2. Thyroid Ultrasound Examination (TUE)

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Part 2 Survey Results

2. Thyroid Ultrasound Examination (TUE)

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1. Purpose

The Great East Japan Earthquake of 2011 ultimately led to a reactor melt-through at TEPCO's Fukushima Daiichi Nuclear Power Plant, which is located on the Pacific coast of Fukushima Prefecture. After the Chernobyl nuclear power plant accident of 1986, there was an increased incidence of thyroid cancer, especially in children, due to the ingestion of food containing radioactive iodine released due to the accident. Considering this fact, concerns also emerged in Fukushima Prefecture about health hazards caused by exposure to radiation from released radioactive materials.

Even if every single case of thyroid cancer is analyzed, it is difficult to know whether or not it is caused by radiation. Rather, it is necessary to look for an increase or decrease in the incidence of thyroid cancer through long-term examinations, but prior to the earthquake, there was neither sufficient data on thyroid cancer among Japanese children, nor comparable data from elsewhere. Since there was a four- to five-year latent period for the rapid increase of thyroid cancer in Chernobyl, it was thought that starting examinations in Fukushima immediately after the disaster would provide data that could be used as a basis for comparison. It was easy to imagine that the number of people in Fukushima Prefecture wishing to undergo ultrasound examinations due to radiation anxiety would increase, even if examinations were not organized, so it was thought desirable to address people's needs and anxieties systematically.¹⁾ The Fukushima Prefectural Assembly also unanimously resolved that thyroid examinations be conducted.

For these reasons, the Fukushima Health Management Survey (FHMS) was launched by Fukushima Prefecture in order to monitor and support the health of Fukushima residents over the long term.^{2), 3)} As part of this Survey, the Thyroid Ultrasound Examination (TUE) program was launched in October 2011 for all residents of Fukushima Prefecture aged 18 and under at the time of the disaster.

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Survey name	Survey		0040	0000	0000									esid			1000	1005	1001	1000	1000
5	year	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000	1999	1998	1997	1996	1995	1994	1993	1992
Preliminary Baseline Survey	FY2011-		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(first-round survey)	2013			Ŭ		0		U	0					0	0				0	0	Ŭ
First Full-Scale Thyroid	FY2014-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Survey (second-round survey)	2015			0		0		0	0	0	0	0	0	0	0	0			0	0	0
Second Full-Scale Thyroid	FY2016-	0	0	_	0	~	0	~	0	0	0	0	0	0	0	0	0	0	0		
Survey (third-round survey)	2017		0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Third Full-Scale Thyroid	FY2018-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
Survey (fourth-round survey)	2019			0		0		0	0	0	0	0	0	0	0	0					
Survey for Age 25	FY2017																				0
(Those born in FY1992)	FI2017																				
Survey for Age 25	EV2010																			0	
(Those born in FY1993)	FY2018																			0	
Survey for Age 25	EV2010																		~		
(Those born in FY1994)	FY2019																		0		

2. Survey method and outline of support

1) Eligible persons

The first round of the survey, or the Preliminary Baseline Survey (PBLS), started on October 9, 2011, for Fukushima Prefecture residents who were born between April 2, 1992 and April 1, 2011, i.e., in the range of 0 to 18 years old as of March 11, 2011. Thus, 367,637 people were eligible for the examination (as of March 31, 2018) (Table 1).

For the Full-Scale Surveys (FSS) from April 2014 onward, in addition to the residents eligible for PBLS, those who were born between April 2, 2011 and April 1, 2012 were also included as eligible for the examination. A total of 381,244 people were eligible for the first FSS (the second-round survey) conducted from FY2014 to FY2015; 336,670 people for the second FSS (the third-round survey) conducted from FY2016 to FY2017; and 294,240 people for the third FSS (the fourth-round survey) conducted from FY2018 to FY2019 (as of March 31, 2020). In addition, from FY2017, a periodic survey for those aged 25 and beyond (Survey for Age 25+) has started, and 22,653 people born in FY1992, 21,889 people born in FY1993, and 22,095 people born in FY1994 were eligible for the examination (as of March 31, 2020).

2) Flow of the TUE

An invitation for examination is mailed to the eligible person, and after obtaining written consent, an appointment for a primary examination and related information are sent. Next, in the primary examination, ultrasound images and ultrasound findings of nodules, cysts, etc. are obtained. These results are evaluated and confirmed by the Thyroid Examination Evaluation Committee of the Radiation Medical Science Center for the Fukushima Health Management Survey (hereinafter referred to as "our/the Center"). If the result is Grade B or C, an invitation for a secondary confirmatory examination is sent to the participant, and again after obtaining written consent, the confirmatory examination will be conducted at a

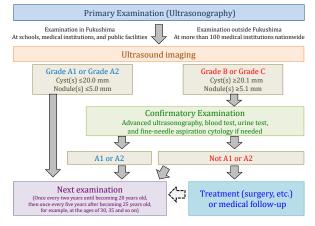


Figure 1. Flow of the TUE

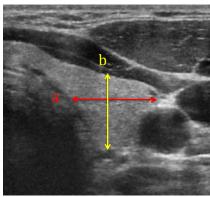
designated specialized medical facility. If the results of the confirmatory examination indicate the need for treatment or follow-up, the participant will be referred for treatment under Japan's system of universal health coverage. Otherwise, the participant will be recommended to receive the next primary examination. Even if the participant is referred for treatment, he/she is still eligible for the next examination (Figure 1).

3) Method of the primary examination

(1) How the examination is performed

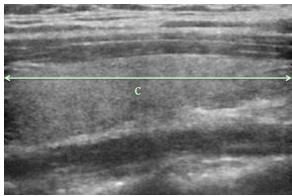
In the primary examination, thyroid ultrasonography is performed.⁴⁾ An ultrasound examination is performed using a linear probe with a frequency of 10 MHz or higher and an ultrasound system with a color Doppler function in addition to B-mode imaging. For on-location examinations in Fukushima Prefecture, a portable system is used. The participant is asked to lie down in a supine position, neck extended using a shoulder pillow during the examination. Still images are obtained and, if necessary, video recordings are stored electronically on the image server of our Center. The examiner measures and records the size of both lobes of the thyroid gland (Figure 2); the presence, location, maximum diameter, and number of cysts (Figure 3A) and nodules (Figure 3B); and other findings.

A (Transverse image)



B (Longitudinal image)

the thyroid gland



a: Transverse diameter, b: Anteroposterior diameter, c: Longitudinal diameter Figure 2. Method of measuring the size of both lobes of



Figure 3A. Ultrasound image of thyroid cysts



Figure 3B. Ultrasound image of a thyroid nodule

(2) Criteria for diagnosis

The ultrasound images recorded at the examinations conducted in and outside Fukushima Prefecture are collected at our Center as digital data in DICOM (Digital Imaging and Communications in Medicine) format, and reviewed by the Evaluation Committee, consisting of several certified specialists, using criteria for the primary examination (Table 2).^{4), 5)} A participant with Grade B or C lesions will be referred to a secondary confirmatory examination. Grade C is defined as one that requires an immediate confirmatory examination. Specifically, thyroid nodules that are suspected to have infiltrated non-thyroidal tissues or those with a large lymph node metastasis (Large N) of 3 cm or more are Grade C. The final result is conveyed to the participant in writing.

Grade		Criteria	Next step
Α		No abnormal findings	
	A1	No cysts or nodules	Undergo another primary examination 2 (or 5) years later
	A2	Nodule(s) with a diameter of 5.0 mm or less* or cyst(s) with a diameter of 20.0 mm or less	Undergo another primary examination 2 (or 5) years later
]	B Nodule(s) with a diameter of 5.1 mm or more or cyst(s) with a diameter of 20.1 mm or more		Undergo a confirmatory examination
(C Cases considered as requiring detailed examination**		Undergo a confirmatory examination immedi- ately

Table 2. Criteria for the primary examination

* Some nodules that are 5.0 mm or less in diameter may be judged as Grade B based on ultrasound images.

** Cases in which thyroid nodules are suspected to have infiltrated non-thyroidal tissues or a large lymph node metastasis (Large N) of 3 cm or more is observed.

(3) Examinations conducted by Fukushima Medical University in Fukushima Prefecture

The primary examination in the PBLS started on October 9, 2011. At first, the examination was conducted at Fukushima Medical University (FMU) on weekends and holidays, until November 13, 2011. During this period, the ultrasound diagnosis systems were customized for the TUE and information was provided to future examiners. The first on-location examinations were conducted at health centers and elementary and junior high schools in Kawamata Town and Minamisoma City. Since the examinations were not conducted at high schools at first, an extremely large number of people who wished to take the examination came to these venues.

Furthermore, in order to implement the examinations throughout the prefecture, municipalities wanted the examinations to be conducted at schools, for reasons such as ensuring equal opportunities for those who wanted to receive the examination, transportation to the examination venues, and reducing the burden on parents/ guardians. In addition, municipal boards of education requested that the examinations be conducted at schools because of the impact on classes if a large number of students would be absent. In response to these requests, we started thyroid examinations at schools after consulting with the prefectural government.

Currently, the TUE program under the FHMS is conducting on-location examinations in Fukushima Prefecture as follows:

- Elementary schools, junior high schools, high schools, etc.
- Public facilities (Sundays and holidays)
- Other universities in Fukushima Prefecture (outside of lecture hours)
- Public facilities (weekdays)
- Public facilities (weekday evenings)

(4) Examinations conducted by FMU outside Fukushima Prefecture

After the Great East Japan Earthquake, more than 30.000 residents needed to evacuate outside the prefecture. Although we have been working to secure medical facilities capable of primary examinations outside Fukushima Prefecture, as described below, there were not enough facilities to accept people in either the Tohoku region or the Tokyo metropolitan area, where many residents were evacuated. Therefore, FMU's Primary Examination Team conducted on-location examinations in Yamagata, Tochigi, Saitama, Chiba, Kanagawa, and Niigata Prefectures from FY2012 to FY2016. Since then, the number of medical facilities capable of primary examinations has increased, and FMU is not currently conducting on-location examinations outside Fukushima Prefecture.

