Ann Med Res 2021;28(5):884-7

Annals of Medical Research
DOI: 10.5455/annalsmedres.2020.05.446

Original Article

Clinical experience in the treatment of spinal cord tumors with cyberknife® fractionated stereotactic radiotherapy

Gulhan Guler Avci[1], Gonca Altinisik Inan[2], Suheyla Aytac Arslan[2], Yildiz Guney[3], Mehtap Coskun Breuneval[4]

[1]Department of Radiation Oncology, Faculty of Medicine, Gaziosmanpasa University, Tokat, Turkey
[2]Department of Radiation Oncology, Faculty of Medicine, Yildirim Beyazit University, Ankara, Turkey
[3]Department of Radiation Oncology, Ankara Memorial Hospital, Ankara, Turkey
[4]Centre Hospitalier Universitaire vaudois CHUV, Lausanne, Switzerland

Abstract

Aim: The aim of the study is to evaluate the efficacy and safety of Cyberknife® fractionated stereotactic radiotherapy (FSRT) in spinal cord tumors. The secondary aim is to present short-term local control of the patients with spinal cord tumors.

Materials and Methods: Ten patients with spinal cord tumors who underwent FSRT between January 2010 and May 2014 were retrospectively analyzed. FSRT was administered in a median dose of 20 Gy (range, 16-40 Gy) in a median 5 fractions (range, 4-6 fractions). Radiological / pathological diagnoses of the patients are meningioma (n = 3), schwannoma (n = 1), neurofibroma (n = 1), hemangioblastoma (n = 1), chordoma (n = 1), recurrent medulloblastoma (n = 1), recurrent ependymoma (n = 2).

Results: The median age was 57 years (range, 22-84 years). The median tumor volume was 3.3 cm^3 (range, 1.8- 74 cm^3). Tumor localization was cervical in six cases, lumbar in three cases, and thoracic in one case. The median follow-up time was 13 months (range, 3-48 months). Clinical improvement was observed by FSRT in all patients except the three cases. Tumor control (no progression) was achieved in all cases. Radiologically, 6 patients were stable, 2 patients had complete and 1 patient had a partial response. No acute toxicity due to FSRT was observed in any cases.

Conclusion: Stereotactic radiosurgery /radiotherapy provides acceptable toxicity and excellent local control results in patients with spinal cord tumors. However, well-designed studies with longer follow-up and a large number of patients are warranted.

Keywords: Cyberknife®; fractionated stereotactic radiotherapy; local control; spinal cord tumors; toxicity

INTRODUCTION

Primary spinal cord tumors constitute approximately 2-4% of central nervous system malignancies and they are classified as intramedullary and extramedullary. Intramedullary tumors constitute one-third of them. Although they are mostly benign tumors, they have severe morbidity and mortality rates. In cases where surgery cannot be performed, radiotherapy (RT) is used to reduce tumor volume, improve neurological symptoms and control pain (1). Chemotherapy or immunotherapy has a partial effect especially for benign spinal tumors (2).

Nowadays, with the technological advances in RT, novel and promising RT techniques are available. In RT of the spinal cord or paraspinal lesions, not exceeding the maximum tolerance dose of spinal cord is the most important for the risk of myelopathy. With the stereotactic radiosurgery (SRS), which is the advanced RT technique, both the spinal cord can be maximally protected with millimeter precision and the ablation dose can be delivered to the target volume. Previous SRS techniques (e.g. Gammaknife) were technically limited, especially for extracranial treatments. Recently, advanced SRS techniques have allowed for a suitable and accurate extracranial radiosurgery by tracing the spinal segments without the need to insert a reference marker (3).

Spinal stereotactic radiotherapy (SRT) seems to be a promising treatment option in the multidisciplinary treatment of spinal cord tumors (4-6). The aim of the SRT is to apply effective treatment by reaching high biological effective doses (BED) (7). In cases with spinal tumors that cannot be operated or have residual tumor after surgery, SRT, especially applied with Cyberknife, appears to be an appropriate alternative treatment method (8). This study aimed to evaluate the efficacy and safety of Cyberknife® fractionated stereotactic radiotherapy (FSRT) in spinal cord tumors. The secondary aim is to present short-term local control of the patients with spinal cord tumors.

