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Applied Radiation Oncology

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Adapting to the Virtual World: An Analysis of Remote Work Policies in Academic Radiation Oncology

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Travel-Related Environmental Impact of Telemedicine in a Radiation Oncology Clinic

## Research

Assessing the Readiness for Climate Change Education in Radiation Oncology in the United States and Canada

## Case Report

Challenges of Methotrexate Administration During Breast Radiation: A Case Report

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Postdoctoral research fellow in radiation oncology, Massachusetts General Hospital, Boston, MA, and Harvard Medical School, Boston, MA

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The COVID-19 pandemic prompted a shift from traditional work environments to working from home (WFH). Because WFH benefits and challenges in radiation oncology (RO) are unknown, the authors conducted a survey-based study to assess WFH policies and perceptions of their impact. They also investigated the role of departmental gender composition in remote work policies.

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This study evaluates the perspectives of US and Canadian radiation oncology program directors and associate program directors on climate change and sustainability education, and its impact on health care. The authors discuss the gap between awareness and action, as well as roadblocks, facilitators, and strategies to incorporate climate change education in these programs.

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**Dr. Suh** is the editor-in-chief of *Applied Radiation Oncology*, and professor and chairman, Department of Radiation Oncology at the Taussig Cancer Institute, Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Cleveland Clinic, Cleveland, OH.

# Green Means Go: Increasing Sustainability in Radiation Oncology

John Suh, MD, FASTRO, FACR

Evolving over decades from a grassroots effort to a global movement, environmental sustainability has become a chief priority for many individuals and businesses alike. Health care—including radiation oncology—is no exception, especially as a significant contributor to global carbon emissions.

With consequences comes responsibility, but are we doing our part? In this issue, several articles explore that question, examining gaps and solutions to reduce radiation oncology's impact on climate change while improving patient and practitioner well-being in the process.

Our lineup includes the timely research article *Travel-Related Environmental Impact of Telemedicine in a Radiation Oncology Clinic*, which illustrates how telemedicine substantially lowered carbon emissions for a large outpatient facility during COVID, while maintaining equitable access to care. The authors posit that by modifying transportation behavior of cancer patients overall, we can measurably reduce greenhouse gas emissions associated with health care.

Discussing another facet of telemedicine is the CME-approved article *Adapting to the Virtual World: An Analysis of Remote Work Policies in Academic Radiation Oncology*. This intriguing study investigates the implementation of work-from-home policies in radiation oncology and explores how departmental gender composition factored into their development. It further highlights interesting and helpful findings involving physician satisfaction, burnout, patient care, and gender equity, noting that more equitable policies may be needed to support female physicians in remote work settings.

A third research article, *Assessing the Readiness for Climate Change Education in Radiation Oncology in the United States and Canada*, assesses program and assistant program directors' views on climate change and sustainability education, finding a discrepancy between awareness and action. This enlightening study also identifies barriers and facilitators to implementing climate change education in these programs, highlighting strategies to reach this goal.

We are also pleased to present the Resident Voice editorial, *Green-ifying Clinical Trials*. With inefficiencies surrounding heavy travel, delivery of trial drugs, and patient enrollment, clinical trials leave a substantial carbon footprint, yet they are crucial to advancing cancer care. The article presents seven steps to mitigate environmental toxicity in US cancer clinical trials—a great resource, especially as federal guidelines in this area are not yet available.

We hope these articles strengthen your interest and understanding of the imperative role of sustainability in radiation oncology. Special thanks to Katie Lichter, MD, MPH, Climate Health Fellow at the University of California San Francisco, for her assistance with this issue and her passion and leadership surrounding climate change and cancer care.

Finally, I want to take this opportunity to announce that *Applied Radiation Oncology* has been accepted to the Committee on Publication Ethics (COPE), which is a tremendous achievement and affirms the journal's editorial/publishing policies meet COPE's rigorous standards! I want to thank our many contributors over the past 11 years, our advisory board, our readers, and Anderson Publishing—and especially thank Sharon Breske and Kieran Anderson for their diligence, focus, and passion in making this achievement possible.

# Adapting to the Virtual World: An Analysis of Remote Work Policies in Academic Radiation Oncology

## Introduction

The COVID-19 pandemic led to a shift from traditional work environments to working from home (WFH). The specific benefits and challenges of WFH in radiation oncology are currently unknown.

To address this gap in knowledge, a survey-based study was conducted to assess WFH policies and perceptions of their impact, as well as explore the role of departmental gender composition in remote work policies.

## Learning Objectives

Upon completing this activity:

1. Clinicians will be able to clarify the role that WFH has on physician well-being, burnout, and gender disparities within radiation oncology.
2. Clinicians will understand how to leverage WFH to maximize physician wellness and patient care.
3. Radiation oncology department leaders will be empowered to establish WFH policies that are both thorough and equitable.

## Authors

Sara Beltran Ponce, MD<sup>1\*</sup>; Amy LoTempio<sup>2\*</sup>; Erin Kaya, MD<sup>3</sup>; Katie Lichter, MD<sup>4</sup>; Shradda M. Dalwadi, MD<sup>5</sup>; Sumi Sinha, MD<sup>4</sup>; Lois Wairiri, MD<sup>6</sup>; William Stadlander<sup>7</sup>; Mary McGunigal, MD<sup>8</sup>; Reshma Jaggi, MD, DPhil<sup>9</sup>; Virginia W. Osborn, MD<sup>10</sup>; Elizabeth Jeans, MD<sup>11</sup>; Gabrielle W. Peters, MD<sup>12</sup>; Jenna M. Kahn, MD<sup>13</sup>

\*Co first authors

**Affiliations:** <sup>1</sup>Medical College of Wisconsin, Milwaukee, WI; <sup>2</sup>State University of New York Upstate Medical University, Syracuse, NY; <sup>3</sup>Oregon Health Sciences University, Portland, OR; <sup>4</sup>University of California San Francisco; <sup>5</sup>MD Anderson Cancer Center, Houston, TX; <sup>6</sup>University of Washington, Seattle; <sup>7</sup>Virginia Garcia Memorial Health Center and Foundation, Newburgh, OR; <sup>8</sup>Veteran Affairs New York Harbor Healthcare System, State University of New York–Downstate Medical Center, New York, NY; <sup>9</sup>Emory University, Atlanta, GA; <sup>10</sup>Massachusetts General Hospital, Exeter, NH; <sup>11</sup>Arizona Center for Cancer Care, Scottsdale, AZ; <sup>12</sup>Yale School of Medicine, New Haven, CT; <sup>13</sup>Kaiser Permanente, Portland, OR.

## Target Audience

- Radiation oncologists
- Related oncology professionals

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# Adapting to the Virtual World: An Analysis of Remote Work Policies in Academic Radiation Oncology

Sara Beltran Ponce, MD;<sup>1†</sup> Amy LoTemplo, BA;<sup>2†\*</sup> Erin Kaya, MD;<sup>3</sup> Katie Lichter, MD;<sup>4</sup> Shradda M. Dalwadi, MD;<sup>5</sup> Sumi Sinha, MD;<sup>4</sup> Lois Wairiri, MD;<sup>6</sup> William Stadtlander, MPH;<sup>7</sup> Mary McGunigal, MD;<sup>8</sup> Reshma Jaggi, MD, DPhil;<sup>9</sup> Virginia W. Osborn, MD;<sup>10</sup> Elizabeth Jeans, MD;<sup>11</sup> Gabrielle W. Peters, MD;<sup>12</sup> Jenna M. Kahn, MD<sup>13</sup>

## Abstract

**Objective:** The COVID-19 pandemic led to a shift from traditional work environments to working from home (WFH). The specific benefits and challenges of WFH in radiation oncology (RO) are currently unknown. To address this gap in knowledge, a survey-based study was conducted to assess WFH policies and perceptions of their impact, as well as explore the role of departmental gender composition in remote work policies.

**Materials and Methods:** Faculty and residents were randomly selected from the 92 American College of Graduate Medical Education-accredited RO residency programs. Descriptive statistics were generated for responses overall and separately among faculty and residents for demographic responses. They were also generated for responses relating to remote policy among departments with at least one-third female faculty/residents and those with less than one-third female faculty/residents. Associations between responses and groups were assessed using chi-square or Fisher exact tests for categorical responses and Wilcoxon rank-sum tests for numerical responses.

**Results:** Although 58.6% of faculty and 59.1% of residents perceived a negative or somewhat negative impact of WFH on patient satisfaction, the majority (> 51%) had positive perceptions of impact on all other measured outcomes, including their time with children, time with partner, time with other family members, and their personal wellness. Additionally, the current study revealed that 93.4% (n = 57) of departments comprised of more than one-third women had WFH policies in place, while only 84.2% (n = 64) of departments comprised of fewer than one-third female members had such policies.

**Conclusion:** These findings highlight the importance of diverse input from all genders as departments implement WFH policies. Further research should explore the durability of changes in workplace flexibility and how they may impact gender disparities within RO.

**Keywords:** work from home, academic radiation oncology, gender disparities

**Affiliations:** <sup>1</sup>Medical College of Wisconsin, Milwaukee, WI. <sup>2</sup>State University of New York (SUNY) Upstate Medical University, Syracuse, NY. <sup>3</sup>Oregon Health Sciences University, Portland, OR. <sup>4</sup>University of California San Francisco, San Francisco, CA. <sup>5</sup>MD Anderson Cancer Center, Houston, TX. <sup>6</sup>University of Washington, Seattle, WA. <sup>7</sup>Virginia Garcia Memorial Health Center and Foundation, Newburgh, OR. <sup>8</sup>Veteran Affairs New York Harbor Healthcare System, SUNY - Downstate Medical Center, New York, NY. <sup>9</sup>Emory University, Atlanta, GA. <sup>10</sup>Massachusetts General Hospital, Exeter, NH. <sup>11</sup>Arizona Center for Cancer Care, Scottsdale, AZ. <sup>12</sup>Yale School of Medicine, New Haven, CT. <sup>13</sup>Kaiser Permanente, Portland, OR. †Dr. Beltran Ponce and Ms. LoTemplo are co-first authors and contributed equally to the work.

**Corresponding author:** \*Amy LoTemplo, BA, 509 Columbus Ave, Apt. 2., Syracuse, NY 13210. (lotempla@upstate.edu)

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**Data sharing statement:** All data generated and analyzed during this study are included in this published article.



## Introduction

The COVID-19 pandemic has led to a significant shift from traditional work environments to working from home (WFH) for many health care workers.<sup>1-3</sup> This transition significantly impacted individuals responsible for family care as school closures required caretakers to balance professional, domestic, and educational roles.<sup>1</sup> These demands disproportionately impact women, who typically bear a greater portion of domestic and childcare responsibilities.<sup>4</sup>

This holds true in academic medicine, where women have been negatively impacted.<sup>5,6</sup> First-author publications by women decreased in the first year of the pandemic, despite a 2020 survey reporting that 41% of women felt they were expected to be more productive throughout COVID-19.<sup>5,6</sup> For instance, when compared with papers published in 2019, Andersen et al found that papers published between January 1, 2020 and May 5, 2020 had 23%, 16% and 16% lower proportion of female first authors, last authors, and general authors, respectively.<sup>5</sup> The misalignment between expectation and reality has placed a burden on women in academic medicine.

Before the pandemic, only 52% of female radiation oncology (RO) residents felt RO was family-friendly, and only 5% reported no symptoms of burnout.<sup>7</sup> Since COVID-19, female physicians have reported high levels of career uncertainty, and 71% of physician mothers with young children reported feeling that the pandemic limited their career advancement.<sup>6</sup>

Because little is known about how RO departments implemented WFH policies and how these policies were perceived in the field, we conducted a study to investigate the implementation of WFH policies

in RO and explore the role that departmental gender composition played in the development of remote work policies. These understandings may aid in the design of equitable remote work policies beyond COVID-19.

## Materials and Methods

This is a survey-based analysis that seeks to describe WFH policies within RO, perceptions of their impact, and whether the gender composition of departments was associated with policy characteristics. The questions of the survey were written by members of the Society for Women in Radiation Oncology (SWRO) and reviewed by the executive committee of SWRO and some members of the senior advisory counsel. The study received institutional review board (IRB) approval.

### Study Sample and Survey Administration

The survey was administered to the RO program director and 1 randomly selected resident from each US academic RO department. These participants were invited to complete an anonymous, web-based survey distributed through RedCap to all 92 American College of Graduate Medical Education-accredited RO residency programs in the United States. If the contacted RO program director or resident did not respond, a random faculty member or resident was chosen. Responses were collected from December 2020 to February 2021, with reminders sent every 2 weeks. If no response was received after the second reminder, an alternate participant was selected from the same institution.

### Survey Development and Measures

The survey consisted of 32 questions and assessed

5 themes: (1) respondent/department demographics, (2) WFH departmental policies, (3) perceived impact of WFH policies on domains of work and personal life, (4) utilization of WFH policy, and (5) sentiments about WFH. The survey assessed domains such as children's education, personal wellness, and time with family, as well as work-related tasks, patient care, educational responsibilities, research duties, and leadership duties. Data were held in RedCap and analyzed using R.

### Statistical Analysis

Descriptive statistics were generated for overall responses. For demographic questions, responses were stratified by the responder's role. For questions relating to remote policy, departments were stratified by those with at least one-third female faculty or residents and those with less than one-third female faculty or residents.

Associations between multiple-choice responses and stratification variables were assessed using Fisher exact tests when the expected value for any response subgroup was less than 5; in other cases, Pearson's chi-square tests were used. For the numerical response, a Wilcoxon rank-sum test was used.

All analyses were performed using R (version 4.0.5) and RStudio (version 1.4.1103) software.

## Results

A total of 146 responses were collected from 77 departments (84% of those contacted). Among the 77 faculty and 69 residents surveyed, 55% identified as female, 58% were White, and 51% were between 31 and 40 years, an age when most residents start to consider having families (**Table 1**). Of the

<b>Table 1. Survey of Participant Demographics</b>				
	<b>OVERALL N = 146</b>	<b>FACULTY (N = 77)</b>	<b>RESIDENT (N= 69)</b>	<b>P VALUE*</b>
Age [n (%)]				< .001
21-30	27 (18%)	1 (1.3%)	26 (38%)	
31-40	74 (51%)	33 (43%)	41 (59%)	
41-50	29 (20%)	27 (35%)	2 (2.9%)	
51-60	11 (7.5%)	11 (14%)	0 (0%)	
> 60	5 (3.4%)	5 (6.5%)	0 (0%)	
Gender [n (%)]				< .001
Female	80 (55%)	57 (74%)	23 (33%)	
Male	66 (45%)	20 (26%)	46 (67%)	
Race/ethnicity [n (%)]				.2
Asian	43 (29%)	24 (31%)	19 (28%)	
Black or African American	1 (.7%)	1 (1.3%)	0 (0%)	
Hispanic, Latino, or Spanish origin	8 (5.5%)	7 (9.1%)	1 (1.4%)	
White or Caucasian	85 (58%)	39 (51%)	46 (67%)	
Other	3 (2.1%)	2 (2.6%)	1 (1.4%)	
Prefer not to answer	6 (4.1%)	4 (5.2%)	2 (2.9%)	
Program location [n (%)]				.7
New England	7 (5.0%)	5 (6.8%)	2 (3.0%)	
Middle Atlantic	26 (19%)	12 (16%)	14 (21%)	
East North Central	27 (19%)	12 (16%)	15 (22%)	
West North Central	9 (6.4%)	3 (4.1%)	6 (9.0%)	
South Atlantic	25 (18%)	14 (19%)	11 (16%)	
East South Central	11 (7.9%)	5 (6.8%)	6 (9.0%)	
West South Central	10 (7.1%)	6 (8.2%)	4 (6.0%)	
Mountain	6 (4.3%)	3 (4.1%)	3 (4.5%)	
Pacific	19 (14%)	13 (18%)	6 (9.0%)	
Not provided	6	4	2	
Population where located [n (%)]				.4
< 2500	1 (.7%)	1 (1.4%)	0 (0%)	
> 20,000	14 (10%)	8 (11%)	6 (9.0%)	
< 250,000	7 (5.0%)	5 (6.8%)	2 (3.0%)	
250,000-1,000,000	37 (26%)	15 (21%)	22 (33%)	
> 1,000,000	81 (58%)	44 (60%)	37 (55%)	
Not provided	6	4	2	
Number of faculty/residents [median (IQR)]	9 (7, 14)	12 (8, 20)	8 (6, 11)	< .001
Not provided	9	6	3	
Faculty/resident demographics				.2
At least one-third female	61 (45%)	35 (49%)	26 (39%)	

**Table 1. continued**

	OVERALL N = 146)	FACULTY (N = 77)	RESIDENT (N = 69)	P VALUE*
Less than one-third female	76 (55%)	36 (51%)	40 (61%)	
Not provided	9	6	3	
Percent with children and/or dependents (female) [n (%)]				< .001
Few (< 10%)	44 (32%)	6 (8.3%)	38 (58%)	
Minority (10-50%)	21 (15%)	9 (12%)	12 (18%)	
Majority (50-80%)	24 (17%)	19 (26%)	5 (7.6%)	
Almost all (> 90%)	37 (27%)	32 (44%)	5 (7.6%)	
I don't know	12 (8.7%)	6 (8.3%)	6 (9.1%)	
Not provided	8	5	3	
Percent with children and/or dependents (male) [n (%)]				< .001
Few (< 10%)	17 (12%)	0 (0%)	17 (26%)	
Minority (10-50%)	45 (33%)	10 (14%)	35 (53%)	
Majority (50-80%)	39 (28%)	27 (38%)	12 (18%)	
Almost all (> 90%)	27 (20%)	26 (36%)	1 (1.5%)	
I don't know	10 (7.2%)	9 (12%)	1 (1.5%)	
Not provided	8	5	3	
Responsibilities prior to the pandemic [n (%)]				
Childcare	19 (13%)	14 (18%)	5 (7.2%)	.05
Child education	10 (6.8%)	7 (9.1%)	3 (4.3%)	.3
Other dependent care	9 (6.2%)	6 (7.8%)	3 (4.3%)	.5
Responsibilities at the onset of the pandemic [n (%)]				
Childcare	23 (16%)	16 (21%)	7 (10%)	.078
Child education	21 (14%)	16 (21%)	5 (7.2%)	.02
Other dependent care	10 (6.8%)	7 (9.1%)	3 (4.3%)	.3

\*Pearson's chi-square test or Fisher exact test for categorical variables; Wilcoxon rank-sum test for number of faculty/residents.

represented departments, 45% (n = 61) reported having less than one-third female-identifying faculty/residents. Among respondents, 48% reported that a majority or almost all males in their program had children or other vulnerable dependents in the household, while 44% responded this way regarding female colleagues. Before the pandemic, 6.8% (n = 10) of faculty and 9.1% (n = 7) of residents reported feeling responsible for child education. These values increased to 14% (n = 21) and 21% (n = 16), respectively, during the pandemic.

Only one department reported having a WFH policy in place before the pandemic (**Table 2**), while 42% reported having an ongoing WFH policy. Of those departments with WFH policies, 78% reported that policy installments were within the first 1-2 months of the onset of the pandemic. Of the departments comprised of at least one-third female members, 93.4% (n = 57) had WFH policies in place, while only 84.2% (n = 64) of the departments comprised of fewer than one-third female members had WFH policies in place. Of the

departments with a WFH policy during the initial phase of the pandemic, most later reduced their WFH allowances (56%, n = 68), while 12% (n = 15) expanded and 31% (n = 38) left them unchanged. In departments with less than one-third female faculty, 18% (n = 8) had policies that allowed for moderate (2-3 d at home) or full remote work policy options while 36% (n = 14) of the departments with at least one-third female faculty members had such policies. **Table 2** provides further details regarding the extent of WFH, rationale for its implementation,

**Table 2. Participant Responses Relating to Questions About Their Remote Work Policy**

	OVERALL (N = 137)	AT LEAST ONE-THIRD FEMALE (N = 61)	LESS THAN ONE-THIRD FEMALE (N = 76)	P VALUE*
Presence of policy [n (%)]				.15
Remote work policy already in place prior to the pandemic	1 (.7%)	1 (1.6%)	0 (0%)	
Remote work policy started during the pandemic, ongoing	57 (42%)	24 (39%)	33 (43%)	
Remote work policy started during the pandemic, now modified	63 (46%)	32 (52%)	31 (41%)	
No remote work policy	16 (12%)	4 (6.6%)	12 (16%)	
When policy started [n (%)]				.4
Within the first 1-2 mo of the onset of the US pandemic (January-March)	94 (78%)	42 (75%)	52 (81%)	
3-4 mo after the start of the US pandemic (April-May)	25 (21%)	14 (25%)	11 (17%)	
June 2020 or thereafter	1 (.8%)	0 (0%)	1 (1.6%)	
No response	17	5	12	
How policy has changed [n (%)]				.9
Expanded	15 (12%)	8 (14%)	7 (11%)	
Contracted	68 (56%)	31 (54%)	37 (58%)	
Unchanged	38 (31%)	18 (32%)	20 (31%)	
No response	16	4	12	
Amount of remote work (initial) [n (%)]				.9
Minimal remote work options (1 d per week at home)	43 (36%)	19 (33%)	24 (38%)	
Moderate remote work options (2-3 d at home)	59 (49%)	29 (51%)	30 (47%)	
Full remote work capability (all remote with only necessary in person interaction)	19 (16%)	9 (16%)	10 (16%)	
No response	16	4	12	
Amount of remote work (current) [n (%)]				.056
No remote work	22 (27%)	12 (31%)	10 (23%)	
Minimal remote work options (1 d per week at home)	34 (41%)	10 (26%)	24 (55%)	
Moderate remote work options (2-3 d at home)	20 (24%)	12 (31%)	8 (18%)	
Full remote work capability (all remote with only necessary in person interaction)	2 (2.4%)	2 (5.1%)	0 (0%)	
Other	5 (6.0%)	3 (7.7%)	2 (4.5%)	
No response	54	22	32	
	OVERALL (N = 121)	AT LEAST ONE-THIRD FEMALE (N = 57)	LESS THAN ONE-THIRD FEMALE (N = 64)	P VALUE*
Department rationale for policy [n (%)]				
Public health (prevalence and risk of COVID-19 in the community)	118 (98%)	55 (96%)	63 (98%)	.6

**Table 2. continued**

	OVERALL (N = 121)	AT LEAST ONE-THIRD FEMALE (N= 57)	LESS THAN ONE-THIRD FEMALE (N = 64)	P VALUE*
Culture (preference spoken by physicians)	25 (21%)	13 (23%)	12 (19%)	.6
Financial (dependents at home)	14 (12%)	11 (19%)	3 (4.7%)	.012
Legal	1 (.8%)	0 (0%)	1 (1.6%)	> .9
Other	3 (2.5%)	2 (3.5%)	1 (1.6%)	.6
Unsure	1 (.8%)	0 (0%)	1 (1.6%)	> .9
Tasks integrated into remote work policy [n (%)]				
Direct patient care (consults, OTVs, follow-up visits)	69 (57%)	36 (63%)	33 (52%)	.2
Clinical documentation	109 (90%)	52 (91%)	57 (89%)	.7
Patient planning (simulation, contouring, plan review/ approval)	105 (87%)	49 (86%)	56 (88%)	.8
Patient treatment (IGRT review)	73 (60%)	31 (54%)	42 (66%)	.2
Departmental requirements (chart rounds, education)	109 (90%)	51 (89%)	58 (91%)	.8
Hospital requirements (tumor board, research grand rounds)	114 (94%)	54 (95%)	60 (94%)	> .9

and tasks included in WFH provisions.

