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Letter to the Editor

Brachytherapy Issues and Priorities in the Context of the Coronavirus Disease 2019 (COVID-19) Outbreak

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To the Editor,

Brachytherapy has a major role in patient cure and cannot be substituted or excessively delayed in patients with rapidly growing tumors (eg, cervical cancer). However, the coronavirus disease 2019 (COVID-19) pandemic requires workflow adaptation to ensure treatment continuity for patients while ensuring safety of health care professionals. Because of a drastic reduction in operating room capacity, with the exception of critical emergencies, it is mandatory to have COVID-19 recommendations applicable to the field of brachytherapy, taking into account specific constraints. Strategies for infection prevention and rationalization of health care resources are discussed. Herein, we place brachytherapy in the context of reduced access to radiotherapy facilities and underscore strategies to be implemented to protect patients and health workers while ensuring that patients will still receive the most appropriate curative treatment.

In the context of the international public health emergency related to the COVID-19 outbreak, radiotherapy facilities have to adapt to ensure safety of caregivers and treatment continuity for patients.[1] As recently highlighted, radiotherapy departments have adapted their practice.[2-4] Staff reorganizations and reduction of patients' access to radiotherapy facilities have been created to minimize the risk of infection transmission and spare health care providers, a population identified as high risk.[5] The management of COVID-19 suspect or positive patients has been addressed for external beam radiotherapy (EBRT), but practical aspects of brachytherapy have not been fully addressed.[6] Guidelines overall tend to prioritize locally advanced, curable disease for EBRT and to suggest limitation of treatments wherever there is no strong clinical benefit for immediate EBRT. Strategies for infection prevention, rationalization of clinical workload, and working practice in the presence of COVID-19 infected patients have been published.[7,8] It seems crucial to extend COVID-19 recommendations to the field of brachytherapy, which has specific constraints related to professional exposure and is an essential component of treatment for patient cure in numerous clinical situations, especially in cervical cancer. Furthermore, the COVID-19 pandemic has led to a drastic reduction of operating room capacity with the exception of critical emergencies.

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Table 1 Brachytherapy prioritization scale

Priority	Indication	Modality	Action in the COVID-19 context
Priority 1	Locally advanced cervical cancer	Boost	Do not postpone
Priority 2	Head and neck (eg, lip)	Exclusive	Do not postpone
	Skin or urogenital squamous cell carcinoma	Exclusive	
Priority 3	Pediatrics indication	Exclusive	To be discussed on an individual basis
Priority 4	Intermediate and high risk prostate	Boost	Postpone (8-12 wk) or opt for external irradiation according to local facilities
	Accelerated partial breast irradiation	Exclusive	
	High-risk endometrial cancer	Boost	
Priority 5	Low risk prostate	Exclusive	Postpone (8-12 wk) or opt for surveillance
	Intermediate risk endometrial cancer	Exclusive	
Priority 6	Basal cell carcinoma	Exclusive	Postpone according to functional risks
Priority 7	Endoscopic procedures (esophagus or bronchus)	Exclusive	Omit and consider external beam options
Priority 8	Keloids	Exclusive	Omit and consider external beam options

Abbreviation: COVID-19 = coronavirus disease 2019.

In addition to recently published EBRT guidelines, we highlight strategies that may be implemented in brachytherapy facilities in this emergency context in order to protect patients and health care workers.

