# Malignant epidural spinal cord compression: the role of external beam radiotherapy

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**Purpose of review**
Spinal cord compression is a common complication of metastatic malignancy. If not diagnosed and treated early when the patient is still able to ambulate, outcomes and survival are poor. The purpose of this study is to review treatment options for patients presenting with metastatic spinal cord compression and emphasize the importance of early diagnosis. This review also aims to highlight the need for ongoing research to improve patient outcomes.

**Recent findings**
Recent literature suggests that treatment choices should take into account overall patient prognosis and ambulation status at diagnosis. In particular, poor prognosis patients can be treated with short courses of radiation and longer courses of radiation may be associated with better local control and therefore should be considered for good prognosis patients. Patient prognosis can be estimated using validated scoring systems. MRI screening may be of benefit in selected patient groups deemed at high risk of developing spinal cord compression.

**Summary**
Despite being a common complication of metastatic bone disease, there is a paucity of high-level evidence to guide treatment practice. Current and future randomized trials are vital.

**Keywords**
metastatic, radiation, spinal cord compression

## INTRODUCTION

Metastatic epidural spinal cord compression (MESCC) is a potentially debilitating and common complication of cancer with an incidence varying between 2.5 and 14% of all cancer patients [1,2]. The most common primary solid tumour sites are breast, prostate, lung and myeloma. Survival after MESCC is related to primary tumour type ranging from 17 to 20 months for breast, prostate and myeloma to only 4 months for lung [3]. Most cases develop in patients already known to have cancer. Untreated, the majority of patients with spinal cord compression become paraplegic. Early detection and treatment when the patient is still able to walk results in the highest chance of ambulation [4,5].

The common early presenting symptoms are back pain, often radicular in nature, and mild sensory or motor changes of the extremities. Often the onset of symptoms is gradual over days to weeks; however, acute presentations with rapidly progressive symptoms do occur. Prognosis can be related to the speed of onset with a better prognosis in those with a longer prelude to the diagnosis being confirmed, one study finding that ambulatory recovery occurred in 86% of patients with a history of more than 14 days compared with only 35% when the history was 1–7 days [6]. In order to maximize ambulatory function, and in turn survival from MESCC, a high index of suspicion is essential in patients with pre-existing malignancy, particularly

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## KEY POINTS

- External beam radiotherapy either alone or in combination with decompressive surgery remains the treatment of choice for patients presenting with metastatic spinal cord compression.
- The optimal fractionation schedule for the treatment of spinal cord compression remains unknown, but new evidence suggests that the schedule should take into account overall patient prognosis.
- New techniques such as radiosurgery and stereotactic radiotherapy may be of benefit for highly selected patients including those with recurrent spinal cord compression.

those with known spinal metastases. Education of healthcare professionals, patients and their care givers can play important part in achieving early diagnosis. Once suspected, whole spine MRI is the diagnostic investigation of choice. For patients in whom an MRI is contraindicated or facilities are unavailable, then a spinal CT scan should be undertaken. Once confirmed, immediate treatment is vital as the treatment outcome is closely related to functional status at diagnosis. The role of screening high-risk patients is also worthy of consideration. A recent study in prostate cancer has suggested that the optimal frequency would be every 4–6 months for patients with previous MESCC, a rapidly rising or serum prostate specific antigen persistent back pain and annually for all others [7▪].

Initial treatment of MESCC is with steroids and either surgery followed by external beam radiotherapy or primary external beam radiation treatment (EBRT) alone. Selection of treatment depends on a range of individual patient factors including overall oncological disease status, burden of spinal metastases and patient performance status.

## INDICATIONS FOR EXTERNAL BEAM RADIATION TREATMENT IN THE MANAGEMENT OF MESCC

External beam radiotherapy remains an essential component in the treatment of metastatic spinal cord compression. It is either used as the primary treatment modality or as an adjuvant treatment in the postoperative setting.

