XXI CONGRESSO NAZIONALE AIRO
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Centro Congressi

Approccio multidisciplinare nel trattamento delle metastasi vertebrali

La Radioterapia

Giovanna Mantini
Facoltà di Medicina e Chirurgia Agostino Gemelli
ROMA

UNIVERSITÀ CATTOLICA del Sacro Cuore

Keywords

- Patient selection: radiotherapy or surgery?
- Timing
- Fractionation
- Technique and retreatment

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Radiotherapy or surgery for spine metastases?

A population-based study of 903 patients in the south-eastern region of Norway

Olga Zaikova[1], Sophie D Fosså[2, 3], Øyvind S Bruland[2, 3], Karl-Erik Giercksky[2, 3], Berit Sandstad[4], and Sigmund Skjeldal[1]

[1]Department of Orthopaedics and [2]Division of Surgery and Cancer Medicine, Norwegian Radium Hospital, Oslo University Hospital; [3]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo; [4]Clinical Trials Unit, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

Table 3. Comparison of the use of surgery and radiotherapy (RT) as primary treatment of spinal metastatic disease in 903 patients [a]

	n	Primary surgery	Primary RT
Primary cancer diagnosis			
Myeloma and Lymphoma	79	19	60
Breast	152	3	149
Prostate	260	11	249
Lung	179	7	172
Kidney	40	3	37
Other	193	15	178
Age			
70+	433	26	40[illegible]
50–69	400	25	375
19–49	70	7	63
Gender			
Female	361	16	345
Male	542	42	500
Time from primary cancer diagnosis to treatment for SM [b]			
Within one year	396	40	356
Between one and 5 years	279	11	268
6 years or more	204	5	199
Motor impairment [c]			
Normal motor status (Frankel E)	607	11	596
Ambulating with minor motor deficit (Frankel D)	176	22	154
Non-ambulatory (Frankel A–C)	98	25	73
Multiplicity of spine metastases			
One vertebra affected	142	26	116
Multiple vertebra	761	32	729

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Table 2. Comparison of the use of multiple-fraction (MF) and single-fraction (SF) radiotherapy (RT) as primary treatment for spinal metastatic disease in 845 patients [a]

	n	MF	SF	p -value	OR (95% CI)
Primary cancer diagnosis				< 0.001	
Myeloma/lymphoma	60	56	4		1
Breast	149	135	14	0.7	0.8 (0.3–3.0)
Prostate	249	200	49	0.02	0.2 (0.1–0.8)
Lung	172	128	44	0.002	0.2 (0.1–0.5)
Kidney	37	34	3	0.5	0.5 (0.1–2.8)
Other	178	151	27	0.1	0.3 (0.1–1.1)
Age				0.04	
70+	407	323	84		1
50–69	375	325	50	0.01	1.8 (1.1–2.8)
19–49	63	56	7	0.4	1.4 (0.6–3.5)
Sex				0.5	
Female	345	294	51		
Male	500	410	90		
Motor impairment [b]				< 0.001	
Non-ambulatory (Frankel A–C)	73	69	4		1
Ambulatory with minor motor deficit (Frankel D)	154	141	13	0.4	0.6 (0.2–1.9)
Normal motor status (Frankel E)	596	486	110	0.005	0.2 (0.1–0.6)
Multiplicity of spine metastases				0.6	
One vertebra affected	116	99	17		
Multiple vertebra	729	605	124		
RT center				< 0.001	
Center 1	90	47	43		1
Center 2	429	385	44	< 0.001	8.3 (4.7–14.8)
Center 3	204	169	35	< 0.001	5.0 (2.7–9.2)
Center 4	122	103	19	< 0.001	5.4 (2.7–10.9)

OR: odds ratio for choice of MF RT vs. SF RT; 95%CI: 95% confidence interval.
[a] Binary logistic regression model.
[b] Motor impairment was unknown for 22 patients.

Radiotherapy

8.0 Gy was used as single-fraction (SF) primary treatment in 141 patients and multiple- fraction (MF) treatment was used in 704 patients. In 1 of 4 RT centers, SF RT was used more frequently. The most frequently used MF schedules were 3.0 Gy × 10 in 554 patients, 4.0 Gy × 5 in 33 patients, and 3.0 Gy × 12 in 13 patients. 94% of the patients completed RT as initially scheduled. 73 patients were non-ambulatory (Frankel A–C) before the start of RT, 154 were ambulatory with minor motor deficit (Frankel D), and 596 patients had no motor impairment (Frankel E).

In the multiple logistic regression model, the type of primary tumor, age, and motor impairment were associated with the use of MF RT as opposed to SF RT (Table 2).

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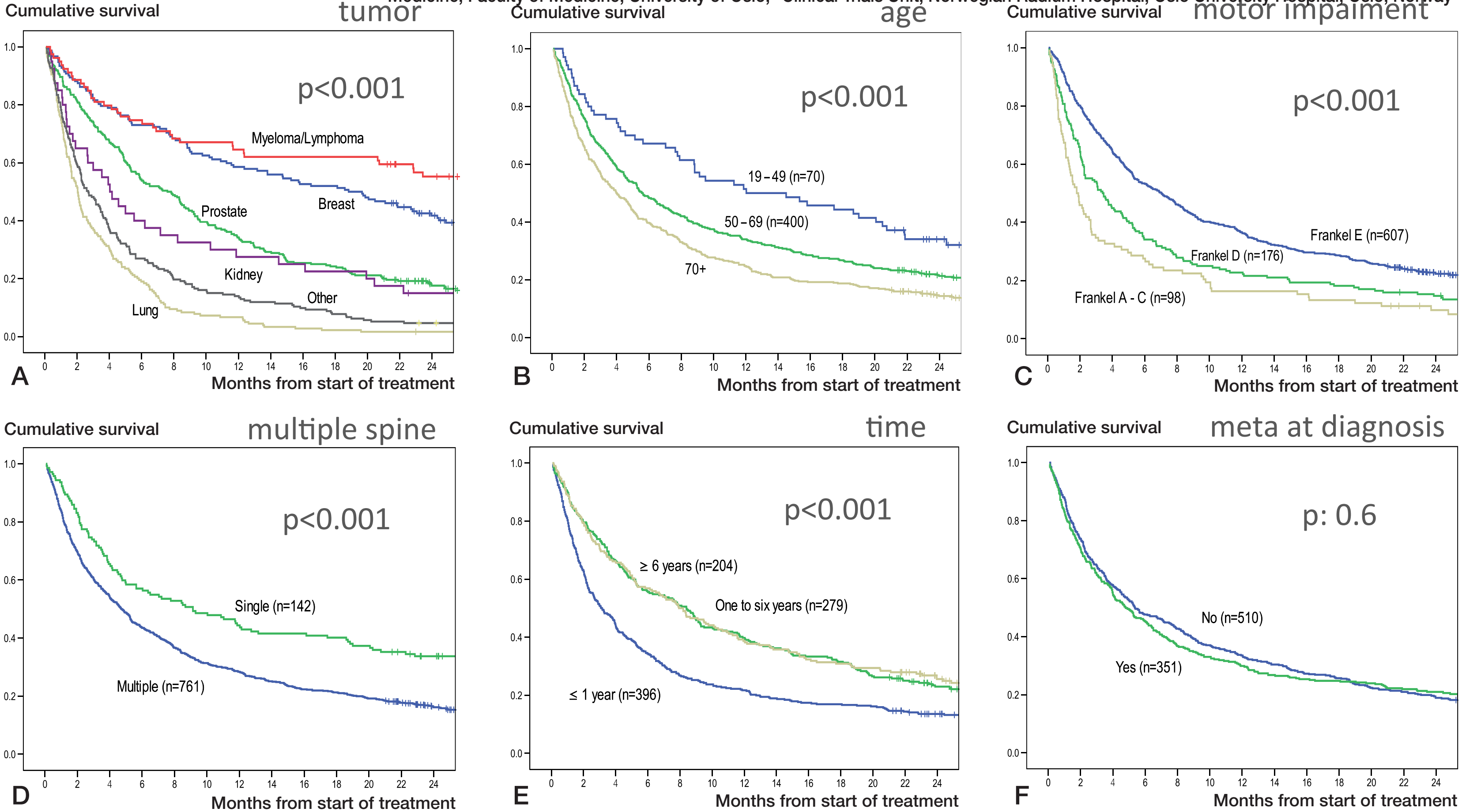

Figure 1. Kaplan-Meier plots with results of log-rank tests of survival related to pretreatment factors. A. Primary tumor ($p < 0.001$). B. Age ($p < 0.001$). C. Motor impairment [a] ($p < 0.001$). D. Multiplicity of metastases in spine ($p < 0.001$). E. Time from diagnosis of cancer to treatment [b] ($p < 0.001$). F. Metastases in spine at the time of primary cancer diagnosis [c] ($p = 0.6$).

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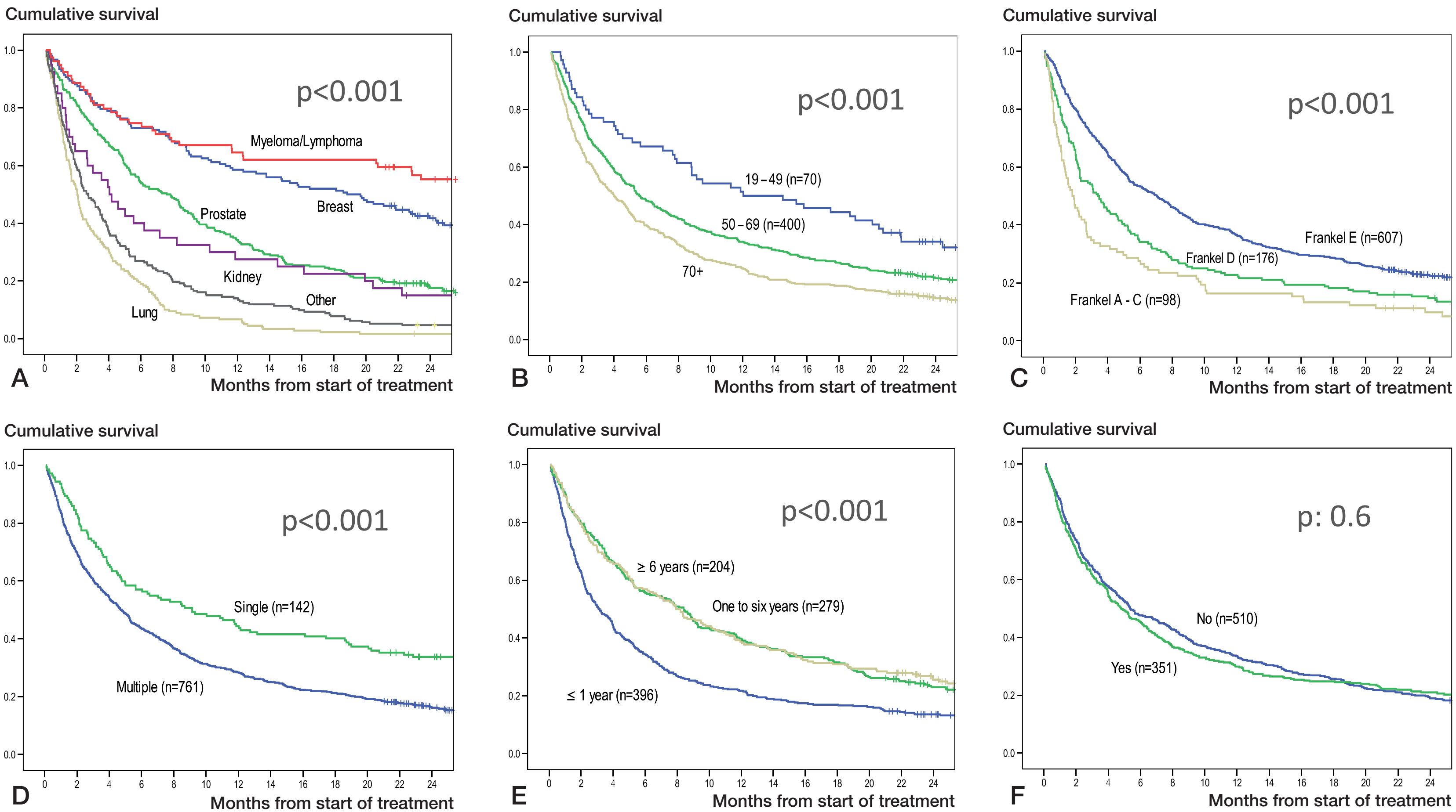

