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Research article

Are radiation oncologists following guidelines? An audit of practice in patients with uncomplicated bone metastases

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ABSTRACT

Background: Best-practice guidelines recommend single-fraction (SFRT) instead of multi-fraction radiation therapy (MFRT) for uncomplicated symptomatic bone metastases. SFRT is comparable to MFRT in relieving pain, convenient for patients, and cost-effective. Patterns of practice in Canada reveal that SFRT is underused, with significant variability across the country. We audited SFRT use and studied factors that may influence treatment decisions at a large academic tertiary care center in Quebec, Canada.
Methods: Patients who received radiotherapy for uncomplicated bone metastases between February 2014 and March 2015 were reviewed. Age, gender, primary histology, site of metastases and performance status were identified as potential factors affecting fractionation. These were explored by Fisher's test on univariate analysis and logistic regression for multivariate analysis. Retreatment rates were analyzed with cumulative incidence and compared with Gray's test.
Results: 254 radiotherapy courses were administered to 165 patients, 85.4% of which were delivered using a single fraction of 8 Gy. Patients age less than 70 years and those with breast histology were more likely to receive MFRT ($p = 0.04$; $p = 0.0046$). Performance status (ECOG) was a significant predictor of fractionation because of high correlations between young age, breast histology, and ECOG status ($p = 0.03$). Follow-up was too short in 40% of patients to derive definitive conclusions on retreatment.
Conclusions: In accordance with current guidelines, our audit confirms that use of SFRT in patients with uncomplicated bone metastases at our center is high. We identified that patient age, primary histology, and performance status influenced fractionation. Incorporation of this quality indicator into our performance dashboard will allow assessment of retreatment differences and other criteria that may also influence treatment choice.

Introduction and background

Painful bone metastases can significantly impair the quality of life in patients with advanced cancer. External beam radiation therapy is the mainstay of palliative management for these patients, with the goal of controlling pain, preserving function, and stabilizing bone [1,2]. Palliative radiotherapy improves symptoms in 50–80% of patients and relieves pain completely in up to one-third [2].

Multiple meta-analyses and systematic reviews have demonstrated equivalence between single- and multiple-fraction radiation therapy (SFRT and MFRT respectively) in terms of pain relief for uncomplicated bone metastases, although SFRT is associated with higher retreatment rates [3–6]. SFRT has been shown to be more convenient for patients in the palliative setting, with fewer treatment visits resulting in less time and financial burden for the patient [4]. In addition, SFRT is a cost-effective treatment modality for radiation oncology departments with both economic and service gains [7–9]. As a result, in 2011, the American Society for Radiation Oncology (ASTRO) first published guidelines advocating for the use of SFRT for all patients in pain with uncomplicated bone metastases [2,10]. Similarly, the Royal College of Radiologists in the UK recommend SFRT use for pain relief from bone metastases as a Grade A recommendation [11]. Doses of 8 Gray in 1 fraction have traditionally been recommended and most commonly compared to multi-fractionation. A recent review concluded that this dose produces better pain response than lower doses and

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should be the standard of care when used to compare alternate single fractionated doses [12].

Despite this, international patterns of practice reveal that many radiation oncologists are still prescribing multiple fraction regimens in this situation [13–15]. A Canadian study reported varying practices within the province of British Columbia where SFRT prescriptions varied from 25.5% to 74.3% amongst different treatment centers. Both patient and physician factors appeared to influence decision making [16]. Patient characteristics that were found to affect use of SFRT include treatment site and site of primary cancer. For physicians, professional affiliation, experience, and country of training also impacted the use of SFRT [13,16]. A national Canadian study reported significant variation between provinces, with 40.3% to 69% of patients with bone metastases receiving MFRT in 2013 [17].

As current data show a reluctance to adopt SFRT despite best-practice recommendations, we hypothesized that this would also be the case at the McGill University Health Centre (MUHC), a large university teaching hospital and cancer center with 15 full-time staff radiation oncologists with diverse backgrounds. Our radiation oncologists have trained in a number of countries and have been practicing for more than 15 years on average. This audit was therefore performed after the publication of these guidelines to evaluate radiation oncology practice for patients with uncomplicated bone metastases at our center.

