From Toshiko Kato and Kosaku Yamada

20 July 2022

Dr Jing Chen

Chair of the UNSCEAR Committee

Dr Mikhail Balonov

Lead Writer

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Dear Dr Chen and Dr Mikhail Balonov

Subject: Author response to

Comments on Kato and Yamada paper 'Individual Dose Response and Radiation Origin of Childhood and Adolescent Thyroid Cancer in Fukushima, Japan'

（From UNSCEAR Secretariat to Mr. Shigeru Taguchi, 15 June 2022）

The authors were told from Mr. Shigeru Taguchi that he received the Comments on our paper 'Individual Dose Response and Radiation Origin of Childhood and Adolescent Thyroid Cancer in Fukushima, Japan' [1] from UNSCEAR Secretariat on June 16, 2022. The UNSCEAR was passing on a rebuttal by unknown UNSCEAR experts to Mr. Taguchi, who is not the author of the original paper. In this case, we authors do not know to whom we should send our response to their rebuttal.

First of all, we protest to UNSCEAR that this is a clear departure from the rules of science. Please give us the name of the main writer of the important comments by UNSCEAR experts.
However, the comment by some UNSCEAR experts has already been distributed. We had to respond formally to the UNSCEAR and posted this letter and attached file "Author response to the Comments by UNSCEAR experts" to the Chairperson of UNSCEAR, Dr. Jing Chen, and Lead writer Dr Mikhail Balonov as well as the comments by UNSCEAR experts (15 June 2022) on the public domain website, UNSCEAR2020/21 report-verification-networks (https://www.unscear2020report-verification.net); we will post your reply to the same website, as many people sincerely wish to know your response.

Summary of authors' response to the comments written by UNSCEAR experts

In this paper, we presented that "Childhood and adolescent thyroid cancer detected in the Fukushima health management survey (FHMS) was associated with individual external dose estimated in FHMS basic survey. Increased childhood and adolescent thyroid cancer in Fukushima could most probably be attributed to radiation exposure from the nuclear accident. Individual dose dependence of thyroid cancer incidence in the second-round screening was studied by dividing 108,980 examinees into three external dose groups, <1mSv, 1–2mSv, and ≥2mSv from the data of Ohira et al. [2]. We also determined the risk coefficient for thyroid cancer based on the external dose dependence of thyroid cancer incidence of dose groups. In order to compare the results with those of Chernobyl and other previous studies, the risk coefficient per millisievert was converted to the thyroid dose estimated in Appendix B of the UNSCEAR 2020/2021 report (an approximation using the proportional relationship between external exposure dose and thyroid dose in 59 municipalities).

This summary accords with the summary by UNSCEAR.

Additional analyses to answer the comments by UNSCEAR experts

The experts had some substantial comments relevant both to dosimetry and epidemiological parts of our paper. We took your comments very carefully and performed some additional analyses: e.g.,

1. The UNSCEAR criticized that the rough estimate of excess relative risk per Gray, ERR/Gy= 213 (95% CI 129, 297) based on only 36 thyroid cancer cases is unbelievable, and commented further that there is an arbitrary assumption that "The mean doses of the first two groups (<1 mSv and 1-2 mSv) were assumed to be 0.5 mSv and 1.5 mSv (a) " without any justification of those numbers.

   We found 36 thyroid cancer cases are comparable to cases in high-quality studies of thyroid cancer risk in Chernobyl (Attached File Table 1). We derived ERR/Gy values for two other assumed mean dose values (0.4, 1.4) and (0.3, 1.3) mSv, and found excellent linear dose dependence. ERR/Gy values were high,

   170 (95%CI=159, 182; p=0.003) for mean dose (0.4, 1.4) mSv of dose groups.

2. The UNSCEAR experts commented that estimated confidence interval ERR/Gy= 213 (95% CI 129, 297) differed from the central (point?) estimate of 213 by less than a factor of 2, which lacks plausibility compared to wider CI values in studies after Chernobyl [Tronko 2006; Zablotska 2011]. We could reproduce the result by Zablotska et al. but 95%CI was a little sharper in the

regression analysis by Microsoft Excel: EOR/Gy =2.21(1.9, 4.2) compared to their EOR/Gy=2.15 (0.81, 5.17). The reason for the difference in CI's of ERR/Gy, as pointed by experts, was presumably the software or definition of 95%CI used in each paper.

After many re-analyses according to your comments, we found that "The high ERR/Gy value is most likely due to the underestimation of the UNSCEAR 2020/2021 thyroid dose assessment and not due to the method of analysis in our paper."

UNSCEAR2020/2021 estimated thyroid dose by adjusting many coefficients to match about half of the simplified measurements of 1080 children. However, the thyroid measurement might have been a great underestimation because 55% of measured thyroid dose were negative or zero, suggesting that some dose other than background was subtracted from the measurements. Inaccurate thyroid dose measurements were evaluated as valid based on the unrealistic assumption that there was "no surface contamination of the body or clothing" (UNSCEAR 2020/2021 Attachment A-2 59) which was contrary to the report of Hosokawa et al. [3] Thyroid dose in all municipalities in Fukushima prefecture might have been severely underestimated. The UNSCEAR can never derive any conclusion about thyroid cancer from such an underestimated thyroid dose.

Please read the attached "Author response to UNSCEAR" carefully, and respond as soon as possible.

We shall post your letter to our website, as many people sincerely wish to know your response. Thank you very much for your comments. We found no necessity for revision to be made on our paper after careful examination of your comments. The conclusion does not change.

