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ADVANCES IN PEDIATRIC RESEARCH

Dose dependence of pediatric thyroid cancer prevalence in the 6 years after the Fukushima nuclear power plant accident

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Abstract

Background: After the Fukushima nuclear accident in March 2011, Fukushima Prefecture initiated thyroid ultrasound screening as part of the Fukushima Health Management Survey (FHMS). Regional differences in external radiation dose were often reported not associated with thyroid cancer prevalence in the first-round screening E-I (2011-2013). The association between childhood thyroid cancer and radiation exposure in the 6 years after the accident is studied by analyzing the results of the first and second-round examinations E-I+II (2011-2015).

Methods: Dose dependence of thyroid cancer proportion in E-I and E-II for all residents aged ≤18 years at the accident was analyzed for FHMS external dose and UNSCEAR effective dose by regression analysis using Microsoft Excel. Two divisions of Fukushima prefecture, O-model in the order of decreasing external dose and S-model according to the initial screening schedule, were adopted.

Results: In O-model, thyroid cancer proportion per 100,000 in E-II and in E-I+II were found to increase linearly to FHMS external dose in 0.2–1.4 mSv range and UNSCEAR effective dose in 1.6–5 mSv range. Thyroid cancer proportion in E-II and E-I+II was observed to increase linearly to effective dose in S-model.

Conclusion: The observed linear prevalence–dose relation after 6 years from the accident and incidence-dose relation during 4-6 years after exposure suggest a possible association between pediatric thyroid cancer and radiation exposure. Regional differences were not obvious in E-I presumably because of the short interval from exposure to screening in high-dose areas. High prevalence of thyroid cancer cannot be attributed only to mass screening effect that does not depend on radiation dose and elapsed time from exposure.

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Introduction

Thyroid ultrasound screening

After the release of radioactive elements from triple meltdown of Fukushima Daiichi Nuclear Power Plant (F1NPP) in March 2011, Fukushima Prefecture initiated thyroid ultrasound screening for all 367,649 residents aged ≤18 years at the accident. The Fukushima Health Management Survey (FHMS) reported the results of the first-round examination (E-I) conducted in fiscal year FY2011-2013 and the second-round examination E-II (FY2014-2015), where 186 confirmed or suspected cancer cases were detected [1-3]. Oversight Committee Meeting for FHMS evaluated that the proportion of thyroid cancer in the first round was several tens of times higher than the prevalence proportion estimated from the Japanese cancer statistics data based on the regional cancer registry [4]. Thyroid cancer proportion in the second round was somewhat lower than that in the first round but still tens of times higher than the cancer statistics data [5].

Members of Fukushima Medical University (FMU), which is responsible for FHMS, often reported that there were no significant differences among evacuation zone and other areas in thyroid cancer prevalence in the first screening E-I [6-8]. From reasons including the absence of obvious regional differences of thyroid cancer prevalence in E-I, both the International Atomic Energy Agency (IAEA) [9] and the FHMS committee [4] summarized that thyroid cancer detected in the first round was unlikely to be associated with radiation exposure. Suzuki et al. further concluded that the high prevalence of childhood thyroid cancer detected in E-I could be attributed to mass screening [7]. It is curious that the same order of thyroid cancer patients was detected in E-II, 2 years after the first ultrasound screening detected thoroughly nonclinical and subclinical thyroid cancers. Thyroid cancer patients seem to increase roughly proportionally to elapsed time from the accident in the time scale shorter than the latency 4-5 years of radiation induced thyroid cancer [6]. This seems to contradict the slow growing nature of sporadic (ordinary) thyroid cancer.

Recently, a preliminary analysis including the second-round examination, E-I+II (FY2011-2015), revealed a linear relationship between thyroid cancer proportion and external radiation dose after 6 years from the accident [10]. The purpose of this paper is to investigate the relation between pediatric and adolescent thyroid cancer in Fukushima and radiation doses: external dose estimated by FHMS [11] and effective dose estimated by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) [12,13], in the 6 years after the accident. We shall utilize several calculation models to assess whether there was an actual increase of the prevalence of thyroid cancer related to the accident or, in contrast, whether the increased prevalence was simply related to mass screening.

Health risk assessment from nuclear accident

Enormous quantities of radioactive material were released into the environment following the meltdown of three nuclear reactors in the F1NPP accident. Internal exposure of radioactive Iodine (I-131) was found to be closely associated with thyroid cancer among children after the Chernobyl accident. Exposure information of I-131 from the Fukushima accident was uncertain because of few measurements of I-131 activity in the thyroid [14]. The authors noted that I-131 has a half-life of 8 days and therefore it was necessary to make activity measurements of I-131 in the thyroid rapidly, but no further examinations were carried out by the local authorities. Estimation of internal thyroid doses involved a lot of uncertainties and provided only representative values for the residents [15]. The World Health Organization (WHO) estimated thyroid doses for 10-years-old children and 1-year-old infants in the most affected areas of Fukushima prefecture to be within 18−122 mSv (Table 6 in [16]).

