Patterns of Radiation Therapy During the COVID-19 Pandemic: Results from the Multicenter, Cross-Sectoral Registry of the German National Pandemic Cohort Network (NAPKON)

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Patterns of Radiation Therapy During the COVID-19 Pandemic: Results from the Multicenter, Cross-Sectoral Registry of the German National Pandemic Cohort Network (NAPKON)

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Simple Summary

Cancer patients receiving or having received radiotherapy were considered a particularly vulnerable group during the COVID-19 pandemic, but systematic data on their clinical course have been limited. Using data from the German National Pandemic Cohort Network (NAPKON), this study describes radiotherapy (RT) characteristics and COVID-19-related clinical features in patients with documented RT and confirmed SARS-CoV-2 infection. Ninety patients were included, most of whom had received a single course of RT with a median dose of 45 Gy. The majority experienced mild or moderate COVID-19 courses, and vaccination rates were high. Overall, these findings suggest that patients with a history of RT documented in NAPKON predominantly had favorable COVID-19 outcomes and demonstrate the feasibility of integrating oncologic subcohorts into national pandemic research infrastructures.

Abstract

Background: Cancer patients receiving or having received radiotherapy (RT) represent a clinically vulnerable group during the COVID-19 pandemic. However, systematic data on their clinical course, comorbidities, and vaccination status are limited. The German National Pandemic Cohort Network (NAPKON), established to systematically collect comprehensive clinical data on COVID-19 patients nationwide, provides a unique opportunity to address this gap. This study aimed to describe radiation therapy patterns and

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COVID-19-related clinical characteristics among patients documented within the NAPKON Cross-Sectoral Platform (SUEP). **Methods:** This multicenter, descriptive analysis was conducted within the framework of the German National Pandemic Cohort Network (NAPKON). All patients with documented RT and confirmed SARS-CoV-2 infection were identified in the SUEP database. RT was classified relative to the documented infection date as occurring before, during, or after infection. Demographic, clinical, laboratory, imaging, and vaccination data were extracted and analyzed descriptively. Due to the small sample size, no correlation or multivariable analyses were performed. **Results:** A total of n = 90 patients were included in the analysis. The median age was 65 years (range 22–90), and 56% were male. Most patients (93%) received one course of RT, most frequently targeting specific organ systems (54%), while total body irradiation was performed in 4%. The median radiation dose was 45 Gy (IQR 30–60). Among 68 patients with evaluable timing information, RT had been administered before infection in 53 patients (77.9%), during infection in 3 patients (4.4%), and after infection in 12 patients (17.6%). At the time of SARS-CoV-2 detection, 76% of patients experienced a phase without complications, 19% a phase with complications, and 2% a critical phase. The majority of vaccinated individuals had received Comirnaty (BioNTech/Pfizer; 80%). COVID-19-typical findings were identified in 18% of chest X-rays and 27% of CT scans. Clinical and laboratory characteristics showed no substantial differences by hospital length of stay. **Conclusions:** Patients with documented RT and SARS-CoV-2 infection in the NAPKON registry predominantly experienced mild or moderate COVID-19 courses and showed a relatively high vaccination uptake. However, due to the descriptive study design and the absence of a control group, these findings should not be interpreted as being attributable to RT itself but rather as a characterization of this registry cohort. Importantly, the cohort mainly comprised patients with a history of RT before SARS-CoV-2 infection, whereas only a small minority received RT during infection. Although the analysis was descriptive and limited by missing data, it demonstrates the feasibility and scientific value of integrating oncologic subcohorts within national pandemic research networks. Continued longitudinal analyses will be essential to further characterize outcomes of patients with cancer and RT in future pandemics.

Keywords: radiotherapy; radiation oncology; COVID-19; SARS-CoV-2; NAPKON; Network University Medicine (NUM); Germany; vaccination

1. Introduction

Since late 2019, the global medical and scientific community has faced an unprecedented health crisis caused by the emergence of a novel betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19) [1]. Coronaviruses are large, enveloped, single-stranded RNA viruses that can infect both animals and humans, with SARS-CoV-2 being the seventh known human coronavirus. Following its first detection in Wuhan, China, the virus spread rapidly across the globe and was declared a pandemic by the World Health Organization in March 2020 [1].

