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# Stereotactic Radiotherapy for Residual Tumor after Chondrosarcoma Surgery: Clinical Case

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ABSTRACT

***BACKGROUND:*** The treatment of chondrosarcoma can be challenging due to the rarity of the tumor, the characteristics of the disease progression, and the variability of its anatomical location. Surgical resection of the tumor is not always feasible, particularly complete resection, due to its proximity to vital organs such as the spinal cord. The low cell sensitivity to chemotherapy and radiotherapy further limits treatment options and poses a poor prognosis. These factors contribute to a high incidence of local relapses, with their frequency reaching 58%. Particular emphasis is hereby placed on the recent advancements in high-dose chondrosarcoma irradiation using stereotactic radiotherapy, a technique that has been demonstrated to effectively overcome the radioresistance exhibited by malignant cells and thereby ensure the comprehensive eradication of the tumor.

***DESCRIPTION OF CLINICAL CASE:*** A female patient diagnosed with chondrosarcoma Th12 underwent Th11-12 laminectomy with the removal of an extratradural extramedullary tumor located on the anterior surface of the dural sac. Contrast-enhanced magnetic resonance imaging revealed a residual tumor two months post-surgery, accompanied by a clinical progression. The relapsed tumor bed was irradiated in a single dose of 9 Gy daily to a total dose of 45 Gy (116 Gy). Five months after the initiation of radiotherapy, a clinical improvement was observed, as evidenced by a decrease in pain on a visual analog scale. Furthermore, the dose of opioid analgesics was reduced. Objectively, based on magnetic resonance imaging findings, the disease stabilized. At the 13-month follow-up, a decrease in the lesion size was documented.

***CONCLUSION:*** Stereotactic radiotherapy for residual tumor following chondrosarcoma surgery has been demonstrated to stabilize the patient's overall condition, reduce the necessity for opioid analgesics, enhance the patient's quality of life, achieve partial regression of the tumor, and attain long-term disease remission.

**Keywords:** chondrosarcoma; residual tumor; stereotactic radiotherapy; spine; SRT.

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# Стереотаксическая лучевая терапия остаточной опухоли после хирургического удаления хондросаркомы: клинический случай

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## АННОТАЦИЯ

**Обоснование.** Лечение хондросаркомы (ХС) представляет собой сложную задачу ввиду редкости данной опухоли, особенностей течения заболевания и вариативности её локализации. Классическое хирургическое удаление злокачественного новообразования не всегда возможно, тем более в полном объёме, ввиду расположения опухоли вблизи таких жизненно важных структур, как спинной мозг, а низкая чувствительность клеток к химиотерапии и лучевой терапии ограничивает лечебные опции и ухудшает прогноз для пациента. Указанные особенности приводят к высоким показателям местных рецидивов, частота которых достигает 58%. Особое внимание привлекает современное высокодозное облучение ХС методом стереотаксической лучевой терапии, которая позволяет преодолеть порог радиорезистентности злокачественных клеток и обеспечивает радикализм лечения.

**Описание клинического случая.** Больная с диагнозом ХС Th12 получила хирургическое лечение в объёме ламинэктомии Th11-12, удаления экстраинтрадурального экстрамедуллярного новообразования передней поверхности дурального мешка. По результатам магнитно-резонансной томографии с контрастным усилением через 2 мес. от даты операции диагностирована остаточная опухоль, отмечалось клиническое ухудшение состояния пациентки. Проведено облучение ложа опухоли с рецидивом в разовой дозе 9 Гр ежедневно до суммарной дозы 45 Гр (116 изоГр). Спустя 5 мес после лучевой терапии отмечается клиническое улучшение, уменьшение болей по Визуальной аналоговой шкале, доза опиоидных анальгетиков снижена, объективно по данным магнитно-резонансной томографии стабилизация заболевания, а через 13 мес. зарегистрировано уменьшение размеров образования.

