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Stereotactic Radiosurgery for Spinal Metastasis

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Disclosures

- None

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A Clinical (“Friday Evening”) Scenario

- Urgent inpatient consult
- 60M with new onset lower extremity weakness
- Metastatic prostate cancer
- MRI shows compressive lesion
- What now?

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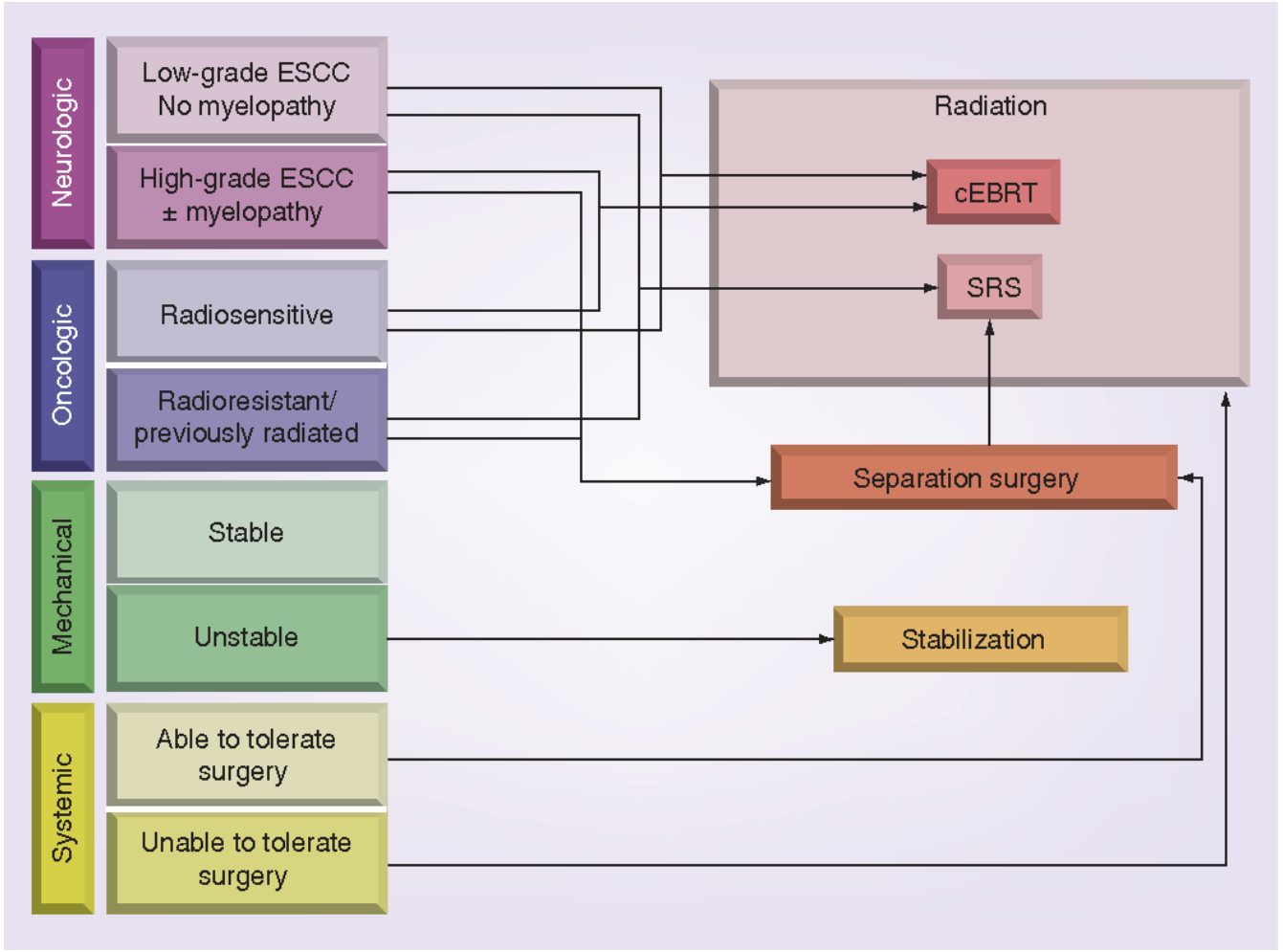
NOMS Decision Support Framework



NEUROLOGIC: Bilsky Epidural Disease Grading System

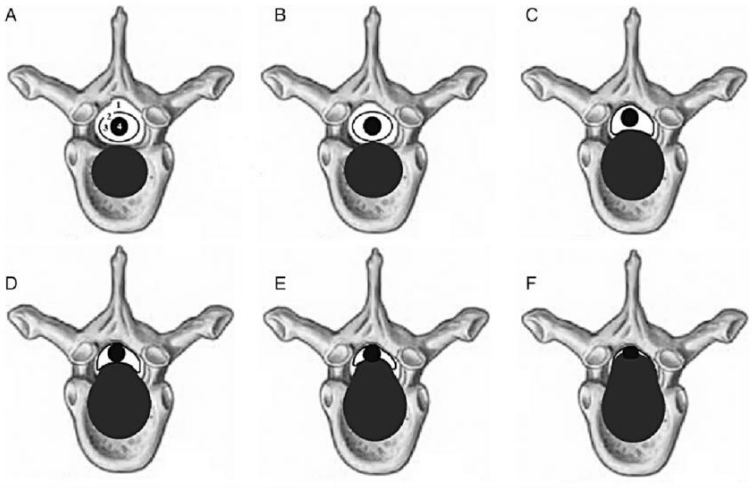


Table 2 Bilsky epidural disease grading system

Grade	Description
0	No epidural disease
1a	Epidural disease impinging on the thecal sac but no deformation
1b	Epidural disease deforming thecal sac but not spinal cord
1c	Epidural disease deforming thecal sac and contacting spinal cord
2	Epidural spinal cord compression with CSF visible
3	Epidural spinal cord compression with no visible CSF

CSF, cerebrospinal fluid.

ONCOLOGIC: Radiosensitive or “Resistant”

Radiotherapy and Radiosurgery for Metastatic Spine Disease: What Are the Options, Indications, and Outcomes?

Gerszten, Peter C.; Mendel, Ehud; Yamada, Yoshiya
Spine34(22S):S78-S92, October 15, 2009.

Table 3. Classification of Radiosensitive and Radioresistant Histologies

Study	Lymphoma, Seminoma, Myeloma	Breast	Prostate	Sarcoma	Melanoma	Gastrointestinal	NSCLC	Renal
Gilbert *et al*[103]	F	U	U	U	U	U	U	U
Maranzano *et al*[79]	F	F	F	U	U	U	U	U
Rades *et al*[20,43]	F	I	I	I	U	I	U	I
Rades *et al*[58]	F	F	F	U	U	U	U	U
Katagiri *et al*[49]	F	F	F	U	U	U	U	U
Maranzano *et al*[22]	F	F	F	U	U	U	U	U
Rades *et al*[23]	F	I	I	I	U	I	U	I

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

SPINE

Classification of Radiosensitive and Radioresistant Histologies

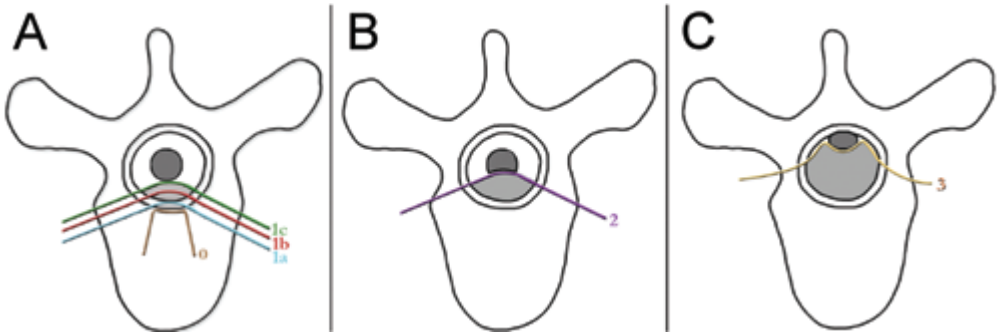
MECHANICAL: Spinal Instability Neoplastic Score (SINS)

	Score
Location	
Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)	3
Mobile spine (C3-C6, L2-L4)	2
Semirigid (T3-T10)	1
Rigid (S2-S5)	0
Pain	
Yes	3
Occasional pain but not mechanical	1
Pain-free lesion	0
Bone lesion	
Lytic	2
Mixed (lytic/blastic)	1
Blastic	0
Radiographic spinal alignment	
Subluxation/translation present	4
De novo deformity (kyphosis/scoliosis)	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% body involved	1
None of the above	0
Posterolateral involvement of spinal elements	
Bilateral	3
Unilateral	1
None of the above	0
Total score	
Stable	0–6
Indeterminate	7–12
Unstable	13–18

SYSTEMIC Disease or/and SURGICAL Candidate

- Tumor Biology
- Disease extent
- Co-morbidities

Spinal cord compression and NOMS Decision Framework



Neurologic	Oncologic	Mechanical	Systemic	Decision
Low-grade ESCC + no myelopathy	Radiosensitive	Stable		cEBRT
	Radiosensitive	Unstable		Stabilization followed by cEBRT
	Radioresistant	Stable		SRS
	Radioresistant	Unstable		Stabilization followed by SRS
High-grade ESCC ± myelopathy	Radiosensitive	Stable		cEBRT
	Radiosensitive	Unstable		Stabilization followed by cEBRT
	Radioresistant	Stable	Able to tolerate surgery	Decompression/stabilization followed by SRS
	Radioresistant	Stable	Unable to tolerate surgery	cEBRT
	Radioresistant	Unstable	Able to tolerate surgery	Decompression/stabilization followed by SRS
	Radioresistant	Unstable	Unable to tolerate surgery	Stabilization followed by cEBRT

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Decompressive Surgery

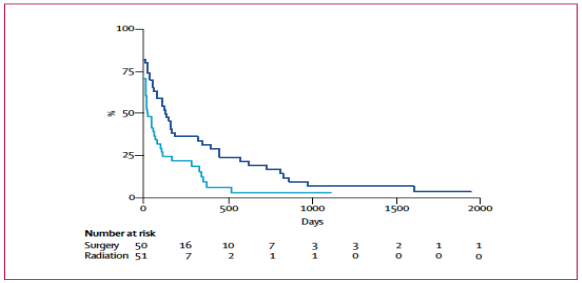

Figure 2: Kaplan–Meier estimates of length of time all study patients remained ambulatory after treatment

	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, R.A., et al., Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet, 2005. 366(9486): p. 643-8.

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Surgical Candidates?

- Single area of compression
- High performance status
- Non-radiosensitive histology
- Prognosis > 3 months
- Can be only ~15% of patients……

Conventional Radiation

- Most common treatment
- Appropriate course is variable
- Short course (4 Gy x 5, 8 Gy x 1) considered when prognosis < 6 months
- Longer-course (3 Gy x 10, 2 Gy x 20) has shown minimal local control benefit
- 10-20% improvement in motor function……

Rades, D. and J.L. Abrahm, The role of radiotherapy for metastatic epidural spinal cord compression. Nat Rev Clin Oncol, 2010. 7(10): p. 590-8.

Randomized Trial of Short- Versus Long-Course Radiotherapy for Palliation of Painful Bone Metastases

William F. Hartsell, Charles B. Scott, Deborah Watkins Bruner, Charles W. Scarantino, Robert A. Ivker, Mack Roach, III, John H. Suh, William F. Demas, Benjamin Movsas, Ivy A. Petersen, Andre A. Konski, Charles S. Cleeland, Nora A. Janjan, Michelle DeSilvio

Parameter	No. of patients (%)		*P**
	8-Gy arm (n = 288)	30-Gy arm (n = 285)	
BPI worst pain score			
0	44 (15)	51 (18)	.854
1–4	99 (34)	98 (34)	
5–6	56 (19)	53 (19)	
7–10	89 (31)	83 (29)	
No answers/2 answers	2	5	
Overall response type			
Complete	44 (15)	51 (18)	.6
Partial	143 (50)	137 (48)	
Stable	74 (26)	69 (24)	
Progressive	27 (9)	28 (10)	

Drug	No. of patients (%)		*P**
	8-Gy arm (n = 318)	30-Gy arm (n = 310)	
None	65 (20)	69 (22)	.483
Nonnarcotic analgesic	40 (13)	30 (10)	
Narcotic	213 (67)	211 (68)	

Conventional RT for MESCC

- 116 patients with pathologically proven metastatic cancer
- 20 Gy in 5 fractions (control) vs. high-dose of 10 Gy in 1 fraction (experimental)
- Primary outcome was mobility based on modified Tomita score
- 10.5% improved mobility in both groups, 2-10% improved bladder function
- ~60-70% had stable symptoms

"ICORG 05-03: Prospective Randomized Non-Inferiority Phase 3 Trial Comparing Two Radiation Schedules in Malignant Spinal Cord Compression not Proceeding with Surgical Decompression," ASTRO 2014

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OUTCOMES OF SBRT FOR SPINE TUMORS

Table 1 – Phase I and II studies assessing single dose stereotactic irradiation to the spine.

