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ORIGINAL ARTICLE

Experience of stereotactic radiation therapy and radiosurgical treatment of metastatic vertebral tumors

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ABSTRACT

Purpose of the study. Evaluation of the effectiveness of extracranial stereotactic radiation therapy in various fractionation regimens in the treatment of patients with metastatic vertebral lesions.

Patients and methods. The study included 12 patients with metastatic spinal lesions who underwent extracranial stereotactic radiation therapy (SBRT) on a Novalis Tx linear accelerator, Varian, in radiosurgery mode (SRS; in 1 fraction) and hypofractionation mode (SFD 5Gy, TFD 25Gy, 5 fractions) in the period from 01/01/2020 to 03/31/2022. The assessment of local control was carried out using positron emission tomography – computed tomography (PET-CT) from 18FDG. The intensity of the pain syndrome before and after radiation was assessed using a visual analog pain scale (VAS).

Results. 19 vertebrae with metastatic lesions were irradiated in 12 patients. The SBRT technique in hypofractionation mode was used in 6 (50 %) patients, in radiosurgery (SRS) mode was used in 4 (34 %) patients, in 2 (17 %) patients a combination of irradiation techniques was used on various affected segments of the spinal column. The general tumor volume (GTV) averaged 30.56 = 7.8 km^2. When using the radiosurgical irradiation regimen, SFD ranged from 16 to 18 Gy. When using the hypofractionation technique, the total focal dose (TFD) was 25 Gy, a single focal dose (SFD) was 5 Gy.

Conclusion. Stereotactic radiation therapy and radiosurgery of metastatic vertebral tumors without compression of neural structures provides local tumor control in 92 % of patients within 6 months and in 83 % of patients within 1 year, regression of pain after irradiation – in 67 % of patients.

Keywords: stereotactic radiotherapy, radiosurgery, spinal metastases

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Compliance with ethical standards: This research has been carried out in compliance with the ethical principles set forth by the World Medical Association Declaration of Helsinki, 1964, ed. 2013. The study was approved by the Committee on Biomedical Ethics at the National Medical Research Center of Oncology, the Russian Federation Ministry of Health (extract from the protocol of the meeting No. 118 dated 06/02/2022). Informed consent was received from all the participants of the study

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3.1.6. Онкология, лучевая терапия
ОРИГИНАЛЬНАЯ СТАТЬЯ

Опыт стереотаксической лучевой терапии и радиохирургического лечения метастатических опухолей позвонков

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РЕЗЮМЕ

Цель исследования. Оценка эффективности экстракраниальной стереотаксической лучевой терапии в различных режимах фракционирования при лечении пациентов с метастатическим поражением позвонков

Пациенты и методы. В исследование включено 12 больных с метастатическим поражением позвоночника, которым была проведена экстракраниальная стереотаксическая лучевая терапия (SBRT) на линейном ускорителе Novalis Tx, Varian, в режиме радиохирургии (SRS; за 1 фракцию) и режиме гипофракционирования (разовая очаговая доза (РОД) 5Гр, суммарная очаговая доза (СОД) 25Гр, 5 фракций) в период с 01.01.2020 по 31.03.2022 гг. Оценка локального контроля осуществлялась с использованием позитронно-эмиссионной томографии – компьютерной томографии (ПЭТ-КТ) с 18ФДГ. Интенсивность болевого синдрома до и после облучения оценивали по визуально аналоговой шкале боли (ВАШ).

Результаты. У 12 пациентов проведено облучение 19 метастатических пораженных позвонков. Методика SBRT в режиме гипофракционирования была применена у 6 (50 %) больных, в режиме радиохирургии (SRS) использована у 4 (34 %) пациентов, у 2 (17 %) больных на различных пораженных сегментах позвоночного столба применялась комбинация методик облучения. Общий объем опухоли (GTV) в среднем составлял 30,56 ± 7,8 см². При применении радиохирургического режима облучения РОД составляла от 16 до 18Гр. При применении методики гипофракционирования СОД составила 25 Гр, РОД – 5 Гр.

