

Case Conference: SBRT for spinal metastases



DANIEL SIMPSON MD

3/27/12

Case



- 79 yo M with hx of T3No colon cancer diagnosed in 2008
 - metastatic liver disease s/p liver segmentectomy 2009 and SBRT in 2011
 - CT abdomen demonstrated a sclerotic lesion in L vertebral body
 - MRI L-spine done in 2012: 2.1 x 1.6 x 2.4 cm enhancing lesion involving the left posterior half of the L1 vertebral body with no extension into the spinal canal and second ill-defined lesion in posterior third of T12
 - Asymptomatic, no pain or neurologic symptoms
 - Tx: SBRT to T12 and L1; 24 Gy/3

Epidemiology



- Spinal metastases account for 70% of bony metastases
- 18,000 new cases in North America every year
- 70% of patients who die of cancer have spinal metastases at autopsy
 - <14% are symptomatic

*Frequencies of primary cancers and metastases seen at
M. D. Anderson, 1984–1994**

Primary Cancer Site	No. of Cases (%)	No. of Spinal Metastases (%)
all sites	113,831 (100)	11,884 (100)
breast	13,977 (12.3)	3,592 (25.7)
blood	12,907 (11.3)	1,213 (9.4)
lung	10,568 (9.3)	2,410 (22.8)
skin	10,844 (9.5)	369 (3.4)
colon	7,107 (6.2)	185 (2.6)
prostate	6,975 (6.1)	1,137 (16.3)
urinary tract	5,692 (5.0)	478 (8.4)
mouth	5,174 (4.5)	72 (1.4)
unknown primary	4,099 (3.6)	344 (8.4)
ovary	2,916 (2.6)	17 (0.6)
uterus	2,224 (2.0)	16 (0.7)
pancreas	1,637 (1.4)	10 (0.6)
bone	1,167 (1.0)	14 (1.2)
other	28,544 (25.1)	2,027 (7.1)

* Patient population was identified through a search of the tumor registry maintained by the Department of Medical Informatics.

Pathophysiology



- Occur primarily via hematogenous spread
 - Skeletal blood flow accounts for 4-10% of cardiac output
 - Skeletal vasculature renders it vulnerable to metastatic deposition
- The most common primary sites are breast, lung, and prostate
- Lumbar and thoracic spine most common sites
- Extradural and intradural
 - 95% extradural

Presentation



- Pain is most common (~90%) presenting symptom
 - Typically constant, present at night
 - Can be poorly characterized such as referred pain to the ribs
- Neurologic signs frequently preceded by pain
 - Radiculopathy, myelopathy, cauda equina syndrome

Diagnostic Imaging



- Bone scan is more sensitive than plain films for sclerotic lesions
 - CT scans are more specific, better for differentiating between
- Plain films and CT are helpful for detecting pathologic fracture
- MRI spine series is indicated in setting of suspected neurologic compromise
- PET/CT similar sensitivity to bone scan, but higher specificity
 - Not effective for more differentiated tumors, ie. Prostate cancer



Conventional Radiation



- Symptomatic relief with conventional RT (ie. 30/10, 8/1) provides unsatisfactory results
- RTOG 97-14
 - Arm 1) RT 8/1 vs. Arm 2) 30/10. Primary outcome pain relief at 3 months
 - Outcome: 3-month complete pain relief 8/1 15% vs. 30/10 18% (NS); partial 50% vs. 48% (NS); stable 26% vs 24%; progressive 9% vs 10%
- TROG 96.05
 - Randomized trial of 8 Gy in 1 versus 20 Gy in 5 fractions
 - Response rate: 53% vs. 61% (p=NS)
 - TTF 2.4 mo vs. 3.7 mo

Image-Guided and Intensity-Modulated Radiosurgery for Patients with Spinal Metastasis

- Ryu et al. (Cancer 2003)
- 10 patients; All pts received external beam radiation therapy (25 Gy/10) followed by SBRT (6–8 Gy single dose) to the site of the spine involvement or spinal cord compression
- Time to pain relief 2-4 weeks

