Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Cole JS, Patchell RA. Metastatic epidural spinal cord compression. *Lancet Neurol*. 2008;7(5):459-466.	Review/Other-Tx	N/A	A review on MESCC.	MESCC is a medical emergency that needs rapid diagnosis and treatment if permanent paralysis is to be prevented: the diagnosis of MESCC is best made with MRI; and corticosteroids, RT, and surgery are all established treatments.	4
2. Loblaw DA, Mitera G, Ford M, Laperriere NJ. A 2011 updated systematic review and clinical practice guideline for the management of malignant extradural spinal cord compression. *Int J Radiat Oncol Biol Phys.* 2012;84(2):312-317.	Review/Other-Tx	28 articles	To update the 2005 Cancer Care Ontario practice guidelines for the diagnosis and treatment of adult patients with a suspected or confirmed diagnosis of MESCC.	A randomized control trial of RT with or without decompressive surgery showed improvements in pain, ambulatory ability, urinary continence, duration of continence, functional status, and OS. 2 randomized control trials of RT (30 Gy in 8 fractions vs 16 Gy in 2 fractions; 16 Gy in 2 fractions vs 8 Gy in 1 fraction) in patients with a poor prognosis showed no difference in ambulation, duration of ambulation, bladder function, pain response, in-field failure, and OS. Retrospective multicenter studies reported that protracted RT schedules in nonsurgical patients with a good prognosis improved local control but had no effect on functional or survival outcomes.	4
3. Shiue K, Sahgal A, Chow E, et al. Management of metastatic spinal cord compression. *Expert Rev Anticancer Ther*. 2010;10(5):697-708.	Review/Other-Tx	N/A	To review pathophysiology, diagnosis and management of spinal cord compression.	No results stated in abstract.	4
4. Fisher CG, DiPaola CP, Ryken TC, et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. *Spine (Phila Pa 1976).* 2010;35(22):E1221-1229.	Review/Other-Tx	N/A	To use an evidence-based medicine process using the best available literature and expert opinion consensus to develop a comprehensive classification system to diagnose neoplastic spinal instability.	A comprehensive classification system based on patient symptoms and radiographic criteria of the spine was developed to aid in predicting spine stability of neoplastic lesions. The classification system includes global spinal location of the tumor, type and presence of pain, bone lesion quality, spinal alignment, extent of vertebral body collapse, and posterolateral spinal element involvement. Qualitative scores were assigned based on relative importance of particular factors gleaned from the literature and refined by expert consensus.	4

Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. 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(4):975-979.	Observational-Tx	98 patients	To investigate the influence of the time of motor deficit development before RT on the post-treatment functional status and to confirm preliminary (less patients, only 2 main subgroups, incomplete follow-up) results.	In the >14-day subgroup, improvement occurred significantly (P<0.001) more often than in the other subgroups (86% vs 29% and 10%) and the post-treatment ambulatory rate was significantly higher (86% vs 55% and 35%, P=0.026). Multivariate analysis revealed the time of development of motor deficits before RT to be the strongest prognostic factor.	1
6. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet.* 2005;366(9486):643-648.	Experimental-Tx	101 patients	To determine the value of surgery in the management of MESCC, the authors undertook a randomized trial comparing the efficacy of direct decompressive surgery plus postoperative RT with that of RT alone.	After an interim analysis the study was stopped because the criterion of a predetermined early stopping rule was met. Thus, 123 patients were assessed for eligibility before the study closed and 101 were randomized. Significantly more patients in the surgery group (42/50, 84%) than in the RT group (29/51, 57%) were able to walk after treatment (odds ratio 6.2 [95% CI; 2.0–19.8] P=0·001). Patients treated with surgery also retained the ability to walk significantly longer than did those with RT alone (median 122 days vs 13 days, P=0·003). 32 patients entered the study unable to walk; significantly more patients in the surgery group regained the ability to walk than patients in the RT group (10/16 [62%] vs 3/16 [19%], P0·01). The need for corticosteroids and opioid analgesics was significantly reduced in the surgical group.	1
7. 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(2):174-179.	Experimental-Tx	303 patients	Phase III trial was planned to determine whether in in patients with MSCC and short life expectancy, 8 Gy single-dose is as effective as 8 Gy x 2.	A total of 303 (93%) patients are assessable, 150 treated with the short-course and 153 with the single-dose RT. No difference in response was found between the 2 RT schedules adopted. Median duration of response was 5 and 4.5 months for short-course and single-dose RT (P=0.4), respectively. The median OS was 4 months for all cases. Light acute toxicity was registered in a minority of cases. Late toxicity was never recorded.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
8. Rades D, Freundt K, Meyners T, et al. Dose escalation for metastatic spinal cord compression in patients with relatively radioresistant tumors. *Int J Radiat Oncol Biol Phys.* 2011;80(5):1492-1497.	Observational-Tx	191 patients; 191 controls	To investigate whether patients with favorable survival prognoses benefit from a dose escalation beyond 30 Gy.	Local control rates at 2 years were 71% after 30 Gy and 92% after higher doses (P=0.012). 2-year PFS rates were 68% and 90%, respectively (P=0.013). 2-year OS rates were 53% and 68%, respectively (P=0.032). Results maintained significance in the multivariate analyses (Cox proportional hazards model; stratified model) with respect to local control (P=0.011; P=0.012), PFS (P=0.010; P=0.018), and OS (P=0.014; P=0.015). Functional outcome was similar in both groups. Motor function improved in 40% of patients after 30 Gy and 41% after higher doses (P=0.98).	2
9. Rades D, Lange M, Veninga T, et al. Preliminary results of spinal cord compression recurrence evaluation (score-1) study comparing short-course versus long-course radiotherapy for local control of malignant epidural spinal cord compression. *Int J Radiat Oncol Biol Phys.* 2009;73(1):228-234.	Observational-Tx	231 patients	To compare the results of short-course vs long-course RT for MSCC.	The PFS rate at 12 months was 72% after long-course and 55% after short-course RT (P=0.034). These results were confirmed in a multivariate analysis (RR, 1.33; 95% CI, 1.01–1.79; P=0.046). The 12-month local control rate was 77% and 61% after long-course and short-course RT, respectively (P=0.032). These results were also confirmed in a multivariate analysis (RR, 1.49; 95% CI, 1.03–2.24; P=0.035). The corresponding 12-month OS rates were 32% and 25% (P=0.37). Improvement in motor function was observed in 30% and 28% of patients undergoing long-course vs short-course RT, respectively (P=0.61). In addition to radiation schedule, PFS was associated with the interval to developing motor deficits before RT (RR, 1.99; 95% CI, 1.10–3.55; P=0.024). Local control was associated only with the radiation schedule. Post-RT motor function was associated with performance status (P=0.031), tumor type (P=0.013), interval to developing motor deficits (P=0.001), and bisphosphonate administration (P=0.006). OS was associated with performance status (P<0.001), number of involved vertebrae (P=0.007), visceral metastases (P<0.001), ambulatory status (P<0.001), and bisphosphonate administration (P<0.001).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
10. 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(2):524-530.	Observational-Tx	265 patients	To compare the local control of different RT schedules for MSCC.	1-year local control was 61% after short-course and 81% after long-course RT (P=0.005). On multivariate analysis, improved local control was associated with long-course RT (P=0.018). Motor function improved in 37% after short-course and 39% after long-course RT (P=0.95). Improved motor function was associated with better performance status (P=0.015), favorable tumor type (P=0.034), and slower development of motor deficits (P<0.001). 1-year survival rates were 23% after short-course and 30% after long-course RT (P=0.28). On multivariate analysis, improved survival was associated with better performance status (P<0.001), no visceral metastases (P<0.001), involvement of only 1 to 3 vertebrae (P=0.040), ambulatory status (P=0.038), and bisphosphonate administration after RT (P<0.001).	1
11. Rades D, Panzner A, Rudat V, Karstens JH, Schild SE. Dose escalation of radiotherapy for metastatic spinal cord compression (MSCC) in patients with relatively favorable survival prognosis. *Strahlenther Onkol.* 2011;187(11):729-735.	Observational-Tx	191 patients treated with 30 Gy/10 fractions; 191 patients receiving higher doses (37.5 Gy/15 fractions or 40 Gy/20 fractions)	To determine whether patients with favorable survival prognoses benefit from a dose escalation beyond 30 Gy.	Local control rates at 2 years were 71% after 30 Gy and 92% after higher doses (P=0.012). 2-year PFS rates were 68% and 90%, respectively (P=0.013). 2-year OS rates were 53% and 68%, respectively (P=0.032). Results maintained significance in the multivariate analyses (Cox proportional hazards model; stratified model) with respect to local control (P=0.011; P=0.012), PFS (P=0.010; P=0.018), and OS (P=0.014; P=0.015). Functional outcome was similar in both groups. Motor function improved in 40% of patients after 30 Gy and 41% after higher doses (P=0.98).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Rades D, Stalpers LJ, Schulte R, et al. Defining the appropriate radiotherapy regimen for metastatic spinal cord compression in non-small cell lung cancer patients. *Eur J Cancer.* 2006;42(8):1052-1056.	Observational-Tx	252 patients	To compare short-course RT (1 x 8 Gy/1 day, 5 x 4 Gy/1 week) and long-course RT (10 x 3 Gy/2 weeks, 15 x 2.5 Gy/3 weeks, 20 x 2 Gy/4 weeks) for functional outcome in NSCLC patients developing MSCC.	Improvement of motor function occurred in 14% of patients, no change in 54%, and deterioration in 32%. Functional outcome was affected by the time of developing motor deficits before RT (>14 days better than 1-7 days and 8-14 days, P<0.001), not by the radiation regimen (P=0.87). In the short-course RT group, functional outcome was similar for 1 x 8 Gy and 5 x 4 Gy (P=0.94). Short-course and long-course RT appear similarly effective for MSCC in NSCLC patients. As 1 x 8 Gy and 5 x 4 Gy showed comparable results, 1 x 8 Gy can be considered appropriate.	2
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(15):3358-3365.	Experimental-Tx	300 patients	Randomized trial to assess the clinical outcome and toxicity of 2 different hypofractionated RT regimens in MSCC.	A total of 276 (92%) patients were assessable; 142 (51%) treated with the short-course and 134 (49%) treated with the split-course RT regimen. There was no significant difference in response, duration of response, survival, or toxicity found between the 2 arms. When short- vs split-course regimens were compared, after RT 56% and 59% patients had back pain relief, 68% and 71% were able to walk, and 90% and 89% had good bladder function, respectively. Median survival was 4 months and median duration of improvement was 3.5 months for both arms. Toxicity was equally distributed between the 2 arms: grade 3 esophagitis or pharyngitis was registered in 4 patients (1.5%), grade 3 diarrhea occurred in 4 patients (1.5%), and grade 3 vomiting or nausea occurred in 10 patients (6%). Late toxicity was never recorded.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
14. Rades D, Hoskin PJ, Stalpers LJ, et al. Short-course radiotherapy is not optimal for spinal cord compression due to myeloma. *Int J Radiat Oncol Biol Phys.* 2006;64(5):1452-1457.	Observational-Tx	172 myeloma patients	To investigate the suitability of short-course RT for spinal cord compression in myeloma patients.	Improvement of motor function occurred in 90 patients (52%). 47% of nonambulatory patients regained the ability to walk. Functional outcome was significantly influenced by the time of developing motor deficits before RT. Improvement of motor function was more frequent after long-course RT than after short-course RT: 59% vs 39% (P=0.10) at 1 month, 67% vs 43% (P=0.043) at 6 months, 76% vs 40% (P=0.003) at 12 months, 78% vs 43% (P=0.07) at 18 months, and 83% vs 54% (P=0.33) at 24 months. A subgroup analysis of the long-course RT group demonstrated a similar functional outcome for 10 x 3 Gy when compared with 15 x 2.5 Gy and 20 x 2 Gy.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Terpos E, Morgan G, Dimopoulos MA, et al. International Myeloma Working Group recommendations for the treatment of multiple myeloma-related bone disease. *J Clin Oncol.* 2013;31(18):2347-2357.	Review/Other-Tx	N/A	To develop practice recommendations for the management of multiple myeloma-related bone disease.	Bisphosphonates should be considered in all patients with multiple myeloma receiving first-line antimyeloma therapy, regardless of presence of osteolytic bone lesions on conventional radiography. However, it is unknown if bisphosphonates offer any advantage in patients with no bone disease assessed by MRI or positron emission tomography/computed tomography. Intravenous zoledronic acid or pamidronate is recommended for preventing skeletal-related events in patients with multiple myeloma. Zoledronic acid is preferred over oral clodronate in newly diagnosed patients with multiple myeloma because of its potential antimyeloma effects and survival benefits. Bisphosphonates should be administered every 3 to 4 weeks intravenously during initial therapy. Zoledronic acid or pamidronate should be continued in patients with active disease and should be resumed after disease relapse, if discontinued in patients achieving complete or very good partial response. Bisphosphonates are well tolerated, but preventive strategies must be instituted to avoid renal toxicity or osteonecrosis of the jaw. Kyphoplasty should be considered for symptomatic vertebral compression fractures. Low-dose RT can be used for palliation of uncontrolled pain, impending pathologic fracture, or spinal cord compression. Orthopedic consultation should be sought for long-bone fractures, spinal cord compression, and vertebral column instability.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
16. Jin R, Rock J, Jin JY, et al. Single fraction spine radiosurgery for myeloma epidural spinal cord compression. *J Exp Ther Oncol.* 2009;8(1):35-41.	Review/Other-Tx	31 lesions in 24 patients	To determine the role of single fraction radiosurgery for epidural spinal cord compression due to multiple myeloma.	Median follow-up was 11.2 months (range 1-55). Primary endpoints of this study were pain control, neurological improvement, and radiographic tumor control. Overall pain control rate was 86%; complete relief in 54%, and partial relief in 32% of the patients. 7 patients presented with neurological deficits. 5 patients neurologically improved or became normal after radiosurgery. Complete radiographic response of the epidural tumor was noted in 81% at 3 months after radiosurgery.	4
17. Laufer I, Iorgulescu JB, Chapman T, et al. Local disease control for spinal metastases following "separation surgery" and adjuvant hypofractionated or high-dose single-fraction stereotactic radiosurgery: outcome analysis in 186 patients. *J Neurosurg Spine.* 2013;18(3):207-214.	Observational-Tx	186 patients	To examine the outcomes of postoperative IG-IMRT delivered as single-fraction or hypofractionated SRS for achieving long-term local tumor control.	The total cumulative incidence of local progression was 16.4% 1 year after SRS. Multivariate Gray competing risks analysis revealed a significant improvement in local control with high-dose hypofractionated SRS (4.1% cumulative incidence of local progression at 1 year, HR 0.12, P=0.04) as compared with low-dose hypofractionated SRS (22.6% local progression at 1 year, HR 1). Although univariate analysis demonstrated a trend toward greater risk of local progression for patients in whom preoperative conventional EBRT failed (22.2% local progression at 1 year, HR 1.96, P=0.07) compared with patients who did not receive any preoperative RT (11.2% local progression at 1 year, HR 1), this association was not confirmed with multivariate analysis. No other variable significantly correlated with PFS, including radiation sensitivity of tumor histology, grade of MESCC, extent of surgical decompression, or patient sex.	2