### Postoperative external beam radiation treatment

Level-one evidence suggests that in selected patients, surgery followed by EBRT is superior to EBRT alone. In 2005 Patchell *et al.* [8] published the results of a trial that randomized patients to surgery and postoperative EBRT or EBRT alone. The study aimed to recruit 200 patients but was prematurely closed after a planned interim analysis demonstrated significant improvement in ambulatory rate in the combined surgery and EBRT arm. The published results are therefore based on 101 patients accrued from seven centres over a 10-year period with 70 of the patients recruited from one centre. The study has been criticized because of the poor results in the radiotherapy-alone arm which contrast with published radiotherapy data and, furthermore, since mechanical causes of cord compression were not stipulated as an exclusion criteria some patients may have been treated inappropriately with radiotherapy alone [9].

A secondary data analysis of this study published in 2009 looked at age stratification and demonstrated a strong interaction between age and treatment effect (hazard ratio = 1.61, $P = 0.01$), such that as age increases, the benefit of surgery is diminished [10]. Using sequential prespecified relative risk ratios, the best estimate for the age at which surgery is no longer superior to radiation alone was calculated to be between 60 and 70 years of age [95% confidence interval (CI)]. Multivariate modelling and Kaplan–Meier curves for stratified treatment groups showed that there was no difference in outcome between treatments for patients aged 65 years or above.

A meta-analysis of surgery vs. EBRT for MESCC published in 2005 found a statistically significant difference between surgery and radiation in the ambulatory success rates [11]. Overall, the surgical patients were 1.3 times more likely to be ambulatory after treatment compared with the radiation patients. However, the surgical data used in this meta-analysis contain primarily uncontrolled cohort studies and preceded the Patchell *et al.* publication. Conversely a matched-pair analysis performed retrospectively on 122 patients treated with surgery followed by EBRT matched using 11 known prognostic factors to 244 patients treated with EBRT alone found that on univariate analysis treatment schedule had no impact on functional outcome ($P = 0.92$) or overall survival (OS) ($P = 0.5$) [12▪]. Multiple subgroup analyses also failed to show any benefit for the addition of surgery. The conclusion stated that a further randomized trial was warranted.

It can be concluded that initial surgical resection followed by EBRT should be considered for a carefully selected group of patients, that is with single-level MESCC and neurological deficits. Other commonly agreed upon indications for surgery

include recurrent compression following radiotherapy, spinal instability, retropulsed bony fragment causing cord compression and an unknown primary requiring histological confirmation for diagnosis.

There remain some unanswered questions related to postoperative radiotherapy in this setting. The Patchell *et al.* study defined radiation fields extending one vertebral body above and below the original lesion starting 14 days after surgery and delivering a dose of 30 Gy in 10 fractions to an undefined prescription point. This may serve as a standard for practice but the optimal volume, dose and timing for postoperative radiotherapy have not been critically explored.

## External beam radiation treatment alone for the management of metastatic epidural spinal cord compression

External beam radiation treatment, in combination with steroids, remains the treatment of choice for the majority of patients presenting with MESCC. Despite this, there is a paucity of randomized data in the literature to support an optimal dose and fractionation schedule. In a systematic review performed by Loblaw *et al.* [9] the data were reviewed from three prospective studies, two case-controlled series, one case series and three retrospective reviews, all of which described radiation dose fractionation schedules. They concluded that no one regime was superior to another in any cohort of patients.

Since 2005, there have been two phase III randomized trials reported in the literature [13,14]. Both trials come from the same Italian research group. The first compared a short-course regimen of 16 Gy in two fractions with a split-course regimen of 30 Gy in eight fractions [13]. The second compared 16 Gy in two fractions to 8 Gy in a single fraction [14]. Neither of these two studies showed evidence of a dose response in terms of pain control and ambulation (Table 1). It is important to note that both of these studies were performed in a poor prognosis population, that is patients with short ($\leq$6 months) life expectancy and the median survival of patients in the latter trial was only 4 months. As would be expected from a poor prognosis group, there were few in field recurrences documented and due to the small number of events, no comment could be made on local control or durability of response. However, responders maintained function until death. Also of note is that a proportion of the patients randomized to this study were diagnosed as a result of active screening of patients with known symptomatic spinal metastases. The authors concluded that short-course hypofractionated therapy (8 Gy/1 fraction) is well tolerated, effective and convenient in patients with poor prognosis.