Received: 07.05.2020 **Accepted:** 27.07.2020 **Available online:** 18.05.2021
Corresponding Author: Gulhan Guler Avci, Department of Radiation Oncology, Faculty of Medicine, Gaziosmanpasa University, Tokat, Turkey **E-mail:** drgulhanguler@hotmail.com

MATERIALS and METHODS

Ten patients with spinal cord tumors who underwent FSRT between January 2010 and May 2014 in Ankara Oncology Hospital were retrospectively analyzed. FSRT was applied in three cases due to postoperative residual tumor, in three cases due to recurrence after surgery, and the remaining four cases underwent FSRT as primary treatment because of no suitable for surgery. Radiological / pathological diagnoses of the patients are meningioma (n=3), schwannoma (n=1), neurofibroma (n=1), hemangioblastoma (n=1), chordoma (n=1), recurrent medulloblastoma (n=1), recurrent ependymoma (n=2). FSRT was implemented as a re-irradiation to patients with one recurrent medulloblastoma and two recurrent ependymoma, while others had no previous history of RT. All patients were premedicated with 8 mg dexamethasone and H2-receptor antagonists (ranitidine) before treatment. The patients and characteristics are shown in Table 1.

Table 1. Patients characteristics

Number of patients	10
Sex, n	
Male	5
Female	5
Age, years	
Median	57
Range	22-84
Tumor level, n	
Cervical	6
Thoracic	1
Lumbar	3
Surgery received, n	
Yes	7
No	3
Pathological / radiological diagnosis, n	
Meningioma	3
Schwannoma	1
Neurofibroma	1
Hemangioblastoma	1
Chordoma	1
Recurrent medulloblastoma	1
Recurrent ependymoma	2
Chemotherapy received, n	
Yes	1
No	9

Treatment Planning

All patients were treated with Cyberknife® (Accuray In corporated, Sunnyvale, CA) device. In 80% of the patients, the X-sight spine tracking technique and in the remaining 20%, the 6D skull tracking technique was used. FSRT was administered in a median dose of 20 Gy (range, 19-40 Gy) in 5 fractions in 8 cases. In two cases with recurrent ependymoma, 16 Gy in 6 fractions and 18 Gy in 4 fractions were delivered as re-irradiation. The prescribed doses were administered with a median 86% (range, 76%-95%) isodose. Details of parameters of treatment with FSRT are illustrated in Table 2.

Table 2. Details of Treatment of Cyberkine FSRT

Parameter of treatment	median (range)
Prescribed dose (Gy)	20 (16-40)
Fraction number (n)	5 (4-6)
Isodose line (%)	86 (76-95)
Volume of PTV (cm^3)	3.3 (1.8- 74)
CI	1.4(1.3-2.7)
HI	1.1 (1.1-2.8)
Beam number (n)	133 (63-190)
Spinal cord Dmax (Gy)	21.2 (4.5-26.8)

FSRT: Fractionated stereotactic radiotherapy, PTV: Planned Target Volume, Dmax: Maximum dose, HI: Homogeneity index, CI: Conformality index

Simulation computed tomography images were obtained with 1.5 mm thick sections. In determining the target volume of the patients, assistance was obtained from the fusion images performed with a magnetic resonance imaging (MRI) scan with a thickness of 3 mm. The contrast-enhancing lesion on the MRI was delineated as gross tumor volume (GTV). The planned target volume (PTV) was created by giving a 1 mm margin around the GTV from all directions. In Figure 1, the plan and isodose lines of Cyberknife® FSRT of the patient with operated-residual meningioma at the C2 vertebra level is demonstrated.

Statistical Analysis

SPSS version 24 was used for the analysis. The continuous (quantitative) variables are presented as the minimum-maximum and median. The categorical variables are presented as number (n) and ratio (%). Since the number of cases is low, no survival analyzes were performed.

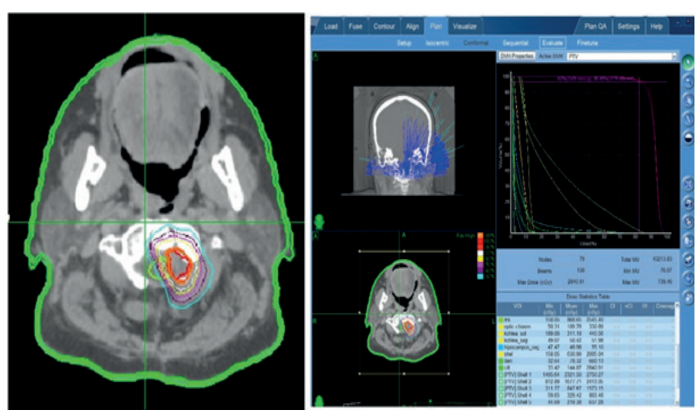

Figure 1. The plan and isodose lines of Cyberknife® FSRT of the patient with operated-residual meningioma at the C2 vertebra level

RESULTS

The median age was 57 years (range, 22-84 years). The gender distribution rate was observed equally. The median tumor volume was 3.3 cm3 (range, 1.8- 74 cm3). In the plans, the median maximum dose of the spinal cord was 21.2 Gy (range, 4.5-26.8 Gy).