While I-131 exposure is clearly important in thyroid cancer, external or effective radiation exposure can also be important. From the preliminary estimation of effective doses ranged from 12 to 25 mSv in the two most affected locations in Fukushima Prefecture, WHO estimated the increased lifetime risk for thyroid cancer by up to around 70% over baseline rates in females exposed as infants in these locations (p.8 in [16]) The study of CT scans among young people, where the exposure consisted entirely of external X-rays, showed that the increased risk of thyroid cancer was greater than the average increased risk for all solid cancers [17]. Lubin et al. reported that relative risk (RR) of thyroid cancer increased with childhood external radiation dose (e.g. through treatment of childhood cancer and benign diseases) without significant departure from linearity at doses <200 mSv: RR=2.1 at 100 mSv and 1.55 at 50 mSv [18].

Methods

Subjects and details of thyroid ultrasound screening

In the thyroid ultrasound screening for all 367,649 residents aged ≤18 years on March 11, 2011, 186 cancer cases: 150 confirmed by surgery and 36 suspected (positives in fine-needle aspiration cytology, FNAC), were detected in E-I and E-II [2,3].

In each examination, results of the primary examination were divided into four categories. A1: no nodule or cyst, A2: nodules <5.0 mm or cysts

<20.0 mm, B: nodules >5.1 mm or cysts >20.1 mm, and C: immediate need for confirmatory examination. In confirmatory examination for those with B and C results, ultrasonography, blood test and urine test were conducted. Positives in confirmatory examination underwent FNAC or medical follow-up. When cancer cells were detected in FNAC, the suspected cancer patients were followed and had surgery at an appropriate time, where malignancy was finally confirmed [2,3]. We abbreviate thyroid cancer cases detected by FNAC as cancer cases for short. Among 187 positive cases in fine needle aspiration cytology in E-I and E-II, 151 cases underwent surgery and 150 cases (99.3%) were confirmed to be cancer, hence possible error may be <1%.

Dose estimation

In the FHMS basic survey, only external radiation doses were estimated based on individual behavioral data of 566,680 residents and daily gamma ray dose rate maps [11,19]. Here, dose response of thyroid cancer was studied for two independent dose estimations, external dose in the FHMS basic survey and effective dose, a sum of external, inhalation, and ingestion of 10-year-old children, in the UNSCEAR 2013 report [12,13]. It should be noted that FHMS External dose and UNSCEAR effective dose are essentially the same quantity because ingestion was assumed be constant for all municipalities and the dominant part of the effective dose was the external dose in the effective dose estimation by UNSCEAR.

External dose of each municipality was estimated from the weighted average of doses by the number of respondents in each municipality, where doses given by intervals <1, 1–2, 2–3, mSv, were assumed to be 0.5, 1.5, 2.5, mSv, respectively [11]. Because dose distribution was given by intervals of 1 mSv, dose values of municipalities in lowest dose areas <0.5 mSv could not be reproduced. Hence dose of municipalities in Aizu and Minami-Aizu were assumed to be their average values 0.2 and 0.1 mSv, respectively. The external dose and effective dose of each area were estimated from the weighted average of dose of each municipality by the number of primary examinees in E-I. In cases where multiple dose estimations were given for a municipality in the evacuation zone, a higher value was adopted.

Models dividing prefecture and statistical analysis

The effect of radiation exposure was studied by adopting two models that divided Fukushima prefecture into four geographic areas.

O-model: Ohira et al. studied the associations between childhood thyroid cancer and external dose on the basis of the data of individual radiation. They classified municipalities into five groups A-E according to the percentage (P') of examinees with external exposure ≥1 mSv based on the data of individual radiation dose (unpublished) , with P'(A) ≥66%>P'(B) ≥55.4% >P'(C) ≥5.7% >P'(D) ≥0.67%>P'(E). [8] In the present O-model, four areas O1-O4 of reasonable statistical size were constructed with similar borders of the percentage (P) of residents who received an external radiation exposure ≥1 mSv: P (O2)≥55.4%>P(O1) ≥5.7% >P(O3) ≥0.9% >P(O4), based on the published data of FHMS basic survey (Figure 1A).

S-model: Suzuki studied the area dependence of thyroid cancer prevalence according to the screening schedule of E-I, which proceeded from expected highest dose area to lowest dose area [6]. In S-model, Suzuki's four areas, S1:13 municipalities of evacuation zone (E-I in FY2011), S2:12 municipalities (E-I in FY2012), S3:17 municipalities in Iwaki and Soma (E-I in FY2013 first half), and S4: Aizu (E-I in FY2013 second half) were adopted (Figure 2A).

Maps in Figures 1A and 2A show that areas O1 and S1 include the evacuation zone, O2 and S2 include the central region with big cities of Fukushima and Koriyama, O3 and S3 are Iwaki and Soma, O4 and S4 include the Aizu area. Dose responses of the four areas in two models were analyzed by simple regression analysis of Microsoft Excel. Odds ratio (OR) and 95% confidence interval (CI) of thyroid cancer proportion were estimated according to the formula of Rothman [20].

