

Management of Metastatic Tumors to the Spine

Alexander R Vaccaro MD, PhD

James Harrop, MD

Professors, Neurosurgery and
Orthopaedics

Thomas Jefferson University

Philadelphia, Pa



Background

- 1.2 million new cases cancer in US/yr
 - 10 – 30% will have spinal mets at time of presentation
 - 60% will develop spinal mets
 - 5 - 14% will develop spinal cord compression
 - Half of these patients will lose ability to ambulate



Location of Tumors

- Region of the Spine
 - Thoracic – 70%
 - Lumbar – 20%
 - Cervical – 10%
- Location within the vertebrae
 - Pedicles & Vertebral Bodies – 85%
 - Epidural Space – 15%

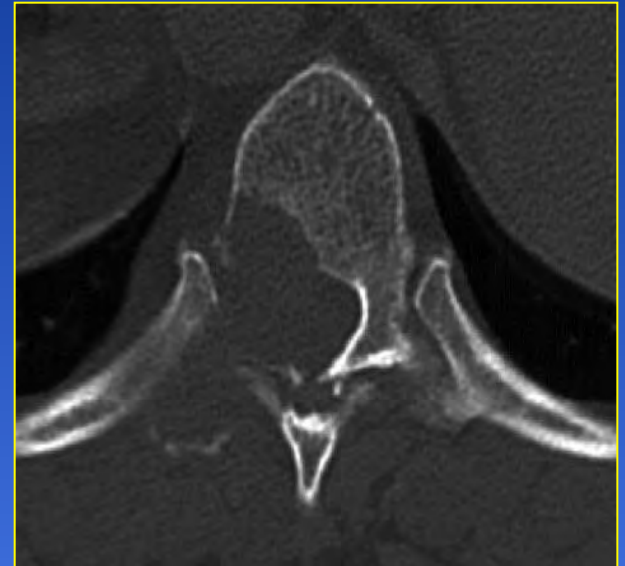


What are the Goals?

- Palliative
 - Reduce pain
- Improve quality of life
 - Improve function, ambulation
- Curative
- Prevent Structural Instability

Factors to be Considered

- **Patient**
 - Neurological Status
 - Pain level
 - Life expectancy
 - Overall health
 - Personal Goals
 - Family / Support system

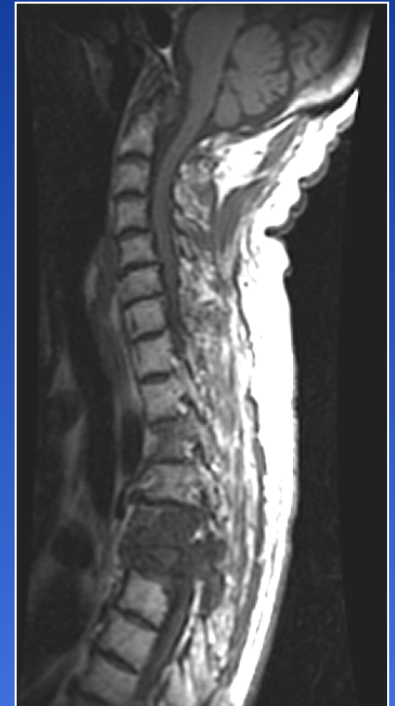


Factors to be Considered

- **Tumor**
 - Histology
 - Sensitivity to various treatments
 - Number of metastasis
 - Aggressiveness of lesions

Factors to be Considered

- **Mechanical**
 - Stability of spine
 - Potential for impending fracture
 - Location of lesion



Treatment Options

- Steroids, Bisphosphonates
- Chemotherapy
- Radiation
- Emobilization
- Kyphoplasty / Vertebroplasty
- Open Surgery
- Combination

Problems

- Literature:
 - Retrospective
 - Poor quality studies
- Poor survivorship
- Confounding variables
- Health issues



Medical Management

- Analgesics:
 - Opiates
 - NSAIDS
- Steroids
- Bisphosphonates



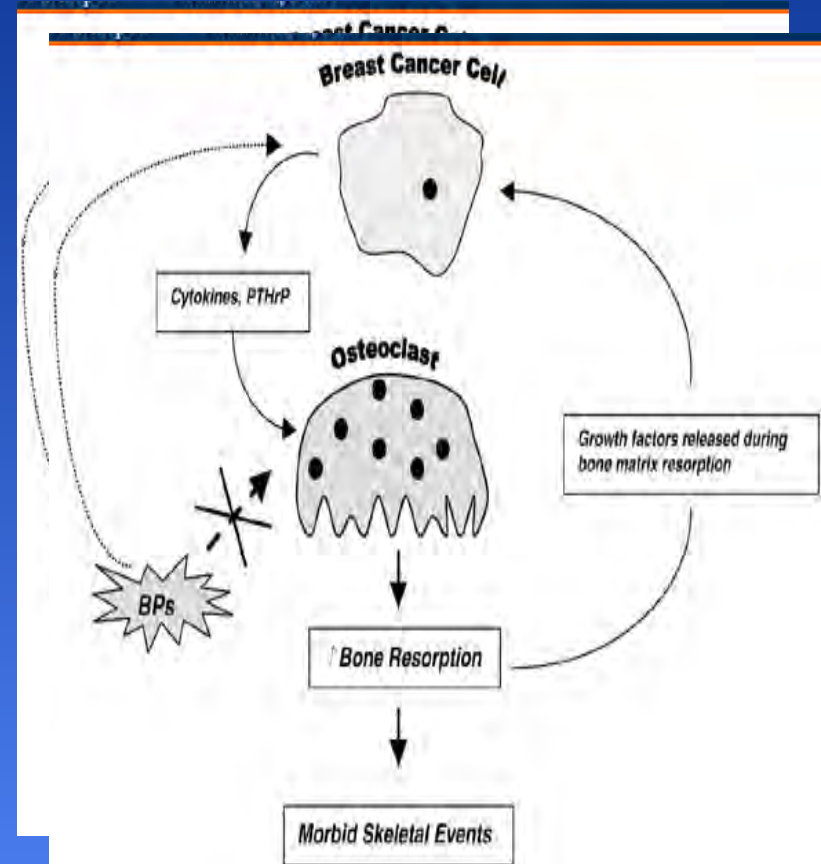
Bisphosphonates

- Mainstay of treatment for metastatic disease
- Reduce risks of
 - Pathologic Fracture (OR 0.6-0.9)
 - Hypercalcemia (OR 0.27-0.73)
 - Need for radiation or surgical treatment (OR 0.67 – 1.0)
- No change in mortality