TABLE 1
Patient Characteristics and Radiosurgery Doses with Clinical Outcome

Diagnosis	Pathology	Site	Radiosurgery (Gy)	Outcome ^a
Lung cancer	Squamous cell	L2	6	Pain relief with reduced medication
Multiple myeloma	Plasma cell	T7-T8	6	Pain reduced at 4 weeks, complete relief at 4 months
Breast cancer	Invasive ductal cell	T7	6	Pain relief 7/10→4/10, progressed at other sites
Multiple myeloma	Plasma cell	T6-T7	6	Pain relief at 1 week, progressed at other sites
Hodgkin disease	Type undetermined	T6	8	Pain relief at 1 week, motor recovery 0/5→5/5
Plasmacytoma	Plasma cell	T2	6	Pain relief with reduced medication
Prostate cancer	Adenocarcinoma	L1	6	Pain relief at 2 weeks, motor recovery 0/5→3/5
Prostate cancer	Adenocarcinoma	T11	6	Pain relief 9/10→3/10
Breast cancer	Invasive ductal cell	T3	6	Pain relief by surgery
Breast cancer	Invasive ductal cell	T10	8	Pain relief at 1 week

Gy: grays.

^a Numeric values indicate motor strength or pain scores.

Radiosurgery for Spinal Metastases

Clinical Experience in 500 Cases From a Single Institution

Peter C. Gerszten, MD, MPH, Steven A. Burton, MD, Cihat Ozhasoglu, PhD,
and William C. Welch, MD, FACS

- Prospective cohort study. 500 cases of spinal metastases (cervical 15%, thoracic 42%, lumbar 22%, sacral 20%), treated with radiosurgery
- Maximum dose 12.5-25 Gy (mean 20 Gy). Prior EBRT 69% (typically 30/10 or 35/14)
- PTV = GTV
- Long-term pain control 86%; at least some improvement in neurologic function in 85%

Table 3. Summary of Pain and Radiographic Outcome for the 4 Most Common Histopathologies (n = 294)

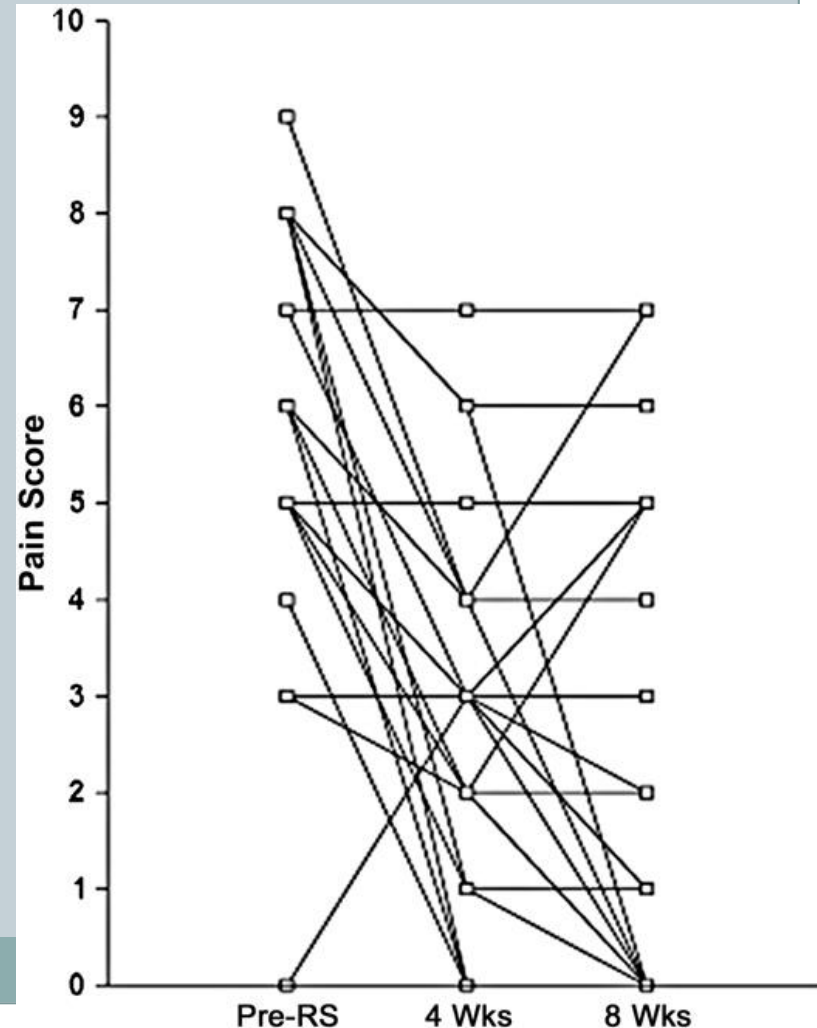
Long-term pain improvement	
All patients	86%
Renal cell	94%
Breast	96%
Lung	93%
Melanoma	96%
Long-term radiographic control	
All patients	88%
Renal cell	87%
Breast	100%
Lung	100%
Melanoma	75%

