



# Radiotherapy during the COVID-19: a review about management and treatment strategies

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## ABSTRACT

**Background:** The administration of radiotherapy should be encouraged despite the emergency of COVID-19; therefore, our aim is to analyze management and therapeutic interventions to be implemented in a Radiotherapy department to allow patients to continue their treatment and health professionals to continue their work safely.

**Materials and methods:** A Pubmed search was performed, in which all articles specific to Radiotherapy and COVID-19 were included. Those articles that were too specific about the COVID-19, surgery and chemotherapy, were excluded.

**Results:** 315 articles were selected, of which 35 were about therapeutic strategies and 25 about management strategies. In the first category, 5 articles were about how radiotherapy could be a weapon to be used for COVID-19 positive patients with important lung problems. While 30 articles described priorities and new treatment plans for oncology patients who have to undergo radiotherapy during the pandemic. In the second category, almost all the articles explained how triage can be a preventive and monitoring way against COVID-19 in an operating unit with many patients and professionals, and other articles developed a telemedicine system, too, which allows patients to make scheduled visits without coming to the hospital and also for the staff, who can work remotely. In addition, 5 articles concerning psychological aspects of both patients and health care providers were included.

**Conclusion:** This document can be used as a summary in the coming months/years, during the recovery phase from COVID-19 pandemic outbreak and as a starting point to be used in case of further pandemic break-out.

**Key words:** radiotherapy; COVID-19; management

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## Introduction

The spread of COVID-19 began in China in 2019 and has had a devastating impact on public health,

delineating a rift in social, health, and economic certainties in the 21st century. Worldwide, there have been 5,200,000 victims of COVID-19 since the beginning of the pandemic by Dec. 1<sup>th</sup> 2021.

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COVID-19 can cause mild, but also severe respiratory complications, requiring hospitalization and intensive care [1].

Coronavirus is one of the greatest challenges of our times, one that all countries of the world are facing. In response to this emergency, all hospitals have been forced to reorganize their workflow, looking for new measures to be taken against the pandemic. Cancer patients are particularly exposed to infections and their potential complications [2], so it can be life-threatening to delay or postpone oncological diagnostic and therapeutic protocols. Therefore, a wide debate about changes in procedures and workflow for cancer patients' management has arisen, which has led to the publication of a large number of papers on the issue. This review, following an accurate bibliographic search, summarizes the various management and therapeutic strategies adopted in radiation oncology departments worldwide.

## Materials and methods

### Inclusion criteria

This review includes all articles in which different radiation oncology departments reported therapeutic and management strategies implemented to cope with the COVID-19 emergency. Considering the particular subject, the systematic approach has been waived due to the lack of a clearly defined endpoint. The purpose of this review is, therefore, to determine the procedures, methods, and workflows adopted during the COVID-19 outbreak in radiotherapy departments worldwide.

### Types of comparators

The selected articles were compared by dividing them into two main categories: 1) therapeutic, and 2) management strategies.

The first group concerns new protocols implemented according to the type and anatomical district in which tumors develop, evaluating the risks and benefits for each diagnosis, according to the possibility to stop or delay the treatment due to COVID-19 diagnosis or quarantine management. The main goal of these works was to allow patients to continue treatment in the shortest possible time, thus reducing the time of exposure to the risk of COVID-19 infection. A subgroup of these papers attempts to propose radiotherapy as a direct weapon

for treating COVID-19 positive patients with major lung problems.

The second group contains management strategies, that is papers that explain different protocols that allow patients to receive radiation therapy safely, as well as to prevent and reduce the risk of exposure for health professionals.

Additionally, further analysis examines the significant impact on psychological well-being that the pandemic has generated on patients and health care professionals.

### Exclusion criteria

Those articles that were too specific about the COVID-19, surgery and chemotherapy, merely mentioning radiotherapy, were excluded.

### Search strategy

An online literature search in the Pubmed database was conducted in February 2021. The key words for conducting this analysis were: "Radiotherapy" and "COVID-19". In Figure 1 the histogram of publications per month is reported.

### Data extraction

Once the Pubmed search was conducted, a number of articles was found, from which the abstracts were extracted. Using these, we could work out what to include (or not) in this review. Using Microsoft Excel, worksheets were created categorizing the various articles according to the selection criteria and the topic covered.