Results

Dose dependence of thyroid cancer based on the O-model

External dose estimated from the FHMS basic survey, effective dose based on UNSCEAR report, number of primary examinees, confirmed or suspected thyroid cancer cases, thyroid cancer proportion per 100,000 people, OR and 95%CI for E-I, E-II, and E-I+II are listed in Table 1. Among 187 cases that were positive by FNAC in E-I+II, 150 cases of 151 surgical cases were confirmed to be malignant. One case found to be benign during surgery was not included in cancer cases. Cancer proportions /100,000 in E-I+II is the sum of those for E-I and E-II. Because screening E-II was carried out for residents excluding confirmed or suspected cancer cases detected in E-I, cancer proportion in E-I and E-I+II represent approximately the prevalence proportion after 4 years and 6 years of the nuclear accident, and cancer proportion in E-II represents approximately the incidence proportion of thyroid cancer in FY2014-2015.

Table 1. External dose, effective dose, and cancer proportion / 100,000 (CP) in E-I, E-II, and E-I+II, in O-model.

Area	External dose/ mSv	Effective dose/ mSv	E-I (FY2011–2013)			E-II (FY2014–2015)				E-I+II (FY2011–2015)		
			Examinees	Cancer cases	CP	Examinees	Cancer cases	CP	OR (CI)	Cancer cases	CP†	OR (CI)
O1	0.74	4.14	55,290	22	39.8	47,918	13	27.1	1.67(0.6-4.7)	35	66.9	1.33(0.7-2.4)
O2	1.37	4.98	134,790	51	37.8	120,015	40	33.3	2.06(0.8-5.2)	91	71.2	1.41(0.8-2.4)
O3	0.51	2.65	78,252	31	39.6	71,761	13	18.1	1.12(0.4-3.1)	44	57.8	1.14(0.7-2.0)
O4	0.2	1.66	32,141	11	34.2	30,817	5	16.2	1 (Ref.)	16	50.4	1 (Ref.)
Average/total	0.91	3.85	300,473	115	38.3	270,511	71	26.2		186	64.5	

† Cancer proportion /100,000 in I + II is the sum of those for I and II.

ORs of thyroid cancer proportion for E-II and E-I+II using the least contaminated area Aizu (O4) as reference decreased in the order O2>O1>O3>O4, which agreed with the order of decreasing FHMS external dose and UNSCEAR effective dose. This suggests an association between thyroid cancer proportion and radiation exposure. The correlation between FHMS external dose and UNSCEAR effective dose in O-model was rather high ($R2=0.91$ and $p=0.048$, Figure 1B).

The proportion of thyroid cancer per 100,000 versus FHMS external dose and UNSCEAR effective dose in E-I, II and I+II are plotted in Figures 1C and 1D, respectively. The regression line and statistics of regression analysis, R2, t- and p-values for slope parameters, are shown in Figure 1. Dose dependence of cancer proportion is not obvious in E-I, in accordance with Ohira et al.'s conclusion that regional differences in external dose were not associated with thyroid cancer prevalence in the 4 years after the accident [8]. However, linear dependences of cancer proportion in E-II (FY2014–2015) and E-I+II (FY2011–2015), detected during 4–6 years from exposure and after 6 years from exposure, respectively, on FHMS external dose and UNSCEAR effective dose were very high, comparable to or higher than the correlation between doses. Prevalence of thyroid cancer after 6 years from exposure (E-I+II) was observed to increase linearly to UNSCEAR effective dose with positive coefficient 6.3 (95% CI = 5.0, 7.5) (cancer cases / 100,000 / mSv) in the 1.6–5 mSv effective dose range.

