FACTORS INFLUENCING THE DEVELOPMENT OF RECURRENCE AND CONTINUED GROWTH OF PRIMARY EXTRAMEDULLARY TUMORS REMOVED USING ND:YAG LASER

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Objective. To assess the significance of clinical factors of extramedullary tumors and new methods of their resection as potential predictors of their recurrence and continued growth.

Material and Methods. The long-term results of removal of primary extramedullary tumors in 412 patients operated on in 1998–2014 were analyzed comparing the use of standard methods of microsurgical technique for tumor removal (277 patients) and of those with additional use of neodymium laser radiation (135 patients).

Results. The use of laser technologies for resection of extramedullary tumors can significantly reduce the number of their recurrences and continued growth, along with other clinical factors is a significant prognostic indicator in determining the nature of the disease course and can be a predictor of their occurrence. The most reliable clinical factors determining the prognosis of a decrease in the incidence of recurrences and continued growth when using laser techniques of surgical resection were repeated operations ($p = 0.002$), the presence of ependymomas of the cone and cauda equina ($p = 0.017$), operations for primary tumors in the thoracic spine ($p = 0.039$) and extramedullary tumors with Grade I anaplasia ($p = 0.007$). An increase in the number of these conditions was associated with operations on the cervical spine ($p = 0.027$), the presence of a tumor with Grade II anaplasia ($p = 0.007$), and a primary extramedullary tumor involving more than three vertebrae ($p = 0.017$).

Conclusion. The use of the laser is indicated for reoperations when removing neoplasms, that have arisen as a result of recurrence or continued growth of extramedullary tumors of any level and length after removal of primary neoplasms with a Grade I malignancy confirmed by intraoperative cytological examination involving no more than three vertebrae in the thoracic, lumbar and sacral spine and during resection of ependymomas with extramedullary growth.

Key Words: extramedullary tumors, recurrence, continued growth, spinal cord tumors, long-term results, meningiomas, neuromas.

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Primary spinal cord tumors represent from 5–10 % of all spinal cord neoplasms in adults and 4.5 % of the total tumors of the central nervous system (CNS) [1]. They occur in about five cases per million for women, three cases per million for men [2] or 1.3 cases per 100,000 population per year [1]. An incidence of extramedullary tumors is 70–80 % of all cases of primary spinal cord tumors and 53.0–68.5 % of those of the total spinal neoplasms [3]. The most common histological variants of extramedullary tumors are meningiomas (24.4 %), ependymomas (23.7 %), and neuromas (21.2 %) [4, 5]. Women aged 50-70 are mainly diagnosed with meningiomas (85–90 % of an overall incidence). Young and middle-aged men, in turn, are more often diagnosed with neuromas [6].

A total microsurgical resection of extramedullary tumors is an entrenched treatment standard. Generally, an approach to the tumor is performed from the back by laminectomy or hemilaminectomy. The latter is used in cases of tumor lateralization in the spinal canal. It reduces injury to the posterior spine support structures. According to G.Yu. Evzikov and V.G. Fomichev [7], in almost all cases radical resection of neuromas can be performed, while in meningiomas it is possible in 93–97 % of cases.

Despite the total resection of these tumors, an overall recurrence rate is quite high. For neuromas and meningiomas – 5 %, and for ependymomas – 15 % [7]. Furthermore, the recurrence rate of spinal meningiomas reaches 4–31 % [5, 7]. In subtotal resection of ependymomas, the frequency of continued growth is about 43 % [8].

Considering the above, the issues of total resection of extramedullary tumors, especially of hard-to-reach localization (craniovertebral junction, hourglass type tumors), and an ultimate decrease in their recurrences are far from final adjudication.