Заключение. Экстракраниальная стереотаксическая лучевая терапия метастатических опухолей позвонков без компрессии невральных структур обеспечивает локальный контроль опухоли у 92 % больных в течение 6 месяцев и у 83 % пациентов в течение 1 года, регресс болевого синдрома после облучения – у 67 % больных.

Ключевые слова: стереотаксическая лучевая терапия, радиохирургия, метастазы в позвоночник

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Соблюдение этических стандартов: в работе соблюдались этические принципы, предъявляемые Хельсинкской декларацией Всемирной медицинской ассоциации (World Medical Association Declaration of Helsinki, 1964, ред. 2013). Исследование одобрено Комитетом по биомедицинской этике при ФГБУ «Национальный медицинский исследовательский центр онкологии» Министерства здравоохранения Российской Федерации (выписка из протокола заседания № 118 от 02.06.2022 г.). Информированное согласие получено от всех участников исследования.

Финансирование: финансирование данной работы не проводилось

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INTRODUCTION

An analysis of the literature shows that 30–50 % of cancer patients have metastatic spinal column lesions, including 70–80 % of patients with breast or prostate cancer and 40 % of patients with advanced lung cancer [1]. In one third of patients, the lesion of the vertebrae is symptomatic. Clinical manifestations are most often represented by pain syndrome, varying in intensity. For a long time, conventional radiation therapy (CRT) has been used in the treatment of this group of patients and in the absence of indications for surgical treatment, which has a satisfactory (up to 80 % of cases) analgesic effect, however, local relapses occur in 60–80 % of patients, and the analgesic effect often develops only 2–3 weeks after treatment, especially with radioresistant tumors [2]. Currently, conformal methods of radiation therapy in the treatment of bone metastases are replacing conventional radiation therapy, despite their disadvantages in the form of the need for longer patient preparation, additional diagnostic studies, and high cost [3]. The main difference between conformal radiation therapy and conventional radiation therapy is the creation of an irradiation field of a given shape with minimal impact on surrounding tissues. The possibility of concentrating the radiation dose without increasing it during conformal radiation therapy in the tumor area is, among other things, a way to overcome its radioresistance. Stereotactic body radiation therapy (SBRT) and radiosurgery (SRS) have taken leading positions among conformal methods in the treatment of spinal tumors. In stereotactic radiation therapy, tumor destruction occurs in several large fractions (5–12 Gy each), in stereotactic radiosurgery – by summing up a radical dose (15–21 Gy) in one session.

The purpose of the study was to evaluate the effectiveness of extracranial stereotactic radiation therapy in various fractionation regimes in the treatment of patients with metastatic vertebral lesions.

PATIENTS AND METHODS

The study included 12 patients with metastatic spinal lesions who underwent extracranial stereotactic radiation therapy (SBRT) on a Novalis Tx linear accelerator, Varian, in radiosurgery mode (SRS; for

Table 1. Characteristics of metastatic vertebral tumors in patients

Indicator	Indicator value (*n* = 19)
The location of a metastatic tumor in the spine according to the Tomita classification	
1 type 5 type 7 type	4 (21 %) 1 (5 %) 14 (74 %)
Localization of the tumor in the vertebra	
body body + peduncle of the arch total defeat	13 (68 %) 3 (16 %) 3 (16 %)
The degree of tumor spread according to the Weinstein-Boriani classification	
B + C A + B + C	18 (95 %) 1 (5 %)
Level of lesion	
Cervical Thoracic Lumbar Sacral	2 (10.5 %) 7 (37 %) 8 (42 %) 2 (10 %)

1 fraction) and hypofractionation mode (SFD 5Gy, TFD 25Gy, 5 fractions) in the period from 01/01/2020 to 03/31/2022.

