Biological Effective Radiation Dose for Multiple Myeloma Palliation

Ruby F. Meredith MD, PhD , John R. Bassler MS ,
Andrew M. McDonald MD , John M. Stahl MD ,
David T. Redden PhD , James A. Bonner MD

PII: S2452-1094(23)00043-X
DOI: https://doi.org/10.1016/j.adro.2023.101214
Reference: ADRO 101214

To appear in: *Advances in Radiation Oncology*

Received date: 13 December 2022
Accepted date: 28 February 2023

Please cite this article as: Ruby F. Meredith MD, PhD , John R. Bassler MS , Andrew M. McDonald MD , John M. Stahl MD , David T. Redden PhD , James A. Bonner MD , Biological Effective Radiation Dose for Multiple Myeloma Palliation, *Advances in Radiation Oncology* (2023), doi: https://doi.org/10.1016/j.adro.2023.101214

Title: **Biological Effective Radiation Dose for Multiple Myeloma Palliation**

Running title: Biological Radiation Dose for Myeloma

Ruby F. Meredith, MD, PhD[1], John R. Bassler, MS[2], Andrew M. McDonald, MD[1], John M. Stahl, MD[1], David T. Redden, PhD[2], James A. Bonner, MD[1]

[1]Department of Radiation Oncology, University of Alabama at Birmingham

[2]Department of Biostatistics, University of Alabama at Birmingham

[*]**Corresponding author:** Ruby F. Meredith, MD, PhD

Dept of Radiation Oncology, 1700 6th Ave. South, Birmingham, AL 35249

Phone: 205 996 4634 FAX 205 975 0784 rmeredith@uabmc.edu

Biostatistics: John R. Bassler, 205 934 2684 jbassl1@uab.edu

David T. Redden, 205 975 9165 dredden@uab.edu

Department of Biostatistics, Ryals Public Health Building,

1665 University Blvd, Birmingham, AL 35233

Supported by Department of Radiation Oncology and the UAB Center for Clinical and Translational Science Award UL1TR003096. No authors have a conflict of interest.

All pertinent data generated and analyzed during this study are included in this published article.

Acknowledgments: the authors wish to thank Roleah Hill for assistance.

Biological Effective Radiation Dose for Multiple Myeloma Palliation

ABSTRACT

Various radiation therapy (RT) dose/fractionation schedules are acceptable for palliation in Multiple Myeloma. Nine years of single Institution RT experience was reviewed to determine the influence of dose/fractionation and other factors pertinent to individualizing therapy.

Methods: 152 items were identified from CPT codes for Multiple Myeloma treatment from 2012 through 6/30/2021. After exclusions, 204 sites of radiation in 94 patients were reviewed. Data were captured from treatment planning and clinical records. To statistically assess the association between biological effective dose (BED_{10}) and variables of interest, BED was first dichotomized to <24 Gy vs. ≥24 Gy. Multivariate analysis used SAS software and a generalized estimating equation approach to account for multiple observations per patient.

Results: Fractions of 1.8 - 8Gy were used in one to 25 fractions. Most patients had no significant toxicity. Grade 1 toxicity was more likely with higher BED radiation courses, as expected [20% vs. 12% for BED <24 Gy]. Pain relief was complete or very good for most sites, with <3 % reporting no pain relief. Eleven sites in 9 patients required retreatment. All retreatment sites had palliation that was lasting, with median of 22 months to last follow-up or death after repeat course (range 0.5-106 months). There was a trend for better pain control and less risk of fracture retreatment with BED ≥24 Gy.

Conclusions: Most patients had good palliation without toxicity. BED ≥24 Gy caused 8% higher risk of grade 1 toxicity and trended towards better pain control plus reduced risk of fracture re-treatment.

INTRODUCTION

Multiple myeloma is a hematologic malignancy that frequently requires radiation therapy (RT) for palliation of painful bony metastases. Various dose/fractionation schedules are acceptable for

palliation in Multiple Myeloma. [1], [2],[3] To further assess dose/fractionation efficacy/toxicity and seek other factors pertinent to individualizing therapy, we reviewed experience for patients identified in the past 9 years.

