

Fukushima Thyroid Examination Fact Sheet: September 2017

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This fact sheet reviews the current status of the Thyroid Ultrasound Examination (TUE) in Fukushima Prefecture. In its seventh year, all the data and information from the TUE have become quite large and complex. Drawing from official meetings, documents, data and publications—some available only in Japanese, some only in English, this fact sheet is intended to act as an English overview.

Introduction

On October 9, 2011, Fukushima Prefecture began the TUE on about 360,000 residents who were age 18 or younger at the time of the March 11, 2011 Fukushima nuclear accident. As the exposure to radioactive iodine dramatically increased the incidence of pediatric thyroid cancer cases after the 1986 Chernobyl nuclear accident, the TUE was implemented as part of the Fukushima Health Management Survey (FHMS),¹ to monitor the exposed children in Fukushima Prefecture. The majority of Fukushima residents did not receive iodine tablets for protection of their thyroid glands.

The FHMS is funded by the central government² and commissioned by the prefectural government to the prefectural-run Fukushima Medical University (FMU).³

Screening protocol⁴

The TUE, conducted every 2 years up to and every 5 years beyond age 20, consists of the primary and confirmatory examinations. The primary examination uses thyroid ultrasound screening to detect cysts and/or nodules. Cysts and nodules that meet certain diagnostic criteria (category B and above, as explained later) are recommended to undergo the confirmatory examination for more detailed ultra-

sound examination including Doppler ultrasound and elastography as well as urine and blood testing. Suspicious cases undergo fine-needle aspiration cytology (FNAC) to examine thyroid cells for signs of malignancy. FNAC positive cases are followed by surgery or observation. Definitive diagnosis of thyroid cancer requires pathological examination of surgically excised thyroid tissue. Thus the TUE results are reported as the number of suspected or confirmed cancer cases. (Note: So far there has been only one case—early in the screening process—that turned out to be benign after surgery).

The first round was expected to produce a baseline*¹ for this population due to a supposed latency of 4 years for radiation-induced thyroid cancer in children based on the Chernobyl data. There has been no thyroid cancer screening of similar magnitude and quality in unexposed children to compare to. Thus the first round screening was called “Initial Screening” at first and later renamed “Preliminary Baseline Screening (PBS).” The second and third rounds are called “First Full-Scale Screening” and “Second Full-Scale Screening,” respectively.

The first round of the TUE was scheduled to be conducted from October 9, 2011 through March 31, 2014, with each fiscal year—from April through the following March—covering residents from a set of municipalities grouped in a descending order of the air dose level of radiation.⁵ In order to boost the participation rate (by 1.5% to 81.7%), the first round was continued through April 30, 2015, concurrent with the first year of the second round. This meant that first time participants were still being registered for the first round while others were already going through the second round.*²

*1—Scientific validity of establishing a baseline in the exposed population is unclear.

*2—Confirmatory examinations from the second and third rounds might be simultaneously ongoing, or there could be

The second round began in April 2014, immediately after the first round was supposedly completed and included residents who were born between April 2, 2012 and April 1, 2013.⁶ The primary examination of the second round with a participation rate of 71.0% and progress rate of 100.0% is essentially complete. But the confirmatory examination with a participation rate of 82.3% and progress rate of 95.4% is still ongoing.

The third round began on May 1, 2016 and is scheduled to run through March 2018—the end of Fiscal Year 2017.⁷ As of March 31, 2017, 120,596 out of the survey population of 336,616 residents—about 45,000 fewer than previous rounds as the milestone screening participants are excluded^{*3}—have participated in the ongoing primary examination at a participation rate of 35.8%. The confirmatory examination began on October 1, 2016 with a participation rate of 48.0% and progress rate of 67.8% so far.

The unique diagnostic categories of A1, A2, B and C for the TUE were established by the “Sectional Meeting for Considering the Diagnostic Criteria of the Thyroid Ultrasound Examination” (referred as the Diagnostic Criteria Subcommittee^{*4} from here in). These diagnostic categories are:

- A1: no nodules or cysts found
- A2: nodules ≤ 5.0 mm or cysts^{*5} ≤ 20.0 mm
- B: nodules ≥ 5.1 mm or cysts ≥ 20.1 mm
- C: requiring immediate confirmatory examination

The A1 and A2 categories are followed in the subsequent round of screening two years later. The B and C categories require confirmatory examination. There has only been one case of the C category which requires confirmatory examination immediately.

Results of the Thyroid Ultrasound Examination

The TUE results are reported at the quarterly Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. English translation of the results are found on the website of the Office of International Cooperation, Radiation Medical Science Center, Fukushima Medical University.⁸ The most current official summaries in English are found in Chapters 14 and 15 of “Thyroid Cancer and Nuclear Accidents.”^{9, 10}

The first cancer case was reported on September 11, 2012,¹¹ exactly a year and a half after the accident. The first 4 cancer cases from the second round were reported on December 25, 2014.¹² At present, the second round results are yet to be finalized due to the still ongoing confirmatory examination, but the most recent data released on June 5[†], 2017,¹³ show 71[†] suspected cancer cases including 49[†] cases surgically confirmed. The current third round screening has so far detected 4 suspected cancer cases with 2 cases surgically confirmed.¹⁴

The Latest Results

Table 1 shows the most recent results reported on June 5, 2017.¹⁵

Transparency and integrity of data

Once the confirmatory examination reveals the need for a closer clinical follow-up, FNAC and/or surgery, the case is no longer part of the TUE and

significant delays in conducting confirmatory examinations due to logistical issues such as the lack of manpower. Originally scheduled screening periods are essentially spread over a longer time period, overlapping with the next round of screening. A precise interpretation of results from each round of screening might be nearly impossible.

*3—Conducted every 2 years up to age 20, the TUE transitions at age 25 to milestone screenings to be conducted every 5 years. Some residents are beginning to participate in the age 25 milestone screening, and if they have never participated in the TUE, their milestone screening results will be added to the second round screening results. Thus the number of the second round screening participants is expected to increase even though the screening period technically ended in March 2016.

*4—The Diagnostic Criteria Subcommittee consists of members from the following seven organizations: Japan Thyroid Association; Japan Association of Endocrine Surgeons; Japan Association of Thyroid Surgery; The Japan Society of Ultrasonics in Medicine; The Japan Society of Sonographers; The Japanese Society for Pediatric Endocrinology; and Japan Association of Breast and Thyroid Sonology. The minutes of the proceeding (in Japanese) have revealed that the Diagnostic Criteria Subcommittee have met regularly behind closed doors where pre-released versions of the results were discussed amongst thyroid experts whose names are not publicized. (Accessible at https://www.i-repository.net/il/meta_pub/ssearch)

*5—“Cysts” in the TUE are said to be colloid or simple cysts with no malignant potential: cysts with any solid components are classified as “nodules” by the size of the cysts themselves. In other words, a 10.0 mm cyst with a solid component would be classified as a 10.0 mm nodule and thus placed in the B category.

