Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Supplemental Table 1. Zubrod Performance Status for Patients who Completed NRPS vs. Those Who Did Not

	Did Not Complete NRPS	Completed NRPS	Chi-Square p-value
Baseline & 1 month	(n=93)	(n=246)	0.047
0	16 (17.2%)	69 (28.0%)	
1	55 (59.1%)	140 (56.9%)	
2	22 (23.7%)	37 (15.0%)	
Baseline & 3 months	(n=125)	(n=214)	0.001
0	19 (15.2%)	66 (30.8%)	
1	76 (60.8%)	119 (55.6%)	
2	30 (24.0%)	29 (13.6%)	
Baseline & 6 months	(n=232)	(n=107)	0.005
0	49 (21.1%)	36 (33.6%)	
1	134 (57.8%)	61 (57.0%)	
2	49 (21.1%)	10 (9.3%)	
Baseline & 12 months	(n=242)	(n=97)	<0.001
0	45 (18.6%)	40 (41.2%)	
1	150 (62.0%)	45 (46.4%)	
2	47 (19.4%)	12 (12.4%)	
Baseline & 24 months			0.007
0	65 (22.3%)	20 (42.6%)	
1	172 (58.9%)	23 (48.9%)	
2	55 (18.8%)	4 (8.5%)	

Other baseline characteristics compared with significant differences noted: age, baseline NRPS score (p=0.03 at 3 months, p=0.04 at 12 months), gender, race, ethnicity, number of spine metastases, location of largest spine metastasis, use of pain medication (p=0.005 at 12 months), type of tumor (p=0.04 at 3 months), and intended SBRT single fraction dose.

Supplemental Table 2. NRPS Patient Compliance

	SRS (n=217)	cEBRT (n=136)
Baseline		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	209 (96.3%)	130 (95.6%)
Month 1		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	153 (70.5%)	93 (68.4%)
Consent withdrawal	3 (1.4%)	9 (6.6%)
Refused due to illness	8 (3.7%)	4 (2.9%)
Unable to contact	6 (2.8%)	7 (5.1%)
Institutional error	6 (2.8%)	2 (1.5%)
Patient refused for other reason	11 (5.1%)	7 (5.1%)
Unknown	3 (1.4%)	2 (1.5%)
Out of time point	19 (8.8%)	6 (4.4%)
Month 3		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	138 (63.6%)	76 (55.9%)
Deceased	17 (7.8%)	12 (8.8%)
Consent withdrawal	6 (2.8%)	13 (9.6%)
Refused due to illness	6 (2.8%)	3 (2.2%)
Unable to contact	11 (5.1%)	3 (2.2%)
Institutional error	4 (1.8%)	4 (2.9%)
Patient refused for other reason	21 (9.7%)	14 (10.3%)
Unknown	4 (1.8%)	1 (0.7%)
Out of time point	2 (0.9%)	4 (2.9%)
Month 6		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	68 (31.3%)	39 (28.7%)
Deceased	53 (24.4%)	28 (20.6%)
Consent withdrawal	8 (3.7%)	15 (11.0%)
Refused due to illness	4 (1.8%)	1 (0.7%)
Unable to contact	9 (4.1%)	7 (5.1%)
Institutional error	7 (3.2%)	6 (4.4%)
Patient refused for other reason	27 (12.4%)	14 (10.3%)
Unknown	5 (2.3%)	5 (3.7%)
Not Received	0 (0.0%)	1 (0.7%)
Out of time point	28 (12.9%)	14 (10.3%)
Month 12		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	59 (27.2%)	38 (27.9%)
Deceased	88 (40.6%)	43 (31.6%)
Consent withdrawal	10 (4.6%)	15 (11.0%)
Refused due to illness	3 (1.4%)	2 (1.5%)

Supplemental Table 2. NRPS Patient Compliance

	SRS (n=217)	cEBRT (n=136)
Unable to contact	15 (6.9%)	6 (4.4%)
Institutional error	8 (3.7%)	3 (2.2%)
Patient refused for other reason	18 (8.3%)	14 (10.3%)
Unknown	3 (1.4%)	2 (1.5%)
Not Received	0 (0.0%)	2 (1.5%)
Out of time point	5 (2.3%)	5 (3.7%)
Month 24		
Clinically ineligible	8 (3.7%)	6 (4.4%)
Complete	31 (14.3%)	16 (11.8%)
Deceased	118 (54.4%)	59 (43.4%)
Consent withdrawal	11 (5.1%)	15 (11.0%)
Refused due to illness	2 (0.9%)	3 (2.2%)
Unable to contact	5 (2.3%)	5 (3.7%)
Institutional error	10 (4.6%)	6 (4.4%)
Patient refused for other reason	18 (8.3%)	15 (11.0%)
Unknown	2 (0.9%)	3 (2.2%)
Not Received	6 (2.8%)	6 (4.4%)
Out of time point	6 (2.8%)	2 (1.5%)

*If the pain score from the date of treatment was missing, the study entry pain score was used resulting in 100% compliance for eligible patients.

