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Progress in Shortening Treatment Courses for Bone Metastases in a Statewide Quality Consortium

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Progress in Shortening Treatment Courses for Bone Metastases in a Statewide Quality**Consortium****Short Running Title:**

Shortening Treatment for Bone Metastases

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Conflict of Interest Statement

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We are not authorized to share MROQC data. The data are individually owned by the member institutions of MROQC.

Short Running Title:

Progress Shortening Treatment Courses for Bone Metastases

Abstract (295 of 300 words)

Purpose

A large body of research has studied varied fractionation regimens for radiation therapy (RT) targeting bone metastases, with evidence that courses with 5 or fewer fractions are isoeffective compared to longer courses. We analyzed practice patterns within a statewide quality consortium following implementation of quality measures promoting single-fraction RT (SFRT) for uncomplicated metastases and ≤ 5 fractions for all metastases.

Materials and Methods:

Consecutive patients receiving RT for bone metastasis with primary breast, lung, melanoma, prostate, or renal cancer(s) between 3/1/18 and 12/31/24 were prospectively enrolled in a statewide quality consortium. SFRT and ≤ 5 fraction quality metrics were implemented 1/1/2020 and 1/1/2022, respectively. Patient, treatment, physician, and facility characteristics were collected and multivariable logistic regression with and without random intercepts for centers were used to account for clustering by center and to assess association with metric adherence.

Results

In total, 4,477 patients were enrolled and received 6,733 RT treatment plans, with 1,105 patients receiving 1,465 plans for uncomplicated metastases and 3,247 patients receiving 4,832 non-stereotactic body RT plans. Use of SFRT and ≤ 5 fraction RT for uncomplicated and any metastases increased from 17.8% to 38.8% and 44.2% to 63.9%, respectively, after implementation of quality measures. In both models, later year of treatment, longer distance to treating facility, higher baseline fatigue, treatment site other than spine, and fewer physician years in practice predicted shorter treatment courses. Patients with >1 site treated for uncomplicated metastases had lower odds of receiving SFRT. Forward planning, uncomplicated

metastasis, retreatment, palliative intent, age ≥ 80 , and ECOG performance status ≥ 2 independently predicted receipt of ≤ 5 fractions.

Conclusions

Our efforts to shorten treatment courses for bone metastases have been successful. The number and variety of factors that predict the use of shorter courses reflect the complexity of clinical decision-making for treatment of bone metastases.

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Introduction

National and international guidelines support the use of varied fractionation regimens for radiation therapy (RT) to bone metastases.^{1,2} ESTRO-ACROP guidelines recommend single-fraction RT for uncomplicated bone metastases.³ RT is commonly used for palliation of painful bone metastases, with a variety of effective fractionation approaches reported in a wide body of literature, with some reports of higher re-treatment rate for single fraction RT (SFRT).⁴⁻⁶ Growing evidence supports the utility of RT for select asymptomatic bone metastases to prevent skeletal events or for patients with oligometastatic disease, often with a stereotactic ablative approach.⁷⁻¹⁰ The selection of fractionation for RT to bone metastases is complex, considering multiple patient-specific factors including treatment indication, anatomic location, and prognosis, among other factors. Treatment in fewer fractions can conserve health system(s) and patient resources and may reduce the environmental impact of radiation therapy.¹¹⁻¹⁴

The Michigan Radiation Oncology Quality Consortium (MROQC) is a collaborative effort among academic and community radiation oncology centers in the state of Michigan that prospectively enrolls and collects data from patients receiving RT for select indications.^{15,16} Within MROQC, we have previously reported real-world data demonstrating heterogeneity in the use of fractionation regimens, including persistent but infrequent use of extended fractionation RT (EFRT, greater than 10 fractions) and use of SFRT reported in a minority of cases.^{17,18} In previously reported efforts, after development and implementation of quality metrics to promote high-value radiation oncology approaches and reduce use of EFRT, we observed a lower rate of EFRT; however, only 12% of plans delivered 8 Gy SFRT and nearly half of plans delivered 10 fractions of RT in this series.¹⁹ National data highlight similar trends in the reduction of EFRT, but limited increase in the use of SFRT.²⁰

MROQC quality metrics to promote the use of SFRT for uncomplicated bone metastases and to promote the use of 5 or fewer fractions for any bone metastasis were subsequently introduced. We hypothesized that practice patterns would remain varied, given the complexity of fractionation selection, with the proportion of patients receiving SFRT and fewer than 5 fractions anticipated to increase with introduction of respective quality metrics.