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18. Ryu S, Rock J, Jain R, et al. Radiosurgical decompression of metastatic epidural compression. *Cancer*. 2010;116(9):2250-2257.	Observational-Tx	62 patients with 85 lesions	A clinical trial was performed to quantitatively determine the degree of epidural decompression by radiosurgery of metastatic epidural compression.	The mean epidural tumor volume reduction was 65 +/- 14% at 2 months after radiosurgery. The epidural tumor area at the level of the most severe spinal cord compression was 0.82 +/- 0.08 cm(2) before radiosurgery and 0.41 +/- 0.06 cm(2) after radiosurgery (P<.001). The cal sac patency improved from 55 +/- 4% to 76 +/- 3% (P<.001). Overall, neurological function improved in 81%.	1
19. Sharp HJ, Brown P, Settle SH, et al. Feasibility of Radiosurgical Decompression of Metastatic Epidural Spinal Cord Compression (MESCC) in Nonoperable Patients. *Int J Radiat Oncol Biol Phys*. 2012;84(3):S282.	Review/Other-Tx	2 trials; 12 patients	To prospectively test the hypothesis that spine SRS used as the primary treatment of inoperable MESCC is both feasible and safe.	Current accrual to the previously irradiated protocol is 5 patients, and radiation naive protocol 7 patients. For these 12 patients, consult to simulation time was 0-19 days (mean 5.25 days, SD 5.86 days). Simulation to treatment time was never longer than 12 days (mean 7.08 days, SD 3.37days). Time from consult to treatment for all patients was 6–23 days (mean 12.33 days, SD 5.71 days). Actual planning times were documented. Utilizing class solutions, time from contour completion to first plan review averaged 8.18 hours (2.25–16 hours, SD 4.48 hours). Initial plan review to plan approval ranged from 0–6 hours (mean 2.42 hours, SD 2.31 hours). Overall, planning start to plan approval averaged 10.6 hours (2.3–18 hours, SD 4.83 hours). With a current mean follow up of 5.07 months (0.59–10.59), 4/12 patients have recurred/progressed, and 4 have died. Mean time to recurrence was 6.42 months (1.41-8.98). At present, no RM has been detected.	4