SARS-CoV-2 primarily affects the respiratory system and is characterized by a broad clinical spectrum ranging from asymptomatic infection to severe viral pneumonia and multi-organ failure [2,3]. The pathogenesis of COVID-19 is closely linked to an excessive host immune response and systemic inflammation, including cytokine dysregulation and endothelial injury, which contribute to the development of acute respiratory distress syndrome (ARDS) and thromboembolic complications [4]. In severe cases, patients fre-

quently progress to COVID-19-associated acute respiratory distress syndrome (CARDS), which carries high morbidity and mortality. Management typically includes optimized oxygenation strategies, non-invasive or invasive ventilation, and corticosteroid therapy, with dexamethasone shown to reduce mortality in severe disease [5].

In response to the pandemic and the urgent need for structured clinical data, the German National Pandemic Cohort Network (NAPKON) was established in 2020 under the umbrella of the Network University Medicine (NUM) to systematically collect and harmonize clinical, laboratory, and biospecimen data across Germany [6]. NAPKON integrates three complementary cohort platforms—the Cross-Sectoral Platform (SUEP), the High-Resolution Platform (HAP), and the Population-Based Platform (POP)—to enable comprehensive and longitudinal observation of patients throughout all phases of SARS-CoV-2 infection. Based on this infrastructure, multiple studies have already provided important insights into long-term health sequelae, post-COVID symptomatology, and quality-of-life outcomes after SARS-CoV-2 infection in Germany [7–9].

Beyond its direct impact on morbidity and mortality, the COVID-19 pandemic profoundly disrupted healthcare delivery worldwide. In oncology, infection control measures, resource constraints, and staff shortages led to considerable changes in diagnostic and therapeutic workflows. Radiotherapy (RT) services—as a cornerstone of cancer treatment—were also affected, prompting adaptations in fractionation schemes, treatment prioritization, and scheduling to ensure continuity of care under pandemic conditions [10].

Analyses from German inpatient data demonstrated that RT utilization patterns shifted during the first pandemic wave: while admissions for cervical cancer decreased markedly, RT for head and neck cancer became more frequently applied, suggesting a temporary reorientation toward non-surgical treatment approaches [11]. These findings highlight the need for comprehensive, registry-based evaluations to better understand how the pandemic influenced RT practice, patient selection, and outcomes.

To date, no systematic analysis has described the clinical characteristics and treatment pathways of irradiated COVID-19 patients in Germany. The present study therefore aims to characterize radiotherapy patterns, patient demographics, and clinical courses among patients with documented RT and SARS-CoV-2 infection within the NAPKON registry. Importantly, this cohort includes patients who received RT before, during, or after infection and therefore does not exclusively represent patients undergoing active RT at the time of COVID-19.

2. Methods

2.1. Study Context and Governance

This analysis was conducted within the framework of the NAPKON, a nationwide research initiative of the Network University Medicine (NUM). Within NAPKON, the "Fach- und Organspezifische Arbeitsgruppe" (FOSA) Strahlentherapie served as the coordinating expert group for radiation oncology. The FOSA facilitates interdisciplinary exchange among clinical experts, supports dataset review and harmonization, and contributes to research agenda setting, data use, and quality assurance within the NUM. In addition, a patient representation group (AG Patient:innenvertretung) ensures the inclusion of patient perspectives in scientific and ethical deliberations.

2.2. Data Source and Cohort

The present study is based on data from the Cross-Sectoral Platform (SUEP) of NAPKON. SUEP is a national, multicenter, minimally interventional, prospective cohort study including patients with confirmed SARS-CoV-2 infection or matched controls, recruited across all levels of healthcare in Germany—ranging from university hospitals and commu-

nity hospitals to outpatient practices. The platform collects standardized clinical, laboratory, imaging, and biosample data at baseline, during follow-up, and up to 12 months post infection. The aim of SUEP is to provide a harmonized, high-quality dataset to enable epidemiological and translational research on COVID-19 and future pandemics.

2.3. Ethical Approval and Data Access

Data use for this project was requested through the official NAPKON Use & Access procedure. The application was reviewed and approved by the NUM Scientific Advisory Board and the Use & Access Committee after presentation in the meeting on 3 May 2024. The project was subsequently approved by the local ethics committee of the University Hospital Halle (Saale) (reference number 2024-087). Data transfer to the study team was initiated after completion of the feasibility assessment and ethical clearance.