Pain Control by Image-Guided Radiosurgery for Solitary Spinal Metastasis

Samuel Ryu, MD, Ryan Jin, MD, Jian-Yue Jin, PhD, Qing Chen, PhD,
Jack Rock, MD, Joseph Anderson, MD, and Benjamin Movsas, MD

*Departments of Radiation Oncology (S.R., R.J., J.-Y.J., Q.C., B.M.), Neurosurgery (S.R., J.R.),
and Medical Oncology (J.A.), Henry Ford Hospital, Detroit, Michigan, USA*

- 49 patients with 61 separate spinal metastases were treated with radiosurgery
- Dose ranged from 10-16 Gy, single fraction
- PTV = involved spinal segment
- Median time to pain relief 14 days, fastest 24 hrs
- 1 yr overall pain control rate 84%
- Strong trend of increasing pain control with dose ≥ 14 Gy



HIGH-DOSE, SINGLE-FRACTION IMAGE-GUIDED INTENSITY-MODULATED RADIOTHERAPY FOR METASTATIC SPINAL LESIONS

YOSHIYA YAMADA, M.D., F.R.C.P.C.,* MARK H. BILSKY, M.D.,† D. MICHAEL LOVELOCK, PH.D.,‡
ENRAPADAM S. VENKATRAMAN, PH.D.,§ SEAN TONER, M.S.,‡ JARED JOHNSON, B.S.,*
JOAN ZATCKY, N.P.,* MICHAEL J. ZELEFSKY, M.D.,* AND ZVI FUKS, M.D.*

Departments of *Radiation Oncology, †Neurosurgery, ‡Medical Physics, and §Biostatistics,
Memorial Sloan-Kettering Cancer Center, New York, NY

- 103 spinal metastases in 93 pts without high-grade epidural spinal cord compression were treated with image-guided intensity-modulated RT to doses of 18-24 Gy (median, 24 Gy) in a single fraction between 2003 and 2006
- The spinal cord dose was limited to a 14-Gy maximal dose
- Actuarial LC 90% at 15 mos
- Radiation dose predicted for local control