Materials and methods

Data collection

All patients that received radiation therapy (RT) for uncomplicated bone metastases at the MUHC between February 1st 2014 and March 31st 2015 were included in this audit. We used the definition of uncomplicated bone metastases of *Cheon* et al., that is, those that are purely in the bone itself without extending into the surrounding soft tissue, and without pathological fracture or spinal cord compression [18]. Exclusion criteria therefore included the existence of pathological fracture, spinal cord or cauda equina compression, soft tissue extension as confirmed by review of physician notes and imaging studies for every patient. Patients who had previously received radiotherapy to the same area were also excluded.

Data obtained from the Varian Aria® electronic medical records system included RT date, dose, fractionation, and treatment site. Patients who received RT within the time period of the study were divided into those that received SFRT and those that received MFRT. The chart review included patient characteristics such as age, gender, primary histology, site of skeletal and other metastases, control of primary disease, and performance status at the time of RT prescription. Retreatment rates for both treatment regimens were collated. We did not include pain scores since this was a retrospective chart review and it was felt that pain scores were either too often missing or not graded on a reproductible scale to be used to generate reliable conclusions.

Statistical analysis

Patient age, gender, primary histology, presence of other metastases by site (lung, brain, liver, other), treatment site (spine or other), control of primary cancer and performance status were explored as potential factors predicting the choice of single vs. multi-fraction radiation regimen. Predictors of fractionation were explored by Fisher's test on univariate analysis. While we recognize that Fisher's exact test and Chi-squared test are both tests used to assess statistical significance in contingency tables, the Chi-squared test is an approximation used when computational resources are more limited and does not readily apply to some situations such as low cell values or extreme imbalances. Fisher's test does not have such constraints and can be applied to any contingency table; however, its main limitations are that it may be more conservative, and it is more computationally demanding. However, this did not pose a problem with our statistical package, SAS v9.4.

We also explored the association between pre-treatment characteristics and the choice of fractionation with multivariate logistic regression to try to correct for imbalances in the treatment populations inherent in retrospective reviews. Finally, retreatment rates were analyzed with cumulative incidence because death before retreatment was considered a competing event. Those rates were compared with Gray's test. Two-sided P-values less than 0.05 were considered statistically significant.

Results

Patient characteristics

A total of 254 RT courses were administered to 165 patients with uncomplicated bone metastases in the time frame of the audit. 85.4% of patients received a single 8 Gy fraction of radiotherapy. Patient characteristics are summarized in Table 1. Patient age ranged from 38 to 93 years, with a median of 69 years. 56.4% were female. The most common primary histologies were lung, prostate and breast (30.3%, 27.3%, and 16.4%, respectively). 56% of the patients had low ECOG scores (ranging from 0 to 2), indicating a fairly preserved performance status. Median follow-up for patients followed at our institution was 8 weeks.

Analysis by treatment

Univariate analysis of patient and disease characteristics influencing fractionation choice is summarized in Table 2 and illustrated in Figs. 1 and 2. Patients under the age of 70 were more likely to receive MFRT rather than SFRT (17% vs. 9%, p = 0.042). Breast histology was associated with higher rates of MFRT use (23%) and prostate histology with SFRT (93%, p = 0.0046). We tried to correct for imbalances in the treatment population using logistic regression and explored the effect of the presence of other metastases such as lung, liver and brain, as well as spinal involvement, but none was found to be a statistically significant predictor of

Table 1
Patient characteristics.

Characteristic	N = 165
Age	
<70 years	87 (52.7%)
≥70 years	78 (47.3%)
Gender	
Male	72 (43.6%)
Female	93 (56.4%)
Primary Histology	
Lung	50 (30.3%)
Breast	27 (16.4%)
Prostate	45 (27.3%)
GI	14 (8.4%)
Other	29 (17.6%)
ECOG	
0	25 (15.2%)
1	44 (26.7%)
2	23 (13.9%)
3	21 (12.7%)
4	4 (2.4%)
N/A	48 (29.1%)

Table 2
Radiation therapy prescriptions.