METHODS

Patient Data Acquisition

Institutional Review Board approval was granted for retrospective study. CPT codes for Multiple Myeloma treatments from 2012 through 6/30/2021 identified 152 items. Only patients treated for local myeloma sites were studied. Nine sites among those patients treated earlier than the capture date were included for a total of 205 sites in 94 patients. Treatment was individualized at the discretion of the care team. Toxicity attributed to radiotherapy was graded using CTCAE version 4.0. Data were captured from treatment planning software and electronic medical records. Statistical Analysis: To assess the association between Biological Effective Dose for early reacting tissue and tumors α/β =10 (BED) and the variables of interest, BED was first dichotomized into two distinct groups, having a BED scale less than 24, or BED scale of 24 or greater.

Statistical Analysis

Descriptive analyses consisted of summarizing variables of interest using measures of central tendency (sample medians), dispersion (interquartile range), and distribution (frequency, percentage). Missing data was assumed to be missing completely at random (MCAR) and was not included in descriptive summaries or models. Multivariate analysis of BED comprised of a generalized estimating equation (GEE) approach to account for multiple observations by participant. [4] Model specification included the logit link function and binomial distribution family, as well as a compound symmetric within-subject correlation structure. Although multiple variables were inspected for appropriateness to include in the longitudinal model, careful attention to the model convergence and factors that could reliably be

estimated are included in the final model. All analyses were conducted using SAS software, version 9.4 of the SAS System for Windows.

RESULTS

Demographics are shown in Table 1 and information about concurrent systemic therapy, termed chemotherapy. Staging was coded as the most updated available. If a patient had data for both International Staging (ISS) and Durie Salmon, ISS was used, and revised ISS if known. Some of the Table 1 factors are known or possible prognostic indicators such as high risk cytogenetics, chromosome 1 abnormalities, race, stem cell transplant and family history of hematologic malignancies. [5, 6] [7] Components of bortezomib, lenalidomide and dexamethasone (VRD) were common 1st line systemic therapy. Most reported responses to initial systemic therapy ranged from good to complete while 8.6 % had stable or progressive disease. Response was unknown for 36 patients.

The supplementary Table has details and radiation parameters that are not included in the Table 2 analysis, which was restricted to six radiation courses. Concurrent systemic therapy was used in the majority. For patients who had more than 3 radiation courses, all were beyond 1st line systemic therapy by then and they received a variety of salvage agents.

Radiation dose per fraction varied from 1.8 - to 8 Gy while the number of fractions varied from one to 25 with delivery in one to 36 days. Some sites with unusual fractionations, such as 3 Gy x 6, were planned for more but the full course was not delivered. Two patients were treated with 1.8 Gy to 45 Gy based on good prognostic factors; one had last follow-up at 105 months and the other died at 57.7 months. The most frequent schedule was 2 Gy x 10 fractions (EQD_2 of 20 Gy) and corresponds to the Biologically Effective Dose for early reacting tissue with an α/β of 10 (BED) of 24 Gy. Table 2 provides Odds Ratios for six parameters using radiation with BED

24 Gy or higher compared to lower dose. With limitations of the statistical model, selection of factors for comparison was influenced by the frequency.

The majority of patients had no reported toxicity (87.8% for BED <24 Gy and 79.5% for ≥24 Gy). As expected, the risk of toxicity was greater for higher BED radiation and the only Grade 2 was gastrointestinal complaint after 3 Gy x 10 fractions to the pelvis. Since most patients continued with systemic therapy, this may also have contributed to toxicity attributed to radiation.

Pain relief was complete or very good for the majority of sites. There was variation of pain response between sites of treatment that were not radiation- or patient dependent. For instance, an individual might have complete pain relief at one site while another site receiving the same radiation had less response.