2.4. Data Extraction and Variables

Data were retrieved from the NAPKON SUEP database using a standardized query. All cases with documented RT were identified via the variable "eonradio" (performed RT) within the module FV2 Diagnosen (Rheuma, Diabetes, Tumor, HIV). Corresponding patient-level information was extracted across relevant tables, including demographic data, baseline and follow-up parameters (BV1, STV1, STV2, FUV1, FUV3), comorbidities, and treatment information. To clarify the temporal relationship between RT and SARS-CoV-2 infection, RT timing was classified relative to the documented infection date (gec_diag_date) as before, during, or after infection.

The SUEP data model comprises hierarchical case and visit structures, including a baseline assessment at the time of initial SARS-CoV-2 diagnosis, followed by acute-phase visits and standardized follow-up assessments at 3 and 12 months. This structure enables longitudinal documentation of clinical characteristics, treatments, and outcomes throughout the acute and post-acute phases of COVID-19.

2.5. Participating Centers

Data contributions were received from multiple NAPKON study sites across Germany. Most patients were recruited at tertiary care centers and large non-university hospitals, resulting in a geographically diverse cohort; however, the sample is not population-representative due to the predominance of high-volume recruiting centers. Detailed site contributions are provided in the Supplementary Materials. Additional university and non-university hospitals participated, resulting in a geographically diverse but not population-representative cohort, as recruitment was mainly conducted in large academic and non-academic hospitals.

2.6. Data Processing and Analysis

After secure data transfer, all datasets were pseudonymized and underwent quality control to ensure completeness and consistency. The analysis focused on descriptive evaluation of patient demographics, clinical characteristics, and treatment parameters among irradiated individuals within the SUEP cohort. In patients with multiple RT courses, the timing of RT was first assessed at the treatment-course level and then summarized at the patient level.

2.7. Statistical Analysis

Given the limited sample size of the analyzed cohort, no correlation or multivariable analyses were performed. Therefore, the statistical approach was primarily descriptive. Categorical variables were summarized as absolute and relative frequencies [n (%)], and continuous variables were expressed as medians with interquartile ranges (IQR) and, where

appropriate, minimum and maximum values. Group comparisons, such as those according to hospital length of stay, were presented descriptively without inferential statistical testing.

All statistical analyses were conducted using RStudio, version 2024.04.2+764 (RStudio, PBC, Boston, MA, USA). During the preparation of this work, the authors used ChatGPT (GPT-5.3, OpenAI Inc., San Francisco, CA, USA) to improve writing style and check grammar and spelling. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the final manuscript.

3. Results

3.1. Patient Characteristics

A total of n = 90 patients were included in the analysis (Table 1). Most patients (93%) received only one course of RT, while 4.4% underwent two courses, and two patients received three or more. The majority of treatments (54%) targeted specific organ systems, whereas total body irradiation was performed in 4.4% of cases; in 41% of patients, the radiation type was not documented.

Table 1. Patient and treatment characteristics (n = 90 patients).

Variable	N = 90 [1]
Number of radiations (per patient)	
1	84 (93%)
2	4 (4.4%)
3	1 (1.1%)
5	1 (1.1%)
Radiation type	
Total body irradiation	4 (4.4%)
Organ system(s)	49 (54%)
No information available	37 (41%)
Radiation region	
Bone	7 (7.7%)
Brain	5 (5.5%)
Breast	7 (7.7%)
Head and Neck region	8 (8.8%)
Other	9 (10%)
Prostate	7 (7.7%)
Rectum	3 (3.3%)
Skin	3 (3.3%)
No information available	41 (45.5%)
Radiation dose (Gy)	
Median [Q1, Q3]; range: Min–Max	45 [30, 60]; range: 5–78
No information available	49 (54.4%)
Radiation duration (days)	
Median [Q1, Q3]; range: Min–Max	31 [4, 44]
No information available	34 (37.7%)
Age at diagnosis (years)	
Median [Q1, Q3]; range: Min–Max	65 [60, 71]; range: 22–90
No information available	1 (1.1%)
Sex	
Female	40 (44%)
Male	50 (56%)
Weight baseline (kg)	
Median [Q1, Q3]; range: Min–Max	79 [62, 90]; range: 43–125
No information available	15 (16.6%)
CRP baseline (mg/L)	
Median [Q1, Q3]; range: Min–Max	10 [2, 30]; range: 0–174
No information available	8 (8.8%)
Creatinine baseline (mg/dL)	
Median [Q1, Q3]; range: Min–Max	0.89 [0.72, 1.13]; range: 0.45–6.40
No information available	3 (3.3%)

