4 пациентов, частичный – у 3 пациентов. Статистически значимое уменьшение высоты опухоли (с 4,69±2,58 мм до 1,36±1,14 мм; p=0,0062) и диаметра ее основания (с 8,54±3,56 мм до 6,65±3,70 мм; p=0,016) сочеталось с выраженным васкуло-окклюзивным эффектом, проявляющимся в полной аваскуляризации опухоли у большинства пациентов по данным ультразвукового исследования (УЗИ) в режиме цветового допплеровского картирования (УЗДГ). Эходенситометрия зафиксировала статистически значимое снижение средней акустической плотности с 35,53±1,26 дБ до 28,97±0,83 дБ (p=0,0002), что может свидетельствовать о деструкции опухолевой ткани. На протяжении всего периода наблюдения не зафиксировано интра– или послеоперационных осложнений, отмечена тенденция к сохранению стабильной остроты зрения. Полученные данные позволяют рассматривать ТСФДТ как перспективный минимально инвазивный органосохраняющий метод лечения МЦТ, требующий дальнейшего изучения для определения его роли в качестве изолированной или комбинированной терапии.

Ключевые слова. Увеальная меланома, меланома цилиарного тела, меланома хориоидеи, офтальмоонкология, фотодинамическая терапия, хлорин е6, транссклеральная фотодинамическая терапия, фотосенсибилизатор.

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Introduction

Melanoma of the ciliary body (CBM) accounts for up to 20% of all cases of uveal melanoma [1,2]. This localization presents significant difficulties for organ-preserving treatment, due to its anatomical location in close proximity to the lens and drainage system of the eye [1-6]. Peripheral localization and "hidden" growth cause a late diagnosis of this process, and also create significant difficulties in choosing the optimal treatment tactics [2,3,6]. Currently, local surgical resection (block excision) and various types of radiation therapy are in the arsenal of organ-preserving methods for CBM [2,4-10]. However, each of these approaches has certain limitations. Thus, block excision is technically difficult, involves the risk of intra- and postoperative complications, including suprachoroidal hemorrhage, detachment of the choroid and retina, and requires the highest qualification of the surgeon [2,6,7]. Radiation treatment methods such as Ru-106/Rh-106 brachytherapy and proton therapy show high efficacy in local tumor control [5,9,10]. At the same time, in the treatment of CBM, they may be associated with a higher incidence of post-radiation complications compared with post-equatorial tumors, which is due to the inevitable irradiation of critical structures of the anterior part of the eyeball [5, 10-12]. An additional difficulty in brachytherapy is the precise positioning of the ophthalmoapplicator in the area of the ciliary body.

Photodynamic therapy (PDT) has been actively studied in recent years as a minimally invasive organ-preserving approach for uveal melanoma [13-20]. The clinical validity of the use in melanoma is confirmed by the presence of officially registered indications for chlorin photosensitizers (PS), such as photolon / fotoran. The greatest experience has been gained with the use of transpupillary PDT (TPPDT), the effectiveness of which, as shown in a number of studies, depends on the initial size of the tumor, as well as the degree of its vascularization and pigmentation [15,16,18-20]. At the same time, the field of application of TPPDT is limited to neoplasms of the posterior pole of the eye, accessible for irradiation through transparent optical media [18-20]. In this regard, transcleral PDT (TSPDT), which provides direct laser radiation to the base of the tumor through the scleral membrane, is a promising alternative to overcome this anatomical limitation [13,21,22]. The possibility of using this approach has been confirmed in previous experimental studies, which have shown the ability of laser radiation with a wavelength of 660 nm to effectively and safely penetrate the sclera [22]. In addition, selective photochemical damage to the choroidal vascular network has been proven [21]. However, there is no data in the literature on the clinical use of TSPDT for the treatment of ocular vascular melanoma. The present study presents the first clinical results evaluating the efficacy and safety of isolated TSPDT with PS chlorin e6 in the treatment of CBM.