Good palliation (Complete or Very Good pain relief) was more likely with BED ≥ 24 Gy than less radiation (51% vs. 68.75% when confounding factors were not assessed). Pain response was usually durable with <10% of patients having a site retreatment with monitoring up to 133 months from initial radiation to death or last follow-up. Most patients in the category of partial, or no pain response, had modest relief. Only 4 patients had no significant pain relief at 6 sites (2.9%), and 2 of the patients had relief at other sites. Three sites given 8Gy fractions had worse pain the next day, consistent with flare response. Confounding factors of no pain relief reports include incomplete radiation course and pain at other sites or medical conditions that interfered with assessment.

Objective measures were helpful in assessing the efficacy of radiation. Images confirmed that a single 4 Gy treatment was adequate to allow fracture healing and complete pain relief although the area remained weak and another fracture in that lesion occurred after trauma at 31 months. Two others with low BED at fractures had short survival and a third patient had no

problem during 72-month follow-up but that fracture had rod stabilization. In concern for higher dose impedance of bone healing, no problem was noted of fractures treated at higher dose. No indication was found that BED ≥30 Gy at 7 fracture sites interfered with healing. Most sites had control until death or last follow-up; the retreatment rate was 5.3% as discussed below.

Positron emission tomography (PET) imaging was helpful for assessing efficacy of radiation and was available for 76 sites (37.0%). PET demonstrated efficacy of low dose RT in some patients, whereas 46% at higher radiation lacked complete resolution. Factors other than radiation dose, such as resistant disease, inflammation not definitively distinguishable from active disease, or larger masses not controlled by usual palliative doses of radiation, were not analyzed.

Most patients who had PET resolution had complete pain relief as shown in Table 3. The observation that a few patients who still had pain at PET resolution suggests other factors contributing to pain such as continued mass effect or other etiologies. There are myeloma patients whose disease does not always appear PET avid, but none were found in this series. PET resolution was more likely with BED ≥24 (53.9%) than BED <24 Gy (38.4%). Each group had one PET progression within 6 mo. and partial pain relief in those sites.

Overall, fracture sites were treated with nearly the whole range of BED (3.9-31.25 Gy). However, fracture sites requiring retreatment tended to received lower initial BED (5.6-31.25 Gy, mean 16.9 Gy, median 14.8 Gy); while fracture associated sites not requiring retreatment received BED of 3.9-31.25 Gy, (mean 22.9 Gy, median 24 Gy). Initial fracture sites treated at 4 Gy x 1 and 2 Gy X 10 (ID31 and 79, respectively) had healing but experienced 2nd fracture after trauma and were retreated (Table 4).

Eleven sites in 9 patients required retreatment, with at least partial overlap of the initial field. No patient had 3 treatments to the same site. Factors are compared in Table 4. Initial dose/fractionations included 1.8 Gy x 4, 2 Gy x 4, 2 Gy x 10, 3 Gy x10, 4 Gy x1, 8 Gy x 1 and one site with 10 fractions of unknown Gy delivered at another institution. The need for retreatment was considered in field progression in 6 and overlap with other lesions in 3. All sites treated at our institution had palliative benefit from both 1st and 2nd courses that was lasting with median of 22 months to latest follow up or death after retreatment.

DISCUSSION

Historically a variety of dose/fractionation schedules have been successfully used for palliation of predominantly bone lesions in multiple myeloma patients [2] [1] [8] [9, 10] [11] [2] [12] Since myeloma is usually more radiosensitive than most solid tumors, lower doses have frequently been satisfactory. ASTRO guidelines for bone metastasis provides a review of outcome with various "practices" and the tradeoff of quicker relief plus convenience for short course radiation versus reduced rate of retreatment for longer courses. [1], [9] One more recent analysis of 87 lesions had less need for re-treatment with Equivalent dose in 2 Gy fractions (EQD2 = $23.33\ \mathrm{Gy}_{\alpha/\beta=10}$) or above. [12] Others found satisfactory results with yet a lower dose range for more selected patients. [12, 13] Price et, al. found that radiation schedules with EQD2 <12 Gy was effective for pain control in 95% of uncomplicated bone lesions. [13] Although the number of lesions was limited to 48 for the high dose and 22 for the low dose, the duration of pain relief and rate of pain recurrence was not statistically different. Retreatment was used for 9.5% of the low dose group and 6.3% of the higher dose group. This

rate of retreatment is similar to that in other reports using a variety of dose/fractionation courses. [1, 10] [2] [14] In keeping with the desire to provide appropriate treatment, that study excluded patients who had epidural lesions and fractures since a prior report found short course radiation to be suboptimal for spinal cord compression in myeloma patient.[15] [10]

