

## Scientific Article

# Radiation Therapy Delivery Challenges in Older Patients During Coronavirus Disease 2019 Pandemic



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## Abstract

**Purpose:** The management of older patients in radiation therapy (RT) departments has been challenging in the context of the Coronavirus Disease 2019 (COVID-19) outbreak. We report our experience of RT adapted schedules or strategy changes in older patients during the COVID-19 pandemic.

**Methods and Materials:** Patients aged  $\geq 75$  years were recruited during weekly chart rounds. All were potentially eligible for a specific intervention to reduce the frequency of patients' visits to the hospital. The effect of deferring radiation and hypofractionation of RT schedules was assessed in terms of the number of courses initially planned and replanned during the lockdown.

**Results:** Twenty patients were identified during the official lockdown in France (March 17 to May 11). Median age was 78 years (75-95 years). Most patients were male ( $n = 12$ , 60%) being treated in the postoperative setting ( $n = 17$ , 85%). RT was delayed in 11 cases (55%) with hormonal therapy prescribed in 10 cases (50%). Altered RT fractionation was proposed for 5 cases (25%); combinations of altered fractionation and deferral of radiation were applied in 3 cases (15%). The number of radiation courses initially planned and replanned according to the pandemic context: 563 and 197, respectively ( $-62\%$ ;  $P < .001$ ). None presented recurrence when RT was initiated, and no patient developed symptomatic COVID-19 infection.

**Conclusions:** In the context of the COVID-19 outbreak, individual risk-based radiation therapy seems to be safe. Systematic screening of patients for COVID-19 before starting radiation therapy is mandatory. In our department the oncogeriatrics expertise availability for daily practice was of great use during the pandemic. Other prospective studies are needed to validate such strategies in case of resurgence of similar outbreaks.

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## Introduction

The world has faced an unprecedented global health crisis triggered by the Coronavirus Disease 2019 (COVID-19) pandemic. The first cases of human infection

from COVID-19 were reported from Wuhan, China, in December 2019. Since then, the virus rapidly spread throughout the entire world, especially in Europe, which became the most affected continent within a few weeks. COVID-19 is associated with high contagiousness related to respiratory droplets that can persist on all surfaces for 3 hours and up to days.<sup>1</sup> Early data from China suggest that older patients<sup>2</sup> and patients with cancer<sup>3</sup> are disproportionately affected by COVID-19, from severe illness and hospitalization to an increased rate of mortality. As acknowledged by various health authorities, the optimal management of these patients was particularly challenging during the early stages of the outbreak. In addition, general guidelines were released by the High Council for Public Health for the general population.<sup>4</sup> More specifically for older patients, geriatric societies emphasized the need to follow and to reinforce these guidelines for older patients. Thus, the publication of national<sup>5</sup> and international guidelines for patients' care from the International Geriatric Radiotherapy Group<sup>6</sup> and the International Society of Geriatric Oncology<sup>7</sup> was of great help in decision-making. However, while some were published late, after the extent of the pandemic in many countries, their application in radiation therapy (RT) departments reduced the risk of contamination and allowed a better patient selection for therapy.

The aim of this study was to assess the ratio of therapeutic effectiveness of radiation and risk of infectious contamination for older patients. However, feedback and sharing of experience for older patients during the pandemic in RT departments is lacking. Here, we report our experience with older patients referred to our department during the lockdown. We will describe a personalized care plan<sup>8</sup> following the guidelines from the international early recommendations for departments organization and cancer management during COVID-19 pandemic<sup>9</sup> in the context of the outbreak, taking into account various aspects of geriatric frailty.

