Radiosurgery for benign tumors of the spine using the Synergy S with cone-beam computed tomography image guidance

Clinical article

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Object. There is a growing body of evidence to support the safe and effective use of spine radiosurgery. However, there is much less experience regarding the use of radiosurgery for the treatment of benign as opposed to malignant spine tumors. This study represents an evaluation of, and reporting on, the technical aspects of using a dedicated radiosurgery system for the treatment of benign spine tumors.

Methods. Forty-five consecutive benign spine tumors were treated using the Elekta Synergy S 6-MV linear accelerator with a beam modulator and cone-beam computed tomography (CBCT) image guidance technology for target localization. The study cohort included 16 men and 29 women, ranging in age from 23 to 88 years (mean age 52 years). There were 14 cervical, 12 thoracic, 14 lumbar, and 5 sacral tumors. Forty-one lesions (91%) were intradural. The most common histological types of tumor were schwannoma, neurofibroma, and meningioma. Indications for radiosurgery included primary treatment in 24 cases (53%) and treatment of recurrent or residual tumor after open resection in 21 cases (47%).

Results. No subacute or long-term spinal cord or cauda equina toxicity occurred during the follow-up period (median 32 months). The mean maximum dose received by the gross tumor volume (GTV) was 16 Gy (range 12–24 Gy) delivered in a single fraction in 39 cases. The mean lowest dose received to the GTV was 12 Gy (range 8–16 Gy). The GTV ranged from 0.37 to 94.5 cm³ (mean 13.7 cm³, median 5.9 cm³). In the majority of cases, a planning target volume expansion of 2 mm was employed (38 cases; 84%). The mean maximum point dose delivered to the spinal cord was 8.7 Gy (range 4–11.5 Gy); the mean volume of the spinal cord that received greater than 8 Gy was 0.9 cm³ (range 0.0–5.1 cm³); and the mean dose delivered to 0.1 cm³ of the spinal cord was 7.5 Gy (range 3–10.5 Gy). The mean maximum point dose delivered to the cauda equina was 10 Gy (range 0–13 Gy); the mean volume of the cauda equina that received greater than 8 Gy was 1.45 cm³ (range 0.0–10.6 cm³); and the mean dose delivered to 0.1 cm³ of the cauda equina was 8 Gy (range 0.5–11 Gy).

Conclusions. In this study the authors describe the contouring and prescribed dose techniques used in the treatment planning and delivery of radiosurgery for benign neoplasms of the spine using CBCT image guidance. This technique may serve as an important reference for the performance of radiosurgery when one believes it is clinically indicated as a treatment modality for a benign spine tumor that is associated with both a high safety profile and a strong positive clinical outcome.

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KEY WORDS • cone-beam computed tomography • spine radiation treatment • spine tumor • stereotactic radiosurgery • meningioma • neurofibroma • schwannoma

STEREOTACTIC radiosurgery for the treatment of a variety of benign intracranial lesions has become widely accepted; it has excellent long-term outcomes and is associated with minimal toxicity.^{17,34,37,51,59} Radiation therapy has been used for the treatment of numerous benign diseases for decades.^{29,31,36,54,57} Benign tumors of the spine represent a wide variety of histologi-

cal types of lesions that occur within the intradural space as well as in epidural, paraspinal, and vertebral body locations. The primary treatment option for many benign spinal neoplasms is open resection. The safety and effectiveness of such surgery has been clearly documented.^{8,32–37} The majority of spinal meningiomas, schwannomas, and neurofibromas are noninfiltrative and can be completely and safely resected using microsurgical techniques.^{2,38,39,43} When complete tumor removal is achieved, recurrence is unlikely.^{7,32,35,41}

In certain circumstances, however, some patients are

Abbreviations used in this paper: CBCT = cone-beam computed tomography; GTV = gross tumor volume; OAR = organ at risk; PTV = planning target volume.

less than ideal candidates for standard open resection because of age, medical comorbidities, recurrent nature of the tumor, or anatomical location of the lesion.¹⁶ Tumors that have recurred after open resection may make safe resection challenging or impossible. Multiple benign spinal tumors, which are commonly found in familial neurocutaneous disorders, may be a pattern of spinal disease better suited for a less invasive radiosurgical option. It is in such clinical circumstances that radiosurgery may serve as an important treatment option for these patients.