The average age of the patients was 55.47 ± 2.89 years, the ratio of men and women was 2:10. Grade 1b epidural compression was detected in only 1 patient. The stability of the spinal column on the SINS scale averaged 5.0 ± 0.59 points. All patients were neurologically intact (Frankel type E) and functionally intact (70–80 points according to Karnofsky). Pain syndrome before the course of radiation occurred in all patients, the average score according to VAS was 5.4 ± 0.67. According to the histological type of the primary tumor, the distribution was as follows: breast

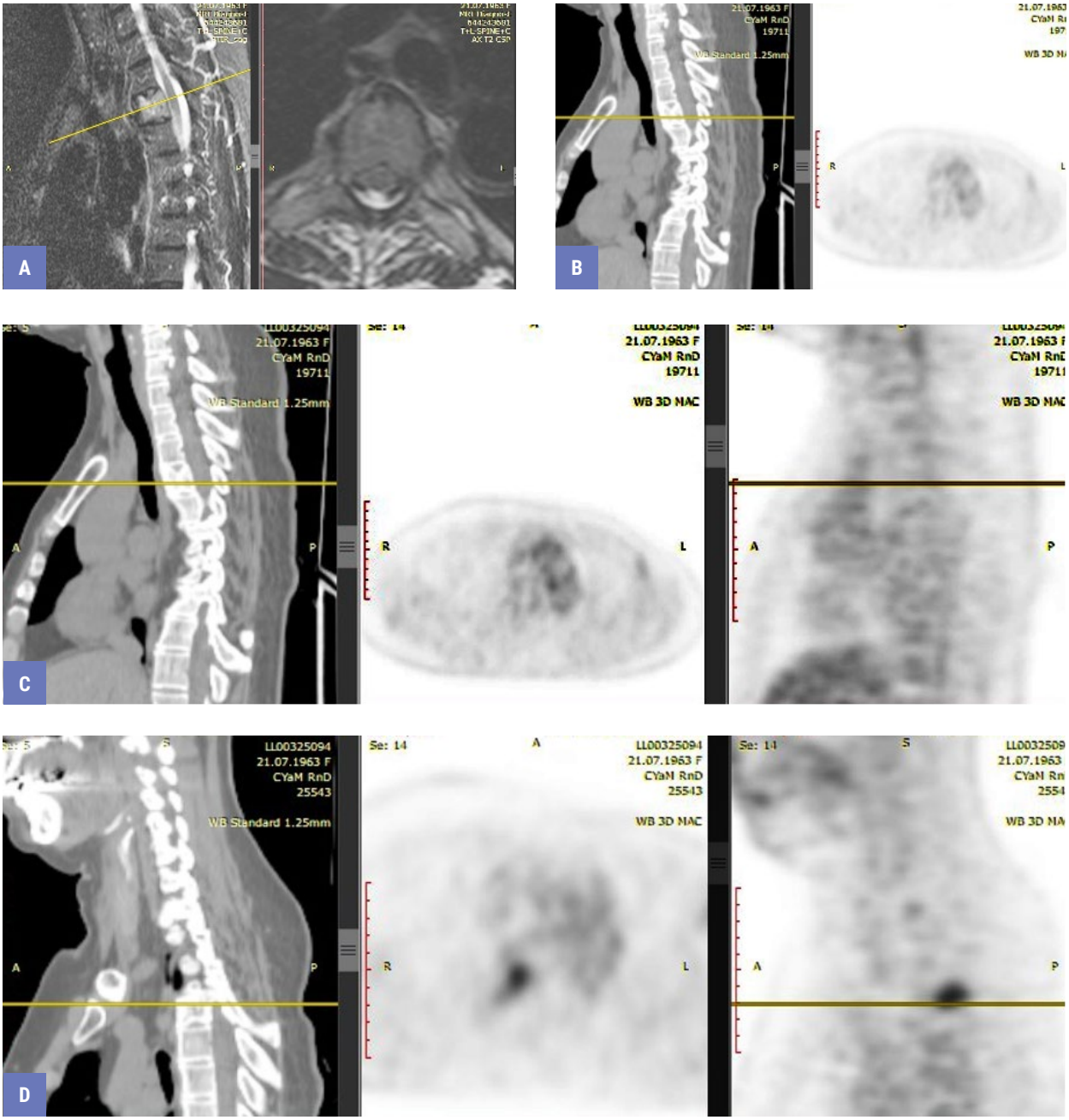

Fig. 1. Assessment of local control after radiation therapy in patient L-o. A, B – MRI and CT data of the thoracic spine before treatment (signs of metastatic lesion of the Th3 vertebra); C – data of the control PET-CT during the observation period 3 months after irradiation (there are no signs of pathological activity in the irradiation zone); D – data of the control PET-CT during the observation period after 12 months after irradiation (signs of recurrence of formation in the area of the vertebral arch peduncle)

cancer – 10 (84 %) patients, skin melanoma – 1 (8 %) patient, without an established primary focus – 1 (8 %) patient. The characteristics of metastatic vertebral tumors in patients with neuroimaging are represented in Table 1.