Bisphosphonates

- Inhibit osteoclasts
- May have direct inhibitory affect on tumor cells



Treatment Options

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Spine Focus Issue

Summary of Management Recommendations in Spine Oncology

Charles G. Fisher, MD, MHSc*, Gunnar B. J. Andersson, MD, PhD,† and James N. Weinstein, DO, MS‡

Spine Oncology Study Group

6 papers (12 recommendations)
regarding metastatic disease

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External Beam Radiation

- Most common treatment for metastatic disease
- 3000cGy divided over 10 doses is most common dosing schedule



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§

- **Meta-Analysis of 49 papers including 7985 patients**
 - Pain reduced in 46-100% of patients
 - Most studies report >80%
 - Ambulation maintained in 60 – 100% of patients

Complications

- Limited data
 - Common, reversible
 - Fatigue, mucositis, bowel irritation
 - More severe
 - Myelitis, esophagitis, fracture
- Dose for 5% risk of myelopathy
 - 50Gy to <5cm of cord

Limitations

- Limited ability to help improve neurological function
 - 0 – 67% regained ability to ambulate
 - Most studies <20%

Radiosensitivity

- Favorable
 - Lymphoma, myeloma, and seminoma
- Intermediate
 - Breast and prostate cancers
- Unfavorable
 - Non-small cell lung, renal cell, melanoma, sarcoma, and GI cancers

Radiosensitivity

Study	Lymphoma, Seminoma, Myeloma	Breast	Prostate	Sarcoma	Melanoma	Gastrointestinal	NSCLC	Renal
Gilbert <i>et al</i> ¹⁰³	F	U	U	U	U	U	U	U
Maranzano <i>et al</i> ⁷⁹	F	F	F	U	U	U	U	U
Rades <i>et al</i> ^{20,43}	F	I	I	I	U	I	U	I
Rades <i>et al</i> ⁵⁸	F	F	F	U	U	U	U	U
Katagiri <i>et al</i> ⁴⁰	F	F	F	U	U	U	U	U
Maranzano <i>et al</i> ²²	F	F	F	U	U	U	U	U
Rades <i>et al</i> ²³	F	I	I	I	U	I	U	I

F indicates favorable; I, intermediate; U, unfavorable.

Neurological Improvement with XRT

Table 4. Improvement in Motor Function After Conventional Radiotherapy

Study	N	Breast	Prostate	NSCLC	Gastrointestinal	Renal	Sarcoma
Maranzano <i>et al</i> ⁴⁵	35	60%					
Rades Strahlentherapie <i>et al</i> ⁴¹	81				14%		
Rades European Urology <i>et al</i> ⁴²	87					29%	
Smith <i>et al</i> ⁷⁰	35		66%				
Rades <i>et al</i> ⁵³	281		33%				
Rades <i>et al</i> ⁵⁵	335	31%					
Bach <i>et al</i> ⁵¹	59			22%			
Rades <i>et al</i> ⁵²	252			14%			
Merminsky <i>et al</i> ⁷²	19						27%*
Rades <i>et al</i> ⁵⁶	142	33%					
	133		40%				
	52			29%			
Maranzano <i>et al</i> ⁴⁶	44		46%				
Totals	512	34%					
	493		36%				
	363			17%			
	81				14%		
	87					29%	
	19						27%

*One patient in this series underwent laminectomy and radiotherapy.

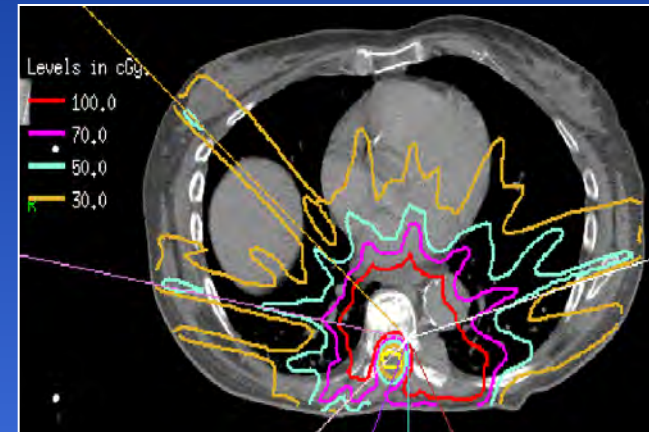
Neurological Improvement with XRT

Breast	34%
Prostate	36%
Non-Small Cell Lung	17%
Gastrointestinal	14%
Renal	29%
Sarcoma	27%

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Sterotactic Radiosurgery

- Also referred to as IMRT
 - Image modulated radiotherapy
- High dose radiation delivered precisely at the site of the tumor
 - 16Gy in one dose



