

# INFLUENCE OF NEODYMIUM LASER RADIATION ON The frequency of recurrence and continued growth of extramedullary tumors

## I.A. Eliseenko<sup>1</sup>, S.G. Struts<sup>2</sup>, V.V. Stupak<sup>1</sup>

<sup>1</sup>Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, Novosibirsk, Russia <sup>2</sup>Institute of Laser Physics SB RAS, Novosibirsk, Russia

**Objective.** To assess the effect of neodymium laser radiation on the recurrence rate and continued growth of primary extramedullary tumors on the basis of clinical data obtained in the long-term follow-up period in operated patients with extramedullary tumors.

Material and Methods. The long-term results of surgical treatment of two groups of patients (n=412) with primary extramedullary tumors operated on from 1998 to 2014 were studied and systematized. Patients of comparison group (n=277;67.2%) underwent removal of tumors using standard microsurgical techniques, and the neoplasms in patients of the study group (n=135;32.8%) were removed with additionally used neodymium (Nd:YAG) laser.

Results. The use of the developed laser technologies for the resection of extramedullary intracanal primary tumors made it possible to reliably reduce the relative number of recurrence and continued growth from 11.1% to 1.2% compared with patients treated with standard surgery methods. The proportion of recurrences was 3.5%, all of them were detected only in the group with the classical technique of tumor resection (p < 0.01).

**Conclusion.** The use of a neodymium laser as an additional technology to the classical microsurgical resection of extramedullary tumors is effective for the prevention of their recurrence and continued growth.

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

Please cite this paper as: Eliseenko IA, Struts SG, Stupak VV. Influence of neodymium laser radiation on the frequency of recurrence and continued growth of extramedullary tumors. Hir. Pozvonoc. 2021;18(3):77–85. In Russian.

DOI: http://dx.doi.org/10.14531/ss2021.3.77-85.

From 5 to 15 % of all spinal cord tumors in adults and up to 15 % of the total number of tumors of the central nervous system account for primary spinal cord neoplasms [1–3]. Their frequency is approximately 5 cases per 1 million for women and 3 cases per 1 million for men, or 1.3 cases per 100 thousand population per year [2–4]. Extramedullary tumors (EMT) arise in 70-80 % of cases of all primary spinal cord tumors. They represent 53-68 % of the total number of spinal cord tumors [2, 5, 6]. The most common histological variants of EMT are meningiomas (24.4 %), ependymomas (23.7 %) and neuromas (21.2 %) [7–9].

Notwithstanding the total resection of these tumors, the overall frequency of their recurrences is quite high and amounts to 5 % for neuromas and meningiomas, as well as 15 % for ependymomas. Furthermore, spinal meningiomas may recur. According to various authors [3, 8], the frequency ranges from 4 to 31 %. If there is a subtotal resection of the ependymomas, the frequency of

continued growth varies about 43 % [2, 10].

In order to find ways to solve these challenges, along with improving surgical approaches [11], for 20 years we have been using high-intensity ND laser radiation with a wavelength of 1.064 microns in the surgical treatment of EMT. The clinical studies performed by V.V. Stupak et al. [12] have shown the advantages of laser technologies used in tumor resection: less injury rate of surgical approach and spinal cord, improvement of the life quality of the patients. Together with this, the number of radical surgeries was increasing. These findings were found in the early postoperative period (up to 5 years from the surgery date). Only a small part of the research is dedicated to the long-term results of surgical treatment (more than 5 years since the tumor resection). Additionally, the clinical findings achieved during the observation of a small group of patients did not provide statistically valid conclusions concerning the effectiveness of advanced laser technologies. The clinical surgical findings of this type of tumors in the long-term period can be a link in the general evidence chain of the effectiveness of the developed laser technologies we apply.

The objective is to assess the effect of neodymium laser radiation on the recurrence rate and continued growth of primary extramedullary tumors on the basis of clinical data obtained in the long-term follow-up period in operated patients with extramedullary tumors.

# **Material and Methods**

Study design: an unblinded observational uncontrolled non-randomized multicenter retrospective study.