Tumor localization was cervical in six cases, lumbar in three cases, and thoracic in one case. The most common symptoms were pain and numbness. Surgery was performed as the primary treatment in 6 of the cases, and 2/3 of them had gross total resection. In spinal schwannoma (1), spinal meningioma (1) and neurofibroma (1) cases, surgery could not be performed, they were diagnosed radiologically and received Cyberknife FSRT as the primary treatment. The patient with recurrent medulloblastoma previously received RT to the craniospinal (36 Gy) and posterior fossa (54 Gy). No surgery was considered in the relapse, and FSRT was primarily applied to the relapse. The two patients with recurrent spinal ependymoma also received postoperative limited field-spinal RT (46.8 Gy and 50 Gy) in their initial treatments and FSRT was delivered as secondary irradiation. Chemotherapy was administered only to the case of recurrent medulloblastoma.

The median follow-up time was 13 months (range, 3-48 months). While three cases were clinically stable, clinical improvement was achieved in the remaining 7 cases. Radiologically, 6 patients were stable, 1 patient had a partial response and 1 patient with recurrent meningioma at 9-months follow-up had a complete response. The patient with recurrent medulloblastoma also had a complete radiological response but relapsed at different localization 14 months after FSRT. One patient had difficulty in reaching the hospital because of the neurological deficit and it was learned to be clinically stable. None of our patients reported acute toxicity due to FSRT.

DISCUSSION

In this study with 10 patients with spinal cord tumors with a 48-month maximum follow-up period, clinical improvement was observed by FSRT in all patients except the three cases. Tumor control (no progression) was achieved in all cases. Radiologically, 6 patients were stable, 2 patients had complete and 1 patient had a partial response. No acute toxicity due to FSRT was observed in any cases.

A large-scale study, assessing the efficacy and safety of spinal radiosurgery in the treatment of spinal cord tumors, has been reported by Dodd et al (9). In their study, 51 patients with 55 benign intradural extramedullary lesions underwent radiosurgery (with Cyberknife) with a radiation dose ranging from 18 to 20 Gy. At the 36-month follow-up, 61% of the lesion did not change, while 31% shrink. As a side effect, only one patient reported that myelopathy developed (9). Another similar large-scale study was performed with 73 patients with spinal cord tumors (neurofibroma (25), schwannoma (35) and meningioma (13)) and radiosurgery was implemented in a single fraction at doses ranging from 15 to 25 Gy (10). At the median 37 months follow-up, radiographic tumor control was achieved in all patients. Radiation-induced spinal cord toxicity developed in 3 patients (10). In the present study, no radiation-induced myelopathy or any adverse effects were observed during the median 13-month follow-up.

Chang et al. (11) also reported their radiosurgery experience in 20 patients with 30 spinal cord lesions. Stereotactic radiosurgery (SRS)/SRT was performed at doses of 14-33 Gy in 1-5 fractions. Whilst shrinkage was observed in the size of 57% of the lesions, no change was observed in 33%. Progression was detected in 10% of the lesions (11). In a study of 39 patients with spinal meningioma and schwannomas, radiosurgery was administered as a median prescribe dose 14 Gy (12). Similar to our study, no progression was observed in any patient. The size of 19 lesions decreased whereas 20 lesions were stable. The reduction of pain level was reported in 8 of 19 patients with pain symptoms (12). In the present small scale study, clinical improvement was observed in 7 of 10 patients. In parallel with the aforementioned studies, tumor control was achieved radiologically in all patients undergoing SRT and no progression was reported in any patient. In only one case, the disease recurred in a different localization.