(5) Examinations conducted by other medical facilities in Fukushima Prefecture

In addition to certified specialists and certified sonographers in Fukushima Prefecture (Table 3), the number of medical doctors, medical technologists, and radiological technologists who can perform primary examinations in Fukushima Prefecture has been increasing as a result of training efforts by the Fukushima Medical Associ-

Examination		Specialist qualification	Certifying organization				
Primary examination	Medical doctor	Certified Endocrine Surgeon Certified Thyroid Surgeon ¹⁾ Certified Specialist Certified Endocrinologist (Pediatrics) ²⁾ Certified Fellow (Thyroid/Body Surface/General) Committee-Certified Physician ³⁾	Japan Association of Endocrine Surgery Japanese Society of Thyroid Surgery Japan Thyroid Association Japan Endocrine Society Japan Society of Ultrasonics in Medicine Fukushima Prefecture Joint Committee for Thyroid Examination Support				
	Technologist, etc. ⁴⁾	Certified Fellow (Body Surface) Committee-Certified Physician ³⁾	Japan Society of Ultrasonics in Medicine Fukushima Prefecture Joint Committee for Thyroid Examination Support				
Confirmatory examination	Medical doctor	Certified Specialist or Certified Endocrine/Thyroid Surgeon and	Japan Thyroid Association Japan Association of Endocrine Surgery, Japanese Society of Thyroid Surgery				
		Certified Fellow (Body Surface/Thyroid)	Japan Society of Ultrasonics in Medicine				

Table 3. Qualifications for examiners

1) The Japanese Society of Thyroid Surgery was merged with the Japan Association of Endocrine Surgery in 2018, and the specialist certification system was also unified into endocrine surgeon certification.

2) A member of the Japanese Society of Pediatric Endocrinology and a certified endocrinologist (Pediatrics) of the Japan Thyroid Association

3) Medical doctors or technologists who participated in thyroid ultrasonography seminars organized by the Fukushima Medical Association (FMA), passed examinations, and are practicing medicine in Fukushima Prefecture

4) Radiological technologists, clinical laboratory technicians, nurses, and assistant nurses

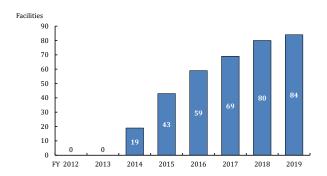


Figure 4. Number of medical facilities conducting primary examinations in Fukushima Prefecture, by year

ation's Joint Committee for Thyroid Examination Support.

As a result, existing medical facilities in Fukushima were credentialled to conduct primary examinations in 2014, and primary examinations were started at medical facilities other than FMU. The number of such facilities increased to 84 by the end of FY2019 (Figure 4). However, as of October 2020, only 24 out of 59 municipalities in Fukushima Prefecture have had primary examination facilities, and further expansion of the number of facilities is considered to be an important issue for the future.

There are many issues to be addressed when conducting the same examination at a large number of medical facilities, such as standardization of examinations and diagnostic criteria, and sharing of methods for dealing with participants during examinations. For this reason, we are visiting medical facilities in Fukushima Prefecture, providing support and guidance on how to conduct thyroid examinations, and conducting simulations of the examination.

The Council of Medical Facilities conducting Thyroid Examinations in Fukushima Prefecture, including medical doctors in charge of the examinations and medical staff at participating facilities, regularly shares information to carry out quality control and uniform reporting standards for the examination.

(6) Examinations conducted by medical facilities outside Fukushima Prefecture

For those who evacuated or relocated from Fukushima Prefecture after the earthquake, we outsource the primary examination to medical facilities in other prefectures where certified spe-

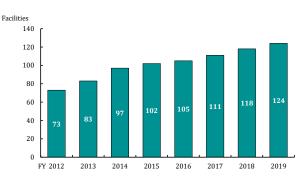
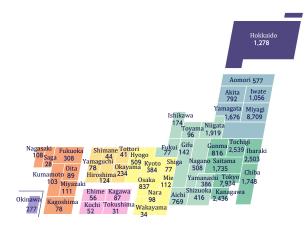


Figure 5. Number of medical facilities conducting primary examinations outside Fukushima Prefecture, by year



Cumulative total from October 2011 to March 2019

Figure 6. Total number, by prefecture, of people receiving primary examinations outside Fukushima Prefecture

cialists are enrolled. In FY2012, 73 medical facilities started conducting the examination, making the primary examination available in all prefectures. Furthermore, with the cooperation of medical facilities across the country, the number of facilities conducting primary examinations has been increasing year by year, and by the end of FY2019, it reached 124 (Figure 5).

The examinations are conducted by certified specialists or technologists who meet the requirements for primary examination providers (Table 3). As in the case of medical facilities in Fukushima Prefecture, information is shared with medical facilities and the quality of examinations is maintained through various opportunities, such as visits to medical facilities before the start of the examinations, hands-on seminars, and the Council of Medical Facilities conducting Thyroid Examinations outside Fukushima Prefecture, including medical doctors in charge of thyroid examinations, medical staff, and administrators from participating medical facilities. To date, primary examinations have been conducted in all prefectures (Figure 6), and by the end of FY2019, a total of 46,785 people had undergone primary examinations at medical facilities outside Fukushima Prefecture.

4) Method of the confirmatory examination

(1) How the examination is conducted

Participants found to have Grade B or C results in their primary examination are invited by mail to take a confirmatory examination. After obtaining written consent for the confirmatory examination, an appointment is made and information is sent to them.

The confirmatory examination includes (1) interview and medical consultation by a medical doctor, (2) detailed thyroid ultrasonography using high-end ultrasound equipment, (3) blood tests for thyroid-stimulating hormone, free thyroid hormone (Free T3, Free T4), thyroglobulin, anti-thyroglobulin antibody, and anti-thyroid peroxidase antibody, and (4) urinalysis (for iodine in urine). In addition, ultrasound-guided aspiration cytology is performed only when an indication for aspiration cytology is determined in accordance with the ultrasound diagnostic criteria for thyroid nodules by the Japan Society of Ultrasonics in Medicine⁶⁾ and a diagnostic flowchart by the Japan Association of Breast and Thyroid Sonology⁷⁾ and after consent is obtained.⁸⁾ At present, cytological diagnosis is made in accordance with the General Rules for the Description of Thyroid Cancer and the Bethesda System, which is a global standard.⁹⁾

(2) Explanation of the examination results and decision on what to do after the confirmatory examination

The results of the confirmatory examination are explained directly to participants and their families, and consultation will be held to discuss what to do after the confirmatory examination. If the result of the confirmatory examination is equivalent to Grade A1 or A2 by the same criteria as that of the primary examination, the examinee will, in principle, be recommended to take the primary examination in the next round. In other cases, we will refer the participant for treatment under Japan's system of universal healthcare, taking into consideration the examination results and the needs of each participant and their family (Figure 1). Even in cases where the participant has been referred for treatment, an invitation to the next primary examination will be sent to them so that they can undergo the primary examination if desired.

(3) Medical facilities that perform the confirmatory examination

Medical facilities that can perform confirmatory examinations are defined as those with a certified thyroidologist or certified endocrine surgeon and a certified ultrasound specialist (body surface, thyroid, general) (Table 3). As of the end of FY2019, five medical facilities. including FMU Hospital in Fukushima Prefecture and 37 medical facilities outside Fukushima Prefecture, were conducting confirmatory examinations.

5) Progress of the TUE

(1) Preliminary Baseline Survey

Primary examinations in the Preliminary Baseline Survey (PBLS) (the first-round survey), which started on October 9, 2011, were, in principle, conducted year-by-year in descending order of post-accident air dose rates: the 13 municipalities of the nationally designated evacuation zone in FY2011 (named on p. 84), most of the Nakadori Area in FY2012, and the Kennan District (a southern part of Nakadori), the Hamadori Area, and the Aizu Area in FY2013 (Figure 7). In some municipalities, examinations continued until April 2015. The confirmatory examinations of the PBLS started in FY2012 and continued until FY2015 (Figure 9).

(2) Full-Scale Surveys

The first Full-Scale Survey (FSS) (the second-round survey) was conducted from FY2014 to FY2015, the second FSS (the third-round survey) from FY2016 to FY2017, and the third FSS (the fourth-round survey) from FY2018 to FY2019 (Figure 9). In the first half of each survey period, examinations were conducted mainly in the 13 municipalities in the designated evacua-

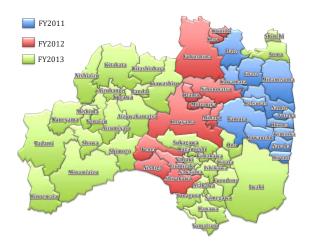


Figure 7. Implementation year of the Preliminary Baseline Survey, by municipality

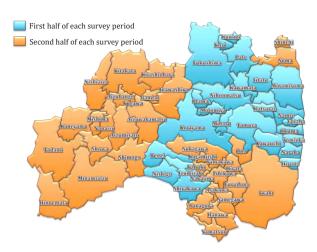


Figure 8. Implementation fiscal year of the FSS, by municipality

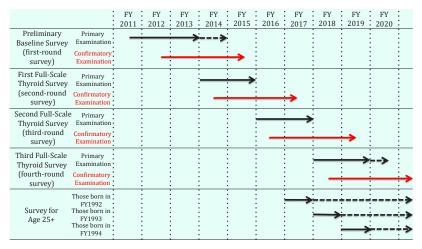


Figure 9. Progress of each survey

tion zone and the Nakadori Area, while in the second half, examinations were conducted in the Kennan district, the Hamadori Area, and the Aizu Area (Figure 8). The Survey for Age 25, which is a part of the FSS, started in FY2017, when the residents born in FY1992, the oldest age group eligible for TUE, turned 25. In FY2018 and FY2019, the primary examination for those born in FY1993 and FY1994, respectively, were conducted (Figure 9). Since there will be a 5-year interval between the Survey for Age 25 and the Survey for Age 30, it is possible for those eligible for the Survey for Age 25 to take the primary examination until the year of turning 29.

