



Perspective

Cancer risk of CT scan in COVID-19: Resolving the dilemma

With an unprecedented surge in the COVID-19 cases in India during the second wave, the number of chest computed tomography (CT) acquisitions in COVID-19 patients also increased dramatically. It prompted the Indian health authorities and policymakers to issue an advisory on the appropriate use of the CT chest in COVID-19¹. A debate then ensued over the probability of CT scans escalating the cancer risk in COVID-19 patients, with various healthcare professionals stuck in the tangle².

CT scan is an invaluable diagnostic tool and has contributed to patient care over many years, and the benefits of an appropriately indicated and timely done CT have far outweighed the risks involved³. Even during the ongoing pandemic, CT chest has played a pivotal role in the diagnosis and management of COVID-19⁴. However, at the same time, it is equally important to understand that a CT scan is not a routine test and should be used judiciously. CT scan involves the use of ionizing X-rays, which are categorized as hazardous radiation. While ionizing radiation can have deterministic effects which are predictable and include skin erythema, burns and hair loss⁵, it happens only when a patient is exposed to high dose of radiation and over a short span of time. Such side effects with medical diagnostic imaging tests such as CT scans are almost never seen in clinical practice barring a few anecdotal incidents of gross medical error.

The primary concern of radiation is the stochastic effect, *i.e.* the ability of the radiation to produce genetic mutations that may lead to the development of cancer, and the increase in the chances of occurrence of cancer with increasing radiation dose⁵. These are the probabilistic, long-term consequences of ionizing radiations, which may take 15-20 yrs or even longer to show up⁶. Thus, the chance of radiation-induced cancer risk is particularly more in children and young people who have a decent life span ahead of them.

Many studies have been done to estimate the carcinogenic potential of ionizing radiation in humans, but the majority of such data are derived from the cohorts of atomic bomb survivors who experienced instantaneous whole-body exposure to X-rays, particulate radiations, neutrons and other radioactive materials^{7,8}. This is the major limitation of these studies as the known biological effects of radiation in these survivors are different from those exposed to radiation from diagnostic medical imaging tests such as CT scan that result in limited radiation exposure to a small portion of the body. In one such study, the chance of getting cancer from one CT scan was estimated to be as high as 1 in 2000⁹. However, this cancer risk estimation from CT was done based on the 'linear no-threshold' (LNT) dose-response model, which is a mathematical formula and calculates only the hypothetical and theoretical risk¹⁰. It lies at a foundation of a postulate that (i) irrespective of however low the radiation dose may be, any exposure to ionizing radiation is harmful and could result in cancer or heritable genetic damage, (ii) its detrimental effects increase proportionately with the radiation dose received, and (iii) these effects are cumulative over lifetime¹⁰. Even though the current radiation safety regulations and practices are based on this hypothesis, it has lately been challenged by various authors and professional organizations including Health Physics Society, United Nations Scientific Committee on the Effects of Atomic Radiation and US Nuclear Regulatory Commission and American Nuclear Society¹¹⁻¹⁴. Furthermore, based on the advances in radiation biology during the last two decades and an improved understanding of carcinogenesis, this model finds little merit when used for calculating the radiation risk, especially at low doses and dose rates of medical radiation exposure. It exaggerates the risks and fails to provide a reliable projection of future cancer incidence as there are statistical uncertainties in biological response at low levels of radiation¹⁵⁻¹⁷.

There have been a few epidemiologic studies published in the last decade that attempted to provide evidence of carcinogenesis in children due to CT scans. Some reported potential evidence of a dose–response relationship between brain tumours and leukaemia in children and CT¹⁸. However, the results of these studies were later considered sub-optimal due to the bias of ‘reverse causation’ - which means that the reported cancer association could also be related to the patients’ underlying health conditions that prompted the CT examination or the factors predisposing to cancer were already present at the time of the scan^{12,19}. Furthermore, Ferrero *et al*²⁰, reported that despite the concerns about ionizing radiation in medical imaging remain, but there is no concrete evidence that can prove an increased cancer risk associated with low-level radiation doses used in medical imaging. While in another large, population-based cohort study from South Korea, Lee *et al*²¹ found that radiation from abdominopelvic CT was associated with a higher incidence of hematologic malignancies. Another multinational study on a cohort of 950,000 patients is underway to provide direct estimates of the risk of solid tumours and leukaemia among children and young adults who had undergone CT at least once before the age of 22 yr²², but its results are still awaited.

