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EDITORIAL

# Research in radiation oncology and the Covid-19 pandemic

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2020 was in many ways different from usual in radiation oncology. The entry of the Covid-19 should prove to have broad consequences for cancer care, including research in radiation oncology.

Early on during the course of the pandemic in Wuhan, it became clear that cancer patients are in high-risk of complicated infection. During the first wave of the Covid-19, cancer patients had a ∼4-fold increased risk of respiratory distress with need of intensive care, mechanical ventilation and death [1]. As a consequence, cancer patients must be offered the highest possible protection.

The society lock-down sent a broad part of the population, and especially the elderly and the more fragile into social isolation. The lock-down also affected hospital services for diagnosis and treatment of conditions that were not considered acute and life-threatening. The intention was to reduce the transmission of Covid-19 to patients and hospital personal through reduced number of patient contacts in the health care sector. Individuals with symptoms of cancer did not seek help at their general practitioner and were therefore not referred for diagnostic tests. This resulted in a huge unintended drop in diagnoses of cancer. An analysis of the National Patient Register in Denmark revealed a 33% [95%CI 26–40%] reduction of total cancer diagnoses from March to May 2020 compared to similar months in 2015–2018 [2]. Significantly reduced incidences were observed for both males and females and in all age groups. In Germany, they observed similar fall in cancer diagnoses during spring 2020 [3,4]. Reduced diagnostic activity resulting in a diagnostic delay was expected to be followed by a bounce of more advanced cancer cases in the second half of 2020, but it is the general impression that it has not come yet.

Varies actions have been suggested to protect patients and personal from Covid-19 infection. Reorganization of the clinical patient flow aiming to omit or reduce the patients' hospital visits, to ensure safety of patients and personal in the hospital, to design management strategies of suspected and confirmed positive patients, to test for SARS-CoV-19 etc. were measures that all cancer centres implemented [5].

An important action was to minimize the patients' contacts to the hospital, aiming at reducing COVID-19 exposure without compromising on the oncological outcome. Within the radiation therapy community it was felt that the use of radiotherapy should be reduced by omitting treatment to those who do not have an absolute indication for radiotherapy, deferring the therapy for those with indolent cancer or shortening the treatment schedules by use of hypofractionation, when appropriate [6]. International guidelines on radiation therapy for breast cancer during the Covid-19 pandemic recommends omission of adjuvant radiotherapy in some low-risk breast cancer patients and hypofractionated schedules for most others, unless it is against evidence supporting normo-fractionation. In prostate cancer, delay of radiotherapy and use of the shortest safe regimen (ultra- or moderately hypofractionated radiotherapy) are recommended for relevant risk-groups [7]. For head- and neck and lung cancer, less altered strategies are recommended. ESTRO-ASTRO Delphi consensus guidelines for the two cancer types recommend thorough triage of individual patients, postponement of therapy of some patients, only to use hypofractionation when appropriate and to continue chemo-radiation of head and neck cancer patients [8,9].

In a population-based study of the English NHS during the first peak of the COVID-19 pandemic, Spencer et al found that mean weekly radiotherapy courses/fractions fell by 19.9%/29.1% in April, 6.2%/31.4% in May, and 11.6%/31.5% in June compared with corresponding months in 2019. The largest reduction was seen in the elderly and in prostate cancer [10]. Other diagnoses saw an increase in radiotherapy use (esophageal, bladder, rectal cancer), and more use of ultra-hypofractionation (breast). The authors conclude that while radiotherapy activity fell significantly, use of hypofractionated regimens rapidly increased and the increase in treatments for some cancers suggests that radiotherapy compensated for reduced surgical activity.

It is generally recommended to do virtual consultations and to avoid all unnecessary visits to the hospital with the intension to minimize transmission of the virus to patients and personal. Participation in a clinical trial often implies a higher number of hospital visits compared to standard of care. Some trials were paused during the first wave of the Covid-19 pandemic and others just slowed down because focus was on the virus and not on research.

In a paper published in the present issue of Acta Oncologica, De et al. report on the impact of the Covid-19 pandemic on clinical radiotherapy research [11]. The authors

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explore the changes in recruitment of patients into three randomized radiotherapy trials at the MD Anderson Cancer Center as direct and indirect effects of stay-at-home orders, restrictions on traveling and general society and hospital close-downs in March 2020. The three trials were the SAPHIRE (hypo- versus conventional fractionation of breast cancer, including loco-regional lymph nodes), the OPAL II (one versus three weeks hypofractionated regimes in early-stage breast cancer) and the EXTEND (systemic antineoplastic therapy with local consolidative therapy versus systemic therapy alone in oligometastatic cancer). A 70% reduction in patient recruitment to the three trials was observed in March through April and a 45% reduction from June to July 2020. The studies were not suspended or stopped during the Covid-19, but they most likely recruited slowly due to a decreased referral to the cancer centre, health-care professionals reduced encouragement or patients' reluctance to participate in the trials.

At the MD Anderson Cancer Center they adopted their procedures during the first wave to allow remote consent, virtual consultation etc. to facilitate clinical trials based on provisions granted by the National Institute (NCI). These and many more actions should be encouraged to maintain possibilities to conduct clinical trials during crises as for the Covid-19 pandemic. The pandemic has lasted for a year and only the most optimistic predictions says that it is over during the first half of 2021. We cannot catch up what was lost in 2020 and trials may run out of funding. We need to adopt to the circumstances and get the clinical trials running again. Otherwise we will lose even more than we lost in 2020.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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