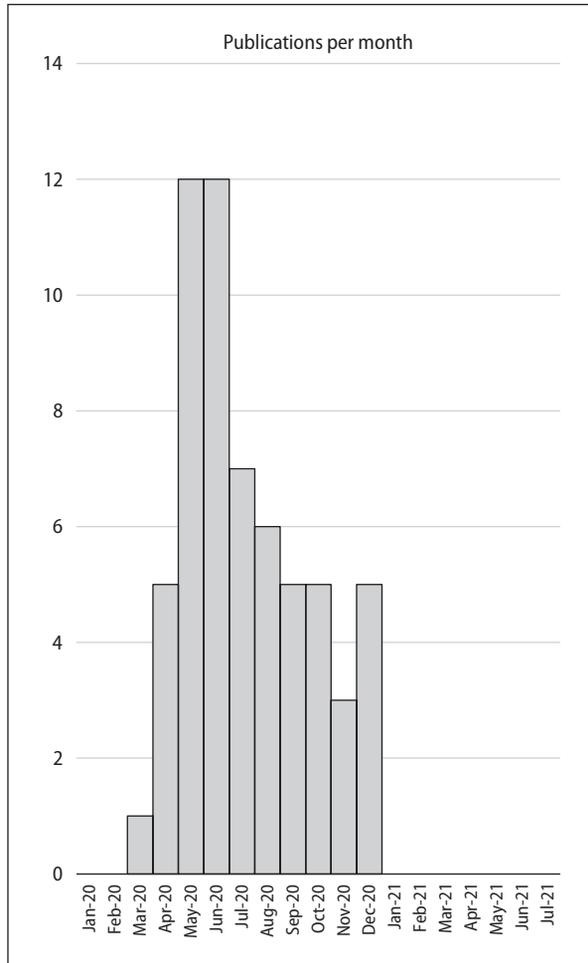
## Results

### Literature search

315 articles were found according to the search: we selected 35 articles concerning therapeutic strategies and 25 concerning management strategies in a radiotherapy department. 5 articles that explored how the pandemic has affected psychological aspects were included. 249 articles were excluded from the Review. In Figure 2 the summary of paper topics is reported.

### Characteristics

In the first category, 5 articles were about how radiotherapy could be a weapon used against COVID-19 in positive patients with important lung problems, while 34 articles described priorities and



**Figure 1.** Histogram of publications per month

new treatment plans for oncology patients who had to undergo radiotherapy during the pandemic, which are divided according to anatomical district:

- 3: breast;
- 5: gynecological;
- 8: head and neck;
- 5: lung;
- 3: prostate;
- 2: palliative;
- 1: pediatric patient;
- 3: brachytherapy.

In the second category, almost all the articles explained how triage can be a preventive and monitoring tool against COVID-19 in an operating unit with many patients and professionals. Other articles developed a telemedicine system, too, which allowed patients to have scheduled check-ups without attending the hospital in person.

Additional paragraphs discuss how patients in a radiotherapy department approached the risk of

contracting COVID-19 and how healthcare professionals responded to the critical issues and difficulties that arose during the pandemic.

### Reporting quality and bias

This review provides a framework, a synthesis of the evidence for specific intervention strategies, which is not intended to be static but rather evolving as the pandemic evolves, resources become available, and therapies or vaccines are developed for COVID-19. Data mining research was conducted in the absence of randomized clinical trials, consequently without study evaluation bias, a limitation imposed by the pandemic.