In the recent 20 years, we have been using a powerful neodymium laser with a wavelength of 1.064 microns for resection of extramedullary tumors. It is done to find solutions to the problems expressed previously, along with improving surgical approaches [9]. V.V. Stupak and V.V. Moiseev [10] described the advantages of laser technologies in resection of extramedullary tumors. They were manifested in less traumatic surgical approach and lesser damage to spinal cord, as well as in improved life quality of patients. In addition, the number of radically performed surgeries has noticeably increased. A major share of these outcomes was obtained from observations of patients in the early (up to 5 years) postoperative period. For a number of objective reasons, only an insignificant part of data was involved in the analysis of long-term postoperative period outcomes (5 years or more since tumor resection). The small volume of clinical treatment outcomes achieved in the long-term period did not provide statistically valid evidence for the effectiveness of the laser technologies developed by us. Nevertheless, it was suggested that the long-term clinical endpoints of surgical treatment of these tumors could be a link in the evidence chain for the effectiveness of used laser technologies.

There are a number of articles [11–14] devoted to surgical treatment outcomes of extramedullary tumors depending on various surgical approaches and technologies of their resection. Yet there are no data regarding the resection technique of extramedullary tumors using high-intensity neodymium laser radiation, its effect on recurrence rate and continued growth of this type of neoplasms. According, the objective of the present study is formulated.

The objective is to assess the significance of clinical factors of extramedullary tumors and new methods of their resection as potential predictors of their recurrence and continued growth.

Material and Methods

Design: an open observational uncontrolled non-randomized monocentric retrospective study.

Compliance criteria: medical records of patients with primary extramedullary tumors operated from July 1998 to January 2014 were used for the study.

Inclusion criteria: 1) the presence of primary extramedullary tumors in patients, cases of their recurrence and continued growth; 2) the presence of pathomorphological confirmation of the diagnosis; 3) surgeries performed in accordance with the standard protocol [13].

Exclusion criteria: 1) multiple metastatic lesions of organs and tissues; 2) deaths in an early postoperative period; 3) deaths as a result of severe concomitant somatic disorder.

The long-term surgical outcomes of 412 patients operated in 1998–2014 for primary extramedullary tumors were analyzed. Before the study, the patients were divided into two groups: patients of comparison group (n = 277; 67.2 %) underwent tumor resection using standard microsurgical techniques; and those of study group (n = 135; 32.8 %) – with additional use of high-intensity neodymium laser radiation.

The resection extent of the neoplasm was identified and the facts of recurrence or continued growth were confirmed using MRI studies of the spine and spinal cord (TOSHIBA Excelart Vantage MRI scanners, Japan) with the administration of a contrast agent. Patients with suspected structural abnormalities of the vertebrae additionally underwent CT of the spine using Toshiba Aquilion 64 CT scanner (Japan).

V.V. Stupak and V.V. Moiseev [10] described the microsurgical and methodological techniques of using a neodymium laser for the resection of extramedullary tumors.

To organize the obtained clinical outcomes and ensure their comparability between the groups, authors considered the radicality of tumor resection, the number of recurrences and continued growth in the long-term postoperative period as well as the relationship with surgical mode.

The research was performed in strict accordance with ethical standards developed under the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", as amended in 2000, and the "Rules of Good Clinical Practice in the Russian Federation", approved by the Order of the Ministry of Health of the Russian Federation No. 200n as of April 1, 2016. The research was approved by the Biomedical Ethics Committee of the medical institution. Data on all patients are depersonalized.

Statistical techniques. The empirical distributions of continuous data were tested for compliance with the normal distribution law according to the Shapiro – Wilk criteria; homoscedasticity between groups was studied by the Fisher's criterion (F test). Among the compared indicators, there were no both normally distributed and homoscedastic. Hence, nonparametric comparison criteria were used.

Descriptive characteristics are given in the form of median [first quartile; third quartile] for continuous data; quantity (percentage) for binary and categorical data.

To statistically test hypotheses concerning the equality of continuous characteristics of sample distributions in the compared groups, the Mann Whitney U test was used. To evaluate the difference in continuous indicators between the groups, the bias of distributions was calculated with the construction of a 95 % confidence interval (CI). To compare binary and categorical indicators, the Fisher's exact test was applied. Multiple category comparisons were corrected using the Benjamini–Hochberg method. To evaluate the difference in categorical and binary data, risk differences (RD) were calculated with the construction of 95 % CI; for binary data, the odds ratio (OR) and the hazard ratio (HR) were estimated with the construction of 95 % CI.