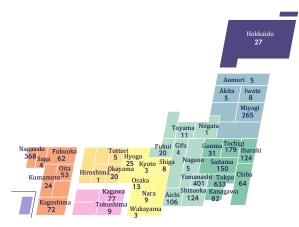
In addition, the confirmatory examination is conducted sequentially after the results of the primary examination are sent.

6) External support and training of examiners in Fukushima Prefecture

(1) External support

Since there were only a limited number of certified specialists and technologists specializing in thyroid diagnosis and treatment in Fukushima Prefecture, we requested the cooperation of seven related academic societies in Japan from the beginning of the TUE program: the Japan Thyroid Association, the Japanese Society of Thyroid Surgery, the Japan Association of Endocrine Surgery, the Japanese Society for Pediatric Endocrinology, the Japan Society of Ultrasonics in Medicine, the Japan Association of Breast and Thyroid Sonology, and the Japanese Society of Sonographers. Medical doctors and technologists from all over the country are participating in the examinations in Fukushima as support examiners. We have also received support from the Med-

2. Thyroid Ultrasound Examination (TUE)



Cumulative total from October 2011 to March 2019

Figure 10. Total number of support examiners from outside Fukushima prefecture for thyroid examinations conducted in the prefecture

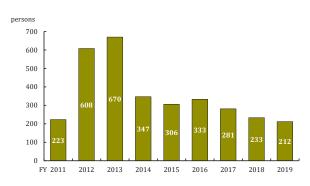


Figure 11. Total number of support examiners from outside Fukushima Prefecture for thyroid examinations conducted in the Prefecture, by year

ical Support Committee for Disaster Victims of the National Council of Medical School Deans and Hospital Directors, which has dispatched examiners from national university hospitals across Japan. As a result, we have received support from almost all over the country (Figure 10), and by the end of FY2019, a total of 3,213 medical doctors and technologists have provided support. Although the annual trend is decreasing (Figure 11), support from certified specialists and technologists is shifting to support the training of examiners in Fukushima Prefecture.

(2) Training of in-house examiners

In order to develop human resources specializing in thyroid ultrasonography, FMU has been training thyroid ultrasonographers.¹⁰⁾ In addition to the basics of neck anatomy, trainees learn an overview of thyroid diseases, ultrasound diagnosis of thyroid nodular lesions, characteristics of the pediatric thyroid gland, and the overall structure of the FHMS. Considerations for participants and their parents/guardians are also explained. In addition, they practice ultrasound examinations on a simulator or on volunteer staff members with cysts or benign nodules, to learn examination techniques. Furthermore, after a senior certified ultrasonography specialist confirms their knowledge, techniques, and manner of communicating with participants, the trainees are allowed to participate in the primary examination as examiners.

(3) Training of examiners in the prefecture

The Fukushima Prefecture Joint Committee for Thyroid Examination Support and the Fukushima Medical Association hold Fukushima Prefecture Thyroid Ultrasonography Seminars in major cities in Fukushima Prefecture for medical doctors, medical technologists, radiological technologists and others working in the prefecture.^{10), 11)} Under this program, certification to conduct primary examinations only in Fukushima Prefecture are granted after the following steps: (1) lectures on thyroid diseases and thyroid ultrasonography for the required number of credits, (2) hands-on practical training (basic and applied), and (3) certification examinations (academic and practical). In addition, support is provided for those who have passed the examination, so that they can conduct primary examinations independently, after (4) participation in thyroid examinations at an examination venue (at least three times).

7) Support for participants and their families

(1) Support to promote understanding of thyroid examinations

Thyroid Newsletters are issued and mailed twice a year to residents who are eligible for the examination and their parents/guardians. The Thyroid Newsletter includes descriptions of upcoming thyroid examinations, the latest aggregate results, current topics, as well as Q & A to address common concerns (Figure 12).

In addition, we provide on-location lectures to schools and on-location information sessions to groups other than schools upon request. Using



Figure 12. Thyroid Newsletters

programs and materials tailored to the age groups of the participants, we explain about ultrasonography; thyroid cysts, nodules, and cancer; the purpose of thyroid examinations; and the advantages and disadvantages of receiving thyroid examinations. We also provide support so that they can make their own decisions about whether to have an examination and how to understand examination results (Figure 13).

Those eligible for the examination and living in the prefecture can take the examination at school through high school, but after graduating, they will have to take the examination outside of school. For this reason, helpful information is printed on materials such as notebooks and file folders, distributed at high school graduation and coming-of-age ceremonies, to explain how and when to take the primary examination.

(2) Support before taking the examination

Before the primary examination, an "Invitation to Thyroid Examination" booklet is mailed to the eligible person, explaining the purpose of the examination (Figure 14) and its advantages and disadvantages (Figure 15). In addition, as a com-



Figure 13. On-location lecture

plement to the written explanations, we provide opportunities to view explanatory videos online, and secure consultation opportunities through our call center, dedicated medical consultation line, a web-based consultation system, etc., to support participants and their parents/guardians in making decisions about whether to undergo the examination.

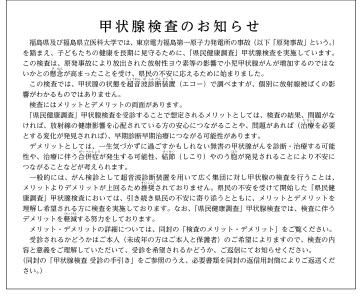


Figure 14. Invitation to Thyroid Examinations

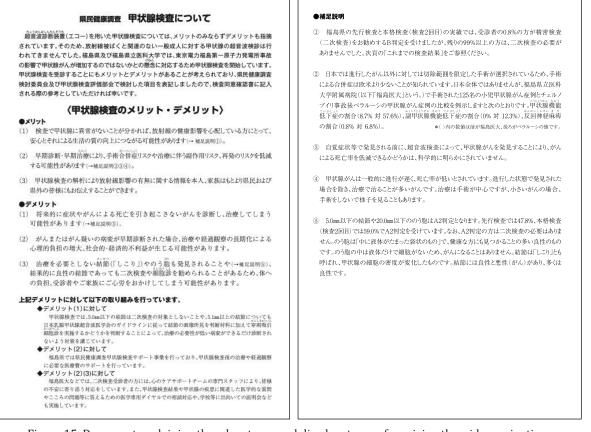


Figure 15. Document explaining the advantages and disadvantages of receiving thyroid examinations

(3) Support at the primary examination

During examinations at general venues in Fukushima Prefecture, where participants can come with their parents/guardians, the provisional results of the primary examination are verbally explained while showing pertinent ultrasound images. At the same time, explanations about thyroid nodules and cysts, responses to concerns about radiation exposure, and explanations about future examinations are also offered (Figure 16).

The explanations at the time of the primary examination are provided by certified specialists from FMU and other professionals from academic societies such as the Japan Endocrine Society and the Japanese Society for Pediatric Endocrinology,

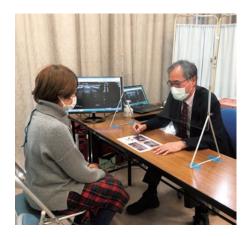


Figure 16. Explanation of the examination at the primary examination venue



Figure 17. Leaflet distributed at the primary examination

and the Japan Radioisotope Association. In addition, we are making efforts so that explanations of examination results can come from the medical doctor in charge when examinees undergo examinations at medical facilities other than FMU.

In addition, since there are cases where parents/guardians cannot be present for explanations, such as primary examinations at school, a leaflet containing explanations of thyroid nodules and cysts and confirmatory examinations is distributed to assist in understanding examination results (Figure 17).

(4) Support at the confirmatory examination

In order to respond to the concerns and anxieties of those who were recommended to take confirmatory examinations, a support team consisting of mental health social workers, general social workers, medical social workers, clinical psychologists, and nurses was established in November 2013 to provide psychological support for those who undergo the confirmatory examination at FMU Hospital.

Specific aspects of the psychological support include attending the examination, talking to the participants during and after the examination, and offering telephone and web consultations before and after the examination. This Thyroid Support Team provides psychological support by speaking with everyone as much as possible, being attentive to any anxieties of the participant and their family, and helping the participant communicate with the medical doctor.

(5) Support during clinical treatment

The activities of the Thyroid Support Team are not limited to the time of the confirmatory examination, but also continue in cooperation with a hospital's medical team even after the participant has been referred for treatment. Support is provided not only during outpatient follow-up visits, but also during pre-admission examinations, during hospitalization, and after discharge if hospitalization is required.

3. Survey results and analyses of survey results

1) Survey results

(1) Preliminary Baseline Survey (PBLS) (the first-round survey)

A) Primary examination results

As of March 31, 2018, there were 300,472 (81.7%) of 367,637 eligible persons who received primary examinations and had their results confirmed. The breakdown of results was as follows: Grade A1 in 154,605 (51.5%); Grade A2 in 143,573 (47.8%); Grade B in 2,293 (0.8%); and Grade C in 1 (0.0%)(Table 4).

The detection rate of nodules and cysts was 0.6% (1,713 people) for nodules of 5.0 mm or less, 0.8% (2,275 people) for nodules of 5.1 mm or more, 47.9% (143,899 people) for cysts of 20.0 mm or less, and 0.0% (12 people) for cysts of 20.1 mm or more.