Materials and Methods:

Consecutive patients receiving RT for bone metastases from primary breast, lung, melanoma, prostate, or renal cancer(s) between 3/1/18 and 12/31/24 were prospectively enrolled in the state-wide Michigan Radiation Oncology Quality Consortium (MROQC) database from participating centers.¹⁵ Data collection instruments measuring patient, treatment, physician, and facility characteristics were prospectively collected via surveys distributed to both patients and clinicians. Treatment characteristics including treatment sites, treatment intent, baseline symptoms, and presence of spinal cord or cauda equina compression were physician-assessed. Collected responses were manually entered into an electronic database. Consecutive patients enrolled in the database were included regardless of insurance status or insurer. The work of MROQC is designated as quality improvement and has been reviewed by the University of Michigan Institutional Review Board (IRB), which has determined that it is exempt from further IRB oversight.

Quality metrics were introduced to participating facilities as a component of an incentive structure through Blue Cross Blue Shield of Michigan (BCBSM), including a facility-level pay-for-performance program, a facility-level prior authorization “gold card” program (facilities with “gold card” status are exempted from BCBSM’s radiation oncology prior authorization

program), and a physician-level value-based reimbursement program. Multiple quality initiatives were used in parallel for selected disease sites. Inclusion and exact weighting of metrics varied by year, and quality metrics across multiple disease sites were included in incentive programs.

A quality metric promoting the use of single fraction RT for uncomplicated bone metastases was initiated 1/1/2020. Uncomplicated metastases were defined as painful, not previously irradiated, and not associated with spinal cord or nerve root compression, fracture, surgery, or a soft tissue component. A provider-facing knowledge transfer project including an educational video followed by a facilitated discussion was conducted at 25 participating centers between 2022 and 2023 to promote SFRT.²¹ A quality metric promoting use of ≤ 5 fraction RT for all bone metastases was initiated 1/1/2022, without penalty for stereotactic body radiation therapy (SBRT) plans in incentive structure. An example annual quality measure benchmark aimed for $\geq 75\%$ of bone metastases to be treated in ≤ 5 fractions at the facility level and $\geq 45\%$ of patients with uncomplicated metastases to be treated with SFRT across the consortium.

Patient, treatment, physician, and facility characteristics were summarized using descriptive statistical methods, including adherence to quality metrics and change in the use of SFRT and ≤ 5 fraction RT over time. Characteristics utilized were assessable at time of receipt of RT. Oncologic outcomes were not assessed.

Utilization of SFRT and ≤ 5 fraction RT were assessed for association with collected variables among patients with uncomplicated metastasis and all enrolled patients, respectively. For analysis of ≤ 5 fraction RT use, SBRT plans were excluded from analysis given that all were ≤ 5 fractions. If multiple areas were treated in a treatment course, the dose and fractionation with the largest number of fractions were used in description and analysis. Planning modality was collected, including forward planning (manually selected beam direction, shape, and weight),

inverse planning (plans optimized from treatment goals for target dose and organ at risk avoidance using commercially available software), or hybrid planning (a combination of the two strategies).

Multivariable logistic regression with and without random intercepts for centers to account for clustering were generated with significance defined as $p < 0.05$. Year of treatment was assessed both as a continuous variable and as defined categorical time periods before and after the launch of applicable quality initiatives for inclusion in models. The distance a patient traveled to treating facility was estimated using the centroids of the U.S. ZIP code(s) for patient residence and treating facility. Distance from the treating facility was reported by tercile in the overall cohort, but a continuous variable with a unit of 10 miles was used for multivariable analyses. Physician years in practice were reported categorically in 10-year intervals. Treatment intent (given all uncomplicated metastases were treated for palliation) and retreatment (defined as treatment to the same site by the treating physician) were excluded from models for uncomplicated metastases given they violated our definition of uncomplicated metastasis.

Statistical analysis was completed with SAS version 9.4.