Materials and methods

The study included 7 patients (7 eyes) with CBM who were treated with isolated TSPDT in the period from 2022 to 2024. The inclusion criteria were: tumor thickness up to 9 mm, base diameter up to 15 mm, absence of signs of extrascleral spread and tumor growth in the corner of the anterior chamber, absence of complications.

Ethical aspects

The research protocol was approved by the local Ethics committee of the Federal State Budgetary Budgetary Institution "IEM" (No. 4/24 dated 10/24/2024).

All patients underwent a comprehensive clinical and instrumental examination, which included visometry with an assessment of best corrected visual acuity (BCVA), biomicroscopy, ophthalmoscopy with a non-contact lens, Maklakov tonometry and ultrasound biomicroscopy (UBM). Ultrasound was performed on a Philips Affinity 50 multifunction scanner (Philips Ultrasound, USA) with an L15-7io sensor to evaluate the metric parameters of the tumor, the characteristics of intracellular blood flow using color Doppler mapping (CDM) and densitometric characteristics of tumor tissue (echodensitometry) with quantitative determination of acoustic density in decibels (dB) with the construction of and analysis of amplitude histograms under standardized conditions. To stage the process and exclude metastatic lesions, multispiral computed tomography (MSCT) of the chest organs, magnetic resonance imaging (MRI) of the abdominal cavity with contrast, and MRI of the brain were performed.

The distribution of patients by stage, size, blood flow characteristics, and acoustic density of the tumor is shown in Table 1.

As the data in Table 1 show, the patients in the study were mainly women (n=6), whose average age was 68.7±15.8 years. All tumors belonged to stage II according to the AJCC classification of the 8th edition (IIA n=4), (IIB n=3). According to the degree of pigmentation, strongly pigmented tumors prevailed (n=4). At the time of diagnosis, the vast majority of neoplasms (n=5) had a hypervascular type of blood flow, while 6 patients had several vessels feeding the tumor. The average acoustic density of the tumor tissue before treatment was 35.53±1.26 dB (26.34-44.42). The average follow-up period was 19.0±5.9 months.

The TSPDT procedure was performed under anesthesia, 3 hours before the laser exposure, chlorin-type PS based on chlorin e6 (photolon/fotoran) was administered intravenously at a dose of 1.0 mg/kg body weight. After conjunctival access and transpupillary diaphanoscopy, transcleral laser irradiation of the tumor base was performed using an ALOD-01 laser (λ=662 nm, Alcom Medica, Russia) and specialized transcleral tip probes to accurately mark the tumor boundaries.

The technical parameters of the exposure were unified: radiation power 0.17 W, power density 0.866 W/cm^2, energy density 519.5 J/cm^2 with an

Таблица 1
Клинико-инструментальные характеристики пациентов с меланомой цилиарного тела до лечения (n=7)

Table 1
Clinical and instrumental characteristics of patients with ciliary body melanoma before treatment (n=7)

Параметр Parameter	Значение Value
Возраст, лет Age, years	68,7±15,8 (37-82)
Женский пол, n Female gender, n	6
Мужской пол, n Male gender, n	1
Срок наблюдения, мес Observation period, months	19,0±5,89 (12-30)
Стадия AJCC, n **AJCC stage, n**	
IIA	4
IIB	3
Пигментация, n **Pigmentation, n**	
Выраженная Significant	4
Умеренная Mild	2
Беспигментная Non-pigmented	1
Васкуляризация исходная, n Initial vascularization, n	
Гиперваскулярная Hypervascular	5
Гиповаскулярная Hypovascular	2
Количество питающих опухоль сосудов, n **Number of vessels feeding the tumor, n**	
Один сосуд One vessel	1
Несколько сосудов Several vessels	6
Средняя акустическая плотность, дБ **Average acoustic density, dB**	35,53±1,26 (26,34-44,42)

exposure duration of 600 seconds (10 minutes) in the field. These parameters were proportionally doubled, taking into account the transmittance of the sclera to provide the necessary therapeutic dose in the tumor area. The exposure was carried out concentrically from the center to the periphery with the overlap of fields on 10-15% of the area.

