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Basic Original Report

Recommendations for Single-Fraction Radiation Therapy and Stereotactic Body Radiation Therapy in Palliative Treatment of Bone Metastases: A Statewide Practice Patterns Survey

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Abstract

Purpose: Single-fraction (SF) radiation therapy is effective and convenient for patients with painful noncomplex bone metastases. Prior survey results reported a low recommendation of SF radiation therapy in the US. We sought to assess contemporary treatment recommendations for the management of bone metastases among diverse physicians participating in a statewide quality consortium.

Methods and Materials: Members of the Michigan Radiation Oncology Quality Consortium were surveyed between April and May 2017. Physicians rated the importance of 31 variables on their choice of dose fractionation. The survey also covered 7 patient scenarios.

Results: Fifty-six physicians responded who were practicing at 18 of 20 centers surveyed. Respondents recommended 23 dose-fractionation schedules across the 7 scenarios. Highest-rated

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factors considered when choosing a dose fractionation regimen were performance status, prognosis, spinal cord compression, and prior radiation therapy. Recommendations for SF overall were uncommon (16.1%). On multivariable analysis, factors associated with SF use included academic employment (odds ratio [OR] 2.04; 95% CI, 1.02-4.08; $P = .044$) and higher palliative case volume (OR 2.59; 95% CI, 1.45-4.63; $P = .001$). Stereotactic body radiation therapy (SBRT) was recommended in 16.4% of scenarios overall, and on multivariable analysis, significant predictors for SBRT use were academic employment (OR 2.99; 95% CI, 1.39-6.44; $P = .005$), more recent residency completion (OR 4.37; 95% CI, 1.26-15.17; $P = .02$), spine location (OR 12.54; 95% CI, 3.96-39.68; $P < .001$), and prior radiation therapy (OR 26.67; 95% CI, 7.86-90.57; $P < .001$). SF rates were higher than in a survey reported in 2009 (16.1% vs 9.4%, $P = .0004$).

Conclusions: SF radiation therapy remains uncommonly recommended, although it may be recommended more now than it was 10 years ago despite the increased utilization of SBRT. We identify multiple key drivers in physician decision making affecting SF recommendations that have not been addressed by prior level one evidence. Further research with evidence-based recommendations to clarify the role of SF and SBRT in management of patients with bony metastases are needed.

Introduction

The use of radiation therapy (RT) for the treatment bone metastases is common. Indications include palliation of pain, prevention of pathologic fracture, amelioration of symptoms of spinal cord compression, or more recent evidence over the past decade demonstrating benefit of metastasis-directed therapy and use of higher doses via stereotactic body radiation therapy (SBRT) to provide durable local control and potentially overall survival benefit.[1] The American Society of Radiation Oncology (ASTRO) guidelines have addressed the use of palliative radiation therapy solely in the context of simple, or noncomplex, bone metastasis and generally recommend the use of a single fraction (SF) of 8 Gy for these patients.[2] This recommendation derives from multiple randomized trials that have demonstrated similar short-term pain response from SF compared with multifraction regimens,[3,4] including in poor-prognosis spinal cord compression.[5] Additionally, SF is more cost-effective and convenient.[6,7]

Despite these recommendations, prior surveys and studies of practice patterns in large databases assessing the use of SF have raised concerns about underutilization of this regimen,[8-10] more so in the US than in other nations.[8,11] The largest physician survey to our knowledge was reported in 2009 and showed a wide variety of palliative dose-fractionation schedules recommended with low SF utilization. Over the past decade, intervening publications have supported SF use, as have updated guidelines from ASTRO. However, additional indications for radiation therapy to bone metastases beyond that of painful uncomplicated bone metastases have also arisen, with numerous completed and ongoing Radiation Therapy Oncology Group and NRG Oncology trials in this space using SBRT (NCT02206334, NCT02364557). Thus, we sought to assess the contemporary acceptance of SF and SBRT use in a statewide survey of radiation oncologists in Michigan.