Time windows : Month 1= + 1 month /- 14 days; Month 3= +2 /- 1 month; Month 6= + /- 1 month; Month 12= + /- 2 month; Month 24= + /- 2 month

Supplemental Table 3. Sensitivity Analyses of Pain Response at 3 Months

	SBRT	EBRT	p-value††
3 month Responder[1]	(n=138)	(n=76)	
No	52 (37.7%)	18 (23.7%)	0.99
Yes	86 (62.3%)	58 (76.3%)	
3 month Responder[2]	(n=192)	(n=118)	
No	81 (42.2%)	30 (25.4%)	0.99
Yes	111 (57.8%)	88 (74.6%)	
3 month Responder[3]	(n=138)	(n=76)	
No	39 (28.3%)	14 (18.4%)	0.96
Yes	99 (71.7%)	62 (81.6%)	
3 month Responder[4]	(n=192)	(n=118)	
No	135 (70.3%)	72 (61.0%)	0.96
Yes	57 (29.7%)	46 (39.0%)	

††one-sided p-value from Fishers exact test

[1]Complete or partial response at 3 month only using index site NRPS (not secondary site(s) and medication increase).

[2]Complete or partial response with no increase in pain meds and no progressive response for the secondary sites at 3 month (assuming all alive patients with consent that are missing NRPS scores are responders).

[3]Complete or partial response using 2 points instead of 3 points at 3 month (Excluded secondary sites response and pain meds criteria).

[4]Complete or partial response with no increase in pain meds and no progressive response for the secondary sites at 3 month (assuming all alive patients with consent that are missing NRPS scores are non-responders).

Supplemental Table 4. Change of NRPS pain score and pain response of the index spine only after treatment

	Mean Change from Baseline Pain score ± Standard Deviation				Cumulative Pain Response	
Time from treatment	SRS	n	cEBRT	n	SRS	cEBRT
1 week*	-1.21±3.44	66	-1.48±2.94	27	37.9%	37.0 %
2 weeks*	-2.59±3.23	56	-2.36±2.90	22	51.8%	54.6%
3 weeks*	-2.72±3.35	47	-2.58±2.89	24	57.5%	62.5%
1 month	-3.03±3.33	153	-2.45±3.28	93	64.7%	55.9%
3 months	-2.98±3.34	138	-3.83±2.97	76	62.3%	76.4%
6 months	-3.07±3.50	68	-3.85±2.56	39	72.1%	82.0%
12 months	-3.34±3.25	59	-3.18±3.23	38	71.2%	63.2%

*Due to unreliable data for patients who had multiple sites treated, only patients who had a single site treated and reported a single pain score were included.
Secondary sites and pain medication were excluded from the pain response definition. SRS=stereotactic radiosurgery; cEBRT=conventional external beam radiotherapy.

Supplemental Table 5. Repeated Measures Proportional Odds Mixed Effects Model for Ordinal NRPS Score

Effect			
A. Complete Case Data	**Odds Ratio**	**95% Confidence Interval**	**p-value[1]**
EBRT vs. SBRT	1.08	0.63, 1.87	0.78
Time			<0.001
3 Months vs 1 Month	1.68	1.13, 2.49	
6 Months vs 1 Month	2.66	1.56, 4.52	
12 Months vs 1 Month	1.30	0.78, 2.16	
Time*Treatment arm	-	-	0.01
Baseline NRPS Index Score	0.75	0.67, 0.84	<0.001
Radioresistant Tumor (vs other)	1.11	0.60, 2.08	0.73
Zubrod 1-2 vs. 0	0.62	0.37, 1.06	0.08
A. Imputed Data	**Estimate**	**95% Confidence Interval**	**p-value[2]**
EBRT vs. SBRT	0.50	-0.20, 1.21	0.16
Time			
3 Months vs 1 Month	-0.01	-0.70, 0.67	0.97
6 Months vs 1 Month	-0.41	-1.96, 1.15	0.60
12 Months vs 1 Month	-1.33	-1.96, -0.71	<0.001
Time*Treatment arm			
3 Months vs 1 Month for SBRT	-1.11	-2.07, -0.15	0.02
6 Months vs 1 Month for SBRT	-1.03	-1.99, -0.07	0.04
12 Months vs 1 Month for SBRT	0.02	-0.88, 0.92	0.97
Baseline NRPS Index Score	0.23	0.15, 0.31	<0.001
Radioresistant Tumor (vs other)	-0.06	-0.70, 0.57	0.84
Zubrod 1-2 vs. 0	0.20	-0.29, 0.69	0.42

Modeling the probability of having lower NRPS scores. Outcome variable is ordinal pain response at 1, 3, 6, and 12 months. Reference levels in parenthesis are for binary variables. Effects of continuous variables are assessed as one unit offsets from the mean.