The effectiveness of treatment was assessed in dynamics after 1, 3, 6, 9, 12 months and further annually, which was based on changes in the nature of intracellular blood flow, densitometric characteristics (acoustic density) and metric parameters of the tumor. The response to treatment was assessed according to the RECIST 1.1 criteria (2009): complete regression (absence of elevation according to color Doppler Imaging (CDI) and blood flow according to CDM), partial regression (decrease in tumor height >30% from the initial one), stabilization (change in height within ±30%) and progression (increase in height >30%). The dynamics of maximum corrected visual acuity and intra- and postoperative complications were also evaluated.

Statistical data processing was carried out using the SPSS 28.0 program. Quantitative data were checked for the normality of the distribution using the Shapiro-Wilk test. The arithmetic mean and standard deviation (M±SD) for parameters with a normal distribution and the median with an interquartile range [Me (Q1; Q3)] for parameters with a distribution other than normal were used for the description. To compare the indicators before and after treatment, the Student's t-test was used for paired samples. Fischer's exact test was used to analyze categorical data. The differences were considered statistically significant at $p < 0.05$.

Таблица 2
Клинико-инструментальная динамика опухолевых, ультразвуковых, денситометрических, допплерографических и функциональных параметров до и после проведения изолированной ТСФДТ

Table 2
Clinical and instrumental dynamics of tumor, ultrasound, densitometric, Doppler and functional parameters before and after isolated TSPDT

Параметр Parameter	До лечения Before treatment	После лечения After treatment	Δ (Изменение) Δ (Change)	p-value
Высота опухоли, мм **Tumor height, mm**	4,69±2,58	1,36±1,14	-3,33±2,41	0,0062
[min-max]	*[2,4 – 8,8]*	*[0,0 – 3,0]*	*[-8,3 – -1,0]*	
Диаметр основания, мм **Base diameter, mm**	8,54±3,56	6,65±3,70	-1,89±1,64	0,016
[min-max]	*[5,0 – 14,0]*	*[2,0 – 11,4]*	*[-3,05 – +0,1]*	
МКОЗ **Best-corrected visual acuity**	0,60±0,34	0,71±0,26	+0,11±0,25	0,25
[min-max]	*[0,03 – 1,0]*	*[0,4 – 1,0]*	*[-0,4 – +0,45]*	
Васкуляризация, n (%) **Vascularization, n (%)**				
Гиперваскулярная Hypervascular	5	1		
Гиповаскулярная Hypovascular	2	1		
Аваскулярная Avascular	0	**5**		
Средняя акустическая плотность, дБ **Average acoustic density, dB**	35,53±1,26	28,97±0,83	-6,56±1,12	0,0002
[min-max]	*[26,34 – 44,42]*	*[19,4 – 34,97]*	*[-12,02 – -2,45]*	
Результат лечения, n (%) **Treatment outcome, n (%)**				
Полный регресс Complete regression	-	4		
Частичный регресс Partial regression	-	3		

Results

The clinical and instrumental dynamics of tumor, ultrasound, densitometric, Dopplerographic, and functional parameters before and after treatment are presented in Table 2.

Clinical and instrumental dynamics of tumor, ultrasound, densitometric, Doppler and functional parameters before and after isolated TSPDT.

Given that the key mechanism of action of PDT is primary vascular occlusive effect, the analysis of the results was primarily aimed at assessing changes in intracellular blood flow. As the results presented in Table 2 show, the most pronounced and early changes were recorded in the nature of intracellular vascularization. Thus, if hypervascularization was observed in 5 patients before treatment, then after TSPDT, all patients in this group showed complete tumor avascularization, which may indicate thrombosis of the vessels feeding the tumor. One patient retained the hypovascular type of blood flow, and only one patient showed signs of moderate hypervascularization.

Next, the dynamics of the densitometric characteristics of the tumor was analyzed. Statistical analysis demonstrated a significant decrease in the average acoustic density of tumor tissue from 35.53±1.26 dB to 28.97±0.83 dB (Δ=-6.56±1.12 dB; p=0.0002), which may indirectly indicate a change in the structural characteristics of the tumor, possibly associated with a direct cytotoxic effect and destruction of tumor tissue.