Author, year	No. patients/no. lesions	Prior RT	Dose/coverage	Constraints/dose to spinal cord	Histology	Median F/U (months)	Local control
Gerszten et al., 2005	50/68	48/68	12.5–22.5 Gy (mean, 19 Gy)/80% IDL	13 Gy (max. dose actually received)	Breast	16	100%
Gerszten et al., 2005	28/36	23/36	17.5–25 Gy (mean, 21.9 Gy)/80% IDL	13.1 Gy (max. dose actually received)	Melanoma	13	93%
Gerszten et al., 2006	77/87	70/87	15–25 Gy (mean, 20 Gy)/80% IDL	12 Gy (max. dose actually received)	Lung	16	100%
Gerszten et al., 2007	393/500	344/500	12.5–25 Gy (mean, 20 Gy)/80% IDL	NR (mean volume of spinal canal dose >8 Gy 0.6 cm³	Mixed	21	88%
Yamada et al., 2008	93/103	0/103	18–24 Gy/100% IDL	14 Gy (max. dose)	Mixed	15	90%
Amdur et al., 2009	21/25	12/25	15 Gy/95% PTV	•12 Gy to 0.1 mL (no previous RT) •5 Gy to 0.5 mL (if previous RT)	Mixed	8	95%
Yamada et al., 2011	412/362	0/363	18–24 Gy/100% IDL	14–15 Gy (max point dose)	Mixed	36	90% (98% in breast and prostate)
Garg et al., 2012	61/63	0/63	16–24 Gy/80–90%	•10 Gy to 0.01 cm³ •12 Gy (spinal cord + 2 mm)	Mixed (renal versus non-renal)	19.7	88%
Ryu et al.,	39/NR	NR	16 Gy/90% PTV	•10% partial spinal cord, max 10 Gy •0.35 cm³ absolute spinal cord, max 10 Gy	NR (no exclusion criteria for histology)	NR	NR

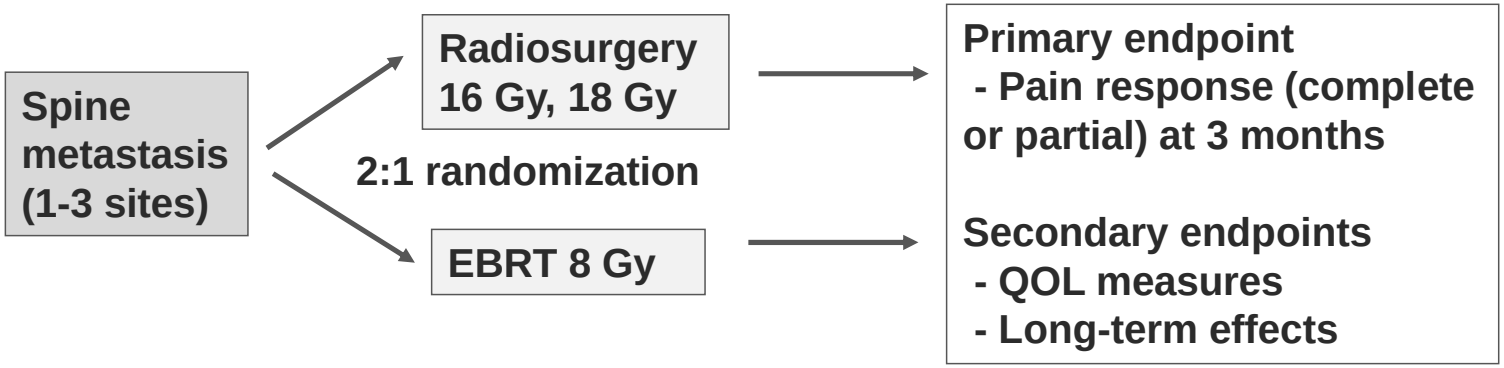
IDL, isodose line.

Radiosurgery/SBRT Compared to External Beam Radiotherapy for Localized Spine Metastasis: Phase III Results of NRG Oncology/RTOG 0631

Samuel Ryu, Snehal Deshmukh, Robert Timmerman, Benjamin Movsas, Peter Gerszten, Fang-Fang Yin, Adam Dicker, Stephen Shiao, Anand Desai, Loren Mell, Puneeth Iyengar, Ying J. Hitchcock, Aaron Max Allen, Steven Burton, Doris Brown, Hadley Sharp, Jason Chesney, Salim Siddiqui, Timothy Chen, Lisa A. Kachnic,

on behalf of NRG Oncology

Study Design

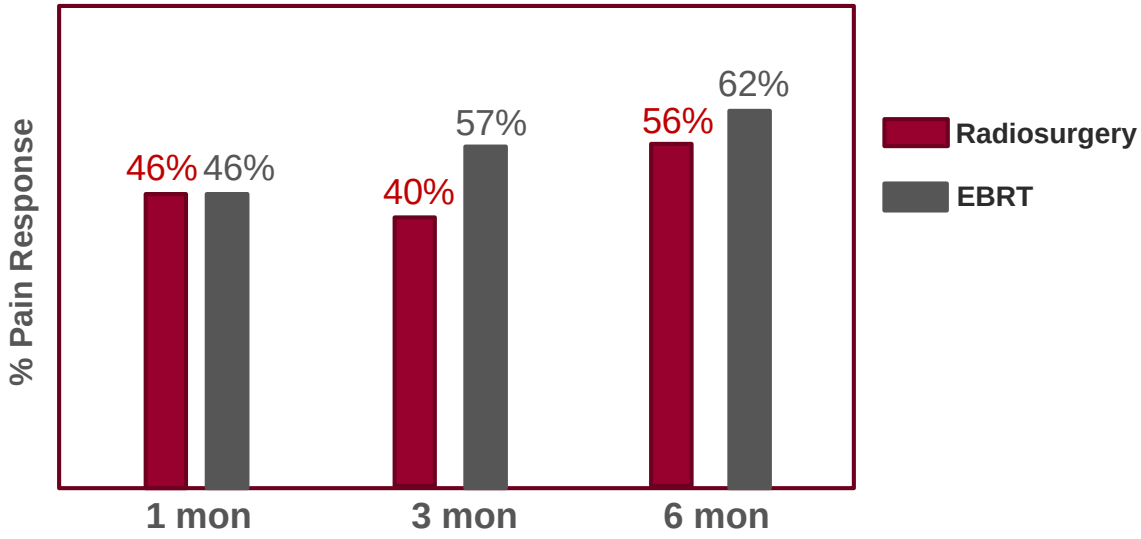


	Radiosurgery (n=209)	EBRT (n=130)	P value
Median Age in Years (range)	63 (23-93)	63 (32-91)	0.21
Gender (% male)	54.5%	53.8%	0.90
Race (% white)	80.9%	77.7%	0.48
Zubrod (% 0-1)	78.0%	90.0%	0.02
2	22.0%	10.0%	
Baseline NRPS (%) 5	23.0%	25.4%	0.50
6-7	39.2%	43.1%	
□	37.8%	31.5%	
% with Single Spine Metastasis	76.6%	76.9%	0.94
Index Spine Met Location (%) C-1 to C-7	0%	10.0%	0.14
T-1 to T-12	38.8%	46.7%	
L-1 to L-5	61.2%	43.3%	
Took Pain Medication	86.6%	88.5%	0.62
Intended 16Gy vs 18Gy if Radiosurgery*	55% vs 45%		0.53
% with Radioresistant Tumor vs Other*	13.9%	11.5%	0.53

Index Site Pain Response (NRPS)

	Radiosurgery (n=139)	EBRT (n=76)
Mean baseline pain score	6.06 (SD=2.61)	5.88 (SD=2.41)
Change in pain at 3 months	-3.00 (SD=3.34)	-3.83 (SD=2.97)
Pain response at 3 months	40.3%	57.9%

(one-sided p=0.99)



NRG ONCOLOGY™

IRB #2015-4957

Adaptive High-Dose Radiotherapy for Metastatic Epidural Disease in the Spine

Montefiore Medical Center
Department of Radiation Oncology
PI: Madhur Garg, MD

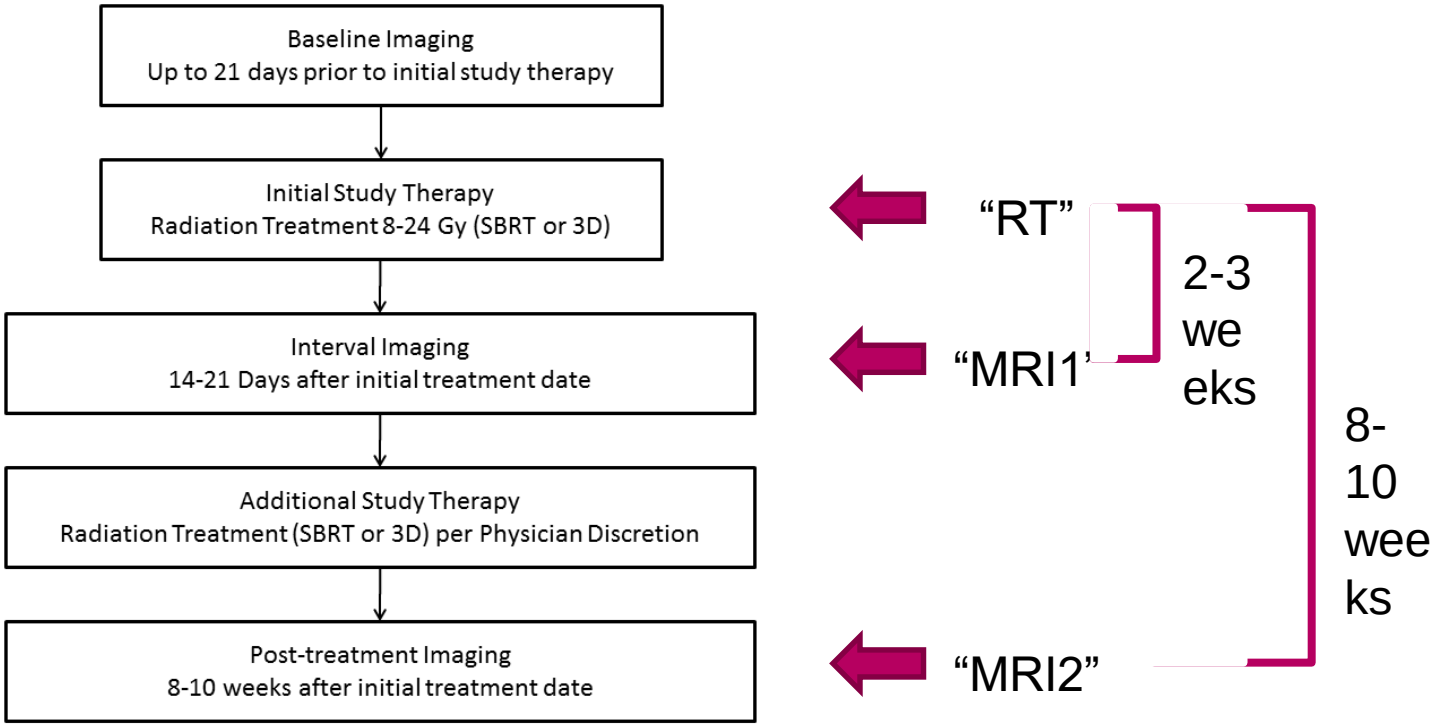
Hypothesis

- MESCC patients who are not surgical candidates can benefit from a staged SBRT approach
  - Short-interval decompression can be noted within 2-3 weeks following radiation
  - An initial dose delivered promptly followed by re-imaging, adaptive planning and targeted boost is feasible if required

Eligibility

- MESCC or epidural extension noted on MRI or CT myelogram not caused primarily by bony retropulsion
- C1 to L5 metastases encroaching within 3mm of the spinal cord
- Non-radiosensitive histology (no lymphoma, multiple myeloma)
- At least 50% preserved vertebral height
- Not proceeding to surgery after multidisciplinary evaluation
- Relative spine stability (SINS <= 12)
- Ability to meet dose constraints accounting for previous RT

Schema



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Radiotherapy Planning & Treatment

- CT myelogram (CTM) performed in Interventional Radiology
- Diagnostic MRI
  - Gadolinium enhanced based on creatinine clearance
  - High-resolution acquisition in area of lesion
- MRI Fusion
  - Rigid or deformable registration (MIM Software™ or Velocity™ packages)
- Contouring
  - GTV (T1 post contrast)= CTV
  - Spinal cord and/or thecal sac (T2MRI and CTM)
  - 1-3mm margin to PTV
- Spinal cord constraints
  - Dmax (0.035 cc) < 12 Gy (1 fraction)

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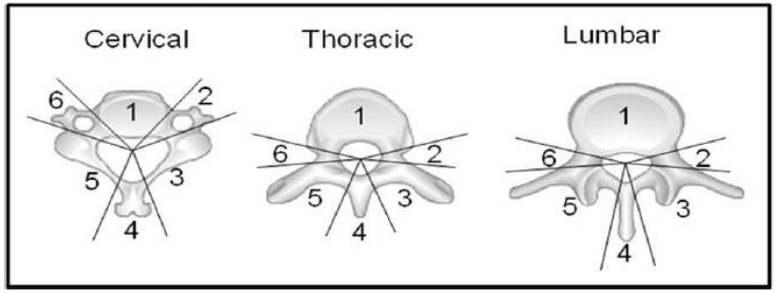
International Spine Radiosurgery Consortium

- Anatomic classification system



GTV involvement	CTV description
Any portion of the vertebral body	Include the entire vertebral body
Lateralized within the vertebral body	Include the entire vertebral body and the ipsilateral pedicle/transverse process
Diffusely involves the vertebral body	Include the entire vertebral body and the bilateral pedicles/transverse processes
GTV involves vertebral body and unilateral pedicle	Include entire vertebral body, pedicle, ipsilateral transverse process, and ipsilateral lamina
GTV involves vertebral body and bilateral pedicles/transverse processes	Include entire vertebral body, bilateral pedicles/transverse processes, and bilateral laminae
GTV involves unilateral pedicle	Include pedicle, ipsilateral transverse process, and ipsilateral lamina, ± vertebral body
GTV involves unilateral lamina	Include lamina, ipsilateral pedicle/transverse process, and spinous process
GTV involves spinous process	Include entire spinous process and bilateral laminae

