Industrial Disease Clinical Research Grants from
Japanese Ministry of Health, Labour and Welfare

Epidemiological Study on the Health Effects in Radiation Workers

(Epidemiological Study of Health Effects in TEPCO Fukushima Daiichi Nuclear Emergency Workers)

The first period (FY2014 to FY2018)

Third Party Committee Report

Chairman Ginji Endo

June 2020

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Introduction

This research started as clinical research for industrial accident diseases by the Ministry of Health, Labour and Welfare in FY2014, four years after the accident at TEPCO's Fukushima Daiichi Nuclear Power Plant. Prior to starting the research, experts were gathered around the Industrial Safety and Health Department Manager of the Labor Standards Bureau in the Ministry of Health, Labour and Welfare in February 2014, a "Review meeting by experts concerning the ideal state of epidemiologic study for emergency workers at TEPCO's Fukushima Daiichi Nuclear Power Plant" (hereafter referred to as "Ideal state review meeting") was established, and conferences were thereafter held five times. In this review meeting, the research method for epidemiologically investigating the health effects on emergency workers due to radiation exposure, etc. were reviewed, and the report showing the basic items regarding the way to proceed with this research was prepared and published based on this.

The study plan of this research was developed following the basic policy of that report, and the research was started in October 2014. The progress status of the research was checked to reveal that some parts progressed according to the policy, while other parts did not. In addition, during this period, the technical advances and the modification of social needs were remarkable, and the necessity of a review of the basic policy became clear.

Concerning how to proceed with this research that is expected to take a long period of time, the report of the review meeting proposed to "establish an independent committee (third-party committee) including researchers whose research achievements are internationally evaluated" "at intervals of once every five years in addition to the usual research evaluation, in order to secure good quality research" and "to implement the evaluation of whether any arbitrary deviation exists that may derive analysis results that are statistically significant or statistically insignificant concerning the selection of the adopted study hypothesis, study plan, exposure factor, statistical technique, etc."

Since five years of the first period has elapsed this time, it was decided to establish this committee as an important place where third party experts not only evaluate the study achievements, but also propose the method for proceeding with the research of the next period based on that. In order to select committee members, we explained to the relevant expert societies about the aim of the committee establishment, asked to recommend committee members and held a third-party committee with the following composition of members:

Name list of the third-party committee

Hirotsugu Ueshima	Specially appointed professor, Center for Epidemiologic Research in Asia, Shiga University of Medical Science
Ginji Endo*	Director, Osaka Labor Health General Center, Japan Industrial Safety and Health Association

Kazuyuki Omae	Professor Emeritus, Keio University
Michiaki Kai	Professor, School of Nursing, Oita University of Nursing and Health Sciences
Takashi Kitaoka	Professor, Ophthalmology and Visual Science, Nagasaki University Graduate School of Biomedical Sciences
Kazuo Sakai	Professor, Higashigaoka and Tachikawa Nursing School, Tokyo Healthcare University
Gen Suzuki	Director, International University of Health and Welfare
Masayuki Tatemichi**	Professor, Dept of Preventive Medicine, Tokai University School of Medicine
Akizumi Tsutsumi	Professor, Public Health, School of Medicine, Kitasato University

*: Chairman **: Vice-chairman

Date and time when Third-party Committee is to be held

1st meeting 10 am to 4 pm, November 5, 2019, Room No. 702, 7th floor, Vision Center in front of Tokyo Station

2nd meeting 1 pm to 3 pm, January 28, 2020, Room No. 701, 7th floor, Vision Center in front of Tokyo Station

3rd meeting June 26, 2020 To be held using documentation*

*Although the third meeting of the committee was planned to be held on March 23, 2020, the meeting was suspended due to the self-restraint request, etc. associated with the novel coronavirus infection, and it was decided to hold the committee using documentation.

The deliberation of the committee was implemented on the committee's own initiative under the mutually elected chairman, and this report was prepared.

We described the details of the establishment of this committee and sincerely thank Director Endo, who acted as the chairman of the third-party committee to establish this committee and prepare the report, along with every committee member, and the parties concerned of Ministry of Health, Labour and Welfare for their great efforts.

On June 26, 2020

Epidemiologic study for emergency workers at TEPCO's Fukushima Daiichi Nuclear Power Plant (Public invitation name: Epidemiologic study concerning health effects on radiation workers)

Study representative Toshiteru Okubo

Third-party committee report

Chapter I　Evaluation of research so far

This chapter summarizes the evaluation, etc. of research achievements in the first period from the aspect of securing research participants, scientific evaluation of health effect by radiation exposure under emergency work and research system.