The investigation is concerned with the medical documentation of patients operated on for primary EMT in the period from July 1998 to January 2014.

Criteria for including medical records in the study:

- 1) the presence of primary EMT, cases of their recurrence and continued growth;
- 2) the presence of pathomorphological evidence of EMT;
- 3) performance of a surgery in accordance with the standard protocol.

Exclusion criteria:

- 1) multiple metastatic lesions of organs and tissues;
- 2) mortality in the early postoperative period;
- 3) mortality as a result of severe somatic pathology in patients.

We studied the long-term results of surgical treatment of 412 patients with primary EMT. All patients were divided into two groups before the study. The comparison group (n = 277; 67.2 %) comprised patients in whom tumor resection was performed using standard microsurgical techniques. The study group (n = 135; 32.8 %) included patients who additionally underwent ND laser resection.

The diagnosis of the resection degree of the tumor and confirmation of the presence of recurrence or continued growth of the tumor was performed using MRI examination of the spine and spinal cord (Excelart Vantage "Toshiba" MR scanners, Japan) with intravenous administration of a contrast agent. The magnetic field intensity was 1.5 T, the section thickness was 4 mm in T1, T2, FLAIR, DWI mode (in three projections). If clinical signs were found accompanied by structural changes in the spine, patients additionally underwent CT of the spine on an Aquilion 64 Toshiba CT scanner, the section thickness was 1 mm.

V.V. Stupak and V.V. Moiseev described the microsurgical technique and methods of using a ND laser for the resection of extramedullary tumors [12].

In order to systematize the obtained clinical results of treatment and compare them between groups, the degree of tumor resection, the number of cases of their recurrence and continued growth in the long-term postoperative period were studied. Additionally, they were compared with the performed surgery type.

The conducted studies correspond to ethical standards developed on the basis of the Helsinki Declaration of the World Medical Association "Ethical principles of conducting academic studies with human participation" (as amended in 2000), and "Clinical Practice Rules in the Russian Federation", approved by the Order of the Ministry of Health of the Russian Federation as of April 1, 2016 No. 200H. The study was approved by the Biomedical Ethics Committee of the medical institution. All data has been depersonalized.

Statistical techniques. The empirical distributions of continuous data were tested for consistency with the normal distribution law according to the Shapiro – Wilk test, homoscedasticity between groups was investigated by the Fisher criterion (F-test). There were no normally distributed and homoscedastic indicators among the compared indicators simultaneously. Therefore, nonparametric comparison criteria were applied.

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

The unpaired two-samples Wilcoxon test was used for hypotheses concerning the equality of continuous characteristics of sample distributions in the groups being compared. To assess the difference in continuous indicators between the groups, the bias of distributions was calculated with the construction of a 95 % confidence interval (CI). 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.

The Propensity Score Matching (PSM) was used to guarantee comparability of the preoperative characteristics of both groups. Considering that sex-specific meningiomas and neuromas prevailed in our sampling (n = 376, 91.2 %), we left the sex parameter as valid for the difference in the PSM. To further control the PSM effect, the comparison tables and

graphs display the findings before and after PSM.

A comparison of the risks of recurrence and continued growth of extramedullary tumors in the groups for five years was performed using a log-rank test. Hazard ratio was evaluated by the Cox proportional-hazards model. The comparison findings are illustrated in the figures of the Kaplan – Meyer curves.

The statistical hypotheses were tested at a significance level of p = 0.05. It means that the difference was considered statistically significant at p < 0.05.

The calculations were done in RStudio (version 1.1.463) in the statistical programming language R.

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

#### Results

Table 1 represents the clinical and demographic features of the studied patients.

A total of 412 individuals underwent surgery. Out of them 313 (76 %) were diagnosed with extramedullary intracanal tumors in various parts of the spine. The other 99 (24 %) individuals had tumors of difficult localization: in 57 (13,8 %) cases, the tumors were of hourglass type; 26 (45,6 %) of these tumors were operated with the use of laser technology; 42 (10,2 %) individuals had tumors at the craniovertebral level; in 8 (19,1 %) cases the tumors were resectioned by ND laser. The ratio between the total number of men (n = 148) and women (n = 264) was 1.0: 1.8 with an average age of  $52.5 \pm 2.3$  years. The maximum and minimum follow-up periods after the surgery reached 16 years (192 months) and 5 years (60 months), respectively, and their average value was  $8.0 \pm 5.5$  years (96.0  $\pm$  65.4 months).

