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Single Fraction Radiotherapy (SFRT) versus Multi-Fraction Radiotherapy (MFRT) for Palliation of Painful Vertebral Bone Metastases: Equivalent Efficacy, Less Toxicity, More Convenient. A Subset Analysis of RTOG 97-14

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Abstract

Background—RTOG 97-14 revealed no difference between radiation delivered for painful bone metastases at 8Gy/1 fraction (SFRT) and 30Gy/10 fractions (MFRT) in pain relief or narcotic use 3 months post randomization. SFRT for painful vertebral bone metastases (PVBM) has not been well accepted, possibly due to concerns about efficacy and toxicity. The present study evaluates the subset of patients treated specifically for PVBM.

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Methods—PVBM includes cervical, thoracic, and/or lumbar spine regions. Among PVBM, differences in re-treatment rates and in pain relief, narcotic use, and toxicity 3 months post randomization were evaluated.

Results—Of 909 eligible patients, 235 (26%) had PVBM. PVBM and non-PVBM patients differed in percentage of males [55% vs. 47%, p=0.03] and patients with multiple painful sites [57% vs. 38%, p<0.01]. Amongst PVBM, more MFRT patients had multiple sites treated [65% vs. 49%, p=0.02]. There were no statistically significant treatment differences in pain relief [62% vs. 70%, p=0.59] or freedom from narcotic use [24% vs. 27%, p=0.76] at 3 months. Significant differences in acute grade 2-4 toxicity [20% vs. 10%, p=0.01] and acute grade 2-4 GI toxicity [14% vs. 6%, p=0.01] were seen at 3 months, with lower toxicities seen with SFRT. Late toxicity was rare. No myelopathy was recorded. SFRT showed higher 3-year re-treatment rates [5% vs. 15%, p=0.01].

Conclusion—Results for the PVBM subset are comparable to those of the entire population. SFRT had less acute toxicity, and a higher rate of re-treatment than MFRT. SFRT and MFRT resulted in comparable pain relief and narcotic use at 3 months.

INTRODUCTION

Pain secondary to osseous metastases is a serious problem in many patients with Stage IV cancer. There are several options for treatment of painful bone metastases. Radiation therapy is an effective treatment, providing pain relief and reducing need for narcotics and other analgesics for management of symptomatic bone metastases. Many randomized trials have shown that various dose/fractionation schedules of radiation can provide comparable pain relief (1,2,3). Several randomized controlled trials have shown equivalency in endpoints measured, such as pain relief and need for narcotic usage after delivery of a single higher dose of radiation compared with several smaller doses of radiation delivered over ten or more treatments. (1,2,3).

In 2005, Hartsell and others (4) reported on the Radiation Therapy Oncology Group (RTOG) study 97-14, which looked at breast cancer and prostate cancer patients diagnosed with painful osseous metastases with an expected median survival of at least three months. These patients received palliative radiation, randomized to two different fractionation schedules: 8Gy in a single fraction (8Gy/1) versus 30Gy delivered in 10 fractions (30Gy/10). The results of this study showed no substantive differences in the end points of pain relief and narcotic usage 3 months post-randomization. The 8Gy/1 group had a lower incidence of acute toxicities, but higher rates of re-treatment than the 30Gy/10 group. RTOG 97-14 included patients with osseous metastases to a wide range of bones throughout the body, excluding the skull, hands, and feet.

Despite overwhelming evidence that equivalent pain relief from painful bone metastases could be achieved from a single radiation treatment, practice patterns among US radiation oncologists still favor a multifraction course of radiation (5,6,7).

The United States radiation oncology community has not well accepted single fraction conventional radiation (SFRT) for use in treatment of painful vertebral bone metastases,

possibly due to provider concerns about efficacy and toxicity. Radiation oncologists have cited concerns about increased risks of acute GI toxicity such as esophagitis, nausea and vomiting, late CNS toxicity such as myelopathy, and potential higher needs for retreatment as reasons not to use SFRT.