The recent development of frameless image-guided radiosurgery allows for the ability to treat benign tumors throughout the body.^{1,16,18,21,50} There is now a substantial body of literature that supports the use of extracranial radiosurgery for the treatment of a variety of malignant spinal tumors.^{3,8–10,12,14,15,22,23,26,28,40,41,44,46,47,49,50,58,61,62} Nevertheless, there is much less experience regarding the use of radiosurgery for the treatment of benign tumors of the spine.

Cone-beam computed tomography image guidance technology now has been adapted for radiosurgical setup with delivery by a variety of radiosurgery delivery systems.^{20,27,53} The clinical experience and current trends at our center for radiosurgery in the treatment of benign tumors of the spine has recently been reported.²¹ Given the gradual widespread adoption of radiosurgery as part of the management of benign spine tumors,⁴² this study was undertaken to carefully evaluate and report on the technical aspects of radiosurgery for benign tumors of the spine using a CBCT image guidance technique.

Methods

Forty-five consecutive benign spine tumors underwent radiosurgery treatment and were evaluated in an institutional review board–approved investigation. Radiosurgery was offered to patients for whom microsurgical resection was believed to be contraindicated or in cases of strong patient preference. All cases had well-circumscribed lesions, no evidence of spinal instability, and generally minimal compromise of spinal cord function. All of the patients were carefully followed up by a dedicated research nurse using Gd-enhanced MRI at 3, 6, and 12 months and yearly thereafter. Neurological examination and the occurrence of any toxicity were evaluated in person at each follow-up imaging time point or by telephone if necessary.

All lesions were treated using the Elekta Synergy S 6-MV linear accelerator with a beam modulator and CBCT image guidance combined with a HexaPOD couch that allows correction of patient positioning in 3 translational and 3 rotational directions. In a plane orthogonal to the linear accelerator, the CBCT image guidance system is mounted on the gantry. Our technique for utilizing CBCT for radiosurgical image guidance has been described elsewhere.^{19,20}

Summary of Study Cohort

The study cohort included 16 men and 29 women, ages 23 to 88 (mean age 52 years). Table 1 lists the characteristics of the treatment group. Lesion location included 14 cervical, 12 thoracic, 14 lumbar, and 5 sacral

tumors. The Karnofsky Performance Scale scores for the cohort ranged from 70% to 90% (mean 88%). The most common histological types of tumor were schwannoma (16 cases), neurofibroma (14 cases), and meningioma (10 cases). The remaining histological types included ganglioglioma, hemangioma, aneurysmal bone cyst, and giant cell tumor. Nine patients had previously diagnosed neurofibromatosis. In 41 cases (91%) the tumors were intradural. Radiosurgery was used as the primary treatment modality in 24 cases (53%) and for tumor recurrence after prior open resection in 21 cases (47%). Nineteen patients (42%) reported a significant component of pain before radiosurgery. Figure 1 demonstrates a representative case.

Six patients (13%) had undergone surgical stabilization at the time of open resection and therefore spinal instrumentation was present at the time of the radiosurgical treatment. All patients were believed to have a stable spine at the time of radiosurgery. Two lesions had been treated with prior radiotherapy at the index location. Magnetic resonance imaging (or CT myelography when the patient could not undergo MRI) was fused with the planning CT scan for contouring purposes in all cases if possible. The prescribed dosage and fractionation were based on tumor size, volume, and location; the degree of potential spinal cord exposure; and history of previous irradiation. The radiosurgery procedure was successfully completed in all patients.