A majority of faculty (> 51%) and residents (> 51%) indicated that WFH was perceived to have a positive or somewhat positive impact on all measured outcomes, except for patient satisfaction with care (**Figure 1**). Both faculty and residents reported that “time with partner” was the most positively impacted domain, with 91.4% of faculty and 95.4% of residents rating this domain as “positively” or “somewhat positively” impacted by WFH. The only domain in which the degree of satisfaction varied significantly between residents and faculty was research. Nearly half of the faculty (44.3%) indicated that their research duties had either been “somewhat negatively” or “negatively” impacted, while only 19.7% of residents shared this sentiment. Subjective

commentary on WFH experiences varied (**Table 3**).

### Discussion

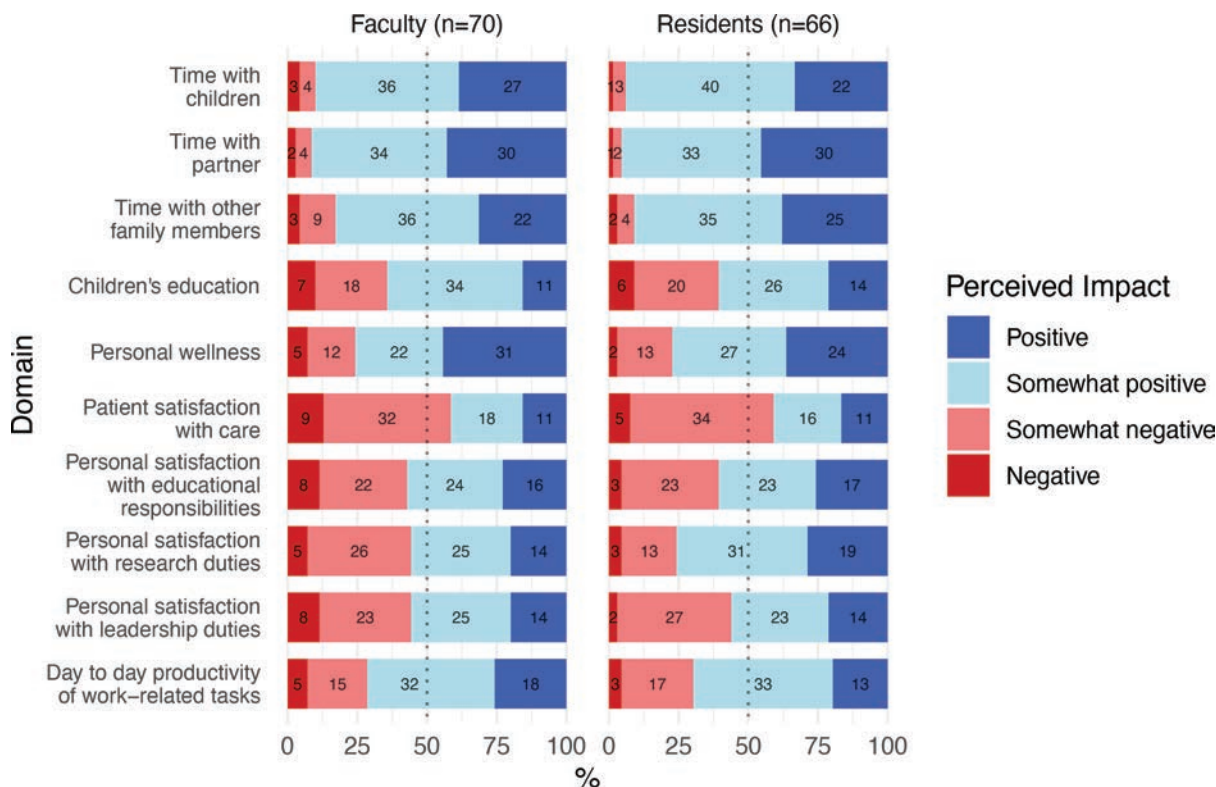
COVID-19 posed significant challenges for RO departments. A total of 87.6% of departments implemented WFH policies in response to the pandemic, reflecting the adaptations that were required to maintain safety and efficiency. This study highlights several aspects of WFH in RO that warrant consideration, including physician satisfaction, burnout, patient care, and gender equity.

Our findings are consistent with current literature relating to RO physician satisfaction during the pandemic, demonstrating that radiation oncologists report decreased burnout with WFH. A

survey by Hoffman et al found higher 2020 pre-pandemic burnout rates compared with rates during the pandemic WFH era (40% vs 32%,  $P < .05$ , respectively), and most employees (74%) reported having a positive experience with WFH.<sup>3</sup> Similarly, we found that RO faculty and residents perceived positive WFH-related impacts. More specifically, 90% of faculty and 93.9% of residents reported a positive or somewhat positive impact on their time with children. Additionally, 75.7% of faculty and 77.3% of residents perceived a somewhat positive or positive impact on their personal wellness. This suggests that WFH may improve the overall quality of life for some RO employees.

Despite the positive impacts of WFH on RO job satisfaction, research suggests that clinical

**Figure 1.** Perceived impact of work from home on domains of work and life.



employees are more likely to experience decreased productivity while working from home. A study by Shih et al found that research (63%) and administrative (75%) employees reported stability or an increase in their productivity, whereas clinical staff reported decreased productivity with remote work, an important consideration for evolving policies. More specifically, some limitations of WFH for clinical care include the inability to reliably take vital signs, the inability to quickly handle emergencies, and the potential degradation of the patient-provider relationship.<sup>8</sup> While telemedicine has drawbacks, it allows for increased access to health care, as patients do not need to travel to their appointments and can decrease lost wages or other financial burdens of attending physician appointments. Additionally, patients

who are immunocompromised, such as cancer patients, can have their appointments without being exposed to other patients who may spread infectious diseases in an office setting.<sup>9</sup> Moving forward, technological advancements will likely improve the quality of virtual health care, reduce patient and provider costs, and streamline electronic communication with patients and colleagues, which may mitigate clinical staff concerns.<sup>10</sup> There may also be a need for identifying tangible performance objectives that ensure RO employees can thrive in all settings. Lastly, our study found that departments with a higher percentage of women were more likely to have WFH policies and more flexible options (Table 2, comments 6-8). Our results also showed that WFH can improve domestic tasks for women with children, but also

highlighted the need for considering the unique challenges faced by female physicians in WFH policy decisions.<sup>5,6</sup> Policy changes that could help with work-life balance include allowing employees to keep their cameras on or off according to their preferences and needs at work meetings, which could allow for more privacy for employees to complete activities such as breastfeeding while participating in work meetings. In addition to flexible on-screen policies, a culture of acceptance for children or pets in the background of video calls that are not patient-facing can normalize the struggles to find balance for all employed people. Finally, designating virtual days on which employees have all of their virtual appointments on 1 day of the week and allowing for those with academic days to complete them remotely can decrease commute

**Table 3. Select Participant Quotes Illustrating the Diversity of Views on WFH in RO, Both in Personal and Professional Aspects****SELECTED RESPONSES FROM PARTICIPANTS REGARDING THEIR PERSONAL EXPERIENCES DURING COVID-19**

<p>“Education and tumor board review via virtual zoom should continue after the pandemic. It is convenient. There is a higher number of participation (easier to sign on than to physically be there).</p> <p>And you can see in detail the radiological image on the shared screen.</p> <p>Plan review with attending and dosimetrists have been very productive virtually (we use Microsoft Teams). Viewing a shared screen is easier than looking over someone else’s shoulder.</p> <p>Remote patient simulation is not possible. You can’t learn how to set up a patient without being there in person. Remote OTV is not helpful. I learn better from physically examining the patient. I would prefer consults and follow-ups in person. Many patients have technological issues that degrade the quality of the interaction with the physician. And the inability to perform a physical exam is big problem.”</p>
<p>“Work from home is doable for Radiation Oncology faculty for part of the week. 1-2 days of work from home are not disruptive and may improve work-life balance.”</p>
<p>“I think working from home has been a positive experience, more time with loved ones at home, more time freed up from less travel to and from work, increased time and energy for patient care, and improved quality of life.”</p>
<p>“In the beginning, there was an overreaction with everyone working from home. That was detrimental to spontaneous casual interactions such as conversations between physics, dosimetry and physicians, which are important for improving departmental capabilities over time and continuously educating members of the department (for example, physician teaching a new dosimetrist different ways of planning and physicist debating merits of a certain technique with physician). These productive interactions were greatly missed, but there is an advantage to having at least some time at home with remote meetings and time to catch up and avoid burnout. Plus, it makes [my] spouse happy to have me at home even if I’m in the home office working. I think our department found a balance that works for us, and I assume it will continue in some capacity moving forward.”</p>
<p>“Some disease sites are more suited to work from home and some really can’t provide good clinical care without in person patient evaluation. If you’re a physician treating brain tumors or routine prostate or breast maybe work from home is ok. If you do head and neck or Gyn requiring more invasive or closer examination not amenable to video then you can’t provide optimal clinical care on a work from home basis, this disproportionately affects people who are in those specialties.”</p>
<p>“It allows me taking care of children education when they are studying from home. I am more efficient using my time without sacrificing patient care. This policy of 1 WFH day will stay in my institution because of good feedback.”</p>
<p>“I had a baby in the NICU and the remote work policy allowed me to keep my baby safe while maintaining clinical productivity.”</p>
<p>“At times difficult to find quiet spot, but productive. Allowed me to continue breastfeeding longer than I could with my first child since I was home.”</p>
<p>“Our therapists and nurses need to be there in person. Physicians and residents should be there managing patients in person with appropriate PPE too. Patient care is optimal in person. I cannot adequately examine a patient through a video screen. One could consider working from home on admin/non-clinical days but that still leaves others to cover clinical work that occurs on those days and that creates additional unnecessary burden on others, esp when working from home may be less productive.”</p>

**Abbreviations:** RO, radiation oncology; WFH, working from home.

time, allow for more personalization of one’s schedule, and increase efficiency.

Limitations of the study include assessing only academic departments with a limited number of participants and a lack of data on the impact of technology on WFH productivity. Additionally, this survey captures only a specific moment in time and therefore is not entirely reflective of the evolving pandemic-related

policy landscape. Further research is needed to improve virtual health care tools and guide policies for clinicians with a balance of tasks that can be completed remotely. These future studies should investigate the effectiveness of hybrid work models, physician satisfaction with these work models, retention of faculty members working with hybrid work models, and patient satisfaction with virtual visits.

Overall, our study highlights the challenges and opportunities presented by WFH in RO during the COVID-19 pandemic. Our findings suggest that more equitable policies may be necessary to support female physicians. Furthermore, this study provides valuable insights that can inform the development of WFH policies that balance the needs of physicians, patients, and the health care system.

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# Assessing the Readiness for Climate Change Education in Radiation Oncology in the US and Canada

Sierra M. Silverwood, BA;<sup>1†\*</sup> Katie E. Lichter, MPH, MD;<sup>2†</sup> Konstandina Stavropoulos, BS;<sup>1</sup> Tyler Pham, BS;<sup>1</sup> James Randall, MD;<sup>3</sup> Leah D'Souza, MD, MSc;<sup>4</sup> Nauman Malik, MD;<sup>5</sup> Jennifer Croke, MD;<sup>5</sup> Jillian R. Gunther, MD;<sup>6</sup> Jeffrey Cao, MD;<sup>7</sup> Joanne Alfieri, MD;<sup>8</sup> Osama Mohamad, MD;<sup>6</sup> Daniel W. Golden, MD, MHPE;<sup>4</sup> Steve Braunstein, MD, PhD<sup>2</sup>

## Abstract

**Objective:** Climate change poses significant challenges to health care, with radiation oncology being no exception. Educational gaps exist among radiation oncology professionals regarding the implications of climate change on patient care and health care delivery. This study aims to assess the perspectives of US and Canadian radiation oncology program directors (PDs) and associate program directors (APDs) on climate change education and its integration into residency programs.

**Materials and Methods:** A survey was distributed to 114 PDs and APDs in the United States and Canada, focusing on attitudes toward climate change education, knowledge and beliefs about climate change and environmental sustainability, and perceptions of its impact on clinical practice. The final survey comprised 15 items, including a 5-point Likert-type scale (1=strongly disagree, 5=strongly agree), multiple-choice, and open-ended questions. Analysis of variance and post hoc least significant difference tests were used for data analysis.

**Results:** Of the 114 individuals contacted, 36 responded (response rate 32%). Respondents rated the importance of incorporating climate change content into residency curricula at an average of  $2 \pm 1.2$ . Significant differences in attitudes were observed based on attendance at prior educational sessions on climate change ( $P < .05$ ); nonattendees rated the importance of this education lower, averaging  $1 \pm 0.0$  vs  $3.3 \pm 1.0$ . Geographical analysis showed that 66% of Canadian respondents were in favor of integrating climate-related material into curricula compared with only 42% of United States counterparts ( $P < .05$ ).

**Conclusion:** Despite varying interest levels and perceived relevance, the study underscores a need for enhanced climate change education in radiation oncology. It suggests exploring alternative educational avenues, such as continuing medical education and professional conferences, to address the challenges highlighted in this study. Incorporating climate change discussions into health care, particularly in training future radiation oncologists, is necessary for the field to adapt to and address the challenges posed by climate change.

**Keywords:** climate change, radiation oncology, medical education, GME, health care sustainability

**Affiliations:** <sup>1</sup>Michigan State College of Human Medicine, Grand Rapids, MI. <sup>2</sup>University of California San Francisco, San Francisco, CA. <sup>3</sup>Northwestern University, McGaw Medical Center, Chicago, IL. <sup>4</sup>RUSH University Medical Center, Chicago, IL. <sup>5</sup>Princess Margaret Cancer Center, Toronto, ON. <sup>6</sup>MD Anderson Cancer Center, Houston, TX. <sup>7</sup>University of Calgary, Calgary, AB. <sup>8</sup>McGill University, Montreal, QC. †Ms. Silverwood and Dr. Lichter served as co-first authors and contributed equally to the work.

**Corresponding author:** \*Sierra M. Silverwood, BA, 15 Michigan St NE, Grand Rapids, MI, 49503. (silverwo@msu.edu)

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## Introduction

The need for medical professionals, including radiation oncologists, to receive education on climate change and its associated impacts on health care is becoming increasingly evident.<sup>1</sup> The rise of extreme weather events linked to climate change is known to disrupt radiation therapy delivery through power outages, damage to crucial infrastructure, and interruptions in transportation networks, thereby adversely affecting patient outcomes, particularly in vulnerable groups such as the elderly and socioeconomically disadvantaged populations.<sup>2-6</sup> Furthermore, these climate-induced changes contribute to the proliferation of diseases and jeopardize essential resources like food and water supplies, as well as access to health care services.<sup>7,8</sup> Recent studies have found that 80% of health care workers, including those in radiation oncology, are urging their employers to prioritize sustainable and environmentally conscious practices.<sup>9</sup> However, 41% of physicians feel ill-prepared to discuss climate change with patients, highlighting a significant knowledge gap and emphasizing the urgency for educational initiatives in this domain.<sup>10</sup>

Efforts to incorporate climate change material into graduate medical education (GME) have been gaining traction across various fields nationally and internationally.<sup>11-15</sup> In June 2019, the American Medical Association (AMA) released a policy statement supporting the inclusion of climate change content throughout GME.<sup>16</sup> Despite the AMA's support for such initiatives, a notable gap remains within the field of radiation oncology.<sup>17</sup>

Our aim was to evaluate the perspectives of US and Canadian radiation oncology program directors (PDs) and associate

program directors (APDs) on climate change and sustainability education, as well as its impact on health care. Furthermore, this survey aims to identify both barriers and facilitators to implementing climate change education in these programs, potentially highlighting effective strategies for its incorporation. In doing so, this study seeks to foster a new generation of radiation oncologists who have the knowledge and skills to effectively address and adapt to the challenges climate change poses.<sup>18</sup>

## Materials and Methods

### Study Population

The study focused on radiation oncology PDs and APDs in the United States and Canada. This group was chosen given their historical role in developing GME and continuing medical education (CME). The University of California San Francisco and Michigan State University Institutional Review Boards approved this study as exempt.

### Survey Development

The survey was developed referencing published studies focusing on understanding perspectives on climate change and education initiatives.<sup>12-14,19-22</sup> Survey questions fell into 3 main categories: climate change education and its integration into radiation oncology residency curricula, knowledge and beliefs about climate change and sustainability, and perceptions of climate change's impact on clinical practice and patient care (see **Supplementary Appendix** for details [available in the online version of this article at [www.appliedradiationoncology.com](http://www.appliedradiationoncology.com)]). Basic demographic information, including participants' gender and location, was also

collected. The survey was piloted with 10 experts in radiation oncology, education, and climate science to improve the clarity, relevance, and structure of the questions.

The final survey comprised 15 items, including a 5-point Likert-type scale, multiple-choice, and open-ended questions. The 5-point Likert-type scale, which ranged from 1 (strongly disagree) to 5 (strongly agree), assessed 10 questions across 3 main categories detailed in the **Supplementary Appendix** (available in the online version of this article at [www.appliedradiationoncology.com](http://www.appliedradiationoncology.com)). Definitions of key terms were provided (see **Supplementary Appendix**) to ensure a uniform understanding. The survey was emailed to 114 PDs and APDs in the United States ( $n=101$ ) and Canada ( $n=13$ ). Participants were allotted 1 month to complete the survey, during which time 2 additional reminders were sent. No incentives were offered. The survey was administered through Qualtrics digital software version XM ©2020, and all data collected were anonymized. In accordance with institutional review board guidelines, participants were not obliged to answer every question.

### Data Analysis

Descriptive statistics (mean and standard deviation [SD]) were calculated to summarize the characteristics of participants and question responses. To investigate the differences in response patterns based on exposure to climate change education (not been offered sessions, have attended, offered but not attended), geographical location (United States, Canada), perceived importance of climate change and sustainability (low, moderate, high), and gender (male, female, other), multiple one-way analysis of variance (ANOVAs) were

**Table 1. Characteristics of Survey Respondents (n = 69)**

STUDY PARTICIPANTS	N (%)
Role	
Program directors	24 (88.9)
Associate program directors	3 (11.1)
Gender	
Female	13 (46.4)
Male	11 (39.3)
Self-described	1 (3.6)
Prefer not to say	3 (10.7)
Region	
Northeast	5 (18.5)
Southeast	5 (18.5)
Midwest	7 (25.9)
Southwest	-
West	4 (14.8)
Hawaii/Alaska	-
Canada	6 (22.2)

employed. For post hoc testing, the least significant difference (LSD) tests were conducted, considering the relatively small number of comparison groups in each analysis. A *P* value of < 0.05 was considered statistically significant for statistical tests. All statistical analyses were carried out using Statistical Software for the Social Sciences (SPSS, IBM).

## Results

### Demographics

Of the 114 PDs and APDs, 36 individuals responded to the survey for an overall response rate of 32%. Of these individuals, 21 (58%) were from the United States, 6 (17%) were from Canada, and 9 (25%) did not report their location (**Table 1**). Within the United States, the Midwest (19%) was the most represented, followed by the Northeast and Southeast (14% each), and the West (11%). Notably, no responses were received from

individuals in the Southwest, Hawaii, or Alaska. Among the participants, 24 (67%) were PDs and 3 (8%) were APDs, with 9 (25%) not specifying their role. Gender distribution varied, with 13 (36%) females, 11 (30%) males, 1 (3%) self-identifying, and another 11 (31%) choosing not to disclose gender.

### Climate and Education

Overall, respondents did not agree that incorporating climate change (mean 2 ± SD 1.2) and sustainability (mean 2 ± 1.2) content into radiation oncology residency curricula is important. There, however, was moderate agreement that residents would be interested in learning these topics (mean 3 ± 1.1), while fewer perceived faculty would share this interest (mean 2 ± 1.1).