Table 1. *Cont.*

Variable	N = 90 [1]
WBC baseline (Gpt/L)	
Median [Q1, Q3]; range: Min–Max	5.3 [3.8, 6.8]; range: 0.3–263.8
No information available	1 (1.1%)
Number of vaccinations	
0	35 (39%)
1	16 (18%)
2	18 (20%)
3	11 (12%)
4	9 (10%)
5	1 (1.1%)
Chest X-ray: COVID-typical finding	
Very typical	1 (1.1%)
Compatible	15 (16.7%)
Not typical	5 (5.6%)
No information available	69 (76.7%)
Chest CT: COVID-typical finding	
Very typical	7 (7.8%)
Compatible	17 (19%)
Not typical	7 (7.8%)
No information available	59 (66%)

[1] n (%)

The most frequently irradiated regions were the head and neck (8.8%), bone (7.7%), breast (7.7%), and prostate (7.7%), followed by brain (5.5%), rectum (3.3%), and skin (3.3%). In 45.5% of patients, no information on the radiation region was available. The median radiation dose was 45 Gy [IQR 30–60], ranging from 5 to 78 Gy, while the median radiation duration was 31 days [IQR 4–44]. Information on radiation dose and duration was missing in 54% and 38% of cases, respectively. To determine whether RT represented a concomitant factor of COVID-19, RT timing was classified relative to the documented infection date. Among 68 patients with evaluable timing information, RT had been administered before infection in 53 patients (77.9%), during infection in 3 patients (4.4%), and after infection in 12 patients (17.6%). Thus, the cohort predominantly consisted of patients with a prior history of RT rather than patients receiving RT concomitantly with SARS-CoV-2 infection.

The median age at diagnosis was 65 years [IQR 60–71; range 22–90], and 56% of patients were male. According to the Clinical Frailty Scale (CFS), 17% of patients were classified as very fit or fit, 29% as managing well or vulnerable, and 32% as mildly to very severely frail; CFS data were unavailable for 21% of patients.

The median baseline weight was 79 kg [IQR 62–90; range 43–125]. The median CRP was 10 mg/L [IQR 2–30; range 0–174], median creatinine 0.89 mg/dL [IQR 0.72–1.13; range 0.45–6.40], and median PCT 0.15 ng/mL [IQR 0.07–0.38; range 0.00–6.11]. The median WBC count was 5.3 Gpt/L [IQR 3.8–6.8; range 0.3–263.8].

Pulmonary comorbidities were documented in 23% of patients, cardiovascular diseases in 9%, and neurological disorders in 19%, while for the majority of patients no information on these comorbidities was available.

Regarding vaccination status, 39% of patients were unvaccinated, 18% had received one, 20% two, 12% three, and 11% four or more COVID-19 vaccinations. Detailed information on symptom prevalence and duration, as well as radiologic findings is provided in the Supplementary Materials (Tables S1 and S2).

3.2. COVID-19 Detection, Contact Exposure, and Vaccination Status

At the time of the first detection of SARS-CoV-2 infection, most patients were in a phase without complications (n = 68, 76%), while 17 patients (19%) experienced a phase

with complications. Two patients (2%) were in a critical phase, and for two patients (2%) no information on the clinical severity was available.

Information on the presumed contact situation prior to infection was documented heterogeneously: 42 patients (47%) reported no known contact with an infected individual, 10 patients (11%) reported contact with a SARS-CoV-2–positive person from their own household, 8 patients (9%) had contact with an infected person outside their household, and 7 patients (8%) reported exposure without further specification. For 25 patients (28%), no data on contact exposure were available.

Regarding vaccination status, the majority of vaccination doses applied were Comirnaty (BioNTech/Pfizer) (n = 98, 80%), followed by Moderna (n = 16, 13%), AstraZeneca (n = 6, 5%), and Janssen (Johnson & Johnson) (n = 2, 2%). One patient had received another vaccine.

In terms of seasonal influenza vaccination, 23 patients (26%) had received a flu shot within the past six months or during the observation period, while 35 (39%) had not been vaccinated; for 35 patients (39%), this information was not available. Concerning other vaccinations within the same period, only two patients (2%) reported additional immunizations, 57 patients (63%) had not received any, and data were missing for 34 patients (38%).

3.3. Hospital Length of Stay and Clinical Characteristics

The median follow-up period for the analyzed cohort was 352 days (11.6 months), with an interquartile range (IQR) of 49–370 days. Table 2 summarizes the distribution of clinical and laboratory characteristics according to hospital length of stay.