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§

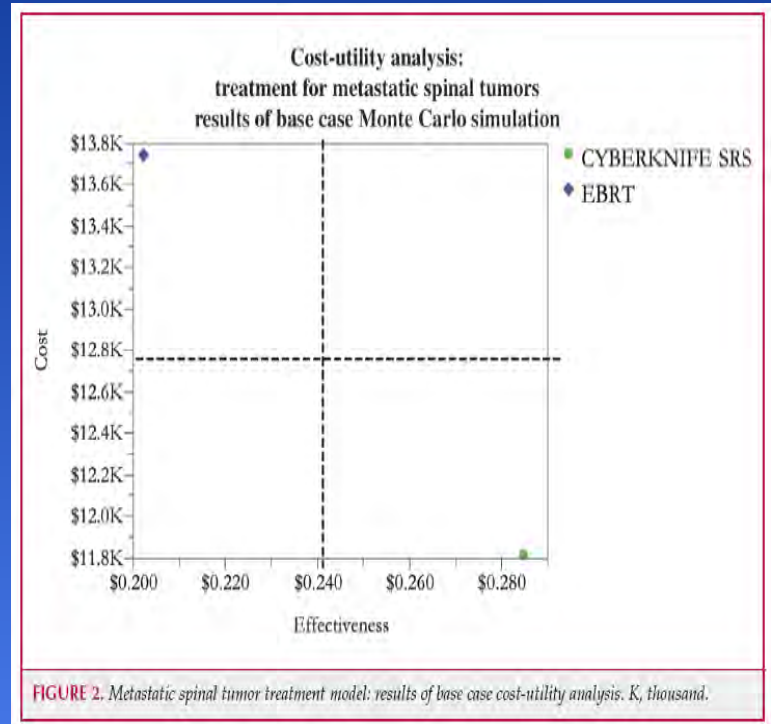
- **Radiosurgery: 27 papers encompassing 1655 patients**
- **Pain**
 - **85% improvement**
 - renal cell, non-small cell lung, melanoma
- **Neurological function**
 - **42 – 90 % improvement**

Cost Effective

TABLE 13. Comparator interventions for metastatic spinal tumors: 95% confidence intervals for costs and effects from base case Monte Carlo simulation^a

Strategy	Cost (U.S. \$)		Effect (QALY)	
	Median	95% CI	Median	95% CI
CyberKnife SRS	\$11 813	\$8083–15 613	0.28	0.21–0.37
EBRT	\$13 682	\$10 216–17 620	0.20	0.13–0.28

^a QALY, quality-adjusted life year; CI, confidence interval; SRS, stereotactic radiosurgery; EBRT, external beam radiation therapy.



Complications

- Generally mild
 - Esophogitis, mucositis, dysphagia, diarrhea, laryngitis, parasthesias, radiculitis
 - 0.5% incidence of post-radiation myelopathy

Spine Oncology Study Group Recommendations: Radiation Therapy

We recommend CRT to reduce pain and maintain ambulation in patients with radiosensitive metastatic disease of the spine without instability. We recommend SBRS over CRT to reduce pain and maintain ambulation in patients with solid-tumor metastases in the setting of oligometastatic disease and metastatic disease resistant to CRT or who have failed CRT and without instability.

Strong recommendation

Low quality evidence

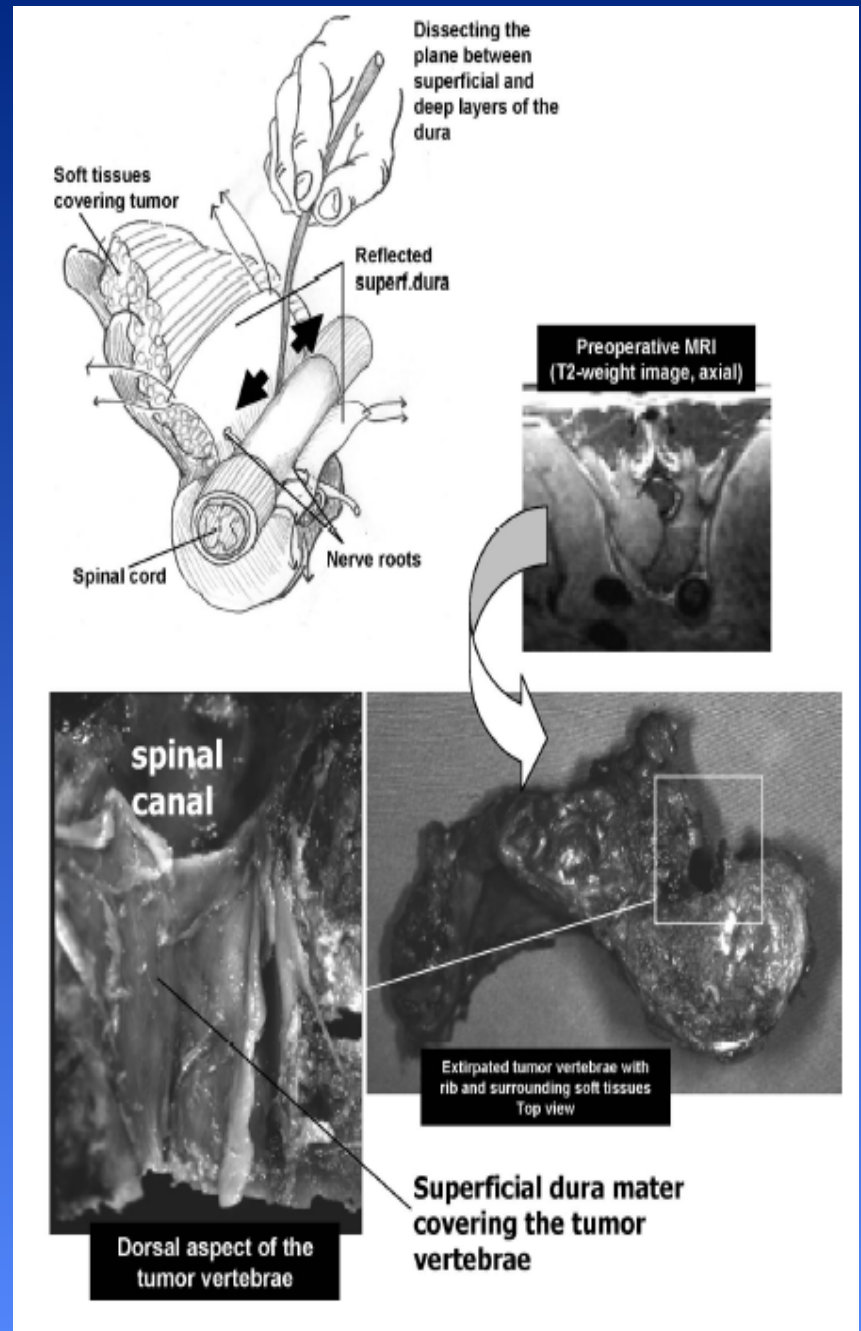
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Renal Cell Carcinoma