1. Securing research participants

In the difficult circumstances whereby survey subjects (19,808) who were emergency workers are dispersed nationwide, and that three or more years have elapsed before the start of survey since the nuclear power plant accident and the end of the subsequent emergency work, the survey was planned, informed consent was obtained, and invitations to the subjects to participate in the health survey were implemented. Although the number of persons who agreed to take the follow-up survey as a cohort survey against the population is currently 7,270, a long time had elapsed before the start of the survey and the locations of subjects were dispersed all over the prefectures. Therefore, considering the difficulty of follow-up of persons who do not belong to the limited region or workplace, it can be well evaluated that suitable invitation to each subject to participate in the research and the following health survey were successfully implemented. Since the participation ratio (36.7% of subjects) with the total number as a denominator is not necessarily high, it is difficult to deny that a sufficient number of participants for clarifying the risk to emergency workers was not secured. However, it is possible to clarify certain health effects due to high dose exposure because the participation ratios for each exposure dose are as high as 79.9% and 78.4% for the population of 100 mSv or more to less than 150 mSv and the population of 150 mSv or more, respectively. In addition, since minute surveys such as a cataract survey and thyroid echo survey were implemented, it can be said this is a valuable research not seen in a conventional exposure survey.

2. Scientific evaluation of health effects by radiation exposure under emergency work

(1) Statistical detection power and analysis method

When applying the evaluation index (end point) to probabilistic events such as cancer, the number of subjects was small in the result so far, and analysis is obliged to be performed with insufficient detection power. As the method for accepting the limitation of insufficient detection power, a regression analysis is planned that takes the event capable of being observed as a response variable, with the exposure dose as an explanatory variable. At least, the risk factor for the outbreak of circulatory disease is possible to analyze because it was surveyed in this cohort. However, although the outbreak factor of circulatory diseases is strongly related to lifestyle habits and the adjustment of a confounding factor is required, it can be well evaluated that the information on the confounding factor has been collected.

(2) Evaluation of radiation dose

Since the quality of dose evaluation for emergency workers is important because the reasonableness of the epidemiologic survey is affected by this quality, this study performs a detailed examination from both the physical and biological aspects of dose evaluation. In the evaluation of the thyroid absorbed dose received by internal exposure through the inhalation of radioactive iodine (mainly I-131) with a large dose contribution, it was recognized that the accuracy of thyroid measurement performed at the time of the accident is sufficiently high even when considering the uncertainty of the position of an examinee, and it was clarified that the volume of thyroid shape obtained from the MRI images shows large personal difference.

Further, the evaluation of the uncertainty regarding the estimated dose, including the effect by acute ingestion of radioactive iodine, the effect of chronic ingestion and the effect on in-body behavior of radioactive iodine due to the ingestion of a stable iodine tablet remains as future tasks. On the other hand, the analysis of iodine 129 in urine sampled for evaluating internal exposure over several months just after the accident is performed using the accelerator mass spectrometry method (AMS). This result will hereafter be the important information for correcting the inhalation ingestion pattern and the personal difference of in-body behavior that will be the uncertainty in the dose estimated from the thyroid measurement.

Concerning external exposure, the dose information of personal dosimeters was further obtained from the central registration center of the Radiation Effects Association based on personal agreement. The evaluation of the reading of a dosimeter and the conversion factor to the organ absorption dose and the verification of the reasonableness of the estimated value of a dosimeter by the chromosome aberration analysis have been advanced, and the total work of dose evaluation progresses steadily.

From the above points, the point of this research to be most highly evaluated is that the dosimetry is accurately identified. In addition, the number of workers whose dosimetry during emergency work exceeds 100 mSv is 174, and we consider that this is important data enabling the evaluation of complex health effects concerning the exposure to 100 mSv or more by hereafter adding medical exposure.

(3) Survey of cause of death and cancer morbidity

The cause of death and cancer morbidity survey subcommittee has the purpose of grasping the cause of death and cancer morbidity. Since matters concerning the cause of death and cancer morbidity above all are major consequences, a high degree of attention is paid, and a high grasp rate and long term follow-up are required. As the follow-up plan, information on the cause of death is periodically understood by obtaining death slips through the procedure of the out-of-purpose utilization of the demographic surveys concerning subjects whose agreement has been obtained. Further, since it is

difficult to obtain consent that was not anticipated at the beginning, we decided to deal with it by opt-out, and take the technique for reviewing the content of opt-out for subjects who continue medical checkups. The periodical application of death slips for the demographic survey of the generation corresponding to the follow-up subjects is planned in order to calculate the standardized death ratio, and the information on the death slips for the demographic survey from March 2011 to December 2016 is already issued.