The general tumor volume (GTV) averaged 30.56 ± 7.8 cm^2. The average radiation dose for single-fraction courses was 26 [13; 16] Gy. When using the hypofractionation technique, the average total focal dose (TFD) was 25 [25; 26] Gy, the average single focal dose (SFD) was 5 [5; 8] Gy.

A single metastatic lesion in the spine at the beginning of treatment was observed in 2 (17 %) patients, in the remaining patients metastatic lesion of the vertebrae was of a multiple nature. In addition to the spine, 6 (50 %) had metastasis to other flat bones of the skeleton, and 4 (34 %) had visceral metastases.

To assess the neurological status and condition of patients, the Frankel and Karnofsky scales were used, the intensity of pain syndrome was assessed using a visually analog pain scale (VAS), and the SINS scale was used to assess instability in the affected spinal-motor segment. All patients were examined on the day of admission, at discharge and every 3 months after completion of the course of radiation therapy. All patients underwent computed tomography (CT) and magnetic resonance imaging (MRI) of the spinal column before treatment, postoperative assessment of local control was carried out using positron emission tomography – computed tomography (PET-CT) with 18F-fluorodeoxyglucose (18-FDG) (Fig. 1).

The irradiation was carried out on the Novalis Tx linear accelerator, Varian. Topometric tomography was previously performed on a Siemens Somatom computed tomograph, and preliminary topometry was processed at the Singo Via virtual simulation station. A full-body vacuum mattress with an ArmShuttle board was used for immobilization and