The choices of dose/fractionation schedules of this experience showed good outcomes and provide data for efforts to improve radiation guidelines. No toxicity was reported for the majority of sites treated regardless of the radiation dose/fractionation schedule and whether or not the radiation was given alone or with systemic agents; mild toxicity was more frequent with higher BED. Similar to other studies, most of our patients received systemic therapy that was not interrupted for radiation. [16]

With individualization, the minority of patients treated with large single fractions had circumstances such as limited life expectancy, other medical conditions and social difficulties. Only 4 had 8 Gy x 1 to the spine, with most patients having multi-fraction courses to the spine in following published guidelines. [1, 17, 18]

Most patients had good palliative benefit; some may have had better pain relief than reported due to early evaluation but limited follow-up. Except for 2.9% of sites, at least modest pain relief was achieved. Consistent with earlier reports, low BED radiation to selected patients had acceptable rates of palliation and risk of retreatment although less than BED $\geq$24 Gy [13]. Single and hypo-fractionated regimens are appropriate for many patients but are not recommended for all sites, such as multi-level spine, cord compression, areas of fracture and large masses.[18] In general, relief was durable. Outcome from retreatment was improved over that reported for bone metastasis from more diverse histologies. [19]

Although treatment courses were based on non-financial factors, the risk of retreatment was cost effective. The billing charges for two single fraction courses versus a single course of 10

fractions, was 9% more. The fact that only 11 of 205 total sites required retreatment reduces health care spending compared to longer courses for all sites.

PET and other imaging was helpful for assessing efficacy of radiation but suggest that there are multiple factors involved in individual site responses. [20]

Conclusions: Most patients had good palliation without toxicity. BED ≥24 Gy caused 8% higher risk of grade 1 toxicity and trended towards better pain control plus reduced risk of fracture re-treatment.

Bibliography

1. Lutz, S., et al., *Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline.* Pract Radiat Oncol, 2017. 7(1): p. 4-12.
2. Tsang, R.W., et al., *Radiation Therapy for Solitary Plasmacytoma and Multiple Myeloma: Guidelines From the International Lymphoma Radiation Oncology Group.* Int J Radiat Oncol Biol Phys, 2018. **101**(4): p. 794-808.
3. Spratt, D.E., et al., *Contemporary Statewide Practice Pattern Assessment of the Palliative Treatment of Bone Metastasis.* International Journal of Radiation Oncology*Biology*Physics, 2018. **101**(2): p. 462-467.
4. Zeger, S.L., K.Y. Liang, and P.S. Albert, *Models for longitudinal data: a generalized estimating equation approach.* Biometrics, 1988. **44**(4): p. 1049-60.
5. Kumar, S., et al., *International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma.* Lancet Oncol, 2016. **17**(8): p. e328-e346.
6. Sonneveld, P., et al., *Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group.* Blood, 2016. **127**(24): p. 2955-62.