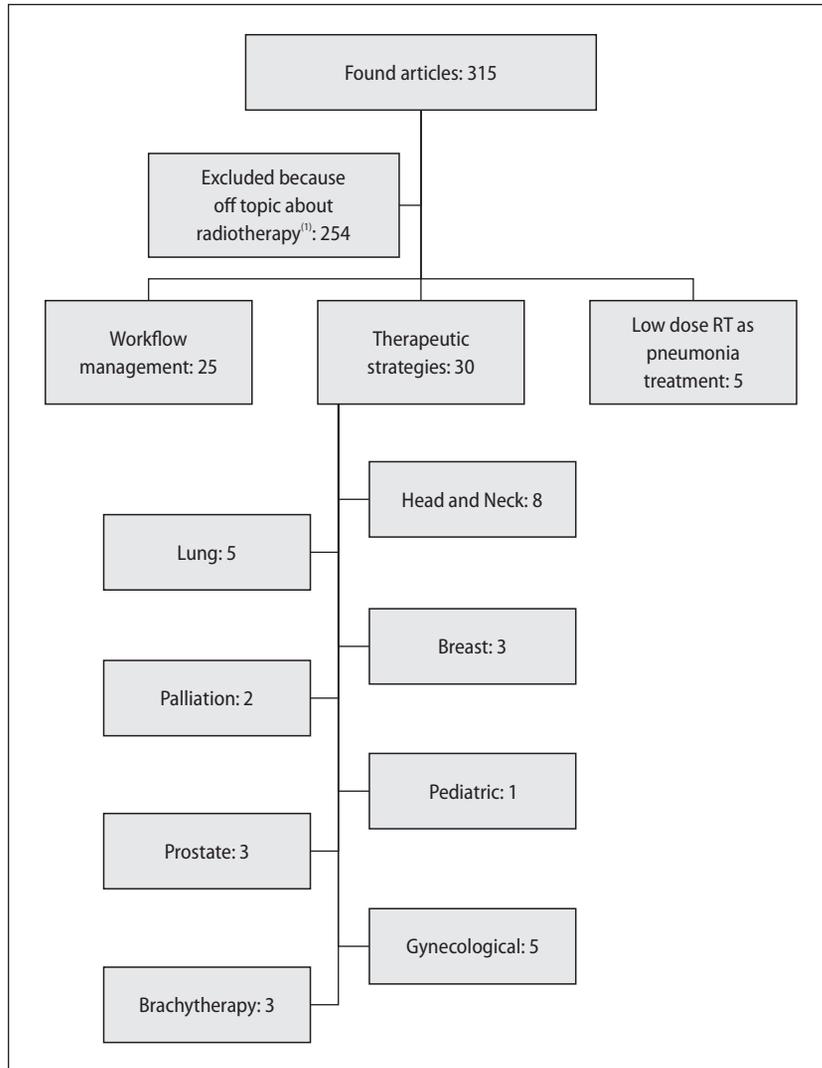
## Discussion

### Summary of main findings

Particular attention has been paid to safety procedures. Several centers have developed guidelines that include different protocols, ranging from accurate triage to identify positive or suspected cases, to limited access to the radiotherapy ward by caregivers, to measures of social distancing and sanitation. All professionals should be adequately trained and periodically updated on the clinical features of COVID-19, the risk of exposure, the correct use of personal protective equipment (PPE) and available prevention and protection procedures [3].

According to the risk of contamination, a division of the department was considered: clean areas where the risk is low (administrative offices, dosimetry) and areas where the risk is high (simulation, console, bunker). Each area increased environmental hygiene, ensuring good ventilation and defining new disinfection procedures. High-risk areas must be cleaned several times a day with a high percentage alcohol-based disinfectant; all systems and equipment must be sanitized at the end of each procedure (simulation or treatment) [4, 5].

Some centers developed two different entrances, one for patients and one for staff. Transfer staff between units should operate in an internal pathway and be kept to a minimum, so they avoid contact with patients or other colleagues. Access to the ward is only for patients; authorization for caregivers is permitted if strictly necessary [4]. In common areas, water and food dispensers have been removed and a distance of 2 meters must be maintained [6]. Protective screens have been placed



**Figure 2.** Summary of paper topics

where staff must communicate with patients verbally [7]. All people entering must be equipped with a surgical mask and disinfect their hands with a personal hydro-alcoholic gel or those installed in the department [6].

Some centers have required staff to perform telephone triage of patients before check-ups, asking if they have symptoms related to COVID-19, such as fever or cough, and if they have had contact with positive cases [8]. When the patient arrives at the Department, the temperature was to be measured and a continuous triage evaluation was required during the radiation treatment [9].

Some departments have planned alternating shifts for radiation oncologists and medical physicists; while for technicians, teams of at least two operators have been created, each one in a specific

bunker, without overlapping or exchanging groups [4]. All operators must always wear PPE, complete for the disinfection procedure: mask, goggles, gown and gloves [10]. Remote communication, by telephone or intranet, has been recommended for all professionals. Where the presence of several professionals is necessarily required, a distance of at least 1 meter must be respected [6]. If there is a suspected case of SARS-Cov-2, diagnosis of COVID-19 is mandatorily required.