Methods and Materials

Participants

Twenty institutions across the state of Michigan participating in the Michigan Radiation Oncology Quality Consortium (MROQC), representing approximately 80% of the radiation oncology volume in the state, were provided a survey (see appendix) to distribute to radiation oncologists in their practices who treat patients with metastatic disease to assess factors that influence their choice of dose fractionation and to assess their preferred treatment method for 7 patient scenarios. The surveys were provided on April 5, 2017, through the software company Qualtrics (Seattle, WA), and data collection was stopped on May 22, 2017. A total of 95 physicians were invited to participate, and 56 participants responded (59%). Eighteen of the 20 centers completed the survey, and the majority of participants answered all questions (99.7% of questions related to treatment factors were answered, and 98.9% of questions related to the scenarios were answered). Missing data was excluded from the analysis. Funding was provided by Blue Bross Blue Shield of Michigan and Blue Care Network, and all authors are members of MROQC.

Survey measures

The questionnaire used was intentionally modeled on a previous study from Fairchild et al[8] to allow comparison of identical scenarios. The survey included the following

components: (1) respondent characteristics, (2) 31 factors influencing the choice of dose fractionation schedules, and (3) 7 hypothetical scenarios. The dose fractionation schedule selected was handwritten in response to each scenario below. Respondents ranked factors as being "a lot," "somewhat," "a little," or "not at all" important in the selection of dose fractionation schemes. A full description of the scenarios and the survey are in Appendix E1 (available online at https://doi.org/10.1016/j.prro.2019.07.005) and are summarized below.

1. Scenario 1 described a patient with breast cancer with painful thoracic spine metastases (case 1 in survey).
2. Scenario 2 described a patient with prostate cancer with both a painful shoulder metastasis and a painless proximal femur metastasis; the scenario asked about treatment of the painful shoulder metastasis (case 2A in survey).
3. Scenario 3 described a patient with prostate cancer with both a painful shoulder metastasis and a painless proximal femur metastasis; the scenario asked about treatment of the painless proximal femur metastasis (case 2B in survey).
4. Scenario 4 described a patient with non-small cell lung cancer with a painful lytic lesion in the lumbar spine (case 3A in survey).
5. Scenario 5 described a patient with non-small cell lung cancer with a painful lytic lesion in the lumbar spine with features of neuropathic pain (case 3B in survey).
6. Scenario 6 described a patient with prostate cancer with both a painful previously irradiated thoracic spine metastasis and a painful previously irradiated right hip metastasis; the scenario asked about retreatment of the thoracic spine metastasis (case 4A in survey).
7. Scenario 7 described a patient with prostate cancer with both a painful previously irradiated thoracic spine metastasis and a painful previously irradiated right hip metastasis; the scenario asked about retreatment of the right hip metastasis (case 4B in survey).

Covariables

A center was defined as an academic institution if the treating radiation oncologists directly supervised residents. The year of respondent residency completion was categorized by decade (1980-1989, 1990-1999, 2000-2009, or 2010 and after). Participants selected the proportion of palliative cases seen in practice as less than 5%, 5% to 25%, or greater than 25% of total case volume. Scenarios were categorized into spine and nonspine lesions. Features in each scenario were coded based on the explicit description of the presence of features of pain, neuropathic pain, prior RT, or lytic features seen on imaging. Scenarios that explicitly described more than 1 metastatic lesion in the description were categorized as having other metastatic sites.

Statistical analysis

Descriptive statistical methods summarized factors associated with dose fractionation decision, which were separated into tumor, patient, and provider factors. Important factors were selected on the basis of the number of physicians that rated the factor as influencing their dose fractionation schedule "a lot." Pooled response rates of SF and SBRT use were assessed by evaluating the combination of all responses to all 7 scenarios. To determine predictors of SF (8 Gy in 1 fraction) recommendation, in addition to SBRT recommendation, univariable and multivariable binary logistic regression models were constructed. Significant variables on univariable analysis were included in the multivariable model. Additionally, position in an academic program for respondents[12] and spinal location of metastasis[13] were selected for inclusion in the multivariate model based on prior data suggesting the impact of these factors on SF use. Results were compared with prior survey data[8] using Fisher exact test. The data were analyzed using the Statistical Package for Social Sciences, version 25 (SPSS, Chicago, IL). Two-sided P values ≤ 0.05 were considered statistically significant.