The use of a shorter course of radiation for supportive care in this palliative situation makes it easier for patients and their caregivers to arrange for the logistics of therapy. One or two visits to the treatment facility for planning and treatment saves time and resources for patients, caregivers and health care providers compared to ten or more visits.

The concerns about efficacy and toxicity due to 8Gy/1 versus 30Gy/10 in patients treated specifically for painful vertebral bone metastases prompted a retrospective subset analysis of RTOG 97-14 patients with painful vertebral bone metastases.

METHODS

Patient Population

Patients were randomized to receive 8Gy/1 on one day or 30Gy/10 over two weeks. Patients were treated for no more than three separate painful sites (multiple spine sites allowed). Patients were identified as vertebral metastases patients (PVBM) if any of the treated sites were at the cervical, thoracic, or lumbar spine. Patients with spinal cord compression or Karnofsky Performance Status <40 were excluded from the study.

The Brief Pain Inventory (BPI) worst pain score was used to assess pain response (8). Eligible patients had a baseline BPI worst pain score ≥ 5 or a score of <5 while receiving ≥ 60 mg morphine equivalent daily. Pain response was determined by the BPI worst pain score at the follow-up assessment occurring 3 months after initiation of radiation. Pain response was categorized as the following: 1) complete response, post-treatment pain score of 0; 2) partial response, post-treatment improvement of at least 2 points; 3) stable response, post-treatment pain score within 1 point of the initial pain score, or 4) progressive response, a post-treatment increase of at least 2 points.

The BPI worst pain score does not incorporate narcotic use. Narcotic use was assessed 3 months after the start of radiation using the following criteria: 1) no pain medication; 2) non-narcotic analgesics (aspirin, buffered aspirin, acetaminophen, ibuprofen and others); 3) mild narcotics, ≤ ½ gram; 4), moderate narcotics, ½-1 gram; or 5) strong narcotics, ≥1 gram.

The decision to re-treat patients, as well as the retreatment dose and fractionation, was left to the discretion of the treating radiation oncologist. Retreatment was not permitted within 4 weeks of completion of initial treatment unless a patient experienced progressive pain.

Adverse events occurring before 90 days after the start of treatment were reported according to the Acute Radiation Morbidity Scoring Criteria and adverse events occurring at least 90 days after start of treatment were reported according to the RTOG/EORTC Late Radiation Morbidity Scoring Scheme (9).

Statistical Methods

The chi-square test was used to test for treatment (8Gy/1 vs. 30Gy/10) differences in the distribution of pain response at the 0.05 significance level. The chi-square test was also used to test for treatment differences in the distribution of narcotic use at the 0.05 significance level.

Retreatment rates were estimated using the cumulative incidence method to account for death as a competing risk. Gray's test was used to test for treatment differences in retreatment rates at the 0.05 significance level (two-sided). Overall survival was estimated using the Kaplan-Meier method. The log-rank test was used to test for treatment differences in overall survival at the 0.05 significance level (two-sided). All data were analyzed using SAS (version 9.1 for Windows, SAS institute, Cary, NC).

RESULTS

RTOG 97-14 accrued 949 patients (909 eligible) of which 235 were PVBM. Most patients were treated at the lumbar (51%) or thoracic (36%) spine. Patients were also treated at the cervical spine or received treatment at multiple spine sites. PVBM were similar the general RTOG 97-14 population (Table 1), although there were some differences. PVBM were older, with a median age of 68 years compared to 66 years for non-vertebral bone patients (non-PVBM) ($p<0.01$). PVBM were mostly male, 55% compared to 47% for non-PVBM ($p=0.03$). PVBM were more likely to have been treated at multiple painful sites, 57% compared to 38% for non-PVBM ($p<0.01$).

Amongst PVBM, most pretreatment characteristics did not differ between patients receiving 8Gy/1 or 30Gy/10, as expected due to randomization (Table 2). However, PVBM receiving 30Gy/10 were more likely to have multiple treatment sites, 65% compared to 49% for patients receiving 8Gy/1 ($p=0.02$).