Treatment purpose is taken into account and a balance is sought between the risk of tumor progression and the change in severe symptoms due to COVID-19 in case of positive patients [11]:

- palliative: performed in any case for a highly symptomatic patient with a life expectancy of more than 3–6 months and no other treatment options;

- curative: if the tumor is potentially curable and is growing rapidly [4].

Additionally, it is recommended to minimize the number of workers exposed, always choosing the same operating unit and Linac, and carrying out the radiotherapy in a specific time slot, preferably at the end of the day, in the case of positive patients, so that the cleaning staff can disinfect the bunker afterwards [9, 7].

The global response to this crisis began with the *#stayathome campaign*, to emphasize the importance of the first measure taken to mitigate the SARS-CoV-2 infection. Around the world, isolation has forced the implementation of telework, i.e. working remotely. It should be noted that the healthcare environment has never implemented any kind of smart working, so the daily work routine had to be revised. Indeed, staff have received training on remote access (with password security and verification from their cell phones) for all resources that are ordinarily used in the workplace [e.g., Treatment Planning System (TPS), Oncology Information System (OIS), Hospital Electronic Medical Record (EMR), Picture Archiving and Communication System (PACS)] [8], thus being able to perform contouring, research and daily meetings online and securely. Additionally, telephone consultations were carried out to reduce the number of on-site patient visits [5, 9].

### Psychological impact of COVID-19 in cancer patients

COVID-19 has had a significant impact on the daily lives of the whole population, but especially for cancer patients, both clinically and psychologically. When receiving the diagnosis of cancer, several psychological issues arise: fear of dying, uncertainty, loss of control, changes in interpersonal relationships and self-image. This burden is carried by patients throughout life-saving treatments [12]. Uncertainty for the future, for the progression of the disease and the outcome of treatments, was already present before COVID-19, but all this now collided with the pandemic and the restrictions to be followed to reduce the spread [13].

While cancer activates awareness and reflection, it also brings more fragility and attacks vitality, as well as creates pain. The pandemic worsens this scenario, amplifying the sense of unreality, denial,

disbelief, disorientation and anger [13]. Patients have experienced a tight emotional state between the need to undergo treatment and the fear of exposing themselves to the risk of infection in the hospital [12].

Additional states of mind emerged such as: catastrophizing (I could die), perceived responsibility (I could be infected and thus infect others), an increase in vulnerability (one is powerless), and attention to negative aspects (the data on mortality and COVID-19 infection). These thoughts were followed by certain behaviors: cognitive (one does not think about it), avoidance (one distracts oneself by doing various activities), relational (experiencing difficulty in expressing emotions) [13]. Physical contact, such as hugging, which until recently represented a resource and was an expression of closeness and care, now represents a danger and is denied.

### Cancer patients in radiotherapy and COVID-19

Radiation therapy technicians' (RTT) "touch" is mandatory to position the patient, and was always intended as protection and consolation; however, patients are now afraid and feel safer when RTT wears gloves [12]. Whatsapp groups, music during the delivery of therapy, or aesthetic changes such as decorating bunker walls can be solutions to help them both to confront emotions and how they are felt [12], to feel less alone and more emotionally close, despite the physical distance [1]. Structured screening questionnaires can detect the presence and severity of distress or anxiety and, if required, establish online psychological sessions [1, 12]. All these psychological approaches for patients are very important in mitigating the fear of contracting COVID-19, which could turn them away from their life-saving treatments [12].

### Psychological wellbeing in healthcare radiotherapy professionals during COVID-19 pandemic

Healthcare workers experienced unknown criticalities and were exposed to continuous distress as well as risk factors for their personal safety. Measures required have changed normal behaviors, making it difficult to find both physical and men-

tal recreational relief [14]. There are many professional experiences characterized by disorientation [15], high stress and burnout risk [13]: exposure to risk, initial difficulty in finding PPE, excessive workload, lack of rest, management of more complex patients; but also the concern for one's own health and for spreading the infection to one's family members, the lack of contact with family and friends, and the difficulty in sharing work-related emotions with them. Add to this the high level of responsibility, the burden of expectations, the fear of not doing enough and the anger towards the institution organization. Indeed, it is important to maintain an effective communication flow, with clear, timely, and regularly-updated information, in order to reduce the sense of isolation and to avoid losing a high level of group cohesion [14]. It is suggested that strategies be established to monitor personal well-being and address stress-management, intervening at the individual or group level, utilizing psychoeducational materials (provided on the work intranet or via webinars) [14], or telematic meetings.