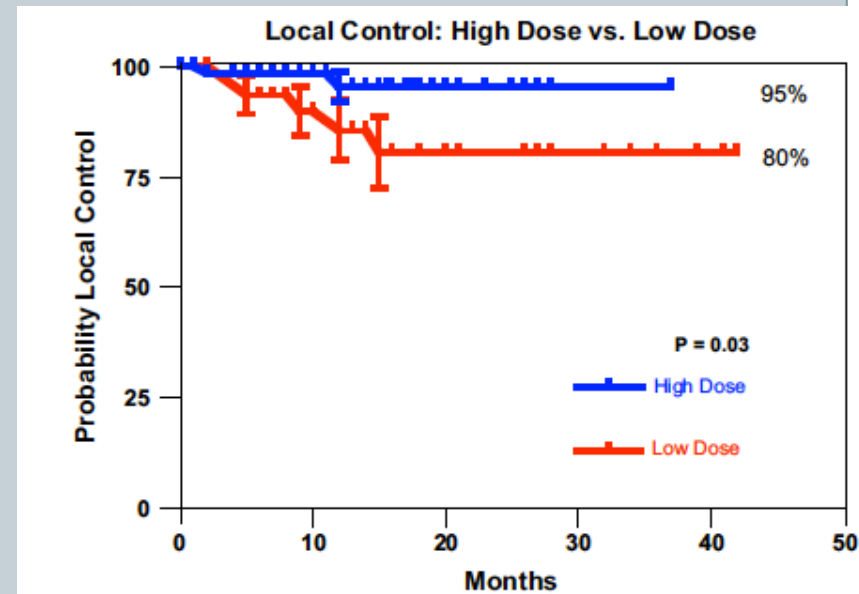


Fig. 3. Local control probability by dose. Statistically significant difference noted for patients treated to 2,400 cGy vs. 1,800–2,300 cGy.

Pattern of Failure



- **Ryu et al (J Neurosurg 2004)**
 - No failures in adjacent vertebral bodies if single segment treated in 49 patients
 - Suggests treating segments above and below is unnecessary
- **Chang et al. (J Neurosurg 2007)**
 - 63 patients with 74 spinal metastases underwent radiosurgery
 - SBRT dose ranged from 27-30 Gy in 3-5 fxs
 - Areas of failure 1) posterior elements and pedicles (17%), and 2) recurrence in the epidural space adjacent to the spinal cord (47%)
 - Authors recommended routine inclusion of the pedicles and posterior elements

Pattern of failure

TABLE 4
Cases involving imaging documentation of tumor progression*

Tumor No.	Patient Age (yrs)	Histology	Original Site	Level	Tumor Vol (cm ³)	TTP (mos)	Prior Treatments	POF	Comment
1	44	oncocytic	VB	T-11	24.1	4	VS, RT	ped, lam	PE†
2	54	HC	VB	T5-7	30.5	2.9	none	ES	PE†
3	69	RCC	prevertebral, VB	T8-10	113	3.5	Vst, RT	ES	PE†, dose‡
4	67	RCC	VB	T-12	42	3.4	kypho	VB	dose‡
5	82	RCC	VB	T4-5	33.8	3.9	VS, RT	prevertebra, paraspinal	MF
6	49	LMS	VB	L-2	30.1	15.7	none	ES	dose‡
7	67	RCC	VB	L-2	42	3.4	kypho	VB	dose‡
8	82	RCC	VB	L-1	27.9	12.0	RT	ES ALL to L-2	dose‡
9	54	RCC	paraspinal	L-4	75	3.0	none	ped, PM	IFF
10	60	ASC	presacral space	S-1	32.2	9.8	RT	presacral space	IFF
11	66	OCCA	paraspinal	L-5	54.8	21.9	none	pelvic side-wall	MF
12	58	LA	paraspinal	C7-T2	12.7	1.9	RT	ES	IFF
13	43	RCC	VB	T-11	39.3	36.6	none	ped, para-vertebral	PE†
14	61	RCC	paraspinal	T6-7	39	17.5	none	T-6, VB, ES	MF
15	23	LMS	paraspinal	L3-5	358	6.3	PRS	ES, VB, para-vertebral	IFF
16	50	LA	VB	L-1 + L-3	149	12.4	none	VB collapse, pain	salvaged w/ VS
17	47	breast	PE	T10-11	32.4	4.3	RT	ES, LMD	dose‡

Kyphoplasty + SBRT



- Gerszten et al. (Neurosurg focus 2005)
- 26 patients with symptomatic compression fractures without canal compromise
- Treated with kyphoplasty followed by SBRT (mean 12 days post-op)
- 16-20 Gy (mean 18) single fraction prescribed to 80%
- Overall pain improvement 92%