## Patients and Methods

### Department organization and preventive actions

In the early weeks of the COVID-19 outbreak, a general overhaul of our radiation oncology department was implemented during the lockdown to protect our patients and our staff. Regarding the safety recommendations for the medical staff (physicians, physicists, and therapists), there was implementation of information sessions, individual preventive actions (hand washing, wearing of masks), collective preventive actions (social distancing, staff turnover), and psychological assistance. Apart from reassessing indications for radiation and postponing whenever possible, strong protective measures were applied for patients: reduced number of visits to the

clinic (hypofractionation, telemedicine), individual preventive actions (hand washing, wearing of masks), and collective preventive actions: social distancing, screening by front desk staff upon check-in, sanitization (waiting room, devices, treatment couch), and individual transportation. The organizational procedures implemented in the early stages of the COVID-19 pandemic in our department were previously reported.<sup>8</sup>

In older patients, the decision to defer radiation therapy or the use of hypofractionation schedules was taken in weekly chart rounds in presence of a radiation oncologist specialized in geriatrics considering comorbidities and frailty of the individual.

### Patient characteristics

Twenty patients were identified during the official lockdown in France from our weekly chart rounds. All patients were potentially eligible for a specific intervention (deferral of radiation or modification of fractionation) that allowed reduction in the number of visits and potential exposure to COVID-19 during the lockdown. Age, sex, and the Rockwood Clinical Frailty score were assessed prospectively in all patients.

### Analyses

The effect of deferring radiation and hypofractionation was assessed in terms of number of courses initially planned and replanned during the lockdown. Pairwise comparisons between the number of radiation courses initially planned from March 17 to May 11 and replanned according to the COVID-19 outbreak were performed using 2-tailed paired Student's *t* test. Statistical analyses were performed using the R software, version 3.5.1 (R project, Vienna, Austria).

## Results

### Patients and comorbidities

The median age of the cohort was 78 (75-95) years. The majority were men ( $n = 12$ , 60%) and were treated in the postoperative setting ( $n = 17$ , 85%). Only 3 patients were free of comorbidity. Thirteen (65%) patients had at least 1 cardiovascular risk factor. Seven patients (35%) had no frailties, and 7 (35%), 4 (20%), and 2 (10%) patients were considered fragile due to their poly-medication or autonomy loss and hearing impairment, respectively (Tables 1 and 2). The Rockwood score was  $\geq 4$  in 14 patients (70%; vulnerable to moderately frail), and 6 patients (30%) were fit (Table 1). All were treated as outpatients.

**Table 1** Patients' management according to comorbidities and frailties

Patient	Medical background	Frailties	Rockwood Clinical Frailty score	Patient management	Type of cancer
1	Diabetes, narrow lumbar canal	Autonomy loss/gait disturbance	6	Delayed RT + HT	Prostate
2	High blood pressure	None	3	Delayed RT + HT	Prostate
3	Arteritis of the lower limbs, hypothyroidism, atrial fibrillation, Crohn disease	Polymedication	4	Delayed RT + HT	Prostate
4	Aortic dissection, high blood pressure	Social isolation, autonomy loss (gait disturbance, balance disturbance)	6	Delayed RT	Cutaneous
5	Osteoporosis, myocardial infarction	Polymedication, social isolation	6	Delayed RT + hypofractionation	Breast
6	None	None	2	Delayed RT + HT	Prostate
7	Endometriosis, Parkinson	Autonomy loss (gait disturbance, repeated falls)	6	Hypofractionation	Breast
8	None	None	2	Hypofractionation	Breast
9	High blood pressure, dyslipidemia	None	2	Hypofractionation	Breast
10	Cataract	None	2	Hypofractionation	Breast
11	Stroke, Dupuytren disease	None	3	Hypofractionation	Sarcoma
12	High blood pressure, myocardial infarction, diabetes	Polymedication	4	Hypofractionation	Cutaneous
13	Asthma	None	3	Hypofractionation	Breast
14	Atrial fibrillation, stroke, knee prosthesis, inguinal hernia	Polymedication, autonomy loss (gait disturbance)	6	Delayed RT + HT	Prostate
15	Colon cancer, kidney cancer	Hearing impairment	5	Hypofractionation	Breast
16	High blood pressure, diabetes, tympanoplasty	Hearing impairment	4	Delayed RT + HT	Prostate
17	Sleep apnea, myocardial infarction, lung cancer, high blood pressure, dyslipidemia	Polymedication	4	Delayed RT + HT	Prostate
18	None	None	2	Delayed RT + HT	Prostate
19	High blood pressure, atrial fibrillation, kidney transplant, hemoptysis, diverticulitis	Polymedication	4	Hypofractionation	Cutaneous
20	High blood pressure, myocardial infarction, arteritis of the lower limbs, diabetes, sleep apnea, hypothyroidism	Polymedication	4	Delayed RT + HT	Prostate

Abbreviations: HT = hormonal therapy; RT = radiation therapy.