Table 1—Latest results (data as of March 31, 2017) *Includes a single case of benign nodules

Screening round	Number of suspicious FNAC cases	Number of surgical cases	Number of confirmed cancer cases	Papillary thyroid cancer	Poorly differentiated thyroid cancer	Other type of thyroid cancer
1st	116*	102*	101	100	1	0
2nd	71	49	49	48	0	1
3rd	4	2	2	2	0	0
Total	191*	153*	152	150	1	1

enters regular medical care under the national health care system. On the premise that “disclosure of clinical information is prohibited in principle,” data from such “follow-up” cases are not shared with the Oversight Committee or Fukushima residents although they have been presented at academic meetings and published in medical journals.

Recently it became known that FMU has not publicized all cancer cases, let alone details, because only cancer cases diagnosed *directly* during the confirmatory examination are reported to the Oversight Committee. This came to light in March 2017 when an unreported cancer case was discovered in a boy who was 4 at the time of the accident.¹⁶ FMU explains that cases followed up under regular medical insurance are deemed outside the boundaries and responsibilities of the TUE, with no obligation or actual system to collect such data for reporting.^{*6} Currently there are about 1250 follow-up cases from the first round, and there is no way to know how many cancer cases might have been diagnosed in this group, if any.

This means the FMU studies^{17, 18} using the official, incomplete data lack scientific integrity.

Surgical and pathological features

Due to the reasons explained above, surgical and pathological details of the cases are not readily available. The most detailed and updated—albeit incomplete—surgical and pathological information on 125 cases operated at FMU, has been published in the aforementioned book, “Thyroid Cancer and Nuclear Accidents.” (The presentation slides can be downloaded from the Radiation Medical Science Center website¹⁹ and information on the slides is explained in detail on the author’s blog post²⁰).

Of 125 cases, 121 (96.8%) were ipsilateral and 4 (3.2%) were bilateral. Hemithyroidectomy was conducted in 114 cases (91.2%) while 11 cases (8.8%) underwent total thyroidectomy.^{*7} All cases underwent the central lymph node dissection, and 24 cas-

es also had dissection of the lateral neck lymph nodes (20 unilateral and 4 bilateral). The intraoperative nerve monitoring system (IONM) was used in all cases to prevent recurrent laryngeal nerve (RLN) injury.

There were no surgical complications such as hypoparathyroidism, permanent RLN palsy, or postoperative bleeding. One case had persistent RLN palsy despite the use of the IONM system.

Histopathological diagnosis showed 121 cases (96.8%) of papillary thyroid cancer (PTC), 3 cases of poorly differentiated thyroid cancer (PDTC), and 1 case of thyroid cancer categorized as “other” in Japan’s thyroid cancer management guideline. Subtypes of 121 PTC included 110 classical variants, 4 follicular variants, 3 diffuse sclerosing variants and 4 cribriform morula variants associated with familial adenomatous polyposis. A special mention was made that no case of solid variant of PTC was found. Absence of solid variant PTC has been one of the distinguishing points between Fukushima and Chernobyl cases.

However, 2 of 3 PDTC cases—one each from FY2011 and FY2012—were reported to have been reclassified as PTC with unspecified subtypes.⁵ Existence of the solid variant PTC in Fukushima is confirmed in a recent study²¹ by Suzuki et al., that covers childhood thyroid cancer cases treated at FMU including cases diagnosed during the TUE: “Cases previously classified as poorly differentiated thyroid cancer in the Sixth Edition of Thyroid Cancer Management Guidelines are reclassified as solid variant PTC in the Seventh Edition. Solid variant PTC is known to be not uncommon in pediatric thyroid cancer cases in Japan, but there have been extremely few cases operated in Fukushima at this time.”

The post-operative TNM classification (Table 2) shows about 60% of tumors with a diameter of 20 mm or less (pT1a & pT1b), 78% with lymph node metastasis (pN1a & pN1b), and 39% with cancer cells spreading outside the thyroid (pEx1).^{*8} Of 44

*6—The case of the 4-year-old remains excluded from the official count.

*7—Japan’s clinical guidelines recommend hemithyroidectomy with prophylactic lymph node dissection unless total thyroidectomy is absolutely indicated.

*8—Review of Suzuki’s presentation video shows that 49

Table 2—Pre-operative (clinical) and post-operative (pathological) TNM findings*⁹
(T = tumor size, N = lymph node metastasis, Ex = extrathyroidal extension, M = distant metastasis)

Pre-op	cTNM	Number(%)	Post-op	pTNM	Number(%)
cT	1a	44(35.2%)	pT	1a	43(34.4%)
	1b	57(45.6%)		1b	31(24.8%)
	2	12(9.6%)		2	2(1.6%)
	3	12(9.6%)		3	49(39.2%)
	4	0		4	0
cN	0	97(77.6%)	pN	0	28(22.4%)
	1a	5(4.0%)		1a	76(60.8%)
	1b	23(18.4%)		1b	21(16.8%)
cEx	0	106(84.8%)	pEx	0	75(60.0%)
	1	19(15.2%)		1	49(39.2%)
	2			2	0
M	0	122(97.6%)			
	1	3(2.4%)			

(Note: Number of cases per Suzuki's presentation slides)

microcarcinoma cases (cT1a cN0M0), 33 had surgical indications such as suspicion of extrathyroidal extension (20), lymph node metastasis (1), RNL invasion (10), tracheal invasion (7), Graves disease (1), and ground-glass opacity of lungs (1).^{*10} Of these, 3 cases turned out to be pT1a pN0 pEx0, justifying surgery in 30 cases. Of 11 cases which opted for surgery against the recommendation of non-surgical observational follow-up, 2 turned out to be pT1a pN0 pEx0. Details of 3 cases with lung metastasis (M1) are: 1) male age 16 at exposure, cT3 cN1a, pT3 pN1a; 2) male age 16 at exposure, cT3 cN1b, pT2 pN1b; and 3) female age 10 at exposure, cT1 cN1b, pT3 pN1b pEx1.

Other thyroid cancer data

A direct comparison between the prevalence obtained by screening of the asymptomatic population and the incidence based on clinical diagnosis is con-

sidered inappropriate. As a reference, thyroid cancer incidence was calculated from the 2012 national incidence estimates in Japan²². For ages 0-19, it was 4.6 per million for both sexes, 1.4 per million for male, and 7.9 per million for female.^{*11}

Assuming all the suspicious FNAC cases are to be confirmed as cancer, excluding the single case surgically confirmed to be a benign nodule, the first round screening data yields thyroid cancer prevalence of 386 per million (116 cancer cases per 300,473 participants) for both sexes in those who were 0-18 years old at the time of the accident.

Officials refer to the so-called "3-prefecture study" as a control study.^{*12} Thyroid ultrasound screening was conducted on 4,365 children aged 3-18 in Aomori, Yamanashi and Nagasaki Prefectures. Cysts and nodules were found in similar proportions to the TUE²³ and one cancer case²⁴ was detected. However, the 3-Prefecture Study is an inappropriate control due to unmatched age range and sex distribution as well as the small size of the study cohort leading to a high margin of error.²⁵ A single case of thyroid cancer diagnosed in the 3-prefecture study makes a point estimate of 229 per 1 million with a 95% confidence interval of 6 to 1,276 per million,²⁶ but the

cases were pT3 due to minimal extrathyroidal extension, i.e. pEx1, rather than tumor > 4 cm limited to the thyroid.