[1]P-value is from Type III Test of Fixed Effects (F-statistic).

[2]P-value is from t-test.

Covariates considered in the model (remained if $p<0.10$): pain medicine at study entry, RT dose, number of mets, time by treatment interaction. Baseline NRPS score, Zubrod score, and radioresistant tumor were forced in the model due to significantly differing between patients with and without completed NRPS scores.

SRS=stereotactic radiosurgery; cEBRT=conventional external beam radiotherapy; NRPS=Numerical Rating Pain Scale.

Supplemental Table 6A. Rapidity of pain response

	SRS				cEBRT			
Month	Estimate (%)	95% CI (%)	Cumulative Pain Responses	At Risk	Estimate (%)	95% CI (%)	Cumulative Pain Responses	At Risk
0	100.0	--	0	209	100.0	--	0	129
3	39.8	(32.8, 46.8)	117	61	50.3	(41.0, 59.5)	57	45
6	29.2	(22.2, 36.1)	132	32	25.4	(16.0, 34.8)	76	15
9	24.4	(17.5, 31.4)	137	19	21.9	(12.6, 31.2)	78	9
12	24.4	(17.5, 31.4)	137	16	21.9	(12.6, 31.2)	78	8

Pain Response/Total: 140/209
Pain Response/Total: 80/130

Log-rank p-value = 0.84
Hazard Ratio [SRS/cEBRT] (95% CI): 0.97 (0.74, 1.28)

This includes weeks 1-3 data. Due to pain medication and pain response at secondary sites not able to be assessed accurately during weeks 1-3, pain medication and secondary sites were excluded from the pain response definition.

Supplemental Table 6B. Duration of Pain Response (Including week 1-3)

	SRS				cEBRT			
Month	Estimate (%)	95% CI (%)	Cumulative Failures	At Risk	Estimate (%)	95% CI (%)	Cumulative Failures	At Risk
0	100.0	--	0	140	100.0	--	0	80
3	98.6	(96.6, 100.0)	2	123	98.8	(96.3, 100.0)	1	75
6	98.6	(96.6, 100.0)	2	100	98.8	(96.3, 100.0)	1	65
9	98.6	(96.6, 100.0)	2	90	98.8	(96.3, 100.0)	1	57
12	97.2	(93.9, 100.0)	3	72	96.9	(92.6, 100.0)	2	51

Pain Response /Total: 6/140
Pain Response /Total: 2/80

Log-rank p-value = 0.44
Hazard Ratio [SRS/cEBRT] (95% CI): 0.54 (0.11, 2.68)

This includes weeks 1- 3 data. Duration of pain response, defined as time from complete or partial pain relief to pain worsening ($\geq$ 3 points); Pain response begins when a patient improves at least 3 points, and pain response ends when the pain score increases by 3 points. Patients assessed at weeks 1, 2, and 3, and 3, 6, 12 and 24 months. Secondary sites are not taken into consideration.

Supplemental Table 7. Repeated Measures Mixed Effects Model for FACT-G Total Score

Variables	Estimate	Standard Error	p- value
A. Complete case data			
Baseline FACT-G Total Score	0.58	0.06	<0.001
Zubrod 1-2 (vs. 0)	0.37	1.91	0.85
Radioresistant Tumor (vs other)	-0.24	2.26	0.92
Non-white (vs. white)	2.56	2.39	0.29
Female (vs. male)	0.32	1.79	0.86
cEBRT (vs. SRS)	1.29	1.75	0.46
Time			
6 months (vs. 3 months)	1.23	2.01	0.54
12 months (vs. 3 months)	-2.20	2.15	0.31
B. Imputed data			
Baseline FACT-G Total Score	0.62	0.12	<0.001
Zubrod 1-2 (vs. 0)	-4.01	4.57	0.38
Radioresistant Tumor (vs other)	5.33	6.60	0.42
Non-white (vs. white)	4.40	5.90	0.46
Female (vs. male)	1.75	4.17	0.67
cEBRT (vs. SRS)	5.02	5.46	0.36
Time			
6 months (vs. 3 months)	2.92	12.03	0.81
12 months (vs. 3 months)	2.22	9.70	0.82