**Primary tumors**

Primary disease was prostate (n = 9, 45%), breast (n = 7, 35%), cutaneous squamous cell carcinoma (n = 3, 15%), and sarcoma (n = 1, 5%).

**Radiation therapy**

Radiation therapy was deferred in 11 cases (55%). During this delay, primary hormonal therapy was prescribed as a “waiting therapy” in 10 cases (9 prostate cancer, 1

breast cancer) and the remaining case was an adjuvant radiation delivered after completely resected cutaneous squamous cell carcinoma. Among those 11 patients, 9 had a severe comorbidity or a high frailty score and 10 were later treated with usual fractionation schemes (Table 1).

Among the 11 patients who had a delayed treatment, 8 had a Rockwood index ≥4 and corresponded to a frail or vulnerable profile. Ten patients who had a delay in their radiation treatment received conventional fractionation. That is related to the fact they were related to prostate cancer treated in the postoperative setting where conventional fractionation is mostly used.

**Table 2** Measures proposed to overcome challenges related to the comorbidities and frailty

Aim	Older challenging specificity	Practical recommendation
Lower risk of infection and ensure tumor control	Undertreatment versus overexposure to infection	Multidisciplinary tumor board case-by-case discussion involving radiation oncologist specialized in geriatrics <sup>8</sup>
Safe treatment conditions	Higher risk of contamination in the clinic	Reduce the number of visits to RT department using altered fractionation: for breast, <sup>9,10</sup> prostate, <sup>11</sup> and skin <sup>12,13</sup> cancers; delaying RT for hormone sensitive cancers (breast) and prostate cancers Personalized treatment plan and schedules <sup>14</sup> Masks and social distancing in waiting rooms <sup>14</sup> Telemedicine for long-term follow up patients <sup>14</sup> Care takers safety (staff rotation, masks)
Adapted care	Reduced mobility	Adapted (simplified) treatment technique

Abbreviation: RT = radiation therapy.

None of the patients presented any locoregional or distant recurrence when delayed RT was initiated. One patient (patient number 5) was treated with hypofractionation to minimize the risk of infection, considering her comorbidities and her frailty. Nine (45%) patients were treated during the outbreak using hypofractionated schedules (Fig. 1). Nine patients with high-risk breast cancer, 1 case of sarcoma, and 2 high-risk cutaneous carcinomas were identified. No patients developed COVID-19 symptoms with a median follow-up of 89 days. The number of radiation courses initially planned and replanned according to the pandemic context was significantly different: 563 and 197, respectively ( $-62%$ ;  $P < .001$ ; Fig. 2).