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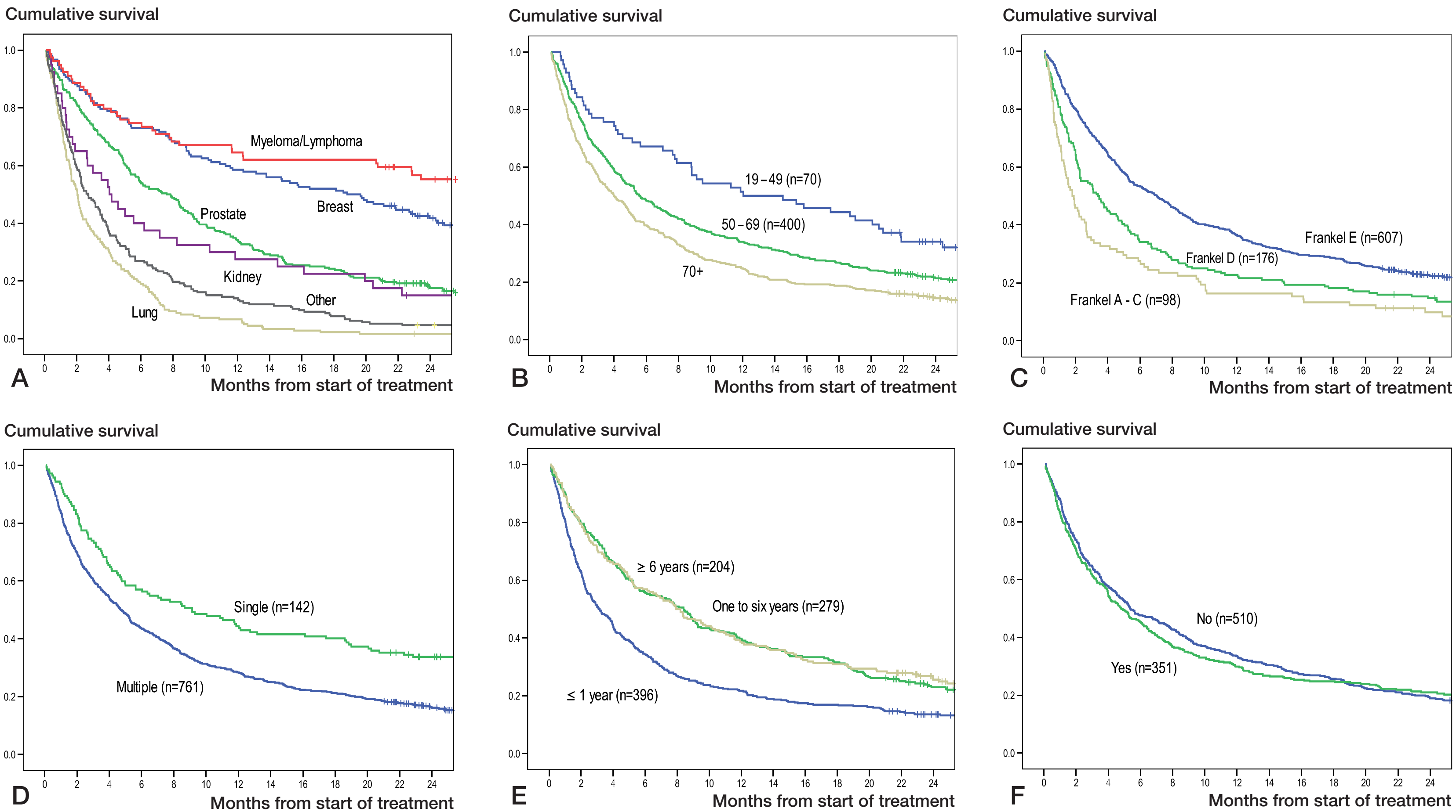

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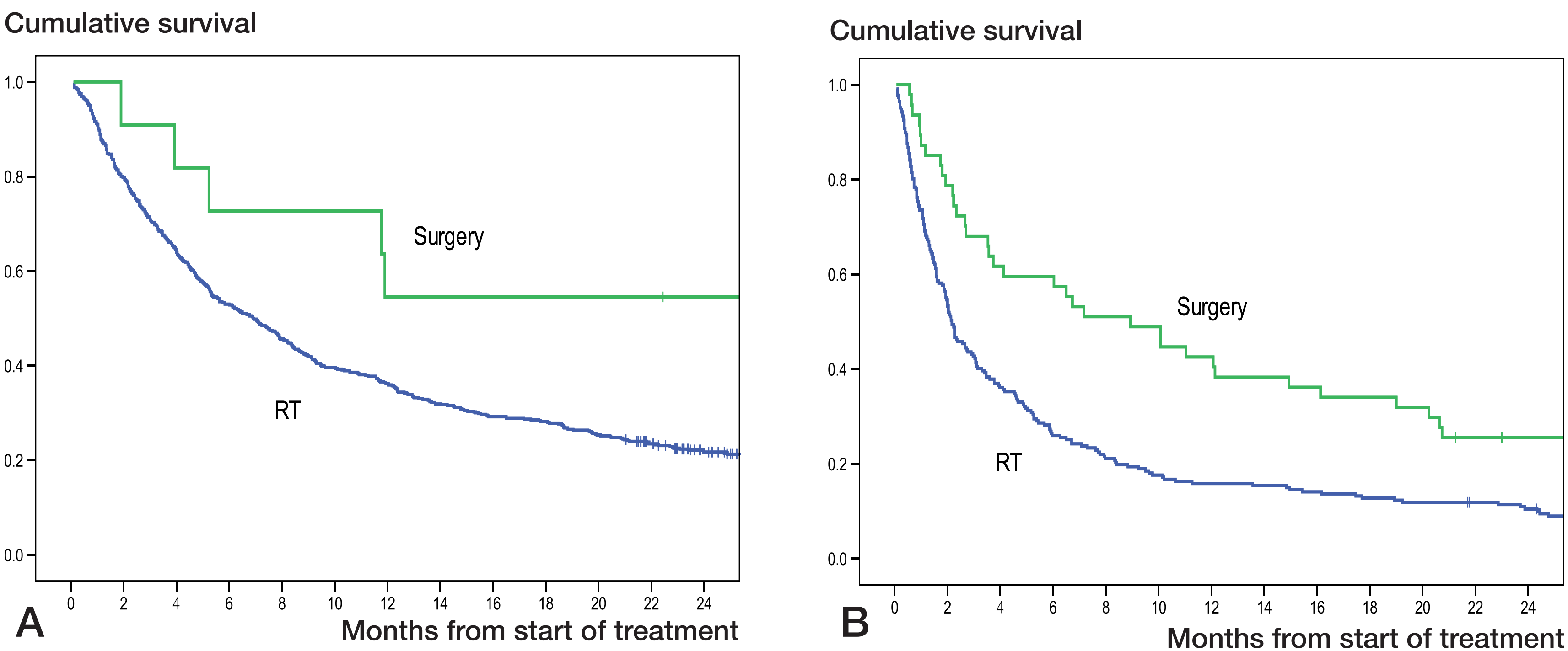

Figure 2. Kaplan-Meier plots with results of log-rank test of overall survival after surgery and radiotherapy (RT) for patients without motor impairment (Frankel E) (panel A; $p = 0.03$), and for patients with motor impairment (Frankel A–D) (panel B; $p < 0.001$).

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The Treatment of Spinal Metastases

by Karl-Stefan Delank, Clemens Wendtner, Hans Theodor Eich, and Peer Eysel

Klinik und Poliklinik für Orthopädie und Unfallchirurgie, Universität Köln: PD Dr. med. Delank, Prof. Dr. med. Eysel

Klinik I für Innere Medizin, Universität Köln: Prof. Dr. med. Wendtner

Klinik und Poliklinik für Strahlentherapie, Universität Köln: PD Dr. med. Eich

Prognostication for patients with spinal metastases [*1]

- **Criteria**
  - – No organ metastasis
  - – No pathological fracture
  - – Solitary skeletal metastasis
  - – No lung cancer
  - – The primary tumor is breast carcinoma, renal cell carcinoma, lymphoma, or myeloma
- **Prognosis**

  The one-year survival rate can be estimated from the number of the above criteria that are positive:

  4–5 positive criteria → one-year survival 50%

  2–3 positive criteria → one-year survival 25%

  0–1 positive criteria → one-year survival 0%

[*1] modified from (11)

Bauer HC, Wedin R: Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. Acta Orthop Scand 1995; 66(2): 143–6.

TABLE

The Tokuhashi Scoring System (5)

Category	Options (%)	Points
General condition (Karnofsky index)	Poor (10–40)	0
	Fair (50–70)	1
	Good (80–100)	2
Number of extraspinal bony metastases	≥ 3	0
	1–2	1
	0	2
Number of spinal metastases	≥ 3	0
	2	1
	1	2
Organ metastases	Unresectable	0
	Resectable	1
	None	2
Primary tumor	Lung, stomach	0
	Kidney, liver, uterus	1
	Thyroid, prostate, breast, rectum	2
Spinal cord damage	Complete	0
	Incomplete	1
	None	2

Recommendation:
≥ 9, radical tumor resection
≤ 5, palliative treatment

Diagnosis and management of metastatic spine disease

A review

Daniel M. Sciubba, M.D.,[1] Rory J. Petteys, M.D.,[1] Mark B. Dekutoski, M.D.,[2] Charles G. Fisher, M.D., M.P.H., F.R.C.S.C.,[3] Michael G. Fehlings, M.D., Ph.D., F.R.C.S.C.,[4] Stephen L. Ondra, M.D.,[5] Laurence D. Rhines, M.D.,[6] and Ziya L. Gokaslan, M.D.[1]

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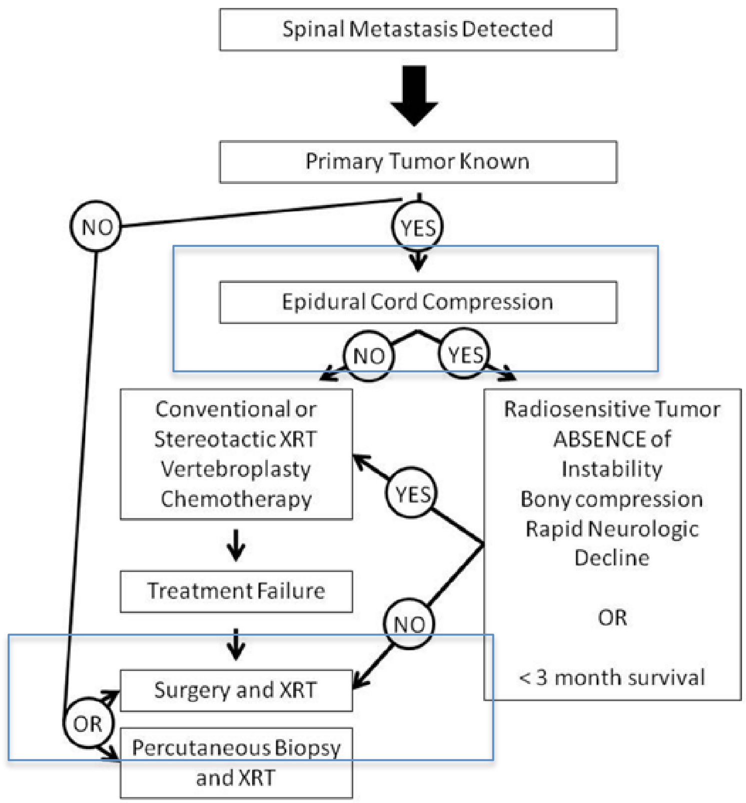

Fig. 2. Flowchart for the management of spinal metastases.

Neurosurg Spine 13:94–108, 2010

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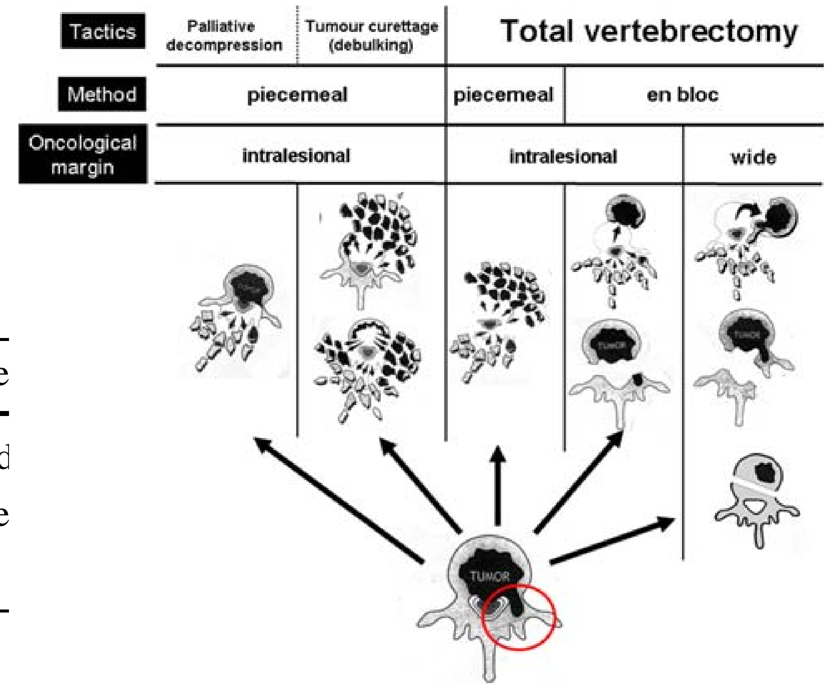
Review of metastatic spine tumour classification and indications for surgery: the consensus statement of the Global Spine Tumour Study Group

David Choi · A. Crockard · C. Bunger · J. Harms · N. Kawahara · C. Mazel · R. Melcher · K. Tomita

Fig. 5 Classification of surgical strategies, as determined by the Global Spine Tumour Study Group



Tomita prognostic score

	Score 1	Score 2	Score
Primary tumour	Slow growth	Moderate growth	Rapid
Visceral metastases		Treatable	Untre
Bone metastases	Solitary	Multiple	

Revised Tokuhashi prognostic score

	Score 0	Score 1	Score 2	Score 3	Score 4	Score 5
Karnofsky's performance (%)	10–40	50–70	80–100			
Extraspinal bone metastases	3 or more	1–2	0			
Vertebral metastases	3 or more	2	1			
Visceral metastases	Unremovable	Removable	None			
Primary site (e.g.)	Lung	Liver	Other	Kidney	Rectum	Breast
Palsy	Frankel A, B	Frankel C, D	Frankel E			