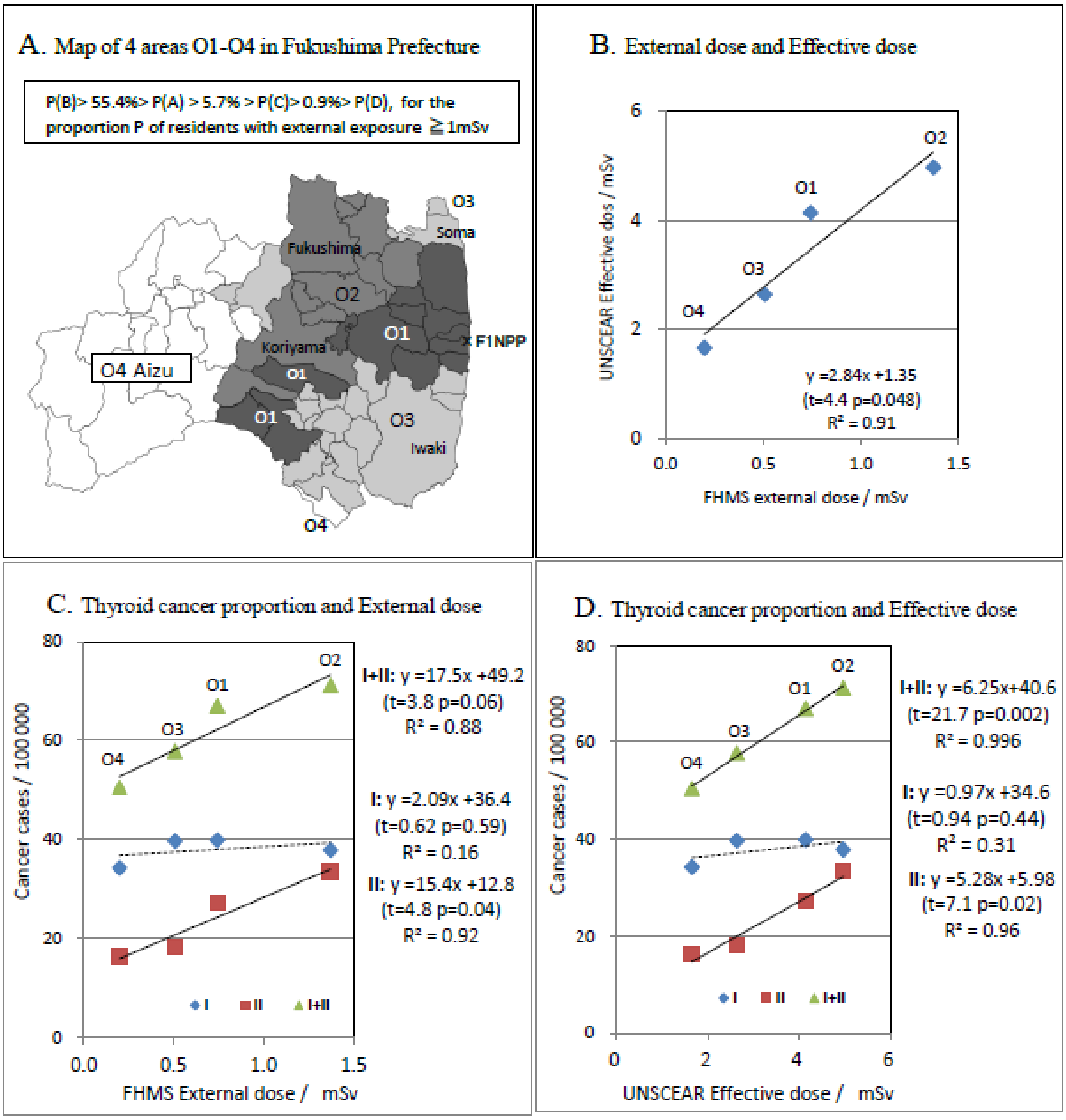

Figure 1. Dose response of thyroid cancer proportion in O-model.
A) Map of four areas O1-O4 in O-model constructed from the percentage of residents exposed ≥1 mSv external dose: P(O2) ≥ 55.4% > P(O1) ≥ 5.7% > P(O3) ≥ 0.9%> P(O4) on the basis of the FHMS basic survey. B) Correlation between FHMS external dose and UNSCEAR effective dose. C) Proportion of thyroid cancer per 100,000 residents aged ≤ 18 years on March 11, 2011 versus FHMS external dose, and D) UNSCEAR effective dose in E-I (FY2011–2013), E-II (FY2014-2015), and E- I+II (FY2011–2015). Dose dependence of thyroid cancer proportion was not observed in E-I for both doses. Linear dependence of cancer proportion in E-II and E-I+II on FHMS external dose and UNSCEAR effective dose were observed.

Dose dependence of thyroid cancer based on the S-model

The results of analysis for areas divided according to the initial screening schedule (S-model) are listed in Table 2. ORs of thyroid cancer proportion in E-II and E-I+II, using the least contaminated area Aizu (S4) as reference, decreased in the order S1>S2>S3>S4, which agreed with the order of decreasing UNSCEAR effective dose, and disagreed partially with the decreasing order of FHMS external dose.

The correlation between FHMS external dose and UNSCEAR effective dose was not high with R2=0.73 (Figure 2B). Cancer proportion per

100,000 versus FHMS external dose and UNSCEAR effective dose in E-I, E-II, and E-I+II are plotted in Figure 2C and 2D, respectively.

Dose dependence of cancer proportion was not obvious in E-I for both doses. This agreed with Suzuki's conclusion that regional differences in the external dose were not associated with thyroid cancer prevalence in the 4 years after the accident [6].

However, cancer proportions in E-II and E-I+II show linear response to UNSCEAR effective dose with R2>0.85 and p<0.08 as shown in Figure 2D. Prevalence of thyroid cancer after 6 years from exposure in E-I+II was observed to increase linearly to effective dose with positive coefficient 7.8 (95% CI = 2.5, 13.0) (cancer cases / 100,000 / mSv) in 1.6 – 5.5 mSv effective dose range. Coefficients of regression lines and linear ranges of effective dose in O- and S-models show reasonable agreement.

On the other hand, plots of cancer proportion in E-II and E-I+II versus FHMS external dose show scatter from linearity. Similar poor correlation patterns between external dose and effective dose (Figure 2B) and between cancer proportion and external dose (Figure 2C) may be the result of an inadequacy of external dose estimation by HHMS, although the estimation was based on detailed behavioral data of 27% of residents in Fukushima Prefecture. FHMS explains that the gamma ray dose rate was the highest in evacuation area S1 followed by the north and middle parts of S2 [19].

Table 2. External dose, effective dose, and cancer proportion / 100,000 (CP) in E-I, E-II, and E-I+II, in S-model.