Respondents rated the most important educational topics in relation to climate change to be cancer (44%), food and water security (38%), and health disparities and inequities (30%). The

preferred methods and challenges for incorporating climate health education are demonstrated in **Figures 1** and **2**.

### Perceptions Around Climate Change

The survey revealed moderate agreement regarding the importance of climate change (mean 3 ± 1.2) and sustainability (mean 3 ± 1.3) for radiation oncologists. The relevance of climate change in addressing health equity also received a mean score of 3 ± 1.2.

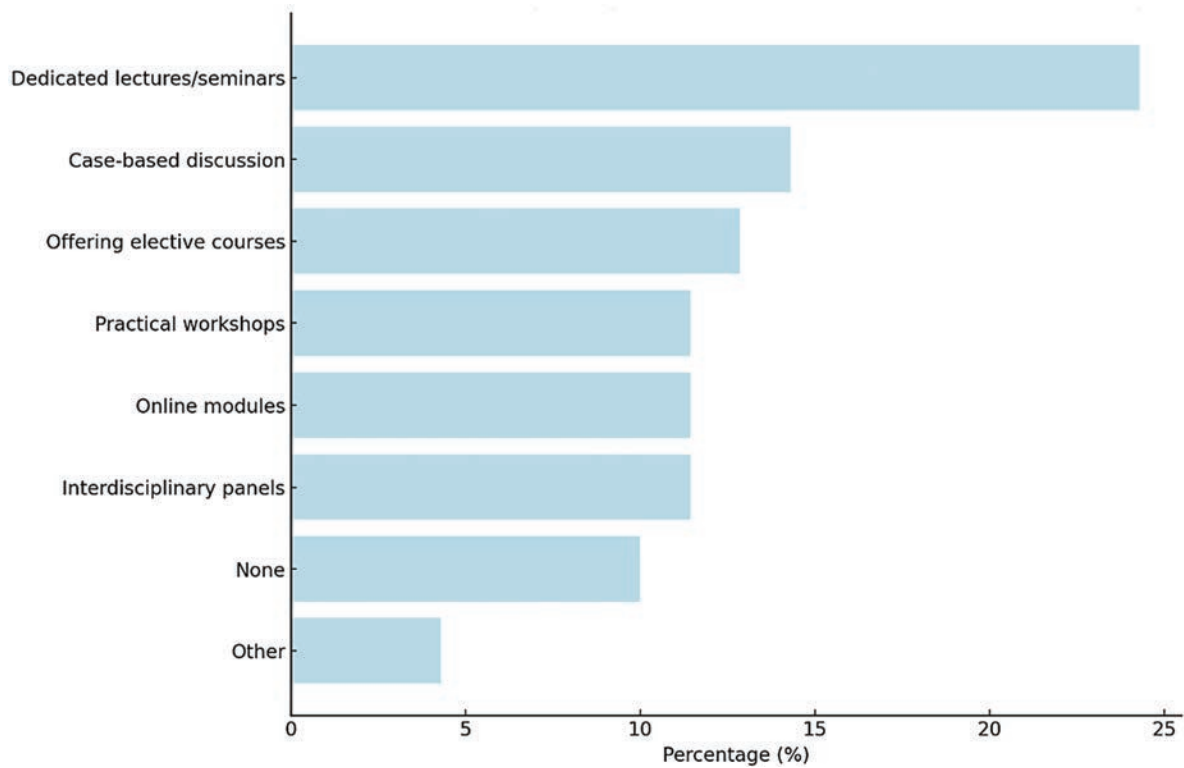
### Perceived Relationship Between Climate Change and Patient Care

While acknowledging the impact of climate change on patients (mean 4 ± 1.1), most respondents doubted the necessity for radiation oncologists to discuss these issues with patients (mean 2 ± 1.5). Only 6% of respondents felt sufficiently prepared to counsel patients on the health impacts related to climate change, whereas 10% expressed confidence in advising patients on protecting themselves against climate-related health impacts (see **Figure 3**).

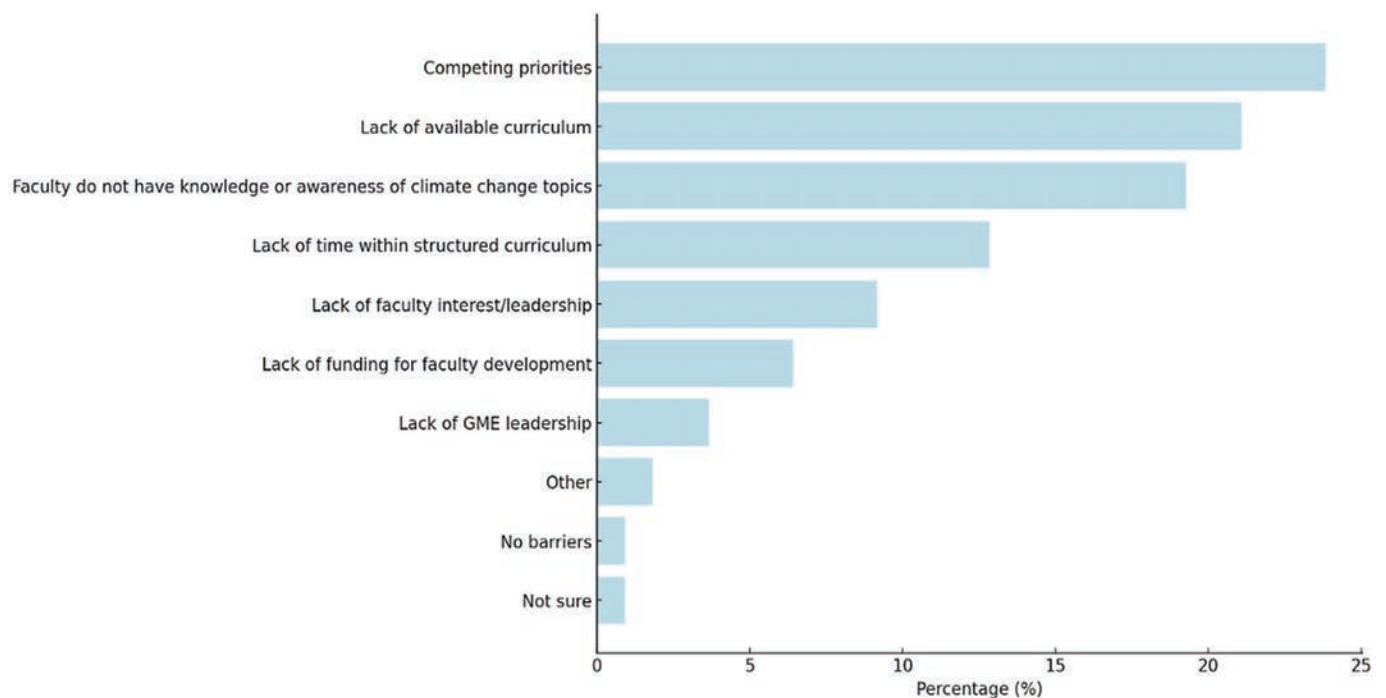
### Impact of Educational Sessions on Attitudes Toward Climate Change

Using ANOVA, significant differences were observed in attitudes toward climate change and sustainability curricula among groups defined by their participation in prior educational sessions (*P* < .05). Key areas where notable disparities emerged included the perceived urgency of addressing climate change in residency curricula, the importance of sustainability in the practice of radiation oncology, willingness to incorporate related materials into educational curricula, and perceptions of faculty interest in these topics among PDs/APDs (**Table 2**).

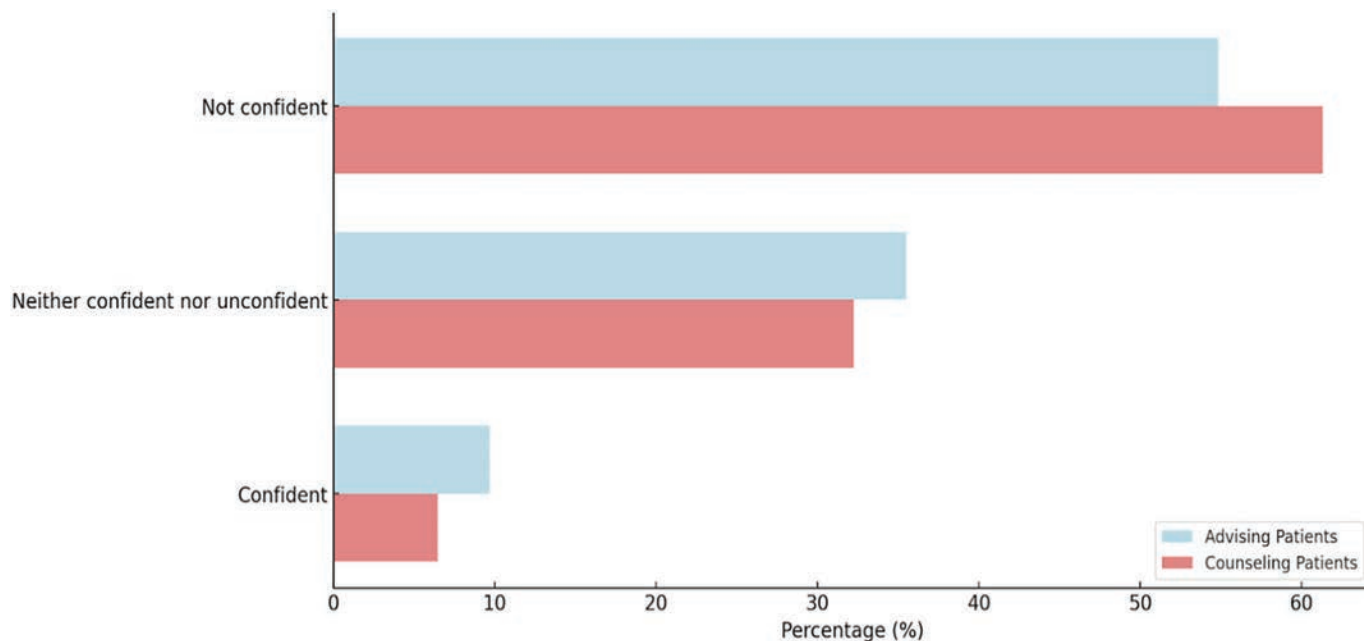
**Figure 1.** Preferred method for integrating climate health education into a residency program (n=36).



**Figure 2.** Respondent's perceived barriers to implementing climate health and sustainability curriculum in radiation oncology programs (n = 31). Note that all individuals responded to this question. GME, graduate medical education.



**Figure 3.** Confidence of program directors (PDs) and associate program directors (APDs) in counseling patients on the health impacts of climate change and advising them on measures they can take to protect themselves from climate change-related impacts (n = 31). Note that all individuals responded to this question.



### Comparative Analysis Based on Session Attendance

Further investigation with post hoc LSD tests (a method used to find differences between group means) showed significant differences among 3 groups: those who attended educational sessions on climate change, those who were offered but did not attend, and those who were not offered any education on the subject ( $P < .05$ ). Specifically, participants who had not been exposed to education on climate change demonstrated significantly lower levels of acknowledgment regarding the importance of climate change and sustainability within their professional domain.

### Perceptions of Climate Change and Sustainability

Similarly, the study revealed that recognizing the significance of climate change and sustainability affects various perceptions, such as equity in responses, the

urgency of incorporating these topics into residency curricula, the fundamental importance of sustainability, and the necessity for radiation oncologists to engage in discussions about these issues with patients ( $P < .05$ ). Further analysis using post hoc LSD tests showed that those who deemed climate change and sustainability important were also more likely to express concern about related topics.

### Perceptions Across North America

Finally, the impact of location (Canada vs the United States) on responses was evaluated using chi-square analysis. A higher percentage of Canadian respondents, compared with their United States counterparts, indicated a willingness to integrate climate-related material into residency curricula if such material was provided (66% vs 42%,  $P < .05$ ). However, for the other questions posed in the study, there were no significant differences in responses between the 2 groups.

### Discussion

This study provides insight into the attitudes and opinions of radiation oncology PDs and APDs in the United States and Canada regarding the integration of climate change education into radiation oncology GME. This investigation is particularly timely, given the growing recognition of climate change's impact on health care delivery and patient outcomes, especially in specialized fields like radiation oncology. The broader trend toward environmental consciousness in health care, as demonstrated by findings from a national study, highlights the importance of incorporating climate change education and sustainability practices into radiation oncology curricula, aligning with the evolving priorities of medical professionals across the nation.<sup>9</sup>

A significant finding from this study is the discrepancy between the recognized importance of climate

**Table 2. Median Scores and Standard Deviations for Likert Scale Responses From PDs/APDs (Scale: 1 = Strongly Disagree, 5 = Strongly Agree) on Climate and Sustainability Survey Questions**

QUESTIONS	ALL RESPONDENTS	PRIOR EDUCATION	OFFERED EDUCATION, BUT DID NOT ATTEND	NOT OFFERED EDUCATION	P VALUE (T TEST)
	N = 36	N = 22	N = 5	N = 4	
	MEAN ± SD	MEAN ± SD	MEAN ± SD	MEAN ± SD	
Climate change is an important issue for radiation oncologists	3 ± 1.2	3.5 ± .9	2.2 ± 1.5	3.0 ± 1.1	.26
Climate change is an important issue for addressing health equity	3 ± 1.2	3.5 ± .9	2.4 ± 1.5	3.0 ± 1.0	.37
It is important to address climate change and its health impacts in the core radiation oncology residency curriculum	2 ± 1.4	3.2 ± 1.0	1.0 ± .0	2.8 ± 1.3	<b>.010</b>
Sustainability and health care decarbonization is an important issue for radiation oncologists	3 ± 1.3	3.5 ± 1.0	1.6 ± 1.3	3.0 ± 1.2	<b>.05</b>
It is important to address sustainability and health care decarbonization in the core radiation oncology residency curriculum	2 ± 1.3	3.3 ± .8	1.8 ± 1.6	2.4 ± 1.1	.22
Climate change currently impacts population health outcomes	4 ± 1.1	3.8 ± .4	2.6 ± 1.2	3.3 ± 1.0	.25
It is important for radiation oncologists to bring the health impacts of climate change to the attention of their patients	2 ± 1.5	2.8 ± .8	1.2 ± .4	2.7 ± 1.6	.12
I would be willing to make time in the curriculum to discuss climate change and sustainability if educational materials were provided	2 ± 1.5	3.3 ± 1.0	1.0 ± .0	3.2 ± 1.4	<b>.01</b>
I believe residents would be interested in learning more about climate change and its health impacts	3 ± 1.1	3.3 ± .8	2.2 ± 1.5	2.9 ± 1.0	.35
I believe other faculty, in addition to residents, would be interested in learning more about climate change and its health impacts	2 ± 1.1	3.0 ± .8	1.4 ± .5	3.0 ± 1.0	<b>.01</b>

Abbreviations: APDs, associate program directors; PDs, program directors; SD, standard deviation.  
 Bolded values are statistically significant.

change impacts on patient health and the low priority given to integrating climate change content into radiation oncology residency curricula. This divergence suggests a gap between awareness and action within the field. The AMA's support for climate change education, echoed by organizations like the American Society for Radiation Oncology (ASTRO) and American Society for Clinical Oncology (ASCO), contrast with our findings of a tepid interest from RO educational leaders (PDs and APDs), underscoring the

need for a broader cultural shift within the specialty.<sup>16,23,24</sup>

Notably, the study revealed that those with prior education or acknowledgment of the significance of climate change were more likely to integrate this knowledge into their medical practice, including finding opportunities to reduce their own "clinical footprint." However, the survey did not detail the nature of this prior education—such as venue (eg, conferences or CME), format (online or in-person), timing, or session quantity. Despite this,

given the wide range of educational opportunities offered by numerous institutions, from formal lectures to informal discussions, the authors inferred that respondents may have participated in such activities.<sup>25-27</sup> This finding suggests that the route to incorporating climate change education into radiation oncology may lie in alternative educational avenues outside the traditional GME structure. CME programs, for instance, could offer targeted courses linking climate change and radiation oncology, as

evidenced by previous successful programs.<sup>25-28</sup> Conferences also provide an expansive platform for workshops, lectures, and panel discussions. Furthermore, the success of platforms like the Radiation Oncology Education Collective Study Group (ROEC SG) and Diversity, Equity and Inclusion in Radiation Oncology (DEInRO) in delivering accessible, customized educational content indicates a promising avenue for disseminating information on climate change and radiation therapy.<sup>29,30</sup>

However, the integration of climate change education into GME remains a crucial long-term objective. The disproportionate impact of climate-related events, such as wildfires, on vulnerable populations and the subsequent exacerbation of health care disparities highlight the urgent need for comprehensive training in this area within oncology.<sup>2,6,31</sup> Such education would not only inform residents about the interplay between environmental factors, public health, and social equity but also empower them to make environmentally conscious decisions in their future clinical practices. Nevertheless, the barriers to implementation highlighted by the survey, such as competing priorities and the need to train and provide educational material to faculty, must be acknowledged and addressed. One approach to bridge these gaps could be the integration of new materials into supplementary didactic sessions rather than embedding them directly into the core radiation oncology curriculum. This strategy could help manage the challenge of overburdening the core curricula while still educating residents on the importance of these topics. Potential pathways for such integration

could involve collaboration with professional radiation oncology bodies, educational committees, or accreditation organizations to develop and disseminate such material. The existence of third-party organizations, such as Climate Resources for Health Education (CRHE)<sup>32</sup>, which are already dedicated to providing educational materials for health care professionals, could facilitate this process and lessen the burden on institutions to develop new content.

The study is subject to several limitations, such as potential response bias and inadequate geographical representation. Certain confounding factors and historical elements, such as regional susceptibilities to climate events, add additional complexity to interpreting the presented data regarding patient vulnerability to climate-related interruptions of care. Additionally, the results may be influenced by social desirability bias, with respondents possibly overestimating the importance of climate change to align with perceived socially acceptable views. The inability to thoroughly analyze the impact of location on survey responses because of the small sample size as well as the structure and phrasing of the survey may both bias responses and limit the interpretation of the findings. Finally, while the response rate is low and limits the generalizability of our study, it is comparable to other studies on this topic.<sup>10,12-14</sup>

Despite these limitations, the findings offer meaningful insights from leaders in radiation oncology education, shedding light on both the facilitators and obstacles to integrating climate change education within the field. In response to the feedback received, we recommend future surveys

specifically address the nuances of integrating climate change topics into the core radiation oncology curriculum. This could involve a careful distinction between the addition of discrete didactic sessions and the broader implications of embedding such content as a core component, thereby ensuring a more nuanced understanding of stakeholders' willingness and the practical challenges involved.

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## Conclusion

In conclusion, while the study indicates a degree of reluctance within the radiation oncology community to prioritize climate change education, it also points to alternative pathways and the need for a multifaceted approach to incorporate this critical subject into the curriculum. The integration of climate change discussions into health care education, particularly in specialties like radiation oncology, is not just a matter of academic interest but a necessity to prepare health care professionals for the challenges posed by a changing climate. Through dedicated efforts to embed these topics into medical training, there is an opportunity to shape a generation of radiation oncologists who are not only skilled clinicians but also informed and proactive in addressing environmental challenges and the associated impact on patient care.

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# Travel-Related Environmental Impact of Telemedicine in a Radiation Oncology Clinic

Melissa A. Frick, MD;<sup>1,2\*</sup> Claire C. Baniel, MD;<sup>3</sup> Katie Lichter, MD;<sup>4</sup> Hilary P. Bagshaw, MD<sup>3</sup>

## Abstract

**Objective:** The environmental impact of telemedicine within radiation oncology has not yet been established. This is particularly relevant as climate change is recognized as one of the largest threats to human health, including oncological outcomes. The health care sector significantly contributes to global carbon emissions, in part due to patient travel. We assessed the impact of telemedicine utilization on patient travel-related greenhouse gas (GHG) emissions for a large radiation oncology clinic located in a densely populated suburban setting.

**Materials and Methods:** All in-person and telemedicine visits scheduled in a radiation oncology clinic over 7 consecutive days in June 2021 were retrospectively reviewed. Care visits with out-of-state patients were excluded. Travel distance between patients' reported home address and the clinic address was estimated using Google Maps. Associated GHG emissions were calculated using a well-to-wheel model. Gas, hybrid, plug-in hybrid, and electric vehicle utilization were accounted for per statewide vehicle registration statistics. GHG emissions were converted into carbon dioxide equivalents (CO<sub>2</sub>e) using 100-year global warming potentials.

**Results:** A total of 156 clinic visits were conducted over the time period; 115 via telemedicine (74%) and 41 in-person (26%). Patients traveling for in-person visits had a median round trip of 44 miles; of those seen via telemedicine, a median of 60 travel miles were saved. Use of telemedicine "saved" an estimated 13,828 travel miles in 1 week, translating into 719,056 miles saved annually. The forecasted annual savings of CO<sub>2</sub>e attributed to telemedicine visits is 339.8 metric tons, the equivalent emissions of 65.7 homes' electricity use for 1 year.

**Conclusion:** Integration of telemedicine within a radiation oncology clinic reduces the environmental impact of patient care. Advocacy efforts should support telemedicine where feasible and clinically appropriate to decrease carbon emissions associated with the practice of radiation oncology, as well as to establish and promote environmentally sustainable behaviors within the field.

**Keywords:** telemedicine, telehealth, virtual health, digital health, sustainability, sustainable health care, greenhouse gas, carbon emissions, climate change

**Affiliations:** <sup>1</sup>Penn Medicine Lancaster General Health, Lancaster, PA. <sup>2</sup>Ann B. Barshinger Cancer Institute, Lancaster, PA. <sup>3</sup>Department of Radiation Oncology, Stanford University, Palo Alto, CA. <sup>4</sup>Department of Radiation Oncology, University of California-San Francisco, San Francisco, CA.