To provide comparability of preoperative characteristics of both groups, the Propensity Score Matching (PSM) technique was used. Since meningiomas and neuromas, which are sex-specific, predominated in our sample (n = 376; 91.2 %), during the PSM we left the sex parameter as valid for distinction. For additional control of PSM effect, the comparison tables show the results of data before and after PSM.

Comparison of risk of recurrences and continued growth of extramedullary neoplasms in the groups for five years was performed using Log-rank test. Hazard ratio was assessed by the Cox proportional hazards model.

The predictors of recurrence and continued growth were identified by constructing one-factor and multivariate logistic regressions.

Statistical hypotheses were tested at a critical significance level of $p = 0.05$, i.e., the difference was considered statistically significant if $p < 0.05$.

Calculations were performed using RStudio (version 1.1.463) in R programming language for statistical computing.

The primary endpoint of this study was the time of recurrence or continued tumor growth since the moment of surgery and histological diagnosis, estimated at 5 years or more.

Results

Table 1 shows the clinical and demographic features of patients. Out of 412 operated patients, 313 (76.0 %) were diagnosed with intracanal extramedullary tumors in various spine departments; and 99 (24.0 %) – with neoplasms of hard-to-reach localization: tumors at the craniovertebral level were detected in 42 (10.4 %), in 8 (19.1 %) of which laser radiation was used during resection; hourglass type neoplasms were detected in 57 (16.5 %) cases, in 26 (38.8 %) of which laser radiation was also used during surgery. The average age of the subjects was 52.5 ± 2.3 y.o. with a ratio of the total number of men (n = 148) and women (n = 264) equal to 1: 1.8. The average follow-up period of patients after surgery was 8.0 ± 5.5 years (96.0 ± 65.4 months) with a maximum value of 16 years (192 months) and a minimum of 5 years (60 months).

Surgical treatment for recurrence and continued growth of neoplasms was performed in a single operation in 361 (87.6 %) patients; and in two operations – in 51 (22.4 %).

Histopathological characteristics of tumors in accordance with the 2007 WHO classification [15] are shown in Table 1: 354 neoplasms corresponded to Grade I (GI) of malignancy, 58 – to Grade II (GII). An average extent of tumors along the vertebral bodies was 1.78 ± 0.9 (min – 1, max – 7) levels.

A gross total resection was performed in 372 (90.3 %) patients, subtotal resection – in 40 (9.7 %). Standard microsurgical technique allowed to perform a complete removal of neoplasms in 245 (88.4 %) cases and near total – in 32 (11.5 %). In the neodymium laser group, such interventions were performed in 127 (94.1 %) and 8 (5.9 %) cases, respectively ($p = 0.078$).

Clinical and MRI postoperative studies have verified the presence of recurrences or continued growth in 51 (12.4 %) of 412 operated patients. The recurrences were observed in 24 (5.8 %), and the continued growth was confirmed in 27 (6.6 %). In other words, complications were presented with almost equal frequency – 47.1 % and 52.9 %. Meanwhile, out of 372 gross total resections in the late postoperative period, 24 (6.4 %) cases of recurrences were detected; among the near total resections of 40 neoplasms, continued growth was confirmed in 27 (67.5 %) cases.

In the comparison group, recurrences and continued tumor growth were detected in 44 (15.9 %) patients. It is worth noting that with gross total resection, recurrences were observed in 21 (7.6 %) cases; in near total resection, continued tumor growth was diagnosed in 23 (8.3 %) cases. In the study group, 7 (5.2 %) patients revealed 3 (3.0 %) recurrences and 4 (5.0 %) cases of continued tumor growth in the follow-up period.