- Highly vascular tumor
- Resistant to conventional XRT and chemotherapy
- Surgery and Stereotactic surgery have been recommended for solitary metastasis

Surgical Treatment

- En bloc spondylectomy
- Limited clinical data
- 4 – 16% local recurrence
- Technically demanding



Sterotactic Radiosurgery

- Local control 87 – 90%
 - Greater with doses $>24\text{Gy}$
- Pain control 89%
- 12.5% required late surgery for progressive neurological symptoms

Spine Oncology Study Group

Recommendations:

Renal Cell Carcinoma

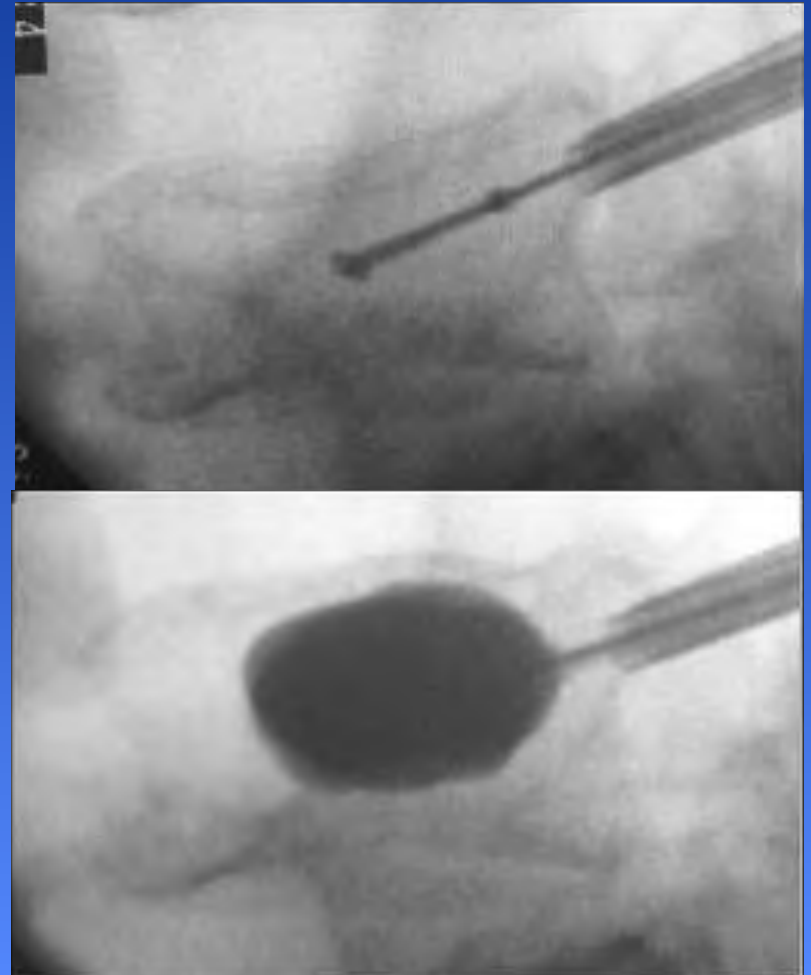
We suggest in patients with solid renal cell carcinoma in the absence or with minimal epidural disease that stereotactic radiosurgery be the first line therapy rather than *en bloc* excision.

Weak recommendation

Very low
quality
evidence

Cement Augmentation

- Vertebroplasty and kyphoplasty
- Used to stabilize pathologic fractures or impending fractures



Advantages

- Limited incision
- Short OR time
- Does not require general anesthesia
- May have cytotoxic and thermal effects on tumor cells



Vertebroplasty

Prospective Study	Method	Scale Best-Worst	Patients	Preop (SD)	Postop (SD)	Follow-up	P
Pain							
Vertebroplasty							
Cahana et al ^{#6}	VRS	0-5	22	4.8 (0.4)	2.3 (1.1)		<0.001
Cheung et al ⁷	SPSS	0-10	13			12 w	<0.001
Ramos et al ^{#8}	VAS	0-10	12	7.5 (2.3)	3.3 (2.1)	4 w	<0.001
Anselmetti et al ^{#11}	VAS	0-10	14	8.1 (1.4)	1.0 (1.0)	6 m	<0.001
Cotten et al ^{9,10}	McGill/Melzack	0-5	37†			36 h	
Function							
Vertebroplasty							
Cahana et al ^{#6}	ECOG-PS	0-4	22	1.9 (1.0)	0.9 (1.0)		<0.001
Cheung et al ⁷	TFAS	1-4	13			12 w	0.223
Ramos et al ^{#8}	ECOG-PS	0-4	12	3.1 (1.0)	2.4 (1.2)	4 w	0.035
Anselmetti et al ^{#11}	ODI	0-100	14	63.3 (14.1)	10.6 (6.5)	6 m	<0.001
Cotten et al ^{9,10}							

Kyphoplasty

Prospective Study	Method	Scale Best-Worst	Patients	Preop (SD)	Postop (SD)	Follow-up	P
Pain							
Kyphoplasty							
Khanna <i>et al</i> ³⁴	SF36-BP	100-0	56	28.2 (15.3)	48.0 (20.5)	55 w	<0.001
Gerszten <i>et al</i> ³⁵	VAS	0-10	26	7.5	2.8	4 w	<0.001
Dudeney <i>et al</i> ³⁶	SF36-BP	100-0	18	23.2	55.4	7.4 m	<0.001
Lane <i>et al</i> ³⁷	VAS	0-10	20	8.2	1.9	3 m	<0.05
Pflugmacher <i>et al</i> ⁴⁰	VAS	0-10	65	8.3 (1.5)	2.9 (0.9)	3 m	<0.001
Kyphoplasty							
Khanna <i>et al</i> ³⁴	SF36-PF	100-0	56	26.2 (22.2)	44.2 (26.2)	55 w	<0.001
Gerszten <i>et al</i> ³⁵	SF36-PF	100-0	18	21.3	50.6	7.4 m	0.001
Lane JM <i>et al</i> ³⁷	ODI	0-100	19	48.9 (16.6)	32.6 (13.6)	3 m	<0.001
Pflugmacher <i>et al</i> ³⁹	ODI	0-100	20	71.5	22.0	3 m	<0.05
Pflugmacher <i>et al</i> ⁴⁰	ODI	0-100	65	8.1 (0.8)	3.3 (0.6)	3 m	<0.001