Treatment was appropriately delivered per protocol. A random sample of 71 (30%) patients was selected for quality assurance review. Ninety-three percent of patients were treated within treatment protocol borders, 96% received total protocol dose, 99% received all fractions, and 99% did not have any treatment delays. Patients were treated with 4-9 MV photons (63%), 10-20 MV photons (23%), 60-Cobalt (11%), or other energies (3%). Acute and late adverse events were minimal. For patients receiving 8Gy/1, there were no grade 4 adverse events, one grade 3 acute non-hematologic (lung) adverse event, and two grade 3 late non-hematologic (CNS) adverse events (grade 3 CNS adverse event definition: neurologic findings requiring hospitalization for initial management). For patients receiving 30Gy/10, there was one grade 4 acute hematologic adverse event, one grade 4 late non-hematologic (lung) adverse event, and three grade 3 acute non-hematologic (GI) adverse events. Radiation myelopathy was not seen in any patient. Significant treatment (8Gy/1 vs. 30Gy/10) differences in acute overall grade 2-4 toxicity [10% vs. 20%, $p=0.01$] and acute grade 2-4 GI toxicity [6% vs. 14%, $p=0.01$] at 3 months were seen, with less toxicity in 8Gy/1.

No significant difference between treatment arms was reported in narcotic use or pain response three months following initial radiation (Tables 3-4). Sixty-three percent of patients on each treatment arm reported moderate or strong narcotic use (p=0.76). Seventy percent and sixty-two percent of patients on the 8Gy/1 and 30Gy/10 treatment arms, respectively, experienced a partial or complete pain response (p=0.59).

Patients treated with 8Gy/1 had significantly higher retreatment rates at 3 years following their initial radiation, 15% compared to 5% (p=0.01) with differences evident at 3 months following initial radiation (Table 5). There were no differences amongst cervical, thoracic, or multiple spine site patients; the differences in retreatment in the overall PVBM population are attributable to patients with lumbar spine metastases. Sixty-eight percent (17/25) of retreated patients were lumbar spine patients. There were no treatment differences in overall survival: the median survival was 9.3 months and 10.6 months in the 8Gy/1 and 30Gy/10 treatment arms, respectively (p=0.51). Survival estimates at three and six months were 83% and 62% in the 8Gy/1 arm and 85% and 67% in the 30Gy/10 arm (Table 6).

DISCUSSION

This is the largest series to date comparing single fraction conventional radiation (SFRT) to a multi-fraction course of radiation (MFRT) for patients with painful vertebral bone metastases (PVBM). Radiation delivered by SFRT or MFRT was equally effective at palliating pain from metastases to the vertebral bone. This result is similar to what was seen in the total population of patients with bone metastases in RTOG 97-14 (4). The pain control seen was comparable to a group of 117 Canadian patients treated with radiation for spinal metastases. (14) The largest series of patients treated with radiation for spinal column metastases-603 patients-comes from Japan. (15) While Mizumoto et al. discuss prognostic factors, local control and survival for this population (15), there is little information on pain relief.

SFRT has not yet found overwhelming support in practice in the United States

There may be many reasons for this—among them a reluctance to adapt a new practice after a long experience with MFRT, concerns about risks of acute morbidity as well as concerns about late CNS toxicity. MFRT is also reimbursed at a higher rate in the US than SFRT. (12)

This analysis provides further evidence that SFRT for vertebral bone metastases is safe and effective, **with less acute effects** and **no difference in late effects** compared with MFRT.

Radiation-induced myelopathy (RM) is the radiation oncologist' greatest concern of iatrogenic toxicity of all concerns about the potential morbidity of radiation. The consequences of radiation damage to the spinal cord can be devastating. As a result, radiation oncologists are loath to give a dose anywhere near that which would be associated with a low risk of damage. It could be uncertainty about the effects of 8Gy/1 to the spinal cord that frightens US radiation oncologists away from this technique. Studies from Maranzano et al. using 8Gy/1 and even two 8Gy fractions spaced a week apart (16Gy total) for vertebral bone metastases causing spinal cord compression have not recorded any late cases of radiation induced myelopathy. (10,11). Macbeth et al. (13) reported five cases of

radiation myelopathy out of 1048 patients treated with radiation for inoperable non-small cell lung cancer. There were three cases of RM out of 524 patients treated with 17Gy in two fractions spaced one week apart, and two cases of RM out of 153 patients treated with 39Gy in 13 fractions over 17 days. There were no reports of radiation-induced myelopathy in RTOG 97-14 patients.