Attention should be paid to the occurrence, duration, and persistence of certain psychophysical symptoms, such as [14]:

- persistent difficulty in relaxing or poor quality of sleep;
- decrease or increase in body weight;
- excessive fatigue, difficulty in recovery, reduced energy, occurrence of physical pain without an organic cause (somatization);
- excessive tension, hypervigilance, nervousness, irritability, aggression, negative thoughts and moods, feeling of inadequacy, apathy, estrangement, confusion.

Radiotherapy has resisted throughout the crisis period [16] and staff has been faced with an ambivalent aspect between the need to reassure patients and personal fear [15]. Studies suggest interventions aimed at gratification, which is useful for the well-being of healthcare workers, who in this way can rediscover the purpose and meaning of their work [15], recognizing contributions made by each individual of the staff [14]. Protecting healthcare workers is an important component and promoting their health is a key element [14].

Radiotherapy departments have had to face two issues: protecting patients and staff from the risk of viral infection, and maintaining the delivery of

radiation treatment that inevitably requires specific skills and organization. All patients need special treatment to prevent, reduce, and avoid all possible risks of infection. For this reason, a new optimization of patients' access to the Radiotherapy Department has been devised, suggesting a reinterpretation of priorities and therapeutic intentions, modifying the scheduling of doses and concomitant chemotherapy regimens. Health education is mandatory for all patients: they must always wear a mask, wash and disinfect their hands properly according to instructions, avoid crowded places and ensure social distancing. It is important to discuss each individual case to understand the risks and benefits in performing a radiotherapy cycle [17]. These recommendations are only intended to provide a framework, remembering that this is not static information and will continue to change during the pandemic.

## Breast cancer

Breast radiation therapy may be delayed in some cases, up to a maximum of 3 months, taking into account the risk of recurrence, expected benefit, and individual risk estimate [18]. Hormone therapy may be taken during the waiting interval [19]. Standard radiation therapy usually means delivering 50 Gy in 25 fractions (2 Gy daily). Adjuvant radiation therapy may be given during this period with a hypofractionation of 42.6 Gy in 16 fractions (or 40 Gy in 15 fractions). This therapy can be omitted in low-risk cases or cases of carcinoma in situ. Boost can be omitted in patients > 50 years of age with small tumors, but is advantageous in high-risk cases. If it is used, one can hypofractionate the radiation therapy by administering 10 Gy in 2 fractions (5 Gy daily) or 13.35 Gy in 5 fractions (2.6 Gy daily) [20].

## Gynecological tumors

Cervical cancer is treated with standard radiation therapy of 45/50 Gy in 25 fractions (1,8/2 Gy daily), adding a boost with external radiation or alternatively with brachytherapy and in advanced states also with concomitant chemotherapy. Hypofractionation with a total dose of 40 Gy in 16 fractions (2.5 Gy daily) leads to a reasonable tumor response and acceptable levels of late toxicity. During COVID-19 emergence the boost should be

integrated concurrently [21, 22]. In endometrial cancer, brachytherapy can be given exclusively and should not be delayed for more than 12 weeks after surgery, otherwise survival may be compromised. Also for early vaginal cancer, brachytherapy has an exclusive role with a daily dose of 7 Gy for 5 fractions; whereas in patients with an advanced stage, chemoradiotherapy treatment can be considered, followed by brachytherapy of 7 Gy in 3 fractions [23].