	а	b		С	Pri	imary exam	ination resu	ılts
	Eligible	Participants	Participants	Participants with confirmed	I	ł	Requ confirmat	iring tory exam
	persons	(% of a)	outside Fukushima	results (% of b)	A1 (% of c)	A2 (% of c)	B (% of c)	C (% of c)
FY 2011	47,769	41,810 (87.5)	2,024	41,810 (100.0)	26,375 (63.1)	15,214 (36.4)	221 (0.5)	0 (0.0)
FY 2012	161,120	139,337 (86.5)	4,267	139,337 (100.0)	76,195 (54.7)	62,154 (44.6)	987 (0.7)	1 (0.0)
FY 2013	158,748	119,325 (75.2)	3,220	119,325 (100.0)	52,035 (43.6)	66,205 (55.5)	1,085 (0.9)	0 (0.0)
Total	367,637	300,472 (81.7)	9,511	300,472 (100.0)	154,605 (51.5)	143,573 (47.8)	2,293 (0.8)	1 (0.0)

Table 4. Primary examination results in the PBLS (as of March 31, 20	
	18)

Table 5. Confirmatory	examination	results in	the PBLS	(as of March 31	, 2018)
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	а	b	С	Confi	rmatory exa	amination results		
	Those recommended	Participants	Participants with	I	Α	Otl	ner	
	to undergo confirmatory exam	(% of a)	confirmed results (% of b)	A1 (% of c)	A2 (% of c)	d (% of c)	FNAC (% of d)	
FY 2011	221	199 (90.0)	198 (99.5)	18 (9.1)	36 (18.2)	144 (72.7)	92 (63.9)	
FY 2012	988	920 (93.1)	903 (98.2)	57 (6.3)	250 (27.7)	596 (66.0)	264 (44.3)	
FY 2013	1,084	1,011 (93.3)	990 (97.9)	57 (5.8)	293 (29.6)	640 (64.6)	191 (29.8)	
Total	2,293	2,130 (92.9)	2,091 (98.2)	132 (6.3)	579 (27.7)	1,380 (66.0)	547 (39.6)	

B) Confirmatory examination results

Of the 2,294 people with Grade B or C results in their primary examination, 2,130 (92.9%) underwent confirmatory examinations, and the results for 2,091 (98.2%) were confirmed: Grade A1 in 132 (6.3%) and Grade A2 for 579 (27.7%) by primary examination criteria. The remaining 1,380 (66.0%) were Grade B, of whom 547 people (39.6%) underwent fine needle aspiration cytology (FNAC) (Table 5).

Of those who underwent FNAC, 116 had lesions malignant or suspicious for malignancy, including 39 males and 77 females. Their ages at the time of confirmatory examination ranged from 8 to 22 years (mean age: 17.3 ± 2.7 years),

and tumor diameters ranged from a minimum of 5.1 mm to a maximum of 45.0 mm (mean tumor diameter: 13.9 ± 7.8 mm) (Table 6).

(2) First Full-Scale Survey (FSS) (the second-round survey)

A) Primary examination results

As of March 31, 2018, there were 270,540 (71.0%) of 381,244 eligible persons who received a primary examination, and the results of 270,529 people were confirmed. The breakdown of the results was as follows: Grade A1 in 108,718 (40.2%); Grade A2 in 159,584 (59.0%); Grade B in 2,227 (0.8%); and Grade C in 0 (0.0%) (Table 7).

	Preliminary Baseline Survey (first-round survey)	First Full-Scale Thyroid Survey (second-round survey)	Second Full-Scale Thyroid Survey (third-round survey)	Third Full-Scale Thyroid Survey (fourth-round survey)	Survey for Age 25
Malignant or suspicious for malignancy	116	71	31	21	7
Male / Female	39 / 77	32 / 39	13 / 18	11 / 10	2 / 5
Age* (min-max)	8 - 22	9 – 23	12 – 23	11 – 20	24 – 27
Age* (mean±SD)	17.3±2.7	16.9±3.2	16.3±2.9	16.6±2.5	25.3±1.0
Tumor size (min-max, mm)	5.1 - 45.0	5.3 - 35.6	5.5 - 33.0	6.1 – 29.4	10.8 – 49.9
Tumor size (mean±SD, mm)	13.9±7.8	11.1±5.6	12.9±6.4	11.6±5.3	22.6±15.6

* Age at confirmatory examination

Table 7. Primary examination results of the first FSS	(the second-round survey) (as of March 31, 2018)

	а	b		С	Pri	mary exam	ination resu	esults		
	Eligible Participants Participants		Participants with confirmed	А		Requiring confirmatory exam				
	persons	(% of a)	of a) Fukushima	results (% of b)	A1 (% of c)	A2 (% of c)	B (% of c)	C (% of c)		
FY 2014	216,866	159,177 (73.4)	11,426	159,171 (100.0)	66,451 (41.7)	91,413 (57.4)	1,307 (0.8)	0 (0.0)		
FY 2015	164,378	111,363 (67.7)	4,232	111,358 (100.0)	42,267 (38.0)	68,171 (61.2)	920 (0.8)	0 (0.0)		
Total	381,244	270,540 (71.0)	15,658	270,529 (100.0)	108,718 (40.2)	159,584 (59.0)	2,227 (0.8)	0 (0.0)		

Table 8. Confirmatory examination	n results of the first FSS (the second-ro	ound survey) (as of March 31, 2018)
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	a b		С	Confirmatory examination results				
	Those recommended	Participants	Participants with	I	Ι	Other		
	to undergo confirmatory exam		confirmed results (% of b)	A1 (% of c)	A2 (% of c)	d (% of c)	FNAC (% of d)	
FY 2014	1,307	1,099 (84.1)	1,075 (97.8)	39 (3.6)	244 (22.7)	792 (73.7)	151 (19.1)	
FY 2015	920	775 (84.2)	751 (96.9)	24 (3.2)	121 (16.1)	606 (80.7)	56 (9.2)	
Total	2,227	1,874 (84.1)	1,826 (97.4)	63 (3.5)	365 (20.0)	1,398 (76.6)	207 (14.8)	

The detection rate of nodules and cysts was 0.6% (1,570 people) for nodules less than 5.0 mm, 0.8% (2,219 people) for nodules of 5.1 mm or more, 59.3% (160,363 people) for cysts less than 20.0 mm, and 0.0% (6 people) for cysts greater than 20.1 mm.

B) Confirmatory examination results

Of the 2,227 participants with Grade B or C results in their primary examination, 1,874 (84.1%) underwent confirmatory examinations, and the results for 1,826 (97.4%) were confirmed: Grade A1 in 63 (3.5%) and Grade A2 in 365 (20.0%) by primary examination criteria. The remaining 1,398 (76.6%) were Grade B, of whom 207 people (14.8%) underwent FNAC (Table 8).

Of those who underwent FNAC, 71 had lesions malignant or suspicious for malignancy, including 32 males and 39 females. Their ages at the time of confirmatory examination ranged from 9 to 23 years (mean age: 16.9 ± 3.2 years), and tumor diameters ranged from a minimum of 5.3 mm to a maximum of 35.6 mm (mean tumor diameter: 11.1 ± 5.6 mm) (Table 6).

(3) Second FSS (the third-round survey)

A) Primary examination results

As of March 31, 2020, there were 217,921 (64.7%) of 336,670 eligible persons who received a primary examination, and the results of 217,920 people were confirmed. The breakdown of the results was as follows: Grade A1 in 76,433 (35.1%); Grade A2 in 139,986 (64.2%); Grade B in 1,501 (0.7%); and Grade C in 0 (0.0%) (Table 9).

The detection rate of nodules and cysts was 0.4% (829 people) for nodules of 5.0 mm or less, 0.7% (1,498 people) for nodules of 5.1 mm or more, 64.6% (140,672 people) for cysts of 20.0 mm or less, and 0.0% (3 people) for cysts of 20.1 mm or more.

B) Confirmatory examination results

Of the 1,501 participants with Grade B or C results in their primary examination, 1,101 (73.4%) underwent the confirmatory examinations, and the results of 1,060 (96.3%) were confirmed: Grade A1 in 9 (0.8%) and Grade A2 in 100 (9.4%) by primary examination criteria. The remaining 951 (89.7%) were Grade B, of whom 78 people (8.2%) underwent FNAC (Table

	а	b	b		Primary examination results			
	Eligible		Eligible Participants Participants With confirmed		А		Requiring confirmatory exam	
	persons	(% of a)	outside Fukushima	results (% of b)	A1 (% of c)	A2 (% of c)	B (% of c)	C (% of c)
FY 2016	191,877	126,396 (65.9)	8,911	126,395 (100.0)	44,045 (34.8)	81,545 (64.5)	805 (0.6)	0 (0.0)
FY 2017	144,793	91,525 (63.2)	3,598	91,525 (100.0)	32,388 (35.4)	58,441 (63.9)	696 (0.8)	0 (0.0)
Total	336,670	217,921 (64.7)	12,509	217,920 (100.0)	76,433 (35.1)	139,986 (64.2)	1,501 (0.7)	0 (0.0)

Table 9. Primary examination results of the second FSS (the third-round survey) (as of March 31, 2020)

Table 10. Confirmatory examination results of the second FSS	S (the third-round survey) (as of March 31, 2020)
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	a b c Confirmatory exa		mination re	mination results			
	Those recommended	Participants	Participants with	A	Ι	Other	
	to undergo confirmatory exam	(% of a)	confirmed results (% of b)	A1 (% of c)	A2 (% of c)	d (% of c)	FNAC (% of d)
FY 2016	805	612 (76.0)	585 (95.6)	5 (0.9)	58 (9.9)	522 (89.2)	40 (7.7)
FY 2017	696	489 (70.3)	475 (97.1)	4 (0.8)	42 (8.8)	429 (90.3)	38 (8.9)
Total	1,501	1,101 (73.4)	1,060 (96.3)	9 (0.8)	100 (9.4)	951 (89.7)	78 (8.2)

10).

Of those who underwent FNAC, 31 had lesions malignant or suspicious for malignancy, including 13 males and 18 females. Their ages at the time of confirmatory examination ranged from 12 to 23 years (mean age: 16.3 ± 2.9 years), and the tumor diameters ranged from a minimum of 5.6 mm to a maximum of 33.0 mm (mean tumor diameter: 12.9 ± 6.4 mm) (Table 6).

(4) Third FSS (the fourth-round survey)

A) Primary examination results

As of March 31, 2020, the primary examination is still in progress; of 294,240 eligible persons, 180,570 (61.4%) have received primary examination, and the results of 177,424 people were confirmed. The breakdown of the results was as follows: Grade A1 in 59,808 (33.7%); Grade A2 in 116,289 (65.5%) Grade B in 1,327 (0.7%); and Grade C in 0 (0.0%) (Table 11).