Concerning cancer morbidity, since grasping the morbidity in periodic cancer tests, the periodic cancer registration in the prefectural regions where the subjects live and nationwide cancer registration were both fully realized, it is planned to submit the list of survey subjects to the National Cancer Center to collect the information from the nationwide cancer registration. Concerning the research, the acquisition of agreement was implemented on a highest priority basis as the activity in the first period, and a lot of labor was spent from the viewpoint that agreement is required in order to use the information on the cancer registration for this research. We have evaluated that the above matter is reasonable as the methodology for the follow-up in the follow-up environment at the beginning of the plan.

(4) Survey of thyroid cancer morbidity

The thyroid cancer survey subcommittee has the purpose of collecting and analyzing 1) the data of 627 subjects who were subjected to thyroid tests among 1,972 subjects of the exposure population of the thyroid equivalent dose of more than 100 mSv during emergency work who are survey subjects of the team research (Sobue team) that was implemented in the special research project of the Health and Labor Sciences Research Grant in FY 2013, 2) the dose evaluation which has been implemented for the control population of 1437 of said dose of 100 mSv or less and 3) the data of thyroid ultrasonic tests (data of the old research team) as task 1, and also to examine the method for implementing thyroid tests for the total number of subjects of about 20,000 emergency workers and to collect and analyze the test results as task 2.

It can be well evaluated that acquiring agreement for using the thyroid test data of the old research subjects and the thyroid test data possessed by TEPCO for “Epidemiologic study for TEPCO Fukushima Daiichi Nuclear Power Plant emergency workers” (Nuclear Emergency Workers Study; NEWS Study) was promoted, and that the agreement from 577 old study subjects and 1,531 TEPCO employees as of January 2019 had been obtained, resulting in the increase of the number of subjects in task 1. Task 2 has decided the policy whereby thyroid tests are conducted for all the subjects, in addition to all the subjects (1,972) exposed to a thyroid equivalent dose of 100 mSv or more among about 20,000 subjects.

Concerning the accuracy control of the thyroid test, the lecture classes for increasing certified bodies and certified engineers for conducting the thyroid ultrasonic test are being conducted, and 123

certified engineers and 60 certified facilities have been recognized as of the end of December 2018. An accuracy control committee was established in Jichi Medical University, and a thyroid ultrasonic test information system that enables the examination of image data and findings by the accuracy control committee has already been established. In addition, 130 facilities acting as bodies for conducting a secondary test for subjects who required one based on the findings in the thyroid test have been secured nationwide. Further, it can be judged that the system for conducting the test from the aspect of research ethics, showing the way of thinking about the judgment result for the written consent explanatory statement was completed.

(5) Survey of cataract

Although the crystalline lens is a tissue sensitive to radiation, the specific evaluation of its effect is difficult because of the presence of some problems. Firstly, although damage to the crystalline lens results in its opacity, usually only alteration by aging results in opacity, and other than aging, the effects of steroid hormones, diabetes, degenerative myopia, etc. sometimes also result in opacity. Therefore, it is difficult to investigate by distinguishing between the effects of aging alteration, steroid hormones, diabetes, degenerative myopia, etc. and the hazard from radiation. Secondly, the quantitative evaluation of crystalline lens opacity and vacuolar degeneration is difficult. This research is meaningful because it intends to establish a new evaluation method and to compare the effects of aging with those of radiation on cataracts in order to conquer this difficulty.

Firstly, the tests are conducted using an anterior ocular segment analysis and photographing apparatus EAS-1000 capable of evaluating the degree of cataract with the most detail, targeting TEPCO employees exposed to a dose of 50 mSv or more. In addition to this, a simplified transillumination camera that is simple to use and enables easy evaluation has been developed by a study group, and the common usage of this with EAS-1000 is expected to enable coping with studies that can be implemented in many facilities in the future.

Although the disease type of crystalline lens opacity is classified in various ways, six disease types are selected this time. These six types are cortex lens opacity (COR), nuclear sclerosis and opacity (NUC), posterior subcapsular opacity (cataract) (PSC), vacuolation in crystalline lens (Vacuoles), retrodot and water cleft (WC). The report this time especially describes the Vacuoles that is the alteration emerging at a comparatively early stage among the six disease types. It shows that each disease type (especially distinguished from posterior subcapsular in Vacuoles) tended to increase from 2014 to 2016. Also concerning this, the judgment whether this is an actual increase or an apparent increase is important.