Eur Spine J (2010) 19:215–222

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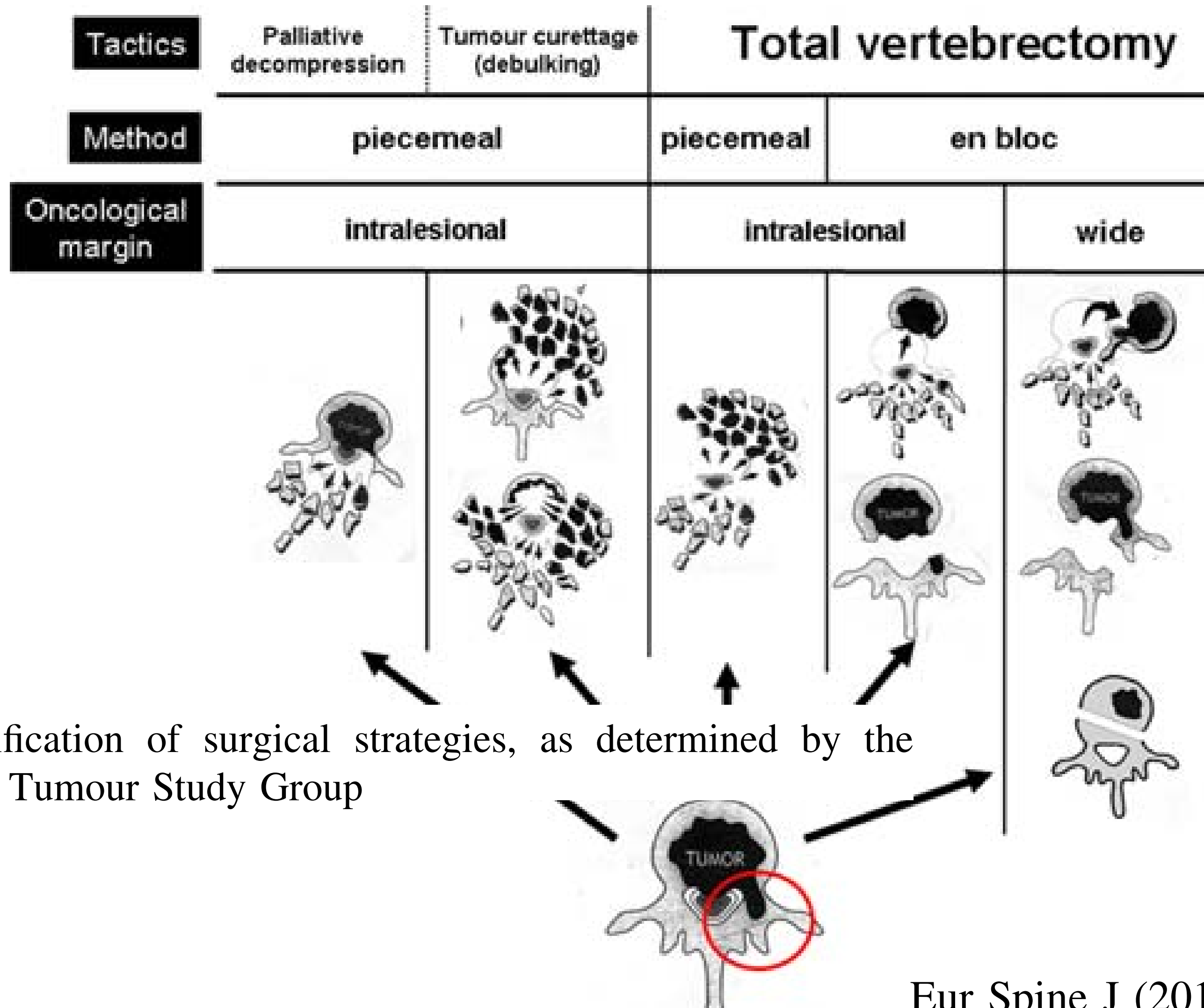

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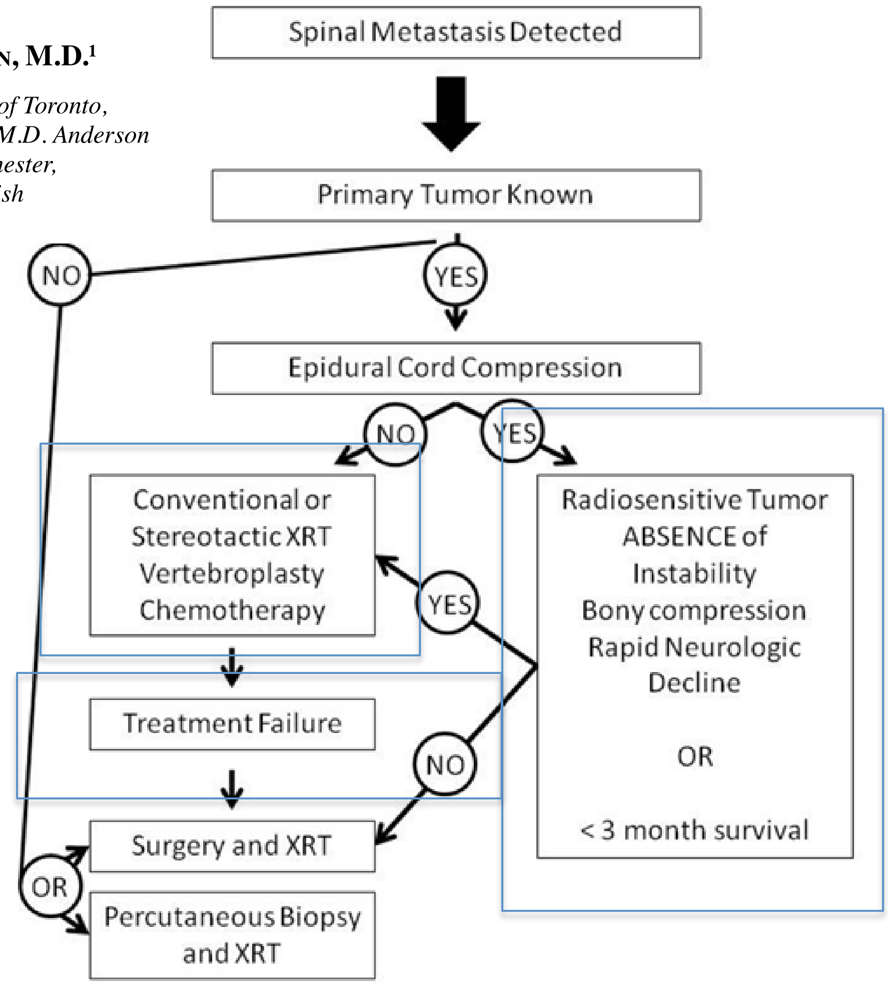

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Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 4, pp. 965–976, 2011

0360-3016/$ - see front matter

ASTRO GUIDELINE

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Suggested inclusion and exclusion criteria for patients considered for surgical intervention for spinal cord decompression

Characteristic	Factors favoring surgical decompression plus postoperative RT
Radiographic	1) Solitary site of tumor progression
	2) Absence of visceral or brain metastases
	3) Spinal instability
Patient	1) Age <65 y
	2) KPS ≥70
	3) Projected survival of >3 mo
	4) Slow progression of neurologic symptoms
	5) Maintained ambulation
	6) Nonambulatory for <48 h
Tumor	1) Relatively radioresistant tumor histologic type (*i.e.,* melanoma)
	2) Site of origin suggesting relatively indolent course (*i.e.,* prostate, breast, kidney)
Treatment	1) Previous EBRT failed

The references listed in Table 7 correspond to those cited in the full manuscript published online and contained in the Supplemental Materials section.

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Radiograph

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1) Previous EBRT failed

Breast Care

Recommendations of DEGRO and AGO on Standard Palliative Radiotherapy

Souchon/Feyer/Thomssen/Fehm/Diel/
Nitz/Janni/Bischoff/Sauer

Guidelines for MSCC

Instability of vertebral column, bony compression and/or paresis/paraplegia	immediate (within maximally 24–48 h) surgical intervention and postoperative RT (LoE 2b)
Spinal cord compression without neurologic deficits	in ambulatory patients: RT (LoE 2b); in case of analgesia as additional goal: short course of RT with increased single doses; in case of remineralization as additional goal: fractionated RT with conventional single doses
Acute onset of paresis/paraplegia	surgical decompression followed by RT; RT when decompression is not possible (LoE 3)
Inoperability	RT; choice of fractionation depending on life expectancy (LoE 3)
After surgical decompression	RT (LoE 2b)
In case of (in-field) recurrence after previous RT	surgery (when possible); re-irradiation (using high-precision techniques) (LoE 4)

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PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Studies investigating surgery and radiotherapy for spinal cord compression

Study	Patients (*n*), histologic type	Treatment regimen	Overall ambulation rate after treatment (%)	Duration of ability to ambulate	Survival	Regained ambulation after treatment (%)	Investigator	Year	Reference
Short-course vs. split-course RT for metastatic spinal cord compression: randomized trial	184, various histologic types	16 Gy/2 Fx, Days 1 and 7	68	3.5 mo	4 mo	29	Marazano	2005	73
		30 Gy/8 Fx (15 Gy/3 Fx then 15 Gy/5 Fx)	71	3.5 mo	4 mo	28			
8-Gy single-dose RT effective for metastatic spinal cord compression: results of Phase III randomized multicenter Italian trial	327, various histologic types	8 Gy/1 Fx	62	5 mo	4 mo	21	Marazano	2009	74
		16 Gy/2 Fx	69	5 mo	4 mo	32			
Surgery and RT vs. RT alone: randomized trial	101, various histologic types	Steroid, surgery, postoperative RT to 30 Gy/10 Fx	84	122 d	126 d	62	Patchell	2005	79
		Steroid, RT to 30 Gy/10 Fx	57	13 d	100 d	19			
Prospective evaluation of 2 RT schedules with 10 Fx vs. 20 Fx for metastatic spinal cord compression	214, various histologic types	30 Gy/10 Fx	60	NR	NR	29	Rades	2004	84
		40 Gy/20 Fx	64	NR	NR	30			

Keywords

- Patient selection: radiotherapy or surgery?
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Timing of surgery and radiotherapy in the management of metastatic spine disease: A systematic review

EYAL ITSHAYEK[1], JOSH YAMADA[2], MARK BILSKY[3], MEIC SCHMIDT[4], CHRISTOPHER SHAFFREY[5], PETER GERSZTEN[6], DAVID POLLY[7], ZIYA GOKASLAN[8], PETER PAUL VARGA[9] and CHARLES G. FISHER[10]

from International panel

Timing of surgery after radiotherapy.

Refs.	Description	Level of evidence (in relation to the primary question)	No. of patients meeting inclusion criteria	Treatment	Results	Conclusion
Ghogawala *et al* (7)	Retrospective	Level III	28	One-stage posterolateral decompression-stabilization	-9 patients suffered wound-related complications -46% complication rate if surgery was per[illegible] withi[illegible]	Spinal radiati[illegible] met[illegible]
Helweg-Larsen *et al* (13)	Prospective	[illegible]	[illegible]	[illegible] due to [illegible]eterioration	[illegible]erative course was not reported	Problem: small series.
[illegible]	[illegible]	[illegible]	14	-Posterolateral vertebrectomy and fusion -All patients were operated on more than a week after completing radio-therapy	-3 patients suffered wound-related complications	Preoperative radiotherapy did not raise the rate of wound-related complications. Problem: radiotherapy-surgery time interval was greater than a week.
Fourney *et al* (16)	Retrospective	Level III	43	Surgery through a posterior or combined anterior-posterior approach	-Timing of radiotherapy in relation to surgery was not specified	Preoperative radiotherapy was significantly related to postoperative complications (p=0.02).
Wang *et al* (15)	Retrospective review of prospectively maintained database	Level III	84	Posterolateral transpedicular vertebrectomy with circumferential fusion	-Median time to failure of radiotherapy was 4.2 months (range 0.1-64.4 months) -Only 6 patients were operated within a week of radiotherapy	No association was found between preoperative radiotherapy and postoperative wound infection (p=0.21). Preoperative radiotherapy within 6 weeks prior to surgery did not increase the infection rate (p=0.29). Problem: radiotherapy-surgery time interval was greater than a week for most patients.

Timing of surgery after radiotherapy.

INTERNATIONAL JOURNAL OF ONCOLOGY 36: 533-544, 2010

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Refs.	Description	Level of evidence (in relation to the primary question)	No. of patients meeting inclusion criteria	Treatment	Results	Conclusion
Holman *et al* (17)	Retrospective	Level III	139	-46 patients were previously irradiated -85 were operated through a posterior or combined anterior-posterior approach		Preoperative radiotherapy was not significantly related to postoperative complications (p=0.17). Problem: association betw[illegible]erative radio-therapy, the speci[illegible] and wound complic[illegible] issue of [illegible]
McPhee *et al* (9)	Retrospective	Level III	75 procedures on 53 patients	-52 were operated through a posterior approach -42 patients had periop[illegible] tive radiother[illegible] a mon[illegible]	-10 patient[illegible] w[illegible]	[illegible]ficantly [illegible] [illegible]ative radiotherapy and not [illegible]ative radiotherapy was investigated as a risk factor for wound complications.
Sundaresan *et al* (18)	Retrospective	Level III	[illegible]	[illegible] posterior approach -40 through a combined anterior-posterior approach -40 patients had preoperative radiotherapy	[illegible] suffered wound complications	Preoperative radiotherapy was significantly related to postoperative complications (p=0.03). Problem: association between preoperative radio-therapy, the specific surgical approach and wound complications was not examined. The issue of timing was not specified.
Sundare[illegible] *et al* (19[illegible]	[illegible]spective	Level III	110	-47 were previously irradiated -59 were operated through a posterior or combined anterior-posterior approach	-40% (4/10) of the patients that were operated due to disease progression while on radiotherapy suffered complications	Complications were significantly more frequent in patients that had preoperative radiotherapy (p<0.001). Problem: association between preoperative radio-therapy, the specific surgical approach and wound complications was not examined.
Wise *et al* (20)	Retrospective	Level II	80	-Patients underwent 88 procedures, 48 through a posterior approach -41 patients had preoperative radiotherapy	-8 patients, who had all had preoperative radiotherapy, suffered wound infection, 7 of them in a posterior approach wound	Preoperative radiotherapy was significantly related to postoperative complications. Problem: when the results were analyzed according to the surgical approach, the number of patients in each group was too small to draw statistically significant conclusions.

Possibility of wound infection

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Timing of radiotherapy after surgery.

