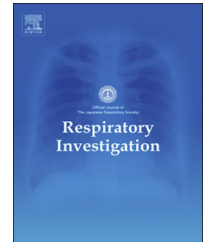


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Review

Risk of thyroid cancer after the Fukushima nuclear power plant accident



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ABSTRACT

The appropriateness of the initial response and countermeasures taken following the Fukushima nuclear power plant accident after the Great East Japan Earthquake on March 11, 2011 should be further examined. Implementation of a prospective epidemiological study on human health risks from low-dose radiation exposure and comprehensive health protection from radiation should be emphasized on a basis of the lessons learnt from the Chernobyl nuclear power plant accident. In contrast, the doses to a vast majority of the population in Fukushima were not high enough to expect to see any increase in incidence of cancer and health effects in the future, however, public concerns about the long-term health effects of radioactive environmental contamination have increased in Japan. Since May 2011, the Fukushima Prefecture started the Fukushima Health Management Survey Project with the purpose of long-term health care administration and early medical diagnosis/treatment for prefectural residents. In this report, risk and countermeasures of thyroid cancer occurrence after nuclear accidents, especially due to early exposure of radioactive iodine, will be focused upon to understand the current situation of risk of thyroid cancer in Fukushima, and the difficult challenges surrounding accurate estimations of low-dose and low-dose rate radiation exposures will be discussed.

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1. Introduction

The worst nuclear power plant accident in Japan occurred just after the Great East Japan Earthquake on March 11, 2011. The scientific understanding about the relationship between radiation exposure dose and health risks continues to be indispensable for proper emergency correspondence immediately after nuclear power plant accidents. According to accumulated data from survivors of the atomic bomb analyzed by the Radiation Effects Research Foundation [1], risks of leukemia and solid cancers occur in a dose-response manner [2,3]. Among human cancer occurrences associated with radiation, thyroid cancer risk increases not only after external exposure, but also after internal exposure to radioactive iodine, as epidemiologically clarified just after the Chernobyl accident [4–6]. Both factors are especially important to understand the health effects of radiation exposure, and a standardized measure of radiation dosage known as the Sievert unit (Sv) should be utilized. Measurements using the Sv unit have indicated that health effects between external and internal exposure are theoretically the same from the standpoint of biological effects.

Although by International Standard, the Fukushima nuclear power plant accident was estimated as a level 7 accident that caused massive environmental radioactive contamination equivalent to the Chernobyl accident, the actual condition and damage scales differ greatly. Thyroid blocking with suitable medication like a stable iodine tablet should be prepared for the reduction and prevention of any internal exposure to radioactive iodine immediately after an accident [7]. Moreover, the safety of food should be strictly controlled by discarding polluted milk and other food items after large-scale accidents. Although the side effects and effectiveness of iodine tablet dosage needs to be verified [8], ample room remains for the development and practical improvement of campaigns toward iodine thyroid blocking in Japan. More specifically, evaluation of the dose of radioactivity is of utmost importance, and longitudinal epidemiologic surveys, such as improvement to the regional cancer registration system and mortality surveys, would be indispensable to our precise understanding of radiation-associated cancer risk. Since thyroid cancer risk principally occurs due to a stochastic effect, and simultaneous comprehensive health risk management and risk communication are necessary for the public. In addition, an understanding of the basics of the molecular mechanisms underlying thyroid biology and carcinogenesis is also required [9].

This report outlines the nuclear accident at Fukushima and summarizes thyroid cancer risk, assuming the possibility of initial exposure to radioactive iodine and drawing lessons from the Chernobyl nuclear accident.