The frequency of detection of nodules and cysts was 0.4% (645 people) for nodules of 5.0 mm or less, 0.7% (1,323 people) for nodules of 5.1 mm or more, 65.9% (116,959 people) for cysts of 20.0 mm or less, and 0.0% (4 people) for cysts of 20.1 mm or more.

B) Confirmatory examination results

Of the 1,327 participants with Grade B or C results in their primary examination, 741 (55.8%) underwent confirmatory examinations, and results for 647 (87.3%) were confirmed: Grade A1 in 2 (0.3%) and Grade A2 in 57 (8.8%) by primary examination criteria. The remaining 588 (90.9%) were Grade B, of whom 49 people (8.3%) underwent FNAC (Table 12).

Of those who underwent FNAC, 21 had lesions malignant or suspicious for malignancy, including, 11 males and 10 females. Their ages at the time of confirmatory examination ranged from 11 to 20 years (mean age: 16.6 ± 2.5 years), and the tumor diameters ranged from a minimum of 6.1 mm to a maximum of 29.4 mm (mean tumor diameter: 11.6 ± 5.3 mm) (Table 6).

(5) Survey for Age 25+

A) Primary examination results

Examinations for those turning 25 years old (born between FY1992 and FY1994) began in May 2017, and by March 31, 2020, there were 5,578 (8.4%) of 66,637 eligible persons who had undergone the examination and the results of 5,234 (93.8%) were confirmed. The breakdown

	а	b		С	Primary examination results			lts
	Eligible		Participants outside	Participants with confirmed	I	ł	Requ confirmat	iring tory exam
	persons	(% of a)	Fukushima	results (% of b)	A1 (% of c)	A2 (% of c)	B (% of c)	C (% of c)
FY 2018	168,033	107,466 (64.0)	7,003	107,023 (99.6)	36,585 (34.2)	69,751 (65.2)	687 (0.6)	0 (0.0)
FY 2019	126,207	73,104 (57.9)	2,796	70,401 (96.3)	23,223 (33.0)	46,538 (66.1)	640 (0.9)	0 (0.0)
Total	294,240	180,570 (61.4)	9,799	177,424 (98.3)	59,808 (33.7)	116,289 (65.5)	1,327 (0.7)	0 (0.0)

Table 11. Primary examination results of the third FSS (the fourth-round survey) (as of March 31, 2020)

	а	b	С	Confirmatory examination results			
	Those recommended	Those recommended Participants		A	ł	Other	
	to undergo confirmatory exam	(% of a)	confirmed results (% of b)	A1 (% of c)	A2 (% of c)	d (% of c)	FNAC (% of d)
FY 2018	687	459 (66.8)	435 (94.8)	2 (0.5)	39 (9.0)	394 (90.6)	38 (9.6)
FY 2019	640	282 (44.1)	212 (75.2)	0 (0.0)	18 (8.5)	194 (91.5)	11 (5.7)
Total	1,327	741 (55.8)	647 (87.3)	2 (0.3)	57 (8.8)	588 (90.9)	49 (8.3)

of the results was as follows: Grade A1 in 2,228 (42.6%); Grade A2 in 2,762 (52.8%); Grade B in 244 (4.7%); and Grade C in 0 (0.0%) (Table 13).

The detection rate of nodules and cysts was 1.9% (101 people) for nodules of 5.0 mm or less,

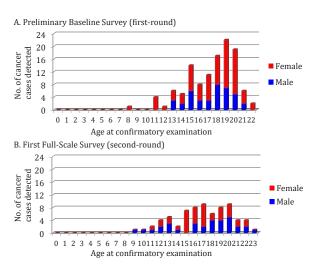


Figure 18. Number of malignant or suspected malignant cases by age at the time of confirmatory examination in the PLBS (the first-round survey) and the first FSS (the second-round survey)

4.6% (243 people) for nodules of 5.1 mm or more, 54.9% (2,872 people) for cysts of 20.0 mm or less, and 0.0% (1 person) for cysts of 20.1 mm or more.

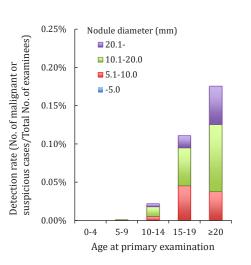


Figure 19. Detection rate of malignant or suspected malignant cases by age at the time of primary examination and by nodule diameter in the PLBS

		а	b		С	Primary examination results				
		Eligible	Participants	Participants	Participants with confirmed	I	ł	Requiring confirmatory exam		
		persons	(% of a)	outside Fukushima	recults		A1 (% of c)	A2 (% of c)	B (% of c)	C (% of c)
	Born in FY1992	22,653	2,250 (9.9)	718	2,249 (100.0)	940 (41.8)	1,211 (53.8)	98 (4.4)	0 (0.0)	
	Born in FY1993	21,889	2,106 (9.6)	751	2,094 (99.4)	942 (45.0)	1,050 (50.1)	102 (4.9)	0 (0.0)	
	Born in FY1994	22,095	1,222 (5.5)	324	891 (72.9)	346 (38.8)	501 (56.2)	44 (4.9)	0 (0.0)	
	Total	66,637	5,578 (8.4)	1,793	5,234 (93.8)	2,228 (42.6)	2,762 (52.8)	244 (4.7)	0 (0.0)	

Table 13. Primary examination results of the Survey for Age 25+ (as of March 31, 2020)

Table 14. Confirmatory	examination results o	f the Survey for A	Age 25+	(as of March 31, 2020)

	а	b	С	Confirmatory examination results				
	Those recommended	Participants	Participants with	I	ł	Other		
	to undergo confirmatory exam	(% of a)	confirmed results (% of b)	A1 (% of c)	A2 (% of c)	d (% of c)	FNAC (% of d)	
Born in FY1992	98	81 (82.7)	78 (96.3)	0 (0.0)	3 (3.8)	75 (96.2)	8 (10.7)	
Born in FY1993	102	84 (82.4)	80 (95.2)	0 (0.0)	7 (8.8)	73 (91.3)	5 (6.8)	
Born in FY1994	44	3 (6.8)	2 (66.7)	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	
Total	244	168 (68.9)	160 (95.2)	1 (0.6)	10 (6.3)	149 (93.1)	13 (8.7)	

B) Confirmatory examination results

As of March 31, 2020, the confirmatory examination for those born from FY1992 to FY1994 was in progress. Of the 244 participants with Grade B or C results in their primary examination, 168 (68.9%) underwent the confirmatory examination, and the results of 160 (95.2%) were confirmed: Grade A1 in 1 (0.6%) and Grade A2 in 10 (6.3%) by primary examination criteria. The remaining 149 (93.1%) were Grade B, of whom 13 people (8.7%) underwent FNAC (Table 14).

Of those who underwent FNAC, 7 had lesions malignant or suspicious for malignancy, including 2 males and 5 females. Their ages at the time of confirmatory examination ranged from 24 to 27 years (mean age: 25.3 ± 1.0 years), and tumor diameters ranged from a minimum of 10.8 mm to a maximum of 49.9 mm (mean tumor diameter: 22.6 ± 15.6 mm) (Table 6).

2) Analyses of the survey results

We have analyzed these results from multiple perspectives and published scientific papers. These are described below.

(1) Detection of malignancy or suspected malignancy

The number of pediatric thyroid cancer cases detected in Chernobyl tended to increase with age, as the younger a child was at the time of the accident, the more likely a thyroid cancer would be detected (Figure 18).¹²⁾ In the analysis of the results of those who received examinations in the PBLS by 2013, an age-dependent increase in the detection rate was observed after the age of 13 in males and after the age of 8 in females. In addition, the diameters of nodules malignant or suspicious for malignancy were classified as 5.1-10.0 mm, 10.1-20.0 mm, and 20.1 mm or larger, and their frequency among males and females combined was examined. As a result, nodules of 10.1-20.0 mm were most frequently observed after the age of 10 (Figure 19).¹³⁾

In the analysis of the results of the first FSS (the second-round survey), the incidence of cancer over a one-year period (between the PBLS and the first FSS) was also examined, and nodules malignant or suspicious for malignancy increased with age and did not differ from the detection rate in the PBLS.¹⁴⁾

(2) Relationship between regional differences in thyroid cancer detection and radiation dose

The prevalence of nodules diagnosed as malignant or suspicious for malignancy was 37.3 out of 100,000 participants in the PBLS; of these, the estimated external radiation dose over the first 4-month period after the nuclear accident, based on Basic Survey data of the Fukushima Health Management Survey, was in a range less than 2.2 mSv.¹⁵)

To assess regionality of detection rates for nodules malignant or suspicious for malignancy in the PBLS, the presence or absence of a general geographic clustering of thyroid cancers by municipality in Fukushima Prefecture was examined in multiple testing, and no statistically significant geographic clustering or significant association with regional indices was found.¹⁶⁾ In addition, there were no clear regional differences in the detection of thyroid cancer in the PBLS results, and the detection rate was within the range that could be predicted by simulations under conditions of no radiation exposure, and it was concluded that there was no strong evidence for a relationship between thyroid cancer and radiation exposure.¹⁷⁾

Based on individual external radiation doses derived from the Basic Survey, the prevalence of thyroid cancer in the PBLS was calculated for the regions of Fukushima Prefecture classified into three groups according to the external radiation dose (Group A for the regions with relatively high radiation doses, Group B for the regions in the middle, and Group C for the regions with the low radiation doses). The age- and sex-adjusted odds ratios for having thyroid cancer compared to Group C were 1.49 (95% confidence interval: 0.36-6.23) for Group A and 1.00 (95% confidence interval: 0.67-1.50) for Group B, thus showing no regional difference in the prevalence of thyroid cancer.¹⁸