Results:

During the observation period, 4,477 patients were enrolled and received 6,733 RT plans. Uncomplicated metastases were observed in 1,105 patients receiving 1,465 plans and were included in analysis of SFRT. After exclusion of SBRT plans, 3,247 patients receiving 4,832 plans were included in analysis of plans delivering ≤ 5 fraction RT for any bone metastasis. SBRT utilization did increase over time from 8.6% of cases in the consortium in 2018 to 29.8% of cases in 2024. Patient, treatment, physician, and facility characteristics for both cohorts are described in Table 1, with many of these characteristics expectedly imbalanced between patients receiving

SFRT and ≤ 5 fraction RT, respectively. All 29 participating centers enrolled patients during the observation period and the number of enrolling providers per center ranged from 1 to 23. The number of participating centers varied by year.

Figure 1 illustrates the use of SFRT and ≤ 5 fraction RT over time. Both overall trended positively over the observation period, with quarterly and annual variation. The use of SFRT for uncomplicated metastases increased from 17.8% prior to 2020 to 38.8% after implementation of the quality measure, while the use of ≤ 5 fractions increased from 44.2% prior to 2022 to 63.9% after quality measure implementation.

The most common fractionations among uncomplicated metastases were 8 Gy in 1 fraction (455 patients, 31.1%), 30 Gy in 10 fractions (389 patients, 26.6%), and 20 Gy in 5 fractions (386 patients, 26.3%). Among all patients included in analysis for ≤ 5 fraction RT, the most common fractionations included 30 Gy in 10 fractions (1763 patients, 36.5%), 20 Gy in 5 fractions (1381 patients, 28.6%), and 8 Gy in 1 fraction (980 patients, 20.3%). All other fractionations represented less than 5% of each cohort.

Multivariable analysis for factors associated with SFRT among uncomplicated metastases and ≤ 5 fraction RT among all bone metastases are presented in Table 2 and Table 3, respectively. After adjusting for co-variables and clustering by center, both models demonstrated that the year of treatment (either as a continuous or categorical variable) was significantly associated with the use of SFRT and ≤ 5 fraction RT. In both models, a longer distance to the treating facility, higher baseline fatigue, treatment site other than spine, and fewer physician years in practice predicted shorter treatment courses. Among uncomplicated metastases, patients requiring treatment to more than one site had lower odds of receiving SFRT. After adjusting for clustering, neither primary histology nor planning type were associated with shorter course use for uncomplicated

metastases. However, among all metastases, there were lower odds of ≤ 5 fraction treatment for breast histology and higher odds of ≤ 5 fraction treatment with the use of forward planning. Uncomplicated metastasis, retreatment, and palliative intent independently predicted use of ≤ 5 fractions. Patients greater than 80 years of age and patients with ECOG performance status ≥ 2 were more likely to receive ≤ 5 fractions.

Discussion:

These results highlight the complexity of decision-making in the treatment of bone metastases. We continue to observe varied practice within the statewide quality consortium; however, we have noted a trend over time towards the utilization of fewer fractions for RT for bone metastases, consistent with the consortium's quality goals. We previously reported that the use of SFRT had increased from 15% to 28% among uncomplicated bone metastases within the first year of metric introduction.¹⁶

While not independently significant after adjusting for clustering, the significance of year as both a continuous and categorical (before vs. after quality measure introduction) variable on multivariable analysis for the use of 5 or fewer fractions suggests a pre-existing time trend driving increased adoption of shorter treatments and the measure was associated with an additional, immediate increase in use beyond what would be expected from the trend alone. Our observation period included the COVID-19 pandemic, with the launch of the SFRT quality initiative just months before the pandemic impacted daily practice. The COVID-19 pandemic was a driver of the use of hypofractionation across multiple disease sites, including bone metastases, to reduce possible patient exposure to the novel coronavirus.²²⁻²⁴ Some evidence suggests a trend towards increased use of fewer fractions for bone metastasis pre-dating the

pandemic, with one institution in our state reporting an estimated inflection point in 2015.²⁵ It is difficult to account for the impact of COVID-19 on fractionation in our consortium and to fully interpret the significance of treatment year in multivariable analyses, although the pandemic is reasonably considered a driver of the use of fewer fractions in the consortium alongside implemented quality metrics.