*9—Japan's own clinical guidelines on cancers use essentially the same classification as the TNM classification, with the exception of the "Ex" notation which refers to the degree of extension outside the thyroid capsule: Ex1, equivalent to T3, means minimal extension (example: extension to sternothyroid muscle or perithyroid soft tissues); and Ex2, equivalent to T4, means further extension.

*10—Numbers in parentheses denote the number of cases which do not add up to 33 because some cases apparently meet more than 2 surgical indications listed.

*11—Thyroid cancer incidence (per million) by age groups for both sexes was 0 for ages 0-4, 0.6 for ages 5-9, 3.1 for ages 10-14, 13.6 for ages 15-19, and 37.5 for ages 20-24.

*12—If the screening prevalence from the first round were indeed the true baseline for Japanese children and no different than the prevalence in the 3-prefecture study, it would suggest nationwide occurrence of pediatric thyroid cancer of similar prevalence as well as stages of cancer progression.

wide bound of the confidence interval weakens the meaningfulness of the point estimate.

Tsuda et al. found a regional variability of the prevalence within Fukushima Prefecture as well as increased incidence rate ratios in most of Fukushima Prefecture compared to the national incidence rate.²⁷ Despite the claim by the authors that the study used standard epidemiological methods based on modern epidemiology, it generated seven criticisms²⁸⁻³⁴ and an authors' response.³⁵

The National Cancer Center research shows the observed/expected ratio of thyroid cancer prevalence to be as much as 30.8, attributing this increase to overdiagnosis.³⁶

Official stance on the high prevalence of thyroid cancer

FMU officials claim that the high prevalence of thyroid cancer diagnosed in Fukushima Prefecture is not excess occurrence but excess detection due to screening of asymptomatic individuals by highly sensitive ultrasound equipment, i.e. screening effect. As early as February 2013 officials began to use the term, "screening effect" and suggested that Fukushima cases constituted diagnosis of indolent "latent" cancer that would not cause any symptoms until much later date, i.e. overdiagnosis.

The National Cancer Center researchers say the high number of thyroid cancer cases detected during the first round is "difficult to explain by screening effect alone" in a document^{*13} submitted to the Thyroid Examination Evaluation Subcommittee in November 2014.³⁷ From available data, Shoichiro Tsugane and Kota Katanoda estimated the 2010 (pre-accident) prevalence of thyroid cancer in ages 0-18 in Fukushima Prefecture to be 2.0. The estimated prevalence was then compared with the first round results of 104 suspected and confirmed thyroid cancer cases at the time: The first round results were 61 times the estimated prevalence before the Fukushima accident. This increase was attributed to either excess occurrence due to some unknown reason or overdiagnosis, and not explainable by screening effect alone.

Researchers claiming screening effect and/or overdiagnosis do not appear to take clinical characteristics of these cancer cases into consideration. Perhaps defending validity of surgery, Suzuki refrains from claiming overdiagnosis, yet he does attribute the high number of thyroid cancer cases diag-

nosed to screening itself. Screening effect presupposes the cancer cases would not have been discovered until much later date, but aggressive features of even microcarcinoma (≤ 10 mm in diameter) make this a weak argument.

Prior diagnostic status of the newly diagnosed cancer cases

For 71 suspected cancer cases found during the second round screening, their first round results were: 33 A1, 32 A2 (7 nodules and 25 others such as cysts), 5 B, and one case that did not undergo the first round. The fifty-eight cases (33 A1 and 25 non-nodular A2) which had no lesions with malignancy potential suggest a few possibilities: 1) missed diagnoses; or 2) rapid growth of cancerous lesions in 2-3 years since the first round screening, contradicting the known latency of 4 years for childhood thyroid cancer.

The official explanation is neither. Akira Ohtsuru, the head of the TUE, states no missed diagnosis was confirmed when prior ultrasound images were reviewed. (This claim has not been independently verified). He rejects the notion of rapid growth, insisting that these are not "newly formed" but "newly detected." His explanations—officially documented in the minutes of the proceedings³⁸—are that even though some of the small nodules are very easy to detect by ultrasound, exceptions arise when 1) the border of the lesion is ambiguous, 2) the density of the lesion is so low that it blends into the normal tissue, or 3) the lesion resembles the normal tissue. Thus, the nodules were simply *not detected even though they were there*. Ohtsuru said that when such previously undetected nodules grow relatively large enough to become detectable by ultrasound, they might look as if they suddenly appeared. (This suggests a possibility that other "newly detected" cancer cases might exist at a similar proportion amongst individuals who received A1 or A2 assessments in the first round and elected not to participate in the subsequent rounds. Such cases would not be in the official count). Ohtsuru added that nodules that have already been detected by ultrasound do not appear to grow very rapidly in general.

An issue of the sex ratio

For thyroid cancer, the female to male ratio is nearly 1:1 in the very young, but it is known to increase with age^{39, 40} and decrease with radiation exposure.⁴¹ The overall female to male ratio was 1.97:1

*13—This document is available only in Japanese, but an unofficial English version is found on the author's blog post.

Table 3—thyroid cancer incidence calculated from the 2012 national incidence estimates in Japan²²

Number of thyroid cancer cases (female/male)						Combined age groups	
Year	Age groups (years)						
	0-4	5-9	10-14	15-19	20-24	5-14	5-19
2000	4/0	3/0	11/11	22/10	98/15	14/11	36/21
2001	5/0	4/0	11/8	25/11	103/14	15/8	40/19
2002	4/0	0/0	10/4	25/8	99/16	10/4	35/12
2003	0/0	0/3	11/0	21/1	89/34	11/3	32/4
2004	0/0	0/1	8/4	43/10	130/23	8/5	51/15
2005	0/0	0/0	4/0	22/18	110/36	4/0	26/18
2006	0/0	0/0	0/0	41/5	103/32	0/0	41/5
2007	0/0	0/0	6/0	41/14	97/34	6/0	47/14
2008	0/0	9/0	4/9	41/9	127/31	13/9	54/18
2009	0/0	0/0	4/3	35/10	97/55	4/3	39/13
2010	0/0	0/0	7/0	56/12	160/40	7/0	63/12
2011	0/0	0/3	18/10	47/10	214/88	18/13	65/23
2012	0/0	0/3	14/4	73/9	188/47	14/7	87/16
Total	13/0	16/10	108/53	492/127	1615/465	124/63	616/190
F:M	13:0	1.6:1	2.04:1	3.87:1	3.47:1	1.97:1	3.21:1

and 1.22:1 in the first and second round, respectively, both much lower than most recent clinically observed ratio of 7.9:1.⁴² Curiously, the FY2015 municipalities have consistently shown a higher number of males than females with the overall female to male ratio of 1:1.38, but this has not been officially investigated.