Table 2. Distribution of clinical and laboratory characteristics according to hospital length of stay. Abbreviations: CRP = C-reactive protein; WBC = white blood cell count; CFS = Clinical Frailty Scale.

Characteristic	≤14 Days N = 42 [1]	>14 Days N = 43 [1]
Age		
<70	28 (68%)	28 (65%)
≥70	13 (32%)	15 (35%)
No information available	1	0
CFS		
<5	18 (56%)	21 (58%)
≥5 (frail)	14 (44%)	15 (42%)
No information available	10	7
CRP		
<10 mg/L	22 (58%)	18 (46%)
≥10 mg/L	16 (42%)	21 (54%)
No information available	4	4
creatinine		
<1.2 mg/dL	29 (74%)	32 (74%)
≥1.2 mg/dL	10 (26%)	11 (26%)
No information available	3	0
WBC		
<10 G/L	36 (88%)	38 (88%)
≥10 G/L	5 (12%)	5 (12%)
No information available	1	0
Sex		
Female	21 (50%)	16 (37%)
Male	21 (50%)	27 (63%)
Number of vaccinations		
0 vaccinations/unknown	15 (36%)	18 (42%)
≥1 vaccination	27 (64%)	25 (58%)

Table 2. *Cont.*

Characteristic	≤14 Days N = 42 [1]	>14 Days N = 43 [1]
Chest CT results compatible with COVID 19		
Other	33 (79%)	28 (65%)
Yes/compatible	9 (21%)	15 (35%)

[1] n (%)

Among patients with a hospital stay of 14 days or less, 68% were younger than 70 years, compared with 65% in those hospitalized for more than 14 days. The proportion of frail patients (CFS $\geq$ 5) was similar in both groups (44% vs. 42%). Elevated CRP levels ($\geq$10 mg/L) were observed in 42% of patients with a shorter stay and in 54% of those with prolonged hospitalization. Correlation analyses between baseline CRP levels and hospitalization duration revealed no statistically significant associations. Spearman correlation coefficients were -0.09 ($p = 0.45$) for total hospitalization time, 0.02 ($p = 0.85$) for mean hospitalization time, and -0.04 ($p = 0.75$) for maximum hospitalization time. These findings indicate that baseline inflammatory activity was not associated with length of hospital stay in this cohort.

Creatinine and white blood cell (WBC) values showed no relevant differences between groups, with approximately three quarters of patients having normal creatinine levels (<1.2 mg/dL) and nearly 90% showing WBC counts below 10 G/L. There was no significant association between baseline renal function and hospitalization duration. Weak positive correlations were observed for mean (Spearman's $\rho = 0.21$, $p = 0.06$) and maximum duration ($\rho = 0.12$, $p = 0.29$), but these did not reach statistical significance. Overall, baseline creatinine levels did not predict the length of hospital stay in this cohort.

Male sex was slightly more frequent among patients with longer hospital stays (63% vs. 50%). A comparable proportion of patients had received at least one COVID-19 vaccination (64% in the ≤14-day group vs. 58% in the >14-day group). Chest CT scans compatible with COVID-19 findings were more often reported in patients with prolonged hospitalization (35%) than in those with a shorter stay (21%).

3.4. Symptom Prevalence and Duration

Table S1 summarizes the prevalence and duration of symptoms as documented by the treating physicians in the NAPKON RT cohort. The most frequently recorded symptoms were coughing and dyspnea, each observed in approximately half of the patients, whereas gastrointestinal symptoms such as nausea, vomiting, and diarrhea were less frequently documented. In many cases, information on symptom duration was incomplete or missing, reflecting heterogeneous documentation across sites. Among the available data, most symptoms resolved within two weeks, although a subset of patients—particularly those with coughing or dyspnea—showed prolonged or ongoing symptoms.

3.5. Radiologic Assessment

Findings from radiologic examinations are presented in Table S2. Chest imaging revealed COVID-typical findings in 18% of X-rays (1.1% very typical, 17% compatible) and in 27% of CT scans (7.8% very typical, 19% compatible). Imaging data were missing in 77% of X-rays and 66% of CT scans.

A chest X-ray was available for 53% of patients, whereas 54% underwent chest CT imaging. Pathological findings were documented in 40% of X-rays and 48% of CT scans. COVID-19–typical imaging patterns were identified in 18% of chest X-rays (very typical or compatible findings) and in 27% of CT scans, indicating a higher diagnostic yield of

CT imaging in this cohort. For a considerable proportion of patients, radiologic data were incomplete or unavailable, highlighting variability in imaging documentation between participating centers.