Furthermore, municipalities in Fukushima Prefecture were reclassified into five groups according to the external exposure doses derived from the Basic Survey, and the relationship between the detection rates of nodules diagnosed as malignant or suspicious for malignancy in the four years after the earthquake and regional external exposure doses was evaluated. The result was that no relationship was found between the detection rate of thyroid cancer and regional differences of external exposure doses.¹⁹

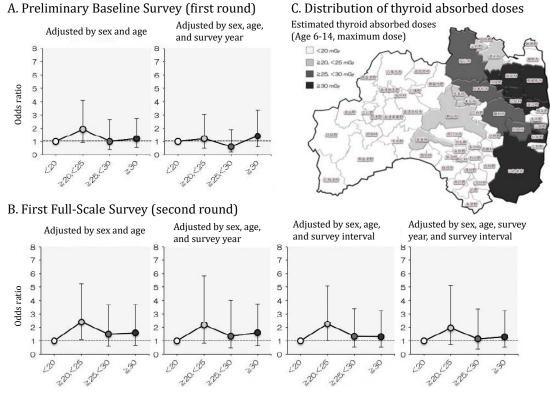
In the results of the first FSS, the relationship between external radiation dose and the detection rate of nodules malignant or suspicious for malignancy was not found when the results were analyzed only for those who had also undergone the PBLS.²⁰⁾

The thyroid gland is an organ that accumulates iodine, and in the case of a nuclear power accident, internal radiation exposure due to the intake and accumulation of radioactive iodine is one of the major factors in the development of thyroid cancer. For this reason, we analyzed the relationship between the estimated thyroid absorbed dose and the detection rate of nodules malignant or suspicious for malignancy by municipality, based on the combination of external and internal dose assessments from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). As a result, no dose-dependent increase in the detection rate proportional to the radiation dose was observed in either of the PBLS or the first FSS (Figures 20 and 21).²¹⁾

(3) Factors associated with detection and increase of thyroid cancer

An analysis of the first FSS results of participants who underwent the PBLS revealed that obesity was a risk factor for thyroid cancer detection, with an adjusted odds ratio of 2.23 (95% confidence interval: 1.01-4.90) compared to nonobese participants.²⁰⁾

There were no significant differences in age, sex, tumor size, observation period, or blood test indices among three groups: those with enlarged, shrunken, or unchanged nodules in the mean 6-month period between the primary and confirmatory examinations in the PBLS, but model analysis confirmed that the larger the nodule diameter at the primary examination, the slower the nodule growth rate.²²⁾



Adjusted odds ratios for detection of malignant and suspicious cases in examinees aged 6-14 at the time of the earthquake, stratified by the estimated maximum thyroid absorbed dose for each municipality (The vertical lines represent 95% confidence intervals. The horizontal axis represents thyroid absorbed doses in mGy.)

Figure 20. Relationship between UNSCEAR-estimated absorbed thyroid dose by municipality and detection rate of malignancy or suspected malignancy (examinees aged 6 to 14 at the time of the earthquake)

In addition, thyroid-stimulating hormone levels tended to be lower in those with nodules, including papillary carcinoma, than in those with no findings or with just cysts in the PBLS, indicating that there may be some relationship between the development of nodular lesions and the regulation mechanism of thyroid hormone levels.²³⁾

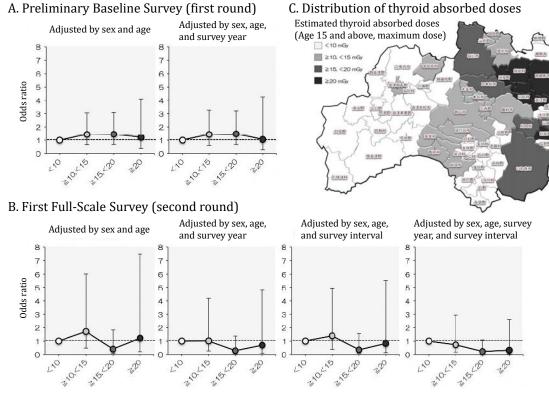
(4) Detection rate of thyroid nodules

In the PBLS, the detection rate of thyroid nodules was 1.0% in males and 1.7% in females among participants who underwent the PBLS within 3 years of the earthquake, showing a clear sex difference.¹³⁾ An age-dependent increase in the detection rate by age group was observed in females aged 10 and above and in males aged 14 and above, and the difference by sex was more pronounced in the age group of 10 and above (Figure 22). Among participants found to have nodules, the percentage of those with multiple nodules was 13.0% in males and 15.0% in females, and remained almost constant at 10% or more in the age group of 7 and above. When the maximum diameter of the nodules was classified as 5.0 mm or less, 5.1 to 10.0

mm, 10.1 to 20.0 mm, and 20.1 mm or more, the frequency of nodules of 5.0 mm or less was the highest in those younger than 10 years, while the frequency of nodules of 5.1 to 10.0 mm was the highest in those aged 10 and above. In all groups, there was an age-dependent increase in frequency (Figure 23). The detection rate of thyroid nodules has remained at a similar level in the subsequent surveys after the PBLS.

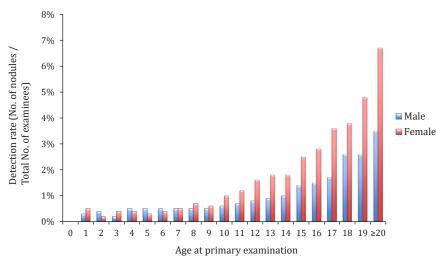
(5) Detection rate of thyroid cysts

The detection rate of thyroid cysts was 45.7% for males and 50.0% for females among participants who underwent the PBLS within 3 years of the earthquake, and the detection rate tended to be slightly higher in females.¹³⁾ By age group, an age-dependent increasing trend was observed among those aged up to 10 years, with a maximum at the age of 11-12 (Figure 24). However, the detection rate showed a decreasing trend in those aged 13 and above, and the decreasing trend is especially conspicuous for the detection rate of cysts 3.0 mm or less. On the other hand, the detection rate of cysts 5.1 mm or more con-



Adjusted odds ratios for detection of malignant and suspicious cases in examinees aged 15 and above at the time of the earthquake stratified by the estimated maximum thyroid absorbed dose for each municipality (The vertical lines represent 95% confidence intervals. The horizontal axis represents thyroid absorbed doses in mGy.)

Figure 21. Relationship between UNSCEAR-estimated absorbed thyroid dose by municipality and detection rate of malignancy or suspected malignancy (examinees aged 15 and above at the time of the earthquake)



Detection rate of thyroid nodules by age at primary examination in those who underwent primary examinations of the PBLS between October 2011 and March 2014

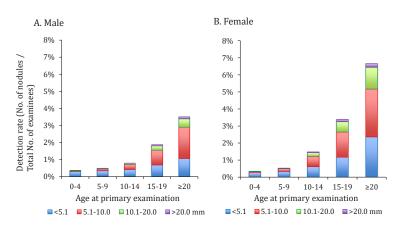
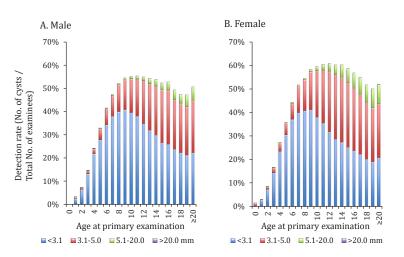


Figure 22. Detection rate of thyroid nodules in the PBLS by age at the time of the primary examination

Detection rate of thyroid nodules by diameter and by age at primary examination in those who underwent primary examinations of the PBLS between October 2011 and March 2014

Figure. 23. Detection rate of thyroid nodules in the PBLS by age at the time of the primary examination group and by nodule diameter



Detection rate of thyroid cysts by diameter and by age at primary examination in those who underwent primary examinations of the PBLS between October 2011 and March 2014

> Figure. 24. Detection rate of thyroid cysts in the PBLS by age at the primary examination and by cyst diameter

tinued to increase after the age of 13, and the median diameter of the largest cyst showed an age-dependent upward trend. Among those who had cysts, 89.3% of males and 89.6% of females had multiple cysts, and this percentages showed an increasing trend up to the age of 6, but remained almost constant after the age of 7.

(6) Other thyroid ultrasound findings

In addition to cysts and nodules, other findings may be observed in thyroid examinations. One such finding is an ectopic thymus within the thyroid gland. The thymus is normally located below the caudal side of the thyroid gland. Ectopic thymus may form in various locations during embryonic development. It has been known that ectopic thymus may occasionally be found in the thyroid gland during thyroid ultrasonography, and since its ultrasound image resembles thyroid cancer, caution is required. In the primary examinations conducted between October 9, 2011 and March 31, 2012, intrathyroidal ectopic thymus was found in 375 (0.99%) of 37,816 participants. Their mean age was 7.0 years (0-18 years). The incidence of intrathyroidal ectopic thymus was inversely correlated with age and body mass index.²⁴⁾

In the primary examination, the size of both lobes of the thyroid gland is measured. We examined the size of the thyroid gland in 34,227 people who underwent primary examinations between October 9, 2011 and March 31, 2012 and for whom measurement data were available. The results showed that the size of the thyroid gland was positively correlated with age and body surface area, as in previous studies. In addition, the right thyroid lobe was larger than the left one, and when the effects of body surface area and age were excluded, the thyroid gland was larger in females than in males.²⁵

Measurement of the size of both lobes of the thyroid gland can also detect the agenesis variants in the thyroid gland. For this reason, we examined the percentage of hemiagenesis variants in 299,908 people in the PBLS conducted from October 2011 to April 2015. We found that the overall freguency of hemiagenesis was 0.022% (67 people), which was similar to or lower than those reported in other countries

(0.02-0.25%). Of these, the left hemiagenesis was significantly more common (55 persons) than the right hemiagenesis (12 persons). In addition, the size of the thyroid gland, corrected for body surface area, was found to be significantly larger as a unilateral lobe present in cases of unilateral variants than in the ipsilateral lobe of those with bilateral lobes, indicating compensatory enlargement.²⁶)

