

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

→ Dirk Rades and Steven Schild

Results of new research show that high-precision radiotherapy, such as radiosurgery, represents an alternative to conventional irradiation for painful spinal metastases in selected patients with a favourable survival prognosis.

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 hypothesised 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 (see opposite).

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 tumour 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 tumour 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 patients (81%) re-irradiated 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 tumour 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. Radiotherapy seems most rational in patients with a favourable survival prognosis, because these patients may live long enough to develop progression of the previously irradiated spinal metastases. Better survival is associated with certain tumour types (breast cancer, prostate cancer), no visceral metastases, and Karnofsky performance score >70.⁵ Radiosurgery seems helpful for patients with less radiosensitive tumours such as melanoma, sarcoma and renal cell carcinoma, or with solitary metastasis. On the basis of

Dirk Rades is associate professor of Radiation Oncology and vice chair of the Department of Radiation Oncology at the University Hospital Schleswig-Holstein, Lübeck, Germany, and Steven Schild is professor of Radiation Oncology and vice chair of the Department of Radiation Oncology at the Mayo Clinic, Scottsdale, Arizona, USA. This article was first published in *Nature Clinical Practice Oncology* 2007 vol. 4 no. 7, and is reproduced with permission. www.nature.com/clinicalpractice, doi:10.1038/ncponc0846, ©2007 Nature Publishing Group

Synopsis

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

Background. Single-fraction stereotactic radiosurgery – an effective treatment for patients with brain tumours 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, non-randomised, 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. Tumour volume ranged from 0.2 to 264 cm³ (mean 46 cm³). 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 analogue 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 tumour control was evaluated by at least two investigators, via direct comparison of the pre-treatment 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 tumour 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 tumour 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 tumour progression at sites adjacent to the irradiated target area. When spinal radiosurgery was employed as the primary treatment modality (65 cases; 13%), tumour 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 tumour control in this cohort, and is a safe and clinically effective treatment for patients with spinal metastases.

Acknowledgement: The synopsis was written by Helen Jaques, Editorial Assistant, *Nature Clinical Practice*.

the study by Gerszten et al., radiosurgery seems both safe and effective.

The role of high-precision radiotherapy for patients with MSSC, who generally have a poor survival prognosis, needs further study. Patients with MSSC 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 MSSC who have a favourable survival prognosis or less

radiosensitive tumours, who cannot receive surgery. The most important role of radiosurgery is for re-treatment of previously irradiated MSSC.

References

1. E Steenland et al. (1999) The effect of a single fraction compared to multiple fractions on painful bone metastases: a global analysis of the Dutch Bone Metastasis Study. *Radiother Oncol* 52:101–109
2. MC Joiner and AJ Van der Kogel (1997) The linear-quadratic approach to fractionation and calculation of isoeffect relationships. In: GG Steel (ed) *Basic Clinical Radiobiology*. Oxford University Press, New York, pp 106–112
3. S Ryu et al. (2003) Image-guided and intensity-modulated radiosurgery for patients with spinal metastasis. *Cancer* 97:2013–2018
4. S Milker-Zabel et al. (2003) Clinical results of retreatment of vertebral bone metastases by stereotactic conformal radiotherapy and intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 55:162–167
5. YM Van der Linden et al. (2004) Prediction of survival in patients with metastases in the spinal column. *Cancer* 103:320–328