The next step was to assess the reduction in tumor size, which is a natural consequence of the cessation of its blood supply. The analysis showed a statistically significant decrease in tumor height: from 4.69±2.58 mm to 1.36±1.14 mm (Δ = -3.33±2.41 mm; p=0.0062). The diameter of the tumor base also significantly decreased: from 8.54±3.56 mm to 6.65±3.70 mm (Δ = -1.89± 1.64 mm; p = 0.016).

According to the criteria of treatment effectiveness RECIST 1.1 (2009), complete regression was achieved in 4 patients, partial regression in 3 patients. There were no cases of stabilization or progression of the disease, which indicates 100% local control of the tumor during the follow-up period.

When assessing functional outcomes, the changes in BCVA did not reach statistical significance, but a tendency to increase was found (from 0.60±0.34 to 0.71±0.26; Δ = +0.11±0.25; p=0.25). The peripheral localization of tumors of the ciliary body in most cases provided initially high visual acuity, which remained at the same level and tended to improve after treatment. It is important to note that during the entire follow-up period, no intra- or postoperative complications related to the TSPDT were recorded.

The results obtained are confirmed by the following clinical observation. Patient E., 58 years old, was sent to the St. Petersburg branch of S. Fyodorov Eye Microsurgery Federal State Institution of the Ministry of Health of the Russian Federation for consultation with an ophthalmologist with suspected neoplasm of the ciliary body of the right eye. The patient noted a decrease in vision in his right eye during the last 4 months. According to the MRI data of orbits with contrast in the inner segment, a solid formation was determined in the projection of the ciliary body. 0,7*0,6*0,8 cm with a cystic component (0.4 * 0.6 cm), closely adjacent to the lens, intensively accumulating contrast. The patient signed an informed consent for a diagnostic examination. According to the results of a standard ophthalmological examination, including biometry, visometry, tonometry, perimetry, biomicroscopy, biomicroophthalmoscopy, it was found that visual acuity was OD = 0.25 sph – 2.0 cyl -1.0 Dax 25 = 0.5; OS = 0.95 sph +0.25 cyl -0.5 D ax 100 = 1.0; intraocular pressure according to pneumotonometry at OD was 19 mmHg, at OS was 16 mmHg. Biomicroscopy of the right eye revealed an enlarged episcleral vessel at 9 o'clock, islet deposits of pigment on the iris from 3 to 5 o'clock, a moderately pigmented pro-inflammatory neoplasm adjacent to the lens was detected behind the pupillary edge from 2 to 5 o'clock, increased lens opacity in the contact zone. Gonioscopy from 2 to 5 o'clock revealed partial closure of the anterior chamber angle by the iris, pigment on the iris with a local round area of hyperpigmentation measuring 1 mm. Ophthalmoscopically the optic nerve disc was pale pink, the borders were clear, in the macular zone there were no features, at the extreme periphery in the upper-inner segment (mainly the inner) a protruding, pigmented neoplasm of a round shape was determined.

The patient underwent additional instrumental examinations: ultrasound, including CDI with color Doppler mapping of the reflected Doppler signal and spectral Doppler imaging on a PHILIPS Affinity 50 multifunctional scanner (Philips Ultrasound, USA) with an L15-7io high-frequency broadband linear transducer in the operating frequency range of 15 to 7 MHz; ultrasound microscopy (UBM) on an Aviso device with a 25 MHz linear transducer; and photo monitoring. The clinical and instrumental examination data are presented in Fig. 1.