Data Collection

The data collected for each case were entered into a database developed by the Elekta Spine Radiosurgery Research Consortium. This is an international research consortium consisting of 6 institutions, all of which have a research and clinical focus on image-guided high-precision radiotherapy with a particular focus on spine radiosurgery. The data set has a particular focus on contouring and prescription techniques as well as toxicity documentation.

Results

The patients were immobilized with the aid of a BodyFix (total body bag, Medical Intelligence) when treatment sites were below T-6; otherwise, a head and shoulder mask with an S-board (CIVCO) was used. The Pinnacle treatment planning system (version 8.0, Philips) and a 1.5-mm CT slice thickness were used to plan all spine radiosurgery treatments. Fourteen patients were immobilized using a mask, and 31 patients were immobilized using the BodyFix.

Imaging Evaluation

The relationship of the tumor to the spinal cord or cauda equina was graded using the scoring system described by Bilsky et al.⁷ for each case based on MRI. The distribution of case by grade was as follows: Grade 0, 7 cases; Grade 1a, 2 cases; Grade 1b, 3 cases; Grade 1c, 1 case; Grade 2, 25 cases; and Grade 3, 7 cases. The degree of circumferential enclosure of the spinal cord or cauda equina was recorded for each case, and then patients were divided into the following groups: 0°–90°, 18 cases; 90°–180°, 18 cases; 180°–270°, 6 cases; and 270°–360°, 3

TABLE 1: Characteristics in 45 patients who underwent radiosurgery for benign spine tumors

Characteristic	Value
age in yrs	
mean	52
range	23–88
sex—no. of patients (%)	
female	16 (36)
male	29 (64)
intradural location—no. of lesions (%)	41 (91)
lesion location—no. of lesions	
cervical	14
thoracic	12
lumbar	14
sacral	5
mean GTV in cm ³ (range)	13.7 (0.4–94.5)
mean prescribed max dose to GTV in Gy (range)	16 (12–24)
histological type—no. of lesions	
meningioma	10
schwannoma	16
neurofibroma	14
other	5
primary indication for treatment—no. of patients (%)	
primary treatment modality	24 (53)
recurrence after open resection	21 (47)

cases. A significant degree of paraspinal involvement of the tumor was present in 13 cases (29%). No evidence of tumor growth was seen on serial images within the GTV during the follow-up period (median 32 months, range 3–55 months).

Contouring and Dosimetric Evaluation

An MRI fusion technique was used for target delineation in 42 cases (93%). The target volume concept employed in all cases was the GTV, as seen on enhanced imaging. A clinical target volume was not used for the benign tumors. In 10 cases, the lesions spanned more than a single vertebra. Our experience has shown that accurate contouring of benign spine tumors is nearly impossible without the use of MRI fusion. High-resolution-sequence MRI often improves resolution degraded by instrumentation. In cases of instrumentation, we have attempted to resolve questions of tumor definition by performing CT myelography. Titanium implants are preferred over stainless steel to decrease the imaging artifact. In some cases in which radiosurgery is already anticipated prior to open surgery, such as in cases involving large “dumbbell” foraminal tumors, spinal instrumentation is only placed on the contralateral side of the tumor to allow for maximum tumor definition for radiosurgery.

The mean maximum radiation dose received by the GTV was 16 Gy (range 12–24 Gy) delivered in a single fraction in 39 cases. In 6 cases in which the tumor was found to be intimately associated with the spinal cord,