The primary surgery was performed in 380 (92.2 %) out of 412 patients; and 32 (7.8 %) underwent reoperation due to the development of recurrence and continued growth of previously removed primary EMT in other city hospitals (Table 1). The same table presents the

histological characteristics and localization of tumors along the spinal axis. The malignancy grade of tumors was the following: I (354 tumors) or II (58 tumors) according to the histopathological classification adopted by WHO in 2007 [13]. The average extent of tumors along the vertebral bodies was  $1.78 \pm 0.9$ ; the minimum value was 1; the maximum was 7 vertebrae.

A total of 372 (90.3%) patients out of 412 underwent total tumor resection; subtotal resection was performed in 40 (9.7%) patients. In the ND laser group, total resection was carried out in 127 (94.1%) cases out of 135, subtotal – in 8 (5.9%). The use of standard microsurgical techniques enabled the complete resection of 245 (88.4%) tumors out of 277 and subtotal - 32 (11.5%; p = 0.078).

Subtotal resection was applied to 11 (11.1 %) out of 99 EMT of difficult localization; the remaining 88 (88.9%) were totally resected. In 26 (45.6 %) patients with hourglass type tumors operated using laser technologies, 23 (88.5 %) total resections were done, 3 (11.5 %) – subtotal (p = 0.510). Using the microsurgical techniques, 25 (80.6 %) total resections were done, 6 (19.4 %) – subtotal. 40 (95.2 %) of 42 tumors at the craniovertebral level were resected totally, 2 (4.8 %) – in a subtotal manner; in 8 cases, when a laser was used, they were completely resected (p = 0.650).

The recurrence and continued growth, confirmed by clinical and MRI-tomographic data, were diagnosed in 51 (12.4 %) people, 24 (5.8 %) had a recurrence, 27 (6.6 %) – continued growth. Therefore, the recurrence of tumors amounted to 47.1 %, and the continued growth – 52.9 % of their total number. In the late postoperative period, 24 (6.4 %) cases of tumor recurrence were revealed out of 372 totally resected tumors; among the subtotal resection of 40 tumors, continued growth was confirmed in 27 (67.5 %) cases.

Among 277 patients in the comparison group, the recurrences and continued growth of tumors were noted in 44 cases (15.9 %). Meanwhile, in cases of total tumor resection, there were 21 (7.6 %) recurrences, while in subtotal cas-

es, 23 (8.3 %) patients had a continued growth of tumors. In the ND laser group, including 135 people, 3 (3 %) recurrences and 4 (5 %) cases of continued growth were found in 7 (5.2 %) patients during the observed period (Table 2).

The tumors of difficult localization most often recurred and displayed a clinical picture of continued growth. Their resection was associated with numerous technical difficulties. The recurrences and cases of continued growth were diagnosed in 12 (12.1 %) of 99 patients operated with such tumors, which accounted for 31.8 % of all 55 cases of such outcomes that developed in our series. Out of 42 people with tumors at the level of craniovertebral junction, 5 (11.9%) similar cases were identified: in 1 (12.5 %) out of 8 patients where laser surgery was used, and in 4 (11.7 %) out of 34 people in the group operated by standard methods (p = 0.670). Among 57 hourglass type tumors, a clinical tomography picture of recurrence and continued growth was observed in 7 cases, which corresponds to 12.2 %. In the group consisting of 21 people operated using laser technologies, there were 2 (9.5 %), without laser use – 5 (13.8 %) out of 36 (p = 0.440).

The number of recurrences and continued growth among 313 cases of extramedullary intracanal tumors was 12.4 % (n = 39), and the use of laser technologies, compared with standard methods, resulted in 4 (1.2 %) and 35 (11.1 %) cases of recurrence, respectively (p < 0.01). The recurrences among these patients amounted to 3.5 % (n = 11). All of them manifested only in the group with the classical resection technique.