Refs.	Description	Level of evidence (in relation to the primary question)	No. of patients meeting inclusion criteria	Treatment	Results	Conclusi[illegible]
Bach *et al* (31)	Retrospective	Level III	91	-Laminectomy followed by radiotherapy -Surgery-radiotherapy time interval was 5-8 days	-No patients were rep[illegible] to suffer wo[illegible] com[illegible]	[illegible]
Gilbert *et al* (32)	Retrospective	Level III	65	-Laminectomy foll[illegible] therapy -7[illegible]	[illegible] ...ys	[illegible] ...ot specified whether [illegible]e patients that had complications were from the preoperative radiotherapy group.
Hall *et al* (33)	Retrospective	Level III	[illegible]	[illegible] 1 week [illegible]	[illegible]o patients were reported to suffer wound-related complications	
Landman [illegible]	[illegible]	[illegible]	[illegible]	-Laminectomy followed by radiotherapy -Surgery-radiotherapy time interval was 2-3 weeks	-No patients were reported to suffer wound-related complications	
[illegible]	[illegible]	Level III	30	-29 patients had a transpedicular vertebrectomy and circumferential fusion -1 patient was operated through a combined anterior-posterior approach -All patients had postoperative radiotherapy -Surgery-radiotherapy time interval was 2 weeks	-2 wound infections, 1 deep and 1 superficial; it was not specified whether these occurred in a posterior or anterior wound -No patients suffered wound dehiscence	

Timing of radiotherapy after surgery.

Timing of surgery and radiotherapy in the management of metastatic spine disease: A systematic review

EYAL ITSHAYEK[1], JOSH YAMADA[2], MARK BILSKY[3], MEIC SCHMIDT[4], CHRISTOPHER SHAFFREY[5], PETER GERSZTEN[6], DAVID POLLY[7], ZIYA GOKASLAN[8], PETER PAUL VARGA[9] and CHARLES G. FISHER[10]

Timing of radiotherapy after surgery.

Refs.	Description	Level of evidence (in relation to the primary question)	No. of patients meeting inclusion criteria	Treatment	Results	Conclusion
Levy *et al* (36)	Retrospective	Level III	38	-Laminectomy followed by radiotherapy -Surgery-radiotherapy time interval was 1 week	-No patients were reported to suffer wound-related complications	
Onimus *et al* (37)	Not specified	Level III	57	-Patients underwent 60 proced... [illegible] ...or non- ...strumented fusion -42 patients had postoperative radiotherapy -Surgery-radiotherapy time interval was 8-10 days -Radiation was adminsitered at a dose of 18-20 Gy in 5 fractions over 5 days		
Wise *et al* (20)	Retrospective	Level III	80	-Patients underwent 88 procedures -48 were through a posterior approach -41 patients had preoperative radiotherapy	-8 patients, who had all had preoperative radiotherapy, suffered wound infection, 7 of them in a posterior approach wound	Postoperative radiotherapy was not significantly associated with postoperative complications. Problem: surgical approach and number of patients that had surgery followed by radiotherapy were not specified, nor was the surgery-radiotherapy time interval.

No wound-related complications

Timing of surgery and radiotherapy in the management of metastatic spine disease: A systematic review

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Timing of radiotherapy after surgery.

Refs.	Description	Level of evidence (in relation to the primary question)	No. of patients meeting inclusion criteria	Treatment	Results	Conclusion
Young *et al* (38)	Randomized prospective	Level III	16	-Laminectomy followed by radiotherapy vs. radiotherapy -Surgery-radiotherapy time interval was 1 week	-No patients suffered wound-related complications	
Ghogawala *et al* (7)	Retrospective	Level III	34	One-stage posterolateral decompression-stabilization procedure followed by radiotherapy	-4 patients suffered wound-related complications	Problem: surgery-radiotherapy time interval was not specified.
Shaw *et al* (28)	Not specified	Level III	2	One-stage posterolateral decompression-stabilization procedure followed by radiotherapy	-No patients suffered wound-related complications	Problem: surgery-radiotherapy time interval was not specified.
Sundaresan *et al* (29)	Not specified	Level III	5	Laminectomy followed by radiotherapy	-No patients suffered wound-related complications	Problem: surgery-radiotherapy time interval was not specified.

Timing of surgery and radiotherapy in the management of metastatic spine disease: A systematic review

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Current radiation treatment planning often includes three-dimensional conformal radiation dosing or stereotactic spinal radiotherapy. These treatment modalities may minimize the radiation dose to the skin at the surgical incision site. These important issues will also require investigation in future studies.

In conclusion, the authors recommend that the radiotherapy-surgery time interval should be at least one week for patients with previous radiotherapy. In the opposite scenario, when radiotherapy is given after surgery, a time interval of at least one week should also be maintained.

INTERNATIONAL JOURNAL OF ONCOLOGY 36: 533-544, 2010

Keywords

- Patient selection: radiotherapy or surgery?
- Timing
- Fractionation
- Technique and retreatment

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JOURNAL OF CLINICAL ONCOLOGY

Short-Course Versus Split-Course Radiotherapy in Metastatic Spinal Cord Compression: Results of a Phase III, Randomized, Multicenter Trial

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From the Radiation Oncology Center, Azienda Ospedaliera, Terni; Radiation Oncology Center, University School of Medicine, and Service of Medical Physics, Policlinico Hospital; Medical Oncology Service, Azienda Sanitaria n.2, Perugia; Radiation Oncology Center, Hospital, Arezzo; Radiation Oncology Center, Hospital, Lucca; and Radiation Oncology Center, University School of Medicine, Careggi Hospital, Firenze, Italy.

Table 1. Patient Characteristics According to Radiotherapy Regimen

Characteristic	Short Course		Split Course		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
All patients	142	51	134	49	276 of 300*	92
Sex						
Male	99	70	92	69	191	69
Female	43	30	42	31	85	31
Age, years						
Range	30-87		34-89		30-89	
Median	66		68		68	
Karnofsky performance status						
≤ 40	46	32	40	30	86	31
50-70	76	54	67	50	143	52
80-100	20	14	27	20	47	17
Back pain						
No	6	4	8	6	14	5
Yes	136	96	126	94	262	95
Motor function						
Walking	93	65	91	68	184	67
Without support	51	36	56	42	107	39
With support	42	30	35	26	77	28
Not walking	49	34	43	32	92	33
Unable to walk	40	28	35	26	75	27
Paraplegic	9	6	8	6	17	6
Sphincter control						
Normal	126	89	120	90	246	89
Abnormal	16	11	13	10	29	11
Histology						
Favorable	50	35	49	37	99	36
Unfavorable	92	65	85	63	177	64

*Twenty-four patients (8%) are not assessable as a result of early death (17 patients) or because they were lost to follow-up (seven patients).

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Table 1. Patient Characteristics According to Radiotherapy Regimen

Characteristic	Short Course: No. of Patients	Short Course: %	Split Course: No. of Patients	Split Course: %	Total: No. of Patients	Total: %
All patients	142	51	134	49	[illegible]	[illegible]
Sex						
Male	99	70	92	[illegible]	[illegible]	[illegible]
Female	43	30	42	[illegible]	[illegible]	[illegible]
Age, years						
Range	30-87		[illegible]		30-89	
Median	[illegible]		[illegible]		68	
Karnofsky performance status						
≤ 40	[illegible]	[illegible]	[illegible]	30	86	31
50-70	[illegible]	[illegible]	[illegible]	50	143	52
80-100	[illegible]	[illegible]	27	20	47	17
[illegible]						
[illegible]	[illegible]	4	8	6	14	5
[illegible]	136	96	126	94	262	95
[illegible]						
[illegible]	93	65	91	68	184	67
Without support	51	36	56	42	107	39
With support	42	30	35	26	77	28
Not walking	49	34	43	32	92	33
Unable to walk	40	28	35	26	75	27
Paraplegic	9	6	8	6	17	6
Sphincter control						
Normal	126	89	120	90	246	89
Abnormal	16	11	13	10	29	11
Histology						
Favorable	50	35	49	37	99	36
Unfavorable	92	65	85	63	177	64

*Twenty-four patients (8%) are not assessable as a result of early death (17 patients) or because they were lost to follow-up (seven patients).

Three hundred patients with MSCC were randomly assigned to a short-course RT (8 Gy × 2 days) or to a split-course RT (5 Gy × 3; 3 Gy × 5). Only patients with a short life expectancy entered the protocol. Median follow-up was 33 months (range, 4 to 61 months).

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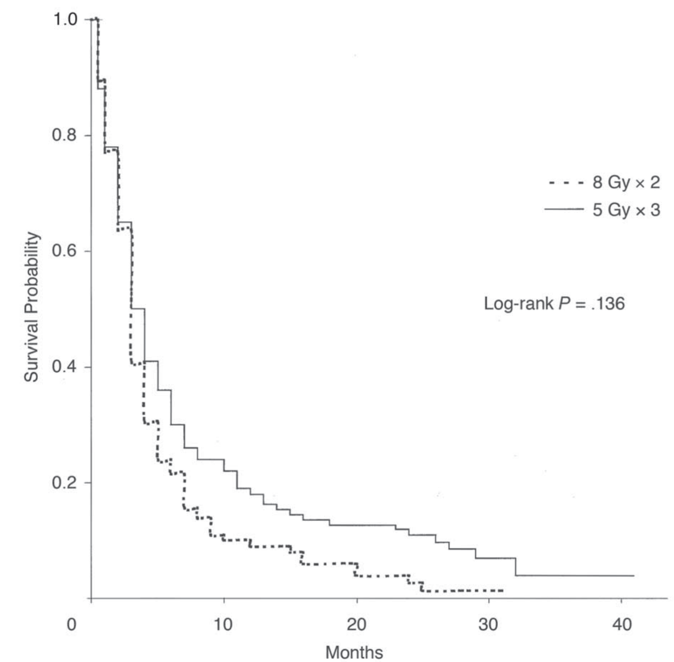
Table 5. Median Duration of Improvement in Motor Capacity per Group

Patient Group	Responders* No.	Responders* Total %	Median Duration of Improvement (months)	*P*
Radiotherapy regimen				
Short course	97/142	68	3.5	
Split course	95/134	71	3.5	
Post-treatment walking patients	192/276	70	4	
Pretreatment status				
Walking patients	167/184	91	4	
Nonwalking patients	26/92	28	3	
Histology				
Favorable	73/96	76	6	
Unfavorable	119/180	66	3	.0001

*Those patients who remained able to walk or regained ability to walk after radiotherapy.



Phase III randomised trial

8 Gy single-dose radiotherapy is effective in metastatic spinal cord compression: Results of a phase III randomized multicentre Italian trial

Ernesto Maranzano [a,*], Fabio Trippa [a], Michelina Casale [a], Sara Costantini [a], Marco Lupattelli [b], Rita Bellavita [b], Luigi Marafioti [c], Stefano Pergolizzi [d], Anna Santacaterina [d], Marcello Mignogna [e], Giovanni Silvano [f], Vincenzo Fusco [g]

Motor and sphincter function before and after treatment according to radiotherapy regimen.

	8 Gy × 2 short-course No. of patients (%)	8 Gy single-dose No. of patients (%)	Total No. of patients (%)
Motor function			
1. Walking pretreatment	101 (67)	98 (64)	199 (65)
Walking	91 (90)	86 (88)	177 (89)
Not walking	10 (10)	12 (12)	22 (11)
2. Not walking pretreatment	49 (33)	55 (36)	104 (35)
Ambulation regained	13 (26)	9 (16)	22 (21)
Not walking	36 (74)	46 (84)	82 (79)
Total of responders	104 (69)	95 (62) *p* = N.S.	199 (66)
Sphincter control			
1. Normal pretreatment	135 (90)	127 (83)	262 (86)
Good sphincter control	129 (95)	121 (95)	250 (95)
Poor sphincter control	6 (5)	6 (5)	12 (5)
2. Abnormal pretreatment	15 (10)	26 (17)	41 (14)
Sphincter control regained	2 (13)	9 (35)	11 (27)
Poor sphincter control	13 (87)	17 (65)	30 (73)
Total of responders	131 (87)	130 (85) *p* = N.S.	261 (86)

Back pain before and after treatment according to radiotherapy regimen.

	8 Gy × 2 short-course No. of patients (%)	8 Gy single-dose No. of patients (%)	Total No. of patients (%)
No analgesic pretreatment	16 (11)	16 (10)	32 (11)
Outcome			
No pain	12 (75)	15 (94)	27 (84)
Appearance of pain	4 (25)	1 (6)	5 (16)
Minor analgesics	10 (7)	15 (9)	25 (8)
Outcome			
No pain	3 (30)	3 (20)	6 (24)
Stable pain	3 (30)	4 (27)	7 (28)
Worse pain	4 (40)	8 (53)	12 (48)
Minor narcotics (codeine)	29 (19)	40 (26)	69 (23)
Outcome			
No pain	10 (34)	14 (35)	24 (35)
Minor analgesics	6 (21)	3 (7)	9 (13)
Stable pain	11 (38)	14 (35)	25 (36)
Worse pain	2 (7)	9 (23)	11 (16)
Major narcotics (morphine)	95 (63)	82 (55)	177 (58)
Outcome			
No pain	10 (11)	10 (12)	20 (11)
Minor analgesics	13 (14)	6 (8)	19 (11)
Minor narcotics	12 (13)	11 (13)	23 (23)
Stable pain	60 (62)	55 (67)	115 (65)
Total responders	80 (53)	80 (52)	160 (53)