**Заключение.** Проведение стереотаксической лучевой терапии остаточной опухоли после хирургического удаления ХС позволило стабилизировать общее состояние больной, уменьшить дозу опиоидных анальгетиков, улучшить качество жизни, добиться частичной регрессии опухоли и длительной ремиссии заболевания.

**Ключевые слова:** хондросаркома; остаточная опухоль; стереотаксическая лучевая терапия; позвоночник.

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# BACKGROUND

Primary bone tumors make up 0.001% of all malignancies, with chondrosarcoma (CHS) being the second most prevalent primary bone tumor (20%–27%) [1–3]. CHS is most commonly found in long bones and pelvic bones; however, it affects the spine in 6.5–10% of cases. The latter is associated with neurological disorders, with clinical signs ranging from nerve root pain to paralysis, depending on the degree of tumor compression of nerve roots and/or the spinal cord [4]. The course of the disease, treatment options, and prognosis are determined by the tumor grade, which ranges from mild (G1) to severe (G3), as well as the tumor location and accessibility for surgical treatment. In small, low-grade CHSs, curative resection is possible, which involves tumor excochleation with a mandatory cavity treatment using local adjuvants (burr [mechanical], 96% alcohol, etc.) [1]. However, total resection of spinal tumors is technically challenging due to anatomical variability and close proximity to vital organs such as the spinal cord. This results in high local recurrence rates ranging from 20% to 58% [5–7]. The low sensitivity of CHS to chemotherapy and radiotherapy (RT) complicates treatment selection; thus, the decision on the need for irradiation must always be consensus-based. Stereotactic radiosurgery (SRS) and stereotactic RT (SRT) are the preferred techniques. These approaches use single- or multi-fraction high ablative doses of ionizing radiation to overcome tumor radioresistance. In CHS, the α/β ratio of 2.45 Gy [8] justifies the use of coarse fractionation and improves the predicted outcome compared to conventional irradiation. Proton RT (PRT) and carbon ion radiotherapy are the best options for CHS in close proximity to critical structures such as the spinal cord. However, costly equipment limits the use of this irradiation; for example, Russia has only four proton irradiation facilities and no carbon ion accelerator facilities [9].

The presented clinical case highlights the challenges encountered in the treatment of rare tumors such as spinal CHS. It also describes a decision-making algorithm and the efficacy of linear electron accelerator-based SRT in achieving long-term remission after non-radical surgery.

# CASE DESCRIPTION

## About the patient

Patient T., female, 75 years old; a history of meningothelial arachnoidal endothelioma resection at the Th6–Th7 level on July 13, 1988. In 2019, the patient began experiencing weakness and pain in the right leg, which increased in severity. On December 22, 2020, the patient was admitted to the Karpovich Krasnoyarsk Interdistrict Clinical Emergency Hospital with the diagnosis of moderate coronavirus disease. Computed tomography (CT) of the chest revealed a lytic lesion of the T12 vertebral body. After recovering from COVID-19-associated pneumonia, the patient was discharged with suspected local tumor recurrence. Magnetic resonance imaging (MRI) of the spine with intravenous contrast revealed an intradural extramedullary tumor of the thoracic spine at the Th12 level, measuring 1.7×2.3×2.3 cm and extending to the intervertebral foramen. Other MRI findings included vertebral destruction and spinal cord deformation and compression (Fig. 1). On November 15, 2022, neurosurgeons at the N.S. Karpovich Krasnoyarsk Interdistrict Clinical Emergency Hospital performed Th11–12 laminectomy and resection of an extra-intradural extramedullary tumor of the anterior dural sac. The tumor extended into the dura mater of the conus medullaris. The patient was diagnosed with low-grade (G1) CHS based on the surgical specimen immunohistochemistry. The specimen was further examined in the anatomic pathology department of the Blokhin National Medical Research Center of Oncology, and the diagnosis was confirmed. A post-operative contrast-enhanced MRI revealed no signs of tumor in the Th12 vertebra and no paramagnetic contrast uptake areas (Fig. 1).