In February 2017, after explaining that the cancer registry showed the female to male ratio close to 1:1 up to around puberty and the autopsy data showed the female to male ratio of 1:1 or smaller in adults, Ohtsuru concluded, “It is scientifically expected that thyroid cancer screening in general leads to a smaller female to male ratio even in adults.”³⁸

His “scientific” explanation does not hold up. An analysis of the cancer registry data from 2000 to 2012 shows the female to male ratio up to puberty is closer to 2:1 than 1:1 (Table 3). Validity of extrapolation from autopsy data to screening is highly questionable, and there is no evidence to show thyroid cancer screening will yield a smaller female to male ratio as evident from South Korea⁴³ where active screening increased the incidence of thyroid cancer.

Official stance on radiation effects

FMU’s stance is summarized in the following excerpt⁹:

The relationship between a high prevalence of thyroid cancer and radiation exposure is

thought to be very unlikely because of several standpoints; e.g., a limited time interval after the accident, very low doses, age and geographic distributions of thyroid cancer patients, driver mutation patterns, and pathological characteristics. This finding suggests overdiagnosis due to screening effects over the past 5 years.

This statement is inconsistent and contradictory. For instance, by “over the past 5 years” officials are clumping the first and second rounds together, contradicting their own assertion that the first round *is* the baseline. Also, differences in age distributions stem from inappropriate comparisons of 1) different post-accident time periods—during (Fukushima) and after (Chernobyl) the first 3-4 post-accident years^{44, 45} or 2) during the first 3 years (Fukushima) and an unspecified number of years (Chernobyl).⁴⁶ When similar post-accident periods were compared, the age distribution of cancer cases in Fukushima was described as “strikingly similar” to that in Ukraine.⁴⁷ These inappropriate comparisons contradict the official claim of the first 4-5 years as a latency period, i.e. cancer in the very young would not have had enough time to grow.

The common notion of radiation carcinogenesis focuses on radiation-induced DNA damage leading to mutations, and “radiation-induced” cancer refers to carcinogenesis “initiated” by radiation. However, radiation is considered a “complete carcinogen”, i.e. able to both initiate and promote cancer development.^{48, 49} In reality it is difficult to completely separate initiation from promotion and progression since radiation-induced DNA damage can activate

myriad pathways that result in genomic instability and may be involved in multiple stages of carcinogenesis.⁴⁸

In fact, ionizing radiation meets at least three of ten key characteristics of carcinogen as defined by the International Agency for Research on Cancer⁵⁰: 1) genotoxic, 2) altering DNA repair or causing genomic instability, and 3) inducing oxidative stress. Oxidative stress produces ROS which are known to contribute to the bystander effect extracellularly and also intracellularly.⁵¹ Thus carcinogenic characteristics of radiation by definition include both genetic and non-targeted effects.^{*14} Induction of oxidative stress leads to cellular injury, affecting the microenvironment. It has been proposed from the systems biology perspective that non-targeted radiation effects create the critical context that promotes cancer development by influencing the microenvironment.^{52, 53}

The minimum latency for all childhood cancers other than lymphoproliferative and hematopoietic cancer has been determined as 1 year in “Minimum Latency & Types or Categories of Cancer,” a policy document used by the Centers for Disease Control and Prevention in the World Trade Center Health Program (accessible from the website, <https://www.cdc.gov/wtc/policies.html>).⁵⁴ The document also establishes 2.5 years as minimum latency for thyroid cancer in adults[†].

It is then plausible to consider that some, if not all, of the thyroid cancer cases in Fukushima may be the result of radiation exposure via promotion of preexisting premalignant cells into malignancy, which constitutes a radiation effect in a broad sense. This in turn invalidates the notion of the first round as the baseline without the radiation effects.

While the total radiation exposure doses in Fukushima may be lower than in Chernobyl, actual doses are unknown for most residents and estimated doses are underestimated on many levels. Contrary to the official claim,⁵⁵ the food testing and ban^{56, 57} was delayed^{*15}; the timing and direction of the actual evacuation was not considered^{58, 59}; and direct mea-

surements in 1080 children (so-called the 1080 survey)⁶⁰ were likely underestimated due to multiple factors. The 1080 survey 1) used a less sensitive survey meter, 2) was conducted after the half-life of radioactive iodine 131 passed, 3) was conducted in the high background levels, and 4) subtracted the radiation level at the individual shoulder—rather than the air dose level—as the background level from the actual measurement, potentially leading to oversubtraction.⁶¹ High readings were never confirmed with a more sensitive thyroid counter “so as not to create worries for and discrimination against the individual, family, and communities.”⁶² ^{*16} Besides, the sample size of 1080 can hardly be considered to represent about 360,000 Fukushima residents who were 18 or younger in March 2011.

Also, doses from short-lived radionuclides such as iodine 132/tellurium 132 and iodine 133 are overlooked.⁵⁹ Furthermore, disputing the official claim,⁶³ a growing body of evidence supports the fact that there is no threshold dose below which radiation has no effect and cancer can be detected at much lower dose than 100 mSv.⁶⁴⁻⁷⁰

High iodine diet in Japan is considered to reduce uptake of radioactive iodine and thus thyroid cancer risk, but actual urinary iodine levels in children show 16.6% with mild to moderate iodine deficiency.⁷¹ A higher risk for iodine deficiency was seen in ages <6 and 12-18, mostly reflecting age groups outside the school lunch program. Furthermore, the lack of iodine supplementation in the infant formula in Japan means a higher risk in the already vulnerable population. As mentioned earlier, iodine tablets were never administered to the vast majority of residents after the accident.

The FMU study¹⁸ suggested no geographical differences after “no significant association between the individual external doses and thyroid cancer prevalence” was found. However, this study suffers from inadequate or inappropriate study designs, an inappropriate geographical classification^{*17} and a mis-

after the accident—and test results of raw milk found to be highly contaminated on March 17 weren’t publicized until March 19.

^{*16}—A document dated April 1, 2011 refers to an opinion of Yoshiharu Yonekura, president of the Japan National Institute of Radiological Sciences and the 2015-2016 chair of the United Nations Scientific Committee on the Effects of Atomic Radiation, that the follow-up with a thyroid counter was not warranted (Supplementary document 23 on page 74 of reference 62).