Secondly, a simplified transillumination camera was introduced in 2016 in addition to the initially used EAS-1000, assuming it would be used in the NEWS study. Therefore, the introduction of the simplified transillumination camera in addition to EAS-1000, the standard for the current cataract

study, raises the detection ratio. On the other hand, the apparent increase of the prevalence rate of cataracts is pointed out as a problem. Further, although the “prevalence rate of cataracts” is described, the definition of cataract is not determined, hence the definition in this study should be clarified. Concerning this point, it is necessary to consider it by dividing in between “cataract” and “alteration of the crystalline lens.” Since it is unclear in which position the setting of focus of the simplified transillumination camera between the anterior and the posterior of crystalline lens enables the identification of findings about Vacuoles, a check of the depth of field and reproducibility of this inspection equipment is required.

(6) Survey of psychological influence

The purpose of the psychological influence survey is to follow-up on mental health over the long term, and the psychological influence is evaluated by questionnaire and composite interviews. Stigma is also a big theme.

Questionnaires were sent to 4,979 persons, and of those 3,784 were analyzed. Training on the WHO World Mental Health Composite International Diagnostic Interview (WMH-CIDI) was conducted for 235 survey executors (public health nurses, etc.). As a result of the CIDI, analyzable data were obtained from 2,130 persons.

In the follow-up on mental health, a wide array of survey items consisting of 1) sevierity of depression, anxiety disorder, sleep disorder, alcohol ingestion disorder, or serious PTSD (post-traumatic stress disorders), and 2) existence of stigma, life event, social assistance, sense of coherence, self-esteem, and self-efficacy were examined, and the analysis of the entry period, the number of working days and work breakdown was made possible. In the questionnaire survey, the relationships between the frequency of depression and action (alcohol ingestion disorder) and the relevant factors were analyzed by comparing with the survey results, etc. targeting the general population. The stigma scale for Fukushima Daiichi Nuclear Power Plant emergency workers was developed, and the stigma after the nuclear disaster and its relevant factors were examined.

It is well evaluated that in spite of the difficulty of surveying, many valuable data were collected by the composite interviews conducted by survey executors who had received training.

(7) Research of radiation biology

A radiation biology research working group performed the search for a biomarker that is expected to be utilized in this research in the tests related to radiation adaptive response and thymic lymphoma-developed model mouse for the purpose of searching for a biomarker for low dose radiation effects, in order to investigate the relationship between low dose radiation exposure and long term health effects. Further, in the test related to human urinary oxidative stress, a field survey was performed in cooperation with a medical institution in Fukushima. The result of the survey of human urinary 8-

OHdG in a specified period for persons who received medical examinations showed a slightly higher value in comparison with a general healthy group, but it cannot be said to be a significant difference.

Although the outcome obtained by five years of research can be evaluated to a certain degree, the selection of the biomarker adaptive to the subjects in this research was not achieved. The research team reported that the biological radiation research has been suspended until the time when a biomarker capable of being utilized in this research can be selected, and we consider this to be reasonable. Currently, biomarkers using metabolomics technology are being energetically studied in various fields with the progress of technology. However, whether the study can be applied to the radiation effects is in the examination stage, and it is necessary to continuously examine the adoption of a new biomarker considering knowledge both inside and outside the research team.

3. Research system

In the first period, the Radiation Effects Research Foundation acts as a research supervision institute, and eleven institutes nationwide participated in the research. Six research groups in charge of clinical survey, exposure dose evaluation, cause of death and cancer morbidity survey, thyroid cancer survey, cataract survey, psychological influence survey and radiation biological research were established to proceed with the survey of the health effects due to radiation exposure during emergency work.