As can be seen from Table 2, a direct comparison of the risks of recurrence and continued growth of tumors between the groups gives statistically significant differences in the late postoperative period both on the initial data and on the data adjusted by PSM. This indicates that the reason for the difference in risks is the surgical technique, and not the heterogeneity of preoperative indicators in the groups.

An additional confirmation of the obtained results is the constructed

Kaplan – Meyer curves of these indicators, depending on the timing of occurrence after the surgeries (Fig. 1–4).

The given Kaplan – Meyer curves, based on the results of the number of recurrences and continued growth after PSM in the long-term postoperative period, indicate that statistically significant differences between the two groups quiet persist, which confirms the positive effect of the applied laser technologies. Furthermore, these differences grow with the follow-up period. This is especially pronounced when using a laser during the resection of tumors with continued growth.

#### Discussion

In this paper, we tried to identify the effectiveness of the original laser technologies used in microsurgical resection of primary EMT by conducting a retrospective uncontrolled non-randomized monocenter cohort study of the clinical results of surgical treatment received in the long-term postoperative period. The data analysis of 412 patients obtained in the long-term postoperative period convincingly proves the advantages of developed laser technologies for microsurgical resection of primary EMT in comparison with traditional neurosurgical methods.

The surgical resection of primary EMT is preferred in almost all cases when choosing a treatment method. It is well recognized that the success of such treatment of this group of tumors and the disease prognosis correlate with the resection degree, thus, surgeons are always focused on the total tumor resection. In the paper by Turel et al. [14], published in 2015, the treatment results of 167 patients with intradural EMT were analyzed. It was shown that total resection of tumors was achieved in 93 % of cases. The same data are published in literature sources based on the study of clinical results of surgical treatment of several large series of patients with extramedullary meningiomas, where their total resection is reported in 82-99 % of cases [12, 15-18].

Clinical and dem	Clinical and demographic features of the studied patients	of the studied pati	ents						
Variable indicators comparison	ors comparison			Before PSM				After PSM	
group (n = 277)		comparison group $(n = 227)$	$\begin{array}{c} \text{study} \\ \text{group} \\ (n=135) \end{array}$	difference [95 % CI]	p-level	comparison group $(n = 161)$	$\begin{array}{c} study \\ group \\ (n=96) \end{array}$	difference [95 % CI]	p-level
Gender, n (%)	Ľ	190 (68.6)	74 (54.8)	1	*600.0	113 (70.2)	53 (55.2)	1	0.022*
	M	7 (31.4)	61 (45.2)			48 (29.8)	43 (44.8)		
Age, years, MED [Q1; Q3]	[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]	*900.0
Tumor size					General comparison: 0.701				General comparison: 0.596
spinal column,				Risk difference				Risk difference	
(%) II	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 levels	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	I	1	1	1
	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					General comparison: 0.033*				General comparison: 0.048*
department, n (%)				Risk difference				Risk difference	
	Ü	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-D	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
	D	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
	D-T	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
	D-L-S	1 (0.4)	0.00)	-0.4 % [-1.0 %; 0.3 %]	>0.999	1 (0.6)	0 (0.0)	-0.6 % [-2.0 %; 0.5 %]	>0.999
	I	83 (30.0)	23 (17.0)	-13.0 % [-21.0 %; -5.0 %]	*9000	50 (31.1)	16 (16.7)	-14.0 % [-25.0%;-4.0%]	0.012*
	$\Gamma$ –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 of				Odds ratio	0.078			Odds ratio	0.054
surgery, II ( %)	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					General comparison: 0.002*				General 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] PP: -3.0 % [-8 %; 2 %]	0.433	17 (11.0)	6 (6.0)	OR: 0.6 [0.2; 1.6] PP: -4.3 % [-11 %; 2 %]	0.269
PSM - Propensite	$PSM-Propensity\ Score\ Matching.\ ^*\ Statistically\ significantly\ different\ indicators.$	* Statistically sig	mificantly diffe	rent indicators.					