Published retrospective and prospective nonrandomized data (Table 2) support the above randomized data in that no dose-fractionation schedule has demonstrated a higher ambulation rate [15,16▪,17]. However, two studies have suggested that local control of MESCC may be superior following long-course compared to the short-course schedules [16▪,17]. The largest published retrospective series of 1304 patients compared short and long-fractionation schedules and showed on multivariate analysis the ambulation success rate was not associated with the higher-dose schedules, but there were fewer documented in-field recurrences in the longer fractionation group [17]. This prompted a prospective nonrandomized fractionation trial (SCORE-1) which was designed to assess local control as a primary endpoint [16▪]. Two hundred and sixty-five patients were recruited from The Netherlands and Germany over a 2-year period from January 2006 to December 2007. Dutch patients received short-course, and German patients long-course EBRT. Most of the follow-up was done by phone between patient and treating physician with immediate recall for MRI if deterioration in motor function was suspected. Whereas the ambulation rates between the two arms were not significantly different, local control (LC) was reported as significantly better in the long course arm (Table 2). On multivariate analysis, improved LC was significantly associated with radiation schedule ($P = 0.018$).

Few studies have documented local control rates for MESCC treated with EBRT based on MRI spine

**Table 1. Randomized phase III trial results (EBRT fractionation)**

| Randomized trial data | Sample size | Arm 1 | Arm 2 | Ambulation response rate | Median survival |
|---|---|---|---|---|---|
| Maranzano *et al.* [13] | 300 | 16 Gy/2 | 15 Gy/3 + 15 Gy/5 split course | 68 vs. 71%* ns | 4 vs. 4m* ns |
| Maranzano *et al.* [14] | 327 | 16 Gy/2 | 8 Gy/1 | 69 vs. 62%* ns | 4 vs. 4m* ns |

ns, Not significant.
*P-value not given in publication.

**Table 2. Nonrandomized studies (EBRT fractionation)**

| Study design | Sample size | Arm/group 1 | Arm/group 2 | Ambulation response rate | LC |
|---|---|---|---|---|---|
| Prospective, nonrandomized [15] | 214 | 30 Gy/10 | 40 Gy/20 | 68 vs. 71%[a] $P=0.791$ | NA |
| | | | | $P=0.578$ | |
| Retrospective [17] | 1304 | 8 Gy/1 | 30G y/10 | | NA |
| | | 20 Gy/5 | 37.7 Gy/15 | | |
| | | | 40 Gy/20 | | |
| Prospective nonrandomized [16▪] | 231 | 8 Gy/1 | 30 Gy/10 | ns* | 61 vs. 81%[b] |
| | | 20 Gy/5 | 37.7 Gy/15 | | $P=0.005$ |
| | | | 40 Gy/20 | | |

LC, local control; NA, not available; ns, not significant.
[a]Ambulation rate at 3 months.
[b]LC at 12 months.
*P-value not given in publication.

follow-up. In a series of 130 hormone-refractory prostate cancer patients, 37 were found to have clinically occult MESCC [7▪]. Following radiotherapy (20 Gy in five fractions), 31/37 (84%) were controlled locally post radiotherapy and the proportion of patients with neurological deficits increased with time at 7.5% at 6 months and 18.7% at 2 years. These data add further weight to the argument for selecting a patient's treatment based on prognosis.

Evidence suggests that until further randomized data are available short-course/single fraction regimens, for example $5 \times 4$ Gy, $2 \times 8$ Gy, or $1 \times 8$ Gy can be used for patients with short life expectancy, whereas fractionated, higher-dose schedules, for example $10 \times 3$ Gy or greater should be considered for patients with better prognosis.

In an attempt to aid prognosis prediction in this group of patients, Rades *et al.* [18], published a scoring system that was derived from a multivariate analysis done on retrospective data from 1852 MESCC patients treated with EBRT alone. The system includes the six prognostic factors found to be significant in that multivariate analysis: tumour type, interval between tumour diagnosis and MESCC, presence of other bone or visceral metastases at the time of radiotherapy (RT), pretreatment ambulatory status, and duration of motor deficits. This scoring system has been validated prospectively for the endpoints survival and ambulatory function [19▪,20].