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20. Al-Omair A, Masucci L, Masson-Cote L, et al. Surgical resection of epidural disease improves local control following postoperative spine stereotactic body radiotherapy. *Neuro Oncol.* 2013;15(10):1413-1419.	Observational-Tx	80 patients	To identify clinical and dosimetric predictors of local control and survival.	The median follow-up was 8.3 months. 35 patients (44%) were treated with 18-26 Gy in 1 or 2 fractions, and 45 patients (56%) with 18–40 Gy in 3–5 fractions. 21 local failures (26%) were observed, and the 1-year local control and OS rates were 84% and 64%, respectively. The most common site of failure was within the epidural space (15/21, 71%). Multivariate proportional hazards analysis identified systemic therapy post-SBRT as the only significant predictor of OS (*P*=.02) and treatment with 18–26 Gy/1 or 2 fractions (*P*=.02) and a postoperative epidural disease grade of 0 or 1 (0, no epidural disease; 1, epidural disease that compresses dura only, *P*=.003) as significant predictors of local control. Subset analysis for only those patients (n = 48/80) with high-grade preoperative epidural disease (cord deformed) indicated significantly greater local control rates when surgically downgraded to 0/1 vs 2 (*P*=.0009).	2
21. Nieder C, Grosu AL, Andratschke NH, Molls M. Update of human spinal cord reirradiation tolerance based on additional data from 38 patients. *Int J Radiat Oncol Biol Phys.* 2006;66(5):1446-1449.	Review/Other-Tx	38 patients	To update a combined analysis of all published clinical data.	The 2005 risk score based on 3 variables (cumulative BED, highest BED of all treatment series in a particular individual, and interval), which discriminate 3 different risk groups, does not require modification. The low-risk group now contains 1 case of RM (RM) after hypofractionated stereotactic reirradiation. Therefore, the rate increased from 0% to 3%. Intermediate-risk patients developed RM in 25%, and high-risk patients in 90%. When the interval between the 2 treatment courses is not shorter than 6 months and the dose of each course is ≤98 Gy(2), the cumulative BED where no case of RM has yet been reported is 120 Gy(2).	4