Clinical findings from November 2022 to January 2023 showed negative changes: worsening of lower paraparesis (from mild to moderate). Subjective complaints included right side back pain radiating to the right leg (pain intensity on a visual analogue scale: 70%–80%), sleep for no more than 2–3 h due to therapy with nonsteroidal anti-inflammatory drugs, weakness, decreased appetite, and tingling in the legs. The patient had difficulty walking and required the assistance of family members. MRI findings two months after surgery (January 2023): a tumor measuring 1.6×1.1 cm along the posterior surface of the Th12 vertebral body, extending to the spinal canal and compressing the adjacent spinal cord segment. Contrast-enhanced MRI revealed a weak, heterogeneous increase in MR signal of the tumor (most likely, residual tumor) (Fig. 2).

## Preliminary Diagnosis

The detected tumor was classified as residual CHS; a telemedicine consultation with the Blokhin National Medical Research Center of Oncology was performed. Recurrent surgery was not indicated, given the absence of spinal cord compression. The patient declined proton RT due to the long-distance commute to the center and her physical status. It was decided to perform photon RT in the primary tumor area in the Kryzhanovsky Krasnoyarsk Territory Clinical Cancer Center.

## Disease Course and Outcomes

In late March 2023, the patient was admitted to a daytime radiotherapy center. A follow-up MRI revealed a tumor measuring 1.5×1.2 cm along the posterior

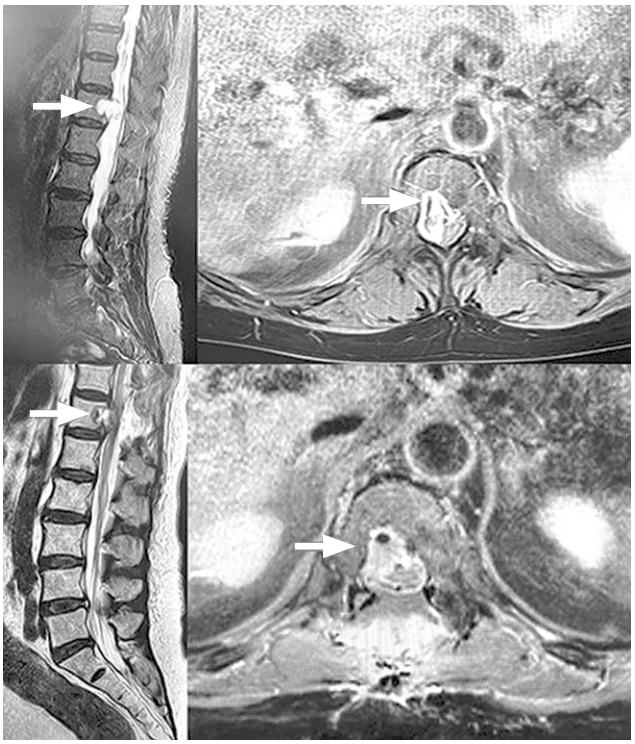

**Fig. 1.** MRI of the spine, T1 mode. The top picture is before surgery (tumor in Th12). The bottom photo is after the operation (the formation is not visualized).
**Рис. 1.** МРТ позвоночника, режим Т1. Верхний рисунок — до операции (опухоль в Th12). Нижнее фото — после операции (образование не визуализируется).

