New evidence for brain cancer risk after a single paediatric CT scan

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Despite the unquestionable benefits of diagnostic radiation exposure, the potential health risks are of considerable concern, particularly for the risk of brain cancer following paediatric head CT examinations. In *The Lancet Oncology*, Michael Hauptmann and colleagues[1] present the results of a large-scale study from nine European countries (the EPI-CT cohort study) to quantify the risks of brain cancer in more than 650 000 patients who had a first head or neck CT examination when they were younger than 22 years. The mean estimated cumulative brain absorbed dose, lagged by 5 years, was 47·4 mGy (SD 60·9). About three quarters of the observed brain cancers were of glioma type (121 [73%] of 165 cases), which is typically a rapidly progressing tumour in adults. Hauptmann and colleagues[1] estimated significant linear dose-response relationships for all brain cancers and for glioma, with excess relative risk estimates per 100 mGy of 5-year lagged cumulative brain dose of 1·27 (95% CI 0·51–2·69) for all brain cancers and 1·11 (0·36–2·59) for gliomas. Risk estimates remained significantly elevated when the analysis included doses only up to 50 mGy or patients who only received a single CT examination. The authors inferred that, per 10 000 people receiving a single head CT examination (giving an average brain dose of 38 mGy), about one radiation-induced brain cancer is expected 5–15 years after the CT examination.[1]

Although it is generally accepted that direct risk estimation from CT exposed cohorts is the best approach, until recently,[2] risks were estimated by a linear extrapolation from studies with relatively high-dose exposures to CT-level doses, which are relatively low. This approach was used not merely because radiation risk at low dose (<100 mGy) is not well quantified, but also because the past CT studies had a relatively small number of participants with short follow-up, study participants were young, and few individual organ dose estimates were available. Furthermore, several studies suggested that estimated radiation risks could have been liable to reverse causation (a situation in which the CT scan might have been taken because of pre-existing disease), confounding by indication (occuring when another condition [not the outcome of interest] causes both CT scan imaging as well as the outcome of interest [brain cancer], without being an intermediate step between them), and other potential biases.[3,4] A 2022 simulation study, however, suggested that the reverse causation bias is unlikely if a reasonable lag time is used in statistical analyses (to exclude cases of brain cancer occurring within 5 years after the first CT scan).[5]

Radiation risk estimates from CT exposed cohorts are generally higher than those from other exposed cohorts (eg, Japanese atomic bomb survivors or occupational radiation workers), as was also the case for this study. The precise mechanism of these differences is not well understood, and would require further investigation, particularly with regards to observed increasing radiation risks with increasing age at exposure. In the EPI-CT cohort study, the highest risks were estimated for those aged 12 years and older (although it is not clear how many cases were observed in each of the age at exposure categories), albeit the trend was not significant.

The EPI-CT cohort study provided a very comprehensive statistical analysis of large and complicated data, with a multitude of sensitivity analyses addressing a number of concerns that have been previously raised in the literature on CT studies. However, several questions remain. First, solid cancers potentially caused by exposure to ionising radiation at young ages might occur not only within a few years but also decades later, and children are generally considered more sensitive to radiogenic brain cancer than adults.[6] The present study, with a relatively short period of follow up (median 5·6 years [IQR 2·4–10·1]), found that after the cumulative brain dose was lagged by 10 years, the association between radiation exposure and brain cancer was no longer significant.[1] Longer follow up would be necessary to understand age trends (average age at the end of follow up was only 22 years and the average age when population rates of glioma start increasing is 30 years). Second, the positive associations for nine countries seem to be driven by the UK data, with no such association found in Sweden and the Netherlands,[1] raising the need to clarify the cause of such intercountry heterogeneity.

Lastly, the authors did not examine how substantial shared errors in dose estimates might affect risk estimates, and this could mean the 95% CIs are wider than reported in the paper.

In summary, the new evidence from the EPI-CT cohort study can be used to give the patients and their parents important information on the risks of CT examination to balance against the known benefits. In recent years, rates of CT use have been steady or declined,[7,8] and various efforts (eg, in terms of diagnostic reference levels) have been made to justify and optimise CT examinations. Such continued efforts, along with extended epidemiological investigations, would be needed to minimise the risk of brain cancer after paediatric CT examination.

We declare no competing interests.

*Nobuyuki Hamada, Lydia B Zablotska
hamada-n@criepi.denken.or.jp

Biology and Environmental Chemistry Division, Sustainable System Research Laboratory, Central Research Institute of Electric Power Industry (CRIEPI), Tokyo 201-8511, Japan (NH); Department of Epidemiology and Biostatistics, School of Medicine, University of California, San Francisco (UCSF), San Francisco, CA, USA (LBZ)

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