Outcomes



Table 3. Summary of clinical outcomes for spinal SBRS

Author/year (study period)	Total no. tumor/patient	No. retx tumor/patient	Follow-up months (range)	Target volume/ contouring imaging technique	Local control/ criteria	Tumor dose/no. fx/Rx isodose	Pain palliation from SBRS (Pain Measure Tool)
Unirradiated patients							
Ryu <i>et al.</i> , 2004 (20) (May 2001– May 2003)	61/49	0/0	6–24	Involved spinal segment/CT or MRI	57 of 61* (93%)/ imaging and pain [†]	10–16 Gy/1/N.R.	52/61 combined CR and PR (verbal/visual analog scale + 0–10 pain score)
Ryu <i>et al.</i> , 2003 (12) (April 2001– December 2001)	10/10	0/10	Mean 6 (3–12)	Site of spine involvement/ CT or MRI	10/10 (100%)/ imaging and pain [†]	EBRT: 25 Gy/10 and SBRS boost: 6–8 Gy/ 1/90%	5/9 CR 4/9 PR [‡] (N.R.)
Reirradiated patients							
Milker-Zabel <i>et al.</i> , 2003 (27) (June 1997– December 2001)	19/18	19/18	Median 12 (4–33)	PTV = GTV plus entire VB/CT with MRI fusion	18/19 (95%)/ imaging [†]	24–45 Gy/aim was 90% Median 39.6 Gy/2/N.R.	13/16 (N.R.)
Hamilton <i>et al.</i> , 1995 (36) (N.R.)	5/5	5/5	Median 6 (1–12)	GTV + areas suspicious of extension/CT	5/5 (100%)/ imaging or clinical [†]	8–10 Gy/1/80– 160% Median 10 Gy/1/80%	N.R.
Mahan <i>et al.</i> , 2005 (24) (N.R.)	8/8	8/8	Mean 15.2	PTV: GTV + 3 mm excluding the cord volume/CT	8/8 (100%) N.R.	20–34 Gy/10– 17/N.R. Median 30 Gy/15/N.R.	6/8 CR 2/8 PR (N.R.)

Overall pain relief ranged from 67 to 100%

Multiple PTV definitions used

Sahgal IJROBP 2008

Outcomes



Postoperative SBRS patients

Rock <i>et al.</i> , 2006 (23) (N.R.)	18/18	1/1	Median 7 (4–36)	Contrast enhancing margin/CT with MRI fusion	17/18 (94%)/ imaging or clinical [†]	4/18: EBRT 25 Gy/10 plus SBRT boost 6–8 Gy /1/ 90% Median: 6 Gy/1/90% 14/18: SBRT only 10–14 Gy/1/90% Median: 14 Gy/1/90%	6/18 CR (N.R)
Gerszten <i>et al.</i> , 2005 (52) (N.R.)	26/26	7/7	Median 16 (11–24)	Postkyphoplasty VB plus areas of extension/ CT	24/26 (92%)/ pain [†]	16–20 Gy/1/80% Mean 18 Gy/ 1/80% Max intratumoral dose 16–20 Gy	Improved 24/26 (10-point verbal visual analog scale)
Mixed patients							
Chang <i>et al.</i> , 2007 (17) (November 2002–March 2005)	74/63	N.R./35	Median 21.3 (1–50)	GTV plus potential spinal structures of extension/CT	57/74 (77%) 1-year FFP: 84%/imaging	(32/63) 6 Gy/5 or (31/63) 9 Gy/3 Prescribed to an isodose line allowing 80–90% target coverage	Narcotic use declined from 60% to 36% at 6 months (Brief Pain Inventory and Narcotic Usage)
Sahgal <i>et al.</i> , 2007 (22) (April 2003–August 2006)	60/38	37/26	Median 8.5 (0.5–48)	GTV = PTV/CT	52/60 (87%) 1-year FFP: 85 % [§] / imaging and pain	8–30 Gy/1–5/ 46–78% Median: 24 Gy/3/64%	31/46 improved (N.R.)