Refining Indications

Compared with EBRT, brachytherapy exposes to a specific risk of perioperative contamination. The difficulty in having a dedicated operative workflow for infected patients in most brachytherapy centers implies that a careful triage evaluation is done before patient hospitalization, in order to preclude access of COVID-19 infected patients to the operating room. Indeed, preparation of a dedicated operating room with dedicated ventilators for COVID-positive patients is usually not possible. Therefore, systematic patient screening for infection by careful questioning and clinical examination, followed by polymerase chain reaction (PCR) testing with or without systematic chest computed tomography (to screen for false PCR-negative patients) have practical implications to avoid contamination of other patients and ensure safety of health care providers. PCR testing of all patients before a brachytherapy procedure should be strongly considered to preclude that an infected patient will enter a brachytherapy operating room. In some countries, such a systematic approach may, however, not be possible owing to test unavailability, as only patients with suspicious symptoms are tested. Patients with symptomatic or even asymptomatic COVID-19, a suspected or a proven infection, should have their treatment postponed and the patient should follow the Centers for Disease Control test-based or nontest-based strategies until COVID negative, and they should be cleared by the infectious disease team before rescheduling the brachytherapy procedure, as for nonurgent procedures per surgical guidelines.[9]

For COVID-19–negative patients, treatment should be scheduled according to the cancer-related clinical condition (Table 1). The dual objective of limiting professional/patient exposure and optimizing operating room activities requires prioritizing radical treatments for patients with nonoperated tumors. Given the major contribution of brachytherapy to patient cure, clear priority should be given to brachytherapy for locally advanced cervical cancers. It has been clearly shown that brachytherapy use is associated with a survival benefit in these patients, with overall survival probability significantly lower among women who do not receive brachytherapy after considering other prognostic factors.[10,11] Therefore, locally advanced cervical cancer patients should be treated with upfront chemoradiation plus brachytherapy and neither EBRT boosts (including stereotactic boosts) nor neoadjuvant approaches should be used given the deleterious effect of these approaches on patient outcome.[12,13] Overall treatment time is another major benchmark for treatment quality and an independent prognostic factor for local control, along with concurrent chemotherapy use.[14] It is therefore appropriate not to postpone brachytherapy in COVID-19–negative patients given the detrimental effect of treatment interruptions and of increasing overall treatment time. Other major indications for brachytherapy include head and neck tumors treated with brachytherapy alone (eg, squamous cell carcinoma of the lip, oral mucosa, or nasal region) and penile glans cancers. In these curative situations for which brachytherapy provides both dosimetric and functional superiority over any other EBRT modality, it seems unsuitable to postpone treatment or to replace brachytherapy with external irradiation.[15] Furthermore, brachytherapy use will decrease constraints for EBRT facilities and minimize economical cost by considerably decreasing the total number of patients travelling. Brachytherapy can therefore be seen as a tool for advanced hypofractionation and therefore for

reduction of patients' access to EBRT facilities (eg, brachytherapy boost in patients with prostate cancer, or interstitial brachytherapy for accelerated partial breast irradiation).[16,17] In the setting of the COVID-19 pandemic, hypofractionation is an attractive therapeutic option in the context of reduced radiotherapy resources and a potential approach to minimize virus spread by limiting patient travel.[18] Brachytherapy boost has been shown to increase progression-free survival when applied to high- and intermediate-risk prostate cancer. However, in this specific case, the benefit of brachytherapy boost should be weighed against the difficulties in accessing operating rooms during the pandemic and the fact that a benefit in overall survival has not been demonstrated. For the same reasons, nonurgent treatments may be postponed (eg, 125-iodine seed implantation for low-risk prostate cancer, treatment of basal cell carcinoma, and others). If the pandemic situation should be long lasting, brachytherapy may be seen as an attractive approach to minimize patients' exposure related to daily standard fractionation EBRT lasting 7 to 8 weeks. In a few highly specialized centers, brachytherapy is indicated in pediatric rhabdomyosarcoma.[19] In this situation, children usually receive chemotherapy first with the timing of local treatment decided according to a personalized approach, taking into account tumor response and a multidisciplinary analysis of the theoretical risk of tumor progression when the patient is on chemotherapy.