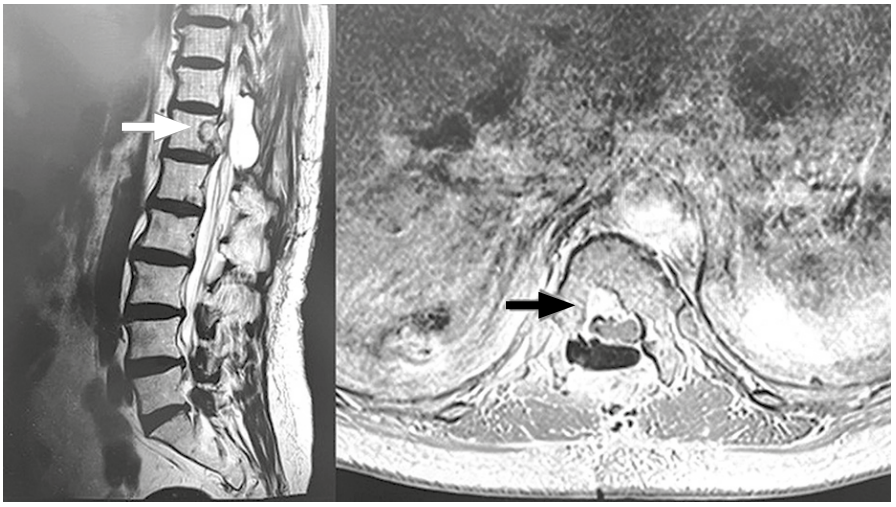

**Fig. 2.** MRI of the spine 2 months after surgery, T1 mode (residual tumor in Th12).
**Рис. 2.** МРТ позвоночника через 2 мес. после операции, режим Т1 (остаточная опухоль в Th12).

surface of the Th12 vertebral body, extending to the spinal canal, with no signs of spinal cord compression (Fig. 2). Subjective complaints included weakness in the right leg, discomfort in soft tissues of the abdomen and back on the right, tingling in the right leg, pain in the right leg, weakness, and fatigue. The patient had difficulty walking and required the assistance of family members. The patient received tramadol, an opioid analgesic, at a dose of up to 400 mg/day.

CT topometry was performed in a prone position with the head and feet fixed, with a 5 mm increment. Following target volume contouring and dosimetry (Fig. 3), a decision was made jointly with the Blokhin National Medical Research Center of Oncology to perform stereotactic radiotherapy of the residual tumor in the Th12 vertebra. The single dose was 9 Gy No. 5 daily, up to the total dose of 45 Gy, which corresponds to 166 isoGy when calculated using a linear quadratic model

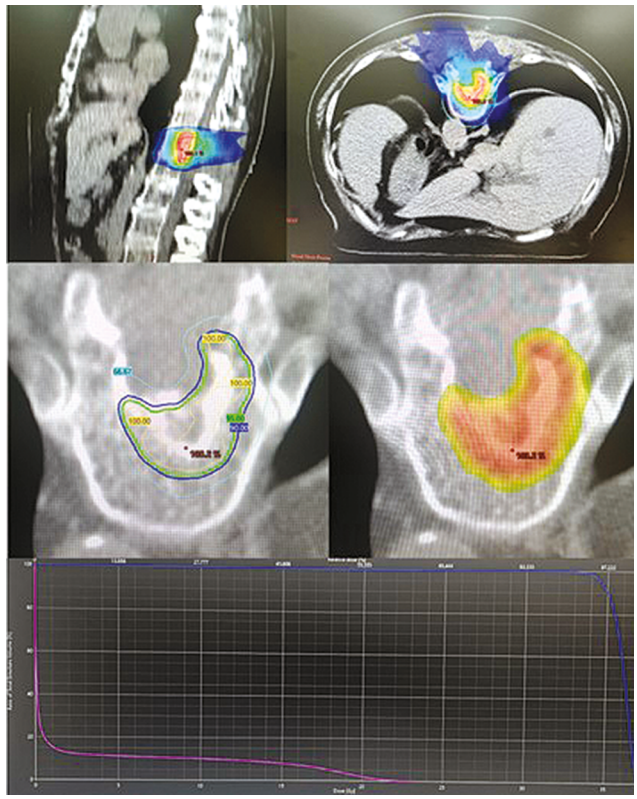

**Fig. 3.** Dose distribution in the radiation volume. Dose-volume (DVH) histogram, spinal cord (lower curve, pink) and PTV (upper curve, blue).
**Рис. 3.** Распределение дозы в объёме облучения. Гистограмма доза-объём (DVH), спинной мозг (нижняя кривая, розовый цвет) и PTV (верхняя кривая, синий цвет).