## Re-irradiation in the setting of recurrent metastatic epidural spinal cord compression

Patients should be followed clinically and/or radiologically to determine whether a local relapse (or a subsequent MESCC episode) develops. The optimal follow-up schedule has not been defined but it has been suggested from one study that in patients who have had a previous episode of MESCC subsequent MRI scanning should be undertaken at every 4–6 months. Documented local relapse rates in the literature range from 4.2 to 45% [21,22].

As with the first presentation of MESCC diagnosis, prognosis, probability of neurologic recovery and time to neurologic recovery are highly dependent on pretreatment neurologic status [9]. Patients should be considered for surgical decompression ± RT first as salvage rates appear better despite higher complication rates [8]. If a patient is not medically and surgically operable, RT ± steroids should be given. The dose and technique of radiation should be chosen to keep the cumulative dose of RT less than BED 120 $Gy_2$ [23,24]. Using this biological threshold, no myelopathy was observed in 24 patients in the series by Maranzano *et al.* [22] and 124 patients in the series by Nieder *et al.* [23]. Newer RT techniques such as spine radiosurgery and stereotactic body RT can be used to minimize cord dose while dose escalating the tumour, and recent guidelines have been published for re-irradiation cord tolerance specific to re-treatment spine radiosurgery [25,26].

Functional outcomes after re-irradiation (re-RT) appear to be similar to de-novo MESCC outcomes. In the prospective Maranzano *et al.* series, 12 of 24 patients were retreated with RT (4–20 Gy in 1–4 fractions; cumulative dose $<120$ $Gy_2$). Six of seven (83%) patients who were ambulatory before re-RT maintained ambulation [22]. None of the non-ambulatory patients recovered ambulation; this is below expectations for naïve MESCC patients. Median OS after re-RT was 5 months in this series.

In the retrospective Rades experience, 36% of 124 improved ambulation (by at least one category

on the Tomita scale; proportion recovering ambulation not reported) and was stable in another 50% [27]. In this series, the median OS was 7 months. On multivariate analysis, the following factors were independently predictive of better survival: *Eastern Cooperative Oncology Group* performance status (3–4 vs. 1–2), ambulatory status before re-RT (ambulatory vs. nonambulatory), time to development of motor deficits (>14 vs. 8–14 vs. >8 days) and visceral metastases (no vs. yes).

## FUTURE DIRECTIONS FOR THE USE OF EXTERNAL BEAM RADIATION TREATMENT IN THE MANAGEMENT OF METASTATIC EPIDURAL SPINAL CORD COMPRESSION

Linear accelerator technology has evolved with multileaf collimation, intensity modulated radiotherapy, systems of image guidance, and robotic technology. This has led to the experimental use of radiosurgery/stereotactic body radiotherapy (RS/SBRT) for the treatment of spinal metastases [28]. With this technology, only the involved vertebral body segment, or even the disease within the vertebrae, is treated to a significantly high-radiation dose as compared with conventional radiotherapy [29–33]. The benefit of this technique lies in dose escalation, reduction in treatment volume, and cord sparing in the setting of previous radiation. This may translate into improved local control in good-prognosis patients with limited spinal metastases. This approach, however, is technically demanding with need for sophisticated radiation units, a reliable body immobilization method, higher treatment cost, and potential risk of radiation-induced myelopathy [29,32,34]. As a result, this treatment is only offered in specialized centres. There may also be a role for radiosurgical epidural decompression in a selected group of MESCC patients; however, this is yet to be defined and RS/SBRT is unlikely to be able to be used as an emergency procedure given the time taken for planning and treatment verification [26]. Radiosurgery is to be compared to conventional radiotherapy as upfront treatment for spinal metastases in a randomized trial. This study is being conducted by Radiation Therapy Oncology Group and will include patients with a limited (1–3) number of spine metastases, with or without minimal epidural compression.

The future direction for research into conventional EBRT is in defining optimal fractionation and dose for both poor and good-prognosis MESCC patients. A multicentre, randomized trial (SCORAD) that is comparing 8 Gy in a single fraction to 20Gy in five fractions is underway in the UK. Opened to accrual in 2006, a similar Irish study (IRCOG) compared 10 Gy in a single fraction to 20Gy in five fractions; however, this trial has been closed before accrual targets were met. The optimal dose and fractionation schedule in the postoperative setting also need to be defined.