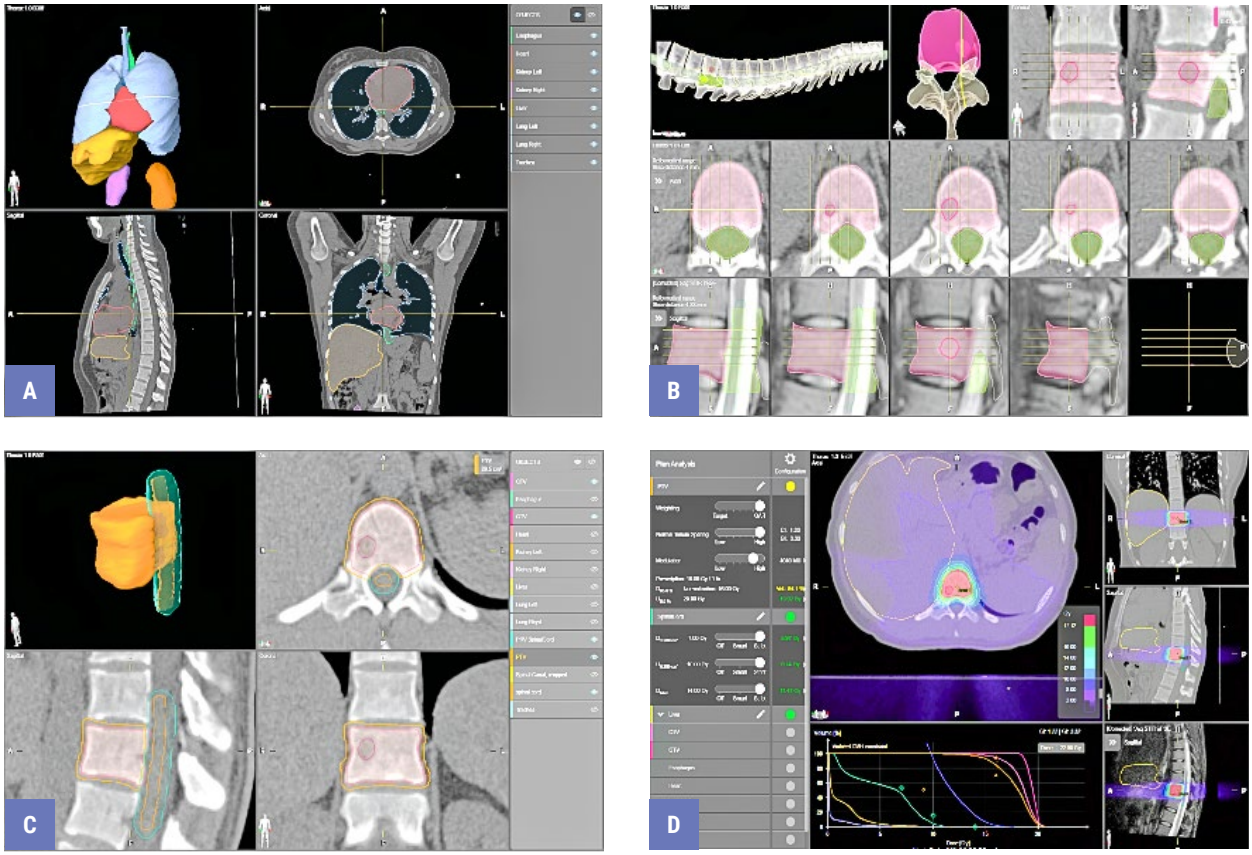

Fig. 2. Radiation planning. A – anatomical segmentation and contouring of critical organs and structures; B – delineation of the GTV volume from images of various modalities and formation of the CTV volume; C – contouring of the spinal cord and the formation of PTV volume; D – dosimetry planning with control of target coverage and load on critical organs and structures, followed by analysis of the calculated irradiation plan

reproducibility of the patient's laying. Using the Elements Brainlab software, segmentation, contouring and formation of a 3D treatment plan for a linear accelerator were performed. The laying and control of the patient's position were performed using orthogonal X-rays using the ExacTrac X-Ray Monitoring BrainLab positioning system. Verification of the calculated stereotactic radiotherapy treatment plan was carried out on a StereoPHAN phantom with a matrix of SRS Mapcheck detectors. Before the radiosurgical treatment session, the absolute dose calibration of the accelerator and the calibration of the positioning system were checked. The dose was delivered using a dynamic volume modulated technique (VMAT).

The clinical volume of the tumor (CTV) was determined in accordance with the International Spine Radiosurgery Consortium Consensus Guidelines [4]. The planned tumor volume (PTV) was calculated by adding a 2 mm edge to the CTV boundaries, minus the PRV (planning risk volume) for the spinal cord (+ 3 mm to the edge of the spinal cord in all directions) and taking into account the location of the risk organs (oropharynx, esophagus, etc.) (Fig. 2).

For each group of indicators, the type of data distribution was determined (histogram construction according to the Kolmogorov – Smirnov test). If the application of the criterion showed a normal distribution of data, the average, the error of the average (M ± m) was used for the description. When the distribution differs from the normal law, the values of the median, 1st and 3rd quartiles (Me [Q1; Q3]) were used for the description. The threshold level of significance for testing statistical hypotheses was assumed to be 0.05.

STUDY RESULTS

In 12 patients, 19 metastatic vertebral tumors were irradiated.