(LQM) with α/β of 2.45 Gy. The therapy was administered in a daytime hospital, using the Varian TrueBeam linear electron accelerator, in volumetric modulated arc therapy (VMAT) mode. The GTV to PTV margin was 0.3 cm; $D_{max}$ for the spinal cord was 23.16 Gy; D 0.15 $cm^3$ was 21 Gy. The irradiation target was positioned daily using cone beam computed tomography (CBCT). The patient was discharged on Day 5 after the start of external beam radiotherapy (the day of the last fraction); no adverse events were reported.

A follow-up MRI in September 2023 (5 months after SRT) revealed a tumor measuring 1.5×1.2 cm in the central parts and along the dorsal surface of the Th12 vertebral body, partially extending to the spinal canal, with moderate compression of adjacent areas of the dural sac and its contents (Fig. 4). The patient reported a decrease in right side back pain and pain in the right leg (pain intensity on a visual analogue scale: 50%–60%). There were no sleep disorders; the dose of tramadol was reduced to 500–100 mg/day (1–2 tablets). The patient was able to walk without the assistance of family members.

A follow-up MRI in May 2024 (13 months after SRT) revealed a tumor measuring 1.3×1.0 cm (previously 1.5×1.2 cm) along the posterior surface of the Th12 vertebral body, extending to the spinal canal, with diffuse, heterogeneous contrast uptake and moderate compression of the dural sac. There were no signs of local recurrence and/or disease progression; the clinical condition was stable (Fig. 4).

### Prognosis

The patient is currently being followed up in the A.I. Kryzhanovsky Krasnoyarsk Territory Clinical Cancer Center. There are no negative changes or imaging findings suggesting a relapse or progression. The prognosis is favorable, considering the low tumor grade (G1) and the performed treatment.

### Time Scale

When summarizing the important stages of this clinical case using a time scale, we arranged them chronologically (Fig. 5).

## DISCUSSION

CHS is a malignant neoplasm of cartilage tissue, accounting for approximately 20%–30% of primary bone sarcomas. This tumor is most commonly found in adults aged 30 to 60 years; it affects internal structures or the surface of a bone [10–12]. Both *de novo* CHS and progression of benign cartilage tissue tumors, such as osteochondromas and enchondromas, to CHS are possible [10]. CHS is most commonly found in pelvic