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Primary Endpoint: Radiographic Decompression

- Cord-disease distance (CDD) of at least 3mm in shortest axial distance

OR

- At least 10% absolute increase in thecal sac patency (TSP), defined as
-

$$TSP = \frac{\text{Thecal sac area at level of max compression}}{\text{Avg. thecal sac area 1 level above/below}}$$

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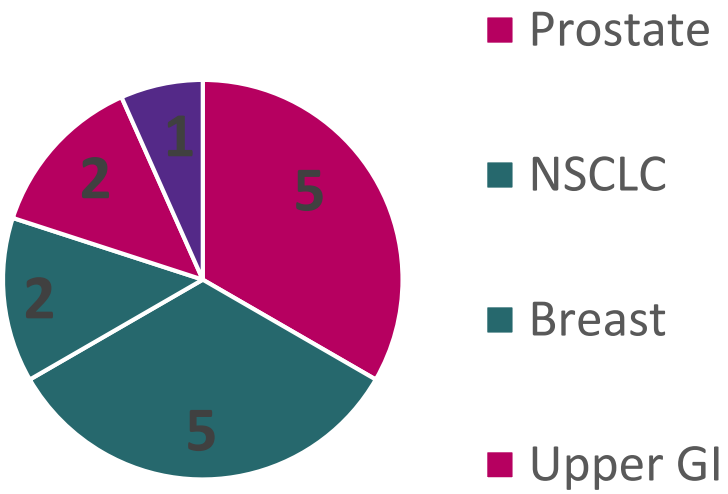
Secondary Endpoints & Statistics

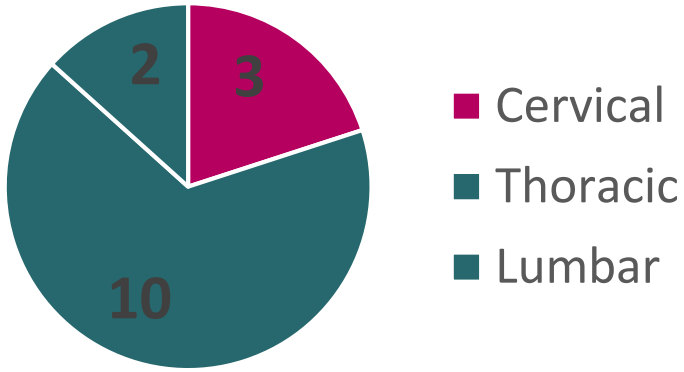
- Pain (NRPS)
- Quality-of–Life (FACT-G)
- Functional Outcomes (Neurologic Assessment)

- Statistics
  - Wilcoxon signed-rank test for comparisons between paired measurements at different time points

Patient and Treatment Characteristics

- 24 patients
- 6 patients received MRI1, no boost fractions given





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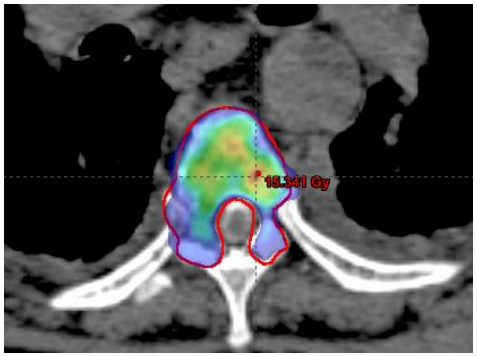
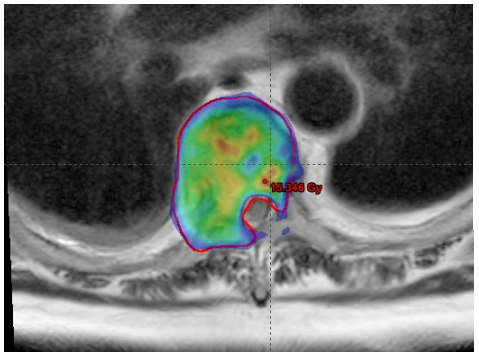
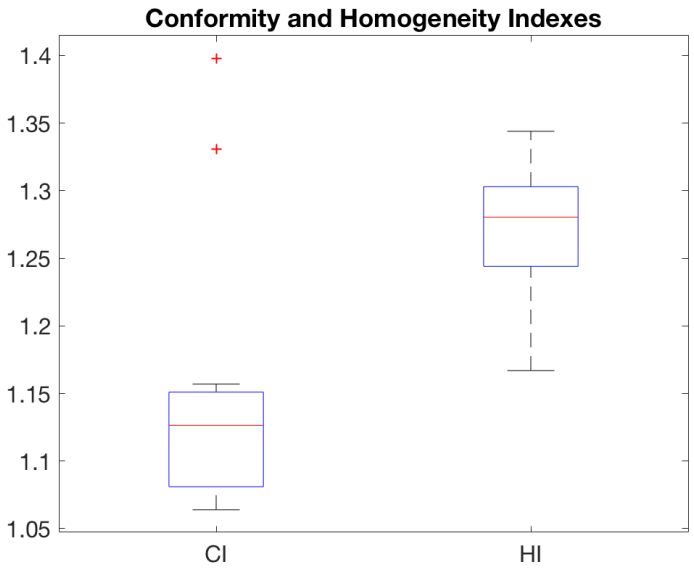
Plan Evaluation







100% isodose

PTV

Dmax

Rx Dose

Median PTV: 34.8cc
Median Dose: 14 Gy
Median Dmax: 128.05%

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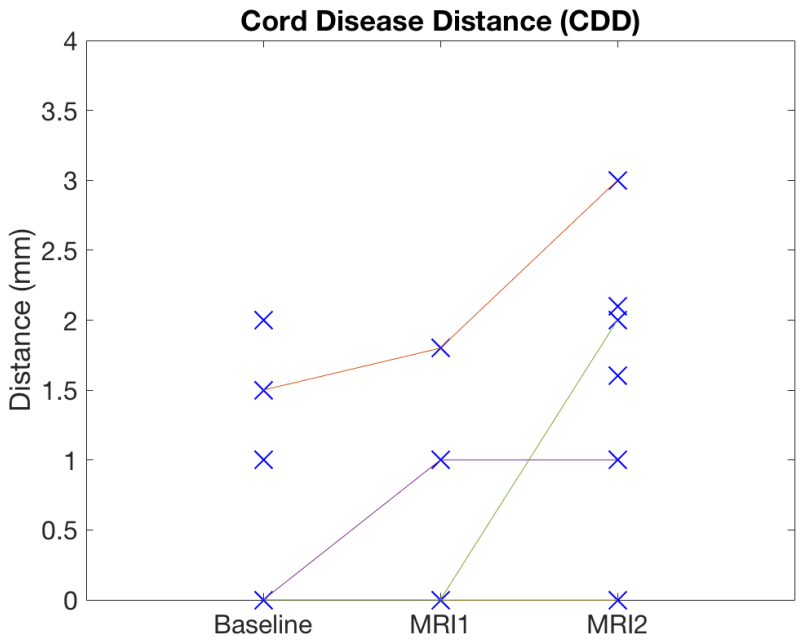
Results: Primary Endpoint (CDD)



- CDD at MRI2 approached significance (WSR p=0.0625)
- Noted canal can be decompressed while cord still abuts disease

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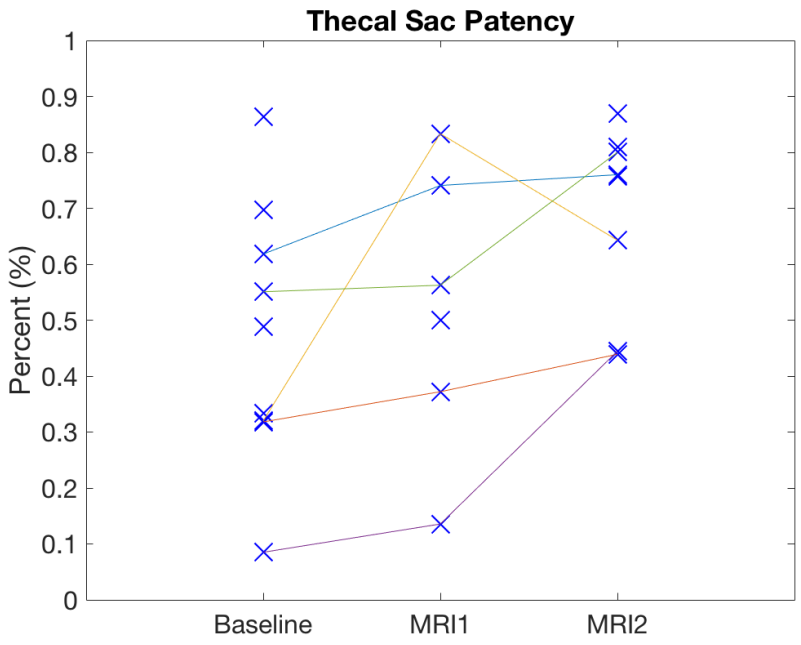
Primary Endpoint: Thecal Sac Patency (TSP)



- TSP difference **significant at both time points (WSR p=0.0312 at MRI1, p=0.0156 at MRI2)**
- 2/6 patients at MRI1 and 6/9 patients at MRI2 met primary endpoint
- 1 patient suffered local failure

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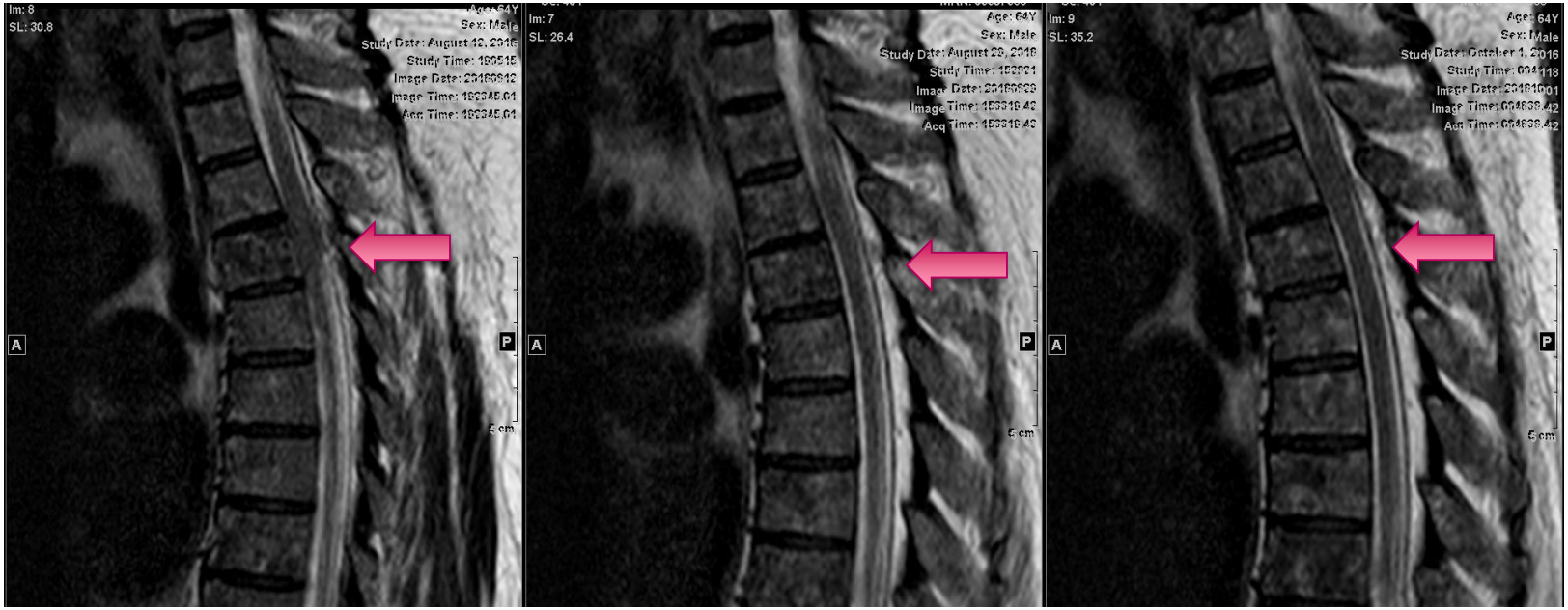
64M with Metastatic Prostate Cancer