Complications

Prospective Studies	Vertebroplasty	Kyphoplasty
No. studies	5	6
No. tumor patients	98	204
No. tumor levels	152*	330†
Tumor types per patient		
Metastases	73 (74.5%)	91 (44.6%)
Multiple myeloma	23 (23.5%)	113 (55.4%)
Hemangioma	2 (2.0%)	0
Complications		
Medical	0	1/204 (0.5%)‡
Neurological	4 (4.1%)	0
Corrective surgery	3 (3.1%)	0
Extravasation		
Total per level	59/101 (58.4%)	12/239 (12.1%)
Symptomatic patients	3/98 (3.1%)	0
Adjacent vertebral fracture	0	6/204 (2.9%)
Corrective surgery	0	3/204 (1.5%)

*Number may be higher, as Cheung *et al*⁷ did not report number of levels per tumor patient.

†Number may be higher, as Khanna *et al*²⁴ did not report number of levels per tumor patient.

‡Khanna *et al*²⁴ reported 1 myocardial infarction without specifying if this was a tumor patient.

Spine Oncology Study Group Recommendations: Cement Augmentation

We recommend cement augmentation in patients with painful compression fractures secondary to metastatic spine disease.

Strong recommendation

Moderate
quality
evidence

Embolization

- Advocated since the 1960's for hypervascular tumors
 - Renal cell
 - Thyroid
- Commonly used as adjunct to surgery



Embolization

- Intraoperative blood loss decreased by >50%
- Decreased rate of operative complications
- 4% risk of neurological complications
 - 1.4% permanent



Spine Oncology Study Group Recommendations: Embolization

We recommend embolization procedures to reduce operative blood loss in hypervascular tumors.

Strong recommendation

Very low quality evidence

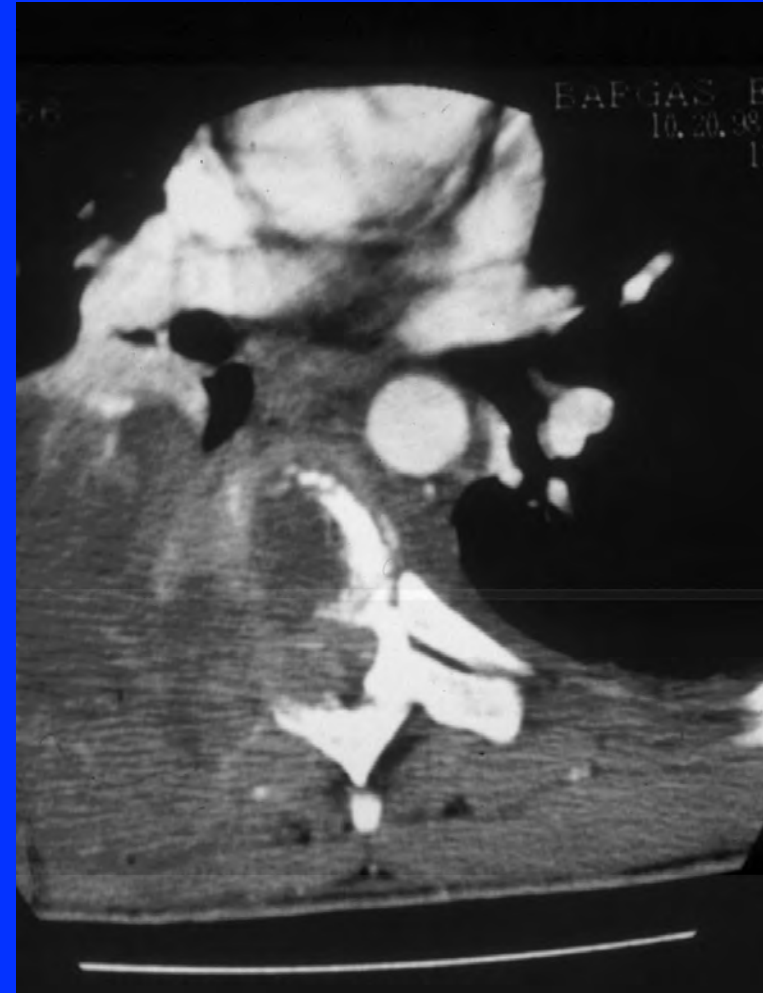
Surgery

Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute – Overall Survival Rates

<u>Site</u>	<u>% of cancers</u>	<u>1-yr</u>	<u>2-yr</u>	<u>3-yr</u>	<u>5-yr</u>	<u>8-yr</u>	<u>10-yr</u>
Prostate	17.4	100.0	99.5	98.9	97.6	94.5	91.7
Breast (in situ)	2.8	100.0	100.0	100.0	100.0	100.0	100.0
Breast (invasive)	16.3	97.8	94.8	91.9	87.1	81.9	79.2
Lung	12.7	42.6	25.9	20.0	15.5	12.4	11.0
Colon/Rectum	11.5	83.3	75.1	69.9	63.6	59.2	57.7
Melanoma	3.5	97.1	94.4	92.4	90.0	88.2	87.9
Urinary Bladder	4.3	91.5	87.1	84.8	81.9	78.9	77.4
Non-Hodgkin Lymphoma	4.2	74.2	66.3	62.1	56.3	49.9	47.0
Uterine Corpus	3.1	93.5	89.5	87.0	84.7	83.1	82.6
Leukemia (all ages)	2.7	67.0	58.0	53.4	47.2	40.7	38.1
Kidney & Renal Pelv.	2.1	80.8	73.8	70.4	65.5	60.9	57.9

SEER 5-Year Survival data in patients with metastatic disease

Prostate	35.8
Breast (invasive)	24.4
Lung	1.9
Colon/Rectum	9.4
Melanoma	14.6
Urinary Bladder	5.8
Non-Hodgkin Lymph	44.3
Uterine Corpus	26.0
Kidney & Renal Pelvis	8.2