Most often, recurrences and continued growth occurred after resection of hard-to-reach tumors. Out of 99 such patients, they were diagnosed in 12 (12.1 %), or in 31.8 % of all 55 similar outcomes in our series. Out of 42 people with tumors at the level of craniovertebral junction, 5 (11.9 %) of such cases were detected: in 1 (12.5 %) after using laser radiation, and in 4 (11.7 %) patients operated with standard techniques ($p = 0.67$). Out of 57 people with hourglass type tumors, a clinical and tomographic picture of recurrence and continued growth was noted in 7 (12.2 %). In the group operated using laser technologies, there were 2 of them (9.5 %), without the use of a laser – 5 (13.8 %); $p = 0.44$. Out of 313 intracanal extramedullary tumors, the total number of recurrences and continued growth cases was 39 (12.4 %): 4 (1.2 %) – in the group using laser technologies, 35 (11.1 %) – in the group with standard surgical techniques ($p = 0.05$). The recurrence rate among these patients was 3.5 % (n = 11); all of them were diagnosed in the group with classical resection technique.

To determine possible predictors of recurrence and continued growth, a logit regression analysis was performed for the entire series of patients, as well as separately for both groups. Tables 2–4 show the results of significant indicators or close to them.

The description of statistical methods indicates that PSM is used to equalize characteristics in groups making them comparable. Meanwhile, it is quite possible that the difference in the number of recurrences found before PSM could disappear due to the existing distinctions in the groups before surgery. Nevertheless, it remained after PSM, which is explained precisely by the use of different techniques for resection of extramedullary tumors.

It follows from logit regression results shown in Tables 2–4 that covariates greater than 1 are risk factors. They increase the chance of recurrences and continued tumor growth. As for covariates less than 1, they are among the favorable factors reducing this risk.

While considering the results of logit regression (Table 2) significant decrease in the risk of recurrences and continued growth in gross total ($p < 0.001$) resection and increase in subtotal resection ($p < 0.001$) seem reasonable. The tumor size factor ($p = 0.091$) raises the risk of developing these conditions by 2.45 times. Ependymomas of medullary cone and filum terminale are the most aggressive tumors in this area. That is why they are much more prone to recurrence ($p = 0.017$). Perhaps this is also associated with decreased risks of tumor localization in the thoracic region, where extramedullary tumors are mainly represented by neuromas and meningiomas. As for ependymomas, they are intramedullary neoplasms. The above factors raise the risks of reoperations ($p = 0.002$).

Studying the group with the use of laser technologies (Table 2), we observe a positive effect of tumor localization in the thoracic region ($p = 0.039$) and a negative effect of its size factor ($p = 0.017$) on the risks of developing these conditions. Cervical localization increases the risk of tumor recurrence ($p = 0.027$). However, it was not observed in tumors of craniovertebral junction ($p = 0.599$). The malignancy factor naturally affects the development of recurrences and continued growth. Nevertheless, the differences for Grade I and Grade II are relevant only for the study group ($p = 0.007$). The use of a laser showed the best outcomes in the removal of Grade I tumors and the worst – of Grade II.

For a number of factors affecting the recurrence or continued growth of removed tumors, similar chances of adverse outcomes are found in the comparison group and in the entire series (Table 2). Particularly noticeable is the factor of subtotal resection, which increases the risk of continued growth in the entire series by 115.5 times, and in the comparison group – by 60.55 times.

In the logit regression of tumor recurrences (Table 3) in the whole series and in the comparison group, the factors of reoperation ($p = 0.004$ for both samples) and ependymomas ($p = 0.008$ and $p = 0.040$) of lumbosacral region raise the recurrence risk. In the study group with a larger number of respondents, these factors, as well as the factor of large tumor size, may raise the recurrence risk ($p > 0.05$).

In the research of factors affecting continued growth (Table 4), an increased risk of their development was observed in neurofibromas ($p = 0.026$) in the general series and in the study group. In the comparison group, a tendency to duration influence of the surgical intervention was revealed. Yet the differences are unreliable, possibly due to a small sample.

Discussion

In this study, we tried to assess a number of clinical factors and the use of laser technologies for resection of extramedullary tumors from the prognostic significance position as potential predictors of recurrence and continued growth of these neoplasms. In the framework of an uncontrolled, nonrandomized, monocentric retrospective study of surgical outcomes of 412 patients, the advantages of using laser technologies in comparison with traditional neurosurgical interventions are convincingly proven.