## Head and neck cancer

Patients with head and neck cancer are even more fragile because they undergo massive surgery and concomitant chemoradiation therapy, which can easily lead to an immunocompromised state. It is recommended that radiotherapy should not be delayed more than 4–6 weeks for oropharyngeal cancer, laryngeal cancer, and oral cavity cancer; high priority has been assigned to squamous cell carcinoma with radical and postoperative radiotherapy for positive margins [24]. Surgery always plays a major role and hypofractionation is not entirely favored over standard radiochemotherapy [25], in which high-dose cisplatin is administered every 3 weeks and 70 Gy in 35 fractions (2 Gy per day). Nevertheless, hypofractionation has been evaluated, providing 60 Gy in 25 fractions (2.4 Gy per day) [26]. Intensified radiotherapy treatment administers a dose of 55 Gy in 20 fractions (2.7 Gy daily), avoiding chemotherapy and significantly improving loco-regional control compared with conventional 66/70 Gy radiotherapy in 33–35 fractions (2 Gy daily) [27]. These patients require the thermoplastic mask, but also special immobilization devices, such as dental guards, bite blocks, or tongue depressors; therefore, during the pandemic they must be trained to be able to insert the intraoral device themselves and with a second mask they must cover tracheotomies [28]. In these treatments, RTTs must use FFP2 and goggles because patients must remove the surgical mask at the time they must put on the thermoplastic mask for treatment [29].

## Lung cancer

Stage T1-T2 non-small cell lung cancer can be treated with stereotactic radiotherapy, although

there is a potential risk of treatment-related toxicity, which is greater for central than peripheral lesions. For central tumors, a five-fraction scheme ranging from 10 to 12 Gy per fraction for a total dose of 50 to 60 Gy delivered every other day has been evaluated. Recommendations allow a dose of up to 48 Gy in four fractions for lesions adjacent to or in contact with the chest wall. Tumors peripheral to or at least 2 cm from the chest wall can be done with extreme hypofractionation with a single 30 Gy fraction [30]. Hypofractionation may be a viable option, with the delivery of 55 Gy in 20 fractions [31]. For locally advanced non-small cell carcinoma, the standard radiotherapy regimen involves administration of 60–66 Gy in 30/33 fractions (2 Gy daily), concurrently with platinum-based chemotherapy. Also, in this case the hypofractionation has been evaluated, sequential to chemotherapy, which foresees the administration in 15/20 sessions of 2.75 to 4 Gy per fraction to the target, with or without an integrated boost.

Radiation therapy also has curative intent for small cell lung cancer, concurrently with chemotherapy. In patients eligible for chemotherapy, administration prior to stereotactic radiation therapy is recommended, as it has been demonstrated that tumor volume can decrease significantly after the first or second cycle of chemotherapy. This therapy should not be delayed more than 4–5 weeks. Standard fractionation is 45 Gy in 30 fractions (twice daily), but hypofractionation, using 40 Gy delivered in 15 fractions (2.6 Gy daily), has also been evaluated. In early stage patients, stereotactic radiotherapy with doses ranging from 50/60 Gy in 5 fractions (10 Gy daily) may be an option [31]. Postoperative adjuvant radiation therapy (PORT) for radically resected tumors can be delayed up to three months after surgery [32] characterised by a fast and global spread during the first months of 2020, has prompted the development of a structured set of recommendations for cancer care management, to maintain the highest possible standards. Within this framework, it is crucial to ensure no disruption to essential oncological services and guarantee the optimal care. This is a structured proposal for the management of lung cancer, comprising three levels of priorities, namely: tier 1 (high priority. Palliative radiation therapy is valuable for inoperable or locally advanced tumors, as well as for treating hemoptysis, severe cough, and secondary dyspnea.

In these cases, it is best to administer a hypofractionated regimen such as 20 Gy in 5 fractions (4 Gy daily), 17 Gy in 2 fractions (8.5 Gy daily), or a single 10 Gy fraction.

### Prostate cancer

Curative radiotherapy is preferable to adjuvant radiotherapy, but it still may be favored over surgery during a pandemic. For low-risk disease, treatment can be postponed; if treatment is necessary, a shorter fractionation, such as the 5- or 7-fraction stereotactic technique, can be adopted, while still maintaining an excellent result in terms of acute and late toxicity. Otherwise, an ultra-hypofractionated treatment of 6 Gy for 6 fractions is used for low volume disease. A moderate hypofractionated regime of 60/62 Gy in 20 fractions (3 Gy daily) can be performed [33]. The use of fiducial markers and rectal spacers must be very selective and should be used only if considered strictly necessary [34].