Toshiteru Okubo	Radiation Effects Research Foundation (RERF)	Consulting Researcher	Principal Investigator	FY 2014 to present
Makoto Akashi	National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Executive Officer	Dose evaluation	FY 2014 to present
Waka Oishi	Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	Clinical survey	FY 2014 to present

Ryuji Okazaki	Department of Radiological Health Science, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health (UOEH)	Professor	Biological survey	FY 2014 to present
Kotaro Ozasa	Hiroshima Department of Epidemiology, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	Cause of death and cancer morbidity	FY 2014 to present
Fumiyoshi Kasagi	(Retired) Institute of Radiation Epidemiology, Radiation Effects Association (REA), Public Interest Incorporated Foundation	Institute Director	Dose evaluation	FY 2014 to 2017
Hiroaki Katayama	(Retired) Department of Information Technology, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	Cause of death and cancer morbidity	FY 2014 to 2017
Kazuaki Kawai	Department of Environmental Oncology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health (UOEH)	Professor	Biological survey	FY 2017 to present
Hiroko Kitamura	Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Deputy Office Head	Clinical survey	FY 2017 to present
Eunjoo Kim	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Researcher	Dose evaluation	FY 2018 to present

Osamu Kurihara	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Department Director	Dose evaluation	FY 2014 to present
Kazunori Kodama	Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Principal Researcher	International matter	FY 2014 to 2017
Hiroshi Sasaki	Department of Ophthalmology, Special Research Division/ Division of Vision Research for Environmental Health, Kanazawa Medical University	Professor	Cataract survey	FY 2014 to present
Jun Shigemura	Department of Psychiatry, Department of Medicine, Faculty of Medical Education, National Defense Medical College	Associate Professor	Psychological effects survey	FY 2015 to present
Yumiko Suto	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Team Leader	Dose evaluation	FY 2014 to present
Tomotaka Sobue	Environmental Medicine and Population Sciences, Department of Social Medicine, Graduate School of Medicine, Osaka University	Professor	Thyroid cancer survey	FY 2014 to present
Kotaro Tani	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Researcher	Dose evaluation	FY 2018 to present

Nobuyuki Taniguchi	Department of Laboratory Medicine, Jichi Medical University	Professor	Dose evaluation	FY 2014 to present
Hisanori Hiro	Department of Mental Health, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health (UOEH)	Professor	Psychological effects survey	FY 2014 to present
Hokuto Hoshi	Hoshi General Hospital, Public Interest Incorporated Foundation	Chairperson	Clinical survey	FY 2014 to present
Megumi Miyagawa	Miyagawa Hospital, Medical Corporation Association Seiikai / Department of Endocrine and Metabolism, Toranomon Hospital, Federation of National Public Service Personnel Mutual Aid Associations	Staff Physician, Dept. of Internal Med (Part-Time)	Thyroid cancer survey	FY 2014 to present
Takuma Momose	Nuclear Fuel Cycle Engineering Laboratories, Sector of Nuclear Fuel, Decommissioning and Waste Management Technology Development, Japan Atomic Energy Agency (JAEA), National Research and Development Agency	Deputy Director and Radiation Control Dept. Mgr.	Dose evaluation	FY 2014 to present
Shinji Yoshinaga	Division of Radiation Bio-Medical Informatics, Department of Environmetrics and Biometrics, Research Institute for Radiation Biology and Medicine, Hiroshima University	Professor	Analysis	FY 2014 to present

Since research participants live nationwide, cooperative medical examination bodies for research are established based on their locations, and the number of such bodies has reached 77 nationwide. Since many persons are in charge of the survey, standardization of the survey method is not easy. Therefore, the standard exchange of collected information is enabled by establishing an information network connecting each of the cooperative bodies, and the responsible person in charge of the health survey of this research and the research coordinator (RC) were appointed to periodically standardize the interview method, and a seminar on professional skills is held.

In addition, in order to keep the technology and methods for medical examination implementation

and the long term preservation of collected blood and urine invariables, specimens collected nationwide are gathered in one inspection body to perform the dispensation of preserved specimens and the biochemical examination unitarily.

It can be said that maintaining a high quality survey is essential in order to avoid variation of the surveys being taken into the risk evaluation. The implementation of the seminar for the standardization by gathering the research coordinators (RC) is well evaluated, and the progress of the improvement of infrastructure for constructing a future research system in the first period including the approaches of inspection, etc. in each of the above-mentioned research fields has also been well evaluated.

Chapter II Proposal to research in the second period

Chapter II describes the proposal about the ideal state of the research in the second period onwards, based on the evaluation, etc. of the research outcome in the first period described in Chapter I.