In choosing the treatment method for primary extramedullary tumors, in almost all cases, favor is given to their surgical removal. It is well known that the success of such treatment and the prognosis of the disease correlate with the resection rate. Hence, surgeons are always focused on gross total resection. According to Mazda et al. [12], the gross total resection of 167 intradural extramedullary tumors was achieved in 93 % of cases. Similar data were presented in publications on several large series of patients with extramedullary meningiomas, which were gross totally resected in 82–99 % of cases [10, 12, 13]. In our series, gross total resection of primary extramedullary tumors was achieved in 90.3 % of cases, and subtotal – in 9.7 % of cases.

The recurrences and continued growth of extramedullary tumors, confirmed by clinical and MRI findings, in the structure of these conditions amounted to 45.5 % and 54.5 %, respectively. Meanwhile, when using a neodymium laser in the long-term postoperative period, these complications were diagnosed in 13.3 % of the operated patients (6.1 % – recurrence, 7.2 % – continued growth). Out of 372 gross total resections, 6.7 % of recurrences were detected in the late postoperative period; among 40 subtotal resections, continued growth was confirmed in 30 cases (75 % of subtotal resections or 7.3 % of the gross total resections). In patients operated with laser in the long-term postoperative period, 4 (3.0 %) recurrences were diagnosed. This is considerably lower than in the group where standard microsurgical technique was applied: 12 (8.0 %); $p = 0.08$.

Out of 313 removed intracanal tumors, their recurrences or continued growth were recorded in 43 (13.7 %) cases. Furthermore, the use of laser technologies, in comparison with standard surgical techniques, ensured a decrease in their frequency from 11.1 to 2.6 % of cases ($p = 0.05$). The recurrence rate among these patients was 3.5 % ($n = 11$). All of them appeared only in the group with the classical resection technique ($p = 0.05$). The outcomes of neuroma resection are explained by the photothermal effect of laser radiation arising from the spinal root ablation from the tumor node. The resection of meningioma has always been followed by its photocoagulation. Then the vaporization of tumor matrix was performed, which more effectively provides apoptosis of neoplastic cells in the tumor growth area compared with bipolar coagulation, both on the inner and outer sides of the dura mater.

Currently, an individual treatment approach to patients with neurooncological pathology depends on modern neuroimaging and surgical techniques, which provides for the use of results obtained in a wide clinical practice. The use of logit regression has revealed clinical situations when the laser is most effective in preventing recurrences and continued growth of extramedullary tumors. A significant correlation with the occurrence of these pathological conditions enables to consider them as predictors.

Generally, the application of laser technologies for resection of extramedullary tumors can considerably reduce the number of recurrences and continued growth. This is a prognostically significant indicator in determining the di-