**Corresponding author:** \*Melissa A. Frick, MD, Radiation Oncology, Penn Medicine Lancaster General Health, 2102 Harrisburg Pike, Lancaster, PA 17601. (melissa.frick@penmedicine.upenn.edu)

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**Data sharing statement:** Data are available upon reasonable request. Deidentified participant data can be requested for further investigation of patient-related emissions from Melissa Frick at melissa.frick@penmedicine.upenn.edu.

## Introduction

Climate change is recognized as one of the largest threats to human health, including oncological outcomes.<sup>1</sup> However, the health care sector significantly contributes to global carbon emissions. In fact, if the global health care sector were a country, it would be the fifth largest emitter of greenhouse gas (GHG) emissions worldwide.<sup>2</sup> Across the health care system, patient and provider transportation-associated GHG emissions account for a significant portion of total emissions. At our institution alone, patient transportation-associated GHG emissions accounted for the largest proportion (75%) of nonsupply chain scope 3 GHG emissions in 2021.<sup>3</sup>

Patients with cancer undergo many appointments across the cancer control continuum, including cancer prevention, screening, diagnosis, treatment, and follow-up care.<sup>4</sup> Radiation oncology in particular requires many in-person visits to coordinate initial evaluation, work-up, treatment, planning, and delivery. The impact of climate change on oncology is just beginning to be understood and often stems from the disruption of the complex health care systems required for multiple aforementioned stages of cancer care. We postulate that altering the transportation behavior of the cancer patient population where possible would have a measurable impact on reducing health care-associated GHG emissions both due to the frequent visits required for optimal treatment and prevalence of cancer in the United States.

Like many others, our radiation oncology department was forced to rapidly integrate telemedicine into practice in response to the COVID-19 pandemic such that patients could

communicate with their health care provider remotely. While there has been an investigation into the implementation, effectiveness, cost, and perceptions of telemedicine, the environmental impact of telemedicine within radiation oncology has not yet been established.<sup>5-7</sup> In light of recent national regulations pertaining to the use of telemedicine, it is imperative to fully understand the potential benefits and limitations of its use. The aim of this study was to assess the impact of telemedicine on transportation-related GHG emissions for a large, academic radiation oncology outpatient clinic located in a densely populated suburban setting.

## Materials and Methods

In-person and telemedicine visits scheduled in our clinic over a consecutive 7-day period in June 2021 were retrospectively reviewed. This time period was selected as COVID cases were at a lull and institutional isolation protocols did not restrict access to in-person visits for those without signs or symptoms of COVID. We define telemedicine as the provision of remote clinical services via real-time two-way communication between patient and health care provider with use of an interactive audiovisual platform. Our institution utilized the VidyoHealth integration with the Epic electronic medical record for telemedicine visits. Visits audited included both new patient consultations and return patient follow-up visits; care visits with patients who resided outside of the state were excluded as well as radiation therapy treatment appointments, as in-person attendance is requisite for treatment. The

shortest possible travel distance between patients' reported home address in the electronic medical record and our clinic address was estimated using Google Maps.<sup>8</sup> As our institution is in a densely populated suburb with limited public transportation accessibility, the analysis was based on patient travel assuming a commute by single-occupancy motor vehicle. Vehicle-related GHG emissions were calculated with the publicly available Greenhouse Gases, Regulated Emissions, and Energy Use in Transportation tool using a well-to-wheel model, which accounts for all emissions related to fuel (ie, gas, electricity) production and use.<sup>9</sup> Gas, hybrid, plug-in hybrid, and electric vehicle utilization were accounted for per published statewide vehicle registration statistics.<sup>10</sup> GHG emissions were converted into carbon dioxide equivalents (CO<sub>2</sub>e) using 100-year global warming potentials (GWPs).<sup>11</sup> GWPs describe the relative potency of a GHG taking account of how long it remains active in the atmosphere and allows comparison of the global warming impact of different GHGs. Annual projections were calculated by multiplying weekly travel distance by 52 weeks. Area Deprivation Index (ADI, a composite measure of socioeconomic disadvantage) scores were obtained for each patient and analyzed per quartile; a higher quartile rank represents a greater disadvantaged block group.<sup>12</sup> Chi-square and simple *t*-test analyses were performed for proportional and continuous variable comparisons, respectively.

## Results

A total of 156 clinic visits were conducted over a 7 days. The

**Table 1. Patient Demographics by Visit Encounter Type**

	TELEMEDICINE (N = 115)	IN-PERSON (N = 41)	TOTAL	P VALUE
Age, mean	61 y	68 y	63 y	.03
Gender, n (%)				.56
Male	51 (49%)	21 (44%)	72 (47%)	
Female	66 (51%)	22 (56%)	88 (53%)	
Race, n (%)				.67
Caucasian	65 (57%)	27 (66%)	92 (59%)	
Asian	23 (20%)	8 (20%)	31 (20%)	
Black or African American	3 (3%)	0 (0%)	3 (2%)	
Other	24 (21%)	6 (15%)	30 (19%)	
Ethnicity, n (%)				.63
Non-Hispanic/non-Latino	97 (84%)	34 (83%)		
Hispanic/Latino	16 (14%)	7 (17%)		
Insurance status, n (%)				.86
Private	40 (35%)	13 (32%)	53 (34%)	
Medicare	66 (57%)	23 (56%)	89 (57%)	
Medical	5 (4%)	3 (7%)	8 (5.1%)	
Other	4 (3.5%)	2 (4.9%)	6 (3.9%)	

**Table 2. Visit Type Stratified by Telemedicine Status and Primary Cancer Site**

	NEW PATIENT VISITS (N = 55)		FOLLOW-UP VISITS (N = 101)	
	IN-PERSON N (%)	TELEMEDICINE N (%)	IN-PERSON N (%)	TELEMEDICINE N (%)
Breast	0 (0%)	8 (100%)	8 (44%)	10 (56%)
Genitourinary	1 (25%)	3 (75%)	3 (20%)	12 (80%)
Thoracic	1 (11%)	8 (89%)	7 (47%)	8 (53%)
Gastrointestinal	2 (25%)	6 (75%)	3 (16%)	16 (84%)
Gynecological	0 (0%)	5 (100%)	3 (50%)	3 (50%)
Head and neck	2 (100%)	0 (0%)	4 (57%)	3 (43%)
Other	1 (7%)	13 (93%)	1 (9%)	10 (91%)
Benign	0 (0%)	4 (100%)	0 (0%)	2 (100%)
Total	8 (15%)	47 (85%)	33 (33%)	68 (67%)

*Other includes sarcoma, cutaneous, pediatric, and lymphoma.*

Telemedicine was utilized similarly across gender, race, ethnicity, and insurance status (**Table 1**). Patients who utilized telemedicine were younger than those who attended in-person visits (mean,

61 years vs 68 years, respectively,  $P = .03$ ) (**Table 1**).

Out of the total 156 clinic visits that occurred over this 1-week span, 115 (74%) were via telemedicine and 41 (26%) were in-person. For

new patient visits ( $n = 55$ ), 8 (15%) were in-person and 47 (85%) were via telehealth. For follow-up visits ( $n = 101$ ), 33 (33%) were in-person and 68 (67%) were via telehealth.

The use of telemedicine varied by disease site and visit type, as demonstrated in **Table 2**. The majority of disease sites utilized telemedicine for new patient visits, with the exception of head and neck new patient consultations, who were exclusively seen in-person. In follow-up, the proportion of in-person visits increased compared with new patient visits, with nearly half of all breast, thoracic, gynecological, and head and neck visits conducted in-person. There was a trend for genitourinary, gastrointestinal, benign, and other sites (sarcoma, cutaneous, pediatric, and lymphoma) to be seen in follow-up via telemedicine ( $P = .09$ ).

On average, patients traveling for in-person visits had a median round

**Table 3. Calculation Model for Greenhouse Gas Emissions Saved by Telemedicine**

	GAS	HYBRID	PHEV	ELECTRIC	TOTAL		
Vehicle fleet, by vehicle type	85%	7%	2%	6%	100%		
Miles driven, by vehicle type	611,198	50,334	14,381	43,143	719,056		
EMISSION TYPE, BY GAS		TOTAL EMISSIONS, BY					EMISSIONS,
	GAS	HYBRID	PHEV	ELECTRIC	GAS (KG)	GWP (100Y)	CO2E (KG)
VOC	179.08	9.82	.92	15.16	204.98	Not defined	-
CO	1772.47	138.92	16.39	6963.63	8891.42	Not defined	-
NOx	241.42	14.54	2.12	.14	258.21	Not defined	-
CH <sub>4</sub>	282.98	16.27	5	15.16	319.42	28	8943.65
CO <sub>2</sub>	277,116.99	16,075.22	3007.02	6963.63	303,162.85	1	303,162.85
NO <sub>2</sub>	81.29	4.79	.1	.14	86.32	298	25,723.25
						Total emissions, CO2e (kg)	337,829.76

*GWPs are not defined for VOC, CO, and NOx due to short-lived atmospheric lifetime of these gases.*  
*Abbreviations: PHEV, plug-in hybrid electric vehicle; GWP, global warming potential; CO2e, carbon dioxide equivalents.*

trip of 44 miles (IQR, 10-98 miles). Of those patients seen via telemedicine, a median of 60 travel miles round trip was saved (IQR, 32-180 miles). Patients who attended in-person visits tended to live closer to the clinic vs those who attended via telemedicine ( $P = .07$ ). Total miles traveled for in-person visits during the 1-week period was 3842 miles; approximately 199,784 miles annually assuming the proportion of in-person to telehealth visits was representative of a typical week. For those who attended visits via telemedicine, 13,828 commuting miles were saved in 1 week and 719,056 miles annually. The forecasted annual saving of CO<sub>2</sub>e attributed to telemedicine visits was 337,829 kg, the equivalent emissions of 65.7 homes' electricity use for 1 year.<sup>13</sup> (Table 3)

ADI, a composite measure of socioeconomic disadvantage, was not associated with the use or avoidance of telemedicine ( $P = 0.22$ ). Patients within each ADI quartile participated similarly in in-person and telemedicine visits (Figure 1).

## Discussion

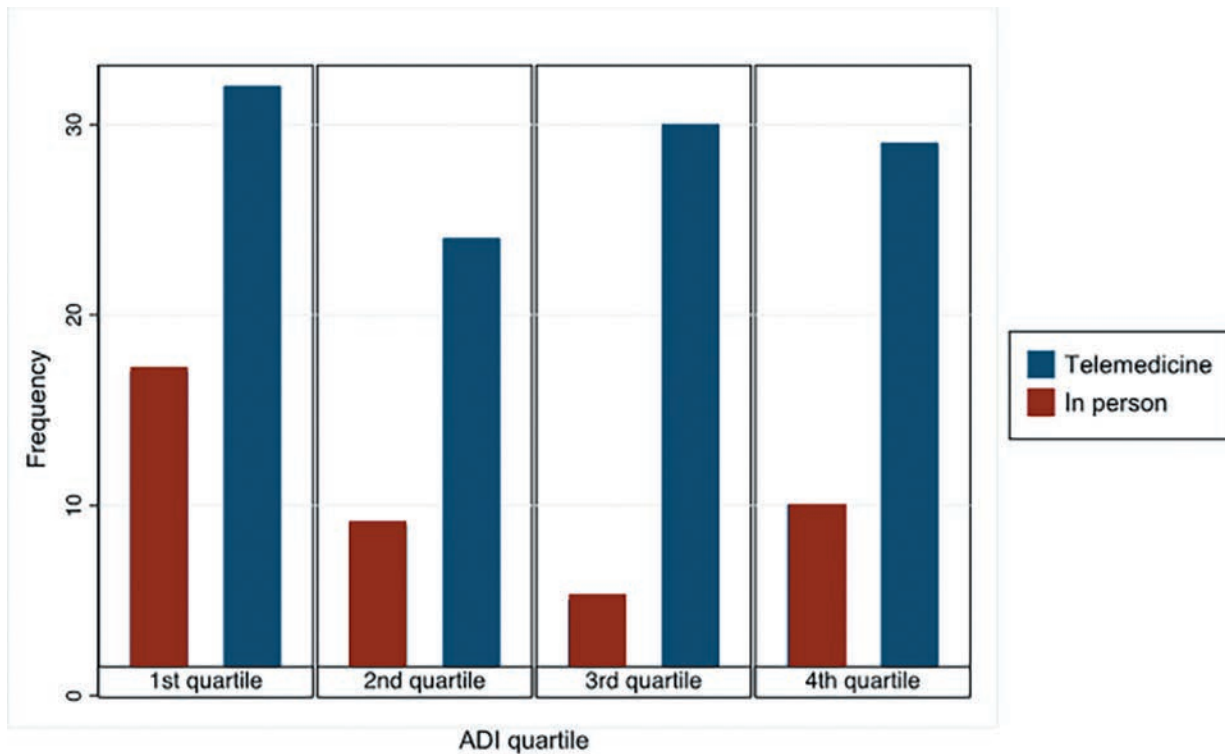
In this cross-sectional single-institution study, integration of telemedicine within a radiation oncology clinic resulted in a substantial reduction in carbon emissions, which when projected annually amounts to 339.8 metric tons of CO<sub>2</sub>e due to obviating the need for patient commute. In total, this translates to the equivalent emissions of 65.7 homes' electricity use for 1 year.

When considering the environmental impact of a health care system (including a radiation therapy delivery center), one must consider both direct and indirect contributions.<sup>1</sup> Patient transportation-associated carbon emissions account for a significant portion of health-care-associated GHG emissions and may be a large and targetable source to reduce carbon emissions.<sup>14</sup> A case series sought to quantify the carbon footprint of the radiation therapy pathway on a

per-patient basis, tallying emissions related to patient travel, energy usage of linear accelerator, energy usage of treatment planning imaging systems, treatment machine sulfur hexafluoride gas leakage, personal protective equipment, and medications required due to radiation therapy. In this series, travel represented the gross majority of a radiation oncology patient's carbon footprint, approaching 75% to 85% of total patient-related carbon emissions and largely dominated other sources such as linear accelerator energy usage (8%-20%) (Rob Chuter, PhD, oral presentation, Christie National Health Service Foundation Trust, September 2022).

Energy usage from linear accelerator-based external-beam radiation therapy was recently estimated, and the energy required for active beam-on treatment time as well as idle time was quantified.<sup>15</sup> The modality with the average highest carbon emissions per course was a 28-fraction course for prostate cancer, which corresponds

**Figure 1.** Frequency of in-person and telemedicine by Area Deprivation Index (a composite measure of socioeconomic disadvantage) quartile. A higher quartile rank represents a more disadvantaged block group.



to CO<sub>2</sub>-equivalent emissions of driving an average of 41.2 miles in a standard vehicle. Based on our data, 1 telemedicine visit saves 60 miles traveled in a standard vehicle, on average. If 1 patient converts to a telemedicine visit from in-person, the CO<sub>2</sub>-equivalent emissions saved are equal to the energy required to power almost 1.5 courses of linear-accelerator-based prostate radiation therapy. Further comprehensive assessments investigating radiation therapy patient care are needed to identify high-impact opportunities to reduce health-care-associated environmental impacts; we posit telemedicine as a potential high-impact intervention that is currently widely in use.<sup>16</sup>

There is concern that telemedicine may increase health care disparities among low-income populations given the cost associated with

telemedicine visits, such as computer, internet, and/or phone service. This is particularly important as vulnerable patient groups are often at greatest risk of poor health outcomes in the face of climate change. Importantly, we demonstrate that telemedicine was used at similar rates across gender, race, ethnicity, insurance policy, and socioeconomic status, and did not differ by ADI score. We have also demonstrated that telemedicine has other positive externalities upon financial toxicities by reducing travel, time, and opportunity costs related to transportation.<sup>17,18</sup> We contend that similarly climate-centered metrics should be considered when informing the choice between in-person and telemedicine visits. For telemedicine to remain accessible and equitable, continued coverage of telemedicine services by insurance payers,

along with improved broadband access for rural communities under recently passed US legislation, will be critical.<sup>19</sup> The Centers for Medicare & Medicaid Services recently announced their plan for revocation of payment parity between in-person and telehealth visits following the end of the public health emergency, during which it was required that insurers reimburse the same payment rate for telehealth services as in-person care. The exact impact on our telemedicine delivery remains to be seen; however, we can safely assume the volumes of telehealth interactions will decrease with negative impacts on health-care-related carbon emissions, health equity, and patient-facing costs.<sup>20</sup>

This piece is particularly timely, with the American Society of Radiation Oncology (ASTRO) having published its inaugural climate

change policy statement earlier this year.<sup>21</sup> In this correspondence, ASTRO recognized that climate change poses a threat to the delivery of cancer care and that these effects result in a considerable cost to patients, providers, and health care systems. They proposed key pillars for focused action against climate change that were within the scope of the society's strategic priorities, including but not limited to (1) a need for education/engagement as well as (2) the promotion of sustainability practices. This investigation not only supports these initiatives posited by ASTRO but also should serve as an interest toward additional oncology societies who are invested in reducing their environmental footprint and increasing practice-related climate resiliency.

One of the primary barriers to standardizing telemedicine is related to patient selection and concerns that telemedicine precludes the ability of physicians to examine patients.<sup>5</sup> Despite this, physicians report that they feel comfortable triaging whether a visit is appropriate for telemedicine or would require an in-person visit.<sup>6</sup> The need for physical examination, or the availability of an acceptable proxy, was the primary factor for most physicians when deciding on telemedicine acceptability.<sup>7</sup> In our experience, we found that patients whose cancer requires a physical examination (ie, nasopharyngoscopy, speculum examination) as part of disease surveillance were seen in-person at higher frequency. Patient-centered factors such as convenience, cost-effectiveness, and preference were also accepted as measures when determining telemedicine utilization. In fact, investigations specific to radiation oncology

telemedicine use report high satisfaction, high utility, that most perceive equivalent or improved visit quality with telemedicine, and that a large majority would want to continue the use of telemedicine.<sup>5-7</sup> Radiation oncology patients, too, demonstrate high satisfaction and confidence in their care, equivalent to in-person visits.<sup>22</sup> Advocacy efforts should promote the use of telemedicine where appropriate in care settings to reduce financial, time, and environmental toxicity in oncology and should involve key stakeholders, including physicians and direct patient care providers, when determining payment models that could significantly limit access to this key component of oncological care delivery.

Our study has several limitations. This is a single-institution experience situated in a densely populated suburban car-centric community; therefore, the primary modality of patient commute was assumed to be by vehicle. Our department is not conveniently accessible by public transportation and few patients live close enough where foot/bike travel is feasible. Institutions in large cities may face different transportation patterns. Additionally, we did not include commutes for patients receiving daily treatment and therefore did not capture the total carbon footprint attributed to all patients commuting to our department daily. Though patient transportation-associated emissions serve as a promising opportunity to reduce the environmental impact of an oncological practice, further studies are needed to comprehensively assess the opportunity to improve care delivery while reducing emissions. The observation that patients who utilized telemedicine visits were more likely to be younger

may potentially signal an age-related inability to access telemedicine and represent a barrier to care for the elderly. Finally, we recognize the limitations of extrapolating a single-week of data to yearly impact, particularly during a time of changing telehealth utilization patterns. Obtaining annual data, however, was time- and resource-prohibitive for the study, and therefore we proceeded with the acceptance that overall validity and applicability may be limited.

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## Conclusion

In conclusion, we demonstrate that integration of telemedicine within a radiation oncology clinic reduces the environmental impact of patient care while maintaining equitable access. Telemedicine should be considered where feasible and clinically appropriate to decrease carbon emissions associated with the practice of radiation oncology, as well as to establish and provide environmentally sustainable health care delivery in oncology.

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# Planning Target Volume Margin Assessment of Retroperitoneal Tumors Using Robotic SBRT With Spine Tracking

Grant McKenzie, MD;<sup>1\*</sup> Maxwell Kassel, BS;<sup>1</sup> Andres Portocarrero Bonifaz, MS;<sup>2</sup> Andrew Willett, BS;<sup>3</sup> Christine Swanson, PhD;<sup>1</sup> Joshua James, MS;<sup>1</sup> Neal Dunlap, MD<sup>1</sup>

## Abstract

**Objective:** Stereotactic body radiation therapy (SBRT) treatment is an emerging salvage modality for treating oligometastatic malignant lesions within the retroperitoneum. Appropriate planning target volume (PTV) margins are essential when delivering SBRT to effectively cover the target volume. Spine tracking uses bony spinal anatomy for localization during treatment delivery on robotic linear accelerator platforms. The aim of this study is to quantify the PTV margin needed when spine tracking is used for intrafraction motion tracking when treating retroperitoneal metastatic lesions with robotic SBRT.

**Materials and Methods:** A single-institution chart review identified 16 patients with retroperitoneal tumors treated with SBRT over 19 courses in 103 fractions. Daily cone-beam CT images registered based on tumor positioning at the time of treatment were analyzed. Van Herk's margin recipe was used to calculate the additional PTV margin required if spine tracking was used instead of daily tumor imaging. Patients' tumors were stratified based on PTV proximity to the vertebral column ( $\leq 1$  cm vs  $> 1$  cm) and location within the retroperitoneum (superior vs inferior to renal artery), with descriptive statistics used to compare the differences of shifts based on location.

**Results:** The additional margins calculated by Van Herk's margin recipe to adequately cover the PTV within the 95% isodose surface for 90% of the entire patient cohort in the vertical, longitudinal, and lateral directions were 2.7, 2.8, and 2.8 mm, respectively. When tumors were stratified by proximity to the vertebral column, average longitudinal ( $P < .001$ ) and total shifts ( $P < .001$ ) were statistically significant.