Initiatives supporting the use of fewer treatment fractions are designed to promote patient convenience, reduce financial toxicity (which has been shown to affect about half of patients receiving palliative RT), decrease the environmental impact of treatment, and support judicious use of healthcare resources.¹¹⁻¹⁴ Given this context, it is unsurprising that patients who traveled a greater distance were more likely to receive 5 or fewer fractions or SFRT in our analyses. Similarly, patients with higher baseline fatigue were more likely to receive fewer fractions. Notably, treatment facility type (academic vs. non-academic) was not independently associated with fractionation. Absolute differences in fractionation selection by facility type were small (<10%) in both analyses, highlighting the effective introduction of quality initiatives and incentive structure across varied practice settings.

We observed that patients undergoing reirradiation (reRT) were more likely to receive 5 fractions or fewer. With continuous improvements in cancer management and patients living longer with cancer, consideration of reRT is expected to increasingly drive decision-making and is not only relevant in the selection of fractionation for reRT to optimize organ at risk (OAR)-sparing versus target dose, but also relevant in the upfront setting with consideration of the durability of response and the ability to re-treat the same location following initial fractionation.^{1,26-28}

In all patients, forward planning was associated with higher odds of receiving 5 fractions or fewer, independent of the presence of uncomplicated metastasis. This is difficult to further characterize or explain with the available data. Forward planning may be used to deliver SFRT to complicated metastases in addition to uncomplicated metastasis, which was a well-represented fractionation in this cohort. Similarly, utilization of forward planning and fewer fractions in conjunction can aid with delivery of expedient RT for palliation, which was a well-represented indication for RT in the cohort assessed for ≤ 5 fraction treatment.

In our assessment of the use of 5 fractions or fewer among all patients, SBRT plans were omitted given these were anticipated to all be delivered in 5 fractions or fewer. Given the incentive structure applied to reward quality consortium participation and meeting quality metrics, some practices achieved exemption from BCBSM prior authorization. We do not characterize here the use of SBRT in such a structure, although this would expectedly confound any analysis and limit generalizability to the greater United States. Given the exclusion of SBRT plans in our analysis of ≤ 5 fractions, and observations of increased use of SBRT over time in our consortium, overall rates of plans delivering 5 fractions or less are higher than reported in this manuscript, especially in more recent years.

Stereotactic approaches may be used more frequently for patients with oligometastatic disease, to prevent skeletal events, or to decrease planning treatment volume margin in the setting of reRT or adjacency of critical OARs. With the increasing role of stereotactic approaches, inclusion of stereotactic treatments in future analyses will be of importance, including the examination of treatment intent and characterizing the use of appropriate OAR delineation and constraints for stereotactic plans.

Notably, histology did predict use of ≤ 5 fractions in our analysis; higher biologically effective dose afforded with treatment in excess of 5 fractions or stereotactic approaches may be differentially preferred for radioresistant histology.¹ Patient sex was not included in our multivariable models, with primary site more likely explanation for differences in treatment by sex given prostate cancer is sex-specific and breast cancer predominantly occurs in females. Additionally, the predisposition for micrometastatic and/or polymetastatic states by histology (e.g. breast cancer) or prognosis and availability of next-line systemic therapy in these states by histology may influence provider decision-making. While we assessed for number of regions treated in each episode, this does not necessarily reflect total systemic disease burden.

A post-pandemic quality initiative involving knowledge dissemination, personalized feedback, and eConsult availability, but without payer involvement, demonstrated improvement over time, yet the post-implementation timeframe was not independently associated with adoption of shorter fractionation.²⁹ Conversely, knowledge transfer campaigns have effectively increased the use of SFRT for bone metastasis within the Canadian health system.³⁰ The MROQC has established a symbiotic partnership between payer and providers to provide incentivized high-quality and high-value care to cancer patients in the state of Michigan and may serve as a model for delivery in other states. Strategic inclusion of fractionation and other dosimetric considerations in quality metrics and knowledge output from the consortia spans all cancer types included in the consortium.^{19,31-34} Metrics within the consortium are measured for all enrolled patients, not just those insured by BCBSM. Similar initiatives span multiple disciplines in our state, suggesting that quality consortia models similar to MROQC's have applicability beyond radiation oncology.³⁵⁻³⁷

Limitations of these data include patients limited to a single state in the continental United States at participating facilities. However, with prospectively collected data from a large cohort of patients in a state that is geographically, socioeconomically, and racially diverse we anticipate that these data will be useful beyond the geographic borders of our quality consortium.