In our series of 412 patients with primary extramedullary tumors, a total resection was achieved in 90.3 %, and subtotal – in 9.7 % of cases The highest percentage of total resection - 90.7 % (n = 284) was received in the group of patients with intracanal EMT. Among them, the use of ND laser allowed to completely resect tumors in 127 (94.1 %) out of 135 patients; the subtotal resection was done in 8 (5.9%). The use of standard microsurgical techniques has given 245 (88.4 %) patients the opportunity to undergo total and 32 (11.6 %) – subtotal resection of tumors (p = 0.15). The original laser technologies developed by us are more effective in increasing the volume of resection and in removing of difficult localization EMT. Therefore, with hourglass-type tumors, these technologies provided their total resection in 88.5 % of cases, and with craniovertebral junction tumors - in 100.0 % of cases (p = 0.65).

The number of recurrences in the postoperative period, which worsen the functional state of the individuals, the course and prognosis of disease, is an essential criterion for the effectiveness of the surgical treatment. In accordance with the predominantly benign nature of EMT, including spinal meningiomas, their recurrences are relatively rare. According to some data, this number varies from 1.3 to 10.0 % [19, 20]. The other sources indicate that the number of recurrences after tumor matrix resec-

tion, compared with coagulation of the meningioma growth zone, is higher and reaches 8.0 % and 5.6 % [21], and 31.3 % and 26.1 % [19], respectively. The authors of the third group do not find a direct relationship between the way the meningioma matrix is treated and the number of occurred recurrences [18]. Baumgartner and Sorenson [21] report 13.0 % of cases of recurrent spinal cord meningiomas that developed within 10 years after the surgeries.

While studying the role of the ND laser in EMT surgery, it was found that among our entire series, recurrences and continued growth, confirmed by clinical data and MRI, were diagnosed in the long-term postoperative period in 13.3 % of the patients. Meanwhile, in 6.1 % of cases there was a recurrence, in 7.2 % – continued growth. The largest part of their total number (54.5 %) was continued growth, and recurrences were manifested in 45.5 % of cases. The spinal tumors of difficult localization, the subtotal resection was performed in 13.0 %, most often gave a clinic of recurrence and continued growth.

Out of 372 totally resected tumors, 6.7 % of recurrences were revealed in the late postoperative period. The subtotal resection of 40 tumors confirmed continued growth in 30 cases, which accounted for 75.0% of all subtotal resections of tumors and 7.3 % of the total number of surgeries. The laser-operated patients were diagnosed with 4 (3 %)

recurrences in the long-term postoperative period, which is significantly lower than in the group where standard microsurgical technique was used -12 (8 %) cases (p = 0.08).

Out of 313 resected intracanal EMT, the relative number of recurrences and continued growth was 13.7 % (n = 43). It should be noted that the use of laser technologies, compared with standard surgical techniques, where they occurred in 11.1 % of cases, allowed statistically significantly reduce these indicators to 1.2 % (p < 0.010). The recurrences among these patients were 3.5 % (n = 11). All of them manifested only in the group with classical resection technique (p = 0.050).

The findings are explained by the photothermal effect (photocoagulation, ablation) of laser radiation on nonremoved tumor cells. In the presence of meningioma, much attention was paid to the treatment of its matrix. According to Crane et al. [22] and Borovich et al. [23], isolated meningiomas are not only the most visible areas of tumor growth in the center of the cell field of the dura mater. However, in 100 % of cases, meningotheliomatous cell clusters were found on its inner surface. Furthermore, infiltration by tumor cells was found at a distance of 2 cm from the visible border of the tumor node [23, 24]. This can account for the high rates of meningioma recurrence after total resection of nodular meningioma. The active photocoagulation and ablation of the meningioma growth zone

 $Table\ 2$  The number of recurrences and continued growth of extramedullary tumors in the long-term 15-year period