2. Chernobyl accident and thyroid cancer risk

On the early morning of April 26, 1986, an explosion occurred in the Chernobyl Nuclear Power Unit No. 4 High Power

Channel-type Reactor, a water-cooled, graphite-moderated nuclear power reactor designed in the former Soviet Union (existing Ukraine). The nuclear reactor and the building that housed the reactor were destroyed by the accident. Subsequently, a fire broke out and spread rapidly due to scattering of hot black lead. Large-scale radioactive material was released into the environment until May 6, 1986. The main radioactive materials emitted were iodine-131, cesium-134, cesium-137, niobium-95, cerium-144, ruthenium-103, ruthenium-106, strontium-90, plutonium-239, and plutonium-240, which reached a total amount of 14 exabecquerel. An exabecquerel is a unit representing 1000 quadrillion times (10^{18}). Although large particles of strontium and plutonium descended in an area less than 100 km from the nuclear plant, other radioactive materials were widely diffused in the Northern Hemisphere around Europe [10].

Immediately after the accident, external exposure became a problem for workers inside the nuclear power plant or in nearby high-dose areas, whereas internal exposure became a problem for nearby residents exposed indirectly to radioactive fallout.

In particular, iodine-131 contamination was found in milk derived from pastured cows that fed on iodine-131-contaminated grass from the surrounding Chernobyl area; this was a critical problem for the local residents. Due to insufficient restriction of the distribution and ingestion of the iodine-131-contaminated milk by the government, people continued to consume the contaminated milk, particularly children from Belarus, Russia, and the Ukraine of the former USSR during the Cold War era. Chernobyl is an inland area that previously lacked iodine contamination. When ingested, the thyroid gland selectively takes in iodine, including iodine-131. Therefore, milk contaminated with iodine-131 was the contributing factor that exacerbated internal exposure to the thyroid glands of children who ingested the contaminated milk. These children were exposed to an estimated dozen to several thousand millisievert dose of radiation to their thyroid gland. As a result, it has been reported that infant thyroid cancer (papillary adenocarcinoma) increased rapidly in children, especially those aged 0–5 years at the time of the accident [11]. The case-control study supports a positive relationship between childhood thyroid cancer occurrence and thyroidal iodine-131 exposure [12]. The dose threshold of radiation-associated thyroid cancer in childhood has not been scientifically clarified, and no consensus exists on the threshold according to the hypothesis of the linear non-threshold (LNT) model [13]. However, some reports using theoretical models from Chernobyl, such as the LNT model, suggest that the critical internal thyroid exposure doses are conservatively more than 50–200 mSv in children [4–6]. Thyroid dose re-evaluation poses many difficulties; however, a comparative study on children who were born before and after the Chernobyl accident supports the etiological role of short half-life radioactive iodine on childhood thyroid cancer, despite a lack of direct measurements of the dose of thyroid exposure [14].

The number of thyroid cancers cases continues to increase, even 25 years after the accident [15], and has amounted to

approximately 6000 thyroid cancer patients [16]. This peak of infant thyroid cancer has shifted to adulthood. The detailed molecular mechanism of thyroid carcinogenesis is still being examined, but signature genes associated with radiation exposure have not been identified [17]. However, high-frequency gene polymorphisms (SNPs) have been found in European populations surrounding Chernobyl [18], and these SNPs were found to be largely, although not fully, overlapping with the original SNPs that are related with cancer risk, according to studies that determined disease-susceptibility genes in thyroid cancer patients [19].

Iodine-131 decays quickly with a half-life of approximately 8 days; however, radioactive cesium remains in the environment much longer. The physical half-life of cesium-134 and cesium-137 is 2 years and 30 years, respectively. Radioactive cesium can contaminate many animals and plants through pollution of the food chain. High-level cesium-137 was detected in mushrooms, grapes, and meat 20 years after the Chernobyl accident, and internal exposure through ingestion continues in parts of Belarus, the Ukraine and Russia [20].

As per a report on Chernobyl published as a joint forum by the International Atomic Energy Agency (IAEA), the World Health Organization (WHO), and others, 20 years after the accident, only infant thyroid cancer was accepted as a consequence of radiation after the accident, while other malignant tumors and changes to the body resulting from cesium including leukemia and other solid cancers were not accepted [21]. Moreover, no difference was seen in the rate of congenital abnormality between cesium-contaminated areas and non-contaminated areas. In the joint forum, it was specified that the greatest health problems after a large accident are mental and psychosocial consequences.