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22. Damast S, Wright J, Bilsky M, et al. Impact of dose on local failure rates after image-guided reirradiation of recurrent paraspinal metastases. *Int J Radiat Oncol Biol Phys.* 2011;81(3):819-826.	Review/Other-Tx	5 x 4-Gy (20-Gy group, n = 42) or 5 x 6-Gy (30-Gy group, n = 55)	To examine the impact of dose on local failure rates in the re-treatment of recurrent paraspinal metastases with IG-IMRT.	The median follow-up was 12.1 months (range, 0.2-63.6 months). The 1-year cumulative incidences of local failure after 20 Gy and 30 Gy IG-IMRT were 45% and 26%, respectively (P=0.04). Of all treatment characteristics examined (20-Gy vs 30-Gy dose group, dose to 95% of the planned and gross target volume, tumor size, histology, receipt of surgery, and interval between first and second radiation), only dose group had a significant impact on actuarial local failure incidence (P=0.04; unadjusted HR, 0.51; 95% CI, 0.27–0.96). There was no incidence of myelopathy.	4
23. Garg AK, Wang XS, Shiu AS, et al. Prospective evaluation of spinal reirradiation by using stereotactic body radiation therapy: The University of Texas MD Anderson Cancer Center experience. *Cancer.* 2011;117(15):3509-3516.	Observational-Tx	59 patients with 63 tumors	To review a prospective series of spinal metastasis patients reirradiated with SBRT.	Mean follow-up was 17.6 months. Actuarial 1-year radiographic local control and OS for all patients were both 76%. Of the tumors that progressed after SBRT, 13 (81%) of 16 patients had tumors that were within 5 mm of the spinal cord, and 6 of them eventually developed spinal cord compression. Toxicity was most commonly grade 1 or 2 fatigue. 2 patients experienced mild to moderate radiation injury (lumbar plexopathy) while remaining independently ambulatory and pain free. Freedom from neurologic deterioration from any cause was 92% at 1 year.	1
24. Mahadevan A, Floyd S, Wong E, Jeyapalan S, Groff M, Kasper E. Stereotactic body radiotherapy reirradiation for recurrent epidural spinal metastases. *Int J Radiat Oncol Biol Phys.* 2011;81(5):1500-1505.	Observational-Tx	60 patients (81 lesions)	To report the use of SBRT for 60 consecutive patients (81 lesions) who had radiological progressive spine metastasis with epidural involvement after previous radiation for spine metastasis.	The median OS was 11 months, and the median PFS was 9 months. Overall, 93% of patients had stable or improved disease while 7% of patients showed disease progression; 65% of patients had pain relief. There was no significant toxicity other than fatigue.	3