Fig. 1. Representative case of a 49-year-old man who presented with a symptomatic left C5–6 neurofibroma associated with spinal cord compression. **A:** Preoperative axial T1-weighted Gd-enhanced MR image demonstrating the tumor. The patient underwent surgical decompression and partial resection of the tumor. **B:** Postoperative axial T1-weighted Gd-enhanced MR image demonstrating residual tumor. The patient had residual weakness and significant radicular pain and was referred for radiosurgery. **C and D:** Axial (C) and coronal (D) CT scans showing the isodose lines of the treatment plan. The GTV was prescribed at 14 Gy, which was delivered in a single fraction with a 2-mm PTV expansion of 12 Gy. The maximum dose delivered to the spinal cord was 10 Gy with a 1-mm safety expansion that received a maximum dose of 9 Gy. **E:** Dose-volume histogram of the radiosurgery treatment plan demonstrating 90% coverage of the GTV and 99% coverage of the PTV. The patient reported significant improvement in his symptoms within 1 month.

with distortion of the spinal cord itself, the prescribed dose to the GTV was delivered in 3 fractions. The mean lowest dose received by the GTV was 12 Gy (range 8–16 Gy). The GTV ranged from 0.37 to 94.5 cm³ (mean 13.7 cm³, median 5.9 cm³).

A PTV expansion was used to account for targeting inaccuracies. In the majority of cases, a PTV expansion of 2 mm was employed (38 cases; 84%). The remaining PTV expansion ranged from 0 to 3 mm. As a rule the PTV prescribed dose was 2 Gy less than the prescribed dose to the GTV. The mean number of beams used to deliver radiosurgical treatment was 10 (median 9 beams, range 7–14 beams).

Clinical Evaluation and Toxicity

No subacute or long-term spinal cord or cauda equina toxicity occurred during the follow-up period (median 32 months, range 3–55 months). Furthermore, no acute radiation-induced dermatitis nor acute dysphagia was encountered. A single patient with a C-2 lesion reported the sensation of neck swelling with questionable dysphagia 1 month after treatment; this completely resolved. No acute fracture secondary to radiation-induced osteopenia was encountered during the follow-up period. There were no deaths in this series.

Nineteen patients (42%) reported a significant component of pain before radiosurgery. Fifteen of these patients reported a significant improvement or complete resolution of pain at the last follow-up. Fifteen patients had a neurological deficit on examination before radiosurgery (motor and sensory in 5 patients and sensory alone in 10 patients). Four motor deficits remained stable as of the last follow-up, and 1 motor deficit worsened in a patient with neurofibromatosis Type 1. Ten sensory deficits improved according to patient reports as of the last follow-up, and 1 sensory deficit worsened again in a patient with neurofibromatosis Type 1.

The planning spinal cord OAR was defined as the spinal cord itself based on MRI or CT myelography in all cases. The planning cauda equina OAR was defined as the nerve roots themselves based on MRI, especially in cases of intradural or foraminal tumors. A 1-mm expansion of the spinal cord OAR was used for lesions at the level of the spinal cord, with a maximum tolerance dose of 1 Gy greater than the spinal cord OAR.

The mean maximum point dose to the spinal cord in this series for the 26 tumors located at the level of the spinal cord was 8.7 Gy (range 4–11.5 Gy). The mean volume of the spinal cord that received greater than 8 Gy was 0.9 cm³ (range 0.0–5.1 cm³). The mean dose to 0.1 cm³ of the spinal cord in these 26 cases was 7.5 Gy (range 3–10.5 Gy).

The mean maximum point dose to the cauda equina for the 18 lesions located at the level of the cauda equina was 10 Gy (range 0–13 Gy). The mean volume of the cauda equina that received greater than 8 Gy was 1.45 cm³ (range 0.0–10.6 cm³). The mean dose to 0.1 cm³ of the cauda equina was 8 Gy (range 0.5–11 Gy).