Results

Respondents included practicing radiation oncologists in the state of Michigan. Of the 20 centers invited to participate, 18 centers completed surveys (90%) for a total of 56 individual participants. Baseline characteristics of respondents are available in Table 1. The majority of respondents were male (82%), which is consistent with

Table 1 Baseline characteristics

		n (%)
Sex, male		46 (82)
Year residency completed		
	1980-1989	8 (14)
	1990-1999	15 (27)
	2000-2009	14 (25)
	2010 +	19 (34)
Patients treated palliatively over past 6 months, %		
	<5	4 (7)
	5-25	29 (53)
	26-50	22 (40)
Academic physicians		16 (29)
Median time to start palliative treatment from simulation in days (range)		2.5 (0-7)

the overall male dominance of the field of radiation oncology in the United States[14]; 34% completed residency in 2010 or later and less than one-third of respondents were academic physicians, again consistent with national trends.[8,14]

Fifty percent of respondents completed residency training in Michigan, and 68% completed training in the Midwest. The majority of respondents indicated that palliative radiation treatments composed a significant proportion of their practices, with 53% having between 5% and 25% of their practice consisting of palliative treatments and 40% having between 26% and 50% palliative cases.

Patient factors were the most important driver of selecting a dose fractionation schedule, which included performance status and prognosis. The most important tumor factors included spinal cord compression or impending spinal cord compression. Important treatment factors included prior radiation or nearby critical normal tissues. Other miscellaneous factors of importance included published evidence and physician experience (Fig 1).

There was variable recommendation for the use of palliative RT, which ranged from 100% (in scenario 2) to only 67% (in scenario 3, Table 2). A total of 23 different dose-fractionation schedules were offered across the 7 scenarios, ranging from 8 Gy in 1 fraction to 44 Gy in 22 fractions. The median absolute dose offered was between 20 and 30 Gy for all scenarios. The most common dose fractionation schedules selected for each scenario are in Figure E1 (available online at https://doi.org/10.1016/j.prro.2019.07.005). The 2 most common dose-fractionation schemes were 30 Gy in 10 fractions (46.8%) and 20 Gy in 5 fractions (17.9%), and 4.3% of dose fractionation schemes used greater than 10 fractions.

Respondents infrequently recommended SF, with 8 Gy in 1 fraction chosen by <33% of respondents for each scenario (range, 3.7%-32.1%) and a total of 16.1% for the entire group. The highest proportion of SF utilization was in the management of a painful shoulder metastasis