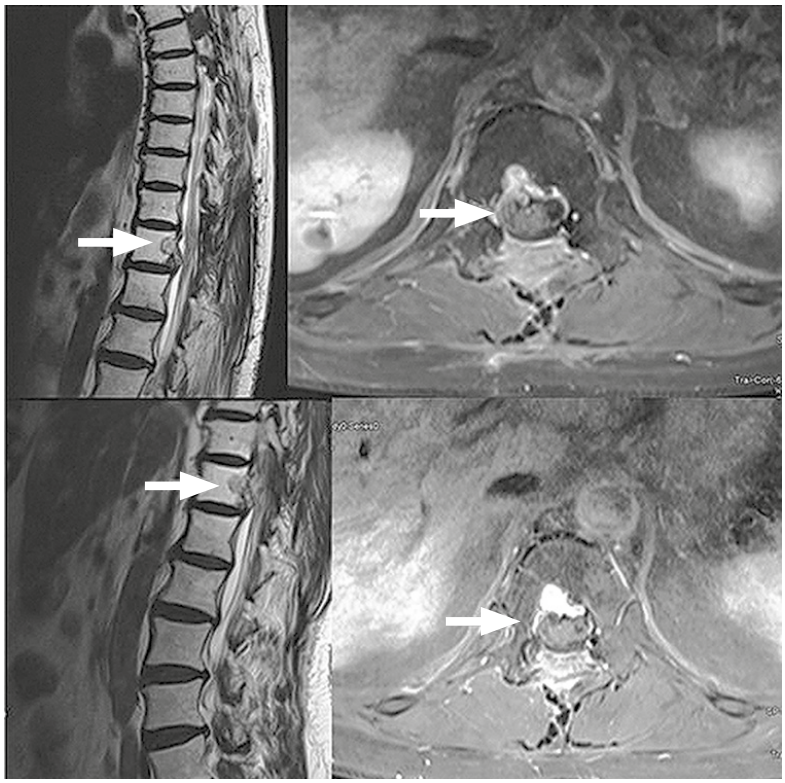

**Fig. 4.** MRI of the spine, T1 mode. The top photo is 5 months after stereotactic radiation therapy (stabilization). The lower photo is 13 months after stereotactic radiation therapy, T1 mode (stabilization).
**Рис. 4.** МРТ позвоночника, режим Т1. Верхнее фото — через 5 мес. после стереотаксической лучевой терапии (стабилизация). Нижнее фото — через 13 мес. после стереотаксической лучевой терапии, режим Т1 (стабилизация).

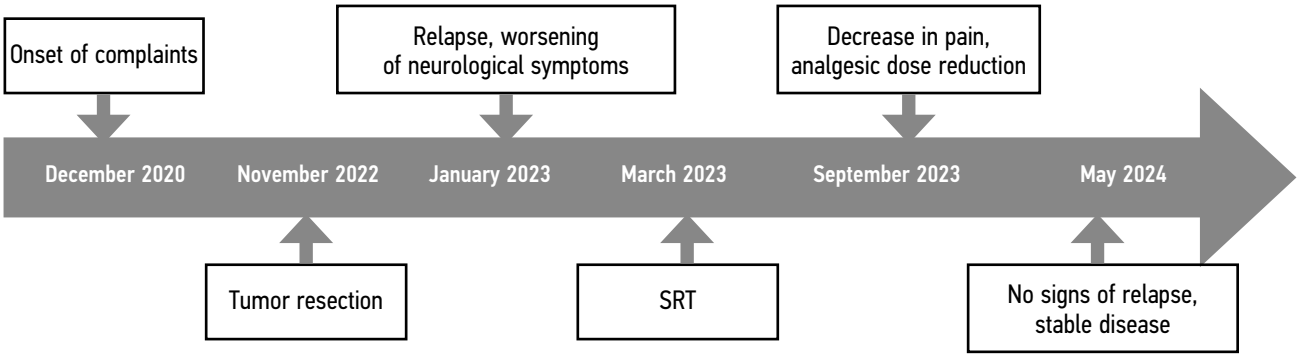


**Рис. 5.** Временная шкала. SRT — стереотаксическая лучевая терапия.
**Fig. 5.** Time scale. SRT — stereotactic radiation therapy.

bones, especially the iliac bone, and more rarely in proximal femoral and shoulder bones, distal femoral bone, and ribs. CHS of other bones is far more uncommon. The symptoms are frequently non-specific, persist for a long time (from several months to several years), and worsen as the tumor grows. The symptoms include pain, pathologic fractures, and multiple lung metastases [12, 13]. According to the World Health Organization data for 2020, there are three main CHS categories (I–III) depending on the tumor grade, tumor matrix characteristics, nuclear grade, and mitotic index [14]. Moreover, there are three subtypes: central, peripheral, and periosteal CHS [10]. The treatment strategy is determined by the age, disease stage, and tumor size, location, and grade [1, 15]. CHS is known to be chemotherapy- and radiotherapy-resistant due to slow cell proliferation, overexpression of the MDR1 protein involved in drug resistance, poor vascularization, and dense extracellular matrix, which impairs the delivery of antineoplastic drugs and causes tissue hypoxia, decreasing radiolysis [16].

Despite the sufficient efficacy of surgical treatment in CHS (particularly G1), these tumors are frequently difficult to access, reducing the possibility of curative surgery and increasing the relapse rate (20%–58%) [5–7]. Mutilating surgeries that reduce the risk of positive resection margin are not always technically feasible. Moreover, these procedures decrease quality of life and require subsequent surgical repair, increasing the risk of infection and anesthetic risks. Modern radiotherapy methods minimize the extent of surgery by exposing the residual tumor to curative doses.