Variable	Before PSM				After PSM			
indicators	comparison	study group	hazard ratio,	log-rank	comparison	study group	hazard ratio,	log-rank
	group	(n = 135), n;	[95 % CI]	test,	group	(n = 96), n;	[95 % CI]	test,
	(n = 277), n;	risk, %		p-level	(n = 161), n;	risk, %		p-level
	risk, %				risk, %			
Recurrences	21; 18 %	3; 3 %	0.15	<0.001*	15; 18 %	3; 5 %	0.25	0.020*
	[9%;27%]	[0%;6%]	[0.04; 0.52]		[8 %; 27 %]	[0%; 10%]	[0.07; 0.88]	
Continued	23; 32 %	4; 5 %	0.12	<0.001*	18; 32%	4; 8 %	0.21	0.002*
growth	[16 %; 45 %]	[0%;9%]	[0.04; 0.36]		[15 %; 46 %]	[0 %; 16 %]	[0.07; 0.23]	

PSM — Propensity Score Matching.

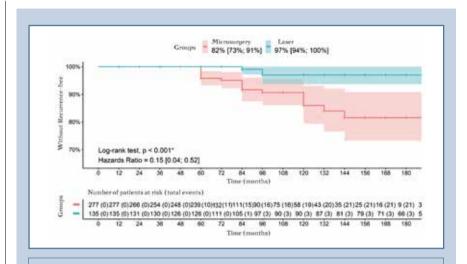
<sup>\*</sup> Statistically significantly different indicators; the risk assessment at the point of 15 years was performed by the Kaplan — Meier estimator; the assessment of the ratio of constant risks was calculated using the Cox proportional-hazards model.

promoted not only apoptosis of meningeal cells and their evaporation on the surface of the matrix remaining after ultrasound removal. These actions result in the thermal destruction of the dura mater for its entire thickness. We consider that this method of matrix processing, in comparison with bipolar coagulation, accounts for the lack of recurrence of these tumors. The excision of the tumor from the spinal cord root was performed using laser radiation at the border with the tumor in the coagulation mode, which also provided an ablastic effect.

#### **Conclusions**

The findings of a comprehensive analysis of clinical, neuroimaging and statistical data obtained during the dynamic observation of 412 patients with primary EMT, collected and systematized before surgery and in the late postoperative period, conclusively showed the following. The application of a laser for the prevention of recurrence and continued growth of tumors is effective as an additional technology to the classical microsurgical resection of tumors of a certain localization, histological structure and size relative to the vertebral bodies. For example, the use of laser technologies for resection of intracanal primary EMT has decreased the relative number of recurrences and continued growth to 1.2 %, compared with 11.1 % of cases in patients treated with standard surgical methods. The share of recurrences was 3.5 %. All of them were found only in the group with the classical tumor resection technique (p < 0.010).

The study had no sponsors. The authors declare that they have no conflict of interest.



**Fig. 1**Kaplan – Meyer curve: recurrences of extramedullary tumors in the long-term 15-year period on data up to PSM

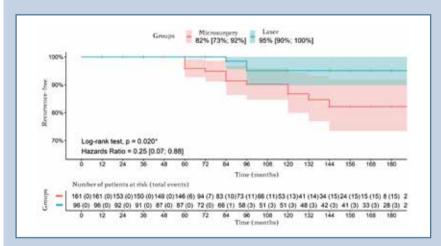
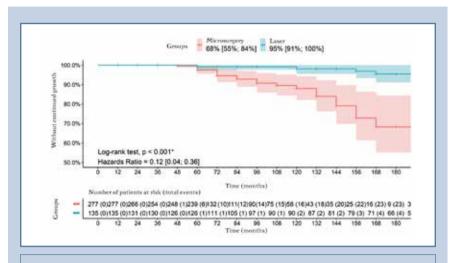
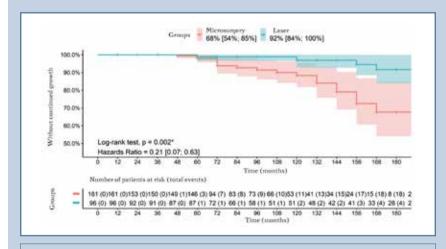