**Conclusion:** When treating retroperitoneal tumors with robotic SBRT, a minimum isometric margin expansion of 5 mm when creating the PTV is recommended if spine tracking is used for intrafraction motion assessment. Target volumes adjacent to the vertebral column may have PTV margins decreased to 4 mm without compromise in target coverage.

**Keywords:** stereotactic, robotic, oligometastatic, retroperitoneal, spine, margin

**Affiliations:** <sup>1</sup>Department of Radiation Oncology, Brown Cancer Center, University of Louisville School of Medicine, Louisville, KY. <sup>2</sup>Central Arkansas Radiation Therapy Institute, Little Rock, AR. <sup>3</sup>School of Medicine, University of Louisville, Louisville, KY.

**Corresponding author:** \*Grant McKenzie, MD, Department of Radiation Oncology, Brown Cancer Center, University of Louisville School of Medicine, 529 S. Jackson St, Louisville, KY 40202. (grant.mckenzie@louisville.edu)

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**Data sharing statement:** The datasets generated during and analyzed within this study are available from the corresponding author upon reasonable request.



## Introduction

Oligometastatic disease (OMD) is defined as a distinct cancer state in patients with a low metastatic disease burden in which a curative treatment is possible.<sup>1</sup> A frequent location for OMD recurrence after local therapy for cancers of the lower abdomen and pelvis is the retroperitoneal lymph nodes. These nodal basins are comprised of the para-aortic, aortocaval, and paracaval lymph nodes.<sup>2</sup> While some retroperitoneal recurrences are amenable to surgical salvage, many patients are either medically fragile and thus poor operative candidates or have a recurrent disease that is technically unresectable.

Stereotactic body radiation therapy (SBRT) has emerged as an attractive nonsurgical salvage option for recurrent tumors in the retroperitoneal region even in the setting of prior radiation therapy treatment.<sup>3</sup> An increasing body of evidence suggests that incorporation of SBRT into metastasis-directed therapy of OMD improves patients' oncological outcomes across a variety of histopathologies.<sup>4-9</sup> Local control after SBRT in patients with limited OMD within the retroperitoneum has been estimated to be between 75% and 90% with favorable toxicity profiles.<sup>10-12</sup>

SBRT is predicated on administering large doses of radiation therapy in a limited number of fractions, resulting in a high biologically effective dose delivery to target tissues. In an effort to minimize normal tissue toxicity, SBRT attempts to achieve highly conformal dose distributions with rapid dose falloff.<sup>13</sup> An important step in the treatment process for SBRT is the determination of margin size when expanding from either the gross target volume (GTV) or internal target volume (ITV) to

the planning target volume (PTV). Appropriate setup margins should account for both systematic errors that influence all fractions of treatment, such as inaccuracies of mechanical equipment and photon beam dosimetry, and random errors such as daily patient setup changes that generally influence only a single fraction.<sup>14</sup> If a chosen PTV margin is too small, the GTV or ITV will not fall within the prescription isodose line during the entire treatment delivery, which may underdose the target. Conversely, if a selected setup margin is made exceedingly large, more normal tissue will be unnecessarily irradiated.

SBRT may be delivered across a variety of radiation therapy treatment platforms with diverse image guidance capabilities. The CyberKnife (Accuray Inc.) is a robotic radiation therapy delivery platform that utilizes 2 ceiling-mounted kV x-ray imaging sources with corresponding in-floor image detectors positioned at 45° such that the generated beams intersect orthogonally at an imaging center.<sup>15</sup> While the CyberKnife was initially designed as a radiosurgical platform, it is commonly used to treat extracranial sites of diseases, including tumors within the spine, lung, pancreas, liver, and prostate.<sup>16-20</sup> Target tracking can be accomplished using the CyberKnife platform through multiple methods depending on the site of treatment; however, all utilize the 2 ceiling-mounted kV x-ray imaging sources. While bony anatomy is readily discernible with kV imaging, soft-tissue delineation is suboptimal, thus making direct target tracking unfeasible for many extracranial treatment sites. In place of direct target tracking, adjacent bony structures such as the spine may be used. With this method of tracking, the spine is monitored during treatment and delivery

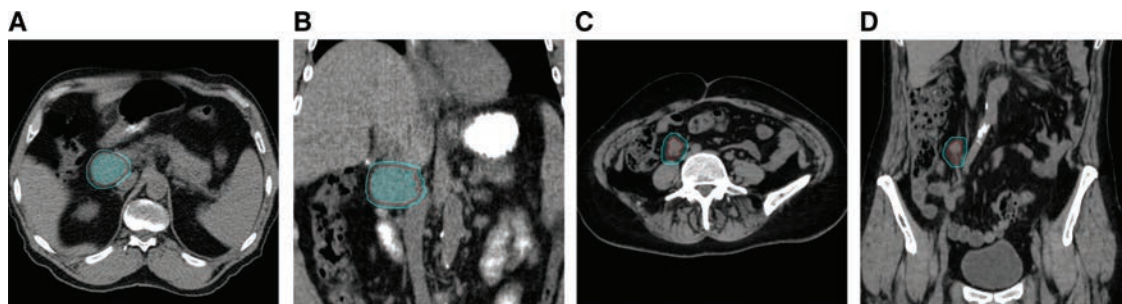
may be interrupted to allow for patient repositioning if necessary. Alternatively, fiducial tracking, which may be used with or without respiratory motion tracking, utilizes small radiopaque markers implanted within or near the tumor and serves as target surrogates identifiable by the kV x-ray imaging sources.

While multiple institutions have previously utilized robotic linear accelerator platforms to deliver SBRT to oligometastatic retroperitoneal lesions, significant variability exists across published literature with respect to treatment planning and delivery.<sup>21-26</sup> While historically PTV margin determination has been largely institutionally defined, modern cooperative protocols investigating the use of SBRT for ablation of systemic OMD allow between 2 and 5 mm PTV margin additions depending on the site of the disease, immobilization technique used, and institutional setup accuracy.<sup>27-29</sup> However, there are no prior reports guiding appropriate PTV margin selection when treating retroperitoneal tumors with robotic stereotactic radiation therapy. Thus, the aim of this study is to quantify the PTV margin needed when spine tracking is used for intrafraction motion tracking when treating retroperitoneal metastatic lesions with robotic SBRT.

## Materials and Methods

A single-institution chart review was performed that identified consecutive patients > 18 years of age treated with linear accelerator-based SBRT for a single site of retroperitoneal OMD between 2015 and 2023. Patients with multiple courses of SBRT were included if they received treatment at an additional site of retroperitoneal disease > 6 months after their

**Figure 1.** Examples of different tumor location classifications. Case 1: Planning target volume (PTV) proximity to the vertebral column  $> 1$  cm and superior to the renal arteries in axial (A) and coronal views (B). Case 2: PTV proximity to the vertebral column  $\leq 1$  cm and inferior to the renal arteries in axial (C) and coronal views (D).



first course of treatment. The retroperitoneal lymph nodes were defined inferiorly at the level of the aortic or inferior vena caval bifurcation and superiorly to the diaphragmatic crura encompassing the para-aortic, aortocaval, and paracaval nodal basins. This study was determined to be exempted by the University of Louisville Institutional Review Board (IRB #22.0219).

To simulate the CyberKnife's spine-tracking system, daily cone-beam CT (CBCT) images acquired using conventional linear accelerator onboard imaging systems at the time of SBRT treatment were rigidly registered to the treatment planning CT scan, aligned to the patient's visible disease, and analyzed. Each CBCT was reviewed in Offline Review software (Aria, Varian). A region of interest, including the spine adjacent to the treatment volume but excluding as much soft tissue as possible, was delineated. Rigid registrations were reperformed within Offline Review using the region of interest and a bone intensity window and level so that the position of the spine on the CBCT was aligned to its position on the planning CT as close as possible to emulate the CyberKnife's spine-tracking system. Per-patient and per-fraction shifts

from the treatment position were recorded. Similar methodologies have previously been described and published by our group in a patient cohort receiving lung SBRT.<sup>30</sup>

Patients' tumors were stratified and compared based on proximity to the vertebral column ( $\leq 1$  cm vs  $> 1$  cm) and location within the retroperitoneum (superior vs inferior location to the renal artery). Stratification of tumor location by proximity to the vertebral column using a distance cutoff of 1 cm was selected based on previously published phantom modeling evaluating the use of spine tracking for abdominal tumors showing smaller dose differentials and higher gamma analysis passing rates using acceptance criteria of dose difference and distance-to-agreement of 5%/5 mm at a distance of 1 cm from reference vertebrae.<sup>31</sup> The renal artery was chosen to stratify superior vs inferior retroperitoneal tumor locations within the abdomen given its readily identifiable nature on CBCT imaging and was used as a surrogate for target proximity to the diaphragm. Tumors were considered superior to the renal artery if the treatment isocenter was superior to the last slice of either the left or right

renal artery, whichever was more superior. Examples of the different types of tumor classifications are demonstrated in **Figure 1**.

After chart review completion, per-patient mean shifts and standard deviations were used to calculate group systematic and random standard deviations. Using Van Herk's margin recipe, additional margins that would adequately treat the patient population if spine tracking were used instead of direct daily tumor imaging by other image guidance techniques were obtained.<sup>32,33</sup> Van Herk's recipe calculates the additional margin in the vertical, longitudinal, and lateral directions for each of the tumor classifications using the following formula:  $2.5\Sigma + 0.7\sigma$ , where  $\Sigma$  is the group systematic standard deviation (standard deviation of the per-patient mean shifts) and  $\sigma$  is the group random standard deviation (standard deviation of the per-patient standard deviation of shifts). Formula coefficients of 2.5 and 0.7 were chosen such that the margin would adequately cover the GTV/ITV within the 95% three-dimensional isodose surface for 90% of the patient cohort. With this method, normal probability distributions were assumed for this patient cohort and different sources of error (eg, target delineation inaccuracies, setup error, organ

**Table 1. Patient Characteristics**

	N (%)
Total patient cohort	16
Treatment courses	19
CBCT images	103
Primary histology	
GU/GYN	10 (63%)
GI	4 (25%)
Other	2 (12%)
PTV (cm <sup>3</sup> )	
≤15	7 (37%)
15-30	4 (21%)
>30	8 (42%)
Spine PTV distance (cm)	
≤1	9 (48%)
>1	10 (52%)
Retroperitoneal location	
Superior	10 (52%)
Inferior	9 (48%)
Motion management	
Yes	12 (63%)
No	7 (37%)

*Abbreviations: CBCT, cone-beam CT; GU/GYN, genitourinary/gynecological; GI, gastrointestinal; PTV, planning target volume.*

motion) were inferred to be statistically independent. Student *t*-test was used to determine whether there was any statistical significance to the difference in shift values based on location. The significance level was set at  $P \leq 0.02$  in alignment with prior investigations by our group.<sup>30</sup> Tumor size and absolute shift dimensions across all fractions were

compared using the Pearson rank correlation coefficient. Statistical analysis and graphical illustrations were performed in Excel (Microsoft).

**Results**

Baseline patient characteristics are listed in **Table 1**. A total of 16 patients with a single site of retroperitoneal OMD were treated over 19 courses in 103 fractions with SBRT between January 2015 and January 2023 and included for analysis. Genitourinary and gynecological histologies comprised a majority of the patient cohort (63%), with gastrointestinal (25%) and other (12%) histologies comprising a minority. Also, 7 treatment courses had PTVs of  $\leq 15$  cm<sup>3</sup> (37%) compared with 4 with PTVs of 15-30 cm<sup>3</sup> (21%) and 8 with PTVs of  $> 30$  cm<sup>3</sup> (42%), respectively. A total of 9 courses (48%) had PTV distances located  $\leq 1$  cm from the vertebral column compared with 10 (52%)  $> 1$  cm. When stratified by tumor location within the retroperitoneum with respect to the renal arteries, 10 courses (52%) had superior retroperitoneal tumor classifications compared with 9 (48%) with inferior tumors. Motion management in the form of a four-dimensional CT (4DCT) scan obtained at the time of CT simulation and an ITV approach was utilized in a total of 12 courses (63%) vs 7 (37%) without. Of the 12 courses where a 4DCT was obtained, 8 were classified as a superior tumor

location within the retroperitoneum in relation to the renal arteries, with mean tumor motion in the superior/inferior dimensions of 4.1 mm (range, 2.0-6.1 mm) vs a mean tumor motion of 1.9 mm (range, 0-3.0 mm) for lesions classified as located inferiorly within the retroperitoneum.

The additional margins calculated by Van Herk's margin recipe to adequately cover the PTV within the 95% isodose surface for 90% of the entire cohort in the vertical, longitudinal, and lateral directions were 2.7, 2.8, and 2.8 mm, respectively, and shown in **Table 2**. The absolute shifts for CBCTs with the maximum total shift based on stratification between tumor location within the retroperitoneum (superior vs inferior) and PTV proximity to the vertebral column ( $\leq 1$  cm vs  $> 1$  cm) are listed in **Tables 3** and **4**. Additional analysis was performed to determine the significance of tumor location within the retroperitoneum and proximity to the vertebral column on both unidirectional and total shifts. When stratified by proximity to the vertebral column, only the average longitudinal ( $P < .001$ ) and total shifts ( $P < .001$ ) were statistically significant and are highlighted in **Table 4**. Further analysis was performed to identify any additional factors other than tumor location and proximity to the vertebral column that would affect shifts. The absolute shifts for each tumor were plotted as a function of PTV (**Figure 2**). No correlation between the magnitude of the shift and PTV size was suggested ( $R^2 = .0222$ ).

When stratified by location within the retroperitoneum, isometric PTV expansions of 3, 4, and 5 mm would have encompassed 82%, 94%, and 100% of the maximum total shifts for lesions superior to the renal artery vs 78%, 94%, and 98% for lesions inferior. Isometric PTV expansions

**Table 2. Additional Planning Target Volume Margin Needed Across the Entire Patient Cohort**

	VERTICAL (MM)	LONGITUDINAL (MM)	LATERAL (MM)
Group systematic standard deviation	.9	.8	.9
Group random standard deviation	.8	1.1	.8
Additional margin	2.7	2.8	2.8

**Table 3. Additional Margin (in mm) Needed When Stratified by Superior vs Inferior Retroperitoneal Classification Using Van Herk's Margin Recipe With P Values Calculated Using Student t-Test**

	CLASSIFICATION	VERTICAL (MM)	LONGITUDINAL (MM)	LATERAL (MM)	TOTAL SHIFT (MM)
Group systematic standard deviation	Superior	.7	.7	.8	.8
	Inferior	1.0	1.0	1.0	1.2
Group random standard deviation	Superior	.7	.9	.7	.8
	Inferior	1.0	1.3	1.0	1.2
Additional margin	Superior	2.2	2.3	2.4	2.5
	Inferior	3.2	3.4	3.3	3.9
P values	-	.073	.474	.598	.834

**Table 4. Additional Margin (in mm) Needed When Stratified by Proximity to Spine ( $\leq 1$  cm vs  $> 1$  cm) Using Van Herk's Margin Recipe With P Values Calculated Using Student t-Test**

	CLASSIFICATION	VERTICAL (MM)	LONGITUDINAL (MM)	LATERAL (MM)	TOTAL SHIFT (MM)
Group systematic standard deviation	$\leq 1$ cm	.6	.5	1.0	.6
	$> 1$ cm	.8	.9	.8	1.0
Group random standard deviation	$\leq 1$ cm	.5	.8	.9	.8
	$> 1$ cm	.9	1.4	.7	1.2
Additional margin	$\leq 1$ cm	1.9	1.8	3.1	2.1
	$> 1$ cm	2.7	3.3	2.5	3.4
P values	-	.056	$<.001$	.340	$<.001$

of 3, 4, and 5 mm would have encompassed 55%, 76%, and 86% of the maximum total shifts for lesions  $> 1$  cm from the vertebral column vs 94%, 100%, and 100% for lesions  $\leq 1$  cm and shown in **Table 5**.

## Discussion

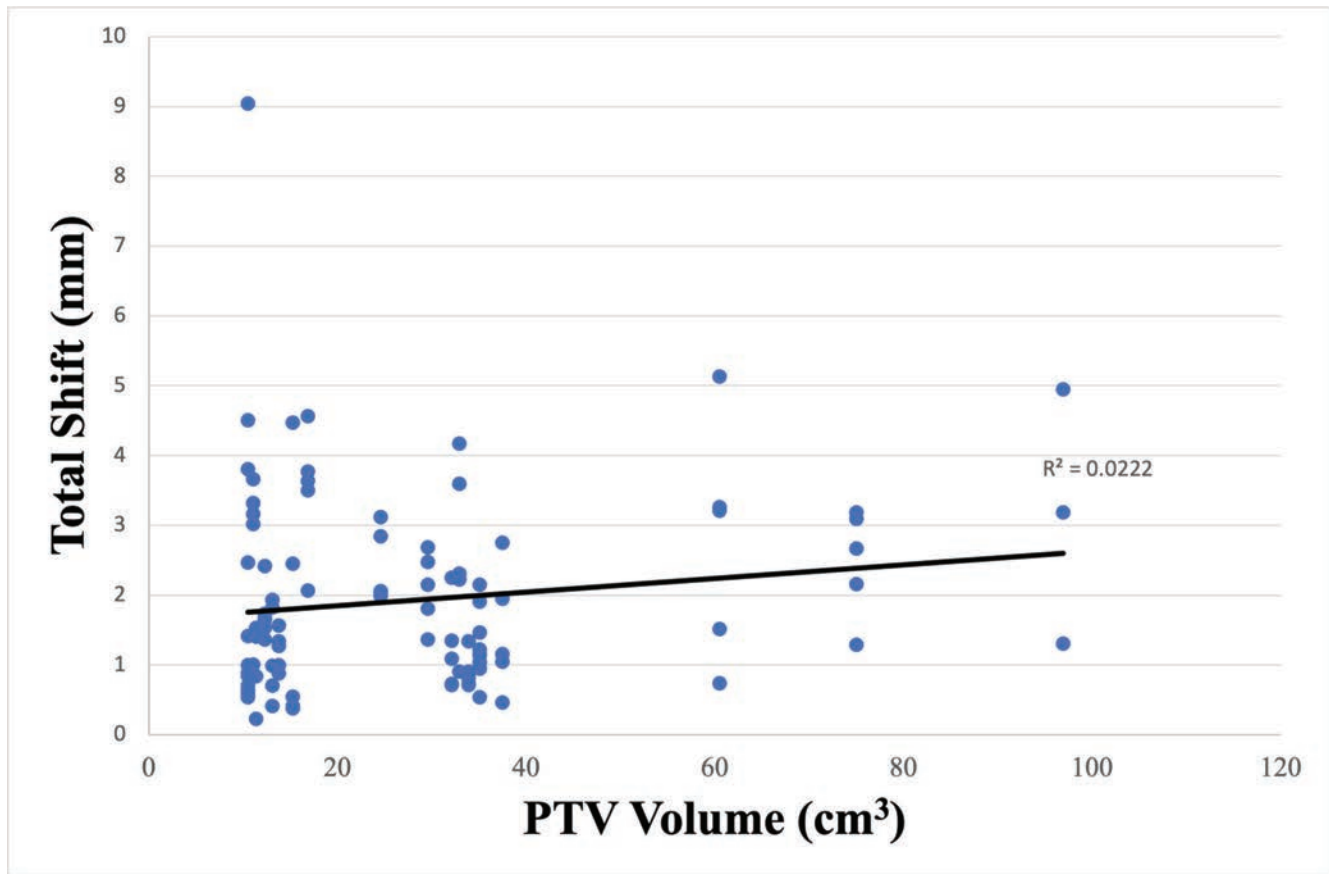
When utilizing robotic radiation therapy delivery platforms to treat retroperitoneal tumors, target tracking may be performed using either fiducial marker tracking or spine tracking. Fiducial tracking within tumors enables sub-millimeter level of tracking accuracy for small target displacements and is often considered the gold standard for target tracking

with robotic radiation therapy delivery platforms.<sup>34</sup> However, fiducial marker implantation is not always feasible due to patient medical comorbidities or tumor anatomic location precluding safe implantation. Additional limitations of fiducial tracking are the requirement of at least 3 implanted fiducials to support 6 degrees of freedom (DOF) corrections and added procedural costs.<sup>35</sup>

Alternatively, intrafraction target tracking using surrogate structures, such as the spine, may be used. Spine tracking allows monitoring of a reference vertebra without the requirement of fiducial implantation using 6-DOF spatial information. A limitation of using spine tracking as a surrogate for the location of a retroperitoneal tumor is that it

assumes the location of the tumor relative to the spine is constant from the time of simulation throughout the duration of treatment. However, treatment uncertainties may be introduced if the distance between the tumor and spine changes between simulation and treatment or if tumor motion patterns vary over time. As a result, an increased setup margin may be necessary, depending on the treatment site, to account for such sources of error. Selection of appropriately sized PTV margins is imperative when delivering high dose per fraction treatment with SBRT. When determining a PTV margin, radiation therapy departments must consider available image guidance within their clinic to ensure accurate dose delivery to target volumes.

**Figure 2.** Correlation between tumor size and absolute shift. PTV, planning target volume.



**Table 5. Isometric PTV Expansions Accounting for Maximum Total Shifts**

CLASSIFICATION		3 MM	4 MM	5 MM
Location (superior vs inferior)	Superior (n = 49)	40 (82%)	46 (94%)	49 (100%)
	Inferior (n = 54)	42 (78%)	51 (94%)	53 (98%)
Spine PTV distance (≤ 1 cm vs > 1 cm)	≤ 1 cm (n = 54)	51 (94%)	54 (100%)	54 (100%)
	> 1 cm (n = 49)	27 (55%)	37 (76%)	42 (86%)

*Abbreviation: PTV, planning target volume.*

Prior to this investigation, within our department, there was no standardized PTV margin addition when robotically treating retroperitoneal metastases with spine tracking. In this study, we found that minimum isometric PTV expansions of 3, 4, and 5 mm would have encompassed 55%,

76%, and 86% of the maximum total shifts for lesions >1 cm from the vertebral column vs 94%, 100%, and 100% for lesions ≤1 cm. Thus, our findings have informed our clinical PTV margin selection when treating with this modality for target lesions adjacent to the spine.