Area	External dose/mSv	Effective dose/mSv	E-I (FY2011–2013)			E-II (FY2014–2015)				E-I + II (FY2011–2015)		
			Examinees	Cancer cases	CP	Examinees	Cancer cases	CP	OR (CI)	Cancer cases	CP †	OR (CI)
S1	0.93	5.54	41,810	14	33.5	34,557	17	49.2	3.17(1.2-8.6)	31	82.7	1.62(0.9-2.9)
S2	1.29	4.59	139,337	56	40.2	124,606	35	28.1	1.81(0.7-4.6)	91	68.3	1.34(0.8-2.2)
S3	0.55	2.65	85,606	33	38.6	79,140	14	17.7	1.14(0.4-3.2)	47	56.3	1.10(0.6-1.9)
S4	0.19	1.67	33,720	12	35.6	32,208	5	15.5	1 (Ref)	17	51.1	1 (Ref)
Average/total	0.91	3.86	300,473	115	38.3	270,511	71	26.2		186	64.5	

† Cancer proportion /100,000 in I + II is the sum of those for I and II.

Many of the S1 residents evacuated from their original location, which is a possible reason for the average dose of S1 is being lower than the average dose of S2. However, if evacuees in S1 first moved to S2 or S3, the external dose of residents in S1 is presumed to be greater than or comparable to the one of S2. (Compare Figure 2A with the integrated amount of Cs-137 on the ground surface, Figure 5 in [16]). External dose decreasing in the order of decreasing effective dose S1>S2>S3 >S4, seems reasonable because external dose is the dominant part of the UNSCEAR effective dose.

Low correlation between FHMS external dose and UNSCEAR effective dose with R2=0.73 in model-S suggests considerable uncertainties in dose estimations, in FHMS external dose or in both, because exact estimation of external and effective doses should give nearly perfect correlation R2=1.

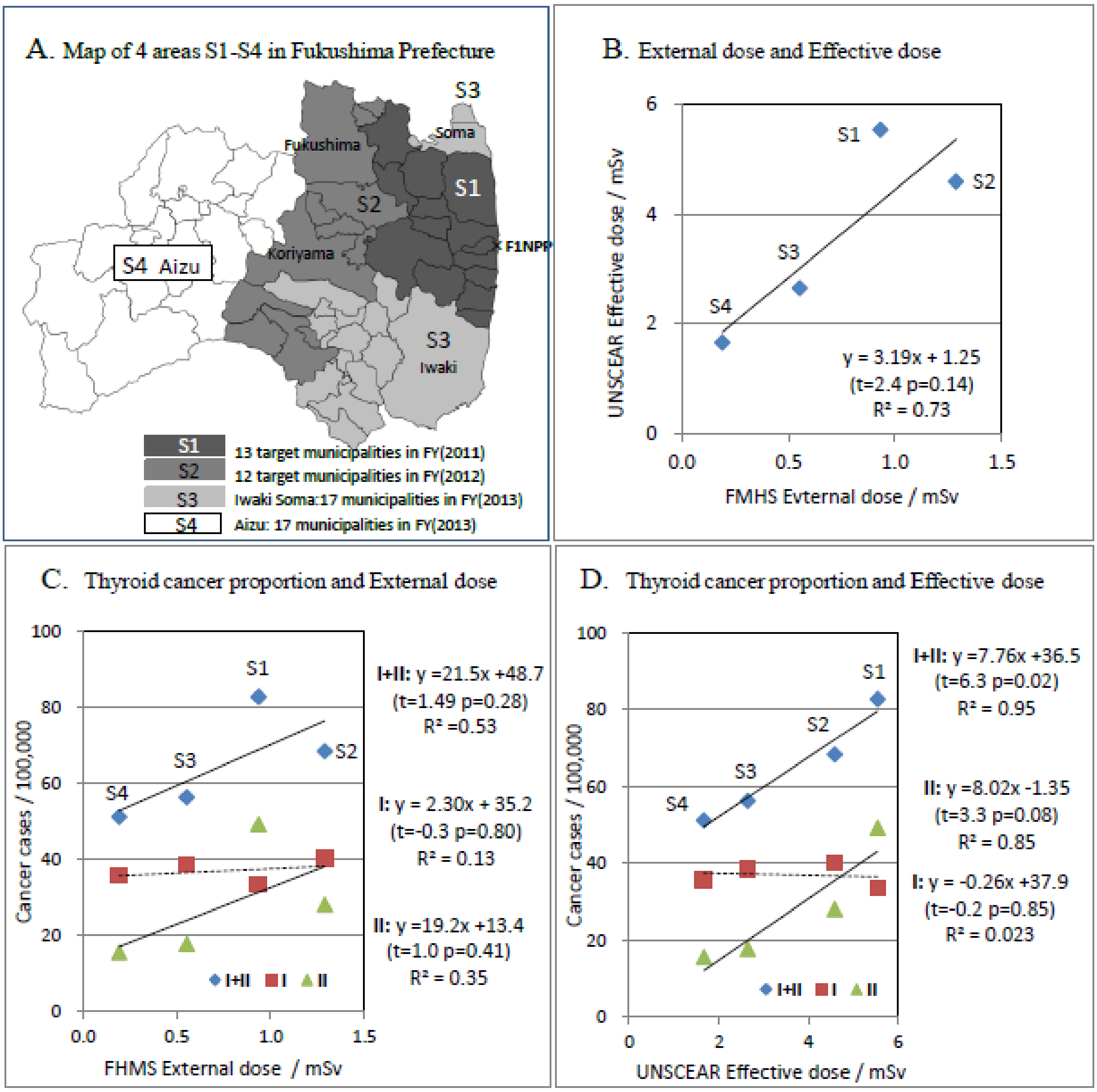

Figure 2. Dose response of thyroid cancer proportion in S-model (A) Map of four areas S1-S4 in S-model according to the initial screening schedule from expected highest dose to lowest dose area. S1: 13 municipalities of evacuation zone, S2: 12 municipalities, S3: 17 municipalities in Iwaki and Soma, and S4: Aizu. (B) Correlation between FHMS external dose and UNSCEAR effective dose. (C) Proportion of thyroid cancer per 100,000 residents versus FHMS external dose, and (D) UNSCEAR effective dose in E-I, E-II, and E-I +II. Dose dependence of thyroid cancer proportion was not observed in E-I for both doses. Linear dependences of thyroid cancer proportion on UNSCEAR effective dose in E-II and E-I+II were observed to be dominant.