1. Securing research participants

In the five years of research in the first period, we had obtained 7,270 participants as of October 2018, and conducted medical examinations for 5,133. Since the locations of subjects are dispersed over many prefectures, considering the difficulty of follow-up for persons who do not belong to a limited region or workplace, it can be well evaluated that a suitable invitation to each subject to participate in the research and the following health survey were successfully implemented. However, an approach to secure and maintain participants over a long period in the future is required. Therefore, it is necessary to examine the above-mentioned approaches to secure and maintain from both the aspect of the research purpose and also the advantages for research subjects. Specifically, we ask that an early study be performed to clarify whether the medical examination items are in accordance with each research policy and are necessary and sufficient to ensure the research is not haphazard, but is looking toward the future and to whether the needs of examinees are being satisfied by the responsible supervising research body. For example, reexamination should be performed from the viewpoint of whether the examination items aiming for the discovery of disease at the time of the survey, such as cancer tests should be conducted in this research, and whether they are examination items enabling observation of the change of the degree of health over the future. Additionally, the research, etc. to check whether the medical examinations are conducted according to the manual, the review of reasonability, etc. of the manual, and whether the research based on the demand survey of the research subjects through questionnaires is performed are also important.

This research requests participation based on free will. We ask for this approach so as to steadily increase research participants. Based on this, it is important to continue planning and devising for maintaining the intent without alteration for long term continuation, even when receiving an offer of research participation once. Subsequent measures such as the improvement of the consulting system

based on the medical examination results and the improvement of the environment for the purpose of utilizing the examination results for self-health control have been so far considered, and it is important that these measures satisfy the needs of the research participants.

The subjects of this research can be roughly divided into the following 3 × 2 groups:

A. Working conditions at the time of survey

① Workers who are still involved in radiation tasks even at this moment

② Workers who were already transferred to a task other than radiation

③ Persons who retired from all professions

B. Category of task at the time of emergency work

(a) Specific emergency worker

(b) Non-specific emergency worker

Each of the specific emergency workers and non-specific emergency workers is included in all the categories of ①, ② and ③. Specific emergency workers are persons with an exposure dose of 50 mSv or more during emergency work, and the Ministry of Labour, Health and Welfare performs long term health control such as cancer tests based on the policy of the Minister. Information on the specific emergency workers necessary for this research team will be provided after submitting an application to the Ministry of Labour, Health and Welfare.

However, retired persons, etc. of ③ who are non-specific emergency workers of (b) (③ × (b) group) are not included as a subject of health control by the companies stipulated in the Industrial Safety and Health Law, such as the general medical examinations and the special medical examinations of the Ordinance of the Prevention of Hazards due to Ionized Radiation, and this group is estimated to increase at a speed of about 500 persons per year. Since the emergency workers are receiving health consultation and guidance from the Ministry of Labour, Health and Welfare, and participation in this research to periodically receive health consultation is useful for the health control of the persons in ③ × (b) group, we should selectively appeal to the persons in this group to have them participate in the research together with MLHW in the second period. In addition, it is also necessary to normalize the health consultation that has been implemented in this research because the number of medical examinees greatly fluctuates year to year.

The matter most difficult and requiring much effort in the cohort survey is to follow up on the survey subjects. The transfer of the subjects is anticipated to be more frequent, and it is inevitable that the follow-up will encounter more difficult situations in the geographical conditions in the future. In addition, the researchers side should continuously maintain the motivation of integrating the long term research over a period of 40 years or more. It is important to establish a follow-up survey system considering these two points in the future.

2. Scientific evaluation of health effects of radiation exposure under emergency work

(1) Statistical detection power and analysis method

Although the figure of 7,200 persons × 40 years = 288,000 person-years is not small in the epidemiologic field targeting persons who suffered radiation exposure by accident that is handled by this research, there is no guarantee that the detection power capable of detecting 80% of a 10% increase in the crisis risk of cancer is obtained even if we follow up this cohort for 40 years. However, this does not mean that no continuous implementation of this cohort survey is required. The important point is contained in the interpretation of the results. That is to say, even when this cohort survey does not clarify the increase of risk, the cohort survey should be continued after recognizing that through interpretation of the results, it cannot necessarily be said that no effect on health is caused by the existing radiation exposure, and the results should be publicized sequentially.

Since the expectation value is large if taking all cancers into account, it is considered that there is a possibility that the data may be significant when taking particular types of cancer (including thyroid cancer) into account, although the detection power at the standardized affection ratio (SIR) = 1.1 corresponding to 10% excessive occurrence may be insufficient. We considered the re-calculation of detection power for each cancer type, including thyroid cancer, against 288,000 person-years.

Although the recruitment of new subjects is important, it has also been judged that ensuring follow-up of the 7,270 persons currently secured is more important. Since neither human nor monetary resources can ever be said to be sufficient, we ask to establish the targets strategically.