In the context of current literature, there is significant variability in treatment planning and delivery across institutions when treating retroperitoneal metastatic disease with robotic SBRT with spine tracking. Napieralska et al retrospectively reported the use of robotic SBRT using spine tracking to treat prostate cancer recurrences in 18 patients with a total of 31 metastatic lymph nodes located in the retroperitoneal region.<sup>26</sup> Treatment doses and fractionation schedules varied, and an isometric GTV to PTV margin expansion of 5 and 4 mm was used in 28 and 3 lesions, respectively. Loi et al retrospectively reviewed 91 patients undergoing robotic SBRT for oligometastatic retroperitoneal failure without fiducial marker

placement for pelvic, para-aortic, and upper abdominal lymph node failures.<sup>25</sup> An isotropic PTV margin was used and varied between 2 and 5 mm around the GTV, with a median margin of 3 mm selected. Jereczek-Fossa et al analyzed 94 patients receiving robotic SBRT to 124 isolated prostate cancer lymph nodal recurrences in both pelvic and extra-pelvic lymph nodes using spine tracking without fiducial marker placement.<sup>21</sup> A 2 mm margin was added to the GTV to obtain the PTV.

Limitations of this retrospective analysis include a small heterogeneous patient cohort treated at a single institution by multiple radiation oncologists over a period of 8 years. During this time, there was no institutionally defined PTV margin added to target volumes receiving SBRT to retroperitoneal sites nor were margins routinely isometric, introducing additional heterogeneity to this study cohort. Further, for purposes of this study, factors influencing group random and systemic errors were assumed to be constant across the entire patient cohort over time. Van Herk's margin recipe assumes the sample population and sources of introduced error are normally distributed across a given study population.<sup>32</sup> However, patient setup errors may not follow a normal distribution if collected over a short period of time in a small sample size.<sup>36</sup>

Additionally, motion management was only assessed in a total of 12 treatment courses (63%) of our cohort. It has been reported that the diaphragmatic motion of abdominal lesions may reach 40 mm even during shallow respiration cycles.<sup>37</sup> Van Herk's margin recipe attempts to calculate the necessary additional PTV margin to ensure adequate dose coverage to a defined clinical target volume (CTV), which includes both gross disease in addition

to subclinical microscopic disease. When utilizing SBRT, the generation of a CTV from a GTV or ITV is often omitted. Additionally, when using a 4DCT to generate an ITV, internal target motion is accounted for within treatment volumes, thus reducing the potential source of both systematic and random errors. Within this study population, a 4DCT/ITV approach was utilized in a total of 12 of 19 courses when delivering SBRT. At our institution, when treating extrathoracic sites of disease with SBRT, use of 4DCT imaging at the time of CT simulation is left to the discretion of the treating radiation oncologist. Thus, a large portion of this study cohort without known internal target motion may underestimate this potential source of error. However, even when using a 4DCT, further treatment uncertainties may arise from interfraction and intrafraction changes of organ motion, motion from unpredictable respiratory cycles, as well as variations between the imaging and treatment sessions.

We identified no significant differences in unidirectional and total shifts when tumors were stratified based on superior or inferior location to the renal arteries. The renal artery was chosen to stratify superior vs inferior retroperitoneal tumor locations within the abdomen given its readily identifiable nature on CBCT imaging. However, this is an unvalidated surrogate for target proximity to the diaphragm and respiratory cycle tumor motion. Within the contexts of this study, use of this landmark for such purposes should be viewed as hypothesis generating and requires additional validation.

Chan et al suggested that when robotic SBRT for lung cancers is delivered with spine tracking, unless effective means are employed to reduce tumor motion, caution should be undertaken when treating

tumors with motion of more than 10 mm due to temporal dose variations from considerable intrafractional target motion.<sup>38</sup> Technical discussions regarding Accuray's Xsight Spine Tracking system utilized by our clinic are beyond the scope of this report but are explained further in detail by Ho et al.<sup>39</sup> Future directions of study for this topic by our group include analyzing dosimetric variables for both organs at risk (OARs) and targets when utilizing the additional calculated Van Herk's margins when treating retroperitoneal sites of disease with robotic SBRT.

Lastly, clinical judgment should be deferred to the treating physician for PTV margin selection in close collaboration with medical physics and dosimetry and performed on a per-patient basis accounting for the size of the treated lesion and proximity to OARs. Nonisometric PTV expansions are also appropriate and frequently used in clinical practice, which varies based on the treating institution. When selecting a setup margin, clinicians must weigh the likelihood of increased treatment-related morbidity from higher integral dose to adjacent normal structures for larger setup margins vs potential target underdosing if smaller margins are used.

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## Conclusions

When treating retroperitoneal tumors with robotic SBRT, an isometric PTV margin expansion of 5 mm is recommended if spine tracking is used for intrafraction motion assessment. Target volumes located near the vertebral column may have PTV margins decreased to 4 mm without compromising target coverage. Additional factors such as target motion, dose per fraction size, and institutional quality assurance

should be considered for patient-specific PTV margin expansions.

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# National Trends in External-Beam Radiation Therapy for Brain Metastases from Lung, Breast, and Melanoma Cancers

Sujay Rajkumar, BA;<sup>1</sup> Jay Desai, BA;<sup>1</sup> Matthew J. Shepard, MD;<sup>1,2</sup> Rodney E. Wegner, MD<sup>1,3\*</sup>

## Abstract

**Objective:** Radiation therapy (RT) in the form of stereotactic radiosurgery (SRS) or whole-brain radiation therapy (WBRT) is fundamental for managing brain metastasis (BM). We analyzed national trends in RT and BM patient survival between 2010 and 2019.

**Materials and Methods:** The US National Cancer Database was queried for patients receiving RT for BMs who were originally diagnosed with primary non-small cell lung cancer (NSCLC), small cell lung cancer, breast cancer, and melanomas from 2010 to 2019. Patients were grouped by WBRT (5-15 fractions; 20-45 Gy) or SRS (1-5 fractions; 10-40 Gy) treatment. Univariate and multivariate logistic regression analyses identified factors associated with receiving SRS over WBRT. Differences in treatment trends were assessed with Kruskal-Wallis tests. Post-treatment survival was assessed using Kaplan-Meier analysis and a Cox proportional hazards model.

**Results:** In total, 59,839 patients were included; 41,197 (68.8%) received WBRT and 18,642 (31.2%) received SRS. Patients who were more recently diagnosed, treated at facilities outside of the East Central regions, insured, diagnosed with NSCLC subtype or melanoma, and who received chemo-/immunotherapy had higher odds of being treated with SRS (all  $P < .005$ ). SRS, a more recent primary diagnosis, conjunctive use of chemo/immunotherapy, and luminal A/B breast cancer histologies (all  $P < .01$ ) correlated with increased survival.

**Conclusion:** The use of SRS has increased with patient survival over the last decade. We hypothesize that in addition to SRS-reducing neurotoxicity, this increase is due to guideline relaxation, improved techniques, and increased accessibility. Increased patient survival also indicates a possible relationship between SRS usage and improved survival.

**Keywords:** radiation therapy, stereotactic radiosurgery, whole-brain radiation therapy, National Cancer Database

**Affiliations:** <sup>1</sup>College of Medicine, Drexel University, Philadelphia, PA. <sup>2</sup>Department of Neurosurgery, Allegheny Health Network, Pittsburgh, PA. <sup>3</sup>Division of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA.

**Corresponding author:** \*Rodney E. Wegner, MD, Division of Radiation Oncology, Allegheny Health Network, 2 Knollwood Dr, Pittsburgh, PA 15215. (Rodney.Wegner@ahn.org)

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## Introduction

Brain metastases (BMs) are a common occurrence in approximately 20% to 40% of patients diagnosed with extracranial cancer, which most often include lung cancer, breast cancer, and melanoma.<sup>1</sup> BMs are a significant source of mortality and morbidity, with multiple studies reporting mean overall survival less than 1 year following diagnosis.<sup>2-4</sup> Radiation therapy (RT), either in the form of whole-brain radiation therapy (WBRT) or stereotactic radiosurgery (SRS), has been used to manage BMs either as an individual treatment or in combination with strategies such as surgery, chemotherapy, or immunotherapy, when warranted.

Within the last decade (2010-2019), SRS has become increasingly employed over WBRT when clinically practical, with the aim of minimizing unwanted neurocognitive toxicity associated with WBRT.<sup>5</sup> While this general trend is well known, there are limited studies quantifying specific factors associated with SRS usage and the survival of patients treated for BMs within the last decade (2010-2019). Using a national clinical oncology database in the US, we analyzed patterns of WBRT and SRS use and the survival of patients treated for BMs originating from lung, breast, and melanoma primary disease types, which are the leading causes of BMs in the US.<sup>3</sup>

## Materials and Methods

### Study Population

The US National Cancer Database (NCDB) was algorithmically queried to select patients diagnosed with BMs originating from non-small cell lung cancer (NSCLC), small cell lung

cancer (SCLC), breast, or melanoma-type cancers between 2010 and 2019 (**Figure 1**). Patients were grouped together based on originating cancer types. The NSCLC patient group was further divided into patients with adenocarcinoma (AC), squamous cell carcinoma (SCC), large cell neuroendocrine carcinoma (LCNEC), or not otherwise specified (NOS) subtypes. The breast cancer patient group was further divided into luminal A, luminal B, triple negative (TN), or HER2-enriched subtypes. For each subtype, patients were then separated by which RT they received (WBRT or SRS). WBRT was defined as 5-15 fractions of RT to the brain, with a total dose of 20-45 Gy. SRS was defined as 1-5 fractions of radiosurgery to the brain to account for techniques similar to SRS such as hypofractionated SRS (fSRS), with a total dose of 10-40 Gy. Patients were excluded from the study if they did not receive brain RT.

### Statistical Analysis

Univariate logistic regression was performed on pre-selected patient, disease, geographic, and socioeconomic variables to determine their association with the clinical use of SRS or WBRT. Variables with  $P < 0.10$  in univariate logistic regression analysis were included in a multivariate logistic regression analysis where significance was indicated by  $P < 0.05$ . General RT trends were analyzed observationally and graphically. The medians of treatment characteristics between WBRT and SRS were compared using Kruskal-Wallis tests. The same analyses were conducted for each type of RT over each diagnostic year. Kaplan-Meier analysis was performed to determine the probability of survival for each year of diagnosis, RT modality,

and primary disease histology, as well as the probability of overall survival for the cohort. A Cox proportional hazards (CPH) model was used to identify survival predictors. Factors that were significant in the univariate CPH analysis ( $P < .10$ ) were used in the multivariate CPH model. Significance in the multivariate CPH model was indicated by  $P < 0.05$ .

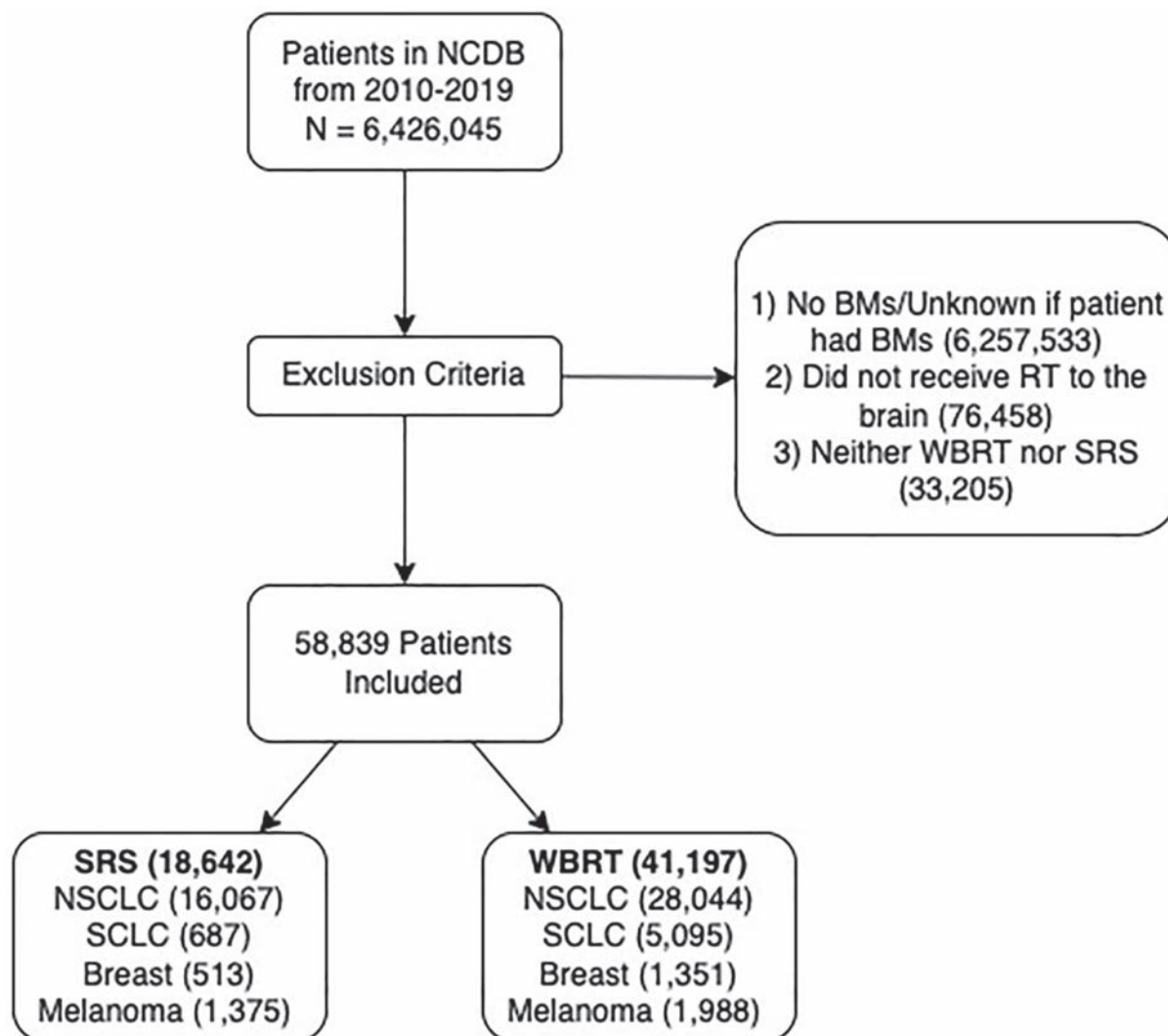
All data organization and analyses were performed using the SPSS Statistics program (version 28.0; IBM) and the following Python (version 3.9.6, Python Software Foundation) packages: Pandas (version 1.4.1), Scikit-learn (version 0.21), SciPy (version 1.6.0), and Lifelines (0.26.4).

## Results

A total of 59,839 patients were included in the study, and of these patients, 41,197 (68.8%) were treated with WBRT and 18,642 (31.2%) were treated with SRS (**Figure 1**). Of note, patients recently diagnosed, treated at facilities outside of the Midwest, insured, diagnosed with SCC or melanoma, and who received chemo-/immunotherapy were more likely to receive SRS (**Table 1**). In contrast, patients diagnosed with SCLC, LCNEC, and breast cancers, as well as patients presenting with extracranial metastases, were more likely to receive WBRT.

From 2010 to 2019, there was an increase in the time from diagnosis to treatment and a shift in the use of some treatments over others. The use of SRS increased: It was used to treat only 13.7% of cases in 2010 compared with 47.2% in 2019 (**Figure 2**). Of SRS-specific technologies, Gamma Knife (GK) (Elekta) usage has increased relative to CyberKnife (CK) (Accuray) usage (167% increase in GK usage vs an

**Figure 1.** Cohort selection flow diagram. The US National Cancer Database (NCDB) was queried to select patients with a brain metastases (BM) diagnosis attributed to non-small cell lung carcinoma (NSCLC), small cell lung carcinoma (SCLC), breast, and melanoma-type cancers from 2010 to 2019. Patients were excluded from the study if they had no radiation therapy (RT) targeting the brain, or whole-brain radiation therapy (WBRT) or stereotactic radiosurgery (SRS) outside our study parameters. Included WBRT patients had total doses of 20-45 Gy and SRS patients had total doses of 10-40 Gy.



86% increase in CK usage between 2010 and 2019). Non-GK and non-CK SRS modalities relatively increased the most during this study period (385% increase).

Median time from diagnosis to RT for WBRT was 17 days compared with 34 days for SRS treatments ( $P < .005$ ; **Table 2**). From 2010 to 2019, the median time from diagnosis to RT increased from 15 days to 20 days

for WBRT ( $P < .005$ ; **Table 3**) and from 32 days to 35 days for SRS ( $P = .014$ ; **Table 4**). Neither dose nor fractions changed appreciably over this time range for either treatment modality.

We also compared survival times for the different cohorts. Median overall survival for all patients (**Figure 3A**) was 6.11 months (CI: 6.01-6.21). Patients receiving WBRT had a median survival of 4.73

months (CI: 4.57-4.89), and patients receiving SRS had a median survival of 11.72 months (CI: 11.50-11.91) ( $P < .005$ ; **Figure 3B**). Median survival consistently increased over the decade from 5.19 months (CI: 5.00-5.38) in 2010-2011 to 7.92 months (CI: 7.59-8.27) in 2018-2019 ( $P < .005$ ; **Figure 3C**). Of the disease histologies, SCC had the lowest median survival at 3.84 months (CI: 3.65-4.00), and luminal

**Table 1. Variables Significant in Univariate Logistic Regression Analysis of Stereotactic Radiosurgery (SRS) Usage ( $P < .10$ ), Presented With Multivariate Logistic Regression Results ( $P < .05$ )**

VARIABLES	LOGISTIC REGRESSION MODEL							
	N		UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	WBRT	SRS	OR	P VALUE	95% CI	OR	P VALUE	95% CI
Age	-	-	1.01	< .005	1.01-1.01	1.02	< .005	1.01-1.02
Race								
White	34,722	15,662		Reference			Reference	
Black	4783	1999	.93	.007	0.88-0.98	.96	.21	.90-1.02
Other	1692	981	1.29	< .005	1.19-1.39	1.04	.374	.95-1.15
Year of diagnosis								
2010	3921	623		Reference			Reference	
2011	3974	742	1.18	.006	1.05-1.32	1.22	< .005	1.08-1.38
2012	4121	905	1.38	< .005	1.24-1.54	1.42	< .005	1.26-1.60
2013	4137	1123	1.71	< .005	1.53-1.90	1.71	< .005	1.52-1.92
2014	4071	1297	2.01	< .005	1.81-2.23	1.92	< .005	1.71-2.15
2015	3660	1517	2.61	< .005	2.35-2.89	2.58	< .005	2.30-2.89
2016	4537	2381	3.30	< .005	2.99-3.64	3.40	< .005	3.06-3.79
2017	4207	2824	4.22	< .005	3.83-4.66	4.29	< .005	3.85-4.78
2018	4451	3552	5.02	< .005	4.57-5.52	5.11	< .005	4.58-5.69
2019	4118	3678	5.62	< .005	5.11-6.18	5.81	< .005	5.20-6.48
Community type								
Metro	33,568	15,759		Reference			Reference	
Urban	6646	2514	.81	< .005	.77-.85	.87	< .005	.82-.93
Rural	983	369	.80	< .005	.71-.91	.92	.289	.80-1.07
Location								
East North Central	9021	3236		Reference			Reference	
East South Central	3732	1239	.93	.045	.85-.99	1.09	.078	.99-1.19
Mid-Atlantic	5745	3398	1.65	< .005	1.56-1.75	1.73	< .005	1.61-1.85
Mountain	1319	747	1.58	< .005	1.43-1.74	1.68	< .005	1.50-1.89
New England	2855	1313	1.28	< .005	1.19-1.38	1.38	< .005	1.26-1.51
Pacific	3466	1776	1.40	< .005	1.31-1.51	1.44	< .005	1.32-1.56
South Atlantic	7982	3840	1.34	< .005	1.27-1.42	1.42	< .005	1.33-1.52
West North Central	4068	1713	1.17	< .005	1.09-1.25	1.19	< .005	1.10-1.30
West South Central	2587	1071	1.15	< .005	1.07-1.27	1.22	< .005	1.11-1.35
Unknown	422	309	2.04	< .005	1.75-2.38	2.62	< .005	2.16-3.17
Insurance status								
Uninsured	2111	469		Reference			Reference	
Private insurance	13,417	6485	2.18	< .005	1.96-2.41	1.95	< .005	1.72-2.20
Government insurance	25,647	11,677	2.05	< .005	1.85-2.27	1.67	< .005	1.48-1.88

Table 1. continued

VARIABLES	LOGISTIC REGRESSION MODEL							
	N		UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	WBRT	SRS	OR	P VALUE	95% CI	OR	P VALUE	95% CI
Unknown	22	11	2.25	.029	1.08-4.67	1.05	.910	.48-2.27
Histology								
NSCLC—adeno	20,219	11,818		Reference			Reference	
NSCLC—SCC	2906	2098	1.24	< .005	1.16-1.31	1.43	< .005	1.33-1.53
NSCLC—LCNEC	928	220	.41	< .005	0.35-0.47	.38	< .005	.32-.45
NSCLC—NOS	3991	1929	.83	< .005	.78-.88	1.06	< .005	.99-1.14
SCLC	10,123	687	.12	< .005	.11-.13	.10	< .005	.09-.11
Breast—luminal A	428	110	.44	< .005	.36-.54	.61	< .005	.48-.78
Breast—luminal B	195	48	.42	< .005	.31-.58	0.43	< .005	.20-0.61
Breast—HER2	141	51	.62	< .005	.45-.85	.62	.012	.43-.90
Breast—TN	262	72	.74	.062	.53-1.02	.66	.005	.50-.89
Breast—NOS	461	232	.68	.096	.43-1.07	.57	< .005	.48-.68
Melanoma	1543	1375	1.76	< .005	1.56-1.98	1.75	< .005	1.59-1.92
Distance to hospital (miles)	-	-	1.00	< .005	1.00-1.00	1.00	< .005	1.00-1.00
Chemotherapy								
No	15,325	6649		Reference			Reference	
Yes	25,872	11,993	1.07	< .005	1.03-1.11	1.60	< .005	1.53-1.68
Immunotherapy								
No	35,459	12,691		Reference			Reference	
Yes	5738	5951	2.90	< .005	2.78-3.02	1.47	< .005	1.39-1.56
Extracranial metastases*								
No	41,048	18,540		Reference			Reference	
Yes	149	102	1.52	< .005	1.18-1.95	.59	< .005	.43-.79

Abbreviations: CI, confidence interval; OR, odds ratio; Adeno, adenocarcinoma; NSCLC, non-small cell lung cancer; WBRT, whole-brain radiation therapy; SCC, squamous cell carcinoma; SCLC, small cell lung carcinoma; LCNEC, large cell neuroendocrine carcinoma; TN, triple negative; NOS, not otherwise specified.

