



Excess Lifetime Cancer Mortality Risk Attributed to Radiation Exposure from Pediatric Computed Tomography Scan

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The important topic of the possible outcome and public health implications of the increasing use of diagnostic computed tomography in children, discussed in the study of Chodick et al. [1] in this issue of the journal, deserves attention, primarily because of its potential for primary prevention of cancer.

The authors estimated the number of excess lifetime cancer deaths related to annual pediatric CT scans performed in Israel, based on several sources: information on CT scan utilization for the period 1999–2003 in the second largest health management organization in Israel, published organ doses for common CT examinations, radiation-related cancer mortality risk estimates from studies on the atomic bomb survivors, and age and gender-specific mortality rates of cancer in Israel. Based on these data, the authors concluded that the performance of 17,686 CTs in a population of 2,236,500 children under the age of 18 years would yield an excess of 9.49 lifetime deaths from cancer among the irradiated individuals (an increase of 0.29% above the expected rates).

From the time of the discovery of the X-ray by Wilhelm Conrad Roentgen in 1895, there has been a dramatic change in the way in which radiation is viewed. News of the discovery spread quickly: within a year, almost 1000 scientific papers and many textbooks on X-rays were published. In February 1896 the *Journal of the American Medical Association* expressed the cautious opinion that X-rays might be useful in the treatment of disease. Soon after, the application of X-rays to diagnosis and therapy became an established part of medical practice. Roentgen was awarded the first Nobel Prize in Physics in 1901 for his discovery [2].

In the first half of the 20th century, ionizing radiation was widely used in medicine for the treatment of benign conditions (e.g., benign breast disease, hemangioma, tinea capitis, postpartum mastitis, acne and even infertility) [3–5]. Later, in the 1970s, the ALARA policy (**as low as reasonably achievable**) was implemented based on the non-threshold linear hypothesis. This idea is based on the concept that any amount of radiation exposure, no matter how small, can increase the chance of negative biological effects such as cancer, albeit by a negligible amount.

It is also based on the principle that the probability of the occurrence of negative effects of radiation exposure increases with cumulative lifetime dose [6]. Nowadays, high doses of ionizing radiation are used with great caution, mainly for the treatment of cancer; however, the use of low dose radiation in diagnostic procedures has been growing continuously [7].

Computed tomography was invented in the early 1970s by Sir Godfrey Hounsfield, a British engineer from EMI (Electrical and Musical Industries), and Dr. Allan M. Cormack, a South African physicist who worked independently on the mathematics of combining multiple X-ray images, at Tufts University. It is interesting to note that EMI is famous for producing the Beatles' recordings and it was rumored that funding for research behind the development of the CT scanner came from the profits brought to EMI by the Beatles. In 1979, Hounsfield and Cormack were awarded the Nobel Prize in "Physiology or Medicine" for their contribution to medicine and science [8].

Since its introduction, CT has become an important tool in medical imaging and serves as the gold standard in the diagnosis of a large number of different disease entities [8,9]. More recently, it is also being used for preventive medicine as a screening tool (e.g., for lung cancer or CT colonography) [10]. Some institutes even offer full body scans for the general population as "screening on demand," although this use has been widely criticized [11]. Official Israeli policy, reflecting awareness of the growing use of CT, was presented in a medical practice statement issued in July 2006 by the Director of Medical Management, which stated that imaging studies should be performed only in cases in which there is a written referral from a physician recommending the examination for the patient. It was emphasized that this applies to all imaging studies, especially those with high levels of radiation such as CTs [12].

CT is regarded as a moderate to high radiation diagnostic technique: the radiation exposure has been estimated to range from 1 to 24 mSv per scan [11]. While technical advances have improved radiation efficiency, there has been simultaneous pressure to obtain higher resolution imaging and use more complex scan techniques, both of which require higher doses of

radiation [9]. Data from the United States and Europe indicate that although only 5–10% of all imaging is performed using CT, 40–67% of all exposure to medical radiation derives from this procedure [9,13].

The risk estimates given by Chodick et al. are for a single exposure, assuming that in a particular year each procedure of CT performed exposed one child [1]. However, the reality is that some children will be repeatedly exposed later on and, even in that year, some children had probably undergone CTs more than once while more children than estimated had never undergone this procedure. In clinical practice there are cases in which CTs are performed once in a lifetime (e.g., due to one specific event of trauma), and there are cases of chronic illness, which require repetitive scanning for diagnostic purposes (e.g., Crohn's disease). An extreme example of such a situation was described by De Jong et al. [14], comparing the survival of cystic fibrosis patients who underwent repeated annual CT scanning with those who did not. When using a model in which the expected median survival of the non-scanned group was 50 years, a 12% excess mortality from solid cancers was shown among those who underwent annual scanning. An additional model, in which patients underwent annual CT scanning only until age 18, showed an excess mortality from solid cancers of more than 6%.