Life Expectancy

Scoring systems:

.Tokuhashi

.Tomita

.Sioutos

.Van der Linden

.Bauer

Recent study comparing seven scoring systems for survival in patients with vertebral mets found most important factors in predicting survival:

1. The primary tumor type
2. The presence or absence of visceral metastases.



Tokuhashi Scoring System

Table 1

Tokuhashi Scoring System for Preoperative Evaluation of Patients With Metastatic Spine Tumor²⁴

Parameter	Score
General condition	
Poor	0
Moderate	1
Good	2
No. of extraspinal bone metastases	
≥3	0
1 or 2	1
0	2
No. of metastases in the spine	
≥3	0
2	1
1	2
Metastases to major internal organs	
Irremovable	0
Removable	1
No metastases	2
Primary site of cancer	
Lung, stomach	0
Kidney, liver, uterus, other	1
Thyroid, prostate, breast, rectum	2
Myelopathy	
Complete	0
Incomplete	1
None	2

Tokuhashi, Spine, 1990

Tokuhashi, Spine, 2005

Tokuhashi Scoring System

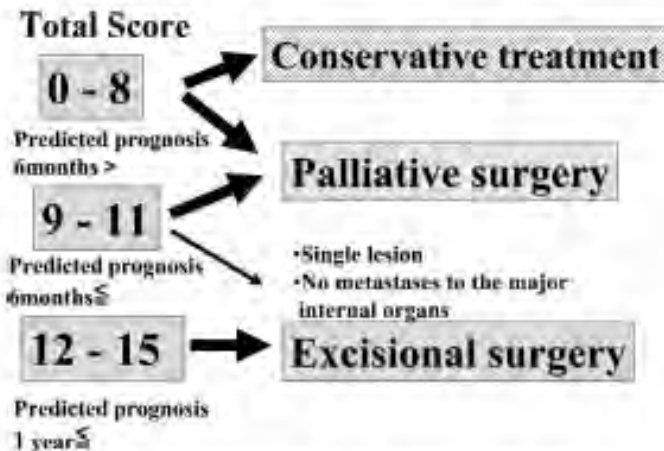


Figure 2. Strategy of treatment for spinal metastases.

Table 3. Distribution of the Total Score and the Survival Period

Total Score	Survival Period		
	<6 mo	6 mo to 1 yr	>1 yr
0-8 (n = 156)	133 (85.3%)	16	7
9-11 (n = 67)	18	29	20 (73.1%)
12-15 (n = 23)		2	21 (95.4%)

*The 73.1% refers to the combination of the 29 and the 20 survivors in this row.

Tomita Scoring System

Scoring System				Prognostic Score	Treatment Goal	Surgical Strategy
Point	Prognostic factors					
	Primary tumor	Visceral mets.*	Bone mets.**			
1	slow growth <small>(breast, thyroid, etc.)</small>	/	solitary or isolated	2	Long-term local control	Wide or Marginal excision
				3		
2	moderate growth <small>(kidney, uterus, etc.)</small>	treatable	multiple	4	Middle-term local control	Marginal or Intralesional excision
				5		
4	rapid growth <small>(lung, stomach, etc.)</small>	un-treatable	/	6	Short-term palliation	Palliative surgery
				7		
				8		
				9	Terminal care	Supportive care
				10		

* No visceral mets = 0 point

** Bone mets: including spinal mets.

Neurological Compromise

Dural Compression

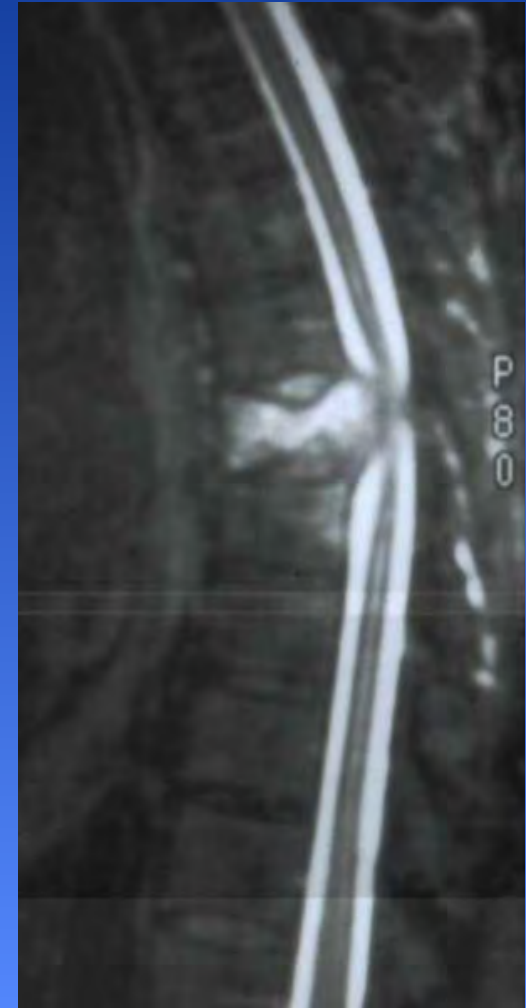
- One of the most common reasons patients with metastatic disease to the spine will require surgical treatment

Dural Compression

Incidence of symptomatic dural compression related to tumor histology:

Breast	22%
Renal	20%
Lung	15%
Prostate	10%

One-third of pts with symptomatic dural compression will have a second non-contiguous area of spinal involvement with dural compression.