Discussion

Linear dose dependence in 6 years after the accident

Dose dependence of thyroid cancer prevalence in Fukushima has been analyzed in the first and second round screening for external dose estimated by FHMS and effective dose estimated by UNSCEAR. In both O- and S- models, no dose dependence of thyroid cancer proportion was observed in E-I. However, thyroid cancer proportion in the next 2 years, E-II, and after 6 years from the accident, E-I+II, have tendency to increase as doses increase in both models.

In O-model, which classified municipalities into four areas in the order of decreasing percentage of residents with external exposure ≥1 mSv, thyroid cancer proportion in E-II and E-I+II were found to increase linearly to FHMS external dose and UNSCEAR effective dose. In S-model of area division according to the initial survey schedule from expected high dose area to low dose area, linear relation between cancer proportion and UNSCEAR effective dose was clearly observed in E-II and E-I+II, while dose response of cancer proportion to FHMS external dose was weak probably because of the inadequacy of external dose estimation by FHMS.

These observations suggest that the association between pediatric and adolescent thyroid cancer in Fukushima and radiation exposure due to the accident is highly probable. If cancer prevalence comes from mass screening effect and cancer patients distribute randomly in Fukushima Prefecture, it would be impossible to see linear prevalence-dose relation by selecting reasonable area division. Comparison of the results of analyses by O- and S-models shows that UNSCEAR effective dose gives a clear explanation for dose dependence of the proportion of pediatric thyroid cancer in E-II and E-I+II, irrespective of models.

Absence of prevalence–dose relation in the first 4 years

In both O- and S- models, no dose dependence of the prevalence was observed in E-I (FY2011-2013), in accordance with conclusions by Ohira et al., [8] Suzuki, [6] and Suzuki et al. [7] that significant area differences in thyroid cancer prevalence were not observed in the first 4 years after the accident.

Difference between dose dependences in the first 4 years and in 6 years after exposure suggests that a possible origin of thyroid cancer prevalence in Fukushima was shortly before thyroid screening. Absence of the prevalence–dose relation in E-I may be due to the difference of intervals from the accident to screening. If cancer occurs due to radiation exposure, the proportion of cancer will increase with elapsed time from exposure. The interval between the accident and screening in E-I changes from ~1.4 years for the expected highest dose area (evacuation zone S1) to ~2.8 years for the lowest dose area (Aizu: O4 and S4) [8], and higher cancer prevalence expected in high-dose areas may have been counteracted by the short interval from exposure to screening. The elapsed time from exposure is around 3.9~4.7 years in E-I+II (FY2011–2015). Increasing cancer prevalence with radiation dose seems to dominate over the effect of relatively small difference of the elapsed time in E-I+II. Thyroid cancer proportion in E-II plotted in Figure 1C and 1D show linear dependence on doses with nearly the same coefficient as in E-I+II. The high coefficient in E-II seems to be the result of high discovery rate of cancers developed between E-I and E-II in high-dose areas because of the low discovery rate in E-I scheduled shortly after the accident.

The prevalence ORs of groups A-D compared with the lowest dose and latest examined group E in E-I were adjusted for elapsed time from the accident in the wrong, low OR direction by Ohira et al. [8]. On the other hand, Tsuda et al. adjusted ORs of higher dose areas for elapsed time from exposure, which indicated a dose–response relationship in E-I [21].

Uncertainty in the dose-dependent prevalence

In order to confirm the uncertainty in the dose-dependent cancer proportion in Figures 1 and 2, the ORs and 95% CIs of thyroid cancer prevalence in E-I+II are plotted versus UNSCEAR effective dose for O- and S-models. (Figure 3) Although CI for each area includes 1, the prevalence ORs show perfect linear prevalence-effective dose response with $p=0.002$ in O-model and $p=0.02$ in S-model. The radiation exposure dose due to diffusion of radioactive plumes should change continuously across regions, and it seems natural that the CIs of the prevalence ORs spread and overlap each other.

Difference in prevalence of areas without overlap of CIs would be unnatural unless there were walls between areas that can control the plume. Additionally, the uncertainties of the dose-estimates themselves give rise to uncertainty in the prevalence-dose response. It is important that linear prevalence-dose relation exists with high precision (low p-value) irrespective of uncertainties in both the prevalence data and dose estimations. Prevalence-dose response may easily disappear if the analysis is based on inadequate dose estimation.