According to ultrasound of the right eye (Fig. 1), in the upper-inner segment in the projection of the ciliary body, a rounded neoplasm with a height of up to 8.8 mm, a diameter of up to 7.4 mm, and an uneven structure with a cyst-like cavity in the thickness were detected. In the CDM mode, multiple color streams were mapped in the projection of a tumor with medium-speed, low-resistance blood flow. During echodensitometry, the average acoustic density of the tumor tissue was 37.4±1.8 dB. According to UBM, in the upper-inner quadrant, a

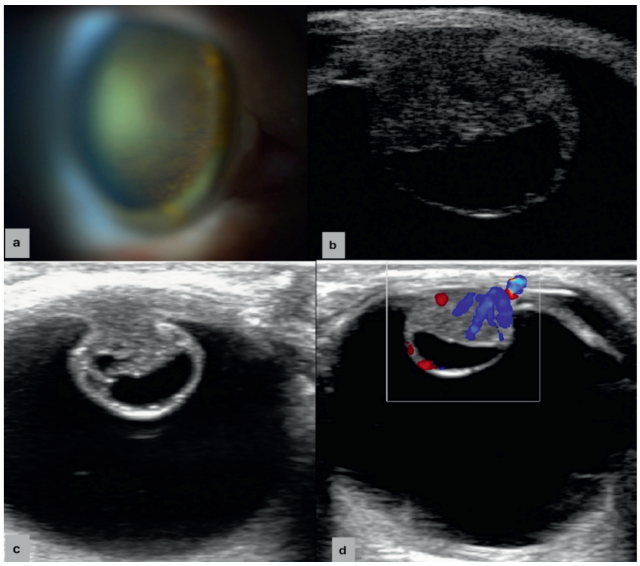

Рис. 1. Диагностические характеристики меланомы цилиарного тела до лечения:
a – пигментированное образование, прилегающее к хрусталику;
b – УБМ проминирующего образования;
c – серошкальное ультразвуковое сканирование;
d – ЦДК внутриопухолевого кровотока.
Fig. 1. Diagnostic characteristics of ciliary body melanoma before treatment:
a – pigmented mass adjacent to the lens;
b – ultrasound biomicroscopy of protruding mass;
c – grayscale ultrasound scanning;
d – color Doppler mapping of intratumoral blood flow.

protruding neoplasm with a height of up to 8.8 mm was visualized in the area of the ciliary body.

To assess the extraocular prevalence of the process, an MRI examination of the abdominal cavity and brain organs, and an MSCT of the lungs were performed. According to the results of additional studies, there are no pathological changes.

Based on the data of a comprehensive clinical and instrumental examination, the patient was diagnosed with T2bN0M0 stage IIB ciliary body melanoma.

Taking into account the size, abundant vascularization and localization of the tumor, the patient was offered treatment in the amount of TSPDT. A voluntary informed consent for treatment has been signed.

On the next day after the TSPDT, ophthalmoscopically, a pronounced reaction was noted in the form of whiteness and swelling of the tumor surface. According to CDI, signs of thrombosis of intracellular vessels were observed (Fig. 2). Echodensitometry data showed an initial decrease in acoustic density to 34.1±2.1 dB.

After treatment, dynamic monitoring was continued. At a follow-up examination 2 months after TSPDT, positive dynamics was noted in the form of partial regression of the tumor according to ultrasound (Fig. 3b) - the height of the tumor decreased to 3.3 mm, the

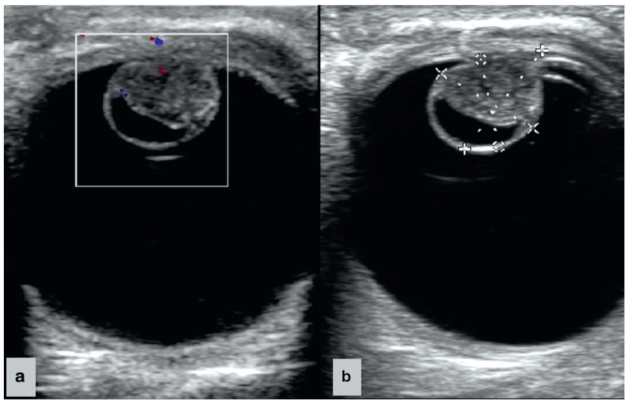

Рис. 2. Ранние изменения после ТСФДТ (1 сут):
a – признаки тромбоза внутриопухолевых сосудов при ЦДК;
b – серошкальное ультразвуковое сканирование.
Fig. 2. Early changes after TSPDT (day 1):
a – signs of intratumoral vessel thrombosis on color Doppler mapping;
b – grayscale ultrasound scanning.