3. Radiation dose estimation after the Fukushima nuclear power plant accident

All nuclear reactors at the first and second TEPCO-Nuclear Power Plants in Fukushima stopped automatically after the Great East Japan Earthquake on March 11, 2011. Continuous cooling is needed for nuclear fuel and spent nuclear fuel in a nuclear reactor or a spent nuclear fuel pool for the decay to remove the heat generated; however, all power supplies to reactors nos. 1-4 for cooling were lost due to the earthquake, tsunami, hydrogen explosion, and other disasters that occurred in succession. As a result, a lot of radioactive material was emitted to the outside environment and spread through the wind. Besides the nuclear power plant workers and surrounding residents who intervened within a 20 km radius of the accident, almost all residents near the nuclear power plant took refuge at least 2-3 km away by March 11, then moved 10 km away, and finally moved 20 km away according to the resident evacuation order on March 12. Within 48 h, approximately 77,000 local residents fled from the 20 km zone and later, many people evacuated from all restricted areas.

Although body surface screening for the evacuees of the Fukushima Prefecture started on March 13, the cutoff value for whole body decontamination at the screening level was up to 100,000 cpm, using the GM survey meter (diameter of

5 cm) on and after March 15. Radioactive material spread from the nuclear power plant to the northwest through the southeastern wind on the afternoon of March 15, and a high spatial dose rate of approximately $20 \mu\text{Sv/h}$ was observed in Fukushima city, about 60 km from the nuclear power plant. According to the environmental data measured in Fukushima, radioactive material dispersed through the wind after the hydrogen explosion occurred at the nuclear power plant and contaminated all surfaces. The main radioactive nuclide emitted from the nuclear power plant was iodine-131. According to measurements of the area using a high spatial dose rate, an immediate declining trend of iodine-131 in the environment was observed. Other radioactive nuclides emitted from the nuclear power plant included cesium-134 and cesium-137, which have a long physical half-life and thus deposit in soil, on roofs, on outer walls of a buildings, and other surfaces for a long time.

Restrictions on shipments and the sales of food containing radioactive iodine and cesium began with milk from the Fukushima Prefecture and spinach from the Fukushima, Ibaraki, and Tochigi Prefectures on March 21. The safe interim standard level for food was set at a maximum annual internal exposure dose of 5 mSv at the end of March following the accident, and shipment restrictions and restrictions on food exceeding this value were implemented. As of April 2012, the annual internal exposure dose became stricter at 1 mSv following the stabilization of the nuclear power plant.

Unfortunately, the calculation and prediction of the concentration of radioactive materials in the air, the radioactive dose, and other measurements immediately after the accident could not be performed due to insufficient information on the source of emission, which was based on the weather survey data, radiation data, wind velocity and System for Prediction of Environmental Emergency Dose Information (SPEEDI). The members of the Radiation Medical Assistance Team dispatched from Nagasaki University stayed in Fukushima from 16:00 on March 14 to 17:00 on March 19 to observe and announce the spatial dose rate of Fukushima and the calculated dose of radioactivity. These levels were predicted to be $1354 \mu\text{Sv}$, but the integrated value read from personal dosimeters was 42-62 μSv over 4 days. Most measurements were taken indoors, while the spatial dose rate was measured at a height of 1 m from the ground outside. In many cases, the actual external exposure dose was relatively low because buildings shielded radiation levels. However, further verification from local residents and evacuees from Fukushima is required, and it is important to utilize these individual effective dose data for appropriate action in the case of future accidents.