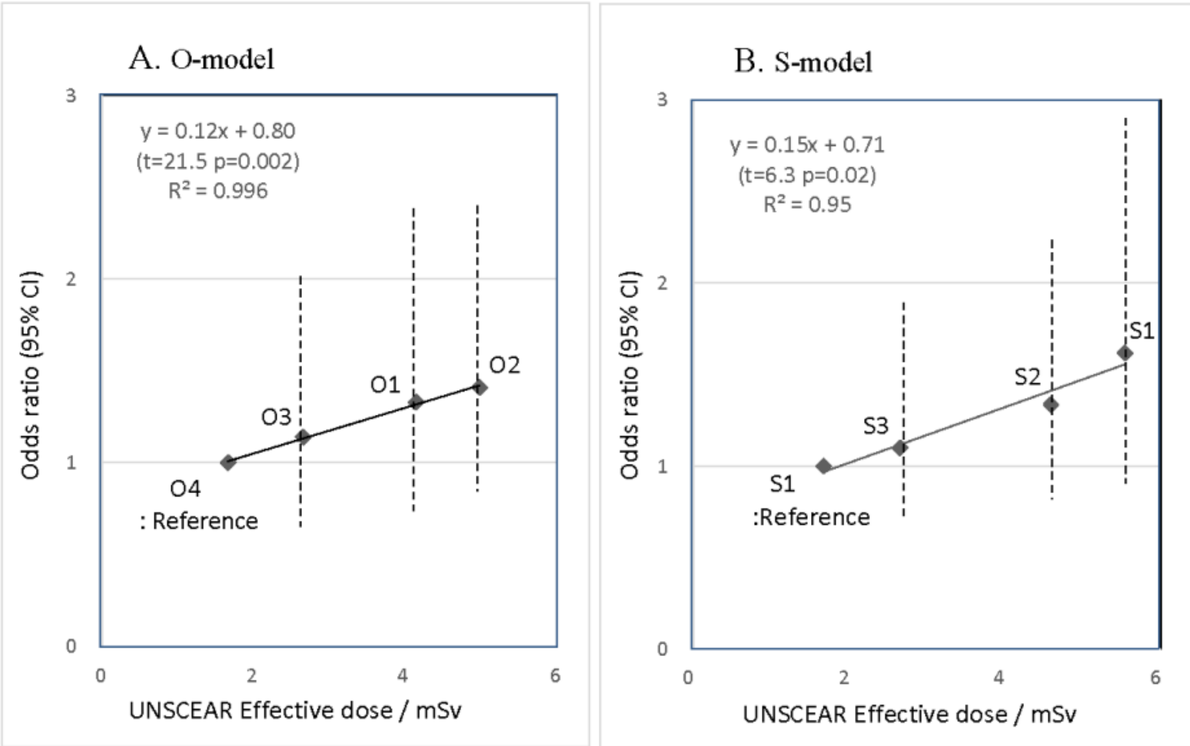

Figure 3. ORs and 95% CIs of thyroid cancer prevalence in E-I+II (2011-2015) versus UNSCEAR effective dose (A) O-model, (B) S-model. Although CI for each area includes 1, the prevalence ORs show linear effective dose response with p=0.002 in O-model and p=0.02 in S-model.

Evaluation of pediatric thyroid cancer by FHMS

FHMS evaluates pediatric thyroid cancer in Fukushima in the Basic survey reports 2012-2019 as follows. Because previous epidemiological studies indicate no significant health effects at doses ≤100 mSv, radiation doses estimated so far are unlikely to cause adverse effects on health, although this conclusion is based on external radiation doses [11]. Contrary to the FHMS view, linear external dose response of thyroid cancer prevalence with positive coefficient of 17.5 (cancer cases /100,000 /mSv) was observed in 0.2–1.4 mSv external dose range in O-model (Figure 1C). Linear dose response of thyroid cancer prevalence was also observed in the 1.6 – 5.5 mSv UNSCEAR effective dose range. Members of FMU often reported that thyroid cancer cases diagnosed in Fukushima were not the result of radiation exposure from the nuclear accident. One reason was the extremely low radiation dose in Fukushima [6]. However, a comparison of radiation doses in Fukushima and Chernobyl will show that both doses may be comparable. According to UNSCEAR 2013 Report, effective dose for adults around Fukushima city (Figures 1A and 2A) in Fukushima Prefecture was 3.5-4.3 mSv (Figure VI in [22]), while the weighted average of effective dose of each soil contamination district by the number of its population in Gomel oblast, Belarus were 3.65 mSv. (UNSCEAR 2008 Report, Table B13 in [23]) Gomel was the highest estimated collective dose area in Chernobyl (B65 in [23]).

The ratio of average values of external dose by FHMS [11], effective dose, and thyroid dose in UNSCEAR report [12,13,24] is around 1:5:30. External dose by FHMS is one-fifth of the effective dose estimated by UNSCEAR, although FHMS uses the term “effective dose” in the same meaning as “external dose” [11]. This seems to be a clear underestimation of effective dose for the public. It should be thyroid dose, ca. 25times of the external dose, to be compared with 100 mSv in the case of thyroid cancer. Thyroid doses of 10-years-old children and 1-year-old infants were estimated to be 15-83 mSv in Fukushima prefecture by UNSCEAR [13,24] and were 15-122 mSv in WHO estimation (Table 6 in [16]).