Outcome variable is FACT-G total score at 3, 6, and 12 months. Reference levels in parenthesis are for binary variables. Number of spine metastases, planned SRS dose, and baseline NRPS score fell out of model ($p>0.10$). Variables found to significantly differ between patients with and without completed FACT-G assessments forced into model. SRS=stereotactic radiosurgery; cEBRT=conventional external beam radiotherapy; FACT-G=Functional Assessment of Cancer Therapy - General.

Supplemental Table 8. Number of Patients with an Adverse Event by Category, Term, and Grade Definitely, Probably, or Possibly Related to Protocol Treatment

Category	SRS (n=202) Grade					cEBRT (n=117) Grade				
Term	1	2	3	4	5	1	2	3	4	5
BLOOD/BONE MARROW	4	8	6	1	0	3	2	1	0	0
Hemoglobin decreased	2	6	2	0	0	1	2	1	0	0
Leukopenia	0	2	1	0	0	1	1	0	0	0
Lymphopenia	0	3	2	1	0	1	0	0	0	0
Neutrophil count decreased	1	1	1	0	0	0	0	0	0	0
Platelet count decreased	2	1	0	0	0	1	0	1	0	0
CONSTITUTIONAL SYMPTOMS	15	8	5	0	0	9	8	0	0	0
Chills	0	0	1	0	0	0	0	0	0	0
Fatigue	14	8	5	0	0	7	6	0	0	0
General symptom	0	0	0	0	0	0	1	0	0	0
Weight loss	1	1	0	0	0	3	2	0	0	0
DERMATOLOGY/SKIN	2	1	0	0	0	3	1	0	0	0
Alopecia	0	0	0	0	0	1	0	0	0	0
Dermatitis radiation	0	0	0	0	0	1	1	0	0	0
Dry skin	1	0	0	0	0	0	0	0	0	0
Pruritus	1	0	0	0	0	0	0	0	0	0
Radiation recall reaction (dermatologic)	0	0	0	0	0	1	0	0	0	0
Rash desquamating	0	1	0	0	0	0	0	0	0	0
GASTROINTESTINAL	11	15	3	0	0	12	4	2	0	0
Abdominal distension	0	0	0	0	0	0	1	0	0	0
Anorexia	5	1	0	0	0	1	0	1	0	0
Constipation	2	1	0	0	0	0	0	0	0	0
Diarrhea	3	1	1	0	0	5	1	0	0	0
Dry mouth	1	1	0	0	0	1	0	0	0	0
Dysphagia	1	2	0	0	0	1	0	0	0	0
Esophageal ulcer	0	0	0	0	0	0	0	1	0	0
Esophagitis	1	0	0	0	0	1	2	0	0	0
Gastrointestinal disorder	0	1	0	0	0	0	0	1	0	0
Nausea	8	8	1	0	0	5	2	0	0	0
Small intestinal obstruction	0	0	1	0	0	0	0	0	0	0
Taste alteration	0	1	0	0	0	0	0	0	0	0
Vomiting	4	5	1	0	0	1	0	0	0	0
INFECTION	0	0	1	1	0	0	0	0	1	0
Pneumonia [with unknown ANC]	0	0	1	0	0	0	0	0	0	0
Sepsis [with unknown ANC]	0	0	0	1	0	0	0	0	1	0
Urinary tract infection [with unknown ANC]	0	0	1	0	0	0	0	0	0	0
LYMPHATICS	0	1	0	0	0	0	0	0	0	0
Edema limbs	0	1	0	0	0	0	0	0	0	0

Supplemental Table 8. Number of Patients with an Adverse Event by Category, Term, and Grade Definitely, Probably, or Possibly Related to Protocol Treatment