Characteristic	SFRT (N = 217)	MFRT (N = 37)	*P-value*
Age			0.042
<70 years	114 (52.5%)	24 (64.9%)	
≥70 years	103 (47.5%)	13 (35.1%)	
Gender			0.46
Male	129 (59.5%)	20 (54.1%)	
Female	88 (40.5%)	17 (45.9%)	
Site of Primary			0.0046
Lung	59 (27.2%)	10 (27.0%)	
Breast	34 (15.7%)	10 (27.0%)	
Prostate	66 (30.4%)	5 (13.5%)	
GI	21 (9.7%)	0 (0%)	
Other	37 (17.0%)	12 (32.5%)	
Spinal Metastases			0.36
Yes	80 (36.9%)	16 (43.2%)	
No	137 (63.1%)	21 (56.8%)	
ECOG			0.03
0	31 (14.3%)	8 (21.6%)	
1	57 (26.3%)	10 (27.0%)	
2	33 (15.2%)	3 (8.1%)	
3	30 (13.8%)	2 (5.4%)	
4	6 (2.8%)	0 (0%)	
N/A	60 (27.6%)	14 (37.9%)	

MFRT use. Performance status (ECOG) was a significant predictor of fractionation choice, essentially because there was a significant correlation of good ECOG with young age and breast histology (p = 0.03). The ECOG score was the most powerful predictor of use of MFRT. Increasing performance status by 1 decreased the rate of utilization of MFRT by 41%.

There was no statistically significant difference in retreatment between SFRT vs. MFRT at 6 months (15.3% vs 17.6%, respectively; p = 0.71). There was also no significant difference in survival at 6 months or 12 months between single and multi-fractionation (9.8% vs. 16.8% at 6 months, 17.2% vs. 24.8% at 12 months, respectively; p = 0.76). However, follow-up was too short in 40% of our patients to derive definitive conclusions on these variables.

Discussion

The main finding of this audit is that the rate of SFRT use for patients with uncomplicated bone metastases at our center during the time frame studied was 85.4%, demonstrating that radiation oncologists at our center are mostly following best-practice guidelines. Our findings are comparable to those of another large academic institution in the United States. They found strong adherence to best-practice guidelines that recommend avoiding the use of more than 10 fractions to palliate painful bone metastases, although SFRT was still underused [19]. Other studies have also shown that SFRT use was greater in academic treatment centers compared to community treatment centers [20,21].

We found that older age was correlated with higher rates of SFRT use, with greater use of MFRT (p = 0.042) in patients 70 years of age or younger. Several other studies have shown a similar correlation between age and choice of fractionation [14,22–27]. We found too that performance status was a significant predictor for the choice of fractionation. Others have also shown that poor patient prognosis is associated with higher rates of SFRT use, which leads one to believe that prognosis can affect treatment choice [16,22–26,28]. Other factors reported to be associated with SFRT use include radiation to sites other than the spine and lung or prostate primaries [14]. We were unable to confirm this in our patient population and also could not make definitive conclusions on retreatment rates given the relatively small sample size and short follow-up. Although we do not have long-term retreatment data, we are confident that the rate is low. This is due to the fact that radiation oncology is very centralized in the province of Quebec (only 12 centers that serve a population of 8.5 million over a very large territory), and if patients were to be retreated, they would be retreated at our center. Patients lost for follow-up are most likely patients that have passed away or that do not need retreatment, as they would have been referred back if their symptoms required retreatment. Unfortunately, because 40% of patients did not have follow-up, it is difficult to state retreatment rates with certainty. This issue has nonetheless been extensively addressed in the literature, where retreatment rates using 8 Gy in 1 fraction are expected to be higher than with 20 Gy in 1 fraction, while pain control rates similar [5,6,29]. Since percentage of patients with uncomplicated bone metastases treated with SFRT is now included on our performance dashboard, we anticipate being able to better identify retreatment differences and other potential predictors of fractionation in the future.