Surgery for Spinal Cord Compression

- Historically patients did not respond well to surgery
 - XRT was used as the treatment of choice
- Before modern surgical techniques



Radiation for Spinal Cord Compression

Author	Year	Quality	Study Type	No. Patients	Post-Treatment Ambulation (%)	Ambulation Regained (%)
Maranzano and Latini ⁴	1995	Very low	Prospective cohort	209	76%	51%
Greenberg <i>et al</i> ⁵	1980	Very low	Retrospective	83	57%	29%
Tomita <i>et al</i> ³	1983	Very low	Retrospective	78	48%	
Martenson <i>et al</i> ¹⁴	1985	Very low	Retrospective	42	64%	21%
Podd <i>et al</i> ¹⁵	1992	Very low	Retrospective	158	31%	18%
Brown <i>et al</i> ¹⁶	1999	Very low	Retrospective	34	65%	22%
Rades <i>et al</i> ¹⁷	2006	Very low	Retrospective	87		25%

Only 18 – 51% of patients regained ambulation

Surgery for Spinal Cord Compression

Table 2. Surgical Series for the Treatment of Epidural Spinal Cord Compression

Author	Year	Quality	Study Type	No. Patients	Post-Treatment Ambulation (%)	Ambulation Regained (%)	Mortality	Morbidity
Patchell <i>et al</i> ²⁹	2005	Moderate	RCT	101	84	62	6	14
Siegal and Tiqva ¹¹	1985	Very low	Prospective cohort	78	80		7	7
Manabe <i>et al</i> ¹⁸	1989	Very low	Retrospective	28		62		
Moore <i>et al</i> ¹⁹	1989	Very low	Retrospective	26		62	31	4
Sunderasan <i>et al</i> ²⁸	1991	Very low	Prospective cohort	54	100	100	6	15
King <i>et al</i> ²⁰	1991	Very low	Retrospective	33		64		
Sundaresan <i>et al</i> ²¹	1995	Very low	Retrospective	110		82		48
Wang <i>et al</i> ²²	2004	Very low	Retrospective	140	90	75	4	14
Jansson and Bauer ²⁴	2006	Very low	Retrospective	282		65	13	20
Mannion <i>et al</i> ²⁷	2007	Very low	Prospective cohort	62	80	50	3	18
Street <i>et al</i> ²⁵	2007	Very low	Prospective cohort	42	73		2	26
Chen <i>et al</i> ²⁶	2007	Very low	Retrospective	31	74	68	6	22

50 – 100% of patients regained ambulation

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Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial

Roy A Patchell, Phillip A Tibbs, William F Regine, Richard Payne, Stephen Saris, Richard J Krucio, Mohammed Mohiuddin, Byron Young

Lancet 2005; 366: 643-48

- Prospective, randomized trial
- Surgery and XRT vs XRT alone
 - 30 Gy in 10 fractions
- Excluded patients with paralysis >48hrs, highly radiosensitive tumors, brain mets, or <3 months survival

Patchell Study

	Radiation group (n=51) median	Surgery group (n=50) median	Relative risk*	95% CI*	P*	Significant predictors**
Maintenance of continence	17 days	156 days	0.47	0.25-0.87	0.016	Surgery RR=0.51 (0.29-0.90) Baseline Frankel Score RR=0.56 (0.3-0.73)
Maintenance of ASIA score	72 days	566 days	0.28	0.13-0.61	0.001	Surgery RR=0.30 (0.14-0.62) Stable Spine RR=0.43 (0.22-0.83) Cervical Spinal Level RR=0.49 (0.26-0.90) Baseline Frankel Score RR=0.65 (0.46-0.91)
Maintenance of Frankel score	72 days	566 days	0.24	0.11-0.54	0.0006	Surgery RR=0.26 (0.12-0.54) Stable Spine RR=0.39 (0.20-0.75) Cervical Spinal Level RR=0.53 (0.74-0.98) Baseline Frankel Score RR=0.62 (0.44-0.88)
Survival time	100 days	126 days	0.60	0.38-0.96	0.033	Surgery RR=0.60 (0.40-0.92) Breast Primary Tumour RR=0.29 (0.13-0.62) Lower Thoracic Spinal Level RR=0.65 (0.43-0.99)

* Based on a Cox model with all covariates included. ** Based on a Cox model with only significant predictors included (stepwise selection).

Table 2: Secondary endpoints

Patchell Study

	Surgery	Radiation
Maintained ambulation	94%	74%
Maintenance of ambulation	153 days	54 days
Regained ambulation	62%	19%
Daily morphine dose	0.4mg	4.8mg
Dexamethasone dose	1.6mg	4.2mg
30 day mortality	6%	14%
Improved Frankel score	91%	61%
Improved ASIA score	86%	60%

Radiation Group

- 10 patients (20%) experienced acute neurological deterioration
 - Treated with surgery
- Only 3 patients regained ability to walk
- 4 patients had a post-operative complication
 - 3 wound infections

Limitations

- In both arms, 38% of patients were considered unstable
 - Based on Cybulski criteria
- Radiation does not provide stability
 - May bias towards surgery

Spine Oncology Study Group Recommendations: Spinal Cord Compression

We recommend that patients with high-grade epidural spinal cord compression from solid tumor metastases undergo decompressive surgery and instrumentation.

Strong recommendation

Moderate
quality
evidence

Surgery for Instability

Kostuick

- Divides vertebral body into 6 segments
- Surgery if 3 or more segments involved