Thyroid cancer might well be expected considering that stable potassium iodide (KI) tablets were not distributed to children except one municipality distributed at its discretion, and so many were unprotected from thyroid cancer in the nuclear disaster. In addition to this failure, urgent need for measurements of I-131 activity in thyroid were warned, but neglected by local authorities [14].

Was there any overdiagnosis of thyroid cancer in Fukushima?

The formal view of FHMS committee is that thyroid cancer detected in E-I was unlikely to be associated with radiation exposure [4]. In a recent paper, Otsuru et al. concluded that ultrasound screening can identify many detectable cancers from a large pool of nonclinical and subclinical thyroid cancers among young people [25]. This conclusion was derived mainly from the similarity of basic clinical characteristics and age patterns between the first and second examinations. They discuss as if there were some overdiagnosis of thyroid cancer in E-I and E-II, and consider that an improvement in screening strategy will be urgently needed to avoid overdiagnosis.

Suzuki submitted “Surgery cases of thyroid cancer” to Oversight Committee Meeting for FHMS on Aug. 31, 2015 as follows [26]. Among 96 Surgery cases of thyroid cancer, in which 93 cases were papillary carcinoma, mild extrathyroidal infiltration pEX1 in 38 cases, lymph node metastasis in 72 cases, multiple lung metastasis in 2 cases, no lymph node metastasis, extrathyroidal invasion, distant metastasis (pT1a pN0 M0) were in 8 cases.

These characteristics of thyroid cancer in Fukushima are similar to the characteristics of radiation related thyroid cancer in Chernobyl [27]. Papillary thyroid carcinoma was the prevalent type (94–98%) and most patients had an advanced stage with a high rate of local lymph node involvement and elevated incidence of distant metastases, including lung metastases. Chernobyl cancers were more aggressive than sporadic cancers despite short-latency. It is interesting that the authors including Yamashita now in FMU, recommended radical thyroid surgery followed by radioiodine treatment.

Were the surgery cases in Fukushima overdiagnosis? Although Otsuru et al. of FMU concern about avoiding overdiagnosis, we should pay more attention to the possibility of cancers becoming serious because of delayed discoveries.

Inaccuracy of the number of thyroid cancer patients

FHMS reports were found not to represent accurately the current status of thyroid cancer patients in Fukushima. Thyroid Cancer Child Fund, which provides aid to people who were ≤ 18 years-of-age at exposure and diagnosed with thyroid cancer after the accident, reported that benefits payed until the end of FY2018 were for 120 people: 85 patients in Fukushima and 35 patients in 15 other prefectures, including 15 cases of radioactive iodine treatment and 8 reoperations due to recurrence or metastasis [28]. One of the benefit recipients, who was four-years-old at exposure and was diagnosed as thyroid cancer, was found not included in cancer cases of FHMS. Then it was announced by FMU that 11 confirmed thyroid cancer cases diagnosed by FMU Hospital, including the four-years-old child, were not included in FHMS data [29]. Among them, seven underwent confirmatory examination and were diagnosed as thyroid cancer during the medical follow-up period. The criteria of cytology examination and follow up for positives in the confirmatory examination are not clearly defined by FMU, and cancer cases diagnosed during follow up period were found not included in the FHMS data [30]. Percentage of cytology examinees has decreased by one-seventh from 64.3% in FY2011 to 9.1% in FY2015 [2,3]. As Ohira et al. of FMU pointed out, the rate of FNAC in confirmatory examination were strongly associated with the detection rate of thyroid cancer [31]. It seems that FMU could control cancer proportion through adjusting the percentage of FNAC.

FHMS canceled the presentation of data by municipality from the third-round examination so that researchers outside FMU cannot study the dose dependence of long-term screening results [32]. In the present analysis of dose response of thyroid cancer proportion for two independent dose estimations in two models, we expected to comprehend the characteristics of childhood thyroid cancer in Fukushima despite inadequacies of the data.

Conclusion

1. On the bases of O-model according to percentage of residents exposed ≥1mSv, thyroid cancer prevalence after 6 years from the accident (E-I+II)

and incidence during 4-6 years after the accident (E-II) showed linear dose dependence in the 0.2–1.4 mSv FHMS external dose range. Cancer prevalence in E-I+II increased linearly to UNSCEAR effective dose in the 1.6–5.5 mSv range with positive coefficient 6.3 (95% CI = 5.0, 7.5) (cancer cases / 100,000 / mSv).

2. In S-model, linear relation between cancer proportion and UNSCEAR effective dose was clearly observed in E-II and E-I+II, while response of cancer proportion to FHMS external dose was weak probably because of the inadequacy of external dose estimation by FHMS.

3. Observed linear dose response of thyroid cancer proportion in E-II and E-I+II, using two models and for two independent dose estimations, suggests that the association between pediatric and adolescent thyroid cancer in Fukushima and radiation exposure due to the accident is highly probable.

4. Regional differences were not observed in the first 4 years presumably because of the short interval from exposure to initial screening in the survey schedule of high-dose areas. It is impossible to attribute high prevalence of thyroid cancer in Fukushima only to a mass screening effect that does not depend on radiation dose and elapsed time from exposure.

5. Similarities between thyroid cancer cases in Fukushima and radiation related thyroid cancer in Chernobyl suggests the importance of thyroid cancer screening in a long term with disclosure of data to the public.

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