In conclusion, we observed that radiation fractionation is complex and multifactorial, reflecting the intricacies involved in decision-making for the treatment of bone metastases with RT. We observed increasing utilization of fewer fractions over time, consistent with the successful implementation of quality measures and the sustained influence on practice within the consortium's incentive structure.

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Table 1: Clinical, patient, and facility characteristics for all patients enrolled with exclusion of SBRT plans. Missing data are excluded. P-values generated via chi-square test. NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer, PFS = progression-free survival, ECOG = Eastern Cooperative Oncology Group, RT = radiation therapy, CNS = central nervous system.

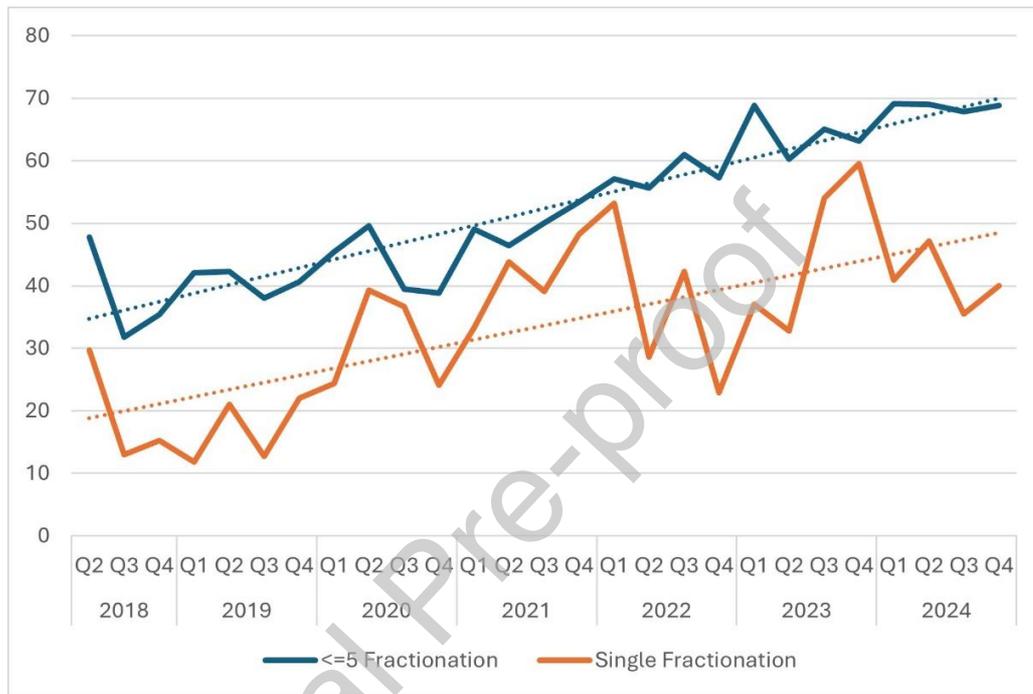


Figure 1: Trends in the percentage of RT plans delivering ≤ 5 and single fractions during the observation period.

Table 2: Multivariable logistic regression and random intercept analysis to adjust for clustering for factors associated with receipt of single-fraction radiation therapy among patients with uncomplicated bone metastases. Lung primary includes both small cell and non-small cell lung cancer. Melanoma was excluded from the analysis due to the small number of patients representing this primary site.

Table 3: Multivariable logistic regression and random intercept analysis to adjust for clustering for factors associated with receipt of ≤ 5 fraction radiation therapy. Lung primary includes both small cell and non-small cell lung cancer. PFS = progression-free survival, ECOG = Eastern Cooperative Oncology Group.