There have been **many randomized comparisons** of 1 or 2 fractions of radiation versus 10 or more fractions for palliative therapy of painful bone metastases (1,2,3). Wu's (3) meta-analysis looking at all randomized control trials reported between 1966 and 2000, showed **no difference in response rates** between SFRT and MFRT. There were **differences seen in the rates of re-treatment**, with patients receiving SFRT having rates of retreatment between 11-25% versus patients receiving MFRT with re-treatment rates between 0-12%. The subset of PVBM from RTOG 97-14 also showed similar rates of retreatment in patients receiving 8 Gy/1 (15%) and 30 Gy/10 (5%)

To put the issue of need for retreatment in perspective, let us illustrate the relative difference of the 8Gy/1 and the 30Gy/10 populations' total visits for radiation. Take a hypothetical sample of 200 patients with painful vertebral bone metastases and treat 100 patients with 8Gy in a single fraction and 100 with 30Gy in 10 fractions. Assume that there is an additional visit required to the radiation therapy department in each case for consultation, planning and simulation. The 8Gy/1 group will have made 200 visits to the department; the 30Gy/10 group, 1100 visits. Factor in re-treatments: 15 from the 8Gy/1 group will make 2 additional visits each (30 total), 5 patients from the 30Gy/10 group, who will each make 11 additional visits (55 total). In aggregate, the 8Gy/1 group will have made 230 visits to the radiation department, while the 30Gy/10 group will have made 1155 visits – a five-fold difference in trips to the radiation department. The 30Gy/10 patient makes, on average, nine more visits for treatment than the SFRT patient.

The **retreatment rates were greatest** in those patients with painful vertebral bone metastases involving the lumbar spine. Decisions on retreatment were left to the discretion of the treating physician. The higher lumbar spine retreatment rate might have been influenced by the absence of the spinal cord below L1, which may have impacted on decisions to retreat. Only 23% of patients were treated with photon energies greater than or equal to 10 MV. Higher photon energy allows for a greater depth of penetration for a given dose, which generally portends for a better dose distribution at depth. The lumbar spine extends deeper in the body than the thoracic or cervical spines. In addition, more information may be gleaned by looking at **allowable treatment techniques** under the radiation therapy treatment plan outlined by the treatment protocol. For the cervical spine, either a posterior field (treated to a depth of 5 cm or other depth as determined from a lateral simulation film) or parallel opposed lateral fields with isocenter set at mid-plane were allowed. For the thoracic spine, a single posterior field was to be used for treatment depth set at the middle of the vertebral body. For the lumbar spine, anterior and posterior opposed lateral fields were suggested with equal weighting. However, unequal weighting could be used with a ratio of doses of 1:2 anterior: posterior, with dose prescribed to mid-thickness of the central axis, or at the center of the target volume if unequal weighting was to be used. Alternatively, a third option for the lumbar spine would have been to treat with a single PA

field, with dose prescribed to mid-vertebral body. Treatment volumes were to include the radiographic abnormalities with at least 2 cm margin. Treatment of the entire bone was not required (1).

One might wonder, with the parameters set for treatment, the percentages of patients treated with lower energy photons, and the treatment volume specified; whether the more centrally located lumbar spine lesions would have indeed received a full and homogeneous dose of radiation, as would be desired. Alternately, **there might been some form of bias** on the part of participating physicians to perhaps use a smaller volume or different dose parameters to reduce dose homogeneity in light of concerns about potential toxicities of SFRT. There was nothing in the study design that required the treating physicians to plan the field to be used prior to randomization. Whether there may have been a bias in the size or orientation of the fields planned based on the randomization to SFRT or MFRT is unknown.