08/12/2016 08/29/2016 10/01/2016

08/14/2016
T4 SBRT
14 Gy x 1

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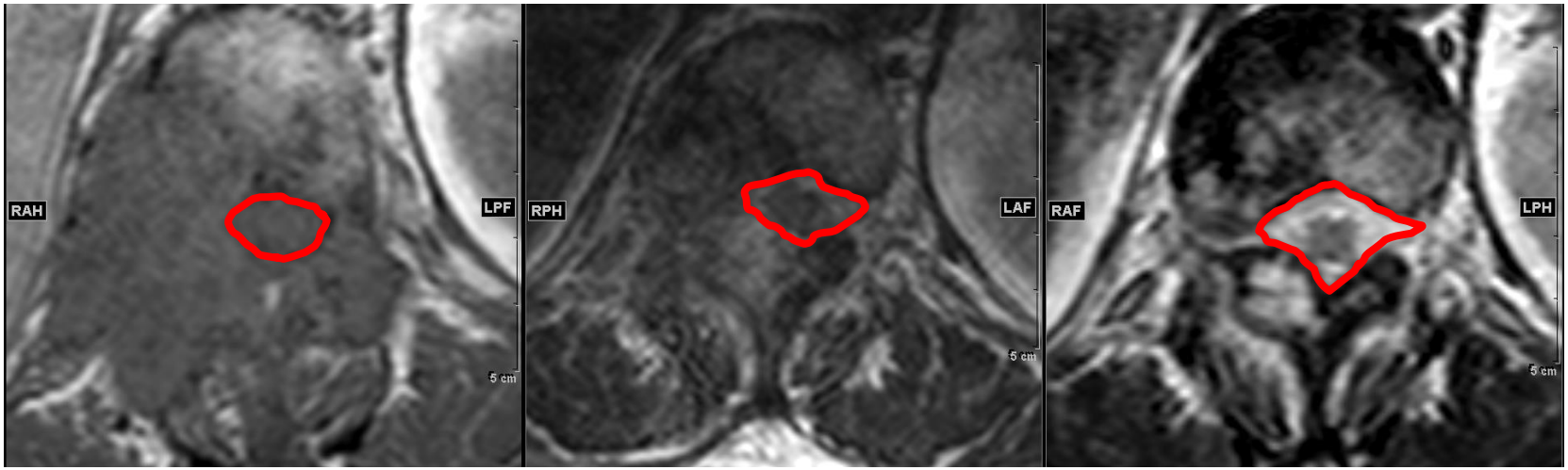
Example Case



Baseline MRI1 MRI2

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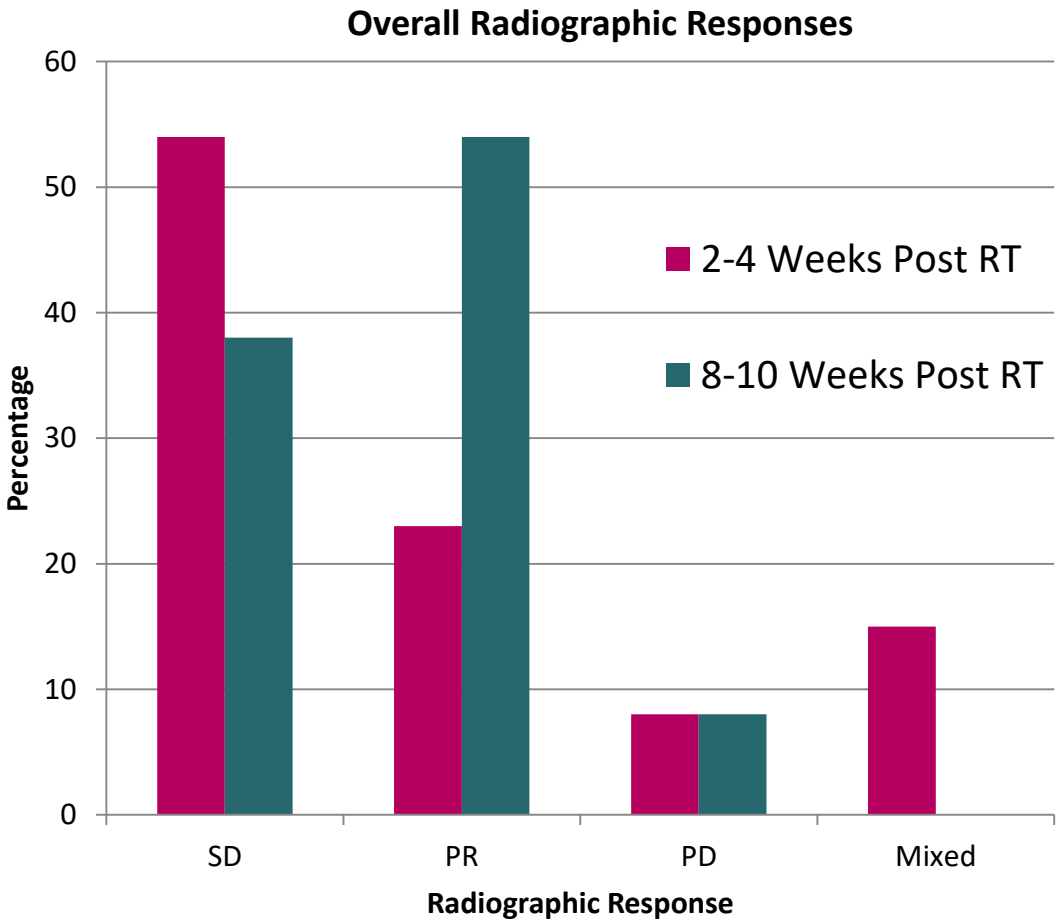
Primary Endpoint Results: Overall Radiographic Responses



- At 2-4 weeks post treatment: (n=13)
  - 7 Patients had stable disease (54%)
  - 3 Patients had a partial response (23%)
  - 2 Patients had a mixed response (15%)
  - 1 Patient had progression of disease (8%)
- At 8-10 weeks post treatment: (n=13)
  - 5 Patients had stable disease (38%)
  - 7 Patients had a partial response (54%)
  - 1 Patient had progression of disease (8%)

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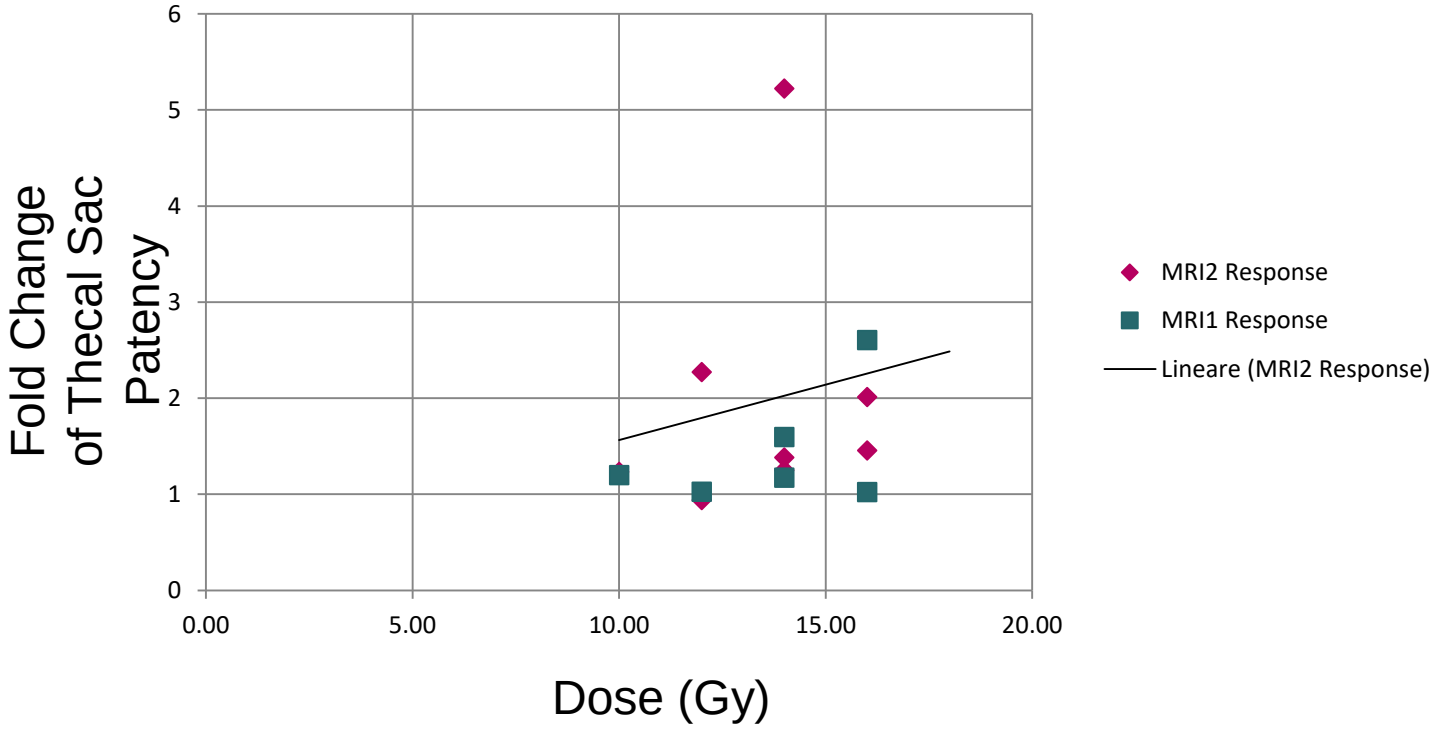
Dose Response Trend (NS)



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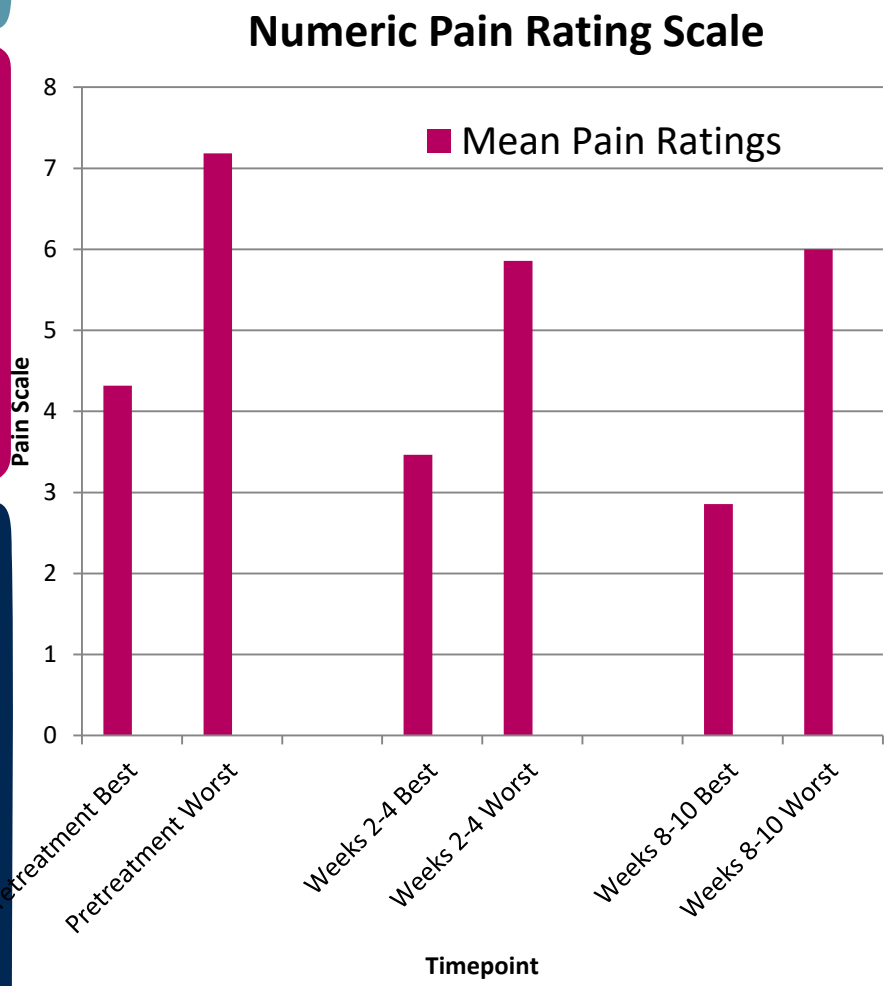
Secondary Endpoint:

Pain control: Pain scores as measured by the Numerical Rating Pain Scale(NRPS) estimation



Numeric Pain Rating Scale			
Pretreament n= 22			
	Mean	Median	SD
Pretreamtent Best	4.318182	4	3
Pretreamtent Worst	7.181818	8	2.8
Weeks 2-4 n= 14			
	Mean	Median	SD
Week 2-4 Best	3.464286	3	2.6
Week 2-4 Worst	5.857143	6.5	3.7
Weeks 8-10 n= 7			
	Mean	Median	SD
Week 8-10 Best	2.857143	3	3.6
Week 8-10 Worst	6	7	3.5

