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Scientific Article

Simulation-Free Radiation Therapy: An Emerging Form of Treatment Planning to Expedite Plan Generation for Patients Receiving Palliative Radiation Therapy

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Abstract

Purpose: Herein we report the clinical and dosimetric experience for patients with metastases treated with palliative simulation-free radiation therapy (SFRT) at a single institution.

Methods and Materials: SFRT was performed at a single institution. Multiple fractionation regimens were used. Diagnostic imaging was used for treatment planning. Patient characteristics as well as planning and treatment time points were collected. A matched cohort of patients with conventional computed tomography simulation radiation therapy (CTRT) was acquired to evaluate for differences in planning and treatment time. SFRT dosimetry was evaluated to determine the fidelity of SFRT. Descriptive statistics were calculated on all variables and statistical significance was evaluated using the Wilcoxon signed rank test and *t* test methods.

Results: Thirty sessions of SFRT were performed and matched with 30 sessions of CTRT. Seventy percent of SFRT and 63% of CTRT treatments were single fraction. The median time to plan generation was 0.88 days (0.19-1.47) for SFRT and 1.90 days (0.39-5.23) for CTRT ($P = .02$). The total treatment time was 41 minutes (28-64) for SFRT and 30 minutes (21-45) for CTRT ($P = .02$). In the SFRT courses, the maximum and mean deviations in the actual delivered dose from the approved plans for the maximum dose were 4.1% and 0.07%, respectively. All deliveries were within a 5% threshold and deemed clinically acceptable.

Conclusions: Palliative SFRT is an emerging technique that allowed for a statistically significant lower time to plan generation and was dosimetrically acceptable. This benefit must be weighed against increased total treatment time for patients receiving SFRT compared with CTRT, and appropriate patient selection is critical.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Introduction

An estimated 30% to 70% of all radiation therapy treatments are for palliative intent.[1,2] Palliative treatment of bone,[3,4] brain,[5,6] and lung metastases,[7,8] among others, is common and has been demonstrated to reduce symptoms in a variety of diseases. Conventional palliative radiation therapy is delivered in 1 to 10 fractions using computed tomography (CT) simulation for treatment planning.[4,7] This process can be time consuming, and simulation in combination with protracted treatment regimens can yield a long overall treatment time. One method to reduce the burden of palliative treatment is to forgo conventional computed tomography simulation radiation therapy (CTRT) and create treatment plans based on diagnostic imaging.[1,9,10] This is known as diagnostic scan-based treatment planning or simulation-free radiation therapy (SFRT).

One of the concerns in planning on diagnostic images is the accuracy in the dose calculation with a generic CT calibration obtained from a simulation CT scanner, which is different from the actual CT scanners used for diagnostic image acquisition. The magnitude of the error in dose calculation is associated directly to the magnitude of the error in the relative electronic density, which is determined from the CT numbers via the CT calibration. According to the International Atomic Energy Agency,[11] the fluctuation of the CT calibrations from various CT scanners is most significant in the high CT number region. They reported that the magnitude of the error in calculated dose on CT images with a generic CT calibration is 2% for a 6MV photon beam in a bony material of 5-cm thickness with a density close to the cranium, lower than the 3% accuracy required by International Atomic Energy Agency.[12]

The feasibility of planning on diagnostic images has been explored in multiple studies. Glober et al reported a retrospective study on the dose difference in plans created on diagnostic and simulation CT images in 10 palliative patients treated for spine metastases.[13] They found a 4% difference in the maximum point dose and a 3% difference in the volume receiving 90% of the prescription dose. Wong et al reported a 2-stage study involving 150 palliative patients receiving CT diagnostic and simulation CT scans.[1] They reported a variation between −2% and 2.5% in the planning target volume coverage at 95% of the prescription dose. Recently, a randomized trial in palliative radiation therapy was open for patient enrollment