Microsurgical resection is an accomplished and effective main treatment in benign spinal cord tumors. However, alternative treatments are needed when surgery harbors high complication probability. Optimal surgery may not be possible not only in terms of complications but also due to multiple lesions, recurrent tumors or medical problems. As an alternative to surgery in such cases, SRS/SRT is an effective, reliable and non-invasive treatment option. In the non-operative management of benign spinal cord tumors, SRT has considerable effects in both local control and pain-symptom control (13-16). In the Korean series of 54 patients with benign tumor (47 spinal schwannomas), a single dose (median 13 Gy) was administered to most of the patients (72%) as a primary treatment. At the median 43-months follow-up, all patients with neurological symptoms recovered and significant improvement in pain scores was reported. Fifty-five percent of the lesions were regressed (14). In their study with 38 patient-47 benign spinal cord tumors, Kalash et al (15) compared low-dose (BED10 Gy≤30) and high dose (BED10 Gy> 30) SRT in terms of local control. No significant difference was reported between the two groups with respect to local control and long-term toxicity (15). Chin and colleagues (16) presented the results of 120 patients with 149 benign spinal tumors treated with 16 Gy in one fraction or 20 Gy in two fractions. The 3-year and 5-year local control rates were 98% and 95%, respectively. Local failure was observed in only 9 patients. In the recurrent cases, there was no difference in respect of prescription dose or minimum dose (16).

Our study has some limitations. It is a retrospective and small series. Objective questionnaires evaluating the pain-symptom scale were not used in the initial admission and routine controls.

CONCLUSION

Stereotactic radiosurgery/SRT provides acceptable toxicity and excellent local control results in patients with spinal cord tumors. However, a large number of patients investigating the importance of SRS/SRT in the treatment of spinal cord tumors and well-designed studies with longer follow-up are warranted.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The Departmental Ethics Committee of University of Health Sciences Ankara Dr. Abdurrahman Yurtaslan Oncology Hospital approved this trial at the meeting number 123, on 4 May 2021.

REFERENCES

1. Grimm S, Chamberlain MC. Adult primary spinal cord tumors. Expert Rev Neurother 2009;9:1487-95.
2. Sioka C, Kyritsis AP. Chemotherapy, hormonal therapy and immunotherapy for recurrent meningiomas. J Neurooncol 2009;92:1-6.
3. Adler JR Jr, Chang SD, Murphy MJ, et al. The Cyberknife: A frameless robotic system for radiosurgery. Stereotact Funct Neurosurg 1997;69:124-8.
4. Sahgal A, Ames C, Chou D, et al. Stereotactic body radiotherapy is effective salvage therapy for patients with prior radiation of spinal metastases. Int J Radiat Oncol Biol Phys 2009;74:723-31.
5. Sahgal A, Chou D, Ames C, et al. Image-guided robotic stereotactic body radiotherapy for benign spinal tumors: the University of California San Francisco preliminary experience. Technol Cancer Res Treat 2007;6:595-604.
6. Sahgal A, Larson DA, Chang EL. Stereotactic body radiosurgery for spinal metastases: a critical review. Int J Radiat Oncol Biol Phys 2008;71:652-65.
7. Ryu SI, Chang SD, Kim DH, et al. Image-guided hypo-fractionated stereotactic radiosurgery to spinal lesions. Neurosurgery 2001;49:838-46.
8. Gerszten PC, Welch WC. Cyberknife radiosurgery for metastatic spine tumors. Neurosurg Clin N Am 2004;15:491-501.
9. Dodd RL, Ryu MR, Kamnerdsupaphon P et al. CyberKnife radiosurgery for benign intradural extramedullary spinal tumors. Neurosurgery 2006;58:674-85.
10. Gerszten PC, Burton SA, Ozhasoglu C et al. Radiosurgery for benign intradural spinal tumors. Neurosurgery 2008;62:887-95.
11. Chang UK, Rhee CH, Youn SM et al. Radiosurgery using the Cyberknife for benign spinal tumors: Korea Cancer Center Hospital experience. J Neurooncol 2011;101:91-9.
12. Kufeld M, Wowra B, Muacevic A et al. Radiosurgery of spinal meningiomas and schwannomas. Technol Cancer Res Treat. 2012;11:27-34.
13. Hwang L, Okoye CC, Patel RB et al. Stereotactic body radiotherapy for benign spinal tumors: Meningiomas, schwannomas, and neurofibromas. J Radiosurg SBRT 2019;6:167-77.
14. Shin DW, Sohn MJ, Kim HS, et al. Clinical analysis of spinal stereotactic radiosurgery in the treatment of neurogenic tumors. J Neurosurg Spine 2015;23:429-37.
15. Kalash R, Glaser SM, Flickinger JC, et al. Stereotactic body radiation therapy for benign spine tumors: is dose de-escalation appropriate? J Neurosurg Spine 2018;29:220-5.
16. Chin AL, Fujimoto D, Kumar KA et al. Long-Term Update of Stereotactic Radiosurgery for Benign Spinal Tumors. Neurosurgery 2019;85:708-16.