Category	SRS (n=202) Grade					cEBRT (n=117) Grade				
Term	1	2	3	4	5	1	2	3	4	5
METABOLIC/LABORATOR	2	1	0	0	0	1	1	1	0	0
Alanine aminotransferase increased	1	0	0	0	0	1	0	0	0	0
Alkaline phosphatase increased	2	0	0	0	0	0	0	0	0	0
Aspartate aminotransferase increased	1	0	0	0	0	0	0	0	0	0
Creatinine increased	0	1	0	0	0	0	0	0	0	0
Hyperbilirubinemia	0	0	0	0	0	0	1	0	0	0
Hyperglycemia	0	0	0	0	0	2	1	0	0	0
Hypocalcemia	0	0	0	0	0	0	0	1	0	0
Hypoglycemia	0	0	0	0	0	1	0	0	0	0
MUSCULOSKELETAL/SOFT TISSUE	3	4	3	0	1	2	1	0	0	0
Fracture	1	1	3	0	0	0	1	0	0	0
Gait abnormal	0	1	0	0	0	0	0	0	0	0
Muscle weakness	1	0	0	0	0	2	0	0	0	0
Muscle weakness lower limb	0	2	0	0	0	0	0	0	0	0
Musculoskeletal disorder	1	1	0	0	1	0	0	0	0	0
NEUROLOGY	5	2	0	0	0	2	2	0	0	0
Anxiety	0	0	0	0	0	1	0	0	0	0
Arachnoiditis	0	1	0	0	0	0	0	0	0	0
Depressed level of consciousness	0	1	0	0	0	0	0	0	0	0
Depression	1	0	0	0	0	0	0	0	0	0
Memory impairment	1	0	0	0	0	0	0	0	0	0
Peripheral motor neuropathy	0	0	0	0	0	1	1	0	0	0
Peripheral sensory neuropathy	2	0	0	0	0	1	0	0	0	0
Radiculitis brachial	1	0	0	0	0	0	0	0	0	0
Speech disorder	0	0	0	0	0	0	1	0	0	0
PAIN	13	18	16	0	0	7	11	5	0	0
Abdominal pain	3	3	1	0	0	0	2	1	0	0
Back pain	9	8	12	0	0	3	8	4	0	0
Bone pain	0	2	1	0	0	0	1	1	0	0
Buttock pain	0	1	0	0	0	0	0	0	0	0
Chest pain	0	1	0	0	0	0	0	0	0	0
Chest wall pain	2	2	0	0	0	0	0	0	0	0
Joint pain	2	1	0	0	0	0	0	0	0	0
Myalgia	1	0	0	0	0	0	0	0	0	0
Neck pain	0	1	1	0	0	1	0	0	0	0
Neuralgia	0	1	0	0	0	0	1	0	0	0
Oral pain	1	0	0	0	0	0	0	0	0	0
Pain [NOS]	1	1	0	0	0	1	2	0	0	0
Pain [other]	0	1	0	0	0	1	1	0	0	0
Pain in extremity	1	3	0	0	0	1	1	0	0	0
Pelvic pain	0	0	1	0	0	0	0	0	0	0
Pharyngolaryngeal pain	0	0	0	0	0	1	0	0	0	0

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Category	SRS (n=202) Grade					cEBRT (n=117) Grade				
Term	1	2	3	4	5	1	2	3	4	5
PULMONARY/UPPER RESPIRATORY	4	1	1	0	0	2	0	0	0	0
Cough	1	0	1	0	0	1	0	0	0	0
Dyspnea	1	1	1	0	0	0	0	0	0	0
Pneumonitis	1	0	0	0	0	0	0	0	0	0
Voice alteration	1	0	0	0	0	1	0	0	0	0
RENAL/GENITOURINARY	0	2	1	0	0	0	0	0	0	0
Cystitis	0	1	0	0	0	0	0	0	0	0
Urinary incontinence	0	1	0	0	0	0	0	0	0	0
Urogenital disorder	0	1	1	0	0	0	0	0	0	0

Includes adverse events where relationship to protocol treatment is missing.
Adverse events were graded with CTCAE version 3.0.

Supplemental Table 9. Time to Compression Fracture

	SRS				cEBRT			
Year	Estimate (%)	95% CI (%)	Cumulative Failures	At Risk	Estimate (%)	95% CI (%)	Cumulative Failures	At Risk
0			0	209			0	130
3	6.8	3.9, 10.8	14	156	10.0	5.4, 16.1	12	88
6	12.7	8.6, 17.7	26	113	15.2	9.4, 22.3	18	64
9	15.2	10.7, 20.5	31	94	17.0	10.8, 24.3	20	55
12	15.7	11.1, 21.1	32	75	18.7	12.2, 26.3	22	48
15	18.4	13.4, 24.1	37	57	20.6	13.7, 28.4	24	35
18	18.9	13.8, 24.7	38	50	21.6	14.6, 29.6	25	31
21	19.5	14.3, 25.3	39	46	21.6	14.6, 29.6	25	30
24	19.5	14.3, 25.3	39	37	21.6	14.6, 29.6	25	20
Compression fracture/Total			39/209				25/130	
p-value (Gray (two-sided))			0.59					