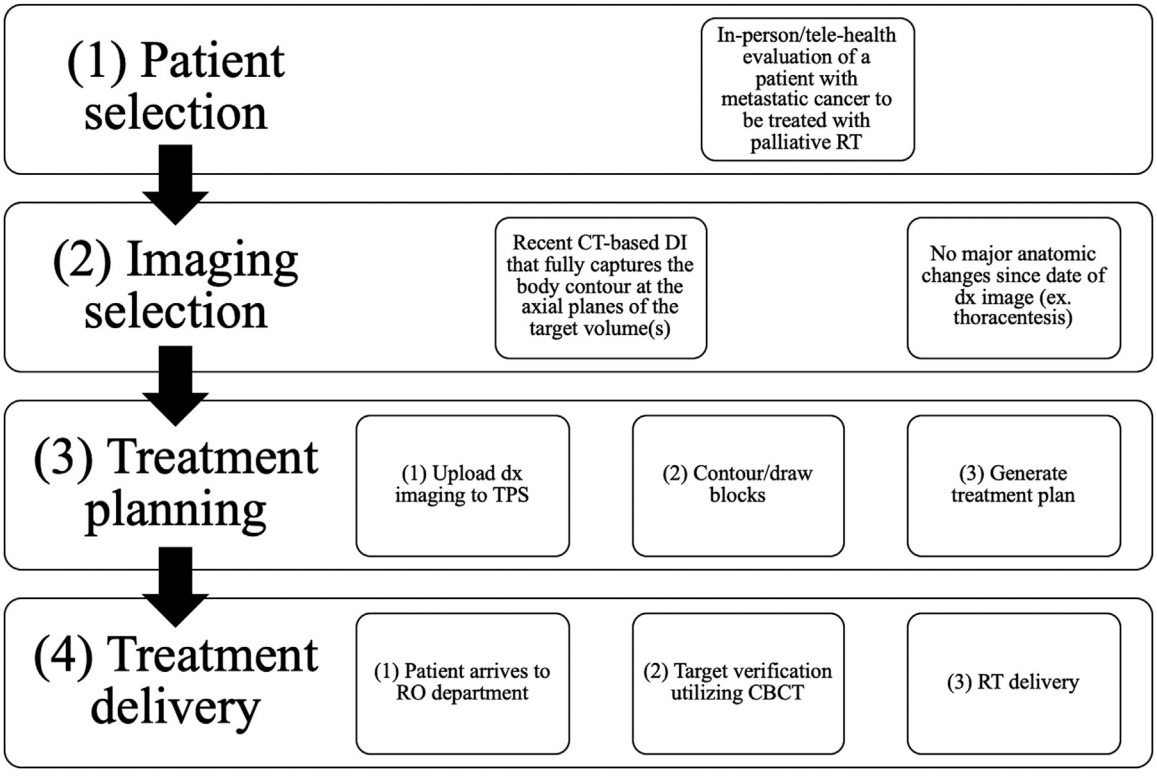

Figure 1 Simulation-free radiation therapy (SFRT) workflow. A workflow diagram of the SFRT workflow. Unique aspects of the SFRT workflow compared with the conventional simulation radiation therapy workflow include diagnostic imaging (DI) selection and target verification using cone beam computed tomography. *Abbreviations:* Dx = diagnostic; RO = radiation oncology; TPS = treatment planning system.

to study the shortening of radiation therapy courses by planning on patients' diagnostic CT.[14]

In this study, we describe our approach to expedite palliative SFRT and report the clinical and dosimetric outcomes from our experience.

Methods and Materials

Patient population

From January 1 to November 30, 2020, 30 sessions of palliative SFRT were performed at a single institution. A session of radiation therapy was a single course of radiation therapy. Multiple fractionation regimens were used for treatment, and all patients were treated on a cone beam CT (CBCT)-guided linear accelerator. Patient eligibility for SFRT was determined by the treating physician. At a minimum, patients eligible for SFRT were required to have recent diagnostic imaging of the intended target site that fully visualized the tissue from beam entry to beam exit at the axial slices of the target. Patients with major anatomic changes since the date of the diagnostic imaging were not eligible. Examples of major anatomic changes include patients with thoracic disease and pleural effusion who had a thoracentesis after the diagnostic image was captured as well as patients with abdominal disease and ascites who had a paracentesis after the diagnostic image was captured. This retrospective review was performed with waiver of informed consent (Institutional Review Board #202008077).