There are numerous benefits to treating with SFRT. SFRT has been shown to be as effective as MFRT in controlling pain [3–6]. Barton et al. surveyed patients before and after treatment and found that most would prefer SFRT for its convenience as long as

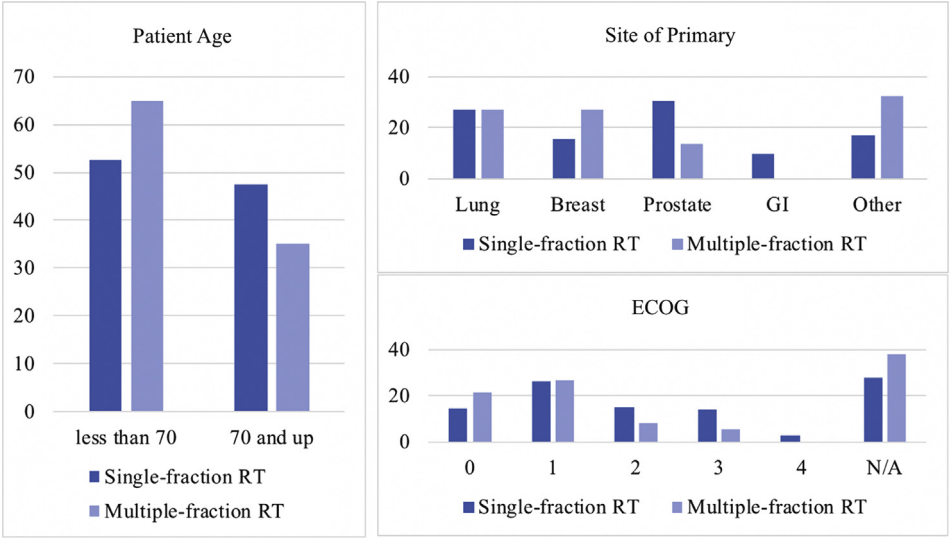

Fig. 1. Statistically significant results – analysis by treatment.

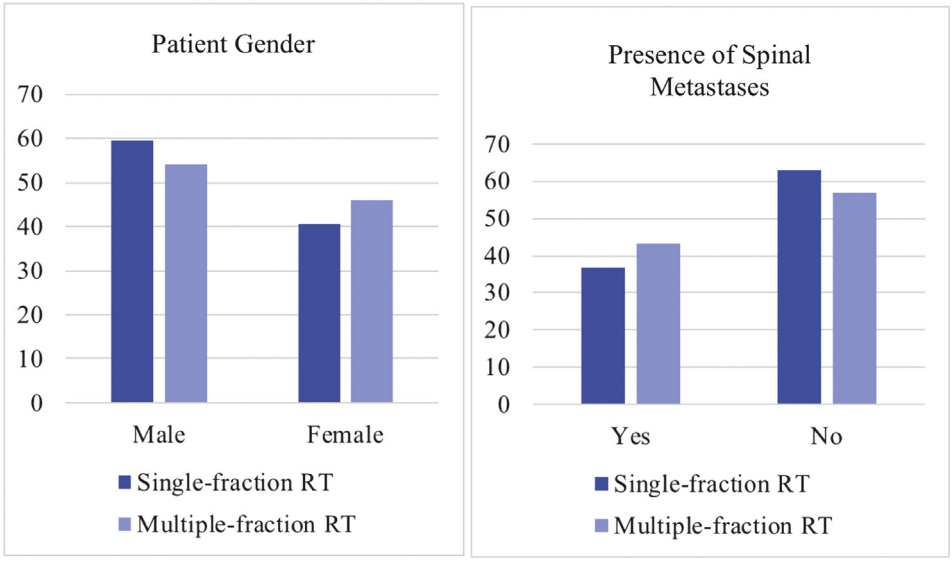

Fig. 2. Other results – analysis by treatment.

outcomes such as durability of pain relief were the same [30]. Szumacher et al. showed that 76% of patients would choose SFRT for its convenience, but a higher rate of bone fracture would dissuade them from choosing SFRT [31]. A study from Singapore revealed that 85% of patients prefer MFRT, most likely due to lower retreatment rates [32]. In terms of medical and societal costs of these two regimens, a Dutch study reviewed treatment costs of radiotherapy, hospitalization, domestic help, and non-medical costs such as those incurred for travel, and concluded that SFRT was cost-effective [9]. A study using a Markov model to evaluate cost-effectiveness of 30 Gy in 10 fractions compared with 8 Gy in one fraction found an incremental cost-effectiveness ratio of 6973 US dollars/quality-adjusted life year, favoring SFRT [8]. In a publicly-funded healthcare model, such as Canada, it is important to recognize the economic gains in providing this treatment.