Estimations of external radiation exposure doses for people residing in Fukushima at the time of the earthquake were conducted as a basic investigation under a prefectural health management survey by the Fukushima Prefecture [22]. The study protocol for this survey has been detailed elsewhere [23]. Data from an original basic survey targeting residents of the evacuation prepared zone were collected from a preliminary investigation conducted over 4 months until July 11, 2011. The maximum estimated external exposure levels of 9747 people (excluding the radiation operation workers) of Kawamata-cho (Yamakiya area), Namie-cho, and Iitate-mura

were found to be 23 mSv. Thus, 94.6% were exposed to doses of <5 mSv per year, and, if including those that were exposed to doses of <10 mSv, 99.3% of the population were exposed. The most recent data released from the Fukushima Prefecture on December 2012 indicated that the average dose of more than 300,000 residents was <1 mSv. The Health Management Survey Committee of Fukushima examined these results and stated, "it is difficult to consider the level of health impairments caused by radiation," but the management of health and efforts toward the reduction of future radiation exposure, such as decontamination and avoidance of contaminated foods, are continuously required.

Children in Iitate-mura and Iwaki Prefecture have been hypothesized to have thyroid radiation exposure possibly reaching 100 mSv by SPEEDI, although they were residing outside the 20 km range. According to a report by Hirosaki University [24], levels of radiation subjected to the thyroid gland may have reached 10 mSv in infants who stayed within 20 km at the time of the accident, and prospective observation of these infants is required. Furthermore, direct measurements of internal exposure soon after the accident suggest a low possibility of any stochastic health effects [25].

The WHO released estimated results of exposure levels around Fukushima in May 2012. Using SPEEDI, prediction data were calculated conservatively from a viewpoint of protection, assuming that the residents did not take refuge for 4 months after the accident in the prepared evacuation area of the nuclear power plant and did not limit their consumption to that of restricted food [26]. According to these assumptions, a 1-year-old child's thyroid radiation dose would be 10–100 mSv in Minami-soma, Iwaki, and Iitate-mura, the prepared evacuation areas, and 1–10 mSv in the prefectures adjacent to Fukushima. However, these data largely deviate from the actual values calculated by thyroid screening and examination using the Whole Body Counter test mentioned above. Further, it is necessary to promote cooperation with international organizations and come to a consensus on accurate dose estimations based on these actual data.

3.1. Thyroid ultrasound examination in Fukushima

Basic investigation of dose estimations in Fukushima including the following measures have begun: (1) thyroid ultrasound, (2) health checkup, (3) mental health performance and lifestyle examination, and (4) examination of expecting and nursing mothers. The progress of these measures are uploaded onto the homepage of the Fukushima Medical University [27]. Results of the environmental radiation dose and investigation into thyroidal radiation exposure dose indicated that there were very few health effects, and these effects were considered restrictive. However, on the basis of a rise in thyroid cancer risk in those exposed to radiation through radioactive iodine ingestion during childhood in Chernobyl, thyroid ultrasound examination was conducted from October 2011 for approximately 360,000 people aged ≤ 18 years. Initial thyroid ultrasound examination of approximately 38,000 people among 48,000 candidates (approximately 80%) of the preparatory evacuation zone was completed by March 2012, and the examination area was enlarged sequentially around Fukushima city after May 2012. Diagnostic criteria

and protocol were introduced and evaluated under an external committee of thyroid specialists in cooperation with associated academic societies. These criteria was developed in response to the need for precision management, evaluation of diagnosis by thyroid ultrasound, and a secondary examination. Most images were considered within a normal range, but examples of minute node and benign findings (e.g., cysts) existed. Standardization of the diagnostic imaging and observation processes was also attained [28]. Approximately 0.5% of those screened required a detailed secondary examination, which included a detailed ultrasound examination, blood test, urinalysis, and cytological diagnosis (Table 1). Although technological changes such as improvements in ultrasound diagnostic instrument that detects small changes (such as cysts and nodules) at a ratio of high frequency have occurred, it is necessary to pay close attention to changes using qualitative diagnosis over time. Hereafter, medical examinations inside and outside the prefecture have been organized using introduction and accuracy control of these criteria, and thyroidal examination will continue for all candidates over the next 2 years. Even if the fixed group of approximately 360,000 people attains an age of >20 years, medical examination will continue to be conducted every 5 years, and the success or failure of the long-term follow-up survey is important.