The employees of large scale enterprises belong to the population where healthy workers effect (HWE) exists, so a simple comparison with the general population having different socioeconomical factors cannot adjust the important socioeconomical confounding factor, and the selection bias cannot be avoided. For example, since the cancer morbidity is lower in comparison with the general population group, there is a high possibility that SIR is underestimated. In order to reduce such selection bias, we consider that we should compare with the emergency workers among TEPCO's employees by adding TEPCO's employees who have the same factor and are not involved in the emergency work to the research subjects as an internal control population. We should not draw a conclusion for carcinogenesis (including thyroid cancer) and cataract that are especially important outcomes only in comparison with the general population.

(2) Confounding factor

Handling of the confounding factor is one of the vital points of this research, and it should be clarified that the department in charge is responsible for the supervisory research institution.

The adjustment of the confounding factor is often implemented by obtaining the answer of "Yes" and "No." For example, LDL-chol (low density lipoprotein cholesterol) has a strong relationship with alcohol drinking and smoking. When handling alcohol drinking and smoking for the adjustment of the cofounding factor, it is expected that the adjustment using a continuous variate and multi-segment

category enables analysis in higher sensitivity, but not using the answers of “Yes” and “No.” It is preferable to adjust the cofounding factor by entering the data in the model formula as a continuous amount if the data can be handled as a continuous amount with no reduction of the information amount.

(3) Dose evaluation

Dose evaluation is important as it affects the detection power and the reasonability of results in the epidemiology of radiation. When examining from this point, the following points can be taken up as tasks:

Since the entire dose distribution deviates to the low dose side, it will be necessary to improve the accuracy of the data of workers who were exposed to doses as high as more than 250 mSv, and to also estimate the dose of organs other than the thyroid due to the inhalation of radioactive iodine that is its main factor. At this time, it is necessary to estimate the contribution of Te-132, I-132, etc. that are radioactive nuclides with a short half-life. Since external exposure has been evaluated based on the effective dose measured by the personal dosimeter, etc. of workers, we recommend to minutely examine the data of the nuclide analysis performed using the whole body counter implemented in the early stage, and to verify the abundance ratio of radioactive nuclides of a short half-life. In addition, in order to investigate the accuracy of dose evaluation of workers who were exposed to doses as high as more than 250 mSv, the investigation of the translocation of peripheral blood lymphocytes should be performed as biological dose evaluation, if necessary.

Since the dose evaluation of only I-131 may cause insufficient evaluation of the early radiation dose from March 12 to 15, 2011 when it is estimated that the exposure to short half-life nuclides other than I-131 was large, the accuracy of dose evaluation should be raised.

In addition, although the exposure evaluation of the thyroid has been so far performed by the National Institute of Radiological Sciences based on the effective dose, it is necessary also to evaluate it based on the thyroid equivalent dose considering thyroid disease.

Although the dose of crystalline lens for the study of cataract is subjected to the dose division based on the effective dose, the subjects should be divided based on the crystalline lens dose evaluation added with β dose. Further, we recommend that the dose evaluation working group examines the verification by sample survey, etc. as to whether the deviation exists between the effective dose distribution and the crystalline lens dose distribution in the early stage.

The largest task when implementing the epidemiologic survey for a long period of time is the medical evaluation of subjects about exposure dose. We should search the method for acquiring the information necessary for dose evaluation, such as photographing condition by clarifying the number of times high-dose IVR (interventional radiology) and CT (computed tomography) were implemented through a questionnaire survey, and obtaining the cooperation of the inspection institution. Therefore, it is necessary to examine the system for establishing and collecting the database of medical exposure

for each worker. In addition, the completion of a system capable of periodically performing information exchange including the dose information in linkage with the epidemiologic survey of radiation workers implemented by the Radiation Effects Association through the entrustment of the Nuclear Regulation Authority should be also examined.

From other viewpoints, it is necessary to examine whether the exposure should be evaluated for the analysis based on the continuous amount or based on the category.

