Is stereotactic radiosurgery the best treatment option for patients with spinal metastases?

Original article Gerszten PC *et al.* (2007) Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine* **32:** 193–199

SYNOPSIS

KEYWORDS CyberKnife®, malignant spinal cord compression, pain, radiosurgery, spinal metastases

BACKGROUND

Single-fraction stereotactic radiosurgery—an effective treatment for patients with brain tumors and brain metastases—is increasingly used to treat patients with spinal metastases.

OBJECTIVE

To evaluate the efficacy and safety of single-fraction spinal stereotactic radiosurgery for the treatment of patients with spinal metastases.

DESIGN AND INTERVENTION

This prospective, nonrandomized, longitudinal, cohort study took place at the University of Pittsburgh Medical Center, Pittsburgh, PA, USA. In total, 393 patients (142 men, 251 women; mean age 56 years) with 500 histologically verified metastases to the spine (73 cervical lesions, 212 thoracic, 112 lumbar, and 103 sacral) from a variety of primary sites were enrolled. Tumor volume ranged from 0.2 to 264 cm^3 (mean 46 cm^3). Study exclusion criteria were neurological deficit due to bony compression of neural elements and evidence of overt spinal instability. Patients were treated with a single radiation dose of 12.5–25 Gy using the CyberKnife® Image-Guided Radiosurgery System (Accuray Inc., Sunnyvale, CA) in conjunction with the Dynamic Tracking System 3.0 software. A 10-point visual analog scale, with 0 representing no pain and 10 representing the worst possible pain, was used to evaluate pain before and after radiosurgery, with pain improvement defined as a pain score improvement of at least three points. Radiographic tumor control was evaluated by at least two investigators, via direct comparison of the pretreatment CT image and the most recent post-treatment CT image. Patients were followed up for a median of 21 months (range 3–53 months).

OUTCOME MEASURES

The main outcome measures were pain improvement and tumor control.

RESULTS

Pain was the primary indication for radiosurgery in the case of 336 lesions (67%), and in the long term, pain improved in 290 (86%) of these cases following treatment. This improvement varied with the primary histopathology of the lesion; improvement was recorded in 96% of women with breast cancer, 96% of patients with melanoma, 94% of patients with renal-cell carcinoma and 93% of patients with lung cancer. In 51 cases (10%), spinal radiosurgery was employed as a 'salvage' treatment after conventional irradiation. Long-term radiographic tumor control in the entire study cohort was 88% for any metastases, 100% for breast and lung cancer metastases, 87% for renal-cell metastases and 75% for melanoma metastases. There were no instances of tumor progression at sites adjacent to the irradiated target area. When spinal radiosurgery was employed as the primary treatment modality (65 cases; 13%), tumor progression was halted in 90% of cases (100% of breast, lung and renal-cell carcinoma metastases and 75% of melanoma metastases). Radiosurgery resulted in at least some improvement in 30 of 35 (85%) patients with progressive neurological deficits before treatment. No spinal cord damage that could be attributable to the treatment was detected.

CONCLUSIONS

Spinal stereotactic radiosurgery achieved long-term pain and tumor control in this cohort, and is a safe and clinically effective treatment for patients with spinal metastases.

COMMENTARY

Dirk Rades* and Steven E Schild

Most patients with vertebral metastases receive radiotherapy for pain relief. Additionally, radiotherapy can prevent pathological fractures and malignant spinal cord compression (MSCC). External-beam radiotherapy (EBRT) results in significant pain relief in 70–80% of patients.[1] After EBRT with 1 × 8 Gy or 6 × 4 Gy, Steenland *et al.* reported a median time to progression of pain of 20 weeks.[1] Hence, there is a need to improve outcome for patients with vertebral metastases. It has been hypothesized that this aim might be achieved with higher doses of radiotherapy, and this is the rationale for the study by Gerszten *et al.*, who presented a large series of patients receiving single fractions of 12.5–25 Gy as radiosurgery, performed with the CyberKnife®.

Total radiation dose is limited by spinal cord tolerance. Biological effectiveness of irradiation depends on total dose and dose per fraction, and is calculated with the equivalent dose in 2-Gy fractions (EQD2), which varies with end point.[2] For tumor cell kill, EQD2 is 50 Gy for 20 Gy in 1 fraction and 20 Gy for 20 Gy in 10 fractions; single large fractions are considered more neurotoxic.

Dose-escalation without exceeding the spinal cord tolerance may be achieved with high-precision radiotherapy. Modern techniques, including image-guided and intensity-modulated radiosurgery, have been reported. These techniques allow the delivery of a high dose to the vertebral tumor without exceeding the spinal cord tolerance. Ryu *et al.* reported 100% pain relief in 10 patients following EBRT with 10 × 2.5 Gy plus a 6–8 Gy radiosurgery boost.[3] Milker-Zabel *et al.* observed significant pain relief in 13 of 16 (81%) patients reirradiated with a median of 39.6 Gy.[4] Gerszten *et al.* presented a retrospective series of 336 patients receiving 12.5–25 Gy in 1 fraction of radiosurgery (EQD2 for tumor cell kill: 23.4–72.9 Gy). Long-term pain relief was observed in 86% of patients. The results seem promising, in particular because toxic effects were minimal.

High-precision techniques can be safely administered only if patient positioning is accurate during the whole treatment. The mean treatment time for radiosurgery with the CyberKnife® is 90 minutes, meaning positioning may be difficult for patients with painful metastases. By comparison, single-fraction EBRT takes a few minutes. Radiosurgery seems most rational in patients with a favorable survival prognosis, because these patients may live long enough to develop progression of the previously irradiated spinal metastases. Better survival is associated with certain tumor types (breast cancer, prostate cancer), no visceral metastases, and Karnofsky performance score >70.[5] Radiosurgery seems helpful for patients with less radiosensitive tumors such as melanoma, sarcoma, and renal cell carcinoma, or with solitary metastasis. On the basis of the study by Gerszten *et al.*, radiosurgery seems both safe and effective.

The role of high-precision radiotherapy for patients with MSCC, who generally have a poor survival prognosis, needs further study. Patients with MSCC are usually treated with decompressive surgery followed by EBRT or, if they do not meet the criteria for surgery, with EBRT alone.

Radiosurgery may be administered to patients with MSCC who have a favorable survival prognosis or less radiosensitive tumors, who cannot receive surgery. The most important role of radiosurgery is for re-treatment of previously irradiated MSCC.

References

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Competing interests
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PRACTICE POINT
High-precision radiotherapy such as radiosurgery represents an alternative to conventional irradiation for painful spinal metastases in selected patients with a favorable survival prognosis