The majority of patients (80 %, *n* = 10) underwent 1 course of radiation therapy, 20 % of patients received 2 courses of radiation. At the same time, irradiation of one vertebra was performed in 8 (67 %) patients, 4 (33 %) received irradiation of two or more segments of the spinal column. The SBRT technique was used in 6 (50 %) patients, radiosurgery (SRS) was used in 4 (34 %) patients. Both SBRT and SRS irradiation techniques were used in 2 (17 %) patients on various affected segments of the spinal column.

The radiation therapy performed was part of the complex treatment in 10 (83 %) patients, combined – in 2 (17 %).

The average duration of follow-up was 12.18 ± 2.23 months. Radiological local control (complete, partial response and stabilization of the disease according to the RECIST criteria) was achieved in 11 (92 %) patients within 6 months, in 10 (83 %) – within 1 year. Progression of the underlying disease during the follow-up period was noted in 6 (50 %) patients. The average survival rate before progression was 9.11 ± 2.69 months. A decrease in back pain after irradiation was noted by 8 (67 %) patients, there were no cases of an increase in pain syndrome.

DISCUSSION

Stereotactic radiation therapy and radiosurgery show high efficiency in the treatment of metastatic tumors of the vertebrae. One of the primary goals of irradiation of tumors that do not compress the spinal cord is the treatment of pain syndrome. Vargo J. A. et al. [5] It is proposed to apply certain modes of irradiation, depending on the purpose of the treatment. If the main task is to relieve pain, then preference is given to radiation for 1 fraction (16–18 Gy). In order to achieve long-term local control, preference is given to fractionated SBRT modes (8–9 Gy × 3 fr., or 6–7 G × 5 fr.).

Randomized studies of the analgesic effect of radiation therapy performed in patients using single-fraction SBRT (16–18 or 24 Gy) and mono-multi-fraction CRT (8 Gy for 1 fraction or 30 Gy for 10 fractions) showed no significant difference between the groups of patients 3 months after treatment, and a significantly better effect of SBRT after 6 months [6, 7]. The limitation of these studies was the lesion of no more than 2 adjacent vertebrae and the presence of a distance of at least 3 mm between the edge of the tumor and the spinal cord (no more than 1b degree ESCC), otherwise the groups could not be randomized. Sahgal A. and co-author. [8] In the course of a randomized multicenter study, the advantages of SBRT (two-fraction 24 Gy) over CRT (20 Gy in 5 fractions) in effectiveness against pain syndrome in metastatic spinal in-

jury were also noted, even during the first 3 months after treatment. The results of randomized studies comparing the effectiveness of CRT and SBRT techniques in relation to local tumor control are currently not available in the literature. Meta-analysis conducted by Singh R. et al. [9], which included 3237 patients, showed the presence of local tumor control in 92.9 % of patients after single-factional SBRT (RS) versus 81 % after CRT or 82.1 % after multi-factional CRT.

Local radiation does not prevent the progression of the underlying disease, so it should be used in combination with chemotherapy treatment. During the follow-up period, progression was noted in 50 % of patients, while local control was achieved by the end of the first year after completion of the radiation course in 83 %.

CONCLUSION

Stereotactic radiation therapy and radiosurgery of metastatic vertebral tumors without compression of neural structures provides local tumor control in 92 % of patients for 6 months. and in 83 % of patients within 1 year, regression of pain syndrome after irradiation – in 67 % of patients.

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Contribution of the authors:

Kit O. I. – performed development of the research design, critical revision with the introduction of valuable intellectual content, final approval of the published version of the manuscript;
Zakondyrin D. E. – contributed to the research design development, analysis of the obtained data, writing the text of the manuscript;
Rostorguev E. E. – review of publications on the topic of the article, a set of clinical material, interpretation of the results;
Sakun P. G. – performed data collection, analysis and interpretation, technical editing;
Voshedskii V. I. – took part in research design development, analysis of the data obtained;
Komandirov M. A. – contributed to the data collection, interpretation, technical editing.