^{*17}—Municipalities wholly or partly in the 20 km zone are included in the middle dose area. UNSCEAR 2013 shows some thyroid dose estimates in the 20 km zone to be higher

^{*14}—Even Otsura Niwa, the current chairman of the Radiation Effect Research Foundation, suggested in 1995 that “radiation induces cancer by enhancement of the spontaneous carcinogenesis process” and that “the first step of radiation carcinogenesis may not be the direct induction of mutation.” (Niwa, O. Epigenetic mechanism of radiation carcinogenesis (NIRS-M-106). Kobayashi, S. (Ed.). Japan. 1995: 193-198. https://inis.iaea.org/search/search.aspx?orig_q=30007142)

^{*15}—Contrary to the official claim that milk and other food-stuffs were swiftly banned, the provisional regulatory limits for food were not established until March 17, 2011—six days

leading reliance on the external doses.^{*18} Thyroid cancer risk should be assessed not by the external doses but the thyroid doses. Inappropriate inclusion of Iwaki City (40 km south of the FDNPP) in the lowest dose group underscores why external dose classifications are unsuitable: Iwaki City's thyroid doses are incongruous with external doses because very little rain caused low ground deposits of radionuclides despite a direct hit by the radioactive plume.⁷² The estimated thyroid doses in Iwaki City are as high as those in the highest dose group such as Iitate Village or Kawamata Town, with the highest thyroid dose from the 1080 survey measured in a child from Iwaki City.⁵⁸

FMU officials divided the entire prefecture into four geographical regions (the evacuation zone plus other 3 geographical regions of Hamadori, Nakadori and Aizu) and reported no regional differences in the proportion of suspected or confirmed cancer cases from the first round (Table 9 of the PBLs report⁵). However, this analysis is not very meaningful due to lack of age adjustment and a weak relationship between the regional division and exposure doses.

Meanwhile, an independent analysis of the *second* round data reveals a lower rate of thyroid cancer—age-adjusted and statistically significant—in the less exposed FY2015 cohort (excluding Iwaki City) compared to the more exposed FY2014 cohort.⁷³ For cancer cases with estimated external doses, a significant difference was found between <1 mSv and ≥1 mSv: the rate of cancer in the ≥1 mSv group was more than twice as large as the <1 mSv group. A further analysis according to the official regional division—even though the division has low statistical power⁷⁴—shows a clear regional difference of thyroid cancer occurrence (per 100,000^{††}) in the second round results: 49.2, 25.7, 19.6 and 15.5 in the evacuation zone, Nakadori, Hamadori^{††}, and Aizu, respectively.⁷⁵ This regional difference, i.e. dose-response, contradicts the official claim dismissing a relationship between the high prevalence of thyroid cancer and radiation exposure.

Different driver mutation patterns—dominance of BRAF point mutation in Fukushima vs. RET/PTC gene arrangement in Chernobyl—does not necessarily rule out radiation effects. Reasons are clearly stated by Gerry Thomas, a British molecular pathologist, in Chapter 12 of the very book the official claims are laid out⁷⁶: “RET rearrangement and BRAF muta-

tion are not related to exposure to radiation, but show a strong association with age of the patient at operation.” That is, RET gene arrangements—often seen in Chernobyl and ascribed to radiation exposure—are actually not related to radiation but to the morphology of PTC which in turn is associated with the age of the patient. RET gene arrangements are not unique to radiation-induced thyroid cancer⁷⁷ and may be related to the dietary iodine status.⁷⁸ BRAF V600E point mutation is more commonly seen in adults and Asian populations⁷⁹ and also related to the dietary iodine status.⁸⁰ As a matter of fact, 40 percent of 62 thyroid cancer cases diagnosed in the Ukrainian-American study had no known mutation including RET/PTC and BRAF.⁸¹ By the same token, the absence of the solid variant PTC in Fukushima (at least officially^{*19})—the only pathological characteristic that purportedly sets Fukushima apart from Chernobyl—most likely simply reflects different age distributions that are inappropriately compared.

Fukushima and Chernobyl are indeed different, but the differences merely underscore the very fact they are different datasets. This misleading emphasis on “differences” has boomeranged by revealing logical inconsistencies.

Concluding remarks

Future of the TUE is a controversial topic. FMU officials who claim overdiagnosis seem to be interested in reducing its scale and facilitating the opt out process in order to lessen psychosocial impacts of cancer diagnosis.⁸² The SHAMISEN project by EU recently issued recommendations on health surveillance after a nuclear accident including a recommendation against a systematic thyroid cancer screening.⁸³ FMU has posted these recommendation on the English website,⁸⁴ implying its endorsement. Meanwhile, Suzuki, an FMU thyroid surgeon, advocates a long-term continuance of the TUE. Changing the course of the TUE seems premature when the second round results have not even been properly analyzed. With FMU's transparency as well as scientific and data integrity in question, it is critical for a truly independent analysis to be conducted by qualified experts, based on the latest evidence.

References

1—Overview of the Fukushima Health Management Survey. Fu-

than some municipalities designated as the middle dose area.

*18—External dose estimates are based on a voluntary, questionnaire survey with a low response rate of 26.4%—hardly representative of the residents.

*19—In Fukushima, reclassification of poorly differentiated thyroid cancer in accordance with updated diagnostic guidelines supposedly added 2 cases of the solid variant PTC to the morphological profile.