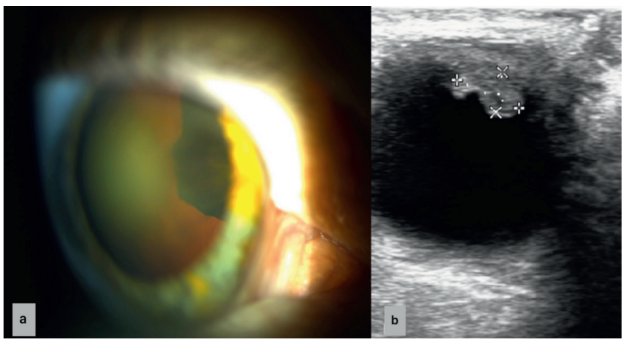

Рис. 3. Динамика состояния через 2 мес после ТСФДТ:
a – биомикроскопия глаза с признаками регресса опухоли;
b – серошкальное ультразвуковое сканирование, демонстрирующее уменьшение размеров опухоли.
Fig. 3. Dynamics at 2 months after TSPDT:
a – biomicroscopy of the eye with signs of tumor regression;
b – grayscale ultrasound scanning demonstrating reduction in tumor size.

diameter of the base decreased to 5.5 mm, according to CDI, blood flow in the tumor was not mapped, and the average acoustic density significantly decreased to 29.2 ±1.5 dB, Biomicroscopically, a decrease in tumor size was noted (Fig. 3a).

Six months after treatment, positive dynamics were noted in the form of tumor regression up to 90%. According to ultrasound data, a decrease in size to 1.1*2.6 mm was observed in the seroscale scanning mode (Fig. 4b), blood flow in the tumor thickness was not mapped during ultrasound with CDM (Fig. 4c), echodensitometry recorded a further decrease in density to 22.6±1.1 dB, biomicroscopically a significant decrease in tumor size was noted (Fig. 4a).

During follow-up examinations 9 months after treatment, the condition is without dynamics. According to ultrasound data in the seroscale scan

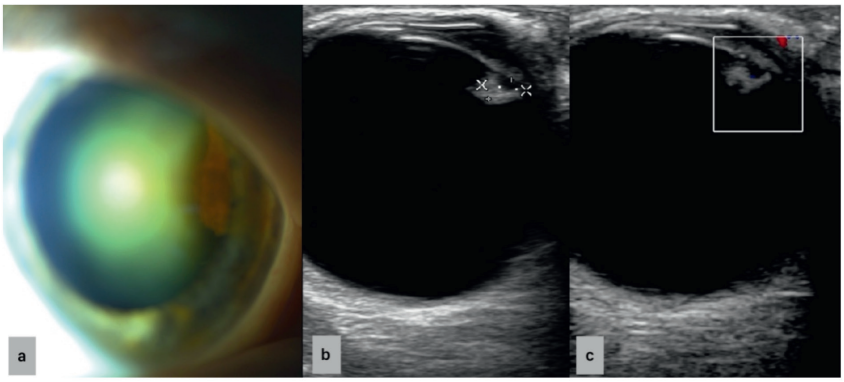

Рис. 4. Динамика состояния через 6 мес после ТСФДТ:
a – биомикроскопия глаза со значительным регрессом опухоли;
b – серошкальное ультразвуковое сканирование, показывающее уменьшение размеров опухоли;
c – ЦДК, подтверждающее аваскулярность опухоли.
Fig. 4. Dynamics at 6 months after TSPDT:
a – biomicroscopy of the eye with significant tumor regression;
b – grayscale ultrasound scanning showing reduction in tumor size;
c – color Doppler mapping confirming tumor avascularity.