Fig. 2

Kaplan – Meyer curve: recurrences of extramedullary tumors in the long-term 15-year period on data after PSM



**Fig. 3**Kaplan – Meyer curve: continued growth of extramedullary tumors in the long-term 15-year period on data up to PSM



Kaplan – Meyer curve: continued growth of extramedullary tumors in the long-term 15-year period on data after PSM

#### References

- Byvaltsev VA, Stepanov IA, Belykh EG, Aliyev MA. Long-term results of surgical treatment in patients with intradural spinal tumors. Annals of the Russian Academy of Medical Sciences (Vestnik Rossiiskoi akademii meditsinskikh nauk). 2018;73(2):88–95. In Russian. DOI: 10.15690/vramn945.
- Arnautovic K, Arnautovic A. Extramedullary intradural spinal tumors: a review of modern diagnostic and treatment options and a report of a series. Bosn J Basic Med Sci. 2009;9 Suppl. 1:\$40–45. DOI: 10.17305/bjbms.2009.2755.
- Cofano F, Giambra C, Costa P, Zeppa P, Bianconi A, Mammi M, Monticelli M, Di Perna G, Junemann CV, Melcarne A, Massaro F, Ducati A, Tartara F, Zenga F, Garbossa D. Management of extramedullary intradural spinal tumors: the impact of clinical status, intraoperative neurophysiological monitoring and surgical approach on outcomes in a 12-year double-center experience. Front Neurol. 2020;11:598619. DOI: 10.3389/fneur.2020.598619.
- Van der Wal EC, Klimek M, Rijs K, Scheltens-de Boer M, Biesheuvel K, Harhangi BS. Intraoperative neuromonitoring in patients with intradural extramedullary spinal cord tumor: a single-center case series. World Neurosurg. 2021;147:e516–e523. DOI: 10.1016/j.wneu.2020.12.099.
- Sudhan MD, Satyarthee GD, Joseph L, Kakkar A, Sharma MC. Primary intradural extramedullary lesions: a longitudinal study of 212 patients and analysis of predictors of functional outcome. J Neurosurg Sci. 2020 Dec 9. DOI: 10.23736/S0390-5616.20.05147
- Byval'tsev VA, Sorokovikov VA, Damdinov VV, Belykh EG, Sereda EV, Panasenkov SYu, Grigor'iev EG. Factors affecting the outcome of surgical management for extramedullary spinal cord tumors: a multicenter study. Zhurnal Voprosy neyrokhirurgii imeni N.N. Burdenko. 2014;78(6):15–23. In Russian. DOI: 10.17116/ neiro201478615-23.
- Aghayev K, Vrionis F, Chamberlain MC. Adult intradural primary spinal cord tumors. J Natl Compr Canc Netw. 2011;9:434–447. DOI: 10.6004/jnccn.2011.0039.
- Bekyashev AKh. Pathogenesis of meningiomas (a review of literature). Head and Neck Tumors (HNT). 2011;(4):26–40. In Russian.
- Houten JK, Cooper PR. Spinal cord astrocytomas: presentation, management and outcome. J Neurooncol. 2000;47:219–224. DOI: 10.1023/a:1006466422143.
- Stupak VV, Shabanov SV, Pendyurin IV, Tsvetovsky SB, Okladnikov GI, Rabinovich SS, Dolzhenko DA. Ependymomas of lumbosacral localization. Long term results of surgical treatment. Advances in Current Natural Sciences. 2015;(5):38–44. In Russian.
- 11. Konovalov NA, Shevelev IN, Nazarenko AG, Asiutin DS, Korolishin VA, Timonin SIu, Zakirov BA, Onoprienko RA. The use of minimally invasive approaches to resect intradural extramedullary spinal cord tumors. Zhurnal Voprosy neyrokhirurgii imeni N.N. Burdenko. 2014;78(6):24–36. In Russian.
- Stupak VV, Moiseev VV. ND-YAG laser in extramedullary tumor surgery. Hir. Pozvonoc. 2004;(1):71–77. In Russian.
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW, Kleihues P. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol. 2007;114:97–109. DOI: 10.1007/s00401-007-0243-4.