(7) Analysis of behavior toward receiving thyroid examinations

Results from an analysis of the behavior of those who underwent the primary examination at the time of the PBLS showed that those aged 16 and above at the time of the earthquake and those who lived in the western part of the prefecture at the time of the earthquake tended not to undergo the primary examination, while those aged 16 and above at the time of the earthquake and those who lived in the Kenchu and the Aizu Districts at the time of the earthquake tended not to undergo the confirmatory examination. These results are thought to be due to the fact that after graduating from high school, opportunities to receive the examinations are limited to those conducted at general venues and medical facilities in Fukushima Prefecture, and that there are regional differences in availability of medical facilities that conduct the primary examination. Therefore, it was thought that it is necessary to increase as much as possible the number of medical facilities where primary examinations can be performed, and to develop a system where residents can receive examinations in their region of residence.²⁷⁾

3) Reporting of survey results to the Oversight Committee and Thyroid Examination Evaluation Subcommittee and their evaluation of the results

In May 2011, Fukushima Prefecture established an Oversight Committee for the FHMS, which consists of outside experts, in order to obtain a wide range of expert advice regarding the FHMS, including the Thyroid Ultrasound Examination (TUE) program. The results of the TUE have been reported to the Oversight Committee since its fifth meeting held in January 2012. In 2013, the Thyroid Examination Evaluation Subcommittee was established by Fukushima Prefecture under the Oversight Committee to conduct a detailed evaluation of the results of the TUE. The TUE results have also been reported to the Subcommittee and made public. The Oversight Committee published its evaluation of the results of the PBLS (the first-round survey) and the first FSS (the second-round survey) as follows:

(1) The PBLS

In March 2016, the Oversight Committee made the following evaluation of the results of PBLS.

Exposure doses due to the accident at the Fukushima Daiichi Nuclear Power Plant were generally lower than those caused by the Chernobyl accident; the period of time from the exposure to the detection of cancers is shorter (mostly from one to four years); cancers have not been detected in those aged five and under at the time of the accident; and there are no substantial regional differences in detection rates. Accordingly, it can be concluded that thyroid cancers found thus far through the Thyroid Ultrasound Examination (TUE) program cannot be attributed to radiation released by the Fukushima accident. However unlikely, the possibility of radiation effects cannot be completely denied at this point in time. Additionally, it is necessary to accumulate information in the long term for accurate evaluation of any effects. Therefore, the TUE should be continued, while meticulously explaining the disadvantages of receiving thyroid examinations and obtaining informed consent from participants.

(2) The first FSS (the second-round survey)

In response to the results of the first FSS (the second-round survey) in July 2019, the Oversight Committee evaluated that at present, no causal relationship between thyroid cancer detected during the FSS (the second-round survey) and radiation exposure can be identified. The reason for this was that an analysis of the relationship between the estimated thyroid absorbed doses published by UNSCEAR and the detection rate of thyroid cancer showed no consistent dose-effect relationship. In addition, the detection rate of thyroid cancer and suspected thyroid cancer in the results of ultrasound examinations, etc., was higher in the older age group at the time of the accident, which was different from the age group in which thyroid cancer was frequently detected after the Chernobyl accident (mainly in younger children).

(3) Recommendations on the ethical aspects

of the TUE and measures to address them The Oversight Committee and the Thyroid Examination Evaluation Subcommittee have recommended that it is important to offer detailed explanations, including the advantages and disadvantages of receiving thyroid examinations, to ensure understanding and informed consent before performing thyroid examinations. In response to this, a document explaining the advantages and disadvantages of receiving thyroid examinations (including a page for elementary school students and one for junior high school students; Figure 25) is sent to the eligible persons before they consent to or forego a thyroid examination.²⁸⁾ The following is the content of the explanation.

\cdot Advantages

- [1] If the examination result shows that there is no irregularity in the thyroid gland, it may lead to peace of mind and an improvement in the quality of life for those who are concerned about the health effects of radiation.
- [2] Early diagnosis and treatment may reduce the risk of complications from surgery, side effects from treatment, and recurrence.
- [3] Analysis of the thyroid examination can provide information on the presence or absence of radiation effects not only to the participant and their family but also to the citizens of the prefecture and people outside the prefecture.

• Disadvantages

- [1] There is a possibility that a cancer that would not cause symptoms or death in the future will be diagnosed and treated.
- [2] If cancerous or suspicious lesions are diagnosed at an early stage, there is a possibility



Figure 25. Document for elementary school students and junior high school students explaining the advantages and disadvantages of receiving thyroid examinations

of postoperative complications, increased psychological burden due to prolonged follow-up, and social and economic disadvantages.

[3] Nodules and cysts that do not require treatment may also be found, and even if the result is a benign nodule, a confirmatory examination or cytological diagnosis may be recommended, which may cause physical burden and emotional distress to the participant and their family.

The following measures are being taken to address the above disadvantages.

Disadvantage [1]: In the TUE, nodules of 5.0 mm or less are not subjected to the confirmatory examination, and for nodules of 5.1 mm or more, FNAC is performed in accordance with the guide-lines of the Japan Association of Breast and Thyroid Sonology.

Disadvantage [2]: Fukushima Prefecture has the Fukushima Health Management Survey Thyroid Examination Support Program to support the medical expenses required for treatment and follow-up after thyroid examinations.

Disadvantages [2] and [3]: FMU has a Thyroid

Support Team of specialists who can help participants and their families with anxiety. In addition, a dedicated medical consultation line is available to answer medical questions and mental health issues related to examination results and thyroid disorders. On-location lectures and information sessions are also held at schools and other venues.

4. Publication of survey results and support/feedback

The latest results of the surveys are published online by the Center. Thyroid Newsletters, which provide an overview of the Thyroid Ultrasound Examination (TUE) program and the results of previous surveys, are prepared twice a year and sent to all eligible persons as well as distributed to relevant organizations such as municipalities and medical facilities.

The survey results are regularly reported to the Oversight Committee and the Thyroid Examination Evaluation Subcommittee for their feedback to improve the program as a whole.

1) Results of support for participants and their families

It has been shown that participation in the TUE program contributes to a reduction of anxiety about health risks due to radiation exposure.²⁹⁾ However, some participants with normal A2 findings were still anxious. Therefore, various risk communication measures were implemented in response to the potential anxiety that may be experienced at each stage of the thyroid examination.³⁰⁾⁻³³⁾

Among the measures implemented to date are the establishment of a call center where questions can be directed to the Center's faculty and staff by phone or e-mail, the mailing of a Thyroid Newsletter twice a year, and the holding of information sessions about the TUE program for parents/guardians, teachers, and the general public. These have proven to be effective in reducing anxiety about radiation.^{31), 34)}

(1) Support at the primary examination

Beginning with the first Full-Scale Survey (FSS) (the second-round survey), an explanation of provisional examination results is provided to the participants and their parents/guardians who underwent the primary examination conducted at general venues in Fukushima Prefecture. As of March 31, 2020, we have provided explanations to a total of 30,836 people and consulted with them not only about their results but also about their anxieties about radiation and other matters.

(2) Support at the confirmatory examination

In order to address the concerns and anxieties of participants who have been recommended to undergo the confirmatory examination, the Thyroid Support Team, established in November 2013, started providing psychological support for confirmatory examinations conducted at Fukushima Medical University (FMU) Hospital. The support team attends the examination, talks to the participants during and after the examination, and provides telephone and web consultation before and after the examination. The support team provides psychological support by communicating with everyone as much as possible, thoughtfully attending to the anxiety of the participant and their family, and helping the participant to communicate effectively with the medical doctor.

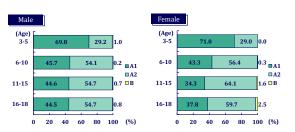
As of March 31, 2020, a total of 1,936 participants (640 males, 1,296 females, 4,041 encounters) have received support in confirmatory examinations at FMU Hospital. The intervention of the support team seems to have been effective in attending to the thoughts and requests of the participants and their families, and to have helped their communication with the medical team, which in turn helped the smooth implementation of the examination and contributed to reducing the burden on participants.³⁵

2) Feedback from the survey conducted in three other prefectures

In the Preliminary Baseline Survey (PBLS), cysts were found in about half of the participants and nodules were found in 1.3% of the participants. Since the prevalence of thyroid gland disorders in Japanese children has not been elucidated until that time,³⁶⁾ a survey on the prevalence of thyroid nodular disease was conducted in three prefectures other than Fukushima (Aomori, Yamanashi, and Nagasaki). In this survey, children in kindergartens, elementary schools, junior high schools, and high schools in the three prefectures cooperated and underwent thyroid ultrasound examinations using the same equipment and methods as in the TUE program. A total of 4,365 children from the three prefectures were included for analysis, and their ages ranged from 3 to 18 years old. The results of the ultrasound examination showed that Grade A1 were found in 42.5%, Grade A2 in 56.5%, Grade B in 1.0% and Grade C in 0.0%. Cysts were found in 56.9% of the students and nodules in 1.7%. These results were similar to the results of the PBLS and the FSS (Figure 26).^{37), 38)}

In addition, of the 44 children with Grade B results in this survey, 31 who agreed to the follow-up survey coeperated to undergo a detailed examination. As a result, 11 (35%) were Grade A. Their lesions were mostly cysts or benign nodules, but two children underwent FNAC, and one was found to have thyroid cancer.³⁹⁾

A. Results of 3-Prefecture Survey



Source: The Japan Association of Breast and Thyroid Sonology, "FY2012 survey report on thyroid nodule observation rates, etc."

B. Comparison with TUE

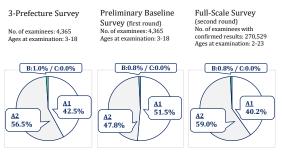


Figure 26. Comparison of the survey results in three prefectures with the TUE results

3) Addressing and evaluating the risk of overdiagnosis in thyroid examinations

In adults, the detection rate of nodules in the thyroid gland is quite common, with nodules found in about 20% of examinees by thyroid ultrasonography,^{40), 41)} most of which are benign adenomatous nodules formed by hyperplasia.⁴¹⁾ However, thyroid cancer is also detected in about 0.5% of cases, most of which are papillary carcinoma.⁴²⁾ The thyroid gland is an organ in which latent cancers are frequently detected at autopsy, and it has been reported that micropapillary carcinomas are found in about 15% of thyroid tissues when sectioned and examined in detail at intervals of 2-3 mm.⁴²⁾ However, most of them are less than 5 mm in diameter.