SFRT treatment planning and delivery

The SFRT workflow (Fig. 1) began with evaluation by the treating physician at consultation. Eligible diagnostic imaging was downloaded to the treatment planning system, and a gross tumor volume and/or radiation therapy block was delineated. Diagnostic imaging was either a diagnostic CT or the CT from a positron emission tomography CT scan. Planning constraints primarily involved limiting the maximum dose (D_{max}) to less than 110% of prescription. Additional target goals and/or constraints were delineated by the treating physician. On the day of treatment, the patient was placed on the treatment couch and cone beam CT (CBCT) was acquired to confirm patient and target alignment. Treatment was delivered with 6 and 10 MV photons. Plan verification was performed after radiation therapy delivery.

SFRT dosimetric evaluation

To determine the fidelity of SFRT, an evaluation of the SFRT dosimetry was performed. The actual dose delivered to the patients was reconstructed on the fractional setup CBCT images. Regions receiving 90% and 100% of the original plan's prescription dose were contoured and propagated to the CBCT images registered to the diagnostic image. Changes in the mean dose to those regions ($Mean_{90}$ and $Mean_{100}$) were reported as the surrogates for the delivery fidelity together with the changes in D_{max}.

Table 1 Baseline and treatment characteristics

Characteristic	SFRT (n = 30)	CTRT (n = 30)
Age (y)	61 (56-73)	62 (55-72)
Sex		
Men	19 (63%)	16 (53%)
Women	11 (37%)	14 (47%)
Primary disease		
Lung	9 (30%)	9 (30%)
Myeloma/lymphoma	7 (23%)	4 (13%)
Sarcoma	4 (13%)	1 (3%)
Prostate	3 (10%)	3 (10%)
Breast	2 (7%)	3 (10%)
Gastrointestinal	2 (7%)	3 (10%)
Head and neck	1 (3%)	4 (13%)
Nonprostate genitourinary	1 (3%)	2 (7%)
Bile duct	1 (3%)	1 (3%)
Outpatient treatment		
Yes	18 (60%)	21 (70%)
No	12 (40%)	9 (30%)
Sites treated per patient		
1	24 (80%)	22 (73%)
2	5 (17%)	3 (10%)
3	1 (3%)	5 (17%)
Sites treated	**n = 37**	**n = 43**
Spine	18 (49%)	22 (51%)
Hip	9 (24%)	8 (19%)
Thorax	4 (11%)	4 (9%)
Rib	2 (5%)	2 (5%)
Head and neck	2 (5%)	1 (2%)
Long bone	1 (3%)	4 (9%)
Abdomen	1 (3%)	2 (5%)
Fractionation		
10 fractions	1 (3%)	1 (3%)
5 fractions	8 (27%)	10 (33%)
1 fraction	21 (70%)	19 (63%)

Abbreviations: CTRT = conventional computed tomography simulation radiation therapy; SFRT = simulation-free radiation therapy. Baseline and treatment characteristics for the 2 cohorts. Continuous variables are presented as median (interquartile range).

Table 2 Timing metrics

Time point	SFRT	CTRT	*P* value
Order approved to plan generation (d)	0.88 (0.19-1.47)	1.90 (0.39-5.23)	**0.02**
Order approved to first treatment (d)	3.60 (1.23-5.91)	4.23 (1.74-8.15)	0.26
Waiting room time (min)	16 (7-26)	12 (8-24)	0.51
Time on couch (min)	25 (12-38)	12 (8-30)	**0.01**
Beam on time (min)	2 (1-3)	2 (1-2)	0.86
Total treatment time (min)	41 (28-64)	30 (21-45)	**0.02**

Abbreviations: CTRT = conventional computed tomography simulation radiation therapy; SFRT = simulation-free radiation therapy.
Timing metrics and statistical comparison for the SFRT and CTRT cohorts. Values in boldface are statistically significant.

Statistical analysis

Patient characteristics as well as treatment and planning time points were collected retrospectively. Time points collected included time of order approval, time of plan generation, and time of first treatment. Waiting room time, total time on the couch, total beam-on time, and total treatment time were also recorded. Additionally, a matched cohort of patients treated with palliative CTRT was acquired via Reweight Mahalanobis Distance Matching matched on age, total dose, and treatment site to evaluate for differences in overall treatment time. Palliative CTRT treatment verification was performed with port films or kV images. Descriptive statistics were calculated on all variables and statistical significance was evaluated using the Wilcoxon signed rank test and *t* test methods.