[a] Radiotherapy Centre, "S. Maria" Hospital, Terni, Italy
[b] Radiotherapy Centre, University Hospital, Perugia, Italy
[c] Radiotherapy Centre, "Mariano Santo" Hospital, Cosenza, Italy
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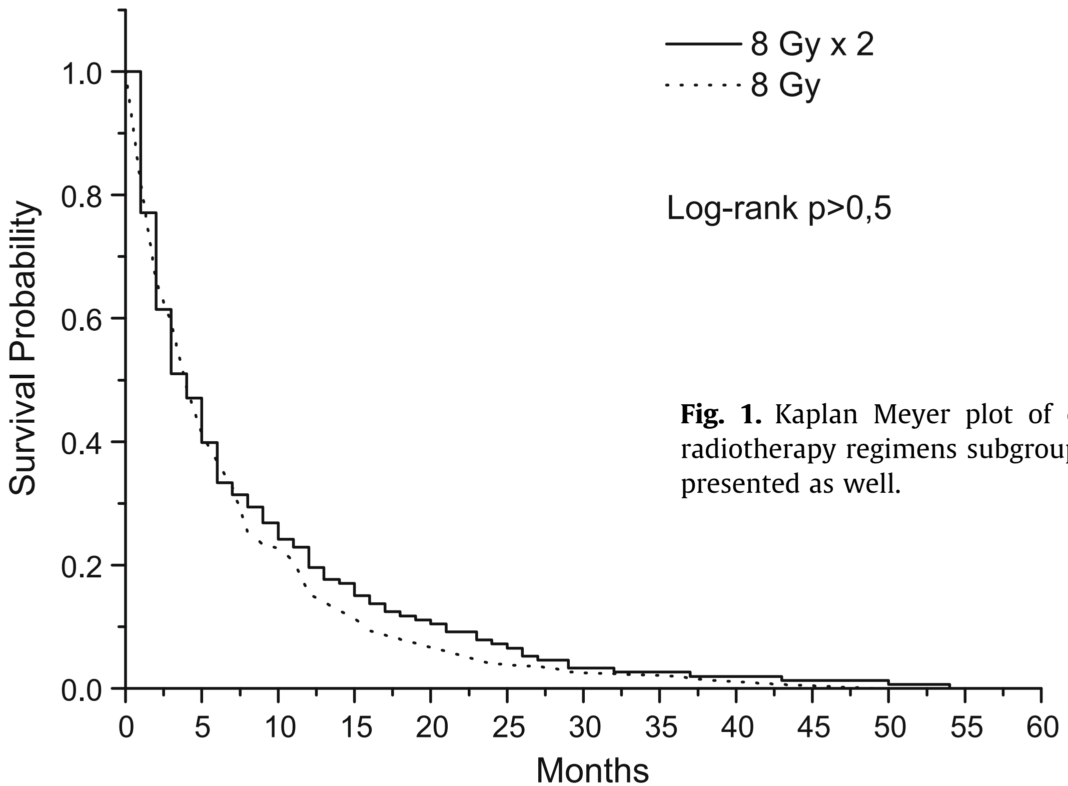

8 Gy x2	150	73	35	12	5	3
8 Gy	153	72	41	17	7	4

Fig. 1. Kaplan Meyer plot of overall survival probability as a function of the radiotherapy regimens subgroups. The Number of patients at risk and *p*-value are presented as well.

Original Article

Palliative Response and Functional Interference Outcomes Using the Brief Pain Inventory for Spinal Bony Metastases Treated with Conventional Radiotherapy

J. Nguyen, E. Chow, L. Zeng, L. Zhang, S. Culleton, L. Holden, G. Mitera, M. Tsao, E. Barnes, C. Danjoux, A. Sahgal

Rapid Response Radiotherapy Program, Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Canada

Patient characteristics at initial consultation ($n = 109$)

Age	
Mean	66.1
Median (range)	68 (33–90)
Karnofsky performance score	
Mean	70.7
Median (range)	75 (0–90)
Worst pain	
Mean	7.57
Median (range)	8.0 (2–10)
Total OMED (mg/day)	
Mean	97.5
Median (range)	30 (0–2600)
Pain relief (%)	
n	90
Mean ± standard deviation	66.4 ± 27.6
Median (range)	70 (0–100)
Primary cancer site	
Breast	31 (28%)
Prostate	30 (28%)
Lung	27 (25%)
Genitourinary	8 (7%)
Gastrointestinal	6 (6%)
Other/unknown primary	5 (5%)/2 (2%)
Radiation site	
SPTL	56 (52%)
SPLS	44 (40%)
SPCT	9 (8%)
Dose fraction Gy/fraction(s)	
8/1	56 (51%)
20/5	49 (45%)
Other	4 (4%)

Clinical Oncology 23 (2011) 485–491

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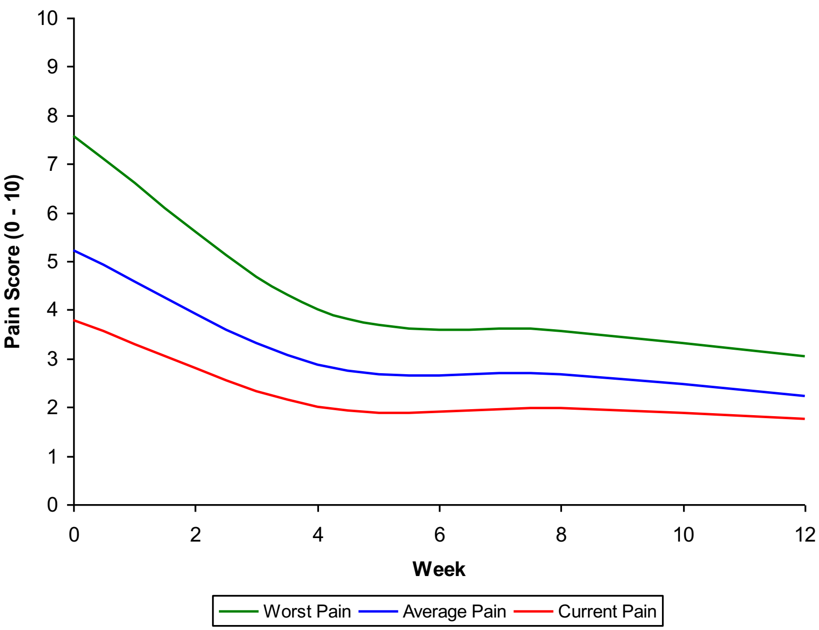
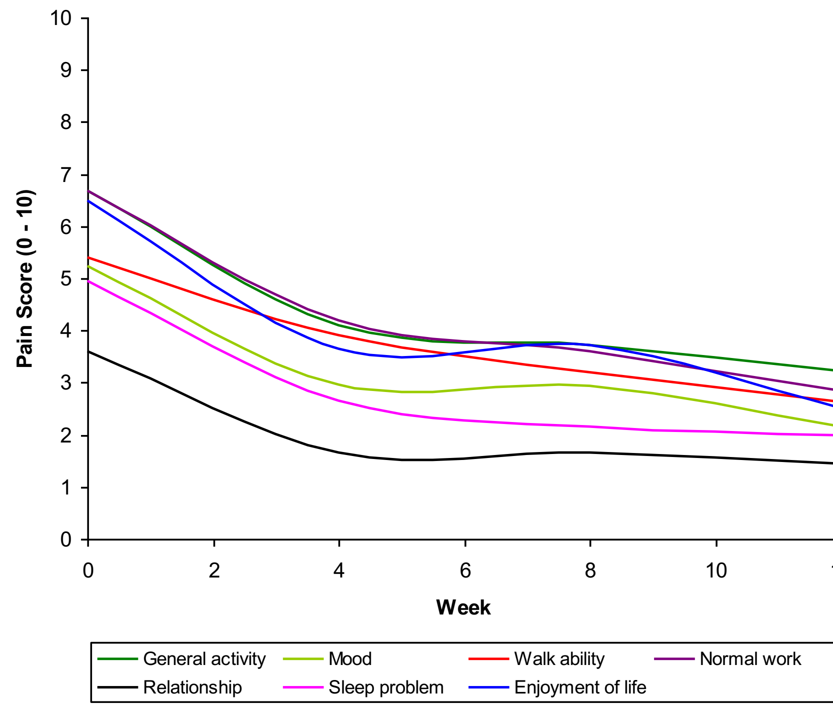
Pain reduction over time.



Brief Pain Inventory functional score changes over time.



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Comparison of patient demographics/characteristics with response to radiotherapy

Variable	Comparing responders versus non-responders (*P* value)		
	Month 1	Month 2	Month 3
Age at radiation	0.27	0.35	0.71
Karnofsky performance score at baseline	0.19	0.18	0.72
Pain relief at baseline (%)	0.06	0.91	0.48
Gender (male versus female)	0.83	0.82	0.10
Primary cancer site (breast, prostate, lung)	0.25	*0.02*	0.37
Radiation site (SPLS, SPLT, SPTC)	0.91	0.05	0.38
Dose fraction (single versus multiple)	0.16	0.27	0.54

SPCT, cervical/cervical thoracic spine; SPTL, thoracic/thoraco-lumbar spine; SPLS, lumbar/lumbosacral spine.

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SPCT, cervical/cervical thoracic spine; SPTL, thoracic/thoraco-lumbar spine; SPLS, lumbar/lumbosacral spin

	Month 3
Primary cancer site (breast, prostate, lung)	0.37
Radiation site (SPLS, SPLT, SPTC)	0.38
Dose fraction (single versus multiple)	0.54

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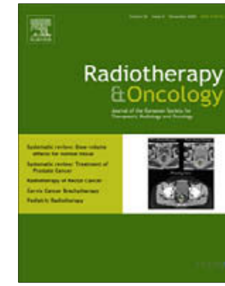

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Walking capacity before and after treatment according to radiotherapy (RT) regimen.

RT regimen	Pretreatment		Post-treatment no. of cases by group*			
(No. of patients)	Group	No. of cases	I	II	III	IV
8 Gy × 2 (150)	I	59	53	4	2	–
	II	42	17	17	6	2
	III	40	2	11	24	3
	IV	9	–	–	2	7
8 Gy (153)	I	55	49	3	3	–
	II	43	9	25	6	3
	III	38	3	5	26	4
	IV	17	–	1	1	15
All patients (303)	I	114	102	7	5	–
	II	85	26	42	12	5
	III	78	5	16	50	7
	IV	26	–	1	3	22

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Back pain before and after treatment according to radiotherapy regimen.

	8 Gy × 2 short-course No. of patients (%)	8 Gy single-dose No. of patients (%)	Total No. of patients (%)
No analgesic pretreatment	16 (11)	16 (10)	32 (11)
Outcome			
No pain	12 (75)	15 (94)	27 (84)
Appearance of pain	4 (25)	1 (6)	5 (16)
Minor analgesics	10 (7)	15 (9)	25 (8)
Outcome			
No pain	3 (30)	3 (20)	6 (24)
Stable pain	3 (30)	4 (27)	7 (28)
Worse pain	4 (40)	8 (53)	12 (48)
Minor narcotics (codeine)	29 (19)	40 (26)	69 (23)
Outcome			
No pain	10 (34)	14 (35)	24 (35)
Minor analgesics	6 (21)	3 (7)	9 (13)
Stable pain	11 (38)	14 (35)	25 (36)
Worse pain	2 (7)	9 (23)	11 (16)
Major narcotics (morphine)	95 (63)	82 (55)	177 (58)
Outcome			
No pain	10 (11)	10 (12)	20 (11)
Minor analgesics	13 (14)	6 (8)	19 (11)
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8 Gy single-dose radiotherapy is effective in metastatic spinal cord compression: Results of a phase III randomized multicentre Italian trial

Walking capacity before and after treatment according to radiotherapy (RT) regimen.

RT regimen	Pretreatment		Post-treatment no. of cases by group*			
(No. of patients)	Group	No. of cases	I	II	III	IV
8 Gy × 2 (150)	I	59	53	4	2	–
	II	42	17	17	6	2
	III	40	2	11	24	3
	IV	9	–	–	2	7
8 Gy (153)	I	55	49	3	3	–
	II	43	9	25	6	3
	III	38	3	5	26	4
	IV	17	–	1	1	15
All patients (303)	I	114	102	7	5	–
	II	85	26	42	12	5
	III	78	5	16	50	7
	IV	26	–	1	3	22

Back pain before and after treatment according to radiotherapy regimen.

	8 Gy × 2 short-course No. of patients (%)	8 Gy single-dose No. of patients (%)	Total No. of patients (%)
No analgesic pretreatment	16 (11)	16 (10)	32 (11)
Outcome			
No pain	12 (75)	15 (94)	27 (84)
Appearance of pain	4 (25)	1 (6)	5 (16)
Minor analgesics	10 (7)	15 (9)	25 (8)
Outcome			
No pain	3 (30)	3 (20)	6 (24)
Stable pain	3 (30)	4 (27)	7 (28)
Worse pain	4 (40)	8 (53)	12 (48)
Minor narcotics (codeine)	29 (19)	40 (26)	69 (23)
Outcome			
No pain	10 (34)	14 (35)	24 (35)
Minor analgesics	6 (21)	3 (7)	9 (13)
Stable pain	11 (38)	14 (35)	25 (36)
Worse pain	2 (7)	9 (23)	11 (16)
Major narcotics (morphine)	95 (63)	82 (55)	177 (58)
Outcome			
No pain	10 (11)	10 (12)	20 (11)
Minor analgesics	13 (14)	6 (8)	19 (11)
Minor narcotics	12 (13)	11 (13)	23 (23)
Stable pain	60 (62)	55 (67)	115 (65)
Total responders	80 (53)	80 (52)	160 (53)

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ASTRO GUIDELINE

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Studies investigating vertebroplasty/kyphoplasty and bone metastases