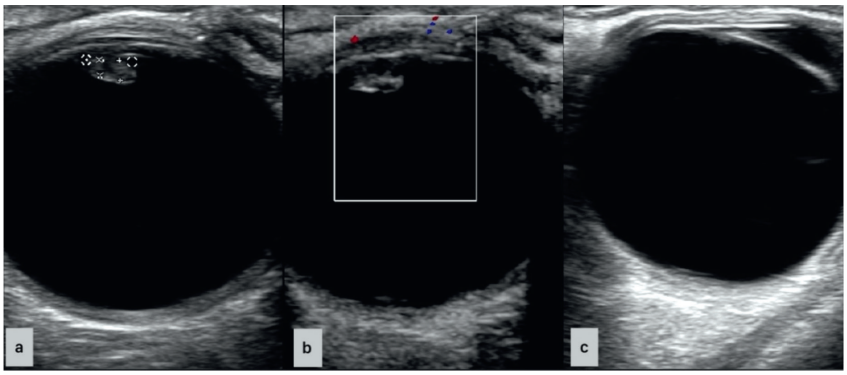

Рис. 5. Отдаленные результаты ТСФДТ:
a – серошкальное ультразвуковое сканирование через 9 мес после лечения;
b – цветовое допплеровское картирование через 9 мес после лечения, аваскулярно;
c – серошкальное ультразвуковое сканирование через 12 мес после лечения, подтверждающее полный регресс опухоли.
Fig. 5. Long-term results of TSPDT:
a – grayscale ultrasound scanning at 9 months after treatment;
b – color Doppler mapping at 9 months after treatment, avascular;
c – grayscale ultrasound scanning at 12 months after treatment, confirming complete tumor regression.

mode, the tumor size was 1.1*2.6 mm (Fig. 5a), in the CDM mode the neoplasm was avascular (Fig. 5b). The acoustic density of the residual tumor tissue was 19.7±0.9 dB. 12 months after the TSPDT, a complete regression of the tumor was achieved, according to ultrasound, the tumor was not visualized (Fig. 5c).

Discussion

TSPDT is an innovative approach in the treatment of intraocular tumors. The key advantage of the technique is the ability of radiation to overcome the scleral membrane with minimal losses and selectively affect the tumor from its base, which is achieved due to the optical properties of the sclera and choroid, which contribute to uniform distribution of energy in the deep layers of the eyeball [14, 22, 23]. The present study presents the first clinical results of the application of this approach for the isolated treatment of melanoma of the choroid of the eyeball.

In the presented series of cases, local tumor control was achieved in all patients during the follow-up period: complete regression was noted in 4 and partial regression in 3 patients with an average follow-up period of 19.0±5.9 months. An important aspect is the absence of cases of local disease progression during follow-up. In cases with insufficient regression dynamics at control examinations within 1-3 months, a timely transition to brachytherapy was used, which excluded wait-and-see tactics. Achieving complete regression in more than half of the patients allows to consider this technology as a potential option for isolated treatment. However, the absence of complete regression in some patients requires further dynamic monitoring and, if necessary, consideration of additional treatment.

The selectivity of PDT, based on the selective accumulation of PS in pathological tissues, minimizes damage to healthy structures of the eye [15, 24-27]. This fact explains the absence of decreased visual acuity and complications characteristic of radiation therapy in the study – post-radiation cataracts, neuroretinopathy, and neovascular glaucoma, which are especially common when tumors of the anterior eye are irradiated and significantly limit the functional results of treatment [5, 11, 12, 13].

The main mechanism of the antitumor effect of PDT is the combined effect on the vessels of the microcirculatory bed of the tumor (vascular occlusive effect) and on tumor cells (direct cytotoxic effect) [15,24,25,28,29]. Complete avascularization of the tumor focus in most patients, which was observed from early follow-up, confirms the pronounced vascular-destroying effect of the method and is consistent with the literature data on tumor vessel thrombosis as a key mechanism of PDT [14-17,19-23].