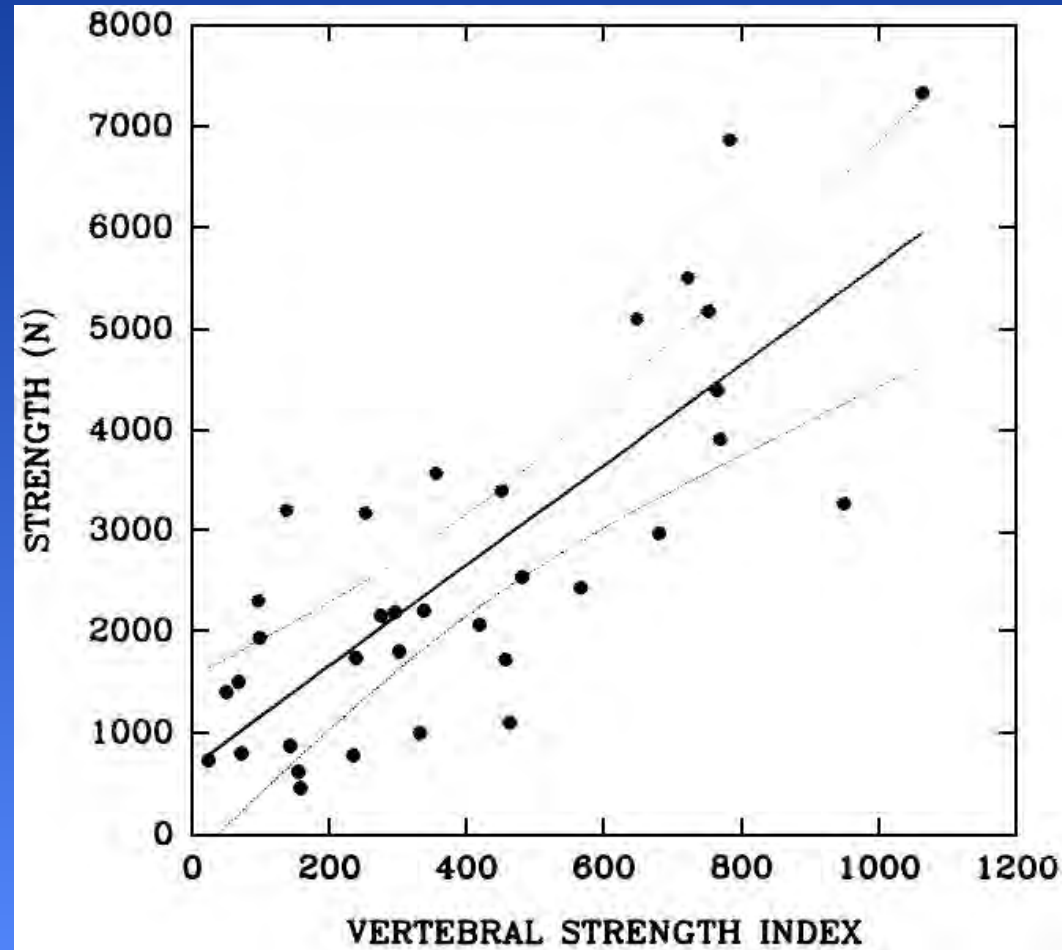


Cybulski Criteria

- 1) Anterior and middle column destruction with greater than 50% loss of vertebral body height
- 2) Collapse of 2 or more adjacent vertebral bodies
- 3) Tumor involving the middle and posterior columns with possible shearing deformity

Cadaver Testing

- Vertebral strength correlates to product of bone mineral density and cross-sectional area of intact vertebral body



Fracture Patterns

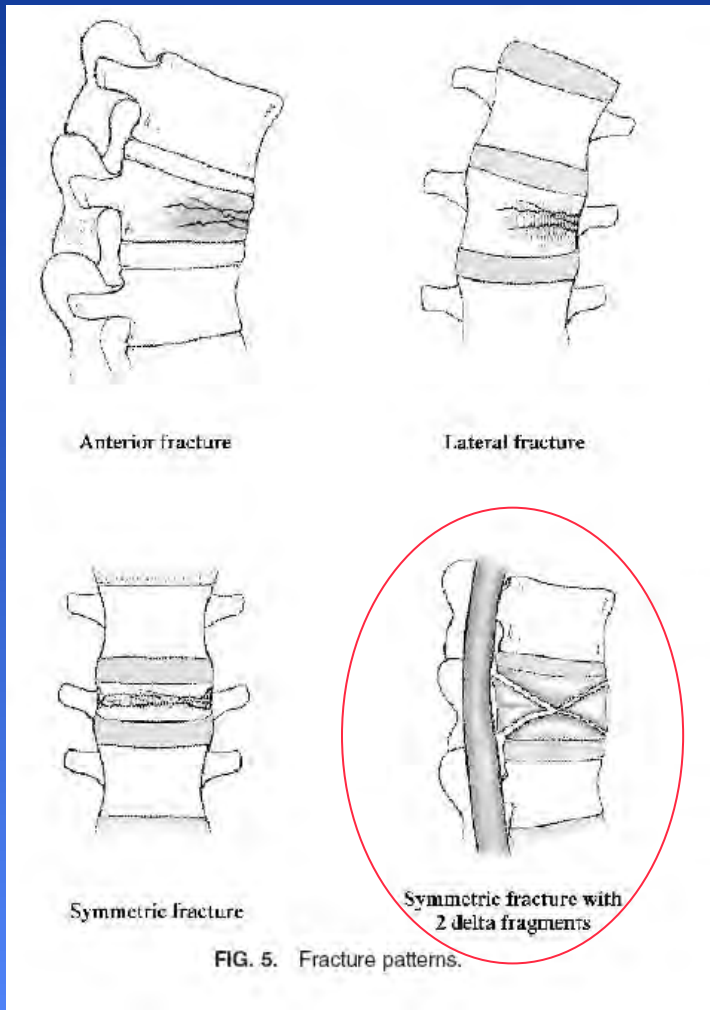


FIG. 5. Fracture patterns.

TABLE 3. *Fracture patterns associated with fragment migration in metastatic spine*

Fracture pattern	Total fractures	No. (%) migrated
Anterior	21	2 (9.5)
Lateral	17	0
Symmetric	40	3 (7.5)
Symmetric with 2 delta fragments	13	9 (69.2)

Spinal Instability

Neoplastic Score (SINS)

- Developed by the Spine Oncology Study Group
- Includes
 - Posterior element involvement
 - Quality and character of pain
 - Location
 - Bone quality
 - Alignment
 - Vertebral collapse

Surgery for Pain Relief

Clinical Study

The value of palliative surgery for metastatic spinal disease: satisfaction of patients and their families

Shunsuke Fujibayashi, MD, PhD^{a,*}, Masashi Neo, MD, PhD^a, Koichi Miyaki, MD, PhD^b, Takeo Nakayama, MD, PhD^b, Takashi Nakamura, MD, PhD^a

- **80% patient satisfaction**
 - Patient satisfaction associated with younger age and neurological improvement
 - Pain was not a factor
 - Family satisfaction associated with improved pain and longer survival

Thank
You

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