- kushima Medical University Radiation Medical Sciences Center website. <http://fmu-global.jp/fukushima-health-management-survey/>. Accessed August 1, 2017.
- 2—Support of the Fukushima Health Management Survey. Ministry of the Environment website. <http://www.env.go.jp/chemi/rhm/support.html>. Accessed August 1, 2017. (in Japanese)
- 3—Cost of the Fukushima Health Management Survey. Access-info Clearinghouse Japan website <https://clearing-house.org/?p=738>. Posted June 6, 2013. Accessed August 1, 2017. (in Japanese)
- 4—Yasumura S, Hosoya M, Yamashita S, et al. Study protocol for the Fukushima Health Management Survey. *Journal of Epidemiology*. 2012; **22**(5): 375–383. doi:10.2188/jea.JE20120105. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3798631/>.
- 5—Thyroid Ultrasound Examination (Supplemental Report of the FY 2016 Survey, Preliminary Baseline Screening). <http://fmu-global.jp/download/thyroid-ultrasound-examination-supplemental-report-of-the-fy-2016-survey-preliminary-baseline-screening/?wpdm=2690>.
- 6—Report of Second-Round Thyroid Ultrasound Examinations (First Full-Scale Thyroid Screening Program). <http://fmu-global.jp/download/thyroid-ultrasound-examination-first-full-scale-thyroid-screening-program-5/?wpdm=2692>.
- 7—Report of Third-Round Thyroid Ultrasound Examinations (Second Full-Scale Thyroid Screening Program). <http://fmu-global.jp/download/thyroid-ultrasound-examination-second-full-scale-thyroid-screening-program-7/?wpdm=2693>.
- 8—The Prefectural Oversight Committee Meeting for Fukushima Health Management Survey, Office of International Cooperation, Radiation Health Medical Science Center, Fukushima Medical University. <http://fmu-global.jp/fukushima-health-management-survey/>.
- 9—Ohtsuru A, Midorikawa S, Suzuki S, Shimura H, Matsuzuka T, Yamashita S. Five-year interim report of thyroid ultrasound examinations in the Fukushima Health Management Survey. In Yamashita S & Thomas G, eds. *Thyroid cancer and nuclear accidents*. Academic Press; 2017:145–153. <https://doi.org/10.1016/B978-0-12-812768-1.00014-9>.
- 10—Suzuki S. The features of childhood and adolescent thyroid cancer after the Fukushima nuclear power plant accident. In Yamashita S & Thomas G, eds. *Thyroid cancer and nuclear accidents*. Academic Press; 2017:155–163. <https://doi.org/10.1016/B978-0-12-812768-1.00015-0>.
- 11—Thyroid Ultrasound Examination, The Eighth Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. <http://fmu-global.jp/survey/proceedings-of-the-8th-prefectural-oversight-committee-meeting-for-fukushima-health-management-survey/>.
- 12—Thyroid Ultrasound Examination, The Twelfth Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. <http://fmu-global.jp/survey/proceedings-of-the-12th-prefectural-oversight-committee-meeting-for-fukushima-health-management-survey/>.
- 13—Thyroid Ultrasound Examination (First Full-Scale Thyroid Screening Program), The 27th Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. <http://fmu-global.jp/download/thyroid-ultrasound-examination-first-full-scale-thyroid-screening-program-5/?wpdm=2692>.
- 14—Thyroid Ultrasound Examination (Second Full-Scale Thyroid Screening Program), The 27th Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. <http://fmu-global.jp/download/thyroid-ultrasound-examination-second-full-scale-thyroid-screening-program-7/?wpdm=2693>.
- 15—The 27th Prefectural Oversight Committee Meeting for Fukushima Health Management Survey. <http://fmu-global.jp/survey/proceedings-of-the-27th-prefectural-oversight-committee-meeting-for-fukushima-health-management-survey/>.
- 16—Hiranuma, Y. Fukushima Prefecture and Fukushima Medical University Fail to Report a Thyroid Cancer Case. Fukushima Voice Version 2e. March 31, 2017. <http://fukushimavoiced-eng2.blogspot.com/2017/03/fukushima-prefecture-and-fukushima.html>. Accessed August 18, 2017.
- 17—Suzuki S, Suzuki S, Fukushima T, Midorikawa S, Shimura H, Matsuzuka T, et al. Comprehensive survey results of childhood thyroid ultrasound examinations in Fukushima in the first four years after the Fukushima Daiichi nuclear power plant accident. *Thyroid*. 2016; **26**(6): 843–851. doi:10.1089/thy.2015.0564. <http://online.liebertpub.com/doi/10.1089/thy.2015.0564>.
- 18—Ohira T, Takahashi H, Yasumura S, Ohtsuru A, Midorikawa S, Suzuki S, et al. Comparison of childhood thyroid cancer prevalence among 3 areas based on external radiation dose after the Fukushima Daiichi nuclear power plant accident: The Fukushima health management survey. *Medicine*. 2016; **95**(35): e4472. doi:10.1097/MD.0000000000004472. http://journals.lww.com/md-journal/Fulltext/2016/08300/Comparison_of_childhood_thyroid_cancer_prevalence.15.aspx.
- 19—Suzuki S. Childhood and adolescent thyroid cancer after the Fukushima nuclear power plant accident. Oral presentation at: The Fifth International Expert Symposium in Fukushima on Radiation and Health: Chernobyl+30, Fukushima+5: Lessons and Solutions for Fukushima's Thyroid Question; September 26, 2016. Available on <http://fmu-global.jp/workshop/symposium/26-27-sep-2016-5th-intl-expert-symposium-in-fukushima-2/>. Accessed July 25, 2017.
- 20—Hiranuma, Y. Clinicopathological Findings of Fukushima Thyroid Cancer Cases: October 2017. Fukushima Voice Version 2e. October 9, 2017. <http://fukushimavoiced-eng2.blogspot.com/2016/10/clinicopathological-findings-of.html>. Accessed August 18, 2017.
- 21—Suzuki S, Suzuki S, Iwade M, Tachiya Y, Ashizawa M, Okouchi C, et al. Ultrasound findings of childhood thyroid cancer. *Official Journal of the Japan Association of Endocrine Surgeons and the Japanese Society of Thyroid Surgery*. 2017; **34**(1): 7–16. https://www.jstage.jst.go.jp/article/jaesjsts/34/1/34_7/_html.
- 22—Hori M, Matsuda T, Shibata A, Katanoda K, Sobue T, Nishimoto H, et al. Cancer incidence and incidence rates in Japan in 2009: a study of 32 population-based cancer registries for the Monitoring of Cancer Incidence in Japan (MCIJ) project. *Japanese Journal of Clinical Oncology*. 2015; **45**(9): 884–91. http://ganjoho.jp/en/professional/statistics/table_download.html. Accessed July 30, 2017.
- 23—Hayashida N, Imaizumi M, Shimura H, Okubo N, Asari Y, Nigawara T, et al. Thyroid ultrasound findings in children from three Japanese prefectures: Aomori, Yamanashi and Nagasaki. *PLoS ONE*. 2013; **8**(12): e83220. <https://doi.org/10.1371/journal.pone.0083220>.
- 24—Hayashida N, Imaizumi M, Shimura H, et al. Thyroid ultrasound findings in a follow-up survey of children from three Japanese prefectures: Aomori, Yamanashi and Nagasaki. *Scientific Reports*. 2015; **5**(1). doi:10.1038/srep09046. <https://www.nature.com/articles/srep09046>.
- 25—Shibuya K, et al. Time to reconsider thyroid cancer screening in Fukushima. *The Lancet*. 2014; **383**(9932): 1883–1884. [http://dx.doi.org/10.1016/S0140-6736\(14\)60909-0](http://dx.doi.org/10.1016/S0140-6736(14)60909-0).
- 26—Hiranuma Y. Professor Tsuda's replies to criticisms regarding the Okayama University study, Part 2. October 30, 2015. Fukushima Voice Version 2. http://fukushimavoiced2.blogspot.com/2015/10/blog-post_30.html. Accessed August 18, 2017. (in Japanese)
- 27—Tsuda T, Tokinobu A, Yamamoto E, Suzuki E. Thyroid cancer detection by ultrasound among residents ages 18 years and younger in Fukushima, Japan: 2011 to 2014. *Epidemiology*. 2016; **27**(3): 316–322. doi:10.1097/EDE.0000000000000385.
- 28—Jorgensen, TJ. Re: Thyroid cancer among young people in