Results

Clinical results

Thirty sessions of palliative SFRT were matched with 30 sessions of palliative CTRT, with the median distance matching being 0.073 (0.018-0.147). Baseline and treatment characteristics are demonstrated in Table 1. The median age of patients treated with SFRT was 61 (56-73), and the median age of patients treated with CTRT was 62 (55-72). Timing metrics are demonstrated in Table 2. Time from order approved to plan generation was significantly shorter in the SFRT group (P = .02), and time on the couch and total treatment time were significantly longer in the SFRT group (P = .01 and .02, respectively).

Dosimetric results

In the SFRT courses, the absolute maximum deviations in the actual delivered dose from the approved plans were 4.1%, 4%, and 3.7% of the prescription dose in D_{max}, $Mean_{90}$, and $Mean_{100}$, and the mean deviations were 0.07%, 0.35%, and 0.78%, respectively. The deviations in

Table 3 Dose deviations

SFRT session	D_{max}	D_{mean90}	$D_{mean100}$
1	0	−1.2	0.9
2	−2.0	−1.0	−0.6
3	−4.1	−4.0	−3.7
4	0.4	0.1	1.5
5	1.5	0.1	0
6	−0.8	−0.9	−1.1
7	−1.1	−1.1	−0.1
8	4.1	1.3	1.8
9	−0.6	1	0.8
10	0.5	1.2	2.2
11	−0.4	0.1	0.4
12	3.6	1.7	2.5
13	−0.3	1.7	1.4
14	−0.2	0.9	1.1
15	3.2	1.5	2.3
16	0.8	1.0	0.7
17	1.0	1.3	0.9
18	2.8	−1.8	0
19	−4.1	1.2	0.5
20	0.9	3	2.4
21	−1.1	0.3	1.5
22	−0.1	1.1	−3.6
23	1.2	1.9	1.5
24	0.2	0.9	0.4
25	−1.4	−0.2	−0.1
26	−3.3	−0.1	0.3
27	1.4	−0.4	1.2
28	0.3	−2.3	−0.4
29	−0.9	2.8	2.0
30	2.8	1.0	2.5

Abbreviations: D_{max} = maximum dose; D_{mean90} = mean dose to 90% or greater of the volume; $D_{mean100}$ = mean dose to 100% of the volume; SFRT = simulation-free radiation therapy.
Deviations from D_{max}, D_{mean90}, and $D_{mean100}$ are presented for each of the 30 sessions of SFRT.

