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COVID-19 Rapid Letter

# Radiotherapy for COVID-19: *Primum non nocere* ☆

Several proposals had been suggested for the use of low dose radiation to treat COVID-19 patients [1,2]. This was quickly followed by suggestions for low dose total body irradiation [3]. We urge caution and careful examination of the evidence and logistics of low dose radiotherapy in COVID-19 patients.

COVID-19 pandemic still currently has no proven cure nor effective therapeutic pharmacology. It is natural for all physicians in the situation of lack of effective options to consider easily accessible, non-invasive treatments. Radiation and particularly environmental radiation exposure has had prior history of causing public panic, particularly as each event was associated with uncontrolled exposures and large numbers of members of the public exposed to doses for example the Chernobyl even though the increased second cancer risks of each individual is very low [4].

As such, responsible radiation oncologists as well as clinical radiologists must bear public responsibility to ensure radiation protection and consider the evidence base carefully. In this instance, we can and should utilise the events of the past to guide current practice.

1) Evidence of absence of harm is not evidence of benefit. The evidence forwarded by Dhawan et al. [5] are mainly historic cohorts of patients treated with low dose radiotherapy for pneumonia. There are many flaws in extrapolating this evidence to support low dose radiotherapy in COVID-19 patients with acute respiratory distress syndrome (ARDS). These historic cohorts do not have a comparator arm therefore attributing radiotherapy as the only cause of cure for pneumonia is not acceptable. These cohorts do not have long term survival outcome and long term follow up on secondary radiation risks. Also, we are only beginning to learn on the pathophysiology of hyper-inflammatory stage in the context of COVID-19 contributing to organ failure which is different to known disease process of pneumonia making a direct comparison invalid.
2) Radiotherapy is not without harm and strong consideration needs to be made to account for the risks of secondary malignancy as a result of radiotherapy. The historic lessons of treating tinea capitis with radiotherapy with subsequent patients developing secondary cancer arising decades later for treatment must not be forgotten [6]. The dose suggested at 0.5 Gy may well be under the threshold for acute toxicities but the risks of secondary malignancy guided by the linear non threshold model needs to be justified by potential benefits of radiotherapy which is in this case is unproven and uncertain [7].
3) A counter factual example is the recent Fukushima Japan earthquake and nuclear reactor meltdown triggered uncontrolled release of radiation with a large number of the public exposed to very low doses of radiation [8]. In the current COVID-19 scenario, the situation is analogous with members of the public not being able to consent carefully potentially due to the hypoxia and intercurrent illness. The difference between the two events being, a natural event (earthquake 2011 versus viral pandemic 2020) resulting in man-made radiation exposure (uncontrolled reactor meltdown versus uncontrolled iatrogenic exposure).
4) The radiotherapy technique proposed with the application of kilovoltage (kV) radiotherapy using portable X-ray machines and unplanned parallel opposed technique is not practical. The low penetration, dominant photo-electric effect of kV resulting in increased bone and lesser lung absorption makes it unsuitable to treat lung tissues as the intended target volume. If the selected patient cohort is critical patients, they would be ventilated and treated in intensive care unit. The logistics of delivering the radiotherapy and radiation protection to staff and other patients are challenging. Portable X-ray machines are not commissioned for delivery of low dose radiotherapy making quality assurance impossible.
5) Defining target volume for treatment with low dose radiotherapy is challenging. The principle of "as low as reasonable achievable" (ALARA) is a central principle of radiation protection. Without a clear biological mechanism, targeting the whole lung for radiotherapy is haphazard. Not able to optimise radiotherapy treatment, account for individual anatomical differences and the suggestion of unplanned radiotherapy technique with kV would make dosimetry impossible and may even cause harm by exposing patients unnecessarily to large radiotherapy fields.
6) Due to the COVID-19 pandemic, national and international guidance has urged prioritisation of resources due to service disruption. One would struggle to get research trials set up where radiotherapy has most evidence in curative setting are being scaled back to accommodate service disruptions from COVID-19 pandemic and research effort being hampered.

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7) Any intervention suggested for COVID-19 must be examined carefully in a trial setting if it is to accrue any benefits to patients. The current RECOVERY trial attempts to assess multiple pharmaceutical agents in randomised multi-arm trial [9]. If radiotherapy is to be suggested to be one of the arm of the trial it would need to be subjected to scientific scrutiny.
8) The issue of low dose radiation exposure has to take into account imaging radiation as well as the doses for anti-inflammation is in the region of the doses for computed tomography (CT) chest scans. Routine diagnostic X-rays and CT scans has been shown to increase the risks of cancer [10,11].

COVID-19 pandemic remains a huge challenge to the medical community at large. The use of radiotherapy in non-cancer diagnoses must be subjected to scientific scrutiny and based on solid evidence base. Oncologists (and radiologists) not learning from lessons of the past on secondary malignancy risks would be condemned to repeat them.

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