\*Bone, lung, liver.

B breast cancer had the highest median survival at 23.56 months (CI: 18.59-28.35). All disease survival rates can be seen in **Figure 3** ( $P < .005$ ).

Multivariate CPH analysis revealed that increased survival correlated with SRS treatment (hazard ratio [HR]: 0.50 CI [0.49-0.52]), recent years of primary diagnosis (2018-2019 hour: 0.67 CI [0.65-0.69]), chemotherapy (HR: 0.49 CI [0.48-0.50]), and immunotherapy

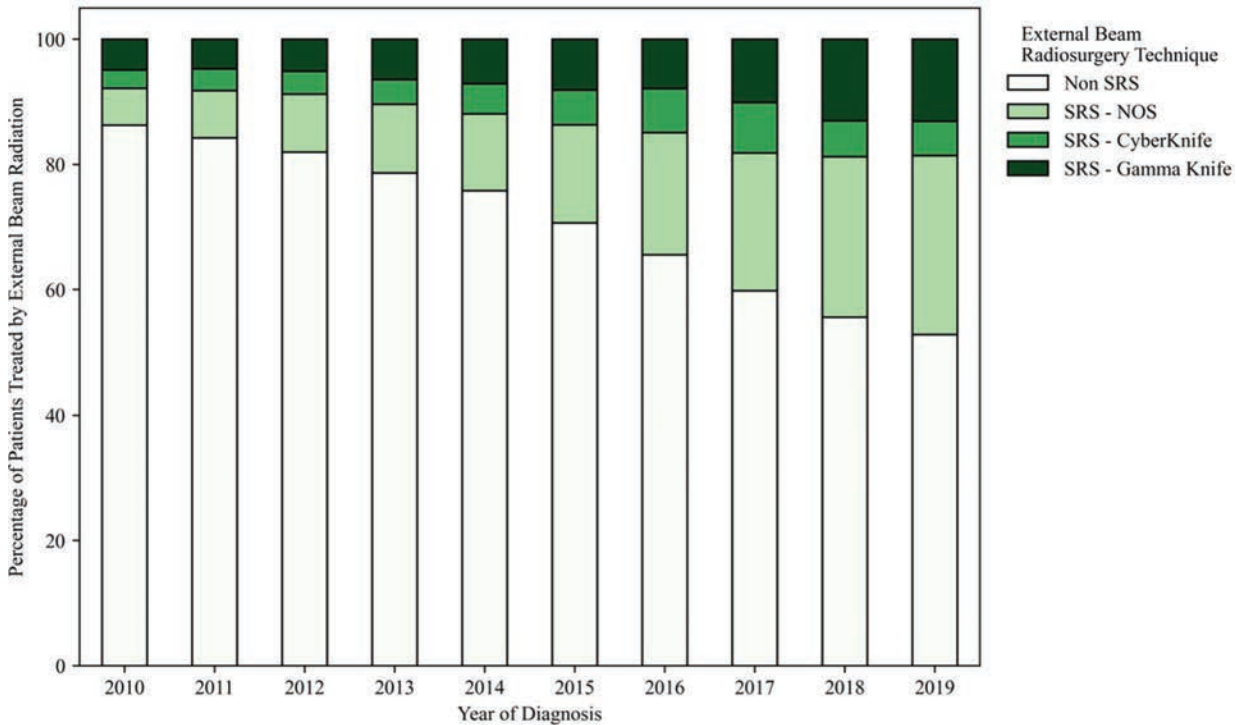
(HR: 0.58 CI [0.55-0.60]) in conjunction with RT, luminal A (HR: 0.67 CI [0.62-0.75]), and luminal B (HR: 0.76 CI [0.66-0.91]) breast histologies. In contrast, decreased survival correlated with WBRT treatment (HR: 2.00 CI [1.92-2.04]), unknown insurance status (HR: 1.25 CI [1.13-2.79]), and certain histologies NSCLC-SCC (HR: 1.40 CI [1.33-1.44]), NSCLC-LCNEC (HR: 1.16 CI [1.07-1.24]), NSCLC-NOS (HR: 1.26 CI [1.22-1.30]), SCLC (HR: 1.31 CI

[1.27-1.34]), and breast-TN (HR: 1.43 CI [1.28-1.63]) histologies. Results of the survival analysis can be seen in **Table 5**.

## Discussion

We found in this large database analysis that SRS is being increasingly utilized for the management of brain metastases. We found several factors, including

**Figure 2.** Relative usage of stereotactic radiosurgery (SRS) (out of all external-beam radiation therapy [RT]) in the US from 2010 to 2019 for the treatment of non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), breast cancers, and melanomas. NOS, not otherwise specified.



**Table 2. Mann-Whitney *U* Analysis Comparing Median Treatment Characteristics for Whole-Brain Radiation Therapy (WBRT) and Stereotactic Radiosurgery (SRS)**

RADIATION THERAPY TYPE	MEDIAN DAYS FROM DX TO RADIATION ( $P < .005$ )	MEDIAN TOTAL DOSE ( $P < .005$ )	MEDIAN FRACTIONS ( $P < .005$ )
WBRT	17 (7-34)	30 Gy (20-45)	10 (6-15)
SRS	34 (22-53)	21 Gy (10-40)	1 (1-5)

Abbreviation: Dx, diagnosis.

updated clinical guidelines, regional availability, and the use of SRS-adjacent techniques, to be associated with increased utilization. One such SRS-adjacent technique is fSRS, which combines the steep-dose gradients and smaller margins of SRS with the radiobiologic advantages of fractionation. The odds of receiving SRS also vary by primary disease type and socioeconomic factors, such as insurance status and proximity to metropolitan environments.

Over the past decade, SRS has been increasingly employed to minimize the risk of neurocognitive decline associated with WBRT while still maintaining similar survival rates for patients with 3 BMs.<sup>6-8</sup> Within the last couple of years, however, its use has been expanded to patients with 4-15 BMs, where WBRT may traditionally have been used.<sup>9</sup> Several studies, including a large-scale retrospective review in 2020 and a meta-analysis in 2022, support the effectiveness

of first-line SRS in patients with a primary SCLC diagnosis who would have otherwise been treated with WBRT.<sup>10,11</sup> Continued evidence depicting SRS's decreased parenchymal tissue damage and comparable effectiveness to WBRT supports relaxing the clinical guidelines and promoting the widespread adoption of SRS over time. Additionally, the rise of frameless GK treatment reduces the logistical constraints and increases patient satisfaction,

**Table 3. Kruskal-Wallis Analysis Comparing Median Stereotactic Radiosurgery Treatment Characteristics from 2010 to 2019**

YEAR OF DIAGNOSIS	MEDIAN DAYS FROM DX TO RADIATION (P = .014)	MEDIAN TOTAL DOSE (P < .005)	MEDIAN FRACTIONS (P < .005)
2010	32 (20-51)	20 Gy (11-40)	1 (1-5)
2011	34 (21-54)	20 Gy (11-40)	1 (1-5)
2012	33 (21-49)	20 Gy (11.7-40)	1 (1-5)
2013	33 (22-52)	20 Gy (10-40)	1 (1-5)
2014	35 (22-53)	20 Gy (10-40)	1 (1-5)
2015	35 (22-52)	20 Gy (10-40)	1 (1-5)
2016	34 (22-53)	21 Gy (10-40)	1 (1-5)
2017	34 (22-52)	21 Gy (10-40)	1 (1-5)
2018	35 (22-53)	21 Gy (10-40)	1 (1-5)
2019	35 (22-54)	21 Gy (10-40)	1 (1-5)

Abbreviation: Dx, diagnosis.

**Table 4. Kruskal-Wallis Analysis Comparing Median Whole-Brain Radiation Therapy Treatment Characteristics from 2010 to 2019**

YEAR OF DIAGNOSIS	MEDIAN DAYS FROM DX TO RADIATION (P < .005)	MEDIAN TOTAL DOSE (P < .005)	MEDIAN FRACTIONS (P < .005)
2010	15 (6-31)	30 (20-45)	10 (6-15)
2011	15 (6-32)	30 (20-45)	10 (6-15)
2012	15 (6-30)	30 (20-45)	10 (6-15)
2013	17 (7-33)	30 (20-45)	10 (6-15)
2014	16 (7-31)	30 (20-45)	10 (6-15)
2015	17 (7-33)	30 (20-45)	10 (6-15)
2016	18 (7-34)	30 (20-45)	10 (6-15)
2017	19 (8-35)	30 (20-45)	10 (6-15)
2018	19 (8-36)	30 (20-45)	10 (6-15)
2019	20 (8-39)	30 (20-45)	10 (6-15)

Abbreviation: Dx, diagnosis.

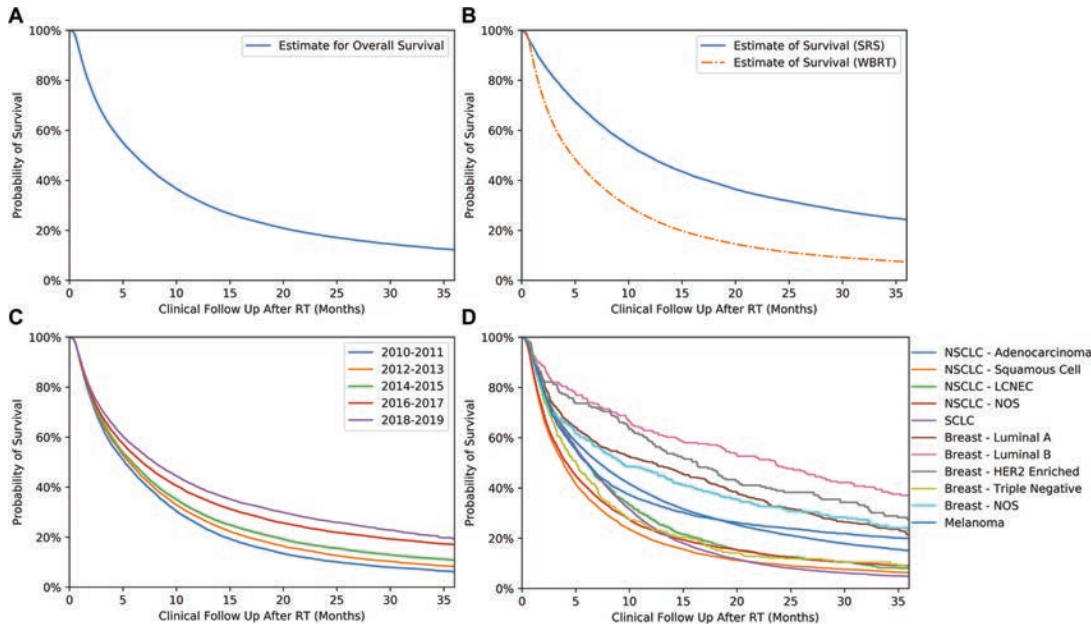
further explaining the observed increase in SRS use.<sup>12,13</sup> Furthermore, adopting fSRS allows for the treatment of metastases that are large or in unfavorable locations.<sup>14</sup>

Our study also demonstrated that regional and socioeconomic discrepancies determine a patient's odds of receiving SRS. A 2012 Canadian study found that on-site SRS availability was the most important factor in receiving SRS treatment.<sup>15</sup> The distribution of SRS systems was surveyed in 2019, and researchers found that

most states in the United States have a ratio of at least 1 SRS machine (GK, linear accelerator, CK) per 1,000,000 people, with a few exceptions. Several states in the South Atlantic, West North Central, West South Central, and New England regions had ratios less than 1, while Vermont, South Dakota, and Wyoming all had 0 machines per 1,000,000 people.<sup>16</sup> Even within certain geographic regions of the United States, proximity to a metropolitan area correlates with higher odds of being

treated with SRS in addition to a higher probability of survival.<sup>17</sup> Likewise, multiple studies concur that insured patients have much higher odds of receiving SRS and a higher probability of survival compared with uninsured populations.<sup>18-20</sup> However, lower survival in uninsured patients and those distant from metro centers may be confounded by an increased disease burden at clinical presentation from a lack of preventative and continued health care.

**Figure 3.** Kaplan-Meier curves depicting estimates of survival following radiation therapy (RT) treatment by overall cohort (A), RT modality (B), year of primary diagnosis (C), and primary histology (D). NSCLC, non-small cell lung cancer; LCNEC, large cell neuroendocrine carcinoma; NOS, not otherwise specified.



Scenarios in which patients receive WBRT include extensive intracranial disease, multiple distant failures, or poor performance status.<sup>7</sup> As a result of these confounding variables, we observed that the risk of mortality was almost halved at the post-treatment 3-year mark among patients who were treated with SRS compared with WBRT. However, a recent 2021 study showed that short-term survival rates are significantly higher for SRS patients than WBRT patients (1-year survival; SRS = 46.4% vs WBRT = 38.8%), when examining crude mortality between a propensity-matched SRS and WBRT cohort.<sup>21</sup> Another study in 2016 claimed that SRS had a larger survival benefit than WBRT in the first 6 months after treatment for postoperative resection cavities ( $P = .003$ ).<sup>22</sup> In our study, we also observed patients living longer with their diagnoses as median overall survival increased by 50% over the last decade. With patients' post-diagnosis

life expectancy increasing, the long-term neurocognitive effects of WBRT must be given greater consideration when developing treatment plans. Investigating the long-term survival rates and neurocognitive preservation for different RT strategies is therefore warranted in future studies.

Primary tumor subtype remains an important prognostic factor for BM patients. In consensus with existing literature, our study found that breast cancer patients (excluding TN subtypes) survived the longest following treatment.<sup>23,24</sup> Within breast cancer subtypes, patients with luminal B and HER2 diagnoses demonstrated the greatest survival, both in this analysis and the literature.<sup>25</sup> Improved survival in BMs associated with HER2-positive breast cancer may be associated with the advent of newer agents such as Enhertu (T-DXd). T-DXd has been proven to have intracranial activity with minimal

toxicity when treating advanced breast cancer patients with BMs.<sup>26</sup> Interestingly, within lung cancer subtypes, patients with SCLC had better survival following treatment than patients with SCC or NOS NSCLC subtypes. Other studies support that patients with SCLC have an increased risk of developing BMs; however, there is no evidence suggesting survival rates are lower among this subgroup compared with other lung cancer subtypes.<sup>27</sup>

This study has several limitations to consider when interpreting results. The NCDB has limited available data, so all analyses used phase I RT data, which do not account for subsequent treatments, such as salvage SRS or WBRT. Furthermore, the NCDB lacks data on the size, number, or location of BMs as well as prognostic factors, such as performance score or tumor grade. It also does not include BM-specific



**Table 5. Variables Significant in the Cox Proportional Hazards Model (CPH) of Survival ( $P < .10$ ), Presented With Multivariate CPH Model Results ( $P < .05$ )**

VARIABLE	COX PROPORTIONAL HAZARDS MODEL					
	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	HR	P VALUE	95% CI	OR	P VALUE	95% CI
Sex						
Male		Reference			Reference	
Female	0.84	< .005	0.83-0.86	0.88	< .005	0.87-0.90
Age						
Analyzed continuously	1.02	< .005	1.02-1.02	1.01	< .005	1.01-1.01
Race						
White		Reference			Reference	
Black	0.93	.007	0.88-0.98	0.92	< .005	0.89-0.96
Other	1.29	< .001	1.19-1.39	0.77	< .005	0.73-0.82
Year of diagnosis						
2010-2011		Reference			Reference	
2012-2013	0.92	< .005	0.90-0.95	0.95	< .005	0.93-0.98
2014-2015	0.86	< .005	0.83-0.88	0.92	< .005	0.89-0.94
2016-2017	0.72	< .005	0.70-0.74	0.78	< .005	0.76-0.80
2018-2019	0.65	< .005	0.63-0.67	0.67	.02	0.65-0.69
Community type						
Metro		Reference			Reference	
Urban	1.12	< .005	1.09-1.15	1.23	< .005	1.09-1.39
Rural	1.16	< .005	1.09-1.24	1.30	< .005	1.15-1.47
Location						
East North Central		Reference			Reference	
East South Central	0.88	< .005	0.84-0.91	0.91	< .005	0.87-0.96
Mid-Atlantic	1.04	8.00E-02	1.00-1.07	1.07	< .005	1.02-1.12
Mountain	1.05	1.00E-02	1.01-1.09	1.09	< .005	1.05-1.15
New England	1.17	< .005	1.12-1.23	1.12	< .005	1.06-1.18
Pacific	1.07	< .005	1.02-1.12	1.11	< .005	1.06-1.17
South Atlantic	0.97	2.20E-01	0.92-1.02	0.98	.45	0.92-1.04
West North Central	0.96	1.80E-01	0.90-1.02	0.96	.30	0.90-1.03
West South Central	0.92	< .005	0.88-0.96	0.97	.22	0.92-1.02
Unknown	0.52	< .005	0.47-0.58	1.05	.44	0.93-1.18
Insurance status						
Uninsured		Reference			Reference	
Private insurance	0.75	< .005	0.71-0.78	0.82	< .005	0.77-0.86
Government insurance	1.04	.06	1.00-1.09	0.88	< .005	0.84-0.93
Unknown	1.25	.28	0.84-1.87	1.75	.01	1.13-2.70
Charlson-Deyo score						

**Table 5. continued**

COX PROPORTIONAL HAZARDS MODEL						
VARIABLE	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	HR	P VALUE	95% CI	OR	P VALUE	95% CI
0		Reference			Reference	
1	1.22	< .005	1.19-1.25	1.11	< .005	1.08-1.14
2+	1.35	< .005	1.31-1.39	1.17	< .005	1.13-1.21
Histology						
NSCLC—adeno		Reference			Reference	
NSCLC—squamous	1.58	< .005	1.53-1.63	1.40	< .005	1.33-1.44
NSCLC—large cell neuroendocrine	1.25	< .005	1.17-1.34	1.16	< .005	1.07-1.24
NSCLC—NOS	1.39	< .005	1.35-1.44	1.26	< .005	1.22-1.30
SCLC	1.35	< .005	1.32-1.39	1.31	< .005	1.27-1.34
Breast—luminal A	0.83	< .005	0.76-0.91	0.67	< .005	0.62-0.75
Breast—luminal B	0.57	< .005	0.50-0.66	0.76	< .005	0.66-0.91
Breast—HER2 enriched	0.67	< .005	0.57-0.79	1.03	.74	0.88-1.25
Breast—TN	1.3	< .005	1.16-1.46	1.43	< .005	1.28-1.63
Breast—NOS	0.81	< .005	0.72-0.91	0.99	.90	0.85-1.21
Melanoma	0.94	.01	0.90-0.99	0.79	< .005	0.75-0.84
Distance to hospital (miles)						
Analyzed continuously	1.00	< .005	1.00-1.00	1.00	.01	1.00-1.00
Chemotherapy						
No		Reference			Reference	
Yes	0.54	< .005	0.53-0.55	0.49	< .005	0.48-0.50
Immunotherapy						
No		Reference			Reference	
Yes	0.54	< .005	0.52-0.56	0.58	< .005	0.55-0.60
Experimental therapy						
No		Reference			Reference	
Yes	0.84	< .005	0.75-0.95	0.88	.05	0.77-1.00
External radiation therapy type						
WBRT		Reference			Reference	
SRS	0.52	< .005	0.51-0.53	0.50	< .005	0.49-0.52

*Abbreviations: CI, confidence interval; OR, odds ratio; Adeno, adenocarcinoma; WBRT, whole-brain radiation therapy; SRS, stereotactic radiosurgery; SCC, squamous cell carcinoma; LCNEC, large cell neuroendocrine carcinoma; TN, triple negative; NOS, not otherwise specified.*

surgical data, even though surgery remains an important treatment for BMs. Additionally, there is a lack of information regarding other downstream effects of BM treatments in the literature, such as leptomeningeal disease and radiation necrosis. Finally, because

patients were partitioned into the general SRS and WBRT groups, it is possible that some treated with unconventional or experimental doses/fractions were excluded.

SRS usage over the last decade has increased nationwide due to relaxation of guidelines, improved

techniques, and accessibility of technology. The increase in patient survival over this same period indicates a possible relationship between SRS usage and improved survival. Finally, patient characteristic discrepancies in RT usage should be explored

to identify ways to overcome BM treatment limitations.