References

[1] Kato T, and Yamada K, Individual dose response and radiation origin of childhood and adolescent thyroid cancer in Fukushima, Japan. Clinical Oncology & Research 2022. https://www.sciencerepository.org/individual-dose-response-and-radiation_COR-2022-2-102

[2] Ohira T, Ohtsuru A, Midorikawa S, Takahashi H, Yasumura S et al. (2019) External radiation dose, obesity, and risk of childhood thyroid cancer after the Fukushima Daiichi Nuclear Power Plant accident: The Fukushima Health Management Survey. Epidemiology 30: 853-860.

[3] Hosokawa, Y., M. Hosoda, A. Nakata et al. Thyroid screening survey on children after the Fukushima Daiichi Nuclear Power Plant Accident. Radiat Emergency Med 2: 82-86 (2013).

Yours sincerely

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日本語訳

課題: UNSCEAR からのコメントに対する著者応答

加藤・山田論文‘Individual Dose Response and Radiation Origin of Childhood and Adolescent Thyroid Cancer in Fukushima, Japan’への UNSCEAR 専門家のコメント

（From UNSCEAR Secretariat to Mr. Shigeru Taguchi, 15 June 2022）

著者らは、田口茂氏から、2022 年 6 月 16 日に UNSCEAR 事務局から我々の論文「福島における小児・思春期甲状腺がんの個人線量反応と放射線起源」［1］に対する Comments を受け取ったと聞かされた。UNSCEAR は、原著論文の著者ではない田口氏に対して、UNSCEAR の無記名の専門家による反論を伝えていた。この場合、我々著者は、彼らの反論に対する回答を誰に送ればよいのかわかりません。

まず、UNSCEAR に対して、これは明らかに科学のルールから逸脱していると抗議します。
UNSCEAR の専門家による重要なコメントの主筆者の名前を知らせるべきと考えます。
しかし、UNSCEAR の一部の専門家によるコメントは既に拡散しています。私たちは UNSCEAR に正式に回答する必要があり、UNSCEAR 議長 Jing Chen 博士、リードライターMikhail Balonov 博士宛に本書簡と添付ファイル「UNSCEAR 専門家への著者応答」を送り、また UNSCEAR expert のコメント（2022 年 6 月 15 日）をパブリックドメインのウェブサイト、UNSCEAR2020/21 report-verification-networks https://www.unscear2020report-verification.net に掲載します。またあなたの回答を知りたい人が多くいますので、同じウェブサイトへも掲載します。

UNSCEAR 専門家からのコメントに対する著者の回答の概要

UNSCEAR 専門家によるコメントに答えるための追加分析

UNSCEAR 専門家からは、本論文の線量評価および疫学的な部分に関して、いくつかの重要なコメントがあった。私たちはそのコメントを慎重に受け止め、いくつかの追加解析を行った。

１．　UNSCEAR は、わずか 36 例の甲状腺がん症例に基づく 1 グレイあたりの過剰相対リスク ERR/Gy=213（95%CI 129, 297）という概算は信じられないと批判し、さらに「最初の 2 群（1mSv 未満と 1-2mSv）の平均線量は、0.5mSv と 1.5mSv（a）とする」いう任意の仮定があり正当性がないとコメントした。
36 例の甲状腺がんは、チェルノブイリにおける甲状腺がんリスクに関する研究の症例と同等であることがわかった（著者回答・表 1）。平均線量については、他の二つの想定平均線量値（0.4, 1.4）, (0.3, 1.3) mSv について ERR/Gy 値を導出し、優れた線形線量依存性を見いだした。ERR/Gy 値は高く、平均線量(0.4, 1.4) mSv の線量群では 170 (95%CI=159, 182; p=0.003) であった。

２．　UNSCEAR 専門家は、推定信頼区間 ERR/Gy=213（95%CI 129, 297）が中央推定値(点推定値ではないか？) 213 とファクター2 以下の差があり、チェルノブイリ後の研究でのより広い CI 値と比較して妥当性に欠けるとコメントしている［Tronko 2006; Zablotska 2011］。
Zablotska らの結果は再現できたが、Microsoft Excel による回帰分析では 95%CI が少し鋭くなった。EOR/Gy = 2.21(1.9, 4.2) と計算されたのに対し、彼らの値は EOR/Gy = 2.15(0.81, 5.17) であった。専門家が指摘した ERR/Gy の信頼区間が異なる理由は、各論文で使用されているソフトウェアまたは 95%CI の定義にあると思われる。
UNSCEAR 専門家からのコメントに従い、いくつかの再解析を行った結果、"ERR/Gy の値が高いのは、UNSCEAR 2020/2021 の甲状腺線量評価の過小評価による可能性が高く、当論文の解析方法によるものではない "ということがわかった。

UNSCEAR2020/2021 では、1080 人の子供の簡易測定値の約半分に一致するように多くの係数を調整して甲状腺線量を推定している。しかし、甲状腺線量測定値の 55％が負またはゼロであり、バックグラウンド以外の何らかの線量が測定値から差し引かれことを示唆していることから、甲状腺測定値は大きな過小評価である可能性がある。不正確な甲状腺線量測定は、引用論文の細川らの報告[3]とは異なった「身体や衣服の表面汚染がない」という非現実的な仮定に基づいて、有効であると評価された（UNSCEAR 2020/2021 Attachment A-2 para.59）。この誤った評価により、 福島県のすべての自治体の甲状腺線量が著しく過小評価された可能性がある。UNSCEAR は、このような過小評価された甲状腺線量から甲状腺がんに関するいかなる結論も導くことはできない。

添付の「UNSCEAR への著者回答書」をよくお読みくださり、できるだけ早くご回答くださいますようお願い申し上げます。多くの人があなたの回答を知りたがっていますので、私たちはあなたの手紙をウェブサイトに掲載することにします。
コメントありがとうございました。ご指摘の内容を精査した結果、論文に修正の必要はないと判断しました。結論は変わりません。
敬具

著者
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