Table 1
Clinical and demographic features of the studied patients

Variable indicators comparison group (n = 277)		Before PSM				After PSM			
		comparison group (n = 227)	study group (n = 135)	difference [95 % CI]	p-level	comparison group (n = 161)	study group (n = 96)	difference [95 % CI]	p-level
Sex, n (%)	F	190 (68.6)	74 (54.8)	–	0.009*	113 (70.2)	53 (55.2)	–	0.022*
	M	7 (31.4)	61 (45.2)			48 (29.8)	43 (44.8)		
Age, y.o., median [Q1; Q3]		55 [44; 64]	50 [42; 58]	-4 [-7.0; -1.0]	0.010*	54 [45; 63]	50 [35; 56.25]	-5 [-9.0; -1.0]	0.006*
Tumor size relative to spine, n (%)					Overall comparison: 0.701				Overall comparison: 0.596
				Разность рисков				Risk difference	
	1 level	115 (41.7)	60 (44.8)	3.0 % [-7.0 %; 13.0 %]	0.595	64 (40.0)	45 (47.0)	7.0 % [-5.0 %; 20.0 %]	0.295
	2 levels	126 (45.7)	57 (42.5)	-3.0 % [-13.0 %; 7.0 %]	0.597	76 (47.5)	40 (42.1)	-5.0 % [-18.0 %;7.0 %]	0.437
	3 levels	22 (8.0)	11 (8.2)	0.2 % [-5.0 %; 6.0 %]	>0.999	11 (6.9)	7 (7.4)	0.4 % [-6.0 %; 7.0 %]	>0.999
	4 levels	6 (2.2)	4 (3.0)	0.7 % [-3.0 %; 4.0 %]	0.735	4 (2.5)	3 (3.2)	0.6 % [-4.0 %; 5.0 %]	0.714
	5 llevels	6 (2.2)	1 (0.7)	-1.4 [-4.0 %; 8.0 %]	0.435	4 (2.5)	0 (0.0)	-3.0 % [-5.0 %; -0.08 %]	0.300
	6 levels	0 (0.0)	1 (0.7)	0.7 % [-0.7 %; 2.0 %]	0.327	–	–	–	–
	7 levels	1 (0.4)	0 (0.0)	-0.3 % [-1.0 %; 0.3 %]	>0.999	1 (0.6)	0 (0.0)	-0.6 % [-2.0 %; 0.6 %]	>0.999
Spine department, n (%)					Overall comparison: 0.033*				Overall comparison: 0.048*
				Risk difference				Risk difference	
	C	57 (21.3)	34 (25.2)	5.0 % [-4.0 %; 13.0 %]	0.312	27 (16.7)	28 (29.2)	12.0 % [2.0 %; 23.0 %]	0.017*
	C–T	8 (2.9)	3 (2.2)	-0.7 % [-4.0 %; 3.0 %]	>0.999	5 (3.1)	2 (2.1)	-1.0 % [-5.0 %; 3.0 %]	>0.999
	T	86 (31.0)	57 (42.0)	11.0 % [1.0 %; 21.0 %]	0.028*	54 (33.5)	39 (40.6)	7.0 % [-5.0 %; 19.0 %]	0.284
	T–L	16 (5.8)	10 (7.4)	1.6 % [-4 .0%; 7.0 %]	0.523	9 (5.6)	6 (6.2)	0.6 % [-5.0 %; 7.0 %]	0.791
	T–L–S	1 (0.4)	0 (0.0)	-0.4 % [-1.0 %; 0.3 %]	>0.999	1 (0.6)	0 (0.0)	-0.6 % [-2.0 %; 0.5 %]	>0.999
	L	83 (30.0)	23 (17.0)	-13.0 % [-21.0 %; -5.0 %]	0.006*	50 (31.1)	16 (16.7)	-14.0 % [-25.0 %; -4.0 %]	0.012*
	L–S	15 (5.4)	2 (1.5)	-4.0 % [-7.0 %; -0.6 %]	0.067	8 (5.0)	1 (1.0)	-4.0 % [-7.0 %; 0.0 %]	0.160
	S	9 (3.2)	6 (4.4)	1.0 % [-3.0 %; 5.0 %]	0.580	7 (4.3)	4 (4.2)	-0.2 % [-5.0 %; 5.0 %]	>0.999
Radicality, n (%)				Odds ratio	0.078			Odds ratio	0.054
	Gross total resection	245 (88.4)	127 (94.1)	2.0 [0.9; 4.6]		140 (87.0)	91 (94.8)	2.7 [0.99. 7.5]	
	Subtotal resection	32 (11.6)	8 (5.9)	0.5 [0.2; 1.1]		21 (13.0)	5 (5.2)	0.36 [0.13; 1.006]	
Histology, n (%)					Overall comparison: 0.002*				Overall comparison: 0.389
				Risk difference				Risk difference	
	Lipoma	1 (0.4)	0 (0.0)	-0.4 % [-1.0 %; 0.3 %]	>0.999	1 (0.6)	0 (0.0)	-0.6 % [-2.0 %; 0.6 %]	>0.999
	Meningioma	106 (38.3)	76 (56.3)	18.0 % [8.0 %; 28.0 %]	<0.001*	65 (40.4)	47 (49.0)	8.5 % [-4.0 %; 21.0 %]	0.195
	Neuroma	140 (50.5)	54 (40.0)	-10.5 % [-21.0 %; -0.4 %]	0.046*	77 (47.8)	44 (45.8)	-2.0 % [-15.0 %; 11.0 %]	0.797
	Neurofibroma	8 (2.9)	1 (0.7)	-2.0 % [-5.0 %; 0.3 %]	0.282	6 (3.7)	1 (1.0)	-2.6 % [-6.0 %; 0.9 %]	0.262
	Ependymoma	22 (7.9)	4 (3.0)	-5.0 % [-9.0 %; -0.7 %]	0.054	12 (7.5)	4 (4.2)	-3.3 % [-9.0 %; 2.0 %]	0.425
Grade, n (%)				Odds ratio	0.451			Odds ratio	0.573
	I	235 (84.8)	119 (88.1)	1.3 [0.7; 2.5]		137 (85.1)	85 (88.5)	1.4 [0.6; 2.9]	
	II	42 (15.2)	16 (11.9)	0.75 [0.4; 1.4]		24 (14.9)	11 (11.5)	0.74 [0.3; 1.6]	
Reoperation, n (%)		24 (9.0)	8 (6.0)	OR: 0.7 [0.3; 1.6] RD: -3.0 % [-8 %; 2 %]	0.433	17 (11.0)	6 (6.0)	OR: 0.6 [0.2; 1.6] RD: -4.3 % [-11 %; 2 %]	0.269