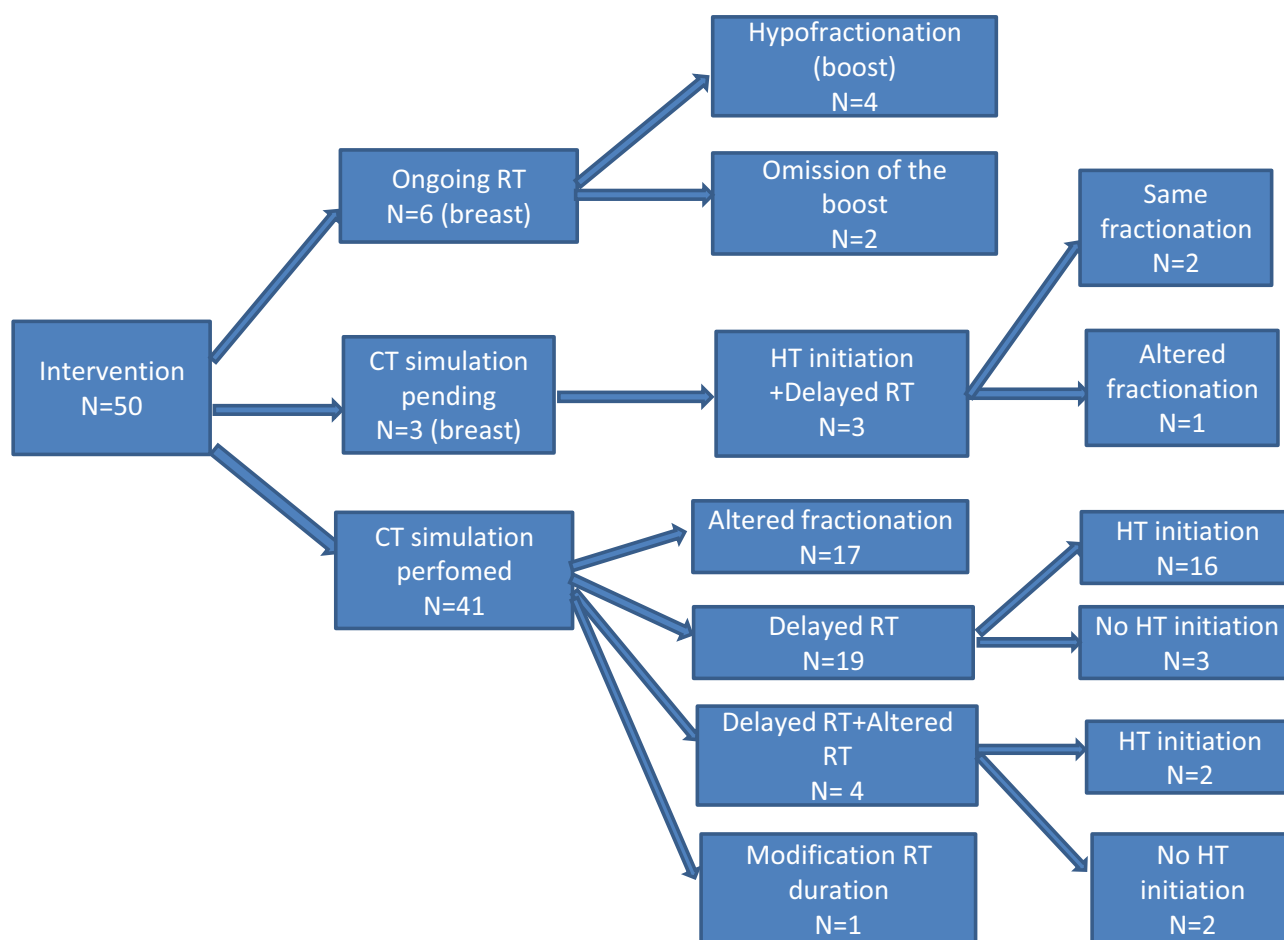
## Discussion

The explosion of new cases of COVID-19 within a few weeks after the first reported case was unexpected. In this context, a complete overhaul of the radiation oncology department was required to protect patients and staff while ensuring the continuity of patient care. Preliminary data showed that patients treated with radiation were at high risk of contracting the virus and were more likely to develop a severe form of the illness due to their underlying immunosuppression related to the cancer and various anticancer drugs.<sup>3</sup> According to general radiation guidelines for older patients,<sup>6,7,14</sup> physicians had to take pragmatic actions to mitigate the negative effects of the COVID-19 pandemic in a vulnerable population while ensuring tumor control.<sup>7</sup> Most focused on systemic therapies and selected oncology guidelines, especially from the international early recommendations for departments organization and cancer management during COVID-19 pandemic<sup>9</sup> that served as a framework for the drafting of a protocol for each tumor location in our department.