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Table 1

	All plans	Plans >5 fractions	Plans <=5 fractions	P-Value	Un-complicated Metastases	Plans >1 fraction	Plans =1 fraction	P-Value
	N (column %)	N (row %)	N (row %)		N (column %)	N (row %)	N (row %)	
Number of Plans	4832	2215	2617		1465	968	497	
Number of Patients	3247	1775	1777		1105	761	401	
Patient/Clinical Characteristics								
Age				<0.0001				0.35176
<=59	1135(23.5%)	560(49.3%)	575(50.7%)		339(23.1%)	235(69.3%)	104(30.7%)	
60-69	1597(33.1%)	752(47.1%)	845(52.9%)		454(31.0%)	303(66.7%)	151(33.3%)	
70-79	1371(28.4%)	634(46.2%)	737(53.8%)		428(29.2%)	277(64.7%)	151(35.3%)	
80+	729(15.1%)	269(36.9%)	460(63.1%)		244(16.7%)	153(62.7%)	91(37.3%)	
Sex				0.2171				0.00172
Female	2401(49.7%)	1122(46.7%)	1279(53.3%)		744(50.8%)	520(69.9%)	224(30.1%)	
Male	2431(50.3%)	1093(45.0%)	1338(55.0%)		721(49.2%)	448(62.1%)	273(37.9%)	
Race				0.418				0.34464
White	3998(82.7%)	1824(45.6%)	2174(54.4%)		1210(82.6%)	795(65.7%)	415(34.3%)	
Black	609(12.6%)	284(46.6%)	325(53.4%)		187(12.8%)	130(69.5%)	57(30.5%)	
Other	155(3.2%)	79(51.0%)	76(49.0%)		36(2.5%)	20(55.6%)	16(44.4%)	
Unknown	70(1.4%)	28(40.0%)	42(60.0%)		32(2.2%)	23(71.9%)	9(28.1%)	
Primary cancer site				0.003				0.00228
Breast Cancer	1489(30.8%)	725(48.7%)	764(51.3%)		485(33.1%)	352(72.6%)	133(27.4%)	
Melanoma	80(1.7%)	30(37.5%)	50(62.5%)		10(0.7%)	8(80.0%)	2(20.0%)	
NSCLC	1445(29.9%)	646(44.7%)	799(55.3%)		418(28.5%)	275(65.8%)	143(34.2%)	
Prostate Cancer	1244(25.7%)	566(45.5%)	678(54.5%)		403(27.5%)	246(61.0%)	157(39.0%)	
Renal Cell Cancer	352(7.3%)	169(48.0%)	183(52.0%)		67(4.6%)	40(59.7%)	27(40.3%)	
SCLC	222(4.6%)	79(35.6%)	143(64.4%)		82(5.6%)	47(57.3%)	35(42.7%)	
Distance from site (miles)				0.2478				0.22034
1st tercile (0-7)	1685(35.0%)	799(47.4%)	886(52.6%)		535(36.6%)	362(67.7%)	173(32.3%)	
2nd tercile (8-19)	1616(33.6%)	732(45.3%)	884(54.7%)		508(34.8%)	343(67.5%)	165(32.5%)	
3rd tercile (>19)	1515(31.5%)	676(44.6%)	839(55.4%)		417(28.6%)	262(62.8%)	155(37.2%)	
Planning type				<0.0001				0.00331

Forward planning	4340(90.0%)	1930(44.5%)	2410(55.5%)		1271(86.9%)	821(64.6%)	450(35.4%)	
Hybrid technique	2(0.0%)	1(50.0%)	1(50.0%)		-	-	-	
Inverse planning	478(9.9%)	276(57.7%)	202(42.3%)		191(13.1%)	144(75.4%)	47(24.6%)	
Uncomplicated bone metastasis				<0.0001				
Complicated	3346(73.2%)	1682(50.3%)	1664(49.7%)		-	-	-	
Uncomplicated	1222(26.8%)	406(33.2%)	816(66.8%)		1465(100%)	968(66.1%)	497(33.9%)	
Opioids use				0.0217				0.43648
No	1183(27.3%)	588(49.7%)	595(50.3%)		364(27.1%)	249(68.4%)	115(31.6%)	
Yes	3153(72.7%)	1444(45.8%)	1709(54.2%)		981(72.9%)	649(66.2%)	332(33.8%)	
Primary Treatment Intent				<0.0001				-
Palliation of Existing Symptoms	3267(68.2%)	1299(39.8%)	1968(60.2%)		1465(100.0%)	968(66.1%)	497(33.9%)	
Curative intent or improvements in PFS	69(1.4%)	32(46.4%)	37(53.6%)		-	-	-	
Durable local control	859(17.9%)	502(58.4%)	357(41.6%)		-	-	-	
Treatment of existing pathological fracture	314(6.6%)	198(63.1%)	116(36.9%)		-	-	-	
Treatment of spinal cord compression	279(5.8%)	166(59.5%)	113(40.5%)		-	-	-	
Anatomic site treated				<0.0001				<0.0001
Hip/Pelvis/Femur	1667(34.5%)	738(44.3%)	929(55.7%)		551(37.6%)	345(62.6%)	206(37.4%)	
Shoulder/Humerus/Scapula/Rib/Sternum/Skull	1216(25.2%)	449(36.9%)	767(63.1%)		423(28.9%)	240(56.7%)	183(43.3%)	
Spine	1949(40.3%)	1028(52.7%)	921(47.3%)		491(33.5%)	383(78.0%)	108(22.0%)	
ECOG >=2				<0.0001				0.7617
<2	2937(66.9%)	1418(48.3%)	1519(51.7%)		977(72%)	641(65.6%)	336(34.4%)	
≥2	1451(33.1%)	578(39.8%)	873(60.2%)		380(28%)	246(64.7%)	134(35.3%)	
Fatigue at baseline, Grade				0.0002				0.00742
0-1	3379(73.5%)	1613(47.7%)	1766(52.3%)		1049(74.1%)	707(67.4%)	342(32.6%)	
≥2	1217(26.5%)	494(40.6%)	723(59.4%)		367(25.9%)	219(59.7%)	148(40.3%)	
Systemic therapy <4 weeks prior to RT				0.164				0.16501
No	2070(43.0%)	972(47.0%)	1098(53.0%)		558(38.2%)	357(64.0%)	201(36.0%)	
Yes	2746(57.0%)	1234(44.9%)	1512(55.1%)		902(61.8%)	609(67.5%)	293(32.5%)	
CNS or Visceral Disease				0.1219				0.01355
No	1934(41.8%)	905(46.8%)	1029(53.2%)		694(48.1%)	481(69.3%)	213(30.7%)	