Study	Patients (*n*)/ levels (*n*)	Diagnoses	Pain scale	Mean preprocedure score	Mean postprocedure score	Symptomatic extravasation rate (%)	Neurologic toxicity	Investigator	Year	Reference
Prospective studies using vertebroplasty										
Percutaneous vertebroplasty and bone cement leakage	14/42	Various histologic types, MM, H	Visual analog scale (0–10)	8	1	0	0	Anselmetti	2008	125
Percutaneous vertebroplasty in octogenarians: results and follow-up	22/48	Various histologic types, MM	Verbal rating scale (0–5)	5	2	0	0	Cahana	2005	126
Percutaneous vertebroplasty in patients with intractable pain from osteoporotic or metastatic fractures	13	Various histologic types	Site-specific pain score (0–10)	NR	NR	8	8	Cheung	2006	127
Percutaneous vertebroplasty for osteolytic metastases and myeloma	37/40	Various histologic types, MM	McGillMelzack (0–5)	Pain relief*	Pain relief*	2	8	Cotton/ Cortet	1996/ 1997	128, 129
Medium-term results of percutaneous vertebroplasty in MM	12/19	MM	Visual analog scale (0–10)	8	3	0	0	Ramos	2006	130
Prospective studies using kyphoplasty										
Kyphoplasty in treatment of osteolytic vertebral compression fractures resulting from MM	18/55	MM	Short form-36 (0–100)	23	55	0	0	Dudeney	2002	131
Combination kyphoplasty and spinal radiosurgery	26/26	Various histologic types	Visual analog scale (0–10)	8	3	0	0	Gerszten	2005	132
Functional outcomes of kyphoplasty for treatment of osteoporotic and osteolytic vertebral compression fractures	56	MM	Short form-36 (0–100)	28	48	NR	NR	Khanna	2006	133
Kyphoplasty enhances function and structural alignment in MM	19/46	MM	NR	NR	NR	0	0	Lane	2004	134
Balloon kyphoplasty in treatment of metastatic disease of spine	65/99	Various histologic types	Visual analog scale (0–10)	8	3	0	0	Pflugmacher	2008	135

Keywords

- Patient selection: radiotherapy or surgery?
- Timing
- Fractionation
- Technique and retreatment

  High conformity

  High precision

  High Dose

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ASTRO GUIDELINE

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Summary of current data for spinal SBRT for spinal metastases

Study	Patients (*n*), tumors (*n*), histologic type	Fractionation	Repeat RT	Pain relief	Complete response	Local control/ definition	Investigator	Year	Reference
Cohort study	69, 127, various histologic types	Mean: 15.5 Gy/2 Fx	15 patients	61/69	NR	96.8% FFP at 10 mo; 123/127 (97%)/ imaging	Tsai	2009	63
Cohort study	38, 60, various histologic types	Median: 24 Gy/3 Fx	37 tumors	31/46	NR	Repeat RT: 34/37 (92%); no previous treatment: 18/23 (78%); entire cohort: 85%, 1-y FFP*/ imaging and pain	Sahgal	2009	64
Cohort study	93, 103, various histologic types	Median: 24 Gy/ 1 Fx	0	NR	NR	90% FFP at 15 mo	Yamada	2008	65
Cohort study	32, 33, various histologic types	Median 18 Gy/3 Fx	22 patients	30/32	13/32 at 1 mo	28/32/imaging and/or pain	Nelson	2008	66
Phase I-II study with defined stopping rules	63, 74, various histologic types	30 Gy/5 Fx (32/ 63) or 27 Gy/ 3 Fx (31/63)	35 patients	Narcotic use declined from 60% to 36% at 6 mo	NR	57/74; 1-y FFP: 84%/imaging	Chang	2007	51
Cohort study	393, 500, various histologic types	Mean 20 Gy/1 Fx	344 tumors	290/336 improvement	NR	440/500/ imaging	Gerszten	2007	57
Cohort study	49, 61, various histologic types	10–16 Gy/1 Fx	0	52/61	NR	57/61/imaging and pain	Ryu	2005	56
Cohort study	21, 21	Median 20 Gy/5 Fx	20 patients	NR	NR	19/21/imaging	Yamada	2005	67
Cohort study	5, 5	10 Gy/1 Fx	5 patients	NR	NR	5/5/imaging and/or pain	Hamilton	1995	68

Stereotactic body radiotherapy for spinal metastases: current status, with a focus on its application in the postoperative patient

A review

only studies reporting on spinal metastases*

Authors & Year	Total No. Tumors/ No. Pts	No. Tumors w/ Retx/ No. Pts	No. Postop Pts	FU in Mos (range)	Local Control/Criteria†	Tumor Dose/No. Frx/Rx Isodose	Pain Response (pain assessment tool)
postop SBRT							
Moulding et al., 2010	21/21	0	21	median 10.3	17 of 21 (81%) w/ 1-yr local control 90.5%/imaging	median 24 Gy/1/100%	NS
Rock et al., 2006	18/18	1/1	18	median 7 (4–36)	17 of 18 (94%)/imaging &/or clinical	4 of 18: EBRT 25 Gy/10 frx + SBRT boost; median 6 Gy/1/90%; 14 of 18: SBRT only; median 14 Gy/1/90%	6 of 18 w/ CR (NS)
Gerszten et al., 2005[17]	26/26	7/7	26	median 16 (11–24)	24 of 26 (92%)/imaging & pain	mean 18 Gy/1/80%	improved in 24 of 26 (VAS)
total	65/65	8/8	65		58 of 65 (89%)		
SBRT for tumors w/ no prior radiation							
Yamada et al., 2008	103/93	0/0	0	median 15 (2–45)	90% at 15 mos, ~93 of 103/imaging	median 24 Gy/1/100%	NS
Ryu et al., 2004	61/49	0/0	NS	median 6.4 (6–24)	57 of 61 (93%)/imaging & pain	10–16 Gy/1/90%	85% comb CR/PR rate (VAS)
Ryu et al., 2003	10/10	0/0	NS	mean 6 (3–12)	10 of 10 (100%)/imaging & pain	EBRT 25 Gy/10 frx + SBRT boost; 6–8 Gy/1/90%	5 of 9 w/ CR, 4 of 9 w/ PR (NS)‡
Sahgal et al., 2009[45]	23/14	0/0	5	median 9 (1–26)	18 of 23 (78%)/imaging &/or pain§	median 24 Gy/3/67%	NS
total	197/166	0/0			178 of 197 (90%)		
SBRT for tumors w/ prior radiation							
Mahan et al., 2005	8/8	8/8	0	mean 15.2	8 of 8 (100%)/NS	median 30 Gy/15/NS	6 of 8 w/ CR, 2 of 8 w/ PR (NS)
Milker-Zabel et al., 2003	19/18	19/18	0	median 12 (4–33)	18 of 19 (95%)/imaging	median 39.6 Gy/2 (aim was 90% coverage)	13 of 16 (NS)
Hamilton et al., 1995	5/5	5/5	0	median 6 (1–12)	5 of 5 (100%)/imaging &/or clinical	median 10 Gy/1/80%	NS
Sahgal et al., 2009[45]	37/25	37/25	0	median 7 (1–48)	34 of 37 (92%)/imaging &/or pain	median 24 Gy/3/60%	NS
total	69/56	69/56	0		65 of 69 (94%)		
studies w/ a mixture of SBRT indications							
Nguyen et al., 2010	55/48	NS/22	15	median 13.1 (3.3–54.5)	43 of 55 (78%; 1-yr FFP 82%)/imaging	30 Gy/5 frx; 24 Gy/3; 24 Gy/1; Rx isodose such that CTV covered by 80%–90%	52% w/ lasting response; pain free at 12 mos (BPI)
Tsai et al., 2009	127/69	NS/15	0	median 10 (3–21)	96.8% at 10 mos, 123 of 127 (97%)/imaging	mean 15.5 Gy/2/80%	61 of 69 w/ improved pain (VAS)
Nelson et al., 2008	33/32	NS/22	0	median 7 (3–21)	29 of 33 (88%)/imaging &/or pain	median 18 Gy/3/NS	13 of 32 w/ CR & 17 of 32 w/ PR at 1 mo (questionnaire)
Chang et al., 2007	74/63	NS/35	29	median 21.3 (1–50)	57 of 74 (77%; 1-yr FFP 84%)/imaging	30 Gy/5 frx (32 of 63); or 27 Gy/3 frx (31 of 63); Rx isodose such that 80%–90% target coverage	narcotic use declined from 60% to 36% at 6 mos (BPI)

A. Sahgal et al. **J Neurosurg Spine 14:**151–166, 2011

Stereotactic body radiotherapy for spinal metastases: current status, with a focus on its application in the postoperative patient

A review

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Authors & Year	Total No. Tumors/ No. Pts	No. Tumors w/ Retx/ No. Pts	No. Postop Pts	FU in Mos (range)	Local Control/Criteria†	Tumor Dose/No. Frx/Rx Isodose	Pain Response (pain assessment tool)
studies w/ a mixture of SBRT indications							
Gibbs et al., 2007	102/74	50/NS	0	mean 9 (0–33)	NS	14–25 Gy/1–5/61%–89%	84% of symptomatic pts w/ resolution or benefit (VAS)
Gerszten et al., 2007	500/393	344/NS	9/500 tumors	median 21 (3–53)	440 of 500 (88%)/imaging	mean 20 Gy/1/80% (7 of 500 w/ comb EBRT + SBRT boost)	290 of 336 w/ improvement (VAS)
Yamada et al., 2005	21/21	20/20	0	median 7 (1–24)	19 of 21 (90%; actuarial 81%)/imaging	median 20 Gy/5 frx	NS for pts w/ metastases only (0–10 self-assessed pain scale)
total	912/700	508/508¶			710 of 809 (88%)		

* BPI = brief pain inventory; comb = combined; CR = complete pain relief; FFP = freedom from progression; FU = follow-up; NS = not specified; PR = partial pain relief; pts = patients; Retx = reirradiation; VAS = visual analog scale.

† Local control for postoperative patients in those nondedicated postoperative mixed cohort series: 4/5 in Sahgal et al.[45]; 10/15 in Nguyen et al.; 23/29 in Chang et al.

‡ One patient obtained pain relief from surgery prior to SBRT; therefore, the number of cases was 9.

§ Details provided by primary author of the publication, although not specified in the paper.

¶ Assumed that the number of patients is the same as number of tumors treated for those not specified, to give a rough estimate to the reader.

Stereotactic body radiotherapy for spinal metastases: current status, with a focus on its application in the postoperative patient

A review

Summary of patterns of failure with spine SBRT

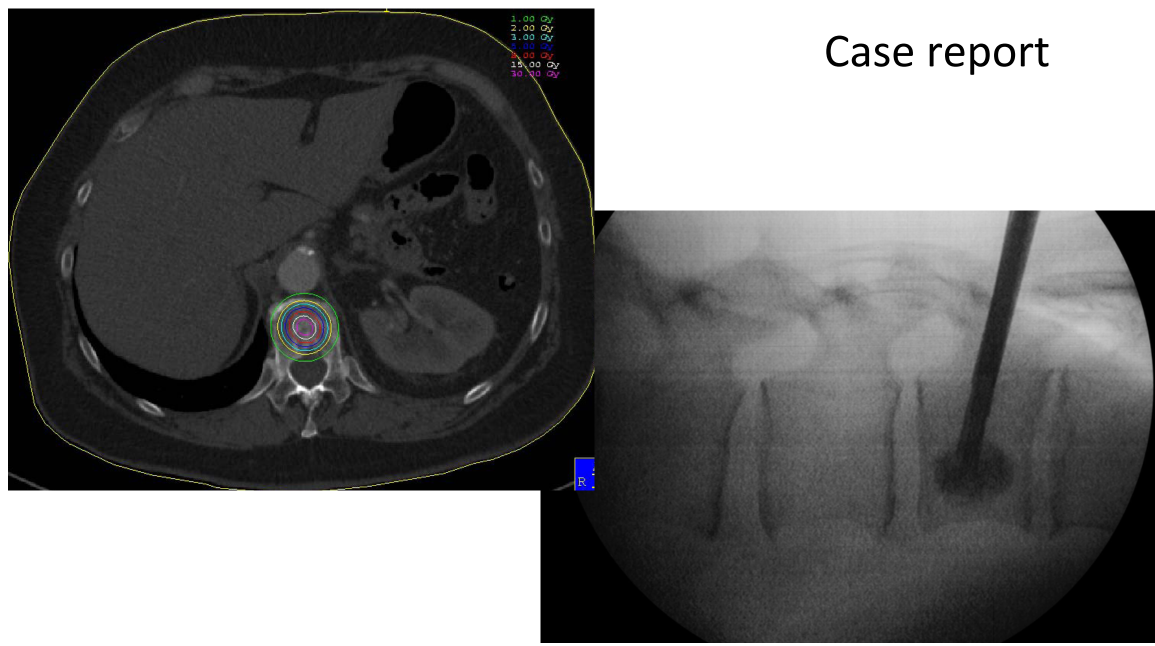
Authors & Year	Incidence
adjacent vertebral segment failure	
Gerszten et al., 2007	0 of 500 tumors
Ryu et al., 2004	3 of 61 tumors
Nelson et al., 2008	0 of 33 tumors
failure at epidural space	
Nguyen et al., 2010	6 of 55 tumors (6 of 12 total failures)
Chang et al., 2007	8 of 74 tumors (8 of 17 total failures)
Milker-Zabel et al., 2003	1 of 19 tumors had “intradural progression”
Gerszten et al., 2007	2 of 35 pts treated for progressive neurological deficits progressed further to complete paraplegia (medically inoperable)
Gibbs et al., 2007	specify that 1 patient w/ preexisting myelopathy continued to progress despite Tx
Nelson et al., 2008	2 of 33 tumors (2 of 4 total failures)
failure sites where anatomy was intentionally excluded	
Nguyen et al., 2010	
posterior elements	5 of 55 tumors (5 of 12 failures)
paraspinal tissue	3 of 55 tumors (3 of 12 failures)
Chang et al., 2007	
paraspinal tissue	4 of 74 tumors (4 of 17 total failures)
posterior elements	3 of 74 tumors (3 of 17 total failures)

A. Sahgal et al. **J Neurosurg Spine 14:**151–166, 2011

Kypho-IORT - a novel approach of intraoperative radiotherapy during kyphoplasty for vertebral metastases

Frederik Wenz[1*], Frank Schneider[1], Christian Neumaier[1], Uta Kraus-Tiefenbacher[1], Tina Reis[1], René Schmidt[2], Udo Obertacke[2]

[1]Department of Radiation Oncology, University Medical Centre Mannheim, Heidelberg University, Mannheim, Germany



Case report

Wenz *et al. Radiation Oncology* 2010, **5**:11

Stereotactic body radiotherapy for spinal metastases: current status, with a focus on its application in the postoperative patient

A review

Spine SBRT is an emerging technique with the potential benefits of delivering high BEDs to the tumor while sparing critical neural structures. Patient selection is highly important

Therefore, the potential for postoperative SBRT to reduce the extent of surgery while providing better tumor control

This application of SBRT requires prospective controlled studies to validate this promising treatment modality.