PSM — Propensity Score Matching. * Statistically and significantly different indicators.

Table 2

Logit regression of recurrences and continued tumor growth

Covariants	One-factor models		Multivariate models	
	OR [95 % CI]	p	OR [95 % CI]	p
A whole series (n = 412)				
Gross total resection	0.01 [0.00; 0.02]	<0.001*	0.01 [0.00; 0.02]	<0.001*
Subtotal resection	115.52 [41.68; 383.54]	<0.001*	–	
Reoperation	5.36 [1.77; 14.79]	0.002*	5.50 [0.84; 28.19]	0.054
Surgery duration	1.01 [1.00; 1.01]	0.016*	–	
Ependymoma	3.32 [1.15; 8.49]	0.017*	8.62 [2.05; 32.05]	0.002*
Dysfunction of pelvic organs before surgery	2.25 [0.95; 4.90]	0.049*	–	
Thoractic spine	0.45 [0.19; 0.96]	0.050*	–	
Age	0.98 [0.96; 1.00]	0.087	–	
Tumor size; 3 or more vertebrae	2.45 [0.81; 6.68]	0.091	–	
Study group (n = 135)				
Grade I	0.14 [0.03; 0.63]	0.007*	–	
Grade II	7.00 [1.58; 29.03]	0.070*	11.71 [2.04; 78.93]	0.006*
Age	0.94 [0.90; 0.98]	0.011*	–	
Tumor size; 3 or more vertebrae	6.61 [1.23; 30.31]	0.017*	8.92 [1.22; 70.43]	0.029*
Cervical spine	4.48 [1.15; 17.49]	0.027*	8.52 [1.61; 57.60]	0.015*
Thoracic spine	0.11 [0.01; 0.61]	0.039*	–	
Reoperation	4.54 [0.60; 23.84]	0.091	–	
Comparison group (n = 277)				
Gross total resection	0.02 [0.00; 0.05]	<0.001*	0.01 [0.00; 0.02]	<0.001*
Subtotal resection	60.55 [20.46; 210.49]	<0.001*	–	
Reoperation	6.53 [1.58; 24.45]	0.006*	16.52 [1.73; 157.12]	0.013*
Ependymoma	3.06 [0.94; 8.62]	0.044*	6.36 [1.24; 30.27]	0.020*

* Statistically significant predictors; "–"– covariants not included in the optimal multivariate model in terms of predictors and expectedness of recurrence as well as continued growth; OR – odds ratio.

sease course. Also, it may serve as a risk predictor.

During the analysis of laser resection techniques in determining the prediction of recurrence reduction and continued tumor growth, the most reliable clinical factors were the following: reoperations (p = 0.002); ependymoma of medullary cone and cauda equina (p = 0.017); surgical removal of primary tumors in thoracic spine (p = 0.039); extramedullary tumors with Grade I anaplasia (p = 0.007). The following factors corresponded to an increased number of these pathological conditions: operations on cervical spine (p = 0.027), tumors with Grade II anaplasia (p = 0.007), primary extramedullary tumor with a length of more than three vertebrae (p = 0.017).