7. Giri, S., et al., *Chromosome 1 abnormalities and survival of patients with multiple myeloma in the era of novel agents.* Blood Adv, 2020. **4**(10): p. 2245-2253.
8. Howell, D.D., et al., *Single-fraction radiotherapy versus multifraction radiotherapy for palliation of painful vertebral bone metastases-equivalent efficacy, less toxicity, more convenient: a subset analysis of Radiation Therapy Oncology Group trial 97-14.* Cancer, 2013. **119**(4): p. 888-96.
9. Wang, S., et al., *Dose Selection for Multiple Myeloma in Modern Era.* Pract Radiat Oncol, 2019. **9**(4): p. e400-e406.
10. Leigh, B.R., et al., *Radiation therapy for the palliation of multiple myeloma.* Int J Radiat Oncol Biol Phys, 1993. **25**(5): p. 801-4.
11. Talamo, G., et al., *Current role of radiation therapy for multiple myeloma.* Front Oncol, 2015. **5**: p. 40.
12. Lee, J.W. and J.E. Lee, *Local radiotherapy for palliation in multiple myeloma patients with symptomatic bone lesions.* Radiat Oncol J, 2016. **34**(1): p. 59-63.
13. Price, J.G., et al., *Effective Pain Control With Very Low Dose Palliative Radiation Therapy for Patients With Multiple Myeloma With Uncomplicated Osseous Lesions.* Adv Radiat Oncol, 2021. **6**(4): p. 100729.
14. Mathis, N.J., et al., *Personalized Treatment Selection Leads to Low Rates of Local Salvage Therapy for Bone Metastases.* Int J Radiat Oncol Biol Phys, 2022. **112**(1): p. 99-105.
15. Rades, D., et al., *Short-course radiotherapy (RT) for metastatic spinal cord compression (MSCC) due to renal cell carcinoma: results of a retrospective multi-center study.* Eur Urol, 2006. **49**(5): p. 846-52; discussion 852.
16. Resende Salgado, L., et al., *The Safety Profile of Concurrent Therapy for Multiple Myeloma in the Modern Era.* Advances in Radiation Oncology, 2019. **4**(1): p. 112-117.
17. Rades, D., et al., *Evaluation of five radiation schedules and prognostic factors for metastatic spinal cord compression.* J Clin Oncol, 2005. **23**(15): p. 3366-75.
18. Rades, D., et al., *A New and Easy-to-Use Survival Score for Patients Irradiated for Metastatic Epidural Spinal Cord Compression.* Pract Radiat Oncol, 2022. **12**(4): p. 354-362.

19. Huisman, M., et al., *Effectiveness of Reirradiation for Painful Bone Metastases: A Systematic Review and Meta-Analysis.* International Journal of Radiation Oncology*Biology*Physics, 2012. **84**(1): p. 8-14.

20. Charalampous, C., et al., *Utility of PET/CT in assessing early treatment response in patients with newly diagnosed multiple myeloma.* Blood Adv, 2022. **6**(9): p. 2763-2772.

Table 1. Demographics by BED at First Course

	BED <24 Gy (N = 27)	BED +24 Gy (N = 67)	Total (N = 94)
Age at Diagnosis (Years)	62.0 (10.09)	60.9 (12.59)	61.3 (11.88)
Stage			
1	5 (26.3%)	7 (15.9%)	12 (19.0%)
2	7 (36.8%)	15 (34.1%)	22 (34.9%)
3	7 (36.8%)	22 (50.0%)	29 (46.0%)
Unknown	8	23	31
Sex (Male)	18 (66.7%)	37 (55.2%)	55 (58.5%)
Stem Cell Transplant (Yes)	12 (46.2%)	35 (53.0%)	47 (51.1%)
Unknown	1	1	2
Total Cytogenetics (Yes)	4 (28.6%)	11 (28.9%)	15 (28.8%)
Unknown	13	29	42
Chromosome 1 Abnormality			

Table 1. Demographics by BED at First Course

	BED <24 Gy (N = 27)	BED +24 Gy (N = 67)	Total (N = 94)
Gain/amp	3 (75.0%)	13 (81.3%)	16 (80.0%)
Del	1 (25.0%)	3 (18.8%)	4 (20.0%)
Unknown	23	51	74
Race			
White or Other	15 (55.6%)	42 (62.7%)	57 (60.6%)
Black	12 (44.4%)	25 (37.3%)	37 (39.4%)
Family History			
Heme C	3 (13.6%)	4 (7.5%)	7 (9.3%)
Other	11 (50.0%)	28 (52.8%)	39 (52.0%)
None	8 (36.4%)	21 (39.6%)	29 (38.7%)
Unknown	5	14	19
Death (Yes)	13 (48.1%)	35 (52.2%)	48 (51.1%)
Response to first Chemo			
CR	6 (35.3%)	9 (22.0%)	15 (25.9%)
VGPR, Near CR	7 (41.2%)	18 (43.9%)	25 (43.1%)
PR, Good	3 (17.6%)	10 (24.4%)	13 (22.4%)
Stable	1 (5.9%)	1 (2.4%)	2 (3.4%)
Progress	0 (0.0%)	3 (7.3%)	3 (5.2%)