Global patterns of practice reveal that SFRT uptake has been slow. Popovic et al. reviewed patterns of radiotherapy practice from 1993 to 2013 and concluded that there has been overall reluctance to prescribe SFRT with geographic location of treatment regarded as an important factor [15]. McDonald et al. published a review showing that the rate of SFRT use varies from 3% to 75%, with SFRT being the least commonly used in the United States [14]. They also found that Western and Northern European countries had higher rates of SFRT, similar to Canadian rates [14]. Another review by Bradley et al. found that more radiation oncologists in non-North American centers prescribe SFRT, a trend that was influenced by financial reimbursement systems [33]. Radiation oncologists employed by academic centers, publicly funded centers, and those paid on a fee-for-service basis, as in Canada, were more likely to prescribe SFRT [33]. One study reported that SFRT was the most commonly used treatment regimen in Canada for bone metastases, although prescribed only 50% of the time [34]. This study also showed that the use of SFRT varied within Canada, ranging from 31 to 60%, depending on the province [34].

The American College of Radiology, ASTRO and the Royal College of Radiologists in the UK all recommend the use of SFRT for patients with uncomplicated bone metastases [2,10,11,35]. The Canadian Partnership Against Cancer, whose purpose is to identify potentially harmful or low-value medical practices in Canadian healthcare, published their findings as part of the Choosing Wisely Canada campaign, and also recommended the use of single fraction of RT in the treatment of uncomplicated bone metastases [36]. Lomas et al. first studied the impact of guidelines on medical practice over 30 years ago and concluded that guidelines may allow physicians to consider changing their practice. However, physicians rarely follow guidelines unless there are incentives to do so [37]. Other studies have supported this, showing that guidelines are most effective when used in combination with other interventions [38]. Future studies should explore ways to improve SFRT use and ensure that this use is maintained. Cancer Care Ontario published guidelines that advocated for the use of SFRT in patients with uncomplicated bone metastases. Immediately following this publication, rates of SFRT prescriptions increased, but this was short-lived [22]. It remains to be seen if releasing provincial guidelines periodically can provide a long-term solution to increasing adherence to guidelines. Another possible initiative to do so was studied in British Columbia, following a study that showed that SFRT was provincially underused [16]. Data from this study were then presented to radiation oncologists across the province at meetings and conferences, and the rates of SFRT prescriptions were measured following this intervention [39,40]. In fact, the authors found an increase in SFRT prescriptions by at least 10% [40]. Our strategy has been to add an indicator "percentage of patients with uncomplicated bone metastases treated with SFRT" to our performance dashboard and provide feedback to all staff on a regular basis. With the implementation of this dashboard, we have maintained a use of SFRT of greater than 80%.

Our audit has important limitations not least its retrospective design and relatively small number of patients in each treatment group. Consequently, patient characteristics may be skewed, impacting the generalizability and applicability of our findings. Moreover, some patient charts were incomplete, and data for performance status, for example, were not available. Furthermore, we could not make definitive conclusions on retreatment rates due to insufficient follow-up time. Incorporating rate of SFRT prescription onto our performance dashboard will allow us to track radiation oncology practice, clarify factors affecting treatment decisions and implement additional strategies as needed to improve adherence to guidelines.

Conclusion

In accordance with best practice, our audit showed that use of SFRT for patients with uncomplicated painful bone metastases is high at our academic center. This audit, that was relatively simple

and largely reassuring, lead to a process for providing regular feedback to clinicians that now serves as a model to address other more complex practice issues at our institution.

Conflict of interest statement

We have no conflicts of interest to disclose.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tipsro.2018.12.001.

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