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25. 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(3):723-731.	Observational-Tx	39 consecutive patients (60 metastases)	To provide actuarial outcomes and dosimetric data for spinal/paraspinal metastases, with and without prior radiation, treated with SBRT.	At last follow-up, 19 patients were deceased. Median patient survival time measured was 21 months (95% CI = 8–27 months), and the 2-year survival probability was 45%. The median total dose prescribed was 24 Gy in 3 fractions prescribed to the 67% and 60% isodose for the unirradiated and re-irradiated cohorts, respectively. The median tumor follow-up for the unirradiated and re-irradiated group was 9 months (range, 1–26) and 7 months (range, 1–48) respectively. 8/60 tumors have progressed, and the 1- and 2-year progression-free probability was 85% and 69%, respectively. For the salvage group the 1 year progression-free probability was 96%. There was no significant difference in OS or progression-free probability between the salvage re-irradiated vs all other tumors treated (P=0.08 and P=0.31, respectively). In 6 of 8 failures the minimum distance from the tumor to the thecal sac was ≤1 mm. Of 60 tumors treated, 39 have ≥6 months follow-up and no radiation-induced myelopathy or radiculopathy has occurred.	2
26. Masucci GL, Yu E, Ma L, et al. Stereotactic body radiotherapy is an effective treatment in reirradiating spinal metastases: current status and practical considerations for safe practice. *Expert Rev Anticancer Ther.* 2011;11(12):1923-1933.	Review/Other-Tx	N/A	To provide an overview of reirradiation spine SBRT and address key issues surrounding safe and effective practice.	No results stated in abstract.	4