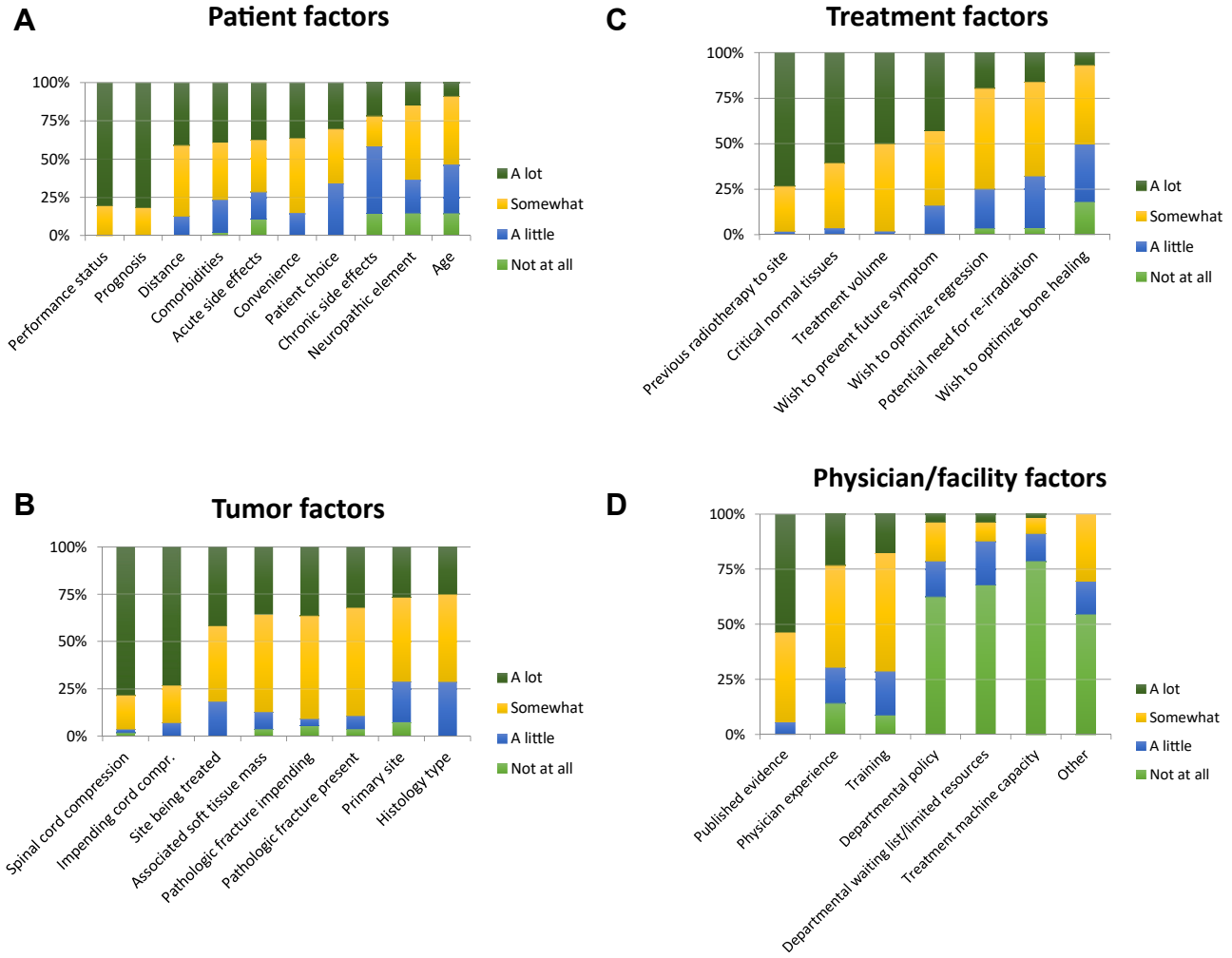

Figure 1 Factors associated with selection of dose fractionation schemes. Stacked bar chart of the factors assessed by physicians as being "a lot," "somewhat," "a little" or "not at all" important in selection of dose-fractionation schemes. (A) Patient factors; (B) tumor factors; (C) treatment factors; and (D) physician and facility factors.

Table 2 Dose fractionation characteristics by scenario

	Radiation recommended		Dose fractionation used			Technique offered				
	Number who would not treat, n (%)	Number who would treat, n (%)	SF used, n (%)	Median, Gy/fractions	Range, Gy/fractions	2D, n (%)	3D without MLCs, n (%)	3D with MLCs, n (%)	IMRT/ VMAT, n (%)	SBRT, n (%)
Scenario 1	2 (4)	54 (96)	4 (7)	30/10	8/1-44/22	15 (28)	15 (28)	21 (39)	3 (6)	2 (4)
Scenario 2	0 (0)	56 (100)	18 (32)	20/5	8/1-35/14	20 (36)	3 (5)	33 (59)	0 (0)	2 (4)
Scenario 3	18 (33)	37 (67)	8 (22)	20/5	8/1-35/14	11 (30)	2 (5)	24 (65)	0 (0)	0 (0)
Scenario 4	1 (2)	55 (98)	3 (5)	30/10	8/1-37.5/15	14 (25)	10 (18)	19 (35)	12 (22)	13 (25)
Scenario 5	2 (4)	54 (96)	2 (4)	30/10	8/1-37.5/15	13 (24)	8 (15)	24 (44)	9 (17)	11 (20)
Scenario 6	14 (25)	41 (75)	8 (22)	20/5	8/1-30/15	3 (7)	0 (0)	13 (32)	25 (61)	24 (60)
Scenario 7	17 (30)	39 (70)	10 (27)	25/10	8/1-35/14	9 (23)	0 (0)	24 (62)	6 (15)	3 (8)

Abbreviations: 3D = 3-dimensional conformal radiation therapy; IMRT = intensity modulated radiation therapy; MLCs = multileaf collimators; SBRT = stereotactic body radiation therapy; SF = single fraction; VMAT = volumetric modulated arc therapy.