Obviously, this situation of repetitive exposure in children over an extended period does not represent the majority of CT use, and the excessive risk estimate mentioned earlier is the consequence of the high cumulative dose of radiation absorbed by this study population. However, this example emphasizes the importance of the attention that must be given to the total number of CTs performed in chronic illnesses in which the cumulative doses of radiation might reach meaningful doses.

One possible solution for limiting the doses of exposure to diagnostic radiation, especially in the era of high dose technologies such as CT on the one hand and computerized medical systems on the other, might be to provide personal information on lifetime ionizing radiation exposure. This information should include the number and type of procedures performed, as well as the age at which they were performed, and calculations of cumulative doses absorbed by different organs. Furthermore, the optimal situation would be if the process of referral of a patient to a procedure involving radiation exposure would mandate that the physician be aware of the patient's history of radiation exposure. This information should be used as a determining factor in deciding if, to what procedure and at what frequency a patient should be referred to a radiation-associated diagnostic examination.

The report by Chodick and team [1] joins several previous publications demonstrating that the irradiation involved in the performance of diagnostic CT is associated with an increase in incidence and mortality rates of cancer in both children and adults [11]. The magnitude of the excess risk described is relatively small. However, from a public health risk perspective, this small individual cancer risk must be multiplied by a large and ever-increasing population of individuals undergoing CT scans [9]. The relatively small lifetime excess of mortality risk of 0.29%

for cancer attributable to ionizing radiation exposure of 17,686 CTs estimated by Chodick et al. was translated into 9.45 radiation-induced deaths. However, since each year children will be exposed to CT (for the first time or repeatedly), this number of deaths will accumulate. Therefore, for 10 years of exposure the excess lifetime deaths will reach 95 cases and even more when multiple exposures occur or when the number of CTs increases.

There are several uncertainties in the estimates used in this and other similar studies that might lead to under- or overestimation of the risk assessment. Most of the quantitative information on radiation-induced cancer risks comes from studies on the A-bomb survivors [15]. Therefore, this cohort is generally used as the basis for predicting radiation-related risks for different populations. Although all age groups are covered in those studies, the risk estimate per specific age group might not be precise enough in this data source, especially when dealing with brain tumors. So far, quantitative data (risk per dose) on the risk to develop brain tumors following an exposure to ionizing radiation have been assessed in only four studies [3,16-18], and their results show some discrepancies regarding risk estimates. The excess relative risk/Sv for childhood exposure derived from the A-bomb studies was 1.2 (for all nervous system tumors excluding schwannoma), and the ERR/Gy seen in an analysis of brain tumors that developed after therapeutic radiation for childhood leukemia was 1.06 for meningioma and 0.33 for gliomas. In contrast, data from a follow-up of the Israeli tinea capitis cohort indicated an ERR/Gy of 4.63 for meningiomas and 1.98 for malignant brain tumors. Results of a pooled analysis of two Swedish cohorts of infants exposed to radiation treatment for hemangiomas are more in line with the tinea capitis cohort findings, with a reported ERR/Gy of 2.7 for all brain tumors combined. While the estimates in the first two studies refer to the age group of ≤ 20 years, the third study deals with children aged ≤ 15 years, and the last study relates to infant exposure. The previously mentioned discrepancies in risk estimates might be partially explained by differences in the age distribution of the cohorts. Therefore, since risk varies with age at exposure, a calculation of excess risk based on radiation-related cancer mortality estimates from A-bomb survivor studies, as performed in the present study, may have led to an underestimation of risk.

An additional source of possible under/overestimation of risk could be the use of models that are based on the assumption of homogenous risk within a certain age group in a population. However, the idea that there are subpopulations that are more sensitive to the effect of radiation is now an accepted paradigm. A recent publication describing a clustering of radiation-associated meningiomas and other cancers in certain families supports the existence of genetic susceptibility for the development of tumors following an exposure to this carcinogen [19]. Such a genetic susceptibility, which may exist in certain subpopulations, might imply that the risk estimate for developing cancer following exposure to radiation could be different in these subgroups from the estimates we use for the general population.

ERR = excess relative risk

Another point that should be considered is that in the Chodick study only the outcome of mortality was examined. Today, survival from cancer is relatively high and continuously rising, with a 5 year survival of about 79% and about 64% among children and adults respectively (U.S. 1995–2000) [20]. However, cancer is a severe disease that has considerable acute and chronic health implications. Therefore, cancer mortality reflects only the tip of the iceberg, and greater attention should be given to the incidence of the disease.

It took more than 50 years to reach the conclusion that ionizing radiation is harmful and that its use should be limited as much as possible. On the other hand, there is no doubt of its importance for therapeutic and diagnostic purposes. As always, the question is whether the benefits of X-ray outweigh the safety concerns. Since CT will remain a major tool in the diagnosis and care of children, it must be used with discretion, in a responsible way, while eliminating inappropriate referrals for CT and limiting the amount of radiation to the essential minimum. Even for small, relative or absolute risks the ancient concept expressed by Hippocrates of *Primum non nocere* (to help, or at least to do no harm) should serve as a guide to achieving the golden mean between risk and benefit accompanying the performance of diagnostic procedures involving ionizing radiation in children.

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