High-risk brachytherapy procedures requiring upper endoscopic procedures for applicator placement (esophagus, pulmonary cancers) should be postponed after careful analysis of the benefit-risk ratio, given the possibility of using alternative noninvasive approaches and the fact that those procedures, at high risk for COVID-19 transmission, are in most cases palliative in intent.[15]

In the adjuvant setting, brachytherapy may be postponed or even avoided where it has not shown a survival benefit and noninterventional options do exist as per international guidelines (eg, postoperative vaginal vault brachytherapy in intermediate risk and high/intermediate risk patients with endometrial cancer, when surveillance is an option, or when the time interval from surgery becomes excessively extended).[20] These cases should be discussed individually on a multidisciplinary basis taking into account clinical situations, local facilities, and epidemiological context.

Finally, treatments for benign disease (eg, brachytherapy for keloids) should be delayed.

Technical Aspects

In the COVID-19 context, it is necessary to protect health care workers and minimize the risk of COVID-19 transmission by avoiding any nonessential exposure of professionals. It is therefore recommended to deny access to the operating room to nonessential people. Each time it is technically feasible, it is necessary to have at maximum 1 operating radiation oncologist, 1 nurse, and 1 physicist (for real-time treatment planning) in the same operating room. In some indications (eg, head and neck or pediatric applications), the treatment may, however, require the presence of additional operators. Guidelines for surgical procedures have been provided elsewhere.[8] Safety issues in the COVID-19 context also apply for brachytherapy. We therefore recommend favoring interventions under local/locoregional anesthesia to minimize health care workers' exposure by avoiding the risks linked to endotracheal intubations, a procedure that can increase the risk of COVID19 diffusion. In the pandemic context, the lack of anesthetists and ventilator equipment should also be taken into account. For endocavitary gynecological applications, there is increasing evidence that proper application can be achieved under local anesthesia. For interstitial brachytherapy procedures, scarce data are available for local anesthesia, but spinal anesthesia is being routinely used in numerous centers, providing good comfort for patients in most cases of pelvic (gynecological, lower gastrointestinal tract, urogenital) malignancies.[21,22] If general anesthesia is still required, a specific anesthesiology protocol should be used, with dedicated protective equipment, taking into account the risk of aerosolized droplet exposure during induction. Those protocols have been described in dedicated international guidelines for anesthetic management of patients during the COVID-19 outbreak.[23]

If technically possible, it is recommended to avoid repeated anesthesia and therefore to favor brachytherapy schemes requiring 1 single implantation (vs repeated implantations). Every effort should be made to minimize total length of stay in the hospital to minimize the risk of COVID-19 transmission during brachytherapy treatment. Those technical aspects may contribute to maintaining high-quality treatments while taking into account the pandemic context and constraints on health care resources. The use of face shields/visor full face protection with surgical masks may reduce the infectious risk and seem therefore appropriate for all health care workers in brachytherapy. Filtering facepiece particles class-2 (N95) masks are mandatory for head and neck implants to minimize the risk of transmission and protect operator and patients. The reinforced hygiene instructions specific to each operating room or hospital service must be maintained to ensure the safety of health professionals, caregivers, and patients in brachytherapy facilities.[6]

Conclusions

Brachytherapy has a major role in patient cure and cannot be substituted or excessively delayed in rapidly growing tumors. This situation of unprecedented challenges, however, requires workflow adaptation, protection

measures for patients and health care workers, and rationalization.[7] If the COVID-19 pandemic should persist, then we do believe it is of utmost priority to provide an appropriate definition of clinical priorities including brachytherapy. It is necessary to ensure that in the emergency context treatment remains guided by clinical evidence and that patients who are in line for curative therapy will not be undertreated.[24] This is especially true for locally advanced cervical cancer patients, for whom utilization of alternative modalities for primary tumor boosting may lead to a poor outcome.[25] At the same time, one should anticipate that the pandemic situation may last as long as systematic large-scale serological tests and an effective vaccination are unavailable. The question of postponing indications may be relevant in the acute phase, but postponing strategies may lead to unsolved issues if resources and treatment capacity should be reduced for an extended period. In this situation, refining brachytherapy indications will be necessary to spare utilization of health care resources, and cancers with the highest therapeutic index, including cervical cancer, should be prioritized.

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