Outcomes



Table 3. Summary of clinical outcomes for spinal SBRS (*Continued*)

Author/year (study period)	Total no. tumor/patient	No. retx tumor/patient	Follow-up months (range)	Target volume/ contouring imaging technique	Local control/ criteria	Tumor dose/no. fx/Rx isodose	Pain palliation from SBRS (Pain Measure Tool)
Gibbs <i>et al.</i> , 2007 (28) (1996– September 2005)	102/74	50 /N.R.	Mean 9 (0–33)	Target lesion + up to 2-mm margin/CT	N.R.	14–25 Gy/1–5/ 61–89%	N.R. specifically for pain (N.R.)
Gerszten <i>et al.</i> , 2007 (19) (N.R.)	500/393	344/N.R.	Median 21 (3–53)	PTV = GTV/CT	440/500 (88%)/ imaging [†]	Maximum intratumor dose 12.5–25 Gy/1/N.R. Mean 20 Gy/ 1/N.R. 7/500 combined EBRT plus SBRT boost and doses N.R.	290/336 improvement (10-point visual analog scale)
Yamada <i>et al.</i> , 2005 (18) (N.R.)	21/21	1/1	Median 7 (1–24)	PTV = GTV + 1 cm except at cord interface/ CT	19/21 (90%) and actuarial: 81% /imaging [†]	20–30 Gy/N.R./ N.R. Median = 20 Gy/5 fractions	N.R. for metastases patients only (0–10 self- assessed pain scale)

ASTRO Consensus



Characteristic	Inclusion	Exclusion
Radiographic	<ol style="list-style-type: none"> 1) Spinal or paraspinal metastasis by MRI (50, 51) 2) No more than 2 consecutive or 3 noncontiguous spine segments involved (50–53) 	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 1) Age ≥ 18 y (50, 54) 2) KPS of ≥ 40–50 (50, 51, 54, 55) 3) Medically inoperable (or patient refused surgery) (50, 51) 	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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) 	<ol style="list-style-type: none"> 1) Radiosensitive histology such as MM⁵⁰⁻⁵² 2) Extraspinal disease not eligible for further treatment⁵¹
Previous treatment	<p>Any of the following:</p> <ol style="list-style-type: none"> 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 	<ol style="list-style-type: none"> 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)

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0631

PHASE II/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

PHASE II COMPONENT	
R	
E	
G	Radiosurgery/SBRT:
I	Single fraction dose of 16 Gy
S	
T	
E	
R	

PHASE III COMPONENT			
S		R	
T	Number of Spine Metastases	A	Arm 1: Radiosurgery/SBRT:
R	1) 1	N	Single fraction dose of 16 or 18 Gy**
A	2) 2-3	D	
T		O	Arm 2: External Beam Radiation Therapy:
I	Type of Tumor	M	Single fraction dose of 8 Gy
F	1) Radioresistant tumor*	I	
Y	2) Other	Z	Randomization ratio (Arm 1: Arm 2) = 2:1
		E	
	Intended Radiosurgery/SBRT Single Fraction Dose**		
	1) 16 Gy		
	2) 18 Gy		

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PHASE II/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

2.1 Primary Objective (8/30/11)

2.1.1 Phase II Component

Determine the feasibility of successfully delivering image-guided radiosurgery/SBRT for spine metastases in a cooperative group setting

2.1.2 Phase III Component

Determine whether image-guided radiosurgery/SBRT (single dose of 16 or 18 Gy) improves pain control (as measured by the 11 point NRPS) as compared to conventional external beam radiotherapy (single dose of 8 Gy)

2.2 Secondary Objectives (Phase III Component) (11/6/09)

2.2.1 Determine whether image-guided radiosurgery/SBRT improves the rapidity of pain response at the treated site(s) as compared to conventional external beam radiotherapy, as measured by the NRPS;