In addition, survivors of the atomic bomb in Hiroshima and Nagasaki were mainly exposed to external radiation, which led to an outbreak of the solid tumors after a 10-year latency period. Therefore, we re-evaluated the statistical differences between cancer risk by radiation exposure, which was higher than 100 (>200) mSv [29]. Furthermore, Furukawa et al. recently reported a significant dose-response relationship between externally exposed organ-dose and thyroid cancer risk estimation at the level of more than 150–200 mSv [30]. Despite of low dose radiation exposure on thyroid glands, efforts toward understanding the public concern in the risk of external and internal radiation-associated thyroid cancer in Fukushima, especially in children, should be further performed.

In contrast to the initial increase of childhood thyroid cancer 4–5 years after the accident in Chernobyl, which was mainly caused by internal exposure to radioactive iodine, the precedent thyroid examination currently conducted at Fukushima also checks for underlying disease in the thyroid gland by a sophisticated screening before evaluating the effect of the nuclear power plant accident. Furthermore, the prevalence of disease is expected to rise due to the implementation of routine thyroid ultrasound screening in Fukushima, but will also clarify the health effects of radiation, protect the health of residents in the long-term, and continue careful correspondence. In particular, countermeasures based on scientific evidence and the international peer-reviewed processes [16], which utilize the lessons of the Chernobyl accident, are required, and the simultaneous development of mental care facilities in Fukushima are needed to meet the social and psychological needs of the residents.

4. Summary

The risk of radiation-associated thyroid cancer in Fukushima is quite different from that of Chernobyl at the standpoint of the level of thyroid dose exposed by the accident. However, we have learned an importance of initial countermeasures

Table 1 – Results of thyroid examinations conducted by the Fukushima Medical University.

Determination	Basis of determination	Number of people	Proportion (%)
A			
(A1)	No nodules or cysts	24,468	64.2
(A2)	Nodules smaller than 5.0 mm and/or cysts smaller than 20 mm	13,460	35.3
B	Nodules larger than 5.1 mm and/or cysts larger than 20.1 mm	186*	0.5
C	Secondary examination required immediately due to state of thyroid gland, involvement of regional lymph nodes, etc.	0	0
Total number of people examined by FMU		38,114	
Explanation of determinations: For A1 and A2, a wait-and-see approach can be taken until the time of the next examination (FY2014 or thereafter). For B and C, a secondary examination is required. (The related individuals are notified of the time and place of the examination and then examined).			
* There were cases where both nodules and cysts were found.			

that efforts toward the administration of stable iodine just before exposure to radioactive iodine released after an unexpected nuclear disaster should be made to increase public safety and avoid unnecessary fear for radioactive iodines released. Administration would prevent the stochastic effect of low-dose, internal exposure of radioactive iodine after a nuclear disaster and the potential increased risk of thyroid cancer among children. Thus, it is necessary to establish a system for long-term follow-up of all children in Fukushima in order not only to overcome a lack of or uncertainty of initial internal thyroid dose estimation but also to keep their physical and mental health in calm and peace for a long time.

There were several lessons to be learned after the Fukushima nuclear power plant disaster, although it is perhaps too early to understand them all. In particular, re-examination of the evacuation preparation area, pre-distribution of stable iodine tablets, correspondence with residents after the accident, re-examination of public risk communication, and the development of an optimal guideline for revival and restoration after a large accident are necessary. Fortunately, there were no victims of acute radiation syndrome in Fukushima, and hypothyroidism resulting from deterministic effects is unlikely.

Finally, debate and contradictory reporting about the management of papillary microcarcinoma of the thyroid with a diameter <1.0 cm exists for those who are diagnosed with subclinical cancer in childhood and adulthood [31–33]. Careful analysis of thyroid ultrasound data that takes into account not only potential screening bias and exaggerated incidence rates of thyroid disease [34], but also the treatment strategies and outcomes is required [35].

Conflicts of interest

The authors have no conflicts of interest.

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