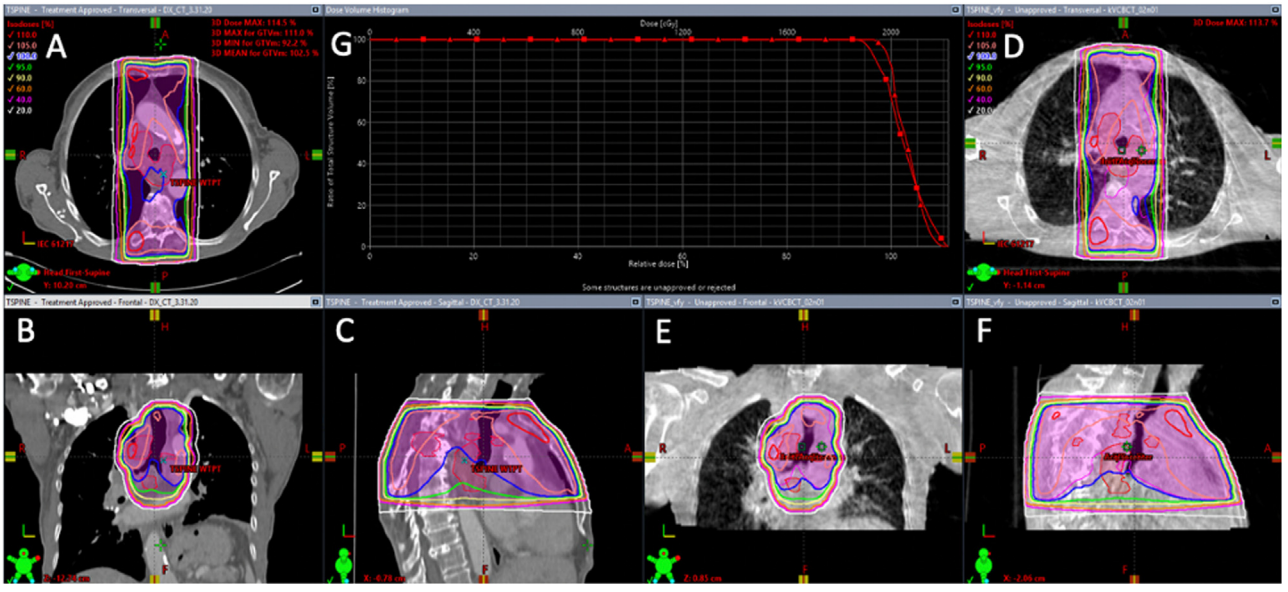

Figure 2 Dose comparison for a thoracic spine simulation-free radiation therapy plan. A thoracic spine simulation-free radiation therapy plan (A-C) alongside the reconstructed plan on the patient's cone beam computed tomography (D-F). On the dose-volume histogram (G), the dose intended to be delivered to the target (triangles) is plotted adjacent to the dose actually delivered to the target based on the cone beam computed tomography reconstruction (squares).

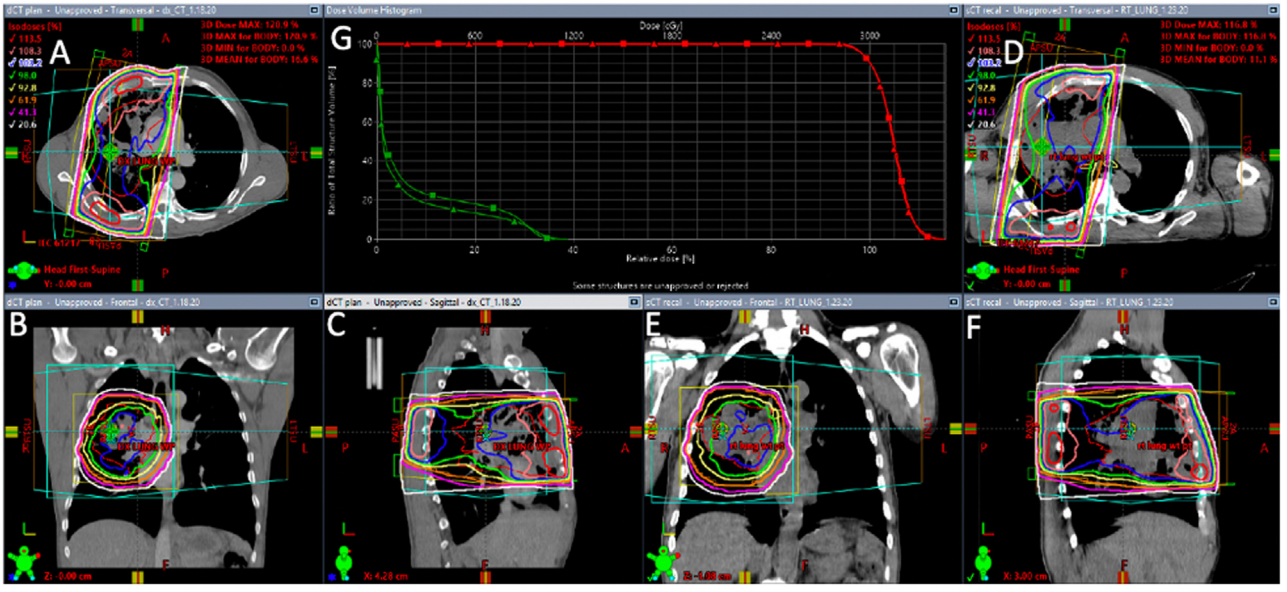

Figure 3 Dose comparison for a thoracic simulation-free radiation therapy plan. A thoracic simulation-free radiation therapy plan (A-C) alongside the reconstructed plan on the patient's cone beam computed tomography (D-F). On the dose-volume histogram (G), the dose intended to be delivered to the target (triangles) is plotted adjacent to the dose actually delivered to the target based on the cone beam computed tomography reconstruction (squares).