Compared to other countries, measures against the risk of overdiagnosis were introduced early on in Japan, with standards for cytological diagnosis and minimal surgical treatment becoming well established. Recently, there has been substantial academic discourse in Japan and abroad on the treatment of low-risk papillary thyroid cancer, and conservative guidelines have emerged overseas that approach the actual practice in Japan. Thyroid cancer in children and young adults is generally considered to have a good prognosis, but there is less knowledge about its natural history compared with cancer in adults, so conscientious treatment and consideration are required. In the TUE program, conducted in the Fukushima Health Management Survey (FHMS), the following measures have been taken in accordance with the guidelines of relevant academic societies to reduce the risk of overdiagnosis. As a result, the number of nodules malignant or suspicious for malignancy detected in the PBLS fall within the 95% confidence interval of the number predicted by a model developed under the assumption that there is no effect of radiation, based on cancer registry data of the National Cancer Center Japan and the sensitivity values of multiple surveys.43)

(1) Measures being taken at the primary examination

In the primary examination, nodules of 5.0 mm or less are Grade A2, and confirmatory examination is not recommended. This measure is expected to exclude most of the latent cancers (cancers that would not be detected until post-mortem autopsy).

(2) Measures being taken at the confirmatory examination

The indications for cytological diagnosis are evaluated according to criteria for the treatment of thyroid nodules of the Japan Association of Breast and Thyroid Sonology.⁶⁾ This prevents excessive cytological examinations and is thought to lead to the postponement of the diagnosis of thyroid cancers that have extremely low risk.

4) Feedback from clinical treatment

To date, a total of 200 surgical cases have been reported to the Oversight Committee: 102 cases in the PBLS (the first-round survey), 54 cases in the first FSS (the second-round survey), 27 cases in the second FSS (the third-round survey), 13 cases in the third FSS (the fourth-round survey), and 4 cases in the Survey for Age 25. The analysis of these cases has provided very important feedback for the TUE program.

(1) Pathological diagnosis of surgical cases

Pathological diagnosis showed papillary carcinoma in 196 cases, follicular carcinoma in 1 case, poorly differentiated carcinoma in 1 case, other thyroid carcinoma in 1 case, and a benign nodule in 1 case. In addition, by the end of June 2017, there were 11 cases of thyroid cancer detected apart from the TUE program that were surgically resected at FMU Hospital, accounting for 5.7% of the 194 cases of malignancy or suspected malignancy that could be identified in the age group eligible for the TUE at that time.⁴⁴⁾

(2) Clinical characteristics of surgical cases

The details of surgical cases were reported for 125 thyroid cancer cases resected at FMU Hospital by March 31, 2016.⁴⁵⁾⁻⁴⁷⁾ In those 125 cases, the male-to-female ratio was 1:1.8, and the pre-operative mean tumor diameter was 14 mm (range 5.0-53 mm). There were 121 cases (96.8%) with unilateral lesions, and 4 cases (3.2%) with bilateral lesions.

Pre-operative TNM (tumor-nodes-metastasis) classification showed T1 for 80.8% (T1a 35.2%, T1b 45.6%), T2 for 9.6%, T3 (Ex1) for 9.6%, no T4, N0 for 77.6%, N1 for 22.4% (N1a 4.0%, N1b 18.4%), M0 for 97.6%, and M1 for 2.4%. On the other hand, post-operative TNM classification was T1 for 59.2% (T1a 34.4%, T1b 24.8%), T2 for 1.6%, T3 (Ex1) for 39.2%, no T4, N0 for 22.4%, and N1 for 77.6% (N1a 60.8%, N1b 16.8%).

When comparing pre- and post-operative findings, the pre-operative rate of T3 (Ex1) and lymph node metastasis was higher than their post-operative rate, with 39.2% compared to 9.6% for T3 (Ex1), and 77.6% compared to 22.4% for lymph node metastasis. The rates of external lymph node metastasis (N1b) were 18.4% and 16.8%, almost the same before and after surgery, while the rates of peribronchial lymph node metastasis (N1a) were 4% before surgery and 60.8% after surgery.

All three M1 cases were suspected of lung metastasis; these three were the only high-risk cases. There were also only three cases with bilateral lesions. The majority (91.2%) of cases were performed hemithyroidectomy, and only 11 (8.8%) had total thyroidectomy. In Chernobyl,

68% of the surgical cases were performed as total or subtotal thyroidectomy and these were treated with post-operative isotope therapy; whereas in Fukushima⁴⁸, more than 90% of the cases had hemithyroidectomy, post-operative isotope therapy was rarely used, and post-operative complications were extremely low.³

(3) Genetic mutations in surgical cases

In Chernobyl, 64-86% of thyroid cancers, especially those with a short latent period of 7-10 years, had *RET/PTC* chromosome rearrangement abnormalities, and RET/PTC3 was particularly common. On the other hand, in the pediatric and young adult thyroid cancer cases operated from February 2013 to September 2014 at FMU, it was found that 63.2% had a BRAF V600E point mutation, while only 8.8% and 1.5% had RET/PTC1 and *RET/PTC3*, respectively.⁴⁹ In addition, a later analysis of 138 cases, including surgeries, conducted after March 2016 also showed that a BRAF V600E point mutation was present in 69.6%, suggesting that it is different from the genetic mutation in thyroid cancer that occurred in Chernobyl. It was also found that patients with BRAF V600E mutation tended to have smaller tumor size and higher incidence of lymph node metastasis than those without BRAF V600E mutation.⁵⁰⁾

(4) Addressing the risk of overtreatment in medical care after completion of thyroid examinations

Patients who are diagnosed with lesions that are malignant or suspicious for malignancy by cytological diagnosis in the TUE program are referred for treatment under Japan's system of universal health coverage. Even after a patient has been referred for treatment, in accordance with the Clinical Practice Guidelines for Thyroid Tumors⁵¹ and with the consent of the patient, low-risk microcarcinomas are not immediately treated surgically, and the course of the tumor is followed.

In a review of microcarcinoma cases that may be eligible for active surveillance (a method of follow-up for consenting patients with cancers of small size and extremely low risk of metastasis or extrathyroidal invasion), there were 44 cases of T1aN0M0 (tumor size of 1 cm or less with no

extrathyroidal invasion, lymph node involvement or distant metastasis) before operation. Of these, 33 cases were indicated for surgery, with 20 suspected cases of T3 (Ex1), 3 suspected cases of N1a, 10 cases of suspected recurrent nerve invasion or in close proximity to the recurrent nerve, 7 cases of suspected tracheal invasion or in close proximity to the trachea, 1 case associated with Graves' disease, and 1 case associated with lung shadowing (with duplication). In addition, 11 cases were proceeded to surgery based on the patient's or their family's wish after non-surgical follow-up was recommended. Of the above 44 patients, only 5 were T1aN0M0 after surgery, and 89% had lymph node metastasis or capsular invasion in the postoperative pathological diagnosis. These results can be attributed to the fact that the confirmatory examination is based on nodule diameter and ultrasonographic findings to evaluate the indications for cytological diagnosis, and in nodules of 1 cm or less, the nodules with almost all malignant findings on ultrasound images are selected for cytological diagnosis.

5. Summary (significance of the TUE)

Starting with the Preliminary Baseline Survey (PBLS, the first-round survey) that started in October 2011, the Thyroid Ultrasound Examination (TUE) program is now in a stage of the fourth Full-Scale Survey (FSS, the fifth-round survey) as of December 2020. Thyroid examinations have been conducted at various locations with consideration for the convenience of participants, such as at designated medical facilities in and outside Fukushima Prefecture; at elementary, junior high, and high schools; at some universities; at public facilities; after hours, and on holidays.

As of March 31, 2020, malignant or suspicious thyroid nodules were detected in a total of 246 people: 116 people in the PBLS, 71 people in the first FSS, 31 people in the second FSS, 21 people in the third FSS, and 7 people in the Survey for Age 25. According to the results of the PBLS and first FSS, there was no clear dose-response relationship between the detection rate of nodules diagnosed as malignant or suspicious for malignancy and the external exposure dose estimates from the Basic Survey or the absorbed thyroid dose estimates from UNSCEAR. The frequency of thyroid cysts, nodules, cancer, and ectopic thymus in children and adolescents by age and sex was also elucidated in the TUE program.

The Oversight Committee evaluated and announced that thyroid cancers found in the PBLS (the first-round survey) cannot be attributed to radiation. The Committee also evaluated results of the FSS (the second-round survey) as follows: At this point, no correlation can be found between thyroid cancers detected so far and radiation exposure.

Apart from this, there have been discussions regarding the possibility of increased anxiety among examinees and their families and the risk of overdiagnosis of thyroid cancer due to thyroid examinations. In response, we have strengthened our efforts in providing detailed explanations about the TUE and support for examinees and their families.

Right after the start of the TUE program, we received a large number of inquiries about the thyroid examination and examination results, but as time has passed and as a result of various support measures, the number of inquiries has been decreasing recently. Also, through continuous public engagement and consultation services, we believe that the eligible persons' understanding of the examination has been deepened. As for support for primary examinations, we provided explanations of the results of examinations at general venues and medical facilities, as well as individual explanations using the call center and dedicated medical consultation line. For those who underwent confirmatory examinations and their families who are highly anxious about thyroid cancer and the health effects of radiation, the Thyroid Support Team listens to their thoughts and complaints, provides appropriate information, and provides psychological and social support so that they can make their own decisions about the future. This is thought to play a role in reducing anxiety among participants.

In the future, we believe that sufficient discussions should be held by the Oversight Committee and others on the design and method of the TUE program, and efforts should be made to provide appropriate examinations based on such discussions.

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