Discussion

Radiosurgery represents a great advance in the treat-

ment of both benign and malignant spine tumors. Radiosurgery has been documented to be an effective treatment modality for a variety of malignant tumors of the spine and spinal cord.^{3,8–10,12,14,15,22,23,26,28,40,41,44,46,47,49,50,58,62} Given their pathological similarities, there is no reason why benign spinal tumors would not be equally as responsive to radiosurgery as their intracranial counterparts.^{10,11,16,32–35,45} Multiple publications have now documented the safety as well as the long-term efficacy of radiosurgery for benign spinal tumors, including a 10-year follow-up experience.^{4,16,21}

There are significant differences between benign and malignant tumors of the spine that have affected the adoption of radiosurgery as a treatment modality for these benign lesions. The primary treatment option for most benign spinal neoplasms is microsurgical removal without adjuvant radiotherapy. The safety and effectiveness of such surgery has been clearly documented.^{13,16,24,30,43,55,56} In certain circumstances, however, some patients are less than ideal candidates for standard open resection because of age, medical comorbidities, the recurrent nature of the tumor, or the presence of multiple lesions occurring in the setting of a phakomatosis.¹⁶ It is in such clinical circumstances that radiosurgery may serve as an important treatment option for these patients.

Because the life expectancy of many patients with metastatic spine disease is rather limited and because radiation injury to normal structures such as the spinal cord can take years to manifest,¹⁶ there is substantial controversy regarding radiosurgery for the management of benign tumors of the spine. These benign tumors most frequently occur in patients with normal life expectancies. These lesions often are also intradural, with a close or sometimes contiguous anatomical relationship to the spinal cord or cauda equina. For this reason, the long-term consequences of neural toxicity secondary to radiosurgery perhaps are of even greater importance to patients with benign tumors than to those with metastatic spine disease. Furthermore, benign spine tumors have their own unique presentation, relationship to the spinal cord, and radiobiological response to radiosurgery, all of which represent unique challenges to the safe and effective application of radiosurgical ablation.¹⁶

Regardless of the delivery system used, in all cases the radiosurgical treatment plan must tightly conform the prescribed dose to the tumor target, while featuring deep dose gradients at the lesion's edge and the immediately surrounding normal tissue.⁶⁰ In the current paper we describe the technique that we have used for contouring benign tumors based on careful target delineation using MR fusion such that the GTV is defined as the edge of the visualized tumor. A PTV expansion of 2 mm is usually used for all tumors of the foramen at the level of the spinal cord as well as for tumors of the cauda equina and those in paraspinal locations. However, in instances in which the tumor is intimately associated with the spinal cord itself, no such PTV expansion is used. For cases in which the spinal cord itself is deformed by a tumor within the spinal canal, radiosurgical treatment is delivered in three separate sessions.

For spine radiosurgery, the spinal cord and cauda equina are the OARs that most frequently limit the pre-

scribed target dose.²⁵ Considerable attention has been given to attempted determinations of the radiation tolerance of the human and animal spinal cord and cauda equina to stereotactic body radiotherapy.^{5,6,48,50,52} In the present study we carefully report on the maximum point dose, mean volume receiving greater than 8 Gy, and mean dose to 0.1 cm³ for both the spinal cord as well as the cauda equina. Such doses to these neural structures were associated with an absence of radiation-induced toxicity.

Conclusions

Radiosurgery is a safe and clinically effective treatment alternative for some benign spinal neoplasms. Such lesions include those in which there is relatively little direct compression on the spinal cord, allowing for the safe delivery of a therapeutic dose of hypofractionated radiation. In this study we describe the contouring and prescribed dose techniques used in the treatment planning and delivery of radiosurgical treatment to benign neoplasms of the spine using CBCT image guidance. This technique may serve as an important reference for the use of radiosurgery when one believes that it is clinically indicated as a treatment modality for a benign spine tumor that is associated with both a high safety profile and a strong positive clinical outcome.

Disclosure

Dr. Novotny is a consultant to Elekta AB. The other authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Gerszten, Flickinger. Acquisition of data: all authors. Analysis and interpretation of data: Gerszten, Chen, Quader, Xu, Flickinger. Drafting the article: Gerszten, Chen. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Gerszten.

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