As radiation oncologists, we had to face several challenges in the management of older patients. The main one was related to the risk of undertreatment of the primary tumor versus the risk of infection. A mass screening program would have allowed identification and confinement of nonsymptomatic COVID-19 infected patients. Atypical inaugural symptoms, including fatigue, loss of autonomy, falls, mental confusion, and diarrhea, may be associated with respiratory symptoms. There is a necessity to allocate specific slots for consultation, simulation computerized tomography, and radiation courses for vulnerable patients, which requires additional human and material resources. Implementation of protective measures from caretakers and telemedicine practice and other social distancing measures may increase the feeling of abandonment, isolation, and incurability.<sup>6,14</sup> In addition, in our department a specific workflow dedicated to older oncologic patients involving a radiation oncologist with oncogeriatric expertise has been implemented prior the pandemic with time slots and a dedicated visits area. This organization was particularly useful in the context of pandemic.

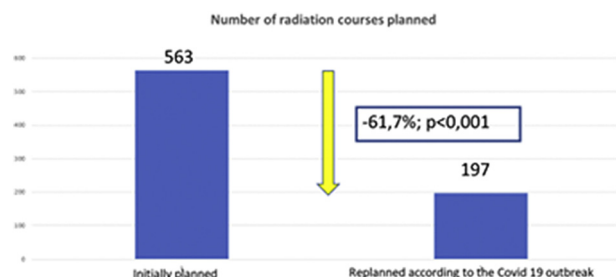
Identification of specific problems related to older patients was the first step of our treatment approach. The next step was to propose a treatment plan based on evidence-based medicine. In terms of radiation therapy planning, radiation dose, fractionation and techniques had to be optimized and adapted to the emergency context. As recommended by the Society of Geriatric Oncology<sup>7</sup> and others,<sup>9</sup> hypofractionated regimens or shorter schedules might be preferable, avoiding a boost in low risk breast cancer, for example.<sup>10</sup> To the best of our knowledge, to date there is no study that has focused on the efficiency of measures taken specifically with radiation therapy for older patients.

Our data show that the application of existent cancer and radiation guidelines can be applicable to older



**Figure 1** Intervention proposed depending on the step of the radiation therapy process. Abbreviations: HT = hormonal therapy; RT = radiation therapy.

patients by considering some specificities related to age and individual vulnerability. Sixty percent of our cohort was represented by vulnerable patients with a median age of 78 years. The weekly chart rounds involving a radiation oncologist and physicians specialized in geriatrics allowed us to select patients who were considered eligible for a specific intervention in the treatment schedule by considering their frailties.



**Figure 2** Impact of interventions (delayed treatment, hypofractionation) in terms of number of radiation courses.

Treatments were delayed in some patients with low-risk profile of cancers. The rationale of delaying therapy was to reduce the risk of exposure to COVID-19 patients with low risk of cancer progression. Among those 11 patients who had a delayed treatment; 8 had a Rockwood index  $\geq 4$  and corresponded to a frail or vulnerable profile. The average length of delay was 2 months for breast cancer and 3 months for prostate cancer. Ten patients who had a delay in their radiation treatment received conventional fractionation. Those corresponded to cases of prostate cancer treated in the postoperative setting where conventional fractionation is mostly used. Patients with breast or prostate cancer were offered primary “waiting” hormonal therapy during the outbreak before undergoing radiation. Such an approach is well established in prostate cancer.<sup>11</sup>

Similarly, hypofractionated radiation consisting of reducing the number of radiation courses was mainly developed for older patients in many cancer types,<sup>12,13</sup> such as breast, prostate, or skin cancer, which represented 95% of our cohort. The modality was particularly adapted for older patients in the context of the pandemic.



Multidisciplinary treatment decision was based on international guidelines<sup>8,9</sup> and on individual comprehensive geriatric assessment during the oncogeriatric visit. We used prospectively a clinical frailty scale according to Rockwood index, which is a multidimensional approach. Unlike Fried Frailty index, the Rockwood scale considers the social, psychological, mood, life expectancy, polymedication, functional dependency for activities of daily living, and instrumental activities of daily living.