An important result of this study, consistent with the data on the direct cytotoxic effect, was the objective confirmation of the destruction of tumor tissue using echodensitometry [30, 31]. A statistically significant decrease in the average acoustic density recorded in dynamics (from 35.53±1.26 dB to 28.97±0.83 dB; p=0.0002) may indicate the development of structural changes in the tumor tissue, presumably associated with necrotic processes, which is also consistent with the data obtained in the presented clinical case. The revealed changes, first of vascularization, and then of acoustic density, naturally contribute to the subsequent regression of the neoplasm.

Tissue pigmentation creates significant limitations for PDT in oncological practice, since melanin absorbs light energy, reducing the depth of radiation penetration and therapeutic effectiveness [18, 32, 33]. In the presented study, the combination of red spectrum radiation (660 nm) with transcleral access minimizes the impact of these limitations. The key advantage of the technique is the direct supply of light to the base of the tumor, partially bypassing the pigment barrier, in contrast to the transpupillary approach, where melanin shields the radiation at the top of the tumor [19-21]. In this series of cases, this approach made it possible to achieve regression even with pronounced pigmented neoplasms.

The depth of penetration and the efficiency of radiation delivery remain important aspects of PDT in the treatment of intraocular neoplasms, since light in PDT procedures is subject to scattering and absorption when passing through biological tissues, including the sclera. The wavelength range used to activate PS is 405-900 nm, while the penetration depth significantly depends on the optical properties of the specific wavelength and absorption spectrum of the drug [20, 25]. In this study, PS chlorin e6 was used, which belongs to the second generation of drugs [15, 16, 25, 34, 35]. Unlike first–generation porphyrins operating in the range of 400-630 nm and providing a penetration depth of up to 1-3 mm, chlorin e6 is activated by 660 nm radiation and provides a significantly greater penetration depth of at least 3.5-4.4 mm, as well as reduced absorption by the main tissue chromophores – melanin and hemoglobin [15, 32, 33, 36, 37]. The results obtained in the presented study are consistent with the data on a sufficient depth of radiation penetration in this spectral range.

The main limitation of this study is the small number of patients in the sample and the relatively short follow-up period, which makes it impossible to draw definitive conclusions about long-term outcomes and the frequency of local relapses. The obtained preliminary data, on the one hand, demonstrate the possibility of using TSPDT as an isolated method in individual patients. On the other hand, given the multicomponent approach adopted in oncology and the fact that brachytherapy remains the "gold standard" for the treatment of ocular vascular melanoma, it is currently advisable to consider the TSPDT method primarily as a component of combination therapy. It should be emphasized that this treatment method does not claim to be a universal solution for all patients with CBM. The demonstrated efficacy was achieved within the selected cohort, which determines the relatively narrow indications for its use as an isolated treatment. The key conditions for success are careful patient selection and strict postoperative monitoring, which allows timely assessment of the response and decision on the need for additional intervention.

Further development of the method is associated with several directions. Firstly, TSPDT can be used to treat small tumors of peripheral localization with hypervascular type of blood flow. Secondly, its use as part of a combined approach seems to be the most reasonable, for example, as a neoadjuvant step before brachytherapy or protonotherapy.

The results obtained, in particular, a significant reduction in the size, vascularization, and acoustic density of the tumor after TSPDT, suggest that such tactics may create prerequisites for reducing the radiation dose during subsequent brachytherapy, which can potentially offset the risks of radiation complications. The method may also be used in adjuvant mode. In addition, a promising direction is the combination of TSPDT with other methods, including TPPDT, for a two-way effect on the tumor.

Conclusion

The study shows that isolated TSPDT with PS based on chlorin e6 can be considered as a promising and safe method of organ-preserving treatment of CBM. Within the selected cohort of patients, the method allowed to achieve a high frequency of local control. In addition to a statistically significant reduction in tumor size and a pronounced vascular occlusive effect, an objective confirmation of the destruction of tumor tissue by echodensitometry was a significant result, which may reflect the direct cytotoxic effect of the method. An important aspect is the preservation of stable visual function and the absence of complications. Given the preliminary nature of the data, the results obtained determine the need for further research to clarify the role of TSPDT in the treatment of vascular melanoma, clarifying the prospects for its use as an isolated method or, most likely, a component of combined treatment.

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