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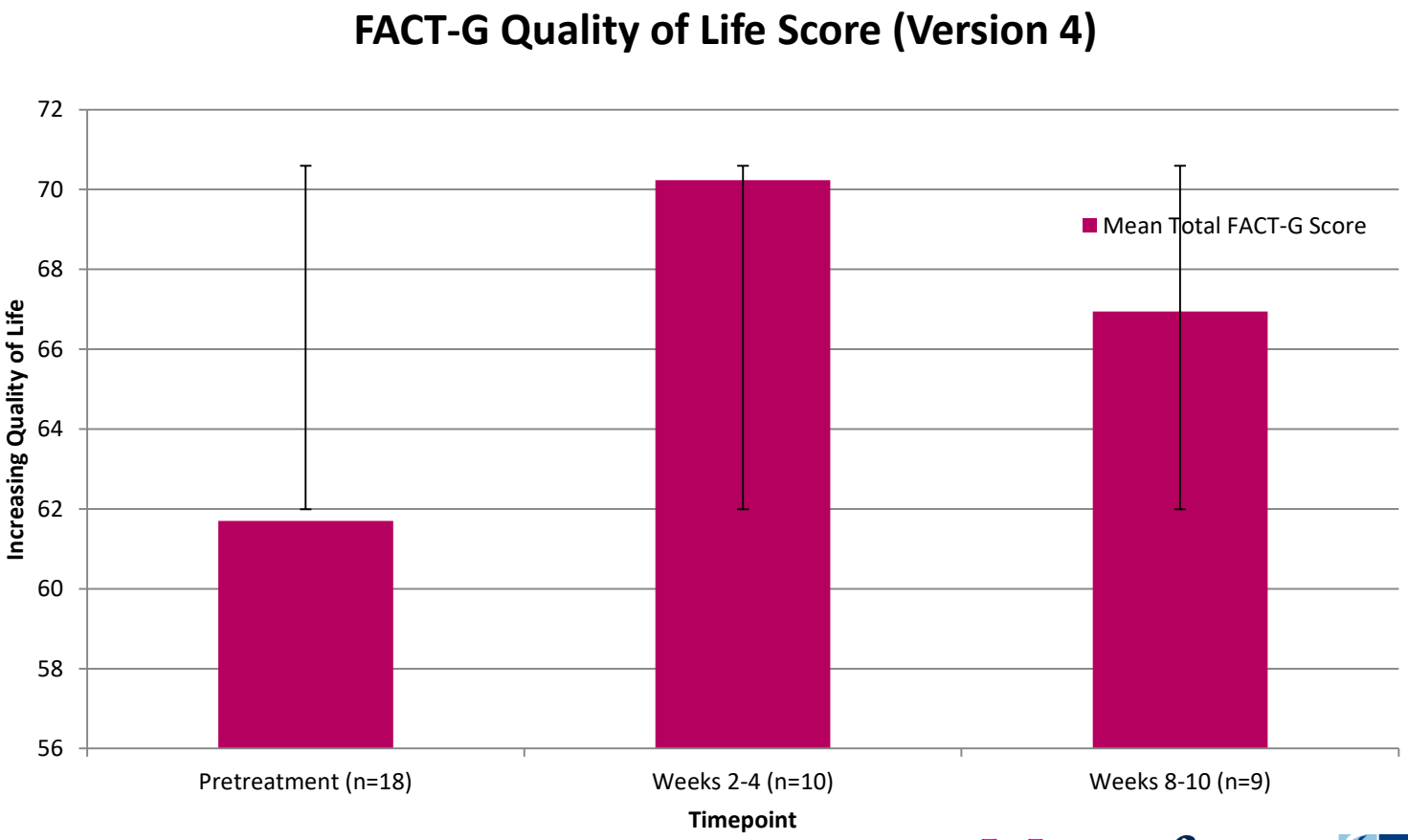
Secondary Endpoint:
Quality of Life: Scores from Functional Assessment of Cancer Therapy (FACT-G)



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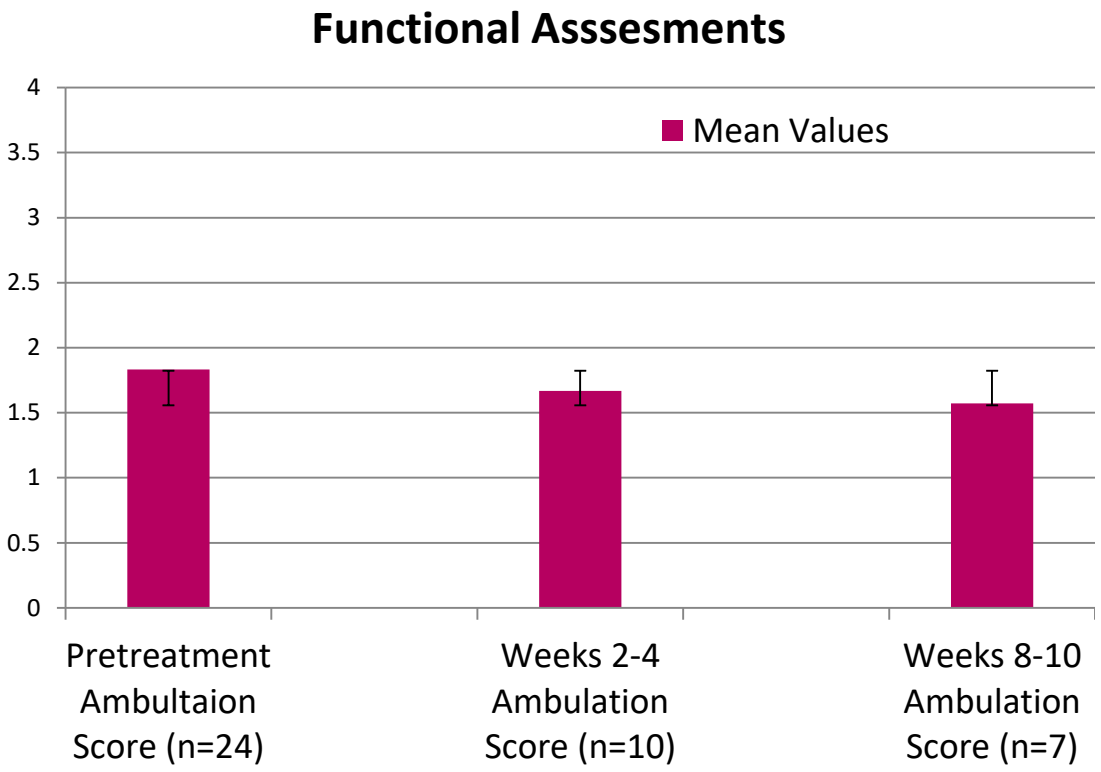
Secondary Endpoint:
Ambulation: Based on ambulation score and standardized neurologic exam



SCALE:
1 = Ambulatory without aid
2 = Ambulatory with aid
3 = Not Ambulatory
4 = Paraplegia

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Secondary Endpoint:
Grade ≥ 2 radiation-induced lung toxicity, scored using CTCAE, v. 4

Secondary Endpoint:
Any grade ≥ 3 treatment-related toxicity, scored using CTCAE, v. 4

- **None noted**

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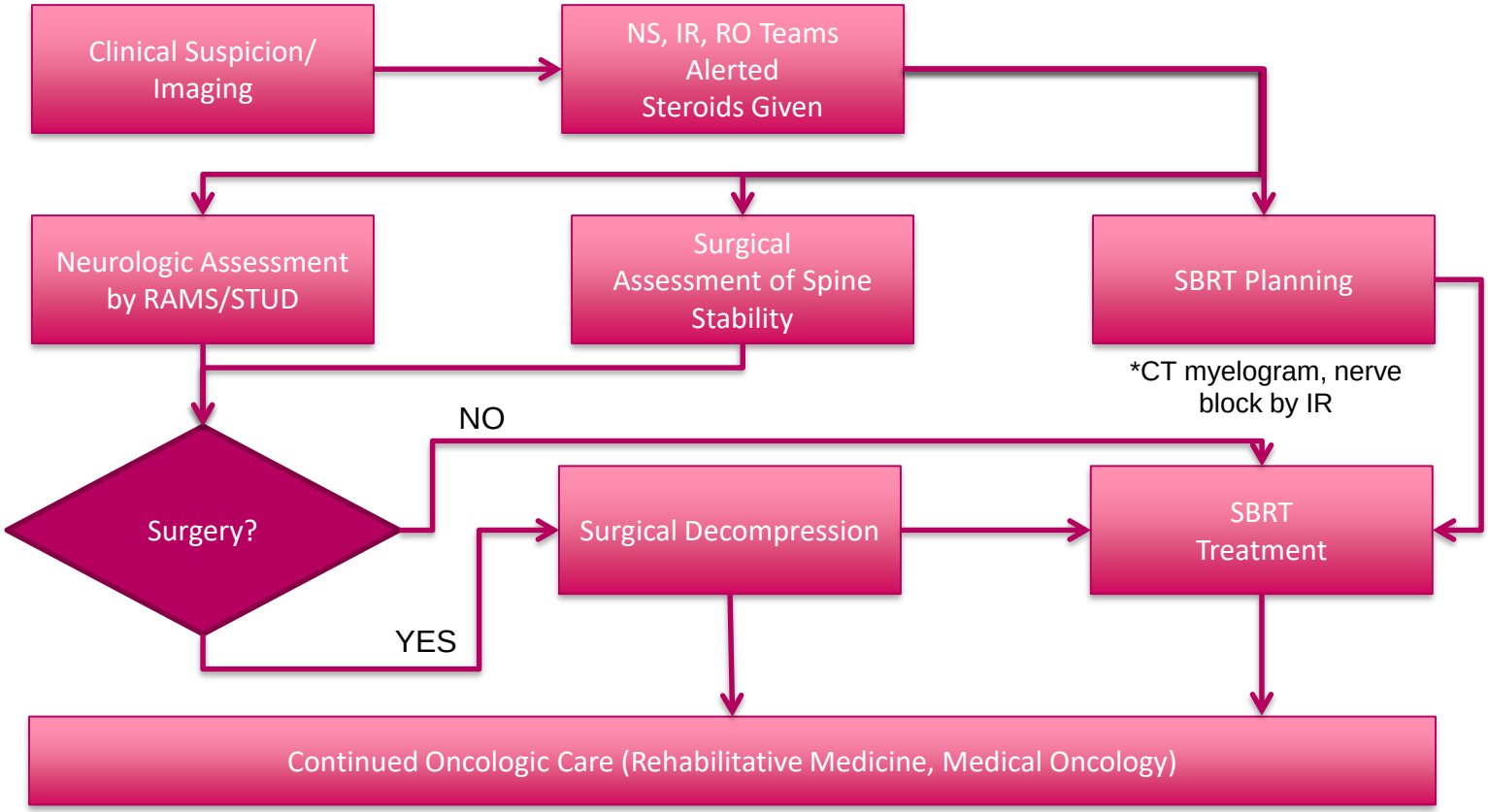
Results

- Radiosurgical decompression can be achieved quickly (~3 weeks) and in greater than 50% of patients
- Rapid improvement in pain and QOL
- Adaptive planning and boost present logistical challenges
  - Position irregularity and registration
  - Planning for uncertainty (flexibility for 2nd fraction)
  - Insurance approval
- Single fraction treatments with highest achievable tumor dose remain a favorable option
- Trend towards dose response above14 Gy

Acute Compression Workflow



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Timelines of Care

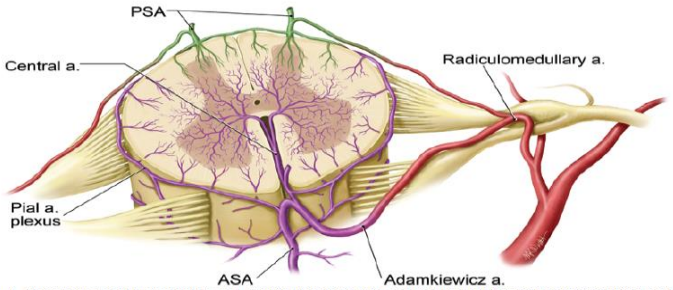

Fig. 1. Vascularization of lumbar spinal cord. Contribution of the ASA and PSA in supplying the blood to the spinal cord. a. = artery/arterial. Used with permission from Nicholas Theodore, M.D.

- Alert NS, NR, RO (immediate)
- Dexamethasone (immediate)
- Surgical/Radiation Evaluation and Imaging Review (1 hour)
- Surgical Decompression if chosen (8 hours)
- Radiation Planning and Treatment (7-10 hours)
  - CT Myelogram (1-2 hours)
  - CT Simulation (1 hour)
  - SBRT Contouring (1-2 hours)
  - SBRT Planning (3-4 hours)
  - Treatment QA and Delivery (1-2 hours)

CONCLUSION

- Conventional EBRT has limited efficacy in patients with spine metastasis
- There seems to be a dose response for SBRT- reason for negative RTOG0631
- SBRT could play a role in epidural disease

Neurologic	Oncologic	Mechanical	Systemic	Decision
Low-grade ESCC + no myelopathy	Radiosensitive	Stable		cEBRT
	Radiosensitive	Unstable		Stabilization followed by cEBRT
	Radioresistant	Stable		SRS
	Radioresistant	Unstable		Stabilization followed by SRS
High-grade ESCC ± myelopathy	Radiosensitive	Stable		cEBRT
	Radiosensitive	Unstable		Stabilization followed by cEBRT
	Radioresistant	Stable	Able to tolerate surgery	Decompression/stabilization followed by SRS
	Radioresistant	Stable	Unable to tolerate surgery	cEBRT
	Radioresistant	Unstable	Able to tolerate surgery	Decompression/stabilization followed by SRS
	Radioresistant	Unstable	Unable to tolerate surgery	Stabilization followed by cEBRT