(scenario 2). The 4 scenarios with spine metastases without prior treatment had the lowest incidence of SF recommendation, ranging from 5% to 7%.

Respondents were more likely to select advanced radiation techniques such as SBRT in scenarios with spinal metastases, including in scenarios of retreatment of spinal metastases (scenarios 4-6). Recommendation for SBRT was 16.4% overall (range 0%-60%, highest in retreatment of spinal metastases, scenario 6).

On univariable analysis, increased likelihood of SF RT recommendation was associated with the proportion of palliative cases seen in practice by the respondent (OR 2.2; 95% CI, 1.30-3.80; $P = .004$), prior radiation therapy of the hypothetical patient (OR 2.07; 95% CI, 1.09-3.92; $P = .026$), and other sites of metastatic disease noted in the scenario (OR 6.17; 95% CI, 2.90-13.14; $P < .001$); decreased likelihood of utilization of SF was associated with spine location of metastasis (OR 0.24; 95% CI, 0.13-0.46; $P < .001$), presence of neuropathic pain (OR 0.17; 95% CI, 0.04-0.72; $P = .016$), and the presence of lytic features (OR 0.17; 95% CI, 0.07-0.45; $P < .001$). On multivariable analysis, academic location of practice (OR 2.04; 95% CI, 1.02-4.08; $P = .044$) and proportion of palliative cases seen in practice remained significant (OR 2.59; 95% CI, 1.45-4.63, $P = .001$, Table 3) for increased recommendation of SF RT.

Predictors of SBRT recommendation were also examined. On univariable analysis, increased likelihood of utilization of SBRT was associated with academic location of practice (OR 2.36; 95% CI, 1.30-4.28; $P = .005$), year of residency completion (completion after 2009 compared with before 1990, OR 3.70; 95% CI, 1.22-11.24; $P = .021$), spine location of metastasis (OR 8.28; 95% CI, 3.20-21.39; $P < .001$), and prior radiation

Table 3 Uni- and multivariable analysis for single-fraction use

Variable	Univariable analysis				Multivariable analysis			
	OR	95% CI		*P* Value	AOR	95% CI		*P* Value
		Lower	Upper			Lower	Upper	
Respondent	1.012	0.994	1.031	.188				
Sex (male vs female)	0.66	0.28	1.53	.33				
Academic practice (vs community practice)	1.58	0.85	2.95	.148	2.04	1.02	4.08	**.044**
Year residency completed								
1980-1989	reference	-	-	-				
1990-1999	0.49	0.18	1.30	.151				
2000-2009	0.49	0.18	1.32	.158				
2010 +	1.14	0.48	2.70	.769				
% palliative cases in practice (ordinal)	2.22	1.30	3.80	**.004**	2.59	1.45	4.63	**.001**
Spine location (vs other sites)	0.24	0.13	0.46	**<.001**	0.79	0.26	2.38	.671
Pain (yes vs no)	0.66	0.28	1.54	.336				
Neuropathic pain (yes vs no)	0.17	0.04	0.72	**.016**	0.66	0.10	4.15	.654
Prior RT (yes vs no)	2.07	1.09	3.92	**.026**	0.92	0.38	2.24	.845
Other metastatic sites (yes vs no)	6.17	2.90	13.14	**<.001**	4.21	0.86	20.61	.076
Lytic lesion (yes vs no)	0.17	0.07	0.45	**<.001**	0.71	0.15	3.40	.669

Abbreviations: CI = confidence interval; OR = odds ratio; RT = radiation therapy.
Boldface indicates $P < .05$.

to site (OR 4.15; 95% CI, 2.26-7.64; $P < .001$). On multivariable analysis, academic location of practice (OR 2.99; 95% CI, 1.39-6.44; $P = .005$), year of residency completion (completion after 2009 compared with before 1990, OR 4.37; 95% CI, 1.26-15.17; $P = .02$), spine location of metastasis (OR 12.54; 95% CI, 3.96-39.68; $P < .001$), prior radiation (OR 26.67; 95% CI, 7.86-90.57; $P < .001$), and lytic lesion remained significant (OR 4.67; 95% CI, 1.47-14.84; $P = .009$, Table 4).