Yes	2690(58.2%)	1197(44.5%)	1493(55.5%)		749(51.9%)	473(63.2%)	276(36.8%)	
Number of Regions treated				0.9195				0.1015
1	2676(56.6%)	1226(45.8%)	1450(54.2%)		847(57.8%)	545(64.3%)	302(35.7%)	
≥2	2054(43.4%)	938(45.7%)	1116(54.3%)		618(42.2%)	423(68.4%)	195(31.6%)	
Retreatment				0.0002				-
No	4345(89.9%)	2031(46.7%)	2314(53.3%)		1465(100%)	968(66.1%)	497(33.9%)	
Yes	487(10.1%)	184(37.8%)	303(62.2%)		-	-	-	
Facility Characteristics								
Facility Type				0.0386				0.05306
Non-academic	3818(79.0%)	1721(45.1%)	2097(54.9%)		1215(82.9%)	816(67.2%)	399(32.8%)	
Academic	1014(21.0%)	494(48.7%)	520(51.3%)		250(17.1%)	152(60.8%)	98(39.2%)	
Physician Years of Practice				<0.0001	304(20.8%)	171(56.3%)	133(43.8%)	0.00025
0-10 years	1399(29.0%)	569(40.7%)	830(59.3%)		466(31.8%)	307(65.9%)	159(34.1%)	
11-20 years	1371(28.4%)	592(43.2%)	779(56.8%)		316(21.6%)	224(70.9%)	92(29.1%)	
21-30 years	875(18.1%)	448(51.2%)	427(48.8%)		379(25.9%)	266(70.2%)	113(29.8%)	
>30 years	1187(24.6%)	606(51.1%)	581(48.9%)		304(20.8%)	171(56.3%)	133(43.8%)	

Table 2

Variable	Multivariable analysis				Random Intercept Analysis			
	OR	95% Confidence limits		p-value	OR	95% Confidence limits		p-value
Year								
2018-2019	(ref)				(ref)			
2020-2024	3.327	2.392	4.626	<0.0001	12.142	5.081	29.015	<0.0001
Primary Malignancy								
Lung	(ref)				-	-	-	-
Breast	0.709	0.528	0.952	0.0055	-	-	-	-
Prostate	1.146	0.851	1.544	0.1473	-	-	-	-
Renal Cell Carcinoma	1.095	0.623	1.926	0.563	-	-	-	-
Distance to treatment center (continuous, unit 10 miles)	1.094	1.029	1.162	0.0041	1.261	1.09	1.458	0.0018
Planning type								
Inverse planning	(ref)				-	-	-	-
Forward planning	1.736	1.183	2.549	0.0048	-	-	-	-
Anatomic site treated:								
Spine	(ref)				(ref)			
Hip/Pelvis/Femur	2.286	1.695	3.083	0.0495	5.367	3.009	9.57	<0.0001
Shoulder/Humerus/Rib/Skull/Other	3.206	2.338	4.397	<0.0001	9.526	4.847	18.72	<0.0001
Fatigue at baseline								
Grade 0-1	(ref)				(ref)			
Grade ≥2	1.53	1.169	2.003	0.0019	2.325	1.246	4.336	0.0081
Number of Regions treated								
1	(ref)				(ref)			
≥2	0.714	0.558	0.912	0.0071	0.397	0.223	0.704	0.0016
Physician Years of Practice								
0-10	(ref)				(ref)			
11-20	0.61	0.44	0.847	0.3577	0.442	0.198	0.988	0.0466
21-30	0.536	0.406	0.846	0.2515	0.45	0.184	1.1	0.0799
>30	0.556	0.392	0.788	0.0846	0.337	0.149	0.764	0.0093