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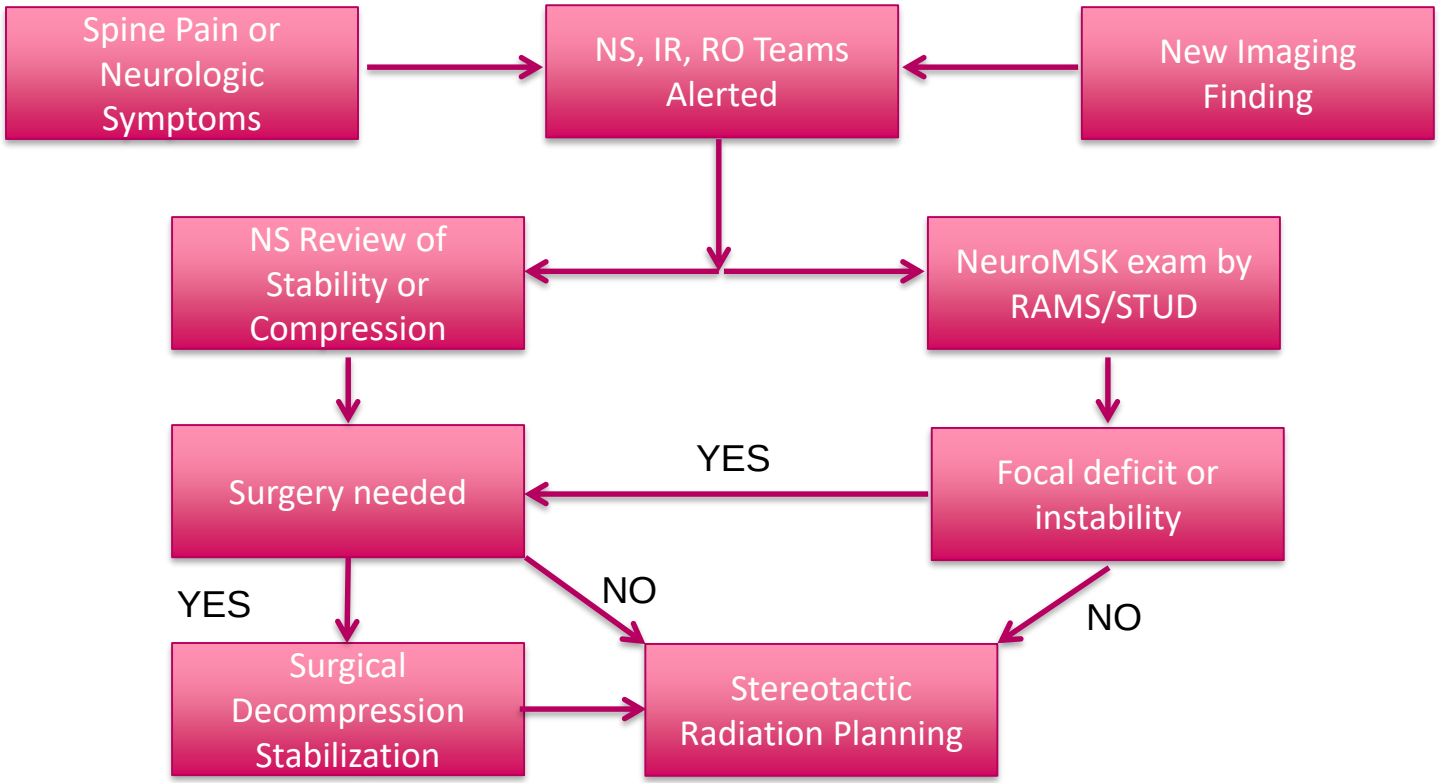
Rapid Assessment of the Malignant Spine (RAMS): A Quality Management Initiative for the Prevention of Cancer-Induced Adverse Spinal Events



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Clinical Team

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- Grigory Syrkin (RHB)
- Rasim Gucalp (MO)
- Hilda Haynes-Lewis
- **Kartik Mani**

Patient Recruitment

- Residents!
- Nurses

Trial Coordinators

- Juhi Purswani
- Alyssa Asaro
- Aviva Berkowitz
- Kwasi Boateng
- Michelle Goggin

Montefiore Medical Center/AECOM

- PRMC
- IRB

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Dose prescription

- RTOG 0631: 16 or 18 Gy
- Cleveland Clinic: 18 Gy
- MSKCC: 24 Gy
- Stanford: 20 Gy
- MDACC: 16-24 Gy
- Sunnybrook: 24 Gy in 2 fractions
- Johns Hopkins: 24 Gy in 2 fractions

$EQD2_{10}$

- 14 x 1 = 28
- 18 x 1 = 42
- 20 x 1 = 50
- 24 x 1 = 68

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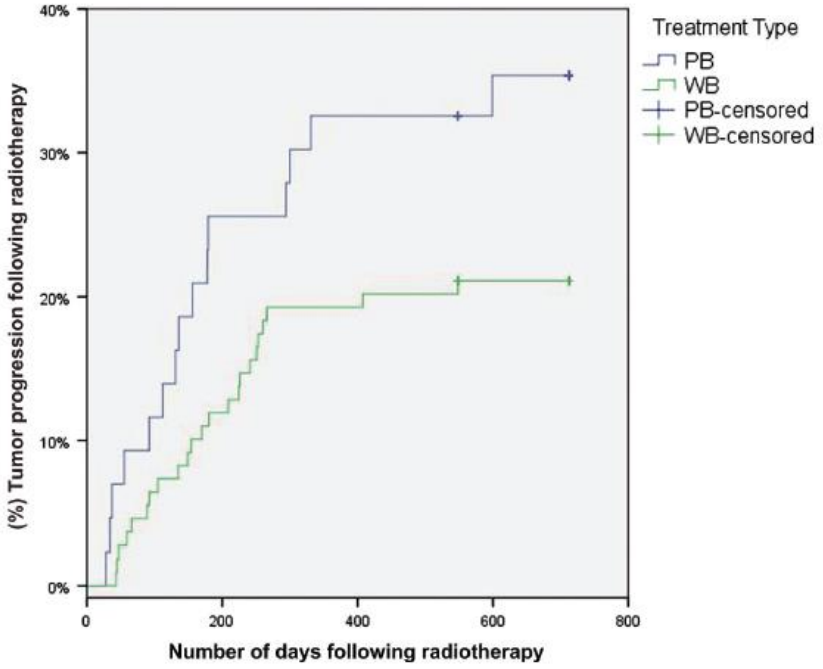
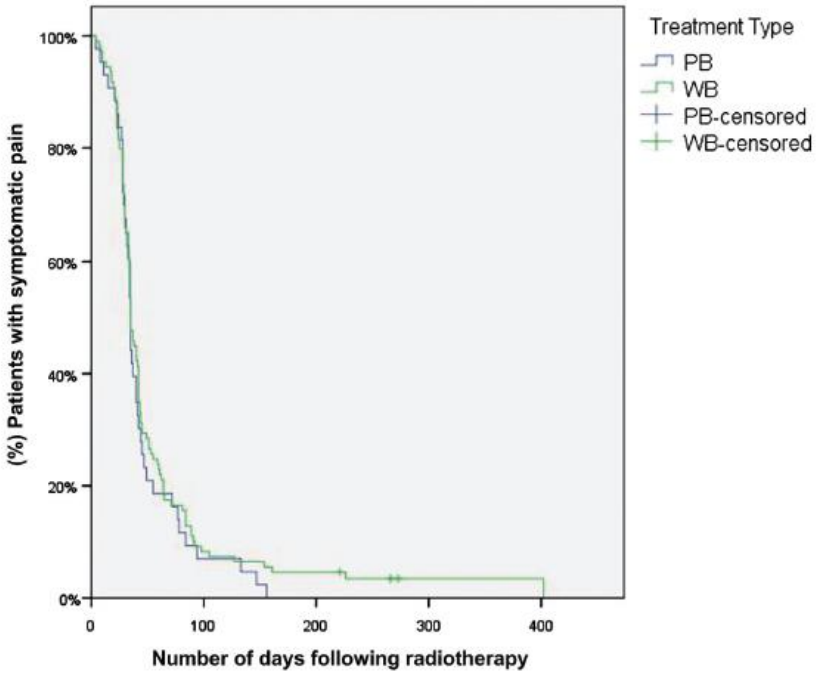
Partial or Whole Vertebra?





Patel et al 2012: U Pitt

Dose or Coverage?

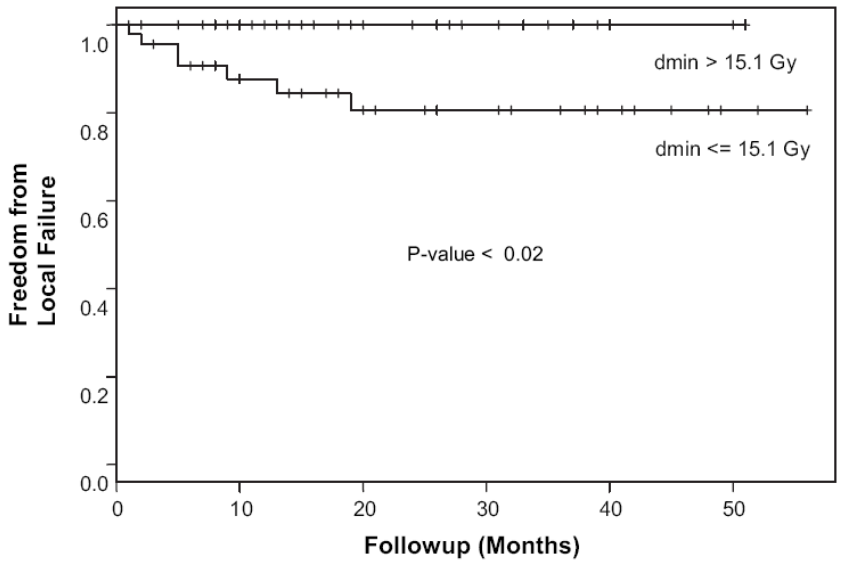


Fig. 3. Kaplan-Meier curves of freedom from local failure for (1) Patients with $D_{min} \leq$ the median D_{min} (15.1 Gy), and (2) Patients with $D_{min} > 15.1$ Gy. The median followup was 17.5 months for patients with $D_{min} < 15.1$ Gy, and 19 months for patients with $D_{min} > 15.1$ Gy.

- Prescription 18-24 Gy
- 1 year LC
  - Dmin > 15 Gy 100%
  - Dmin $\leq$ 15 Gy ~ 80%

Lovelock IJROBP 2010

Minimal coverage and LC

- n=332 at MDACC
- For all patients -1 year LC 88%
- If GTV BED D_{min}-
  - 1 year LC:
    - >33.4 Gy_{10}: 94%
    - <33.4 Gy_{10}: 80%
    - **33.4 Gy_{10} in 1 fraction is: ~14Gy_{10}**

Bishop et al. IJROBP, 2015

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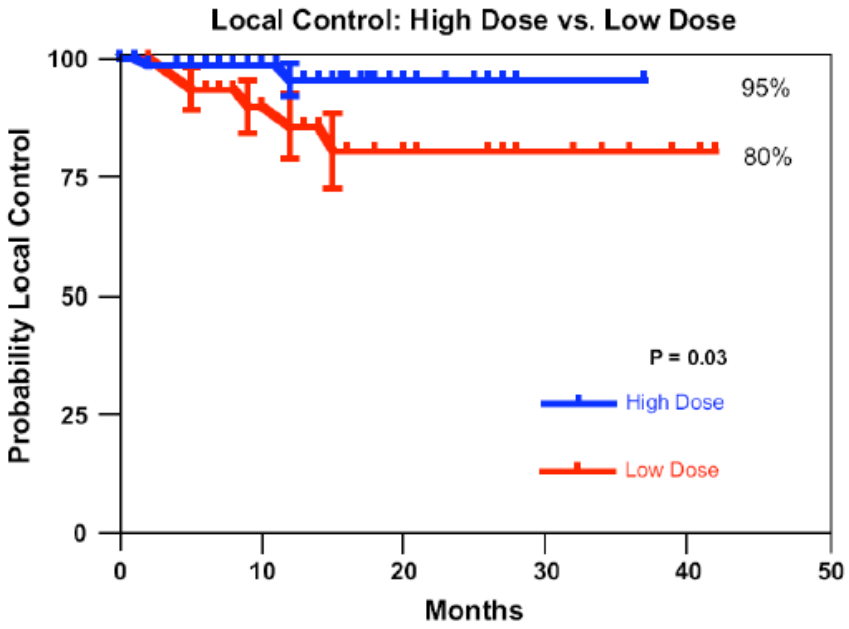
Dose and Local Control

n=103

2003-2006

18–24 Gy x 1



24 Gy

<24 Gy

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

Yamada IJROBP 71, 2008

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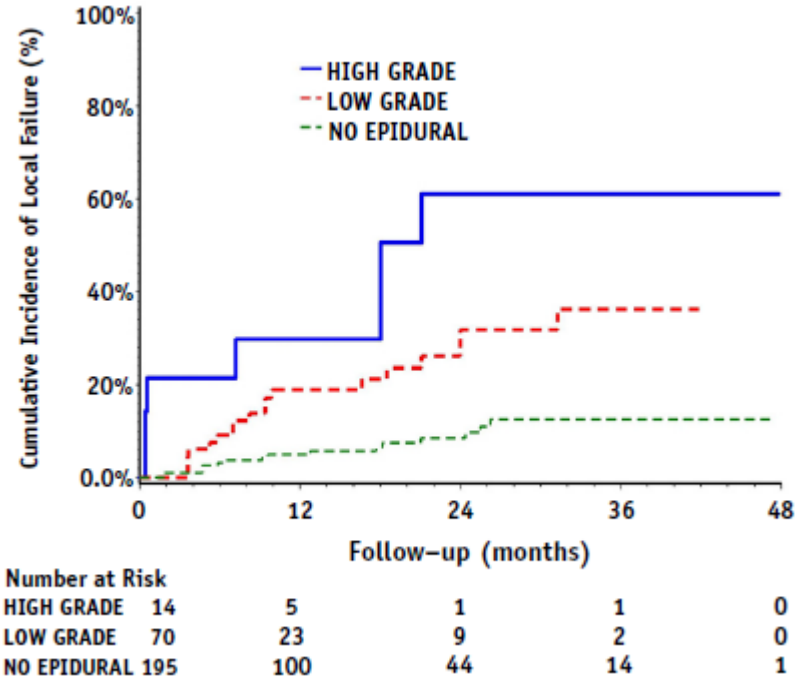
Epidural disease and Local Failure



Tseng et al: IJROBP 2012

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Department of Radiation Oncology
Policies and Procedures
Treatment Planning: SBRT for Spine

- **Dose specifications and Planning Objectives:**
- ***Maximum Dose:*** must be within PTV
- ***Prescription Isodose:*** If Prescription Dose (PD) = 100%, maximum dose must be at least 111% but not more than 167%
- ***Prescription Isodose Surface Coverage:***
- PTV constraints shall be applied to the PTV_Eval if one exists.
- 95% of PTV is conformally covered by the prescription isodose surface (PTV V100% = 95%) and 99% of PTV receives a minimum of 90% of the prescription dose (PTV V90% > 99%).
- ***High Dose Spillage:***
- The cumulative volume of all tissue outside the PTV receiving a dose > 105% of prescription dose should be no more than 15% of the PTV volume. Conformality of PTV coverage will be judged such that the ratio of the volume of the prescription isodose to the volume of the PTV is ideally < 1.2 (refer to Appendix III). These criteria will not be required to be met in treating very small tumors (< 2.5 cm axial GTV dimension or < 1.5 cm craniocaudal GTV dimension) in which the required minimum field size of 3.5 cm results in the inability to meet a conformality ratio of 1.2.
-
- ***Intermediate Dose Spillage:***
- The falloff gradient beyond the PTV extending into normal tissue structures must be rapid in all directions and meet the following criteria:
- Location: The maximum total dose over all fractions in Gray (Gy) to any point 2 cm or greater away from the PTV in any direction must be no greater than D2CM where D2CM is given by Appendix III Table.
- Volume: The ratio of the volume of 50% of the prescription dose isodose to the volume of the PTV must be no greater than R50% where R50% is given in Appendix III Table.