- Turel MK, D'Souza WP, Rajshekhar V. Hemilaminectomy approach for intradural extramedullary spinal tumors: an analysis of 164 patients. Neurosurg Focus. 2015;39:E9. DOI: 10.3171/2015.5.FOCUS15170.
- Kwee LE, Harhangi BS, Ponne GA, Kros JM, Dirven CMF, Dammers R. Spinal meningiomas: Treatment outcome and long-term follow-up. Clin Neurol Neurosurg. 2020;198:106238. DOI: 10.1016/j.clineuro.2020.106238.
- Wong AP, Lall RR, Dahdaleh NS, Lawton CD, Smith ZA, Wong RH, Harvey MJ, Lam S, Koski TR, Fessler RG. Comparison of open and minimally invasive surgery for intradural-extramedullary spine tumors. Neurosurg Focus. 2015;39:E11. DOI: 10.3171/2015.5.FOCUS15129.
- 17. Hirano K, Imagama S, Sato K, Kato F, Yukawa Y, Yoshihara H, Kamiya M, Deguchi M, Kanemura T, Matsubara Y, Inoh H, Kawakami N, Takatsu T, Ito Z, Wakao N, Ando K, Tauchi R, Muramoto A, Matsuyama Y, Ishiguro N. Primary spinal cord tumors: review of 678 surgically treated patients in Japan. A multicenter study. Eur Spine J. 2012;21:2019–2026. DOI: 10.1007/s00586-012-2345-5.
- Helseth A, Mork SJ. Primary intraspinal neoplasms in Norway, 1955 to 1986. A population-based survey of 467 patients. J Neurosurg. 1989;71:842–845. DOI: 10.3171/jns.1989.71.6.0842.
- Klekamp J, Samii M. Surgical results for spinal meningiomas. Surg Neurol. 1999;52:552–562. DOI: 10.1016/S0090-3019(99)00153-6.
- Solero CL, Fornari M, Giombini S, Lasio G, Oliveri G, Cimino C, Pluchino F. Spinal meningiomas: review of 174 operated cases. Neurosurgery. 1989;25:153–160. DOI: 10.1227/00006123-198908000-00001.
- Baumgartner JE, Sorenson JM. Meningioma in the pediatric population. J Neurooncol. 1996;29:223–228. DOI: 10.1007/BF00165652.
- Crone KR, Challa VR, Kute TE, Moody DM, Kelly DL Jr. Relationship between flow cytometric features and clinical behavior of meningiomas. Neurosurgery. 1988;23: 720–724. DOI: 10.1227/00006123-198812000-00006.
- Borovich B, Doron Y. Recurrence of intracranial meningiomas: the role played by regional multicentricity. J Neurosurg. 1986;64:58–63. DOI: 10.3171/jns.1986.64.1.0058.
- Mariniello G, Spaziante R, Cappabianca P, Donzelli R, Del Basso de Caro ML, De Divitiis E. Multicentrical growth of meningiomas: «spatial» or «temporal» phenomenon. J Neurosurg Sci. 1995;39:241–247.

## Address correspondence to:

Eliseenko Ivan Alexeevich Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, eliseenkoivan@gmail.com

Received 24.01.2021 Review completed 12.05.2021 Passed for printing 17.05.2021 I.A. ELISEENKO ET AL. INFLUENCE OF NEODYMIUM LASER RADIATION ON THE FREQUENCY OF RECURRENCE AND CONTINUED GROWTH OF TUMORS

Ivan Alexeevich Eliseenko, neurosurgeon, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0002-9927-7557, eliseenkoivan@gmail.com;

Sergey Grigorievich Struts, leading engineer Institute of Laser Physics SB RAS, 13/3 Akademika Lavrent'eva prospect, Novosibirsk, 630090, Russia, ORCID: 0000-0002-5978-7536, sgs@laser.nsi.ru;

Vyacheslav Vladimirovich Stupak, DMSc, Prof, Head of Neurosurgical Department, Novosibirsk Research Institute of Traumatology and Orthopedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0003-3222-4837, VStupak@niito.ru.