2.2.2. Determine whether image-guided radiosurgery/SBRT increases the duration of pain response at the treated site(s), as compared to conventional external beam radiotherapy, as measured by the NRPS;

2.2.3 Compare adverse events between the two treatments according to the criteria in the CTEP Active Version of the CTCAE;

2.2.4 Evaluate the long-term effects (24 months) of image-guided radiosurgery/SBRT on the vertebral bone (such as compression fracture) and the spinal cord by MRI;

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PHASE III/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

- Target volumes

- Based on MR fused T1 and T2 images
- Should include the entire vertebral body and the pedicles as well as paraspinal (≤ 5 cm) and epidural (≥ 3 mm from cord) components

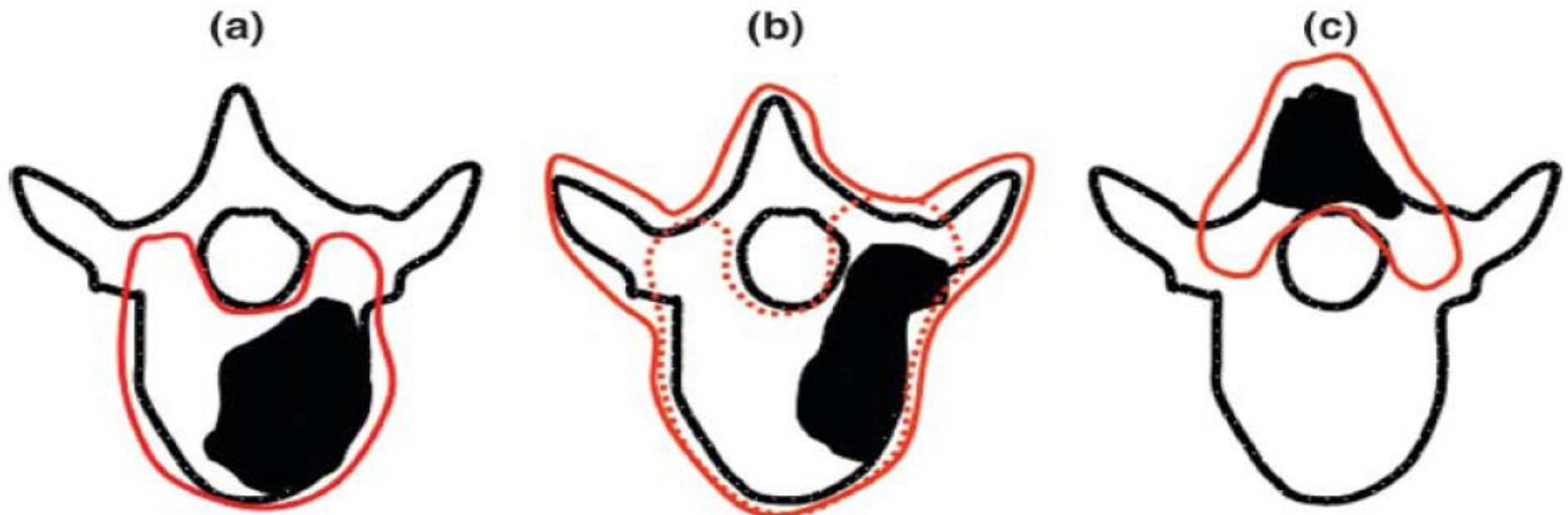


Figure 2: Diagram of Spine Metastasis and Target Volume

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PHASE III/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

- Spinal cord contouring
 - Partial cord volume (5-6 mm above and below target) based on fused T1 and T2 images
 - Dose constraint set at 10 to 10% of partial spinal cord volume
 - Max dose of 14 Gy to 0.03 cc

Summary



- Dose escalation provides potential to improve local control and symptom relief over conventional treatment especially in the setting of oligometastases and prolonged survival
- SBRT makes dose escalation possible while limiting dose to the spinal cord
- Rapid pain control
- Spares bone marrow especially in patients with multiple segments involved
- Shorter overall treatment time more convenient and less likely to interfere with systemic therapy