Frequency of recommending SF in the current study was compared with the study by Fairchild et al[8] using the same scenarios (Fig 2). Respondents in the present study more frequently recommended SF than US ASTRO members in the prior study (16.1% vs 9.4%, $P = .0004$). Analysis by scenarios showed that this difference was primarily driven by a 2-fold increase in SF recommendation for scenario 2 (32.1% vs 15.6%, $P = .0045$). Differences in all other scenarios were nonsignificant. Although the respondents and sample selection are not directly comparable between these studies, utilization of the same survey reflects the continued low recommendation of SF.

Discussion

This study offers a contemporary assessment of the dose fractionation schemes recommended for palliation of various common scenarios of bone metastases by radiation oncologists practicing in the US. The recommendation of SF remains low, ranging from 4% to 32% in this survey. The recommendation of multifraction regimens remained more common, with 30 Gy in 10 fractions and 20 Gy in 5 fractions used most often. We validated multiple previous covariables that appear to drive SF recommendation or its avoidance. We also identified multiple novel predictors of SBRT recommendation.

These results add to the existing literature regarding the treatment of patients with bone metastases. Although other practice pattern studies have been reported, physician surveys are particularly important in identifying the drivers of patterns of care. The publication of guidelines by ASTRO supporting SF use[2] presumably would drive increased utilization in the United States. However, previous analysis of practice patterns in Canada has shown that the publication of guidelines endorsing the use of SF in uncomplicated bone metastases resulted in only a transient increase in the use of SF.[15] Similarly, we found only small increase in the rate of SF recommendation in this study compared with a previous survey from 2009 despite the updated ASTRO guidelines strongly endorsing SF use. This is consistent with trends nationally.[16]

Many of the drivers that influence dose fractionation that we identified are importantly not well represented or addressed by the prior randomized trials and meta-analyses conducted in the 1970s to the 1990s. For example, prognosis and performance status are tightly correlated and are one of the strongest drivers for use of SF RT. The prognosis of patients in many of the trials conducted over 30 years ago had an overall survival of less than 6 months. Currently, many patients with bone metastases live multiple years, and the median survival for hormone-sensitive metastatic prostate cancer is nearly 5 years.[17] Thus, the known short-term and temporary 3-month response rates from the randomized evidence with SF RT may not be ideal for patients with favorable prognosis. Additionally, recent data has supported clinically meaningful improvements in progression-free

Table 4 Uni- and multivariable analysis for SBRT use

Variable	Univariable analysis				Multivariable analysis			
	OR	95% CI		*P* Value	AOR	95% CI		*P* Value
		Lower	Upper			Lower	Upper	
Respondent	1.000	0.982	1.018	.980				
Sex (male vs female)	0.86	0.40	1.88	.71				
Academic practice (vs community practice)	2.36	1.30	4.28	**.005**	2.99	1.39	6.44	**.005**
Year residency completed								
1980-1989	reference	-	-	-	reference	-	-	-
1990-1999	1.58	0.48	5.21	.454	2.11	0.54	8.22	.28
2000-2009	1.14	0.33	3.93	.836	1.08	0.27	4.28	.91
2010 +	3.70	1.22	11.24	**.021**	4.37	1.26	15.17	**.02**
% palliative cases in practice (ordinal)	0.70	0.43	1.13	.14				
Spine location (vs other sites)	8.28	3.20	21.39	**<.001**	12.54	3.96	39.68	**<.001**
Pain (yes vs no)	-	-	-	-				
Neuropathic pain (yes vs no)	1.36	0.65	2.83	.419				
Prior RT (yes vs no)	4.15	2.26	7.64	**<.001**	26.67	7.86	90.57	**<.001**
Other metastatic sites (yes vs no)	1.07	0.60	1.91	.824				
Lytic lesion (yes vs no)	1.80	1.00	3.25	**.052**	4.67	1.47	14.84	**.009**

Abbreviations: CI = confidence interval; OR = odds ratio; RT = radiation therapy.
Boldface indicates $P < .05$.