According to the latest information available on the official website of the National Cancer Institute, United States, the lifetime risk of cancer in children from a single CT scan is estimated at 1 in 10,000²³. However, this calculation is also based on the same LNT theory, which is being debunked lately as there is definite latency threshold for ionizing radiations that could, and arguably should, be considered in cancer risk estimation²⁴. The risk of radiation-induced oncogenesis for exposures <50-100 milli-Sievert (mSv is a unit to measure effective radiation dose) is non-existent or too small to be detected⁹. This is because at such low-dose exposures, if there occurs any injury to the cells, the body has the inherent ability to overcome cell damage as it can repair DNA, along with the elimination of aberrant cells through apoptosis or other types of mitotic death¹⁵. Furthermore, even if there remains any chance of theoretical increase in the risk of cancer incidence, it should always be considered in the context of the plethora of clinical benefits that CT provides.

The precise amount of minimum radiation exposure that can cause cancer is not measurable.

There is a subset of individuals who can be more vulnerable and are at an increased risk of developing cancer, secondary to radiation exposure - such as those who are genetically predisposed with congenital/acquired genetic mutations or defective genes²⁵. In addition, it is also not possible to predict how much radiation from medical imaging a person might receive in the remaining years of their life. Thus, as per the guidelines issued by International Commission of Radiation Protection (Ottawa, Ontario, Canada), it is imperative to follow the basic, as low as reasonably achievable principle through – justification and optimization²⁶. In medical imaging, justification is an important strategy to limit radiation exposure to an individual patient and the population as a whole. Three key questions that should be answered before any CT scan are: (i) why is the CT scan needed?, (ii) will the CT results change the treatment protocol?, (iii) is there an alternative test that does not involve radiation? However, if the test is deemed clinically justified, then the principle of optimization should be followed, wherein every attempt should be made to expose the patient to the minimum possible radiation while achieving the necessary diagnostic information.

The radiation dose from a CT scan varies from patient to patient and depends upon the age, sex, size of the body part examined, the type of scan and the type of CT equipment and its operation²⁷. The calculated values of radiation dose delivered to a patient on imaging are only an estimate and so is the risk involved. On an average, a standard dose chest CT delivers radiation of 3.5-7 mSv²⁸. American College of Radiology Appropriateness Criteria[®] guidelines revised in February 2020 recommend that lifetime diagnostic radiation exposure be limited to 100 mSv at which there is only one per cent risk of development of solid cancer or leukaemia²⁹. Moreover, this estimated risk of cancer from diagnostic radiation is much less than the average lifetime risk of developing cancer from other causes which stands at 40.14 and 38.7 per cent in men and women, respectively³⁰.

The first CT scan was commercially launched in 1972, and since then, it has come a long way. Recently, there have been rapid technological advances in both the CT scan hardware and software, and the radiation delivered to the patient in each CT examination has considerably reduced. The methods to achieve low radiation exposure during a CT scan include automatic exposure controls, decreasing the tube current (mA)

and tube voltage (kV), acquisition at a high pitch and usage of iterative reconstruction algorithms^{31,32}. Furthermore, tweaking these CT acquisition parameters, low-dose CT (LDCT) and ultra-low-dose CT (ULDCT) can be done on the contemporary CT scanners and further reduction in the radiation dose can be achieved. Recently, Dangis *et al*³³ and Hamper *et al*³⁴ reported accuracy and reproducibility of LDCT in the evaluation of COVID-19 pneumonia, while the radiation dose delivered to the patients in each scan was less than 1 mSv. In another recent study, Samir *et al*³⁵ compared the detection accuracy of ULDCT with LDCT in 250 patients of COVID-19 and found it to be around 90.38-93.84 per cent with mean effective dose of only 0.59 mSv in ULDCT. This radiation exposure with LDCT and ULDCT is even less than the average natural background radiation dose which stands at 3 mSv/y²⁴. Thus, an attempt should be made to utilize LDCT or ULDCT more frequently, wherever possible.

However, constraint must be exercised and CT should be done only in specific case scenarios of COVID-19 where it is clinically indicated, and its results are expected to have an impact on the treatment decisions³⁶. This becomes more important especially in situations when mass-level CT scans are done in high number and sometimes also repeated multiple times in the same patient as reported during the ongoing COVID-19 pandemic. The cumulative radiation dose from recurrent CT imaging can predispose few vulnerable individuals to increased lifetime attributable risk of radiation-induced cancer^{37,38}.

According to the current understanding, there is no conclusive evidence of cancer caused by low-level radiation exposure from medical imaging (<50-100 mSv) despite using X-rays for more than 125 years and CT for nearly 50 years now. On the contrary, not doing a CT scan fearing the hypothetical risk of radiation-induced cancer in a clinically relevant indication can delay treatment and cause more harm.

In conclusion, even though there is no definite evidence of any increased risk of cancer due to CT scan in COVID-19 patients, rational and judicious use of CT is warranted and caution needs to be exercised to avoid unnecessary and repeat scans.

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