## CONCLUSION

The treatment controversies regarding MESCC are similar today to those of 1980s. EBRT remains the most appropriate first-line treatment for the majority of MESCC patients; however, for selected patients surgery is recommended with EBRT given postoperatively. For those patients being treated with EBRT alone the optimal fractionation schedule is yet to be defined; present evidence suggests that it should be customized according to the individual patient's prognosis with the use of short courses in patients who have poor prognoses and longer courses in those with better expected outcomes. Prognostic scoring systems based on primary tumour type, systemic disease status, ambulatory and performance status and duration of history may help to predict clinical outcome and be used to optimize treatment.

This debilitating condition continues to impact on the workload of radiation oncology departments worldwide, and late diagnosis has a negative impact on the patient and care givers in terms of quality of life and survival. With greater international collaboration we can complete current and future randomized trials that will improve the treatment of MESCC.

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### Conflicts of interest

*There are no conflicts of interest.*

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 124–125).

1. Bach F, Larsen B, Rohde K, *et al.* Metastatic spinal cord compression. Occurrence, symptoms, clinical presentations and prognosis in 398 patients with spinal cord compression. Acta Neurochir (Wien) 1990; 107 (1–2):37–43.
2. Loblaw DA, Laperriere NJ, Mackillop WJ. A population-based study of malignant spinal cord compression in Ontario. Clin Oncol 2003; 15:211–217.
3. Prewett S, Venkitaraman R. Metastatic spinal cord compression: review of the evidence for a radiotherapy dose fractionation schedule. Clin Oncol (R Coll Radiol) 2010; 22:222–230.
4. Greenberg HS, Kim JH, Posner JB. Epidural spinal cord compression from metastatic tumor: results with a new treatment protocol. Ann Neurol 1980; 8:361–366.

5. Prasad D, Schiff D. Malignant spinal-cord compression. Lancet Oncol 2005; 6:15–24.
6. Rades D, Heidenreich F, Karstens JH. Final results of a prospective study of the prognostic value of the time to develop motor deficits before irradiation in metastatic spinal cord compression. Int J Radiat Oncol Biol Phys 2002; 53:975–979.
7. ■ Venkitaraman R, Sohaib S, Barbachano Y, *et al.* Frequency of screening magnetic resonance imaging to detect occult spinal cord compromise and to prevent neurological deficit in metastatic castration-resistant prostate cancer. Clin Oncol 2010; 22:147–152.

The results of this study suggest that in order to prevent symptomatic spinal cord compression the optimum frequency of screening with MRI is every 4–6 months for patients with previous SCC, rapidly rising or high PSA or back pain and annually for asymptomatic patients.

8. Patchell RA, Tibbs P, Regine W, *et al.* Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet 2005; 366:643–648.
9. Loblaw DA, Perry J, Chambers A, *et al.* Systematic review of the diagnosis and management of malignant extradural spinal cord compression: the Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. J Clin Oncol 2005; 23:2028–2037.
10. Chi JH, Gokaslan Z, McCormick P, *et al.* Selecting patients for treatment with metastatic epidural spinal radiosurgery cord compression: does age matter?: results from a randomised trial. Spine 2009; 35:431–435.
11. Klimo P Jr, Thompson C, Kestle J, *et al.* A meta-analysis of surgery versus conventional radiotherapy for the treatment of metastatic spinal epidural disease. Neuro Oncol 2005; 7:64–76.
12. ■ Rades D, Huttenlocher S, Dunst J, *et al.* Matched pair analysis comparing surgery followed by radiotherapy and radiotherapy alone for metastatic spinal cord compression. J Clin Oncol 2010; 28:3597–3604.

Matched-pair analysis of radiation and surgery patients showing no difference in outcomes including ambulation status post treatment, improvement in ambulation and overall survival.