### Palliative

During the pandemic, oral analgesics are the first option; if this is not possible, a single fraction of 8 Gy radiation therapy can be given for bone metastases. The evidence is insufficient to justify systematic adjuvant radiotherapy in the spine or peripheral bones, so radiotherapy may be deferred (if there are progressive postoperative signs), otherwise fractionated treatments of 30 Gy in 10 sessions (3 Gy daily) or 20 Gy in 5 sessions are suggested (4 Gy daily) [35].

In metastatic epidural spinal cord compression (MESCC), surgical treatment is favored; adjuvant radiation therapy can be deferred from 4 to 12 weeks, whereas if surgery is contraindicated or inappropriate, radiation therapy can be performed exclusively with a single 8 Gy fraction [35]. In patients with brain metastases, in whom long-term survival is expected, the standard 3 Gy fractionation in 10 fractions can be changed to 20 Gy therapy in 5 fractions; while for patients with a poor prognosis, observation is favored to avoid the risk of contracting COVID-19 [36]. Radiation therapy is also an option for tumor-related bleeding, in which 3.7 Gy  $\times$  4 fractions (twice daily) repeated at 3-week intervals during the pandemic period is administered; 4 Gy may also be delivered to avoid twice-daily treatment [36].

### Pediatric patients

During COVID-19 emergence it has been suggested to postpone pediatric radiation therapy whenever possible, administering standard or maintenance chemotherapy in the interim and performing active surveillance [37]. Conventional radiation therapy can be changed to a hypofractionated 2 Gy scheme instead of 1.6/1.8 Gy, especially in patients with a poor prognosis or highly proliferative tumors [37]. In high-risk neuroblastoma, a dose of 3 Gy per fraction can be delivered; in intermediate-risk neuroblastoma, treatment can be delayed for up to 4 weeks [37]. In Ewing's sarcoma, hypofractionation may be a strategy and 3 Gy per fraction is delivered [37]. A simultaneous integrated boost (SIB) of 2.2 Gy can be combined with standard radiotherapy treatment of 1.8 Gy in pediatric patients with soft tissue sarcoma [37]. In leukemia cases, total body irradiation (TBI) is currently administered twice daily with a dose of 12 Gy in 6 fractions (2 Gy, twice a day); standard therapy should be performed when possible, but it is also safe, in terms of disease control and survival, to administer a single daily dose of 3/4 Gy. Replacing TBI with chemotherapy-only regimens can be considered, but there are slightly inferior results and greater toxicity to be expected [37]. In medulloblastoma in children older than newborn age, adjuvant craniospinal radiotherapy with boost gives excellent survival results, so it should not be delayed beyond 40 days after surgery, with chemotherapy support. It administers 59.4 Gy in 33 fractions (1.8 Gy daily), and hypofractionation is not recommended; a slight dose modification to 54 Gy in 30 (1.8 Gy daily) fractions is recommended for very young children (< 12 months) or those undergoing multiple surgeries for tumors near the brainstem [37].

### Brachytherapy

Brachytherapy treatment follows a priority list in the gynecological setting [38]:

1. Curative for cervical cancer (stage I, III) and vaginal cancer (stage I, locally advanced stage);
2. Adjuvant for endometrial cancer (stage I with intermediate risk, stage II with favorable prognosis);
3. Adjuvant if associated with external beam radiotherapy for endometrial cancer (stage II with

unfavorable prognostic factors, stage I with high risk).

To minimize the risk of exposure to COVID-19 and to make up for the hypothetical lack of anesthesiologists, the number of fractions in brachytherapy for cervical cancer was reduced: 7 Gy in four fractions in two insertions one week apart (2 fractions per day separated by a 6-hour interval) or 9 Gy in two fractions one week apart (for small tumors that responded well to external beam radiotherapy) [22]. If there are patients older than 70 years or with significant comorbidities, EBRT and a schedule of 9 Gy per fraction in two fractions 1 week apart may be performed [38]. Vaginal vault brachytherapy (VVB) is recommended in intermediate-risk endometrial cancer because it significantly reduces the recurrence rate; the schedule of 7 Gy for 3 fractions for a dose depth of 0.5 cm, with an acceptable interval of 14 days, can be considered. In cases of stage II endometrial tumors, adjuvant VVB exclusively or in combination with EBRT can be postponed for a maximum of 1 to 2 months. For advanced stages, radiochemotherapy followed by vaginal brachytherapy of 7 Gy in 3 fractions can be evaluated [38, 39].