A. Sahgal et al. **J Neurosurg Spine 14:**151–166, 2011

Keywords

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PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Data describing repeat treatment of painful spinal metastases

Study	Patients (n), tumor histologic type	Initial dose	Retreatment fractionation	Pain relief	Comments	Investigator	Year	Reference
Local repeat RT	30, various histologic types	Mostly 30 Gy/10 Fx	10 Gy/5 Fx to 26 Gy/13 Fx	50%	Better pain relief for those with initial CR vs. PR	Hayashi	2002	39
Prospective randomised trial of 4 or 8-Gy single doses for metastatic bone pain	40, various histologic types	4 Gy/1 Fx 8 Gy/1 Fx	Most received 8 Gy/1 Fx; some received 20 Gy/5 Fx	71% 44%	No difference in response by histologic type	Hoskin	1992	13
Single 4-Gy repeat RT for painful bone metastases after single-fraction RT	109 initial responders, 26 nonresponders, various histologic types	4 Gy/1 Fx 6 Gy/1 Fx 8 Gy/1 Fx	4 Gy/1 Fx	74% initial responders; 46% nonresponders	31% CR	Jeremic	1999	40
Second single 4-Gy repeat RT for painful bone metastases	25, various histologic types	4 Gy/1 Fx, plus repeat RT, 4 Gy/1 Fx 6 Gy/1 Fx plus repe[illegible] treatmen[illegible]	4 Gy/1 Fx (second re-RT[illegible]	80[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Repeat RT for pai[illegible] m[illegible]	[illegible]	[illegible] [illegible] 59%	[illegible] Fx, 28 Gy/7 Fx, 30 Gy/10 Fx	87%	Patients treated were initial nonresponders	Mithal	1994	42
Low-[illegible] sing[illegible] RT f[illegible] metas[illegible] bone pain	[illegible] types	4 Gy/1 Fx	4 Gy/1 Fx to initial responders, multifraction or 8 Gy/1 Fx to nonresponders	100%, initial responders; 0%, nonresponders	2 patients underwent re-RT second time	Price	1988	43
Single-dose RT (6 Gy): palliation of painful bone metastases	18, various histologic types	6 Gy/1 Fx	6 Gy/1 Fx	72%	Long intervals between primary and repeat treatment	Uppelschoten	1995	45
Repeat treatment and Dutch Bone Metastasis Study	173, various histologic types	8 Gy/1 Fx 24 Gy/6 Fx	8 Gy/1 Fx, 46 patients Multifractions, 91 patients 8 Gy/1 Fx, 27 patients Multifractions in 9 patients	66% 46%	Single fraction therapy effective initial treatment or repeat treatment	van der Linden	2004	28

463 patients, various schedules of treatment

Spinal cord radiotherapy

Reirradiation of metastatic spinal cord compression: Definitive results of two randomized trials

Ernesto Maranzano *, Fabio Trippa, Michelina Casale, Paola Anselmo, Romina Rossi

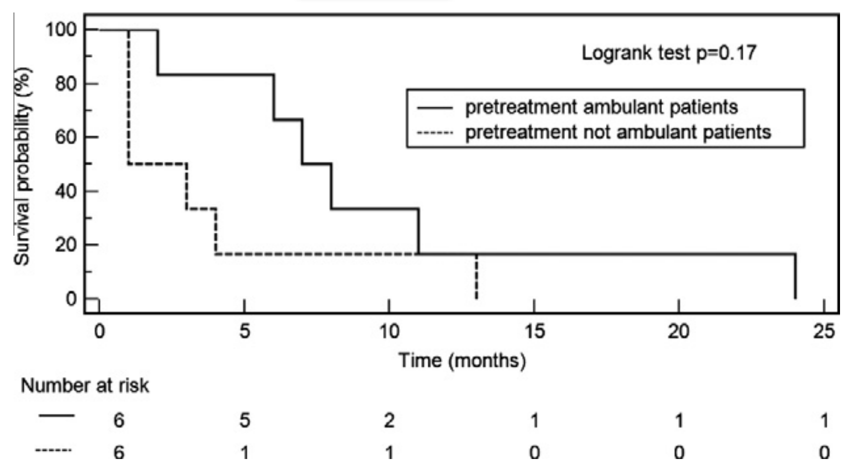
Treatment characteristics according to the first and second radiotherapy regimens.

Patient	First radiotherapy schedule (Gy)	BED[a] (Gy_2)	Reirradiation schedule (Gy)	BED[a] Gy_2	Interval between first and second treatment (months)	Cumulative BED[a] (Gy_2)
1	2 × 8	80	5 × 3	37.5	7	117.5
2	2 × 8	80	7	31.5	3	111.5
3	2 × 8	80	5 × 3	37.5	5	117.5
4	2 × 8	80	4	12	5	92
5	2 × 8	80	8	40	4	120
6	8	40	8	40	31	80
7	8	40	2 × 8	80	9	120
8	8	40	8	40	9	80
9	8	40	8	40	5	80
10	2 × 8	80	8	40	11	120
11	8	40	8	40	2	80
12	8	40	5 × 4	60	4	120

Motor function before and after reirradiation according to fractionation schedules.

Patient	First radiotherapy schedule (Gy)	Tomita group before reirradiation	Reirradiation schedule (Gy)	Tomita group after reirradiation
1	2 × 8	I	5 × 3	I
2	2 × 8	III	7	III
3	2 × 8	II	5 × 3	II
4	2 × 8	II	4	III
5	2 × 8	III	8	III
6	8	I	8	I
7	8	II	2 × 8	II
8	8	III	8	IV
9	8	II	8	II
10	2 × 8	III	8	III
11	8	II	8	II
12	8	III	5 × 4	III

Tomita group I–II: ambulant patients; Tomita group III–IV: not ambulant patients.



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ASTRO GUIDELINE

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Suggested inclusion and exclusion criteria for patients enrolled in trials to evaluate stereotactic body radiotherapy for spinal bone metastases

Characteristic	Inclusion	Exclusion
Radiographic	1) Spinal or paraspinal metastasis by MRI (50, 51) 2) No more than 2 consecutive or 3 noncontiguous spine segments involved (50–53)	1) Spinal MRI cannot be completed for any reason (50, 51) 2) Epidural compression of spinal cord or cauda equina 3) Spinal canal compromise >25% (58) 4) Unstable spine requiring surgical stabilization (50, 51, 54, 57) 5) Tumor location within 5 mm of spinal cord or cauda equina (50, 51) (relative*)
Patient	1) Age ≥18 y (50, 54) 2) KPS of ≥40–50 (50, 51, 54, 55) 3) Medically inoperable (or patient refused surgery) (50, 51)	1) Active connective tissue disease (50) 2) Worsening or progressive neurologic deficit (50–52, 57) 3) Inability to lie flat on table for SBRT (50–52) 4) Patient in hospice or with <3-month life expectancy
Tumor	1) Histologic proof of malignancy (50, 51, 56) 2) Biopsy of spine lesion if first suspected metastasis 3) Oligometastatic or bone only metastatic disease (50)	1) Radiosensitive histology such as MM[50-52] 2) Extraspinal disease not eligible for further treatment[51]
Previous treatment	Any of the following: 1) Previous EBRT <45-Gy total dose 2) Failure of previous surgery to that spinal level (50–52) 3) Presence of gross residual disease after surgery	1) Previous SBRT to same level 2) Systemic radionuclide delivery within 30 days before SBRT (50–52) 3) EBRT within 90 days before SBRT (50–52) 4) Chemotherapy within 30 days of SBRT (50–53)

The references listed in Table 3 correspond to those cited in the full manuscript published online and contained in the Supplemental Materials section.

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Patient	1) Age ≥18 y (50, 54) 2) KPS of ≥40–50 (50, 51, 54, 55) 3) Medically inoperable (or patient refused surgery) (50, 51)
Tumor	1) Histologic proof of malignancy (50, 51, 56) 2) Biopsy of spine lesion if first suspected metastasis 3) Oligometastatic or bone only metastatic disease (50)
Previous treatment	Any of the following: 1) Previous EBRT <45-Gy total dose 2) Failure of previous surgery to that spinal level (50–52) 3) Presence of gross residual disease after surgery

lusion
mpleted for any reason (50, 51)
spinal cord or cauda equina
>25% (58)
surgical stabilization (50, 51, 54,
mm of spinal cord or cauda
e*)
disease (50)
neurologic deficit (50–52, 57)
le for SBRT (50–52)
<3-month life expectancy
such as MM[50-52]
ligible for further treatment[51]
level
livery within 30 days before
fore SBRT (50–52)
days of SBRT (50–53)
terials

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ASTRO GUIDELINE

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

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... The use of stereotactic body radiotherapy holds theoretical promise in the treatment of new or recurrent spine lesions, although the Task Force recommended that its use be limited to highly selected patients and preferably within a prospective trial. Surgical decompression and postoperative radiotherapy is recommended for spinal cord compression or spinal instability in highly selected patients with sufficient performance status and life expectancy. The use of bisphosphonates, radionuclides, vertebroplasty, and kyphoplasty for the treatment or prevention of cancer-related symptoms does not obviate the need for external beam radiotherapy in appropriate patients.

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Radiotherapy and Radiosurgery for Metastatic Spine Disease

What Are the Options, Indications, and Outcomes?

Peter C. Gerszten, MD, MPH,*† Ehud Mendel, MD,‡ and Yoshiya Yamada, MD§

Spine Oncology Study Group Recommendations

From the Departments of *Neurological Surgery and †Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA; ‡Department of Neurological Surgery, The Ohio State University, Columbus, OH; and §Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY.

Study Design. Systematic literature review.

Objective. To determine the options, indications, and outcomes for conventional radiotherapy and radiosurgery for metastatic spine disease.

Methods. Three research questions were determined through a consensus among a multidisciplinary panel of spine oncology experts. A systematic review of the literature was conducted regarding radiotherapy and radiosurgery for metastatic spine disease using PubMed, Embase, the Cochrane Evidence Based Medicine Database, and a review of bibliographies of reviewed articles.

Research questions:

1. What are the clinical outcomes of the current indications for conventional radiotherapy alone and stereotactic radiosurgery for metastatic spine disease?
2. What are the current dose recommendations and fractionation schedules for conventional spine radiotherapy and stereotactic radiosurgery for metastatic spine disease?
3. What are the current known patterns of failure and complications after conventional spine radiation and stereotactic radiosurgery for metastatic spine disease?

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Radiotherapy and Radiosurgery for Metastatic Spine Disease

What Are the Options, Indications, and Outcomes?

Peter C. Gerszten, MD, MPH,*† Ehud Mendel, MD,‡ and Yoshiya Yamada, MD§

Study Design. Systematic literature review.
Objective. To determine the options, indications, and

Research questions:

1. What are the clinical outcomes of the current indications for conventional radiotherapy alone and stereotactic radiosurgery for metastatic spine disease?
2. What are the current dose recommendations and fractionation schedules for conventional spine radiotherapy and stereotactic radiosurgery for metastatic spine disease?
3. What are the current known patterns of failure and complications after conventional spine radiation and stereotactic radiosurgery for metastatic spine disease?

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Summary of Results of Systematic Review for Conventional Radiotherapy

Author	N	Ambulatory Status	Pain Status	Survival	Quality of Evidence
Helwig Larsen et al[39]	153	91% remained ambulatory/50% regained ambulation	78% resolved		Low
Spiegel et al[40]	114			2.5 mo	Very low
Rades et al[41]	81	86% remained ambulatory/14% regained ambulation		4 mo	Low
Rades et al[42]	87	87% remained ambulatory		7 mo	Low
Rades et al[43]	199	27% improved motor function		4 mo	Low
Rades et al[44]	32	6% improvement/16% deterioration		4 mo	Low
Maranzano et al[45]	56	100% remained ambulatory/60% regained ambulation	89% resolved	66% 12 mo survival if ambulatory 10% if [illegible]	Moderate
Maranzano et al[46]	44	100% remained ambulatory/46% regained ambulation	100% improved	[illegible]	Low
Rades et al[47]	922	21% improvement in motor function		14 mo	Low
Hoskin et al[48]	102	84% remained ambulatory/55% regained ambulation at 2 mo	58% using narcotic pre[illegible]therapy, [illegible]% 2–6 mo post-treatment	3.5 mo	Low
Katagiri et al[49]	101	64% remained ambulatory (8[illegible]% of responsive group)	5[illegible]% overall pain relief (87% of favorable group)	7 mo poor responder, 25 mo good responder	Low
Rades et al[50]	143	69% remained ambulatory/10% regained ambulation		4 mo	Low
Bach et al[51]	102	[illegible] 10[illegible]% remained ambulatory/15% regained ambulation/NSCLC 95% remained ambulatory/22% regained ambulation		1.5–3.5 mo	Low
Rades et al[52]	252	68% remained ambulatory/15% regained ambulation			Low
Rades et al[53]	281	84% remained ambulatory/34% regained ambulation		17 mo	Low
Kraiwattanapong et al[54]	31	23% regained ambulation	77% improved		Low
Rades et al[55]	335	89% remained ambulatory/39% regained ambulation		20 mo	Low
Ingham	17	6/17 regained ambulation		1.5 mo	Very low
Rades et al[56]	521	94% remained ambulatory/54% regained ambulation		12 mo	Low
Brown et al[57]	34	95% remained ambulatory/22% regained ambulation		4.1 mo	Low
Rades et al[58]	1852	76% ambulatory at 3 yr		12 mo	Low
Maranzano et al[22]	49	38% regained ambulation	67% improved	5 mo	Low