13. Maranzano E, Bellavita R, Rossi R, *et al.* Short-course versus split-course radiotherapy in metastatic spinal cord compression: results of a phase III, randomized, multicenter trial. J Clin Oncol 2005; 23:3358–3365.
14. Maranzano E, Trippa F, Casale M, *et al.* 8Gy single-dose radiotherapy is effective in metastatic spinal cord compression: results of a phase III randomized multicentre Italian trial. Radiother Oncol 2009; 93:174–179.
15. Rades D, Fehlauer F, Stalpers L, *et al.* A prospective evaluation of two radiotherapy schedules with 10 versus 20 fractions for the treatment of metastatic spinal cord compression: final results of a multicenter study. Cancer 2004; 101:2687–2692.
16. ■ Rades D, Lange M, Veninga T, *et al.* Final results of a prospective study comparing the local control of short-course and long-course radiotherapy for metastatic spinal cord compression. Int J Radiat Oncol Biol Phys 2011; 79:524–530.

Prospective, nonrandomized trial of short course vs. long irradiation for MESCC that showed 1-year local control was statistically better with long course compared to short course.

17. Rades D, Stalpers L, Veninga T, *et al.* Evaluation of five radiation schedules and prognostic factors for metastatic spinal cord compression. J Clin Oncol 2005; 23:3366–3375.
18. Rades D, Dunst J, Schild SE. The first score predicting overall survival in patients with metastatic spinal cord compression. Cancer 2008; 112:157–161.
19. ■ Rades D, Douglas S, Veninga T, *et al.* Validation and simplification of a score predicting survival in patients irradiated for metastatic spinal cord compression. Cancer 2010; 116:3670–3673.

A previously developed and published scoring system to predict survival of patients presenting with MESCC is validated and the scoring system simplified from 5 prognostic groups to a 3.

20. Rades D, Douglas S, Huttenlocher S, *et al.* Validation of a score predicting post-treatment ambulatory status after radiotherapy for metastatic spinal cord compression. Int J Radiat Oncol Biol Phys 2011; 79:1503–1506.
21. Huddart RA, Rajan B, Law M, *et al.* Spinal cord compression in prostate cancer: treatment outcome and prognostic factors. Radiother Oncol 1997; 44:229–236.
22. Maranzano E, Trippa F, Casale M, *et al.* Reirradiation of metastatic spinal cord compression: definitive results of two randomized trials. Radiother Oncol 2011; 98:234–237.
23. Nieder C, Grosu A, Andratschke N, *et al.* Update of human spinal cord reirradiation tolerance based on additional data from 38 patients. Int J Radiat Oncol Biol Phys 2006; 66:1446–1449.
24. Wong CS, Van Dyk J, Milosevic M, *et al.* Radiation myelopathy following single courses of radiotherapy and retreatment. Int J Rad Onc Biol Phys 1994; 30:197–202.
25. Mancosu P, Navarria P, Bignardi M, *et al.* Re-irradiation of metastatic spinal cord compression: a feasibility study by volumetric-modulated arc radiotherapy for in-field recurrence creating a dosimetric hole on the central canal. Radiother Oncol 2010; 94:67–70.
26. Ryu S, Rock J, Jain R, *et al.* Radiosurgical decompression of metastatic epidural compression. Cancer 2010; 116:2250–2257.
27. Rades D, Rudat V, Veninga T, *et al.* Prognostic factors for functional outcome and survival after reirradiation for in-field recurrences of metastatic spinal cord compression. Cancer 2008; 113:1090–1096.
28. Sahgal A, Larson DA, Chang EL. Stereotactic body radiosurgery for spinal metastases: a critical review. Int J Radiat Oncol Biol Phys 2008; 71:652–665.
29. Chang EL, Shiu A, Mendel E, *et al.* Phase I/II study of stereotactic body radiotherapy for spinal metastasis and its pattern of failure. J Neurosurg Spine 2007; 7:151–160.
30. Gerszten PC, Burton S, Ozhasoglu C, *et al.* Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. Spine (Phila Pa 1976) 2007; 32:193–199.
31. Ryu S, Fang Yin F, Rock J, *et al.* Image-guided and intensity-modulated radiosurgery for patients with spinal metastasis. Cancer 2003; 97:2013–2018.
32. Ryu S, Yin J, Yin R, *et al.* Partial volume tolerance of the spinal cord and complications of single-dose radiosurgery. Cancer 2007; 109:628–636.
33. 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; 74:723–731.
34. Gibbs IC, Patel C, Gerszten P, *et al.* Delayed radiation-induced myelopathy after spinal radiosurgery. Neurosurgery 2009; 64 (2 Suppl):A67–A72.