Another factor not controlled in the RTOG 97-14 trial was initial pain management techniques and pain control in the time prior to initiation of radiation, and also how pain was managed during the course of treatment and thereafter. Only 1% (3/235) of patients reported baseline narcotic use. Randomized patients who worked with a radiation oncologist or other health care professional who was more cognizant of 1) appropriate narcotic and non-narcotic pharmacologic pain management with frequent pain assessment, 2) application of long acting analgesics, 3) judicious use of short acting medications for breakthrough pain, 4) the appropriate use of co-analgesics and non-narcotic interventions, 5) the use of pain diary monitoring, and other pain management techniques, may have confounded information on pain control by having different techniques applied for the patient's active pharmacologic management.

Can this data be extrapolated to patients with **other histologies**? The RTOG 97-14 study enrolled only patients with breast and prostate cancer histologies. However, in the absence of any contrary data, it would seem that the results of this study could be extrapolated to patients with vertebral bone metastases of other histologies (10,11).

Can this data be extrapolated to patients who have had **other local interventions** such as vertebroplasty, kyphoplasty, corpectomy or other form of stabilization procedure? The answer is unknown at present.

What is clear is that both regimens studied are safe and effective for palliation of painful vertebral bone metastases. No late grade IV CNS toxicity was seen in either group. There were no reports of radiation myelopathy in RTOG 97-14 patients. GI toxicity was less in the 8Gy/1 group. 10% (1 in 10) more patients in the 8Gy/1 group underwent retreatment than in the 30Gy/10 group. The 30Gy/10 group required nine more visits, on average, in the hypothetical population sample described above, allowing for retreatment rates appropriate to each group, than the 8Gy/1 group. Howell et al. (12) reported a cost analysis for Medicare Region 1 allowable reimbursement for seven different schemas for treatment of bone metastases which showed a nearly tenfold difference in Medicare reimbursement depending on the technology used for treatment, the setting for treatment delivery, and the number of fractions utilized.

On a humanitarian note, the use of SFRT in this clinical setting saves the patient and their caregivers from having to make an additional nine visits to the radiation oncology facility. It saves direct and indirect costs of additional time off of work, transportation, lodging, childcare and other costs. The use of SFRT also saves time for healthcare providers and radiation therapists, as well as reduces linear accelerator usage.

Based on the results of RTOG 97-14, single fraction conventional radiation (SFRT) is safe and effective for the treatment of ***vertebral bone*** **metastases.**

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Table 1

Pretreatment Characteristics All RTOG 9714 Eligible Patients

Characteristics	Non -Vertebral Patients (n= 674)		Vertebral Patients (n=235)		p-value*
Age					
Median (years)	66		68		<0.01
Range	31-92		33-92		
	n	%	n	%	
Treatment Arm					
8 GY	336	50	124	53	0.45
30 GY	338	50	111	47	
Gender					
Male	318	47	130	55	0.03
Female	356	53	105	45	
Race/Ethnicity					
White	488	72	166	71	0.27
Black	101	15	41	17	
Hispanic	34	5	6	3	
Other	51	8	22	9	
KPS					
40 – 60	159	23	56	24	0.65
70 – 80	355	53	134	57	
90 – 100	160	24	45	19	
Receiving bisphosphonates					
Yes	170	25	51	22	0.28
No	504	75	184	78	
Painful sites					
Solitary	415	62	102	43	<0.01
Multiple	259	38	133	57	
BPI Worst Pain Score, Baseline					
<5	15	2	3	1	0.39

Characteristics	Non -Vertebral Patients (n= 674)		Vertebral Patients (n=235)		p-value*
5 – 6	194	29	60	26	
7 – 10	465	69	172	73	

*Chi-square test, except for age (t-test)