3.6. Anti-Infective and Immunomodulatory Therapy

Administration of anti-infective or immunomodulatory medication was documented in 76 of 90 patients (84.44%). The recorded substances encompassed a broad range of antibacterial, antiviral, antifungal, antiparasitic, and immunomodulatory agents. Frequently administered drugs included beta-lactam antibiotics such as amoxicillin, ceftriaxone, cefuroxime, and piperacillin/tazobactam, macrolides such as azithromycin and clarithromycin, and corticosteroids including dexamethasone, prednisolone, and methylprednisolone. In several cases, antiviral agents such as aciclovir, ganciclovir, valaciclovir, and emtricitabine/tenofovir/bictegravir, antifungal drugs such as amphotericin B, caspofungin, voriconazole, and isavuconazole, and immunosuppressive or immunomodulatory medications such as tacrolimus, mycophenolate mofetil, everolimus, tocilizumab, pembrolizumab, and baricitinib were also recorded. This heterogeneity reflects the complexity of clinical management during the pandemic, where overlapping infectious, inflammatory, and oncologic conditions frequently necessitated broad anti-infective or immunomodulatory coverage.

4. Discussion

Before this study, there was little systematically collected evidence on the real-world characteristics of patients with documented RT and SARS-CoV-2 infection, and the broader context of RT care during the COVID-19 pandemic in Germany.

While several international centers published rapid-response recommendations and small institutional reports, standardized, multi-center analyses were lacking, particularly for patients with hematologic and solid malignancies treated during the pandemic period.

This study therefore aimed to provide a comprehensive overview of RT patterns, treatment adaptations, and patient outcomes during the COVID-19 era based on data from the German NAPKON cohort, which allows standardized and cross-institutional data collection.

An important finding of the present analysis is that RT was not a concomitant treatment factor in most evaluable cases. Nearly four fifths of patients with available timing data had received RT before SARS-CoV-2 infection, whereas only 4.4% underwent RT during infection. Therefore, this cohort should primarily be interpreted as a population of patients with a history of RT and COVID-19, rather than as a cohort of patients actively receiving RT during acute infection. An important methodological consideration of the present analysis is the absence of a control group. As a result, the observed clinical characteristics and outcomes cannot be attributed to RT itself. Rather, the findings describe the clinical profile of patients with documented radiotherapy and SARS-CoV-2 infection within the NAPKON registry. The predominance of mild or moderate COVID-19 courses and the vaccination distribution in this cohort may also reflect the broader epidemiological context in Germany during the study period, including evolving vaccination coverage, improvements in clinical management, and changes in circulating viral variants.

In summary, the analysis revealed a broad heterogeneity of tumor entities and treatment intents, with a significant proportion of palliative RT cases. RT was delivered in all participating centers during the pandemic; however, the available NAPKON data do not permit conclusions on treatment continuity or nationwide utilization patterns. However, fractionation details were often unavailable, with only total dose consistently documented, which limits the ability to draw direct conclusions about changes in treatment schedules.

Nevertheless, shorter RT treatment durations in several cases suggest that hypofractionated radiotherapy (HFRT) was adopted during the pandemic period.

HFRT emerged as a key adaptive strategy to minimize patient visits and potential viral exposure while preserving oncologic efficacy. Antony, Dubey et al. reported excellent local control and response rates with HFRT in patients with hematologic malignancies treated during the pandemic. Using regimens equivalent to approximately 39 Gy in 13 fractions, the study achieved an overall response rate of 94% and a two-year freedom from local progression of 76%, with minimal toxicity [12]. These findings support the safety and effectiveness of shorter, high-dose-per-fraction regimens in both consolidative and definitive settings.

Similarly, Detti, Ingrosso et al. highlighted hypofractionation as an essential part of adaptive prostate cancer management during COVID-19, recommending ultra-hypofractionated schedules for unfavorable-risk patients and moderate hypofractionation for high-risk disease [13]. Their work underscores how fractionation adaptation can reconcile infection control with oncologic quality of care.

The shorter treatment durations observed in our study are consistent with these international findings and likely reflect similar pragmatic adaptations in German centers, even in the absence of national harmonized guidelines. Although detailed fractionation data were missing, the trend toward abbreviated treatment courses supports the notion that HFRT became a preferred option where clinically feasible.