Table 1. Continued

Author	N	Ambulatory Status	Pain Status	Survival	Quality of Evidence
Hill et al[75]	43	100% remained ambulatory/47% regained ambulation		4 mo	Low
Tombolini et al[76]	95		82% improved		Very low
Juremic et al[77]	36	63% improved motor function/75% regained ambulation	85% improved		Very low
Patchell et al[78]	51	74% remained ambulatory/19% regained ambulation	4.8 mg daily morphine equivalent (0.4 m[illegible] for surgery)	3 [illegible]	High
Maranzano et al[79]	276	67% remained ambulatory/26% regained ambulation	57% impr[illegible]	4 mo	High
Young et al[80]	13	60% remained ambulatory/33% regained ambulation	4[illegible]% improved	5 mo	High
Maranzano and Latini[81]	209	82% remaine[illegible]/6[illegible]% regained a[illegible] status	77% improved	6 mo	Moderate
Rades et al[20]	214	[illegible] remained ambulatory/30% regained ambulation		12 mo	Moderate
T[illegible] et al[82]	[illegible]7	81% remained ambulatory/12.5% regained ambulatory status	73% improved	2 mo	Moderate
Greenberg et al[83]	83	89% remained ambulatory/35% regained ambulation			Moderate
Sorensen et al[59]	149	78% remained ambulatory/16% regained ambulation		3.1 mo	Low
Rades et al[60]	62	40% improved motor function (re-irradiation)		8 mo	Low
Rades et al[61]	231	12% vs. 10% worse motor function in favor of long radiotherapy 0.006		12 mo	Low
Schiff et al[62]	54	88% remained ambulatory/16% regained ambulation		5 mo	Low
Rades et al[23]	247	55%–61% improvement in ambulatory status (1 yr)			Low
Tazi et al[63]	12	58% ambulatory			Very low
Aass et al[64]	49	60% maintained independent mobility			Low
Podd et al[65]	158	18% regained ambulation	58% improved	3 mo	Very low
Huddart et al[66]	62	67% regained ambulation		3.5 mo	Very low
Kovner et al[67]	79	90% remained ambulatory/33% regained ambulation		2 mo	Very low
Zelefsky et al[68]	42	88% remained ambulatory/77% improved extremity weakness	92% experienced relief	8 mo	Low
Solberg et al[69]	58	68% remained ambulatory/9% regained ambulation	82% significant reduction	4.1 mo	Low
Smith et al[70]	26	85% remained ambulatory/67% regained ambulation	81% improved		Low
Kim et al[71]	25	83% remained ambulatory/0% regained ambulation			Low
Merimsky et al[72]	19	32% motor function improved	80% improved	5 mo	Low
Rades et al[73]	131	3%–70% improvement in motor function, depending upon time to start RT		5 mo	Low
Ampil et al[74]	16	100% remained ambulatory/50% regained ambulation	85% improved	11 mo	Low

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Summary of Results of Systematic Review for Stereotactic Radiosurgery

Author	Description	of Evidence	Outcomes	Conclusions
Hamilton *et al*[27]	Case series	Very low	5 patients with 5 lesions	Feasibility study with no injuries
Ryu *et al*[10]	Prospective cohort study	Very low	5 patients with 5 lesions	Feasibility study with no injuries
Shiu *et al*[11]	Case series	Very low	3 patients with 3 lesions	Feasibility study. No injuries
Milker-Zabel *et al*[17]	Prospective cohort study	Low	18 patients with 19 lesions	Retreatment after prior radiation resulted in 95% local control rate. 81% clinical improvement. No injuries
Ryu *et al*[84]	Prospective cohort study	Low	10 patients with 10 lesions	100% clinical improvement. No injuries
Bilsky *et al*[14]	Prospective cohort study	Very low	4 patients with 4 lesion	All had clinical improvement in pain. No injuries
DeSalles *et al*[16]	Prospective cohort study	Low	10 patients with 11 lesions	90% clinical improvement. No injuries
Benzil *et al*[13]	Prospective cohort study	Low	31 patients with 35 lesions	94% clinical improvement. No injuries
Ryu *et al*[31]	Retrospective case series	Low	49 patients with 61 lesions	85% clinical improvement. No injuries
Chang *et al*[15] (continuation of Shiu study)	Case series	Very low	15 patients with 15 lesions	Feasibility study. No injuries
Degen *et al*[85]	Prospective cohort study using quality of life outcomes measures	Low	38 patients with 58 lesions	97% clinical improvement. 95% local control rate. No injuries
Yamada *et al*[86]	Prospective cohort study	Low	21 patients with 21 lesions	90% clinical improvement. 75% local control rate. No injuries
Mahan *et al*[87]	Case series	Very low	8 patients with spinal cord compression	Pilot feasibility study. No injuries
Gerszten *et al*[88]	Prospective cohort study	Low	28 patients with 36 lesions with melanoma primary	96% clinical improvement. 75% local control rate. No injuries
Gerszten *et al*[89]	Prospective cohort study	Low	50 patients with 68 lesions with breast primary	96% clinical improvement. 100% local control rate. No injuries
Gerszten *et al*[90]	Prospective cohort study	Low	48 patients with 60 lesions with renal primary	89% clinical improvement. 87% local control rate. No injuries
Ryu *et al*[84]	Prospective cohort study	Low	177 patients with 230 lesions	Focusing on the complications of single-dose radiosurgery, 1 case of spinal cord injury
Chang *et al*[93]	Prospective cohort study	Low	63 patients with 74 lesions	84% progression-free incidence. No injuries. Pattern of failure emphasized
Jin *et al*[94]	Prospective cohort study	Low	196 patients with 270 lesions	85% clinical improvement. No injuries
Gerszten *et al*[95]	Prospective cohort study	Low	393 patients with 500 lesions	86% clinical improvement. 89% local control rate. No injuries
Gagnon *et al*[96]	Prospective cohort study with matched controls	Low	18 patients with 18 lesions with breast cancer primary	Salvage radiosurgery is as efficacious as initial conventional radiotherapy without added toxicity
Gibbs *et al*[97]	Prospective cohort study	Low	72 patients with 102 lesions	84% clinical improvement. 3 spinal cord injuries
Ryu *et al*[98]	Prospective cohort study	Low	49 patients with 61 lesions	84% clinical improvement. No injuries
Yamada *et al*[99]	Prospective cohort study	Low	93 patients with 103 lesions	90% local control rate. No injuries
Kim *et al*[100]	Prospective cohort study	Very low	7 patients with 7 lesions	All had radiographic control. No injuries
Gagnon *et al*[101]	Prospective cohort study	Low	151 patients with 151 lesions Outcomes evaluation included visual analog scale and SF-12 survey	Significant decrease in pain scores, quality-of-life improvement, SF-12 Physical Component scores demonstrated no significant change throughout follow-up period. No injuries
Gibbs *et al*[102]	Prospective cohort study	Low	6 cases of radiation-induced myelopathy in a series of 1075 patients	Radiation injury occurred over a spectrum of dose parameters that prevented identification of specific dosimetric factors contributing to the complication

Clinically Relevant questions (1)

- Clinical outcomes:
  - *Conventional RT (over 5000 patients):*

  Ambulatory status: 60-80% remained

  20-60% regained

  Pain: 50-70% palliated

  Sphincter dysfunction: 70% improved

  - *Stereotactic radiosurgery (27 single-institutions):*

  Pain: 85-100% palliated

  Neurologic symptoms: 57-92% improvement

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questions (2)

Current dose recommendations:

– *Conventional RT (3 prospective studies):*

No significant impact of dose-fractionation schedule on ambulatory status

Favorable histology enjoy a more durable response

Conventional fractionation do not influence outcome in unfavorable histology

Benefit for long- course radiation only in follow-up >9m

Short-course radiation for patients with a limited life expectancy

– *Stereotactic radiosurgery (27 single-institutions*

hypofractionation (4Gy, 4,6Gy, 5,8Gy, 3,9Gy X 3) and single dose (16-24Gy): no consensus

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Clinically Relevant questions (3)

- Patterns of failure:
  - *Conventional RT (885 patients):*

    Local Control: 61-89% (mean 77%)

    Clear impact of histology

  - *Stereotactic radiosurgery (27 single-institutions):*

    Local Control: 75-100% (majority 90%)

    Certain histology may do worse (melanoma and renal carcinoma)

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Spine Oncology Study Group Recommendations

Key Points

- Conventional radiotherapy is safe and effective with good symptomatic response and local control, particularly for radiosensitive histologies, such as lymphoma, myeloma, and seminoma.
- A strong recommendation can be made with moderate quality evidence that conventional fractionated radiotherapy is an appropriate initial therapy option for patients with spine metastases in cases in which no relative contraindications exist.
- Radiosurgery is safe and effective with durable symptomatic response and local control for even radioresistant histologies, regardless of prior fractionated radiotherapy.
- A strong recommendation can be made with low-quality evidence that radiosurgery should be considered over conventional fractionated radiotherapy for the treatment of solid tumor spine metastases in the setting of oligometastatic disease and/or radioresistant histology in which no relative contraindications exist.

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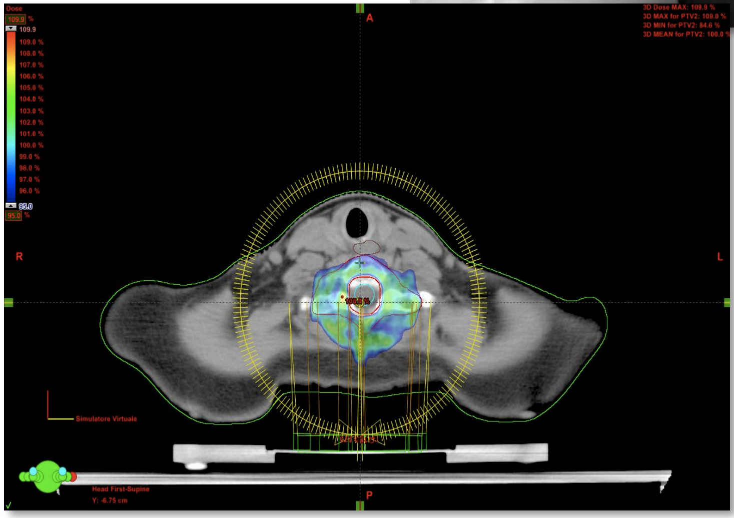
Take Home

- Patient selection
- Goal of treatment
- Multidisciplinary management
- Technology and EBM
- “Net-work”



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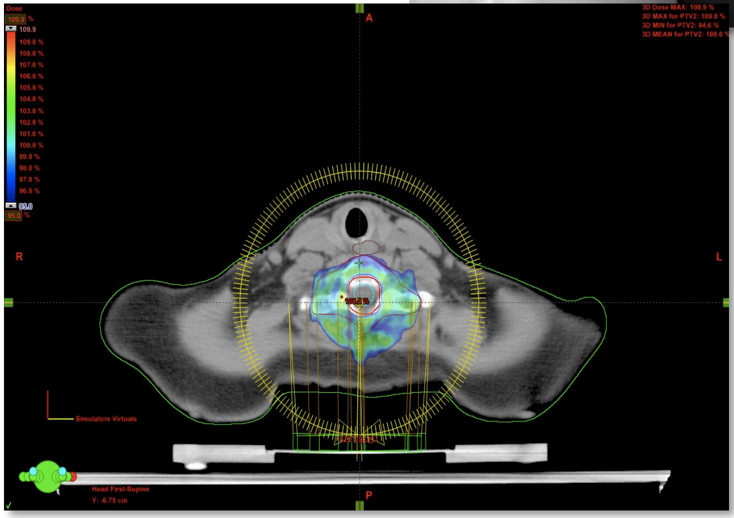

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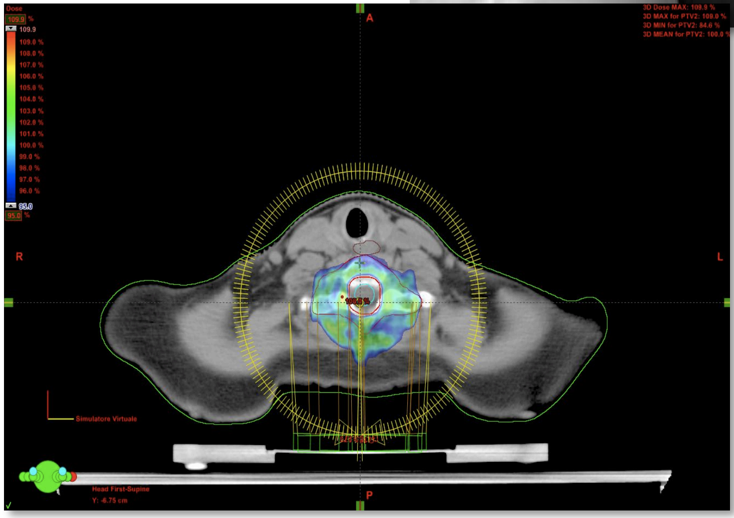

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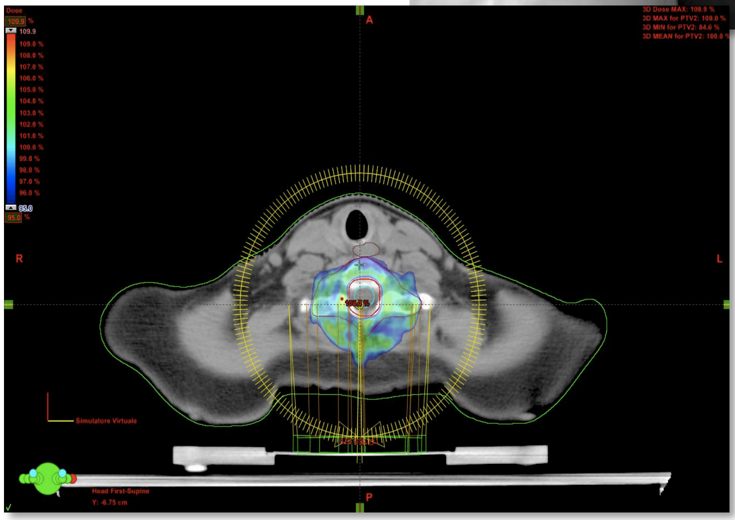

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