Table 1. Demographics by BED at First Course

	BED <24 Gy (N = 27)	BED +24 Gy (N = 67)	Total (N = 94)
Unknown	10	26	36

- Table statistics reported as Mean (Standard Deviation) for continuous factors, and Frequency (Column Percentage %) for categorical factors
- Unknown values are reported and not included in summary statistics

Table 2. GEE model results

	Course 1		Course 2		Course 3		Course 4		Course 5		Course 6		Adjusted Odds Ratio ¥ (95% CI)
	BED <24 Gy (N = 21)	BED +24 Gy (N = 78)	BED <24 Gy (N = 9)	BED +24 Gy (N = 29)	BED <24 Gy (N = 4)	BED +24 Gy (N = 13)	BED <24 Gy (N = 4)	BED +24 Gy (N = 5)	BED <24 Gy (N = 3)	BED +24 Gy (N = 7)	BED <24 Gy (N = 1)	BED +24 Gy (N = 1)	
Stem Cell Transplant													
Yes	7 (14.6%)	41 (85.4%)	7 (28.0%)	18 (72.0%)	2 (18.2%)	9 (81.8%)	4 (57.1%)	3 (42.9%)	1 (16.7%)	5 (83.3%)	1 (50.0%)	1 (50.0%)	1.26 (0.48, 3.33)
No	14 (27.5%)	37 (72.5%)	2 (15.4%)	11 (84.6%)	2 (33.3%)	4 (66.7%)	0 (0.0%)	2 (100.0%)	2 (50.0%)	2 (50.0%)	0 (0.0%)	0 (0.0%)	REF
Race													
White or Other	16 (24.6%)	49 (75.4%)	6 (30.0%)	14 (70.0%)	2 (16.7%)	10 (83.3%)	3 (50.0%)	3 (50.0%)	1 (20.0%)	4 (80.0%)	1 (100.0%)	0 (0.0%)	0.99 (0.36, 2.72)
Black	5 (14.7%)	29 (85.3%)	3 (16.7%)	15 (83.3%)	2 (40.0%)	3 (60.0%)	1 (33.3%)	2 (66.7%)	2 (40.0%)	3 (60.0%)	0 (0.0%)	1 (100.0%)	REF
Site													
Pelvis	6 (15.8%)	32 (84.2%)	1 (20.0%)	4 (80.0%)	0 (0.0%)	5 (100.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	1.71 (0.74, 3.93)
Spine	4 (13.3%)	26 (86.7%)	5 (26.3%)	14 (73.7%)	1 (25.0%)	3 (75.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	1.76 (0.66, 4.71)
Other	11 (35.5%)	20 (64.5%)	3 (21.4%)	11 (78.6%)	3 (37.5%)	5 (62.5%)	3 (42.9%)	4 (57.1%)	2 (33.3%)	4 (66.7%)	1 (50.0%)	1 (50.0%)	REF
Known fracture at time of treatment													
Yes	6 (17.1%)	29 (82.9%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	5 (100.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100.0%)	0 (0.0%)	1.44 (0.55, 3.75)