Although the decision making for patient management was based on a combination of factors, the Rockwood index was one of the most influential parameter. Patients who had a Rockwood score <4 typically received upfront radiation, whereas patients who had  $\geq 4$  had a delayed treatment. The rationale of delaying therapy was to reduce the risk of exposure to COVID-19 patients with low risk of cancer progression.

Our strategy allowed our patients aged >75 years to be spared from COVID-19 infection, but oncology outcomes of our cohort is yet to be reported. Because the vast majority of institutions do not have radiation oncologist specialized in oncogeriatrics. A multi-institutional study was not feasible.

## Conclusions

The optimal management of older patients is often challenging in radiation oncology and requires geriatrics expertise. In our department, a specific workflow dedicated to older patients involving one radiation oncologist with oncogeriatrics expertise is used in daily practice. This has been proven particularly useful during the pandemic as the COVID-19 outbreak can make the treatment decision even more complicated. A thorough individual assessment was performed for all patients  $\geq 75$  considering the risk of infection and the poorer outcomes in this population.

Based on the published guidelines and our weekly chart rounds that involved a physician specialized in geriatrics, we were able to propose individual risk-based treatments to all our older patients. Prospective studies are needed to validate such strategies in case of a resurgence of future similar outbreaks.

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## References

1. Li Q, Guan X, Wu P, et al. Early Transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.* 2020;10:1056.
2. Liu K, Chen Y, Lin R, et al. Clinical feature of COVID-19 in elderly patients: A comparison with young and middle-age patients. *J Infect.* 2020;80:e14-e18.
3. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. *Lancet Oncol.* 2020;21:335-337.
4. You B, Ravaud A, Canivet A, et al. The official French guidelines to protect patients with cancer against SARS-CoV-2 infection. *Lancet Oncol.* 2020;21:619-621.
5. Falandry C, Filteau C, Ravot C. Challenges with the management of older patients with cancer during the COVID-19 pandemic. *J Geriatr Oncol.* 2020;11:747-749.
6. Nguyen NP, Vinh-Hung V, Baumert B, et al. Older cancer patients during the COVID-19 epidemic: Practice proposal of the International Geriatric Radiotherapy Group. *Cancers (Basel).* 2020;12:1287.
7. Battisti LNM, Mislav AR, Cooper L, et al. Adapting care for older cancer patients during the COVID-19 pandemic: Recommendations from the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group. *J Geriatr Oncol.* 2020;11:1190-1198.
8. Belkacemi Y, Loganadane G, Grellier N, et al. Radiation therapy department reorganization during the Coronavirus Disease 2019 (COVID-19) outbreak: Keys to securing staff and patients during the first weeks of the crisis and impact on radiation therapy practice from a single institution experience. *Adv Radiat Oncol.* 2020;5:644-650.
9. Belkacemi Y, Grellier N, Ghith S, et al. A review of the international early recommendations for departments organization and cancer management priorities during the global COVID-19 pandemic: Applicability in low- and middle-income countries. *Eur J Cancer.* 2020;135:130-146.
10. Coles CE, Aristei C, Bliss J, et al. International guidelines on radiation therapy for breast cancer during the COVID-19 pandemic. *Clin Oncol.* 2020;32:279-281.
11. Pinninti R. Management of geriatric cancer patients during the COVID-19 pandemic. *Cancer Res Stat Treat.* 2020;3:S71-S75.
12. Zaorsky NG, Yu JB, McBride SM, et al. Prostate cancer radiotherapy recommendations in response to COVID-19. *Adv Radiat Oncol.* 2020;5:659-665.
13. Simcock R, Thomas TV, Mercy CE, et al. COVID-19 global radiation oncology's targeted response for pandemic preparedness. *Clin Trans Radiat Oncol.* 2020;22:55-68.
14. Frederick JT, Steinman LE, Prohask T, et al. Community-based treatment of late life depression an expert panel-informed literature review. *Am J Prev Med.* 2007;33:222-249.