It was determined that during reoperations for recurrence or continued tumor growth, the use of a laser considerably downgrades the number of recurrences in comparison with the standard microsurgical technique. Laser technologies did not substantially increase the recurrence risk and continued growth during surgical treatment of ependymoma of medullary cone and cauda equina. During surgeries at the thoracic level, the use of a laser considerably reduced these risks. It did not affect interventions in the lumbar and sacral regions, but raised risks in the cervical region by 4.48 times. The effectiveness of laser surgeries was also affected by the histological type of the neoplasm. In Grade I tumors, laser technologies for resection of extramedullary tumors reduced the recurrence risk, and in Grade II – increased it by 7 times. If a tumor with a length of more than three vertebrae was resected, they significantly raised by 11.3 times.

Conclusions

The comprehensive analysis of clinical, neuroimaging and statistical data, which were gathered and systematized during observation of patients with primary extramedullary tumors before surgery and in the late postoperative period, has convincingly proved the scientific validity and effectiveness of laser as a prevention of recurrences and continued growth of new neoplasms. It can be used as an additional technique

Table 3
Logit regression of recurrences

Covariants	One-factor models		Multivariate models	
	OR [95 % CI]	p	OR [95 % CI]	p
A whole series (n = 412)				
Reoperation	14.5 [4.06; 47.53]	0.004*	9.21 [1.62; 43.95]	0.007*
Ependymoma	6.39 [1.66; 20.54]	0.008*	9.94 [2.21; 40.69]	0.002*
Study group (n = 135)				
Reoperation	16.57 [0.61; 450.56]	0.056	–	
Craniovertebral junction	16.57 [0.61; 450.56]	0.056	–	
Tumor size; 3 or more vertebrae	12.67 [0.47; 339.04]	0.081	7.49 [0.20; 469.67]	0.251
Comparison group (n = 277)				
Reoperation	19.33 [4.34; 81.03]	0.004*	17.29 [2.49; 118.09]	0.003*
Ependymoma	6.54 [1.64; 22.44]	0.040*	7.42 [1.41; 36.65]	0.013*

* Statistically significant predictors; "–"– covariants not included in the optimal multivariate model in terms of predictors and expectedness of recurrence; OR – odds ratio.

Table 4
Logit regression of continued tumor growth

Covariants	One-factor models		Multivariate models	
	OR [95 % CI]	p	OR [95 % CI]	p
A whole series (n = 412)				
Neurofibroma	6.84 [0.94; 33.76]	0.026*	6.84 [0.94; 33.76]	0.026*
Study group (n = 135)				
Grade I	0.09 [0.02; 0.45]	0.002*	–	
Grade II	10.70 [2.24; 52.09]	0.002*	12.80 [2.50; 73.30]	0.002*
Tumor size; 3 or more vertebrae	13.50 [1.17; 311.27]	0.042*	–	
Thoracic spine	0.15 [0.01; 0.85]	0.075	–	
Comparison group (n = 277)				
Surgery duration, min	1.01 [1.00; 1.01]	0.055	1.01 [1.00; 1.01]	0.055

* Statistically significant predictors; "–"– covariants not included in the optimal multivariate model in terms of predictors and expectedness of continued tumor growth; OR – odds ratio.

to the classical microsurgical resection of tumors of a certain localization, histological structure and size. The effectiveness of laser radiation in resection of extramedullary intracanal primary tumors is demonstrated.

It was found that the use of developed laser technologies not only reduces the number of recurrences and continued growth of extramedullary tumors. Moreover, it can be considered as their predictors. The following factors are the most informative for predicting a decrease in unfavorable disease development. Firstly, reoperations aimed at removing recurrences or continued growth of extramedullary tumors of any level and extent. Secondly, the removal of primary neoplasms with a length of no more than three vertebrae with Grade I malignancy, confirmed by intraoperative cytological diagnostics in thoracic, lumbar and sacral spine. Finally, these factors also include resections of ependymomas with extramedullary growth.

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