Table 3

Variable	Multivariable Analysis				Random Intercept Analysis			
	OR	95% Confidence Limits		P-Value	OR	95% Confidence Limits		P-Value
Year (continuous)	1.211	1.118	1.312	<0.0001	1.508	1.403	1.621	<0.0001
Year								
2018-2021	(ref)				-	-	-	-
2022-2024	1.395	1.054	1.846	0.02				
Age								
≤59	(ref)				(ref)			
60-69	1.245	1.028	1.508	0.6926	1.221	0.901	1.653	0.1971
70-79	1.224	0.999	1.499	0.5112	1.2	0.878	1.639	0.2522
80+	1.729	1.346	2.22	0.0001	1.898	1.294	2.783	0.0011
Primary Malignancy								
Lung	(ref)				(ref)			
Breast	0.753	0.632	0.899	0.0163	0.67	0.503	0.892	0.0062
Melanoma	1.301	0.749	2.257	0.1185	1.241	0.51	3.023	0.634
Prostate	0.831	0.685	1.008	0.2668	0.765	0.573	1.021	0.0689
Renal Cell Carcinoma	0.803	0.605	1.067	0.2644	0.679	0.453	1.019	0.0615
Distance to treatment center (continuous, unit of 10 miles)	1.045	1.013	1.078	0.0056	1.072	1.021	1.125	0.0049
Planning type								
Inverse planning	(ref)				(ref)			
Forward planning	1.678	1.299	2.169	<0.0001	2.143	1.499	3.064	<0.0001
Uncomplicated metastasis								
No	(ref)				(ref)			
Yes	1.906	1.585	2.292	<0.0001	2.478	1.882	3.263	<0.0001
Treatment Intent								
Palliation for existing symptoms	(ref)				(ref)			
Curative intent or improvements in PFS	0.913	0.496	1.678	0.2228	0.991	0.4	2.454	0.9842
Durable local control	0.59	0.481	0.723	0.1775	0.499	0.37	0.673	<0.0001
Treatment of existing pathologic fracture	0.444	0.333	0.593	0.0013	0.317	0.209	0.48	<0.0001
Treatment of spinal cord compression	0.581	0.429	0.787	0.2711	0.344	0.204	0.581	<0.0001
Anatomic site treated:								
Spine	(ref)				(ref)			
Hip/Pelvis/Femur	1.408	1.192	1.663	0.9592	1.651	1.343	2.03	<0.0001
Shoulder/humerus/rib/skull/other	1.997	1.656	2.408	<0.0001	2.524	1.969	3.234	<0.0001
Fatigue at baseline								
Grade 0-1	(ref)				(ref)			
Grade ≥2	1.573	1.332	1.858	<0.0001	1.689	1.307	2.182	<0.0001
ECOG								
0-1	(ref)				(ref)			
≥2	1.275	1.089	1.494	0.0026	1.484	1.182	1.862	0.0007
Retreatment								
No	(ref)				(ref)			
Yes	1.879	1.464	2.413	<0.0001	2.058	1.474	2.874	<0.0001
Physician Years of Practice								
0-10	(ref)				(ref)			
11-20	0.842	0.695	1.02	0.0982	0.834	0.612	1.138	0.2522
21-30	0.653	0.525	0.812	0.031	0.607	0.425	0.866	0.0059
>30	0.611	0.501	0.743	0.0005	0.538	0.394	0.736	0.0001

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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