Hypofractionated Radiation Therapy for Unresectable or Metastatic Sarcoma Lesions Provides Durable Tumor Control and Effective Palliation

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PURPOSE / OBJECTIVE(s)

Response rates for unresectable and/or metastatic sarcomas are generally poor with most patients progressing on systemic therapy.[1]

In this setting, conventional palliative radiation therapy (RT) provides both limited tumor control and symptom relief.[2]

Recent studies suggest that aggressive local therapy, such as surgery and/or RT, may improve oncologic outcomes.[3,4]

Given the relative radioresistance of sarcomas and their often large size, dose escalated, hypofractionated (HF) RT may improve oncologic outcomes over traditional RT.

We Investigated the efficacy of HFRT in improving survival outcomes, palliation, and duration of systemic therapy breaks in patients with sarcoma.

MATERIALS & METHODS

With IRB approval, we retrospectively reviewed 73 consecutive patients with sarcoma who received >10 fractions of HFRT from 2017-2020.

HFRT was delivered most commonly using intensity modulated radiation therapy (IMRT) with a simultaneous integrated boost to further escalate the dose.

The rationale for HFRT included the following clinical scenarios :

1. palliative/symptomatic (34%)
2. an unresectable primary (27%)
3. oligometastatic disease (16%)
4. oligoprogressive disease (23%)

Oligometasatic disease was defined as < 5 sites of metastasis based on CT or PET imaging.

Oligoprogressive disease was defined as a limited sites of progressive disease in patients with otherwise stable metastatic disease.

RESULTS

Table 1. Treatment Characteristics

Variable	Value or No. (%) (n=73)
Median lines of systemic therapy preceding RT	2 (IQR 1-3)
Systemic therapy immediately preceding RT	
Chemotherapy	33 (45)
Tyrosine kinase inhibitor	9 (12)
Immunotherapy	8 (11)
None	23 (32)
Best radiographic response of tumor prior to RT	
Progressing	56 (77)
Stable	8 (11)
Partial response	9 (12)
Prescription dose to tumor	
Median	45 Gy
IQR	42- 45 Gy
≥ 45 Gy	43 (59)
< 45 Gy	30 (41)
Best radiographic response to RT	
Decreased size	30 (41)
Decrease size & enhancement/avidity	19 (26)
Decreased enhancement/avidity only	5 (7)
Stable only	16 (22)
Unknown	3 (4)

Table 2. Patient and Tumor Characteristics

Variable	Value or No. (%) (n=73)
Follow-up time all patients, months	
Median	9
IQR	5-13
Age, years	
Median	51
IQR	35-69
Sex	
Female	29 (40)
Male	44 (60)
Irradiated Tumor	
Primary Tumor	47 (64)
Metastasis	26 (36)
Irradiated Location	
Head and neck	20 (27)
Upper Extremities	2 (3)
Trunk	48 (66)
Lower Extremities	3 (4)
Sarcoma type	
Soft tissue sarcoma	53 (73)
Bone sarcoma	20 (27)
Maximum Tumor Dimension, cm	
Median	7
IQR	4-12

Table 3. Symptoms Related to Tumor and Radiation Toxicity

Variable	Value or No. (%) (n=73)
Symptoms related to tumor	
None	34 (47)
Pain only	28 (38)
Neurologic only	1 (1)
Pain and neurologic	7 (10)
Other	3 (4)
Symptomatic benefit RT	
Yes	37 (51)
No	2 (3)
Absence of symptoms prior to RT	34 (46)
Acute toxicity	
None	37 (51)
Pain flare	15 (21)
Lower GI	13 (18)
Upper GI	14 (19)
Acute GI Toxicity Grade	
Grade 1	20 (74)
Grade 2	7 (26)
Grade 3-5	0 (0)
Late Toxicity	
Respiratory	2 (3)
GI	0 (0)
Neurologic	0 (0)
Late Toxicity Grade	
Grade 1	2 (3)
Grade 2-5	0 (0)

Figure 1

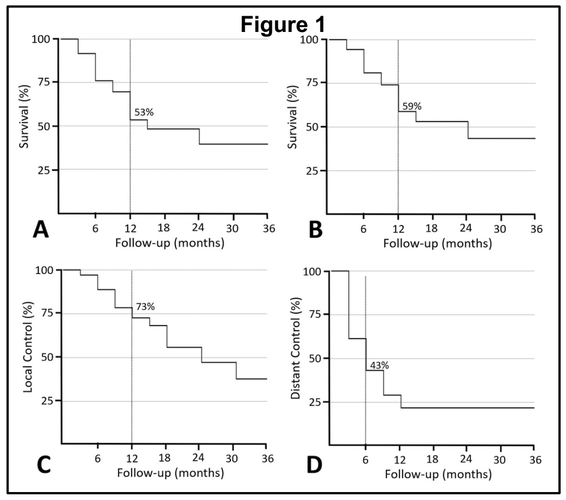
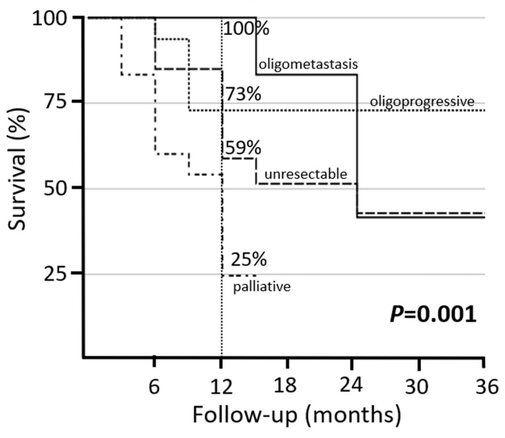


Figure 2



The 1-year disease specific survival was 59%, which was more favorable for patients receiving HFRT for oligometastatic (1-y 100%) or oligoprogressive (1-y 73%) disease (*P*=0.001).

The 1-y targeted lesional control (TLC) was 73% with 26% developing progression at a median time of 7.5 m (IQR, 5.5-13).

A metastatic target (1-y 95% vs 60% primary, *P*=0.02; HR 0.27, *P*=0.04) and soft tissue origin (1-y 78% vs 61% bone, *P*=0.01; HR 0.33, *P*=0.02) were associated with better TLC on univariate and multivariable analyses.

For patients not planned for adjuvant systemic therapy (n=53), **the median systemic therapy break was 9 m** (IQR, 4-23), and notably longer in oligometastatic (13 m), oligoprogressive (12 m) or unresectable (13 m) disease.

The rate of distant failure was high with a 6-month DMFS of only 43%. HFRT use for unresectable (*P*<0.001, HR 0.14) and oligometastatic (*P*=0.003, HR 0.25) disease were the only factors associated with improved DMFS on multivariable analysis.

CONCLUSIONS

HFRT is an effective treatment strategy for patients with unresectable or metastatic sarcoma to provide durable TLC, symptom relief, and meaningful systemic therapy breaks with limited toxicity.

Patients with unresectable or oligo-metastatic/progressive disease benefited from longer systemic therapy breaks and lower rates of distant relapse.

If overall disease control is the primary goal for HFRT, patient selection remains crucial as distant relapse is high.

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