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Montefiore Medical Center
Department of Radiation Oncology
Policies and Procedures
Treatment Planning: SBRT for Spine

(11/1/12) Table 1: Conformality of Prescribed Dose for Calculations Based on Deposition of Photon Beam Energy in Heterogeneous Tissue

PTV Volume (cc)	Ratio of Prescription Isodose Volume to the PTV Volume		Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50\%}$		Maximum Dose (in % of dose prescribed) @ 2 cm from PTV in Any Direction, D_{2cm} (%)		Percent of Lung Receiving 20 Gy Total or More, V_{20} (%)	
	Deviation		Deviation		Deviation		Deviation	
	None	Minor	None	Minor	None	Minor	None	Minor
1.8	<1.2	<1.5	<5.9	<7.5	<50.0	<57.0	<10	<15
3.8	<1.2	.<1.5	<5.5	<6.5	<50.0	<57.0	<10	<15
7.4	<1.2	<1.5	<5.1	<6.0	<50.0	<58.0	<10	<15
13.2	<1.2	<1.5	<4.7	<5.8	<50.0	<58.0	<10	<15
22.0	<1.2	<1.5	<4.5	<5.5	<54.0	<63.0	<10	<15
34.0	<1.2	<1.5	<4.3	<5.3	<58.0	<68.0	<10	<15
50.0	<1.2	<1.5	<4.0	<5.0	<62.0	<77.0	<10	<15
70.0	<1.2	<1.5	<3.5	<4.8	<66.0	<86.0	<10	<15
95.0	<1.2	<1.5	<3.3	<4.4	<70.0	<89.0	<10	<15
126.0	<1.2	<1.5	<3.1	<4.0	<73.0	<91.0	<10	<15
163.0	<1.2	<1.5	<2.9	<3.7	<77.0	<94.0	<10	<15

Note 1: For values of PTV dimension or volume not specified, linear interpolation between table entries is required.
Note 2: Protocol deviations greater than listed here as “minor” will be classified as “major” for protocol compliance (see Section 6.7).

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Policies and Procedures
Treatment Planning: SBRT for Spine

Serial tissue	Max critical volume above threshold (cc)	Threshold dose (Gy)
Cauda Equina	<0.03	16
	<5	14
Thecal Sac	<0.03	14
	<0.35	10
True Cord	<0.03	12
Brachial Plexus	<0.03	17.5
	<3	14
Colon	<0.03	18.4
	<20	14.3
Duodenum	<0.03	12.4
	<5	11.2
	<10	9
Esophagus	<0.03	15.4
	<5	11.9
Great vessels	<0.03	37
	<10	31
Heart/pericardium	<0.03	22
	<15	16
Jejunum/ileum	<0.03	15.4
	<5	11.9
Larynx / Trachea & Large Bronchus	<0.03	20.2
	<4	10.5
Rectum	<0.03	18.4
	<20	14.3
Sacral Plexus	<0.03	16
	<5	14.4
Skin	<0.03	26
	<10	23
Stomach	<0.03	12.4
	<10	11.2
Parallel tissue	Minimum critical volume below threshold (cc)	Threshold dose (Gy)
Kidney (Total)	>200	8.4
Liver	>700	9.1
Lung (Total)	>1500	7
	>1000	7.4

Serial tissue	Max critical volume above threshold (cc)	Threshold dose (Gy)
Cauda Equina	<0.03	24
	<5	21.9
Thecal Sac	<0.03	21.9
	<0.35	18
True Cord	<0.03	15.9
Brachial Plexus	<0.03	24
	<3	20.4
Colon	<0.03	28.2
	<20	24
Duodenum	<0.03	22.2
	<5	16.5
	<10	11.4
Esophagus	<0.03	25.2
	<5	17.7
Great vessels	<0.03	45
	<10	39
Heart/pericardium	<0.03	30
	<15	24
Jejunum/ileum	<0.03	25.2
	<5	17.7
Larynx / Trachea & Large Bronchus	<0.03	30
	<4	15
Rectum	<0.03	28.2
	<20	24
Sacral Plexus	<0.03	24
	<5	22.5
Skin	<0.03	33
	<10	30
Stomach	<0.03	22.2
	<10	16.5
Parallel tissue	Minimum critical volume below threshold (cc)	Threshold dose (Gy)
Kidney (Total)	>200	16
Liver	>700	19.2
Lung (Total)	>1500	11.6
	>1000	12.4

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Spinal cord constraints

	1 fraction Pmax limit (Gy)	2 fractions Pmax limit (Gy)	3 fractions Pmax limit (Gy)	4 fraction Pmax limit (Gy)	5 fraction Pmax limit (Gy)
1% Probability	9.2	12.5	14.8	16.7	18.2
2% Probability	10.6	14.6	17.4	19.6	21.5
3% Probability	11.5	15.7	18.7	21.2	23.2
4% Probability	12.0	16.4	19.6	22.2	24.4
5% Probability	12.4	17.0	20.3	23.0	25.3

Sahgal et al. IJROBP 2013

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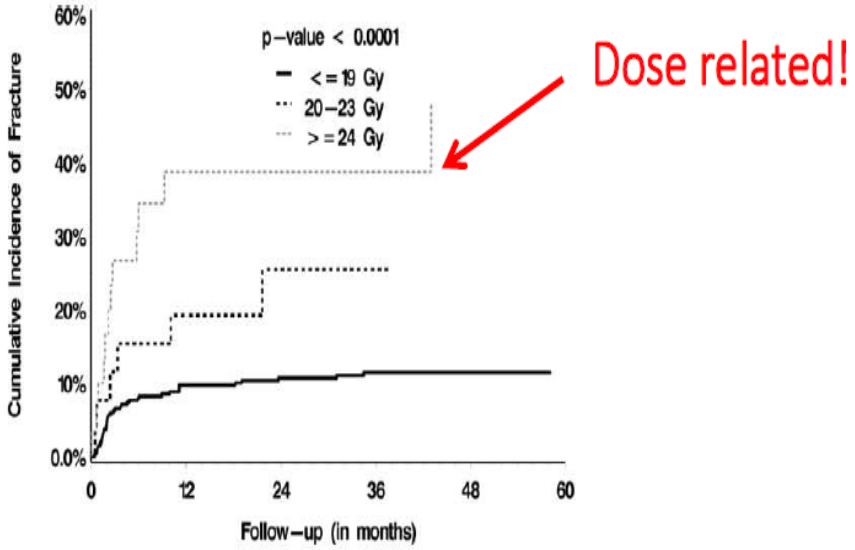
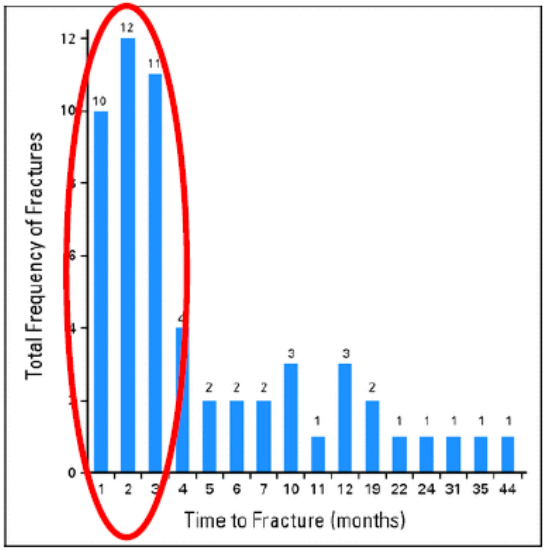
Caution: Vertebral Fracture and Spine SBRT

- Fracture risk ~ 15-40%
- CT appearance, lesion location, and percent vertebral body involvement independently predicted fracture progression.
- Lesions located between T10 and the sacrum were 4.6 times more likely to fracture than were lesions above T10 (95% CI, 1.1–19.7).
- Lytic lesions were 6.8 times more likely to fracture than were sclerotic and mixed lesions.
- As percent vertebral body involvement increased (40% or greater), so did the odds of fracture.
- Fracture yields significantly poorer clinical outcomes.
- Prophylactic or elective vertebroplasty should be considered

Vertebral Fracture





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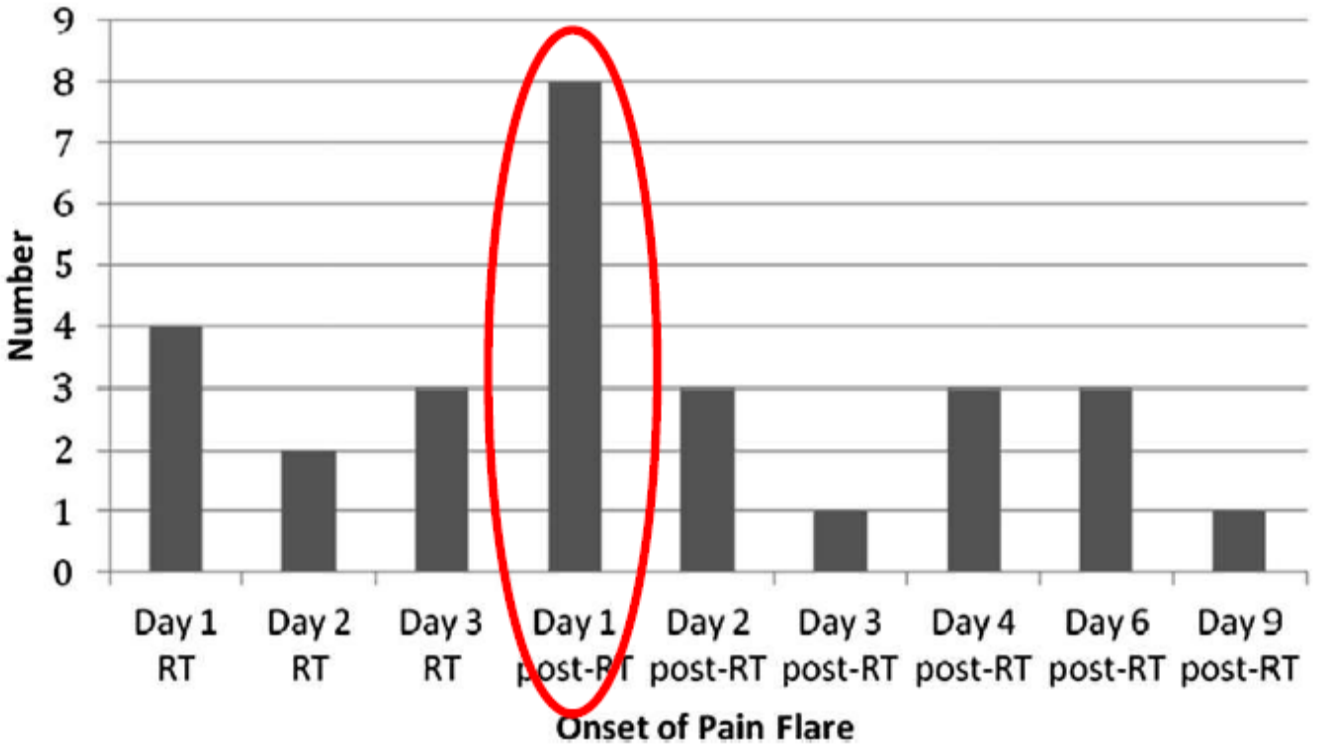
Acute Pain Flare



Chiang et al. IJROBP 2013

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What is the symptom?