- Fukushima. *Epidemiology*. 2016; **27**(3): e17. doi: 10.1097/EDE.0000000000000465.
- 29—Takamura N. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e18. doi: 10.1097/EDE.0000000000000464.
- 30—Körblein, A. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e18–e19. doi: 10.1097/EDE.0000000000000466.
- 31—Suzuki S. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e18–e19. doi: 10.1097/EDE.0000000000000462.
- 32—Shibata, Y. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e19–e20. doi: 10.1097/EDE.0000000000000461.
- 33—Wakeford R, Auvinen A, Gent RN, Jacob P, Kesminiene A, Laurier D, et al. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e20–e21. doi: 10.1097/EDE.0000000000000466.
- 34—Takahashi H, Ohira T, Yasumura S, Nollet KE, Ohtsuru A, Tanigawa K, et al. Re: Thyroid cancer among young people in Fukushima. *Epidemiology*. 2016; **27**(3): e21. doi: 10.1097/EDE.0000000000000467.
- 35—Tsuda T, Tokinobu A, Yamamoto E, Suzuki E. The authors respond. *Epidemiology*. 2016; **27**(5): e36. doi: 10.1097/EDE.0000000000000468.
- 36—Katanoda K, Kamo K-I, Tsugane S. Quantification of the increase in thyroid cancer prevalence in Fukushima after the nuclear disaster in 2011—a potential overdiagnosis? *Japanese Journal of Clinical Oncology*. 2016; **46**(3): 284–286. doi:10.1093/jjco/hyv191.
- 37—Tsugane S. The estimated number of prevalent cases of thyroid cancer in Fukushima prefecture. The Fourth Session of the Thyroid Examination Assessment Subcommittee of the Prefectural Oversight Committee Meeting for the Fukushima Health Management Survey. November 11, 2014. <https://www.pref.fukushima.lg.jp/uploaded/attachment/91000.pdf>. (in Japanese)
- 38—Minutes of Proceedings, The 26th Oversight Committee Meeting for Fukushima Health Management Survey. February 20, 2017. <https://www.pref.fukushima.lg.jp/uploaded/attachment/215168.pdf>. (in Japanese)
- 39—Hogan AR, Zhuge Y, Perez EA, Koniaris NG, Lew JI, Sola JE. Pediatric thyroid carcinoma: incidence and outcomes in 1753 patients. *Journal of Surgical Research*. 2009; **156**(1): 167–172. <http://dx.doi.org/10.1016/j.jss.2009.03.098>.
- 40—Harach HR, Williams ED. Childhood thyroid cancer in England and Wales. *British Journal of Cancer*. 1995; **72**(3): 777–783. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2033913/>.
- 41—Williams ED, Abrosimov A, Bogdanova T, et al. Morphologic characteristics of Chernobyl-related childhood papillary thyroid carcinomas are independent of radiation exposure but vary with iodine intake. *Thyroid*. 2008; **18**(8): 847–852. doi:10.1089/thy.2008.0039.
- 42—Bogdanova TI, Saenko VA, Hirokawa M, et al. Comparative histopathological analysis of sporadic pediatric papillary thyroid carcinoma from Japan and Ukraine. *Endocrine Journal*. 2017. doi:10.1507/endocrj.ej17-0134.
- 43—Ahn HS, Kim HJ, Kim KH, et al. Thyroid cancer screening in South Korea increases detection of papillary cancers with no impact on other subtypes or thyroid cancer mortality. *Thyroid*. 2016; **26**(11): 1535–1540. doi:10.1089/thy.2016.0075.
- 44—Takamura N, Orita M, Saenko V, Yamashita S, Nagataki S, Demidchik Y. Radiation and risk of thyroid cancer: Fukushima and Chernobyl. *The Lancet*. 2016; **4**(8): 647. [http://dx.doi.org/10.1016/S2213-8587\(16\)30112-7](http://dx.doi.org/10.1016/S2213-8587(16)30112-7).
- 45—Hiranuma Y. Misrepresented risk of thyroid cancer in Fukushima. *The Lancet*. 2016; **4**(12): 970. [http://dx.doi.org/10.1016/S2213-8587\(16\)30322-9](http://dx.doi.org/10.1016/S2213-8587(16)30322-9).
- 46—Williams D. Thyroid growth and cancer. *Eur. Thyroid J*. 2015; **4**: 164–173. <https://doi.org/10.1159/000437263>.
- 47—Tronko MD, Saenko VA, Shpak VM, Bogdanova TI, Suzuki S, Yamashita S. Age distribution of childhood thyroid cancer patients in Ukraine after Chernobyl and in Fukushima after the TEPCO-Fukushima Daiichi NPP accident. *Thyroid*. 2014; **24**(10): 1547–1548. doi:10.1089/thy.2014.0198.
- 48—Barcellos-Hoff MH, Blakely EA, Burma S, et al. Concepts and challenges in cancer risk prediction for the space radiation environment. *Life Sciences in Space Research*. 2015; **6**: 92–103. doi:10.1016/j.lssr.2015.07.006.
- 49—Fry RJM, Ley RD, Grube D, Staffeldt E. Studies on the multi-stage nature of radiation carcinogenesis. *Carcinogenesis*. 1982; **7**: 155–165. http://www.iaea.org/inis/collection/NCLCollectionStore/_Public/13/668/13668558.pdf.
- 50—Smith MT, Guyton KZ, Gibbons CF, et al. Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. *Environmental Health Perspectives*. 2016; **124**(6): 713–721. doi:10.1289/ehp.1509912.
- 51—Desouky O, Ding N, Zhou G. Targeted and non-targeted effects of ionizing radiation. *Journal of Radiation Research and Applied Sciences*. 2015; **8**(2): 247–254. doi:10.1016/j.jrras.2015.03.003.
- 52—Barcellos-Hoff MH, Nguyen DH. Radiation carcinogenesis in context: how do irradiated tissues become tumors? *Health physics*. 2009; **97**(5): 446–457. doi:10.1097/HP.0b013e3181b08a10.
- 53—Barcellos-Hoff MH, Adams C, Balmain A, et al. Systems biology perspectives on the carcinogenic potential of radiation. *Journal of Radiation Research*. 2014; **55**(Suppl 1): i145–i154. doi:10.1093/jrr/rrt211.
- 54—Howard, J. Minimum latency & types or categories of cancer. World Trade Center Health Program. <https://www.cdc.gov/wtc/policies.html>. Revised January 6, 2015. Accessed July 30, 2017
- 55—Yamashita S. Fear is a killer: Nuclear expert reveals radiation's real danger. *New Scientist*. 2017; 3125. https://www.newscientist.com/article/mg23431250-600-fear-is-the-killer-nuclear-expert-reveals-radiations-real-danger/?utm_campaign=RSSNSNS. Accessed July 18, 2017.
- 56—Results of the inspection on radioactivity level in raw milk. Excel file for March 11, 2011–March 31, 2011. Ministry of Agriculture, Forestry and Fisheries. Accessed August 24, 2017. http://www.maff.go.jp/e/policies/food_safety/emerg/livest/milk.html.
- 57—Foods exceeding the regulatory limits: deal with them calmly. *NHK*. March 19, 2011. http://www3.nhk.or.jp/news/genpatsu-fukushima/20110319/2010_s_shokuhin-taiou.html. Accessed August 5, 2017. (in Japanese)
- 58—Kim E, Tani K, Kunishima N, Kurihara O, Sakai K, Akashi M. Estimation of early internal doses to Fukushima residents after the nuclear disaster based on the atmospheric dispersion simulation. *Radiation Protection Dosimetry*. 2016; **171**(3): 398–404. <https://doi.org/10.1093/rpd/ncv385>.
- 59—Ohba T, Hasegawa A, Kobayagawa Y, Kondo H, Suzuki G. Body surface contamination levels of residents under different evacuation scenarios after the Fukushima Daiichi nuclear power plant accident. *Health Physics*. 2017; **113**(3): 175–182. doi: 10.1097/HP.0000000000000690.
- 60—Kim E, Kurihara O, Suzuki T, Matsumoto M, Fukutsu K, Yamada Y, Sugiura N, Akashi M. Screening survey on thyroid exposure for children after the Fukushima Daiichi Nuclear Power Station accident. In: Proceedings of the 1st NIRS Symposium on Reconstruction of Early Internal Dose in the TEPCO Fukushima Daiichi Nuclear Power Station Accident. National Institute of Radiological Sciences. Chiba, Japan, July 2012. NIRS-M-252 2012: 59–66. Available on www.nirs.qst.go.jp/publication/irregular/pdf/nirs_m_252.pdf. Accessed July 30, 2017. (in Japanese)
- 61—study2007. For re-assessment of the early childhood thyroid

screening: factors leading to underestimation. *Kagaku*. 2014; **84** (4): 406–414.