Table 2. GEE model results

	Course 1		Course 2		Course 3		Course 4		Course 5		Course 6		Adjusted Odds Ratio ¥ (95% CI)
	BED <24 Gy (N = 21)	BED +24 Gy (N = 78)	BED <24 Gy (N = 9)	BED +24 Gy (N = 29)	BED <24 Gy (N = 4)	BED +24 Gy (N = 13)	BED <24 Gy (N = 4)	BED +24 Gy (N = 5)	BED <24 Gy (N = 3)	BED +24 Gy (N = 7)	BED <24 Gy (N = 1)	BED +24 Gy (N = 1)	
No	15 (23.4%)	49 (76.6%)	8 (22.2%)	28 (77.8%)	4 (33.3%)	8 (66.7%)	3 (37.5%)	5 (62.5%)	3 (33.3%)	6 (66.7%)	0 (0.0%)	1 (100.0%)	REF
Toxicity													
1 or 2	5 (26.3%)	14 (73.7%)	0 (0.0%)	6 (100.0%)	0 (0.0%)	4 (100.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.31 (0.14, 12.56) [1]
0	16 (20.0%)	64 (80.0%)	9 (28.1%)	23 (71.9%)	4 (30.8%)	9 (69.2%)	4 (57.1%)	3 (42.9%)	3 (30.0%)	7 (70.0%)	1 (50.0%)	1 (50.0%)	REF
Pain Scale Category													
Complete or Very Good Relief	11 (16.9%)	54 (83.1%)	5 (18.5%)	22 (81.5%)	4 (44.4%)	5 (55.6%)	0 (0.0%)	3 (100.0%)	2 (22.2%)	7 (77.8%)	0 (0.0%)	1 (100.0%)	-
Partial or No Relief	10 (29.4%)	24 (70.6%)	4 (36.4%)	7 (63.6%)	0 (0.0%)	8 (100.0%)	4 (66.7%)	2 (33.3%)	1 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	-

- Table statistics reported as Frequency (Row Percentage %) for all categorical factors
- Total of 175 observations used in model, or 85.4% of all available observations (175/205) from 85 of the available 94 patients
- ¥ Odds are based on the probability that BED +24
- [1] Odds ratio and CI are stratified by Pain Scale (Complete of Very Good Relief)

Table 3. PET Resolution Compared to Pain Relief *

	PET Result		
	Resolution	Residual	Progression
Pain Relief			
Complete	16	5	0
Partial	20	28	2

- Table statistics reported as Frequency
- * 5 lesions with PET images were excluded due to unknown pain response

Table 4. Comparison of features associated with initial RT and retreatment

ID	Fracture	BED		Pain		Toxicity		PET Response		Months 1st-2nd RT	Months to Last FU/dod
		1st RT	2nd RT	1st RT	2nd RT	1st RT	2nd RT	1st RT	2nd RT		
31	yes	5.6	5.6	CR	PR	0	0	na	na	32	22
31	yes	5.6	5.6	CR	PR	0	0	na	na	16	22
31	yes	5.6	5.6	CR	PR	0	0	na	na	15	22

Table 4. Comparison of features associated with initial RT and retreatment

ID	Fracture	BED		Pain		Toxicity		PET Response		Months 1st-2nd RT	Months to Last FU/dod
		1st RT	2nd RT	1st RT	2nd RT	1st RT	2nd RT	1st RT	2nd RT		
42	-	9.6	9.6	PR	PR	0	0	na	Low residual	11	23
46	yes	24	24	Near CR	PR	0	1	na	na	27	31
53	yes	31.25	43.75	CR	CR	na	na	na	CR	18	106
79	yes	24	24	PR	PR	0	0	na	na	7	94
146	yes	unk	37.5	CR	PR	na	1	na	Low residual	90	11
172	-	8.49	31.25	PR	PR	1	1	na	na	16	12
184	-	30	28	CR	CR	0	0	residual	residual	2	1
229	yes	14.4	24	PR	PR	1	0	progress	na	7	3

- Months from 1st to 2nd RT and Months to last follow-up or death are rounded to nearest month. Pain and PET response CR = complete, PR = Partial, na = not available

Disclosure

Supported by Department of Radiation Oncology and the UAB Center for Clinical and Translational Science Award UL1TR003096. No authors have a conflict of interest.

All pertinent data generated and analyzed during this study are included in this published article.