D_{max}, $Mean_{90}$, and $Mean_{100}$ for all 30 sessions are demonstrated in Table 3. One-sided 1-sample *t* tests were 0.42% ($P = .66$), 1.51% ($P = .93$), and 2.56% ($P = .99$) for D_{max}, $Mean_{90}$, and $Mean_{100}$, respectively. Dose comparisons for thoracic spine and thoracic cases are demonstrated in Figs. 2 and 3. All deliveries were within a 5% threshold and clinically acceptable.

Discussion

These data demonstrate that SFRT reduced time to plan generation compared with CTRT while requiring one less visit to the radiation oncology department when treating with patients with palliative radiation therapy. The dosimetric analysis demonstrates the fidelity of

SFRT, suggesting SFRT is reproducible and safe to deliver in the clinical setting. These data are clinically and dosimetrically consistent with recent SFRT studies and help confirm the feasibility of this paradigm.[1,9,10]

This research is pertinent in light of the recently opened DART trial (NCT05233904).[14] This is a randomized trial evaluating SFRT against standard CT-simulated palliative radiation therapy. Thirty-three patients are planned for accrual, and the primary outcome of this study is time in center on treatment day. We applaud the leaders of this trial for planning to evaluate SFRT in a prospective, randomized fashion, and we eagerly await the results.

In recent years, an emphasis has been placed on reducing palliative treatments from protracted regimens (≥10 fraction) to similarly efficacious, contracted regimens (1-5 fractions).[15-18] This may reduce overall treatment visits, time, and cost for a near-end-of-life population. SFRT represents an additional avenue to reduce treatment visits for radiation oncology's sickest patients. This drive to reduce treatment visits has been further amplified by COVID-19, as physicians have had to balance the risk of infection in a high-risk population with the need for treatment of oncologic disease and its symptoms.[19-23]

While our institution has adopted SFRT for the palliative treatment of certain metastases, the technique does have limitations, and patient selection is key. SFRT requires the acquisition of a CBCT to confirm target alignment when treating a patient, which can be time consuming. This is in comparison to CTRT, which usually requires a port film or kV image for treatment localization. When treating multiple sites, the need to acquire a CBCT for each site may increase patient time on table. This is corroborated by our data which demonstrate that median time on table and total treatment time were higher for SFRT compared with CTRT. Additionally, in our department, time is spent during setup for SFRT patients on making patient marks as well as taking pictures, which is typically done during the simulation appointment for CTRT patients. Depending on the departmental specific palliative radiation therapy protocol, this may be less of a significant factor for other departments who are interested in installing a SFRT program. Treatment of the distal extremities is also challenging, as the increased range of motion makes the matching of a CBCT with a diagnostic image difficult. Alternatively, the decreased range of motion for pelvis and spine cases makes these disease sites optimal SFRT cases. Therefore, we suggest that ideal candidates for SFRT have 1 to 2 lesions of the spine or pelvis intended for palliative treatment and do not have bony pain which precludes them from laying on the treatment table for an extended period.

There are multiple factors unrelated to patient selection that also may increase the utility of SFRT. Recently, a CT simulation machine was replaced at our institution. At a high-volume center such as our own, this led to a significant reduction in available CT simulation appointments, and so in response the utilization of SFRT temporarily increased. While the replacement of a CT simulation machine does not happen often, this technique would also be useful if a simulation machine were to break down and require repairs. Another situation in which SFRT may be at high-volume sites where simulation appointments are harder to schedule in quick fashion or for patients unable to be seen on call over the weekend for whom an early Monday simulation appointment cannot be secured.

Conclusion

SFRT is an emerging technique for palliative radiation therapy that allowed for a statistically significant lower time-to-plan generation and was dosimetrically acceptable. However, patient selection is key as total treatment time was longer for SFRT, possibly due to the need to acquire multiple CBCTs in patients with multiple sites intended to be treated, and further research is warranted to identify the ideal SFRT patient.

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