- Pain
  - Local: Periosteal stretching
  - Radicular: nerve root compression
  - Axial: vertebral fracture and/or instability

- Neurologic compromise
  - Sensory
  - Motor

Technical Considerations

- RTOG 0631, a prospective randomized phase III trial pain relief with single dose 8 Gy versus 16 Gy SBRT. **>3mm distance criteria between tumor and thecal sac**

- Pattern-of-failure analysis with spine SBRT showed that **47% of the recurrences occurred in the epidural space adjacent to the spinal cord**, likely due in part to tumor underdosing in the region due to spinal cord constraints which had been set to a dose of 9–10 Gy. (Chang et al)

Dosimetric and Technical Considerations in Spine SBRT

- 0% (0/114) risk of collateral radiation-induced **myelitis when the dose to the spine was** 10 Gy in a single fraction (Macbeth et al)
- A myelopathy risk of ≤5% was observed when limiting the thecal sac **Pmax volume dose to 12.4 Gy in a single fraction**. (Sahgal et al)
- Single dose of **10 Gy to 10% of the cord segment** that is adjacent to a targeted tumor plus 6 mm above and below this segment, with a risk of radiation-induced myelopathy of <0.5%. (Ryu et al)
- An analysis of **set-up inaccuracies during spine irradiation** has documented translational errors of up to 1 mm with a vector of 1.8 ± 1.0 mm and rotational errors of up to 1.6 ± 1.3◦ which may yield up to 18% errors in D(95). (Kim et al)

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Spinal Cord Compression

- An oncologic emergency that requires true multidisciplinary coordination and management
- Clinical workflow can be disrupted by many factors
- Many avenues for systemic improvement
- Can be prevented with appropriate coordination

Spinal Cord Vasculature

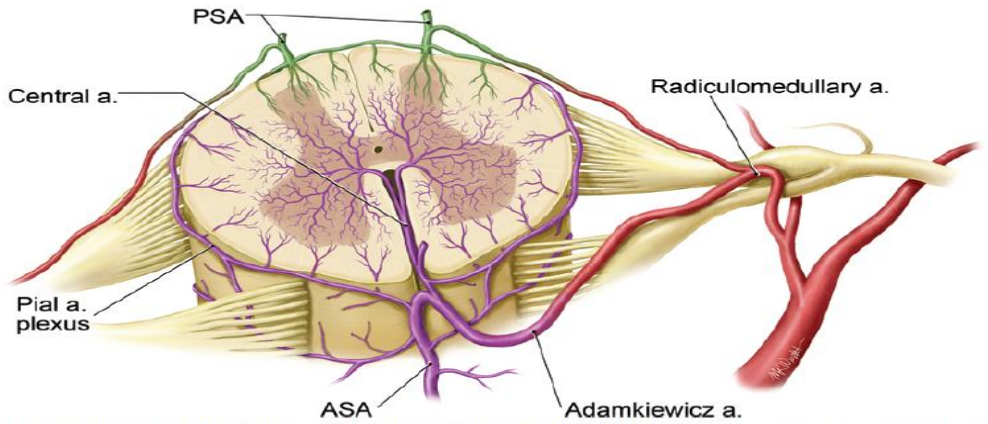

FIG. 1. Vascularization of lumbar spinal cord. Contribution of the ASA and PSA in supplying the blood to the spinal cord. a. = artery/arterial. Used with permission from Nicholas Theodore, M.D.

- Lack of collateral circulation
- Venous occlusion results in reversible edema
- Arterial occlusion causes cord ischemia, then frank infarction

Martirosyan, N.L., et al., Blood supply and vascular reactivity of the spinal cord under normal and pathological conditions. J Neurosurg Spine, 2011. 15(3): p. 238-51.

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P. Price, P. J. Hoskin, D. Easton, D. Austin, S. G. Palmer and J. R. Yarnold*

Division of Radiotherapy, The Royal Marsden Hospital, Downs Road, Sutton, Surrey SM 2 5PT, U.K.

(Received 28 November 1985, revision received 19 March 1986, accepted 21 March 1986)

Key words: Bone pain; Bone metastases; Single fraction radiotherapy

Summary

A prospective randomised trial comparing a single fraction of 8 Gy with 30 Gy in 10 daily fractions relief of metastatic bone pain was performed. In 28 months, 288 patients were randomised. Pain was using a questionnaire completed by the patient at home on a daily basis. No difference was foun speed of onset or duration of pain relief between the two treatment regimes, and pain relief was inde of the histology of the primary tumour.

Results

During the 28 months of the trial, 288 patients were entered; 140 were randomised to receive a single fraction of 8 Gy and 148 were randomised to receive 30 Gy in 10 fractions. There were 25 treatment protocol violations, 91% of the patients receiving the fractionation schedule as randomised.

The mean age of the patients receiving a single fraction was 61.4 years (± 12.5 S.D.), and of those receiving multiple fractions was 62 years (± 12.4

Incidence of response in relation to initial pain score.

(a) *Initial pain score: severe*

1 Week

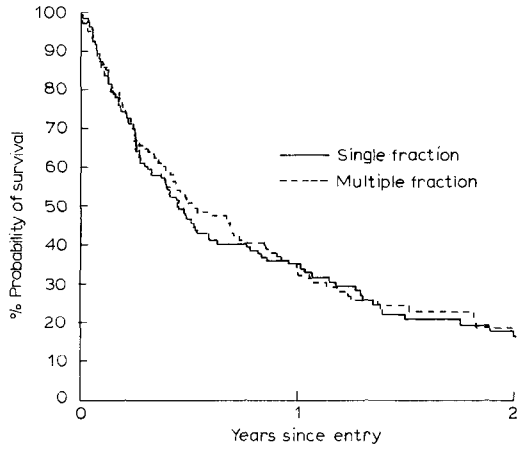
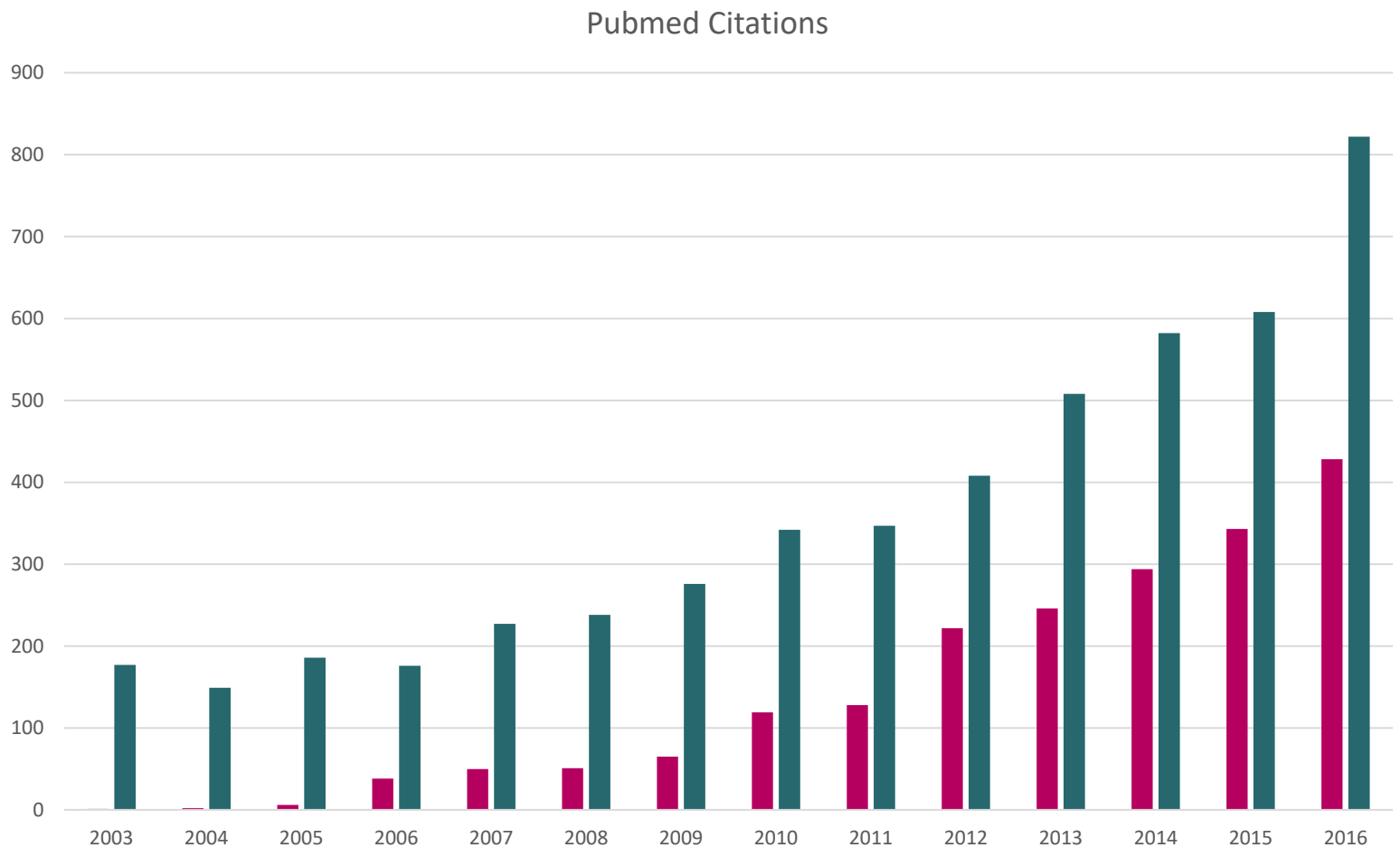


Fig. 1. Survival by treatment allocation

Rising Hypofractionation Interest



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Radiotherapy Simulation

- CT myelogram (CTM) performed in Interventional Radiology
- Vac loc/blue bag immobilization with vacuum seal
- Aquaplast mask for C-spine
- 1.25mm axial slices
- Oral contrast or esophageal paste optional based on location

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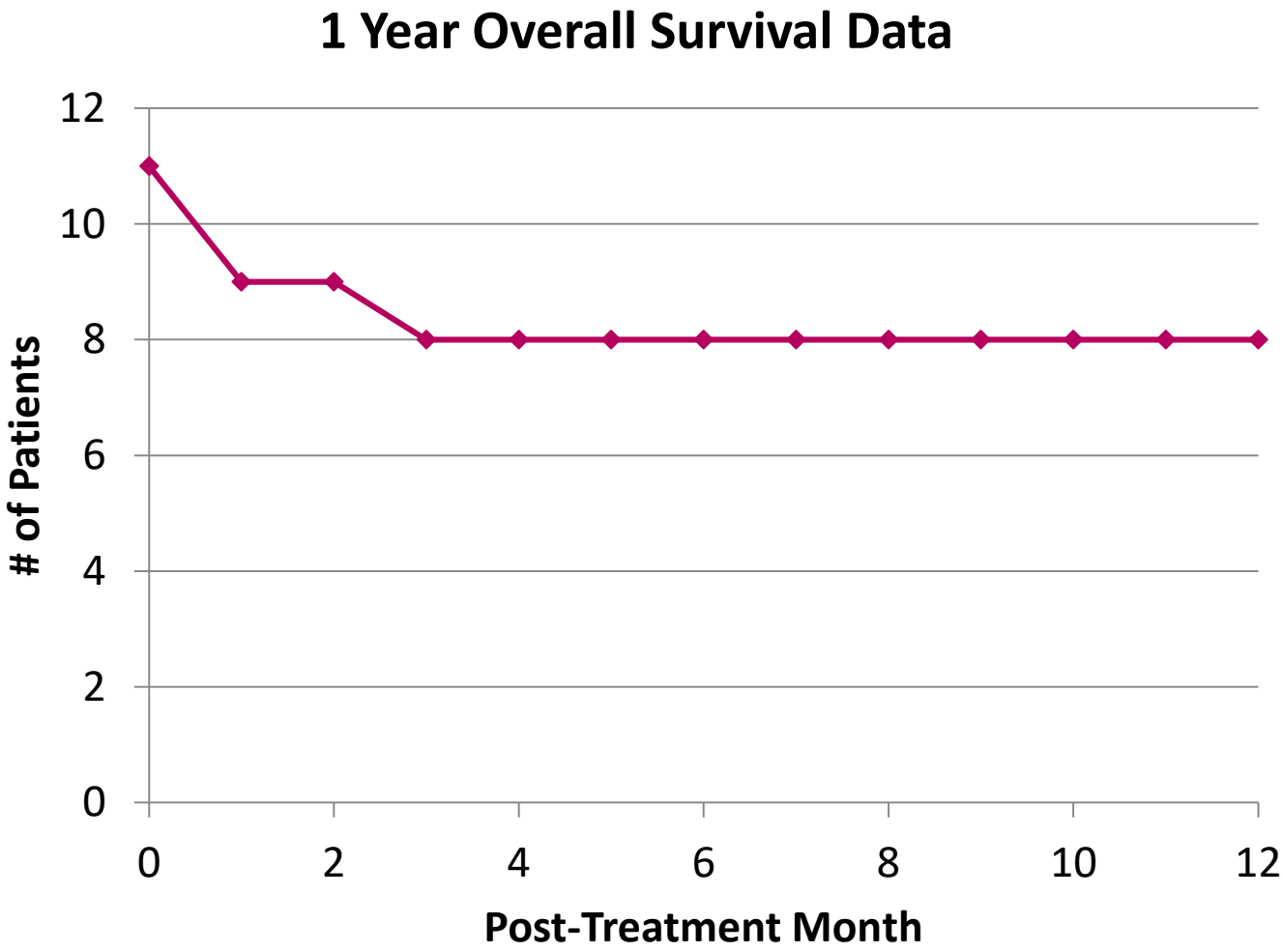

Sample Size = 11: Excluded 6 patients with unknown status, and 7 patients >1 year out from treatment

73% one year OS