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# Challenges of Methotrexate Administration During Breast Radiation: A Case Report

Mona Arbab, MD, MEd;<sup>1\*</sup> Meng-Lun Hsieh, MD, PhD;<sup>1</sup> Vlad Zaha, MD;<sup>2</sup> Sangeetha Reddy, MD;<sup>3</sup> Asal Rahimi, MD<sup>1</sup>

## Abstract

An increased number of patients with cancer who are receiving methotrexate for autoimmune conditions or immune checkpoint inhibitor (ICI) myocarditis are presenting to the radiation oncology department. In this article, we report a case of a patient with ICI myocarditis on methotrexate who received radiation to the chest wall and nodes. In this case, methotrexate did not increase the risk of severe acute toxicities of radiation.

**Keywords:** methotrexate, myocarditis, radiation, breast cancer

## Case Summary

A 29-year-old White woman presented with a palpable mass in the right breast. On examination, there was a mass at 9:00 in the right breast in addition to matted axillary nodes. Initial work-up including an ultrasound, breast MRI, and ultrasound-guided core needle biopsy revealed an infiltrating ductal carcinoma (IDC), grade 3, triple negative with Ki-67 of 75%, cT2N2M0, anatomic stage IIIA, and prognostic stage IIIC. The patient initiated neoadjuvant chemotherapy (NAC) and received 4 cycles of carboplatin, paclitaxel, and pembrolizumab, followed by doxorubicin, cyclophosphamide, and pembrolizumab for 4 cycles. After her first 4 cycles of NAC, she

had a complete clinical response. This was consistent with her right breast mammogram and ultrasound, which were notable for complete response in the breast. The patient underwent right partial mastectomy and sentinel lymph node biopsy with pathological complete response, ypT0N0. The patient continued on pembrolizumab.

Considering the presence of bulky matted lymph nodes, young age, and triple-negative IDC, she was advised to receive comprehensive RT treatment to the right whole breast, right axilla, right internal mammary nodes, and right supraclavicular nodes. The planned dose was 50.4 Gy in 28 fractions using the deep inspiration breath hold technique (**Figures 1, 2**). Of note, the mean heart dose was 100.7 cGy (**Figure**

**2**). The patient was simulated and within a few days prior to the start of radiation, presented to the emergency department with left-sided chest pain, nausea, and headache. Work-up revealed an elevated troponin of 404 ng/L, elevated C-reactive protein of 15.6 mg/L, and a normal electrocardiogram. Cardiac MRI was notable for normal biventricular size and systolic function in addition to late gadolinium enhancement pattern within the mid-inferolateral left ventricular wall and diffuse ventricular edema (global T2 of 68 ms) consistent with acute myocarditis per modified Lake Louise criteria.<sup>1</sup> She was diagnosed with non-fulminant ICI myocarditis. The myocarditis was considered to be caused by both pembrolizumab (ICI) and anthracycline chemotherapy in the setting of alcohol consumption prior to chemotherapy initiation. Pembrolizumab was subsequently discontinued after she developed myocarditis. The patient was treated with 1 g of intravenous solumedrol as an inpatient, and then transitioned

**Affiliations:** <sup>1</sup>Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, TX. <sup>2</sup>Department of Cardiology, UT Southwestern Medical Center, Dallas, TX. <sup>3</sup>Department of Medical Oncology, UT Southwestern Medical Center, Dallas, TX.

**Corresponding author:** \*Mona Arbab, MD, MEd, Department of Radiation Oncology, UT Southwestern Medical Center, 2280 Inwood Rd, Dallas, TX 75235. (Mona.Arbab@utsouthwestern.edu)

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**Figure 1.** Axial view of the patient's CT-based radiation treatment plan summary. The right whole breast and regional lymph nodes (axillary, supraclavicular, internal mammary) were treated utilizing a 3D conformal technique. A dose of 5040 cGy was delivered in 28 fractions of 180 cGy each. The dose was delivered using 10 MV photons, prescribed to the planning target volume (PTV). Custom multileaf collimator blocking was used to shield uninvolved tissue. This was followed by a boost to the tumor bed delivered with 10 MV photons, utilizing a 3D conformal technique, prescribed to PTV. A boost dose of 1000 cGy was delivered in 5 fractions of 200 cGy each. Dose color wash is represented in cGy.



to prednisone 80 mg with a taper over 4 months down to 1 mg prednisone per os (PO) every other week (**Figure 3**). At diagnosis of myocarditis, she was also started on methotrexate 15 mg PO weekly 5 days prior to the start of RT. At the start of RT, she remained on 15 mg of weekly methotrexate PO, and by day 9 of radiation, her methotrexate was increased to 20 mg weekly. She remained on 20 mg of weekly methotrexate throughout her RT treatment, and by approximately week 13 of methotrexate dosing and 5 weeks after completing radiation, her methotrexate was tapered down to 17.5 mg weekly. The start of methotrexate coincided with the beginning of RT; however, we discussed the possible toxicities

of combining both treatments and decided not to delay her RT treatment and proceed with concurrent treatment, given her initial advanced stage disease and young age. Of note, this was a right-sided breast cancer, so the heart was not in proximity to the radiation field. The patient did not develop severe toxicity during radiation and concurrent oral methotrexate at her 1-month follow-up. During RT treatment, she had presented with grade 2 dermatitis in the right supraclavicular area and neck. She also developed nausea, for which she was prescribed ondansetron as needed, and mild grade 1 oral mucositis. Weekly complete blood count and troponins were checked

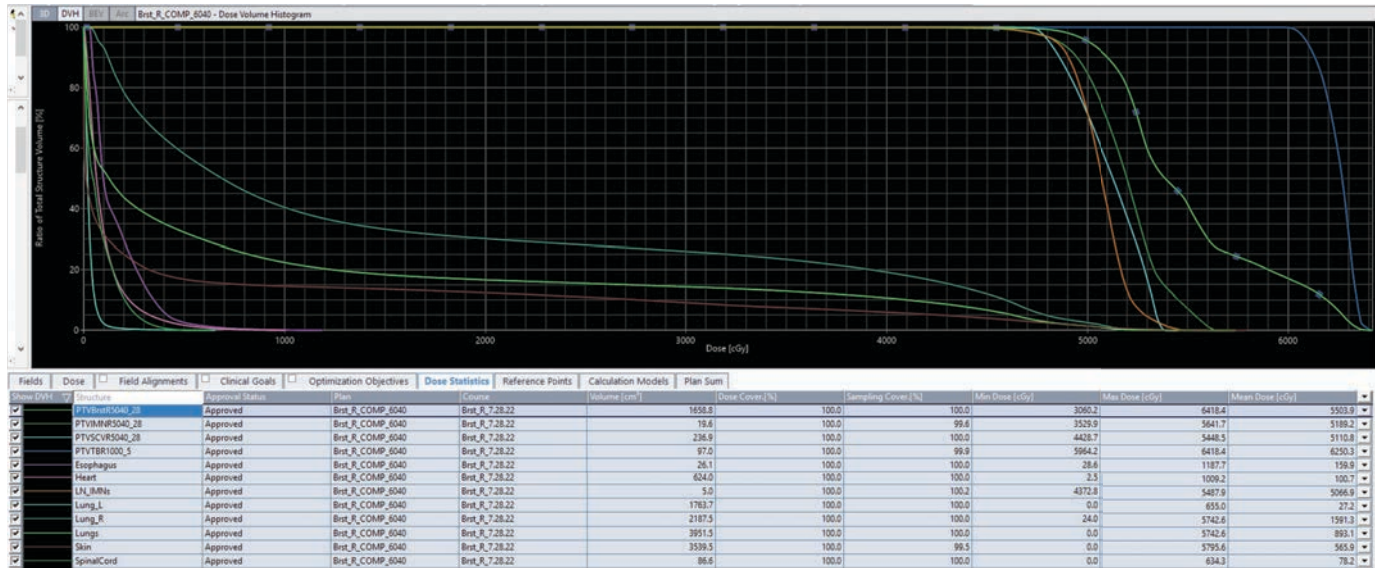
during her treatments (**Figure 3**, **Table 1**). Her troponin levels peaked at 285 ng/L during her diagnosis of myocarditis prior to RT. During her fourth week of radiation, her troponin levels normalized and continued to stay in normal range 2 months after completion of radiation. When starting RT, her hemoglobin levels were slightly low (10.6 and 11.7 g/dl), but these normalized after the first week of RT.

## Discussion

Methotrexate is an antimetabolite, commonly used to treat rheumatoid arthritis, psoriasis, Crohn's, and other autoimmune conditions. In addition, methotrexate is also used to treat ICI myocarditis, a condition that is more common nowadays in patients with cancer. Patients who are on methotrexate can be referred to radiation oncologists for treatment of their cancers, and the common concern is the possible toxicities of combined methotrexate with RT, which can include bone marrow suppression, mucositis, and nausea. Due to the chronicity of these medical conditions, it is not always possible to stop methotrexate during RT. To our knowledge, there are no published data on the safety of oral methotrexate during breast RT. Therefore, in this case report, we shared our experience.

With the recent results from the Keynote 522 trial, which showed an improvement in pathological complete response in patients with triple-negative breast cancer who received pembrolizumab with NAC, we expect to see more immunotherapy being used in the coming decade.<sup>2</sup> Thus, with increased immunotherapy use, patients will most likely experience an increase in common side effects

Figure 2. Dose volume histogram of the radiation treatment plan summary.

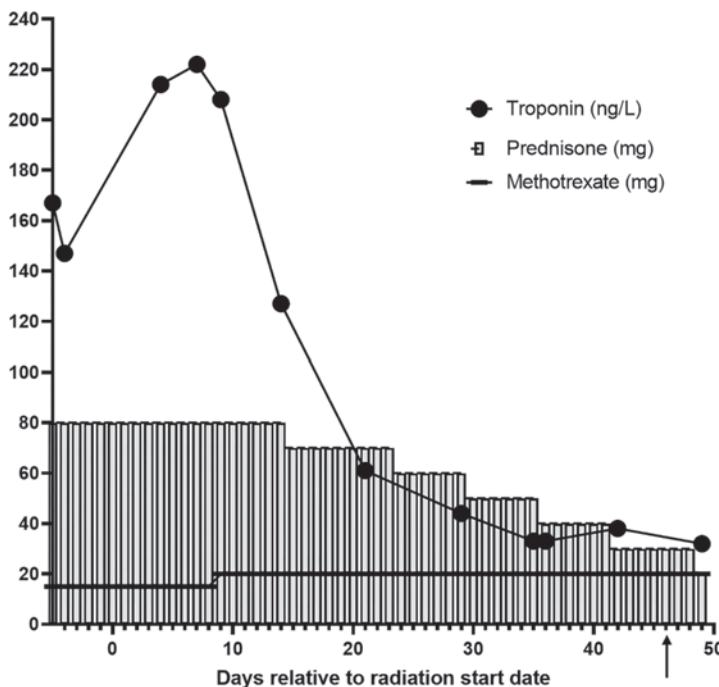


such as febrile neutropenia, anemia, as well as myocarditis, a relatively rare but serious and potentially fatal side effect.<sup>2</sup> Though ICI-related

myocarditis has a reported incidence of 0.04% to 1.14%, compared with other immune-related adverse events, ICI-related myocarditis is associated with a significantly higher mortality of 25% to 50%.<sup>3</sup> Per the European Society of Cardiology guidelines,<sup>4</sup> ICI myocarditis usually occurs within the first 12 weeks of ICI administration but later cases (after 20 wk) can happen. Common treatments for myocarditis include intravenous methylprednisolone at high doses (500-1000 mg daily for 3-5 d) with subsequent tapering with clinical improvements (troponin reduction by 50% within 24-72 h in addition to resolved left ventricular dysfunction, atrioventricular block, and arrhythmias). If the patient does not respond to steroids, other immunosuppressive agents such as methotrexate can also be added.

Currently, to our knowledge, there are no data examining the safety of methotrexate with concurrent RT to the breast or chest wall. However, Recchia et al reported the outcomes of a chemotherapy regimen including methotrexate with

Figure 3. Trending troponin (ng/L) levels are shown before, during, and after radiation therapy, as is the correlation with prednisone (mg) and methotrexate (mg) dosing relative to the number of days before, during, and after radiation treatment. The black arrow on day 46 indicates the end of radiation treatment. The increase in the troponin level after the initiation of RT is not due to the RT treatment but is likely due to the ongoing toxic effect of the alcohol.



**Table 1. Complete Blood Count Trends Before, During, and After Radiation Therapy (RT)**

	PRE-RT	1ST WEEK OF RT	END OF 3RD WEEK OF RT	5TH WEEK OF RT	END OF 6TH WEEK OF RT	5 WK POST-RT
White blood cell 4.00-11.00 × 10 <sup>9</sup> /L	9.63	9.07	8.76	6.43	5.43	2.74
Hemoglobin 12.0-15.0 g/dL	<b>10.6</b>	<b>11.7</b>	12.4	13.3	13.0	12.5
Hematocrit 34.0%-44.0%	<b>31.7</b>	37.3	39.8	42.2	40.6	38.1
Platelet 150-450 × 10(9)/L	285	280	221	240	186	247
Neutrophils 1.50 × 7.40 × 10(9)/L	<b>8.22</b>	<b>7.81</b>	<b>7.95</b>	4.92	4.16	
Lymphocytes 1.10-3.90 × 10(9)/L	<b>.95</b>	<b>.81</b>	<b>.33</b>	<b>.91</b>	<b>.61</b>	
Monocytes 0.10-0.90 × 10(9)/L	.42	.31	.37	.47	.56	
Eosinophils 0.00-0.70 × 10(9)/L	.00	.08	.02	.04	.02	
Basophils 0.00-0.20 × 10(9)/L	.00	.02	.01	.03	.02	
Granulocytes 0.00-0.06 × 10(9)/L	.01	.04	<b>.08</b>	.06	.06	

*Bolded numbers indicate abnormal values.*

concurrent RT in axillary-node-positive patients.<sup>5</sup> In this study, 200 patients with node-positive breast cancer received chemotherapy with adriamycin and docetaxel, followed by RT concurrent with 6 courses of cyclophosphamide, methotrexate, and 5-fluorouracil (CMF). Two courses of dose-dense chemotherapy with ifosfamide, carboplatin, and etoposide, supported by pegfilgrastim, were administered to patients with >5 histologically confirmed axillary lymph node metastases. The radiation dose was 50 Gy in 25 fractions to the chest wall/residual breast tissue and axillary nodes (level II and III), and supraclavicular nodes in patients with >4 positive axillary lymph nodes, followed by a 10 Gy boost to the tumor bed. The

methotrexate dose was 60 mg/m<sup>2</sup> administered every 3 weeks. The most common acute toxicity for patients receiving CMF + RT was nausea and vomiting (13%), followed by mucositis (8%), diarrhea, and leukopenia (3%). Only 3% required discontinuation of treatment due to leukopenia. This study used a higher dose of methotrexate and also added other agents to the treatment but did not show severe acute toxicities. In a retrospective study by Livi et al, concurrent CMF regimen with RT was compared with RT alone and CMF alone.<sup>6</sup> The mean RT dose was 50 Gy to the whole breast, followed by a boost of 6-16 Gy to the tumor bed. The methotrexate dose was 40 mg/m<sup>2</sup> repeated on days 1 and 8, every 28 days for 6 cycles. There was no

difference in late toxicity. However, grade 2 acute skin toxicity was higher in the concurrent arm (21% vs 11%) and RT was interrupted more in the concurrent arm (8.5% vs 4.1%). Another study by Pan et al looked at concurrent RT (40 Gy in 20 fractions to whole brain with/without spinal RT) with intrathecal methotrexate for treating leptomeningeal metastasis.<sup>7</sup> Patients received intrathecal methotrexate at a dose of 12.5 to 15 mg weekly for 4 weeks. In addition, 20% of patients developed moderate-to-severe toxicity, and the main toxicity was leukoencephalopathy (68%), followed by bone marrow suppression (22%) and mucositis (20%). This regimen was more toxic due to the extent and location of the radiation

field, in addition to intrathecal administration of methotrexate and a worse baseline condition of the patients.

Based on the above findings and a lower methotrexate dose in our patient, we decided to proceed with treatment while monitoring her potential toxicities. The patient did not develop any severe toxicity from the treatment. Further research and investigations are needed as ICI-related toxicities become more prevalent and more patients may require concurrent chemoradiation with methotrexate.

### Conclusion

Based on the limited available studies involving concurrent methotrexate and RT in patients with breast cancer, it seems that the combination of both treatments does not increase the risk of

severe acute toxicities; however, there might be an increase in grade 2 skin toxicity and these patients should be monitored closely until more data are accumulated. The most common side effects might be nausea, vomiting, mucositis, leukopenia, and skin toxicity, which can be monitored during treatment and addressed as needed.

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# Green-ifying Clinical Trials

Rachel Shenker, MD;\* Julie Bloom, MD; Katie Lichter, MD, MPH

In oncology, clinical trials are of utmost importance to advance treatment options and management of cancer care. However, there is growing awareness concerning the environmental impact of health care practices. This has led to urgent demands for action.<sup>1-5</sup> Research conducted in the United Kingdom has revealed that the carbon footprint of clinical trials is substantial, with the main contributors including travel required for these trials, the delivery of trial drugs, and the inefficiencies in enrolling participants.<sup>6</sup> Of the 350,000 clinical trials registered across the globe, it is estimated that this equates to a carbon consumption of 27.5 million tons.<sup>7</sup> As part of the National Health Service, the Sustainable Healthcare Coalition has set up resources and a working tool to test on clinical trials to measure carbon emissions, and the National Institute for Health and Care Research has published a Carbon Reduction Guide. However, in the United States, such measures have not been implemented. Thus, we present the following suggestions for the reduction of environmental toxicity within US cancer clinical trials.

## 1. Explore opportunities for decentralized clinical trials:

Recognizing that patients frequently face the challenge of traveling long distances to participate in trials,<sup>8</sup> we encourage the leveraging of community partnerships aimed at exploring the feasibility of decentralizing clinical trials. Recent studies have indicated that travel and driving distance for individual radiation therapy treatments are significant contributors to emissions

related to cancer care.<sup>9-11</sup> By exploring this approach, we could potentially reduce travel-related emissions while also expanding access, thereby mitigating financial burdens and socioeconomic disparities in trial enrollment.<sup>12</sup>

## 2. Enhanced transportation and housing assistance:

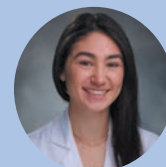
To address the issue of long travel distances, we advocate for increased access to public transportation, charity care, and affordable housing for patients requiring multiday treatments. This strategy may significantly lessen both the environmental impact and financial strain associated with travel for clinical trials.

## 3. Streamlined appointment scheduling:

We suggest partnering with cancer care navigators to effectively streamline and consolidate appointments for patients during clinical trial enrollment. Such strategic coordination has the potential to minimize the need for frequent long-distance travel, thereby leading to a more efficient trial participation process and contributing to a reduction in emissions.

## 4. Enhanced utilization of telehealth:

Given the increasing adoption of and documented advantages of telehealth, such as the 36% reduction in greenhouse gas emissions observed at Stanford Health Care since 2019,<sup>13</sup> integrating telemedicine into the clinical trial framework is advisable. Studies indicate that telehealth



**Dr. Shenker** is a PGY5 resident physician, Duke University Hospital.



**Dr. Bloom** is a PGY5 resident physician, The Mount Sinai Hospital.



**Dr. Lichter** is a PGY4 resident physician, UC Climate Health Fellow, University of California San Francisco.

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**Corresponding author:** \*Rachel Shenker, MD, Department of Radiation Oncology, Duke University Hospital, 20 Duke Medicine Cir, Durham, NC, 27710. (rfs9@duke.edu)

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in oncology not only lowers carbon emissions associated with cancer care but also mitigates financial toxicities for patients and increases access to those in rural settings.<sup>14-16</sup> Its application is especially beneficial in assessing patient eligibility and reducing unnecessary travel.

#### 5. **Prospective environmental data**

**collection:** We advocate for the proactive collection of environmental impact data from the onset of the start of clinical trials. This initiative should be conducted in collaboration with environmental science schools or departments and involve climate health experts. Precise tracking of emissions throughout each phase of a trial is crucial for making well-informed decisions.

#### 6. **Integration of environmental considerations in regulatory frameworks:**

We encourage consideration of modifying the clinical trial authorization and regulatory submission processes to include an assessment of the environmental impact of the trials. This environmental evaluation should be considered as critical as the evaluation of cost, equity, and access in the regulatory process.

#### 7. **Interdisciplinary collaboration:** We call for a concerted effort among oncology teams, environmental specialists, and cooperative groups to devise holistic strategies. These strategies should aim to lower the costs for patients and health care institutions, broaden the accessibility of clinical trials, and reduce the overall carbon footprint associated with these trials.

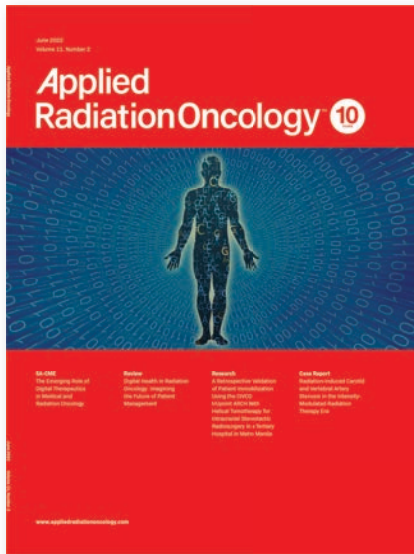
By implementing these recommendations, we can address the environmental impact of clinical trials while improving accessibility and reducing financial burdens on patients.

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