62—Nuclear Safety Commission. Circumstances surrounding the pediatric thyroid survey. https://www.iwanami.co.jp/kagaku/20120913_2.pdf. Published September 13, 2012. Accessed August 27, 2017. (in Japanese)

63—Yamashita S. Adolescent thyroid cancer after the Fukushima nuclear power plant accident: mass screening effect of a real increase? ASCO Daily News. <https://am.asco.org/daily-news/adolescent-thyroid-cancer-after-fukushima-nuclear-power-plant-accident-mass-screening>. Published May 26, 2016. Accessed July 30, 2017.

64—Bithell JF, Stewart AM. Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford Survey. *British Journal of Cancer*. 1975; **31** (3): 271–287.

65—Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, et al. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. *BMJ*. 2005; **331**. <https://doi.org/10.1136/bmj.38499.599861.E0>.

66—Spycher BD, Lupatsch JE, Zwahlen M, Röösl M, Niggli F, Grotzer MA, Rischewski J, Egger M, Kuehni CE, for the Swiss Pediatric Oncology Group and the Swiss National Cohort. Background ionizing radiation and the risk of childhood cancer: a census-based nationwide cohort study. *Environ Health Perspect*. 2015; **123**: 622–628. <http://dx.doi.org/10.1289/ehp.1408548>.

67—Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, et al. Cancer risk in 680 000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. *BMJ*. 2013; **346**: f2360. <https://doi.org/10.1136/bmj.f2360>.

68—Leuraud K, Richardson DB, Cardis E, Daniels RD, Gilles M, O'Hagan JA. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS) : an international cohort study. *The Lancet Hematology*. 2015; **2** (7): e276–e281. [http://dx.doi.org/10.1016/S2352-3026\(15\)00094-0](http://dx.doi.org/10.1016/S2352-3026(15)00094-0).

69—Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, et al. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). *BMJ*. 2015; **351**: h5359. <https://doi.org/10.1136/bmj.h5359>.

70—Veiga LHS, Holmberg E, Anderson H, Pottern L, Sadetzki S, Adams MJ, et al. Thyroid Cancer after Childhood Exposure to External Radiation: An Updated Pooled Analysis of 12 Studies. *Radiation Research*. 2016; **185** (5): 473–484. <https://doi.org/10.1667/RR14213.1>.

71—Tsubokura M, Nomura S, Watanobe H, Nishikawa Y, Suzuki C, Ochi S, et al. Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident. *Thyroid*. 2016; **26** (12): 1778–1785. <https://doi.org/10.1089/thy.2016.0313>.

72—Hosoda M, Tokonami S, Tazoe H, Sorimachi A, Monzen S, Osanai M, et al. Activity concentrations of environmental samples collected in Fukushima Prefecture immediately after the Fukushima nuclear accident. *Scientific Reports*. 2013; **3** (2283). doi:10.1038/srep02283.

73—Makino J. Scientific literacy after 3.11, No.57. *Kagaku*. 2017; **87** (8): 709–711. (in Japanese)

74—Hamaoka Y. Issues regarding the thyroid examination in Fukushima. *Kagaku*. 2016; **86** (11): 1090–1101. (in Japanese)

75—Makino J. Scientific literacy after 3. 11, No. 58. *Kagaku*. 2017; **87** (9): 830–833. (in Japanese)

76—Thomas G. Somatic genomics of childhood thyroid cancer. In Yamashita S & Thomas G, eds. *Thyroid cancer and nuclear accidents*. Academic Press; 2017: 121–132. <https://doi.org/10.1016/B978-0-12-812768-1.00012-5>.

77—Nikiforov YE, Rowland JM, Bove KE, Monforte-Munoz H, Fagin JA. Distinct pattern of ret oncogene rearrangements in mor-

phological variants of radiation-induced and sporadic thyroid papillary carcinomas in children. *Cancer Res*. 1997; **57** (9): 1690–1694. <http://cancerres.aacrjournals.org/content/57/9/1690.long>.

78—Williams ED, Abrosimov A, Bogdanova T, Demidchik EP, Ito M, LiVolsi V, et al. Morphologic characteristics of Chernobyl-related childhood papillary thyroid carcinomas are independent of radiation exposure but vary with iodine intake. *Thyroid*. 2008; **18** (8): 847–852. <https://doi.org/10.1089/thy.2008.0039>.

79—Bychikov A. Prevalence of BRAF V600E mutation in Asian patients with thyroid cancer. *Malays. J. Pathol*. 2017; **39** (1): 95–96. <https://www.ncbi.nlm.nih.gov/pubmed/28413212>.

80—Song YS, Lim JA, Park YJ. Mutation Profile of Well-Differentiated Thyroid Cancer in Asians. *Endocrinology and Metabolism*. 2015; **30** (3): 252–262. doi:10.3803/EnM.2015.30.3.252.

81—Leeman-Neill RJ, Brenner AV, Little MP, Bogdanova TI, Hatch M, Zurnadzy LY, et al. RET/PTC and PAX8/PPAR γ chromosomal rearrangements in post-Chernobyl thyroid cancer and their association with iodine-131 radiation dose and other characteristics. *Cancer*. 2013; **119**: 1792–1799. doi:10.1002/cncr.27893.

82—Midorikawa S, Ohtsuru A, Suzuki S, Tanigawa K, Ohto H, Abe M, Kamiya K. Psychosocial impact of the Thyroid Examination of the Fukushima Health Management Survey. In Yamashita S & Thomas G, eds. *Thyroid cancer and nuclear accidents*. Academic Press; 2017: 165–173. <https://doi.org/10.1016/B978-0-12-812768-1.00016-2>.

83—Oughton D, Albani V, Barquinero F, Chumak V, Clero E, Crouail P, et al on behalf of the SHAMISEN Consortium. Recommendations and procedures for preparedness and health surveillance of populations affected by a radiation accident. July 2017. http://www.crealradiation.com/images/shamisen/Anim2/Radiation_accident.pdf.

84—SHAMISEN recommendation booklet is available. Office of International Cooperation, Radiation Health Medical Science Center, Fukushima Medical University. <http://fmu-global.jp/2017/08/07/shamisen-recommendations-booklet-is-available/>. Published August 7, 2017. Accessed August 10, 2017.

Note: Corrections made as of October 27, 2017 are marked with a dagger symbol (†).

Corrections made as of August 30, 2018 are marked with a double dagger symbol (††).