Table 2

Pretreatment Characteristics All Vertebral Metastases Patients

Characteristics	8 GY (n= 124)		30 GY (n=111)		p-value*
Age					
Median (years)	69		68		0.85
Range	36 -92		33-91		
	n	%	n	%	
Gender					
Male	68	55	61	55	0.96
Female	55	45	50	45	
Race/Ethnicity					
White	86	69	80	72	0.35
Black	26	21	15	13	
Hispanic	2	2	4	4	
Other	10	8	12	11	
KPS					
40 – 60	29	23	27	24	0.80
70 – 80	73	59	61	55	
90 – 100	22	18	23	21	
Receiving bisphosphonates					
Yes	23	19	28	25	0.22
No	101	81	83	75	
Painful sites					
(Vertebral & Non Vertebral)					
Solitary	63	51	39	35	0.02
Multiple	61	49	72	65	
Treatment site					
Weight bearing	48	39	36	32	0.32
Non-weight bearing	76	61	75	68	
Vertebral site					

Characteristics	8 GY (n= 124)		30 GY (n=111)		p-value*
Cervical	12	10	7	6	0.78
Thoracic	44	35	40	36	
Lumbar	63	51	58	53	
Multiple sites	5	4	6	5	
BPI Worst Pain Score, Baseline					
<5	2	2	1	1	0.68
5 – 6	34	27	26	23	
7 – 10	88	71	84	76	

*Chi-square test, except for age (t-test)

Table 3

Narcotic Use, 3 months from start of RT

	8 GY		30 GY		p-value*
All Vertebral Patients	(n=84)		(n=89)		
	n	%	n	%	
None	17	20	15	17	0.76
Analgesics	6	7	6	7	
Mild Narcotic	8	10	12	13	
Moderate Narcotic	21	25	17	19	
Strong Narcotic	32	38	39	44	
Cervical Spine Patients	(n=9)		(n=5)		
	n	%	n	%	
None	2	22	1	20	0.86
Analgesics	1	11	0	0	
Moderate Narcotic	1	11	1	20	
Strong Narcotic	5	56	3	60	
Thoracic Spine Patients	(n=28)		(n=33)		
	n	%	n	%	
None	7	25	8	24	0.97
Analgesics	4	14	3	9	
Mild Narcotic	3	11	3	9	
Moderate Narcotic	4	14	5	15	
Strong Narcotic	10	36	14	42	
Lumbar Spine Patients	(n=42)		(n=47)		
	n	%	n	%	
None	5	12	5	11	0.13
Analgesics	1	2	3	6	
Mild Narcotic	3	7	9	19	
Moderate Narcotic	16	38	8	17	

	8 GY		30 GY		p-value*
Strong Narcotic	17	41	22	47	
Multiple Spine Site Patients	(n=5)		(n=4)		
	n	%	n	%	
None	3	60	1	25	0.08
Mild Narcotic	2	40	0	0	
Moderate Narcotic	0	0	3	75	

Mild narcotic, ≤ ½ gr. Moderate narcotic, ½-1 gr. Strong narcotic, ≥1 gr.

*Chi-square test (Fisher's Exact test for Multiple Spine Patients).

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Table 4

Pain Response, 3 months from start of RT

	8 GY		30 GY		p-value*
All Vertebral Patients	(n=77)		(n=76)		
	n	%	n	%	
Complete	15	19	13	17	0.59
Partial	39	51	34	45	
Stable	14	18	21	28	
Progressive	9	12	8	10	
Cervical Spine Patients	(n=10)		(n=5)		
	n	%	n	%	
Complete	1	10	0	0	0.42
Partial	5	50	1	20	
Stable	2	20	3	60	
Progressive	2	20	1	20	
Thoracic Spine Patients	(n=26)		(n=25)		
	n	%	n	%	
Complete	6	23	5	20	0.75
Partial	14	54	13	52	
Stable	5	19	4	16	
Progressive	1	4	3	12	
Lumbar Spine Patients	(n=38)		(n=44)		
	n	%	n	%	
Complete	6	16	7	16	0.45
Partial	20	52	20	45	
Stable	6	16	13	30	
Progressive	6	16	4	9	
Multiple Spine Site Patients	(n=3)		(n=2)		
	n	%	n	%	

	8 GY		30 GY		p-value*
Complete	2	67	1	50	--
Stable	1	33	1	50	

Pain response based on Brief Pain Inventory (BPI) Worst Pain Score.