Vordermark (2020) further described a temporary paradigm shift favoring RT—often in hypofractionated form—over surgical approaches for several tumor entities (e.g., head and neck, gynecologic, or esophageal cancer), given the high infection risk associated with surgical procedures [14]. Collectively, these findings emphasize the adaptability and resilience of radiation oncology in maintaining effective treatment pathways during a public health crisis.

Maintaining treatment continuity under pandemic conditions was a critical challenge worldwide. Yu, Hu et al. analyzed patients in Wuhan whose RT was interrupted for more than 45 days and demonstrated that such unplanned breaks were associated with worse outcomes, especially in advanced-stage disease [15]. This underscores the oncologic importance of uninterrupted treatment delivery even amid external disruptions.

Conversely, Wei, Zheng et al. presented an exemplary infection-control strategy from Hubei Cancer Hospital, where strict zoning, patient triage, and disinfection measures enabled uninterrupted RT operations through the peak of the outbreak—without any reported in-hospital infections among patients or staff [16].

The findings from our study mirror these observations: despite significant strain on the healthcare system, RT departments in Germany were able to continue operating, with only limited delays or cancellations. This demonstrates that, through structured triage, protective equipment, and workflow adaptation, safe and continuous RT was feasible even during the height of the pandemic.

Hospitalization risk and treatment delay were strongly influenced by both oncologic and infection-related factors during COVID-19. Several recent studies help contextualize our findings. Zhang, Mi et al. and Garbin, Leite et al. identified older age, comorbidities, obesity, and chronic respiratory disease as predictors of prolonged hospitalization [17,18], while Lucijanić, Marelić et al. confirmed these factors in a large tertiary cohort, adding poor functional status and complications such as bacterial sepsis as independent predictors [19]. Similarly, Vahey, McDonald et al. found that age $\geq$ 65, male sex, hypertension, metabolic syndrome, and obesity were all significantly associated with hospital admission [20]. In our dataset, 76 out of 90 patients (84.44%) received anti-infective or immunomodulatory therapy. These treatments included a wide range of antibiotic, antiviral, antifungal, antipar-

asitic, and immunomodulatory agents, including beta-lactams, macrolides, antifungals and immunosuppressants.

The frequent use of corticosteroids and broad-spectrum antibiotics reflects the complex clinical status of many cancer patients during the pandemic, in whom differentiation between tumor-related, infectious, or treatment-related symptoms was often challenging.

This observation aligns with findings from Friedrichs, Wenz et al., who demonstrated that empirical antibiotic therapy in moderate COVID-19 was not associated with clinical benefit and, in fact, correlated with higher rates of deterioration after two weeks [21]. The broad use of anti-infective agents in our cohort therefore likely represents cautious overtreatment during a phase of diagnostic uncertainty, underscoring the need for more tailored infection management strategies in patients treated with RT.

Furthermore, Epsi, Powers et al. showed that patients with respiratory/systemic symptom clusters had higher hospitalization rates and stronger inflammatory responses (elevated CRP and IL-6) [22], which may also explain the frequent administration of corticosteroids and immunomodulators in our population. Taken together, these findings highlight the delicate balance between infection control and the risk of overtreatment in immunocompromised cancer patients during the pandemic. A major strength of this work is that it constitutes the first systematic German analysis RT documentation in patients with SARS-CoV-2 infection during the COVID-19 pandemic.

Utilizing the standardized framework of the NAPKON study ensured high data quality and comparability across multiple centers. The dataset includes a comprehensive set of clinical, demographic, therapeutic, and infection-related parameters, enabling a multifactorial analysis of RT delivery during a national health crisis.

The study also captures a broad spectrum of tumor entities and treatment intents, providing a multicentric overview of real-world RT practice. The finding that most departments maintained treatment continuity despite the pandemic demonstrates the adaptability and operational resilience of German RT centers. Furthermore, the integration of radiotherapeutic, infectious, and pharmacologic data allows for an interdisciplinary understanding of crisis management, offering valuable insights for future preparedness planning.

Nevertheless, the study has several limitations. Documentation of RT parameters was incomplete in many cases; specifically, details on fractionation (dose per fraction, number of fractions) were missing, limiting the ability to quantify hypofractionation. Only total prescribed doses were consistently recorded.

The cohort was heterogeneous in terms of tumor sites, stages, and treatment intents, and in many cases, the irradiated organ or target volume was not specified. The relatively small sample size restricted the ability to perform robust subgroup or multivariate analyses.

Furthermore, the absence of a non-irradiated control cohort prevents assessment of whether the observed clinical outcomes differ from those of other COVID-19 patient populations.