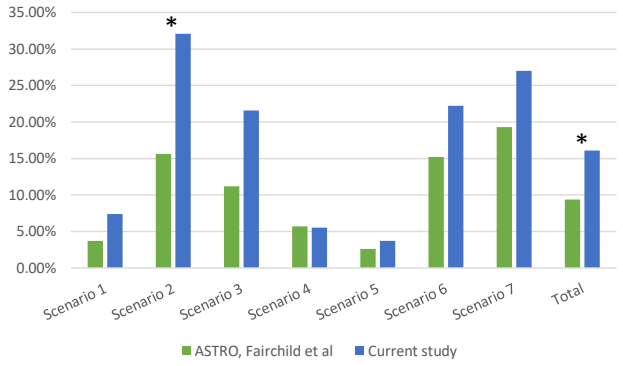

Figure 2 Comparison of single-fraction recommendation between prior survey published by Fairchild et al focusing on the subgroup representing the American Society of Radiation Oncology and the current study. *$P < .05$.

survival and even overall survival from the treatment of limited sites of bone metastasis using SBRT.[1,18] For this reason and others, there is an increased focus on the importance of local control, which is reflected in our survey of patients more commonly receiving SBRT for spine location where treatment failure could be more morbid. Although the use of SF in spinal metastases offers similar pain relief from the randomized trials as multifraction regimens, SF is associated with inferior local control and may be best suited for patients with poor expected survival.[13] In this survey, the recommendation of SF in spinal metastases remained low, potentially reflecting these concerns. Despite this, 95.7% of radiation oncologists queried in this survey used fractionation schemes of 10 fractions or less, consistent with widely recognized reasonable patterns of care such as Choosing Wisely.[19]

Unlike SF RT, the use of SBRT in palliative treatment of bone metastases has not been well-defined. Both retrospective and prospective data have shown that SBRT for bone metastases can offer excellent local control with low toxicity.[20-25] SBRT has been most well studied in spinal metastases, where the advantage of improved local control near the spinal cord is important. Our study shows high rates of willingness to use SBRT, with rates as high as 60% in some of the survey scenarios. An increased likelihood of offering SBRT was associated with employment in an academic site and more recent residency graduation among other factors, suggesting greater familiarity with SBRT in these populations. Thus, a barrier to using SBRT may be lack of training in providers trained before the increased utilization of SBRT for bone metastases. MROQC has the capability to evaluate this potential barrier and others. Given the surge in data suggesting potential survival benefits to using SBRT for patients with limited metastatic burden, this barrier needs to be addressed.

These survey results can be appropriately questioned because self-report in a series of idealized case scenarios may diverge from actual practice. Limitations of this study include its small size and geographic restriction in practice of the surveyed radiation oncologists, limiting generalizability. However, the results of this survey are highly consistent with a recent publication from our group of actual practice patterns for the treatment of bone metastases that found an overall use of SF RT in 8% of patients and 13% of patients who had uncomplicated bone metastases.[26] In practice there is much greater diversity in tumor histology, performance status, burden of metastatic disease, prior and concurrent therapies, and many other factors that are outside of routine case scenarios. Other drivers that were not addressed in this survey include payer models or the influence of financial incentives, which have been shown to affect practice patterns. Regardless, our survey indicates that a minority of patients are recommended SF RT, even for simple noncomplex bone metastasis, and these data provide a unique vantage point to help understand the drivers of these patterns of care.

In an effort to build further on the present work, MROQC has launched a prospective collection of data across its consortium for patients with bone metastases. MROQC is comprised of diverse practices from academia to private practice, variable department size, financial structure, insurance mix, and patient populations. It is the hope of the consortium to better understand real-time practice patterns and address some of the limitations and potential barriers.

Conclusions

In conclusion, recommendation for SF RT for bone metastases remains infrequent, albeit slightly more common than a decade ago, despite the presumed increased utilization of SBRT. We identify multiple key drivers in physician decision making affecting SF recommendations that have not been addressed by prior level one evidence. Further research with evidence-based recommendations to clarify the role of SF and SBRT are needed and may significantly affect practice.

Supplementary Material

Supplementary material for this article can be found at https://doi.org/10.1016/j.prro.2019.07.005.

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