Complete response, post-RT pain score of 0.

Partial response, post-RT pain score decrease ≥ 2 points from baseline score.

Stable response, post-RT pain score within 1 point of baseline score.

Progressive response, post-RT pain score increase ≥ 2 points from baseline score.

*Chi-square test

Table 5

Retreatment Rates

		8 Gy		30 Gy	
		% Retreated*	At Risk	% Retreated*	At Risk
All Vertebral Patients					
Time to Retreatment (Months)					
3		10	94	2	93
6		10	68	2	74
12		15	40	3	53
36		15	15	5	16
60		15	4	5	7
	Failures/Total	19/124		6/111	
	p-value (Grey's Test)	0.01			
Cervical Spine Patients					
Time to Retreatment (Months)					
3		25	9	0	5
6		25	8	0	2
12		25	4	0	2
36		25	2	0	0
60		25	1	0	0
	Failures/Total	3/12		0/7	
	p-value (Grey's Test)	0.16			
Thoracic Spine Patients					
Time to Retreatment (Months)					
3		0	35	0	33
6		0	22	0	27
12		2	16	0	17
36		5	6	3	2
60		5	2	5	1
	Failures/Total	2/44		2/40	
	p-value (Grey's Test)	0.94			

		8 Gy		30 Gy	
		% Retreated*	At Risk	% Retreated*	At Risk
Lumbar Spine Patients					
Time to Retreatment (Months)					
3		14	45	3	49
6		14	33	3	39
12		21	18	5	30
36		21	5	7	12
60		21	1	7	4
	Failures/Total	13/63		4/58	
	p-value (Grey's Test)	0.03			
Multiple Spine Site Patients					
Time to Retreatment (Months)					
3		0	5	0	6
6		0	5	0	6
12		20	2	0	4
36		20	2	0	2
60		20	0	0	2
	Failures/Total	1/5		0/6	
	p-value (Grey's Test)	0.27			

*Estimates based on cumulative incidence, death considered competing risk.

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Table 6

Overall Survival

		8 Gy		30 Gy	
		% Alive*	At Risk	% Alive*	At Risk
All Vertebral Patients					
Time (Months)					
3		83	103	85	94
6		62	77	67	74
12		40	50	49	54
24		26	32	26	29
60		5	5	8	8
	Failures/Total	116/124		102/111	
	Median Survival (months)	9.3		10.6	
	p-value (Log-Rank Test)	0.50			
Cervical Spine Patients					
Time (Months)					
3		92	11	71	5
6		83	10	29	2
12		33	4	29	2
24		17	2	0	0
60		8	1	0	0
	Failures/Total	11/12		7/7	
	Median Survival (months)	9.1		4.5	
	p-value (Log-Rank Test)	0.11			
Thoracic Spine Patients					
Time (Months)					
3		80	35	83	33
6		50	22	68	27
12		36	16	43	17
24		27	12	25	10
60		5	2	3	1

		8 Gy		30 Gy	
		% Alive*	At Risk	% Alive*	At Risk
	Failures/Total	42/44		39/40	
	Median Survival (months)	6.0		8.3	
	p-value (Log-Rank Test)		0.89		
Lumbar Spine Patients					
Time (Months)					
3		83	52	86	50
6		63	40	67	39
12		43	27	53	31
24		24	15	29	17
60		5	2	10	5
	Failures/Total	58/63		52/58	
	Median Survival (months)	10.3		12.4	
	p-value (Log-Rank Test)		0.29		
Multiple Spine Site Patie	nts				
Time (Months)					
3		100	5	100	6
6		100	5	100	6
12		60	3	67	4
24		60	3	33	2
60		0	0	33	2
	Failures/Total	5/5		4/6	
	Median Survival (months)	26.6		17.3	
	p-value (Log-Rank Test)		0.46		

*Kaplan-Meier Estimates