Another important limitation is the relatively high proportion of missing data for several variables. This reflects the multicenter registry design of the NAPKON cohort, in which documentation completeness varied between study sites and clinical modules during the pandemic period. Consequently, certain variables—such as tumor localization, procalcitonin levels, and specific comorbidities—were unavailable in a substantial proportion of patients. To ensure transparency, missing values were explicitly reported, and percentages were calculated relative to the total study population. Nevertheless, these findings should be interpreted cautiously and primarily as descriptive observations rather than precise estimates.

Additionally, data collection was partly retrospective and conducted under pandemic conditions, raising the possibility of incomplete or inconsistent documentation. Missing information on treatment-related toxicity and patient-reported outcomes further limits the

comprehensive assessment of treatment quality. Fractionation details (dose per fraction, number of fractions) were missing in the majority of cases, which limits interpretation of hypofractionation trends.

Despite these limitations, the present analysis provides valuable initial insight into the real-world situation of RT during the COVID-19 pandemic in Germany. It establishes an important foundation for future prospective studies that can incorporate more detailed RT parameters, toxicity data, and outcome measures.

Future research should focus on prospective and standardized documentation of RT parameters, including fractionation details, total dose, and target volume, to allow robust evaluation of adaptive treatment strategies such as hypofractionation. Integration of patient-reported outcomes, infection-control data, and medication profiles will be essential to assess both oncologic efficacy and patient safety comprehensively.

Building upon the NAPKON infrastructure, national registries could facilitate continuous monitoring of RT practice in future public health emergencies. Such data-driven approaches will enhance evidence-based preparedness and ensure that essential oncologic care remains accessible, safe, and effective—even under extraordinary circumstances.

5. Conclusions

In this registry-based cohort, patients with documented RT and SARS-CoV-2 infection predominantly experienced mild or moderate COVID-19 courses and showed substantial vaccination uptake. However, because this analysis was descriptive and lacked a control group, no conclusions can be drawn regarding the effect of radiotherapy on COVID-19 severity. The data reflect a heterogeneous, mainly elderly and moderately frail patient population with a wide range of tumor entities and treatment histories. Most infections were associated with mild or moderate disease courses, and only a small proportion of patients experienced severe or critical phases. Importantly, most evaluable patients had received RT before infection, while only a small minority underwent RT during SARS-CoV-2 infection. Accordingly, this cohort mainly reflects patients with a history of RT rather than concomitant RT during acute COVID-19.

The majority of patients had received at least one COVID-19 vaccination, most commonly with Comirnaty (BioNTech/Pfizer). Nevertheless, COVID-19-typical findings were documented radiologically in approximately one quarter of CT scans, underlining the relevance of imaging diagnostics in this vulnerable group.

Due to the small sample size and the descriptive nature of the analysis, no inferential conclusions can be drawn regarding the relationship between clinical characteristics and outcomes. However, the results illustrate the feasibility and value of systematic data collection within the NAPKON framework and highlight the importance of continued documentation and analysis of oncologic patient subgroups to better understand the impact of SARS-CoV-2 infection and vaccination in individuals treated with RT.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/radiation6020013/s1, Table S1: Symptom prevalence and duration distribution in the NAPKON Radiotherapy cohort; Table S2: Radiologic assessment (X-ray and CT findings).

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Informed Consent Statement: Patient consent was waived due to the use of pseudonymized registry data collected within the framework of the German National Pandemic Cohort Network (NAPKON). The study involved no direct patient contact and no identifiable personal data.

Data Availability Statement: The data presented in this study are available upon reasonable request through the official Use & Access procedure of the German National Pandemic Cohort Network (NAPKON). Due to data protection regulations and ethical restrictions, the data are not publicly available. Researchers may apply for data access via the NAPKON Use & Access Committee.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

CI	Confidence interval
COVID-19	Coronavirus disease 2019
CRP	C-reactive protein
CFS	Clinical Frailty Scale
CT	Computed tomography
ECOG	Eastern Cooperative Oncology Group
Gy	Gray
HFRT	Hypofractionated radiotherapy
HR	Hazard ratio
IQR	Interquartile range
NAPKON	National Pandemic Cohort Network
NUM	Network University Medicine
OR	Odds ratio
PCT	Procalcitonin
RT	Radiotherapy
SUEP	Cross-Sectoral Platform (Strukturierte Übergreifende COVID-19-Erkrankten-Plattform)
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WBC	White blood cell count

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