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27. Sahgal A, Larson DA, Chang EL. Stereotactic body radiosurgery for spinal metastases: a critical review. *Int J Radiat Oncol Biol Phys.* 2008;71(3):652-665.	Review/Other-Tx	N/A	To address the current status of stereotactic body radiosurgery for spinal metastases with respect to its apparatus, clinical indications, outcomes and techniques, and spinal cord tolerance.	The field of spinal stereotactic body radiosurgery is in its formative years. Studies from a limited number of centers suggest that stereotactic body radiosurgery used in the treatment of spinal metastases appears to be safe and effective both in terms of radiographic tumor control and pain relief. This is particularly important as a viable noninvasive option for the previously irradiated patient with painful spinal metastases, as these patients have not had many noninvasive therapeutic options available in the past.	4
28. Huang Z, Mayr NA, Yuh WT, Wang JZ, Lo SS. Reirradiation with stereotactic body radiotherapy: analysis of human spinal cord tolerance using the generalized linear-quadratic model. *Future Oncol.* 2013;9(6):879-887.	Review/Other-Tx	5 RM patients and 14 no-RM patients	To reanalyze published dosimetric data from patients with RM after reirradiation with spinal SBRT using the generalized linear-quadratic model.	Total (conventional RT + SBRT) mean P(max) nBED generalized linear-quadratic was lower in no-RM than RM patients: 59.2 Gy2/2 generalized linear-quadratic (range: 37.5-101.9) vs 94.8 Gy2/2 generalized linear-quadratic (range: 70.2–133.4) (P=0.0016). The proportion of total P(max) nBED generalized linear-quadratic accounted for by the SBRT P(max) nBED generalized linear-quadratic was higher for RM patients. No RM were seen below a total spinal cord nBED generalized linear-quadratic of 70 Gy2/2 generalized linear-quadratic.	4
29. Sahgal A, Ma L, Weinberg V, et al. Reirradiation human spinal cord tolerance for stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys.* 2012;82(1):107-116.	Review/Other-Tx	5 RM patients (5 spinal segments) and 14 no-RM patients (16 spine segments)	To review the treatment for patients with spine metastases who initially received conventional EBRT and were reirradiated with 1-5 fractions of SBRT who did or did not subsequently develop RM.	The initial conventional RT nBED ranged from ~30 to 50 Gy(2/2) (median ~40 Gy(2/2)). The SBRT reirradiation thecal sac mean P(max) nBED in the no-RM group was 20.0 Gy(2/2) (95% CI, 10.8–29.2), which was significantly lower than the corresponding 67.4 Gy(2/2) (95% CI, 51.0–83.9) in the RM group. The mean total P(max) nBED in the no-RM group was 62.3 Gy(2/2) (95% CI, 50.3–74.3), which was significantly lower than the corresponding 105.8 Gy(2/2) (95% CI, 84.3–127.4) in the RM group. The fraction of the total P(max) nBED accounted for by the SBRT P(max) nBED for the RM patients ranged from 0.54 to 0.78 and that for the no-RM patients ranged from 0.04 to 0.53.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Rades D, Hakim SG, Bajrovic A, et al. Impact of zoledronic acid on control of metastatic spinal cord compression. *Strahlenther Onkol.* 2012;188(10):910-916.	Observational-Tx	98 patients with MSCC receiving RT plus zoledronic acid; 196 patients receiving RT alone	To investigate whether the addition of zoledronic acid to RT could improve control of MSCC.	The 1-year local control rates were 90% after RT plus zoledronic acid and 81% after RT alone (P=0.042). The 1-year overall control rates were 87% and 75%, respectively (P=0.016), and the 1-year survival rates were 60% and 52%, respectively (P=0.17). Results were significant in the Cox proportional hazards model regarding local control (P=0.024) and overall control (P=0.008).	2
31. Mhaskar R, Redzepovic J, Wheatley K, et al. Bisphosphonates in multiple myeloma. *Cochrane Database Syst Rev.* 2010(3):CD003188.	Review/Other-Tx	17 trials with 1,520 patients analyzed in bisphosphonates groups, and 1,490 analyzed in control groups	To determine the clinical role of bisphosphonates in multiple myeloma.	This review includes 17 trials with 1,520 patients analyzed in bisphosphonates groups, and 1,490 analyzed in control groups. In comparison with placebo/no treatment, the pooled analysis demonstrated the beneficial effect of bisphosphonates on prevention of pathological vertebral fractures (RR= 0.74 (95% CI: 0.62 to 0.89), P=0.001), total skeletal related events (RR= 0.80 (95% CI: 0.72 to 0.89), P<0.0001) and on amelioration of pain (RR = 0.75 (95% CI: 0.60 to 0.95), P=0.01). We found no significant effect of bisphosphonates on OS, PFS, hypercalcemia or on the reduction of nonvertebral fractures. The indirect meta-analyses did not find the superiority of any particular type of bisphosphonate over others. Only 2 randomized control trials reported osteonecrosis of jaw. The identified observational studies suggested that osteonecrosis of jaw may be a common event (range: 0% to 51%).	4

Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
32. Berenson J, Pflugmacher R, Jarzem P, et al. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. *Lancet Oncol.* 2011;12(3):225-235.	Experimental-Tx	134 patients randomized to kyphoplasty (n=70) or nonsurgical management (n=64)	To assess the efficacy and safety of balloon kyphoplasty compared with nonsurgical management for patients with cancer who have painful vertebral compression fractures.	65 patients in the kyphoplasty group and 52 in the control group had data available at 1 month. The mean Roland-Morris disability questionnaire score in the kyphoplasty group changed from 17.6 at baseline to 9.1 at 1 month (mean change -8.3 points, 95% CI; -6.4 to -10.2; P<0.0001). The mean score in the control group changed from 18.2 to 18.0 (mean change 0.1 points; 95% CI; -0.8 to 1.0; P=0.83). At 1 month, the kyphoplasty treatment effect for Roland-Morris disability questionnaire was -8.4 points (95% CI; -7.6 to -9.2; P<0.0001). The most common adverse events within the first month were back pain (4/70 in the kyphoplasty group and 5/64 in the control group) and symptomatic vertebral fracture (2 and 3, respectively). 1 patient in the kyphoplasty group had an intraoperative non-Q-wave myocardial infarction, which resolved and was attributed to anesthesia. Another patient in this group had a new vertebral compression fracture, which was thought to be device related.	1
33. Lutz S, Spence C, Chow E, Janjan N, Connor S. Survey on use of palliative radiotherapy in hospice care. *J Clin Oncol.* 2004;22(17):3581-3586.	Review/Other-Tx	480 facilities	To survey hospice professionals to assess the perceived need for palliative RT in the hospice setting, investigate factors that limit the access of hospice patients to RT, and to suggest areas of future collaboration on education, research, and patient advocacy.	The findings suggest that the majority of hospice professionals feel that RT is important in palliative oncology and that RT is widely available in the United States. Yet, less than 3% on average of hospice patients served by hospices responding to the survey actually received RT in 2002. The most common barriers to RT in hospice care include RT expense, transportation difficulties, short life expectancy, and educational deficiencies between the specialties. Multiple barriers act to limit the use of palliative RT in hospice care. Finding ways to surmount these obstacles will provide opportunity for improvement in the end-of-life care of cancer patients.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

BED = Biologic effective dose

CI = Confidence interval

EBRT = External-beam radiation therapy

HR = Hazard ratio

IG-IMRT = Image-guided intensity-modulated radiotherapy

MESCC = Metastatic epidural spinal cord compression

MRI = Magnetic resonance imaging

MSCC = Metastatic spinal cord compression

nBED = Normal biologic effective dose

NSCLC = Non–small-cell lung cancer

OS = Overall survival

PFS = Progression-free survival

RM = Radiation myelopathy

RR = Relative risk

RT = Radiation therapy

SBRT = Stereotactic body radiotherapy

SD = Standard deviation

SRS = Stereotactic radiosurgery