As previously mentioned, conventional low-dose radiotherapy (conventional fractionation 1.8–2 Gy) has demonstrated low efficacy in clinical studies due to biological characteristics of tumors and their microenvironment [17]. Local control of CHS requires doses above 70 Gy; however, these doses are difficult to achieve with conventional conformal RT, because they exceed the permissible radiation exposure for surrounding tissues, where the permissible dose is significantly lower (e.g., 50 Gy for the spinal cord). Modern radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT), stereotactic radiosurgery (SRS), and proton radiotherapy (PRT), can overcome these limitations owing to the high beam aiming accuracy [18]. Studies demonstrate promising long-term outcomes in patients with spinal tumors when using IMPT and IMRT for the treatment of CHS [19]. Survival parameters depend on the dose, age, tumor size, and extent of surgical treatment; however, the precision of radiotherapy still needs to be improved for a greater therapeutic effect [20]. Proton radiotherapy (PRT) and carbon ion radiotherapy (CIRT) are the preferred techniques. However, these methods are significantly (3–5 times) more costly than conventional linear electron accelerator (LINAC)-based RT. Moreover, they are less accessible to patients (Russia has only four proton irradiation facilities and no CIRT facilities) [9]. Considering the age, severity of the condition, and long-distance commute to specialist centers, it is critical to achieve a balance between the availability of photon RT and the precision of heavy particle therapy. Thus, experience with conventional electron accelerator-based stereotactic radiation therapy in IMRT and VMAT modes is particularly relevant for Russian oncologists.

The majority of published works on proton radiotherapy in CHS (and other conditions) use passive scattering techniques, preventing an objective comparison between intensity-modulated PRT and stereotactic photon irradiation. Publications on proton radiotherapy largely focus on conventional fractionation, and experience with hypofractionated heavy particle irradiation is currently limited [21]. There are very few direct comparisons, partly due to the low incidence of CHS. However, available studies demonstrate comparable efficacy. For example, Ahmed et al. [22] found that stereotactic photon irradiation was 70% effective for local tumor control. Cho et al. [23] demonstrated that the efficacy of photon SRT in local tumor control was 88.9% after 3 years and 80% after 5 years. In a study by Iyer et al. [24], local tumor control with stereotactic photon RT as a combination therapy reached 68%. According to Jiang et al. [25], this parameter reached 80% during primary CHS treatment, whereas Kim et al. [26] found that it was 100% after 2 years and 80% after 5 years. Proton radiotherapy is more effective at local tumor control: from 94.4% according to Weber et al. [27] to 97.5% according to Feuvret et al. [28]. Given the lack of direct comparisons and the rare nature of the disease, the difference in therapeutic efficacy between stereotactic photon RT and proton RT is unknown. However, it is evident that patients with CHS must be treated at specialty photon radiotherapy centers delivering IGRT and IMRT (VMAT), or at proton radiotherapy centers.

## CONCLUSION

Radiotherapy in spinal CHS is challenging in real-world practice. Proton radiotherapy and carbon ion radiotherapy are the best treatment options for these neoplasms. These techniques minimize irradiation of surrounding critical structures, such as the spinal cord, while providing maximum radiation exposure for the tumor. However, these radiotherapy techniques are costly and not always available, if not completely unavailable, in Russia. Thus, intensity-modulated stereotactic photon RT, which also ensures high-precision tumor irradiation, is used as an alternative option. The modern external beam radiotherapy technique described in this paper overcomes radioresistance of chondrosarcomas, ensuring long-term remission in this patient population.

## ADDITIONAL INFORMATION

**Authors' contribution.** D.V. Chernyaev — patient supervision and treatment, writing an article; V.A. Kozin — advising on the choice of patient treatment tactics, assistance in writing an article; R.A. Zukov — scientific guidance, review of the article and making edits. All authors approved the manuscript (the version for publication), and also agreed to be responsible for all aspects of the work, ensuring proper consideration and resolution of issues related to the accuracy and integrity of any part of it.

**Consent for publication.** The patient voluntarily signed an informed consent form for the publication of personal medical information in an impersonal form in the Russian Journal of Oncology, as well as for the transfer of an electronic copy of the signed informed consent form to the editorial staff of the journal dated June 03, 2024.

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