In early-stage breast cancer, neoadjuvant hormone therapy has been recommended to delay surgery [40]; accelerated partial irradiation (APBI) with balloon or multicatheter brachytherapy, inserted intraoperatively or under local anesthesia, has been considered to shorten the duration of treatment compared with EBRT [41].

Treatments should begin within 12 weeks and no longer than 20 weeks of surgery [40]. The main fractionation option involves 7.5 Gy  $\times$  3 APBI for patients who have had breast conservation surgery, otherwise 34 Gy in 10 fractions given twice daily or 32 Gy in 8 fractions given twice daily can be delivered [40].

In the pandemic setting, soft tissue sarcoma can be treated with brachytherapy in the adjuvant setting, but it is recommended to deliver 60/66 Gy with 1.8/2 per fraction rather than iridium-192 wires to decrease the length of hospitalization [41].

Brachytherapy can also be performed for high-risk prostate cancer, exclusive (13.5 Gy  $\times$  2 fractions) or subsequent to ERT in a single session (15 GY), whereas for low- or intermediate-risk treatment can be deferred for 3-6 months (13.5 Gy  $\times$  2 fractions [41, 40].

## Low dose radiotherapy (LDRT) against COVID-19

Lung irradiation to treat pneumonia was performed in 1905 until 1946; patients had severe pneumonia and were treated historically with low doses of radiotherapy (0.35–1.5 Gy, acceptable risk threshold dose of 0.5 Gy) [36]. Using the same technique for COVID-19 patients has been considered, but there are limitations: small sample of patients, inappropriate control group, toxicity, logistic and technological issues [36, 37].

It is recommended that Volumetric Modulated Arc Therapy (VMAT) be started as early as possible, which allows a good coverage of the entire lung tissue and spare organs at risk. However, it is expensive, requires increased delivery time, extends the treatment time, and an interdisciplinary team is required (with a good link to intensive care) [36].

Research has shown that the anti-inflammatory mechanisms of LDRT suppress the effects of cytokines in critical COVID-19 patients (where other therapies have not worked or are not feasible [38]). In fact, clinicians proposing this type of treatment should monitor inflammatory markers both before and after treatment to validate its efficacy [38]. This is a contentious topic, as there are concerns about possible carcinogenic effects from radiation exposure. It is a small risk, however, that there are organs within the treatment field, whose stochastic effects should not be overlooked [36]. Risk-benefit assessment is still difficult because of the novelty of the treatment. Furthermore, ethical concerns have also been raised because of the speed of clinical deterioration of patients and the need for timely decision making [37]. It is also important to note whether the benefit gained comes directly from radiation treatment or from combination with other therapies [36].

## Limitations

Since this research was carried out, further therapeutic strategies were implemented by most of the centers. Regarding the management strategies, some departments had problems concerning common spaces, e.g. waiting rooms, and the availability of individual protection, which were given first to those working in the COVID-19 departments.

## Conclusions

Considering all the topics discussed, we can say that the common denominator is always the oncological patient, as a fragile subject and more prone to develop comorbidities. The administration of radiotherapy should be encouraged despite the pandemic, however, to evaluate each case according to the risk/benefit ratio. Hypofractionation is one of the most frequently used strategies to overcome the risk of crowding in radiotherapy department, aiming to reduce the waiting lists and the number of patients simultaneously undergoing treatment. Organizational strategies (like ward rules or telemedicine) have been implemented to continue offering medical service, albeit readapted to the context, always ensuring a high level of safety for both patients and operators.

At the time of writing this Review, Countries around the world, especially USA and the EU, have begun administering the COVID-19 vaccine. The general expectation is that the pandemic will end soon and a similar situation will not reoccur quickly, but further pandemics cannot be ruled out. For this reason, United Nations developed the “National Influenza Pandemic Preparedness and Response Plan” back in 2005 [40], which defined the objectives and activities to be implemented to avoid being overwhelmed by a pandemic. This document can represent a summary to be used in the coming years, where lessons and strategies can be found for a Radiotherapy department to start from in the event of a new pandemic (unless there are further technological developments and new types of treatment).

### Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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