(4) Survey of cause of death and cancer morbidity

a. Follow-up on cause of death and cancer morbidity

The cause of death and cancer morbidity working group considers that the acquisition of agreement and follow-up are most difficult. Since the opinion exists that the comparison with death slips of the vital statistics of the population has no problem if it explained that the occurrence of diseases and life-and-death situations are followed up at the survey start stage concerning the agreement of follow-up on the cause of death, it is necessary to verify again what level of agreement is required. Although agreement is not considered to be necessary concerning death and the follow-up on cause of death at the start of the first period research, the necessity of the agreement was judged from the opinions, etc. of the competent authorities, and the acquisition of agreement "concerning the follow-up on cause of death as research" was implemented through medical examinees, mail and the Web. The agreement for the follow-up survey of cause of death and for the comparison with resident cards has actually been acquired from 6,164 persons among 7,270 research participants as of October 31, 2018, and agreement for the collection of cancer registration information has been acquired from 6,220 participants. These are the result of great effort, and the consent ratio is about 1/3 of the total number of subjects. Therefore, it is necessary to aim for the improvement of the ratio of agreement consent in cooperation with the survey project of existing conditions of emergency workers being implemented by the government in order to make efforts to further acquire agreements.

Although it is said that the development of software for comparing the name and date of birth with a death slip is performed to verify the death and cause of death, there is a possibility that persons having the same first and last names cannot be distinguished. It is necessary to clarify the rate of accuracy of comparison with the death slip of vital statistics that can be performed in the early stage of the second period research. It is necessary to minutely investigate the accuracy of grasping this point because the subjects are distributed nationwide and the acquisition of address information is limited, and to further examine the follow-up method if the grasp rate is low. On the other hand, since the government performs follow-up work of emergency workers addresses to make sure of the situation, it is also planned to identify the cause of death by referring to the death slip based on the information obtained by the application to Ministry of Labour, Health and Welfare.

It is necessary to minutely examine with how much accuracy death identification can be performed based on the information from MLHW in the early stage of the second period.

Although the comparison work with the cancer registration for cancer morbidity was not performed in the first period, it is necessary to verify the grasp rate that can be compared with the cancer registration information in the research of the next period. Although cancer registration was performed in prefectures all over Japan, there is prefectural variation in the accuracy, and the comparison work should also be improved. If there is a challenge in comparison with cancer registration, the utilization of receipt information for grasping cancer morbidity is helpful. Since it is said that agreement to the comparison with receipt information was obtained from some health insurance societies, the method for obtaining and utilizing this receipt information should be examined.

b. Scientific evaluation

In order to analyze the cause of death and to calculate a standardized death ratio and the standardized morbidity ratio to evaluate the causal relation to exposure, the determination of the information on the exposure dose distribution and the linkage between the analyses of cause of death, standardized death rate and standardized morbidity rate, as well as the information on exposure dose distribution is the premise of the analyses.

The accurate evaluation of radiation effects is difficult based on information in the stage short on follow-up years. Concerning the period of the analysis of the cause of death and the cancer morbidity, follow-up over the lifetime is required because the analysis of the cause of death requires at least 10 years or more considering the sample size, and the detection power and the result of the trial calculation that the determination of an increase of 10% requires 40 years or more were publicized, especially concerning cancer morbidity.

In addition, we should examine the necessity, etc. for adding TEPCO's employees who have the same socioeconomic factors and are not involved in emergency work to the internal control population, considering HWE for starting analysis.

(5) Survey of thyroid cancer morbidity

a. Radiation exposure and adult thyroid cancer

Almost all the results of the surveys concluded that no relevancy was recognized between radiation exposure and adult thyroid cancer (Note 1). It is anticipated that no increase of thyroid cancer due to exposure will be recognized in the Fukushima Nuclear Power Plant accident where the number of subjects was small and the majority of workers are adult males when judging from these epidemiologic survey reports. However, it is estimated that owing to the screening effect of ultrasonic tests, thyroid cancer will be discovered exceeding the morbidity of the general population that is not subject to ultrasonic test screening. Incidentally, the frequency of potential thyroid cancer

in adult Japanese is 1.5% to 21% even in males, although it varies depending on the method of sampling slices at the time of autopsy. In order to correctly judge the dose effect relationship, it is necessary to conduct the thyroid test in the same extraction rate not only for the high dose population but also for the low dose population to avoid the generation of bias.

Note 1. Epidemiologic survey of survivors exposed to the atomic bomb in Hiroshima/Nagasaki (life survey LSS and adult health survey AHS) has examined the long term radiation effect on the thyroid. The dose effect relationship dependent on age is strongly recognized in thyroid cancer, the younger a subject is at the time of exposure, the higher the cancer risk is, and the risk is small when a subject is 20 years old or more at the time of exposure. The analysis by Furukawa revealed that no significant risk rise is observed for both male and female adults even when continuing follow-up for 60 years (Int. J. Cancer: 132: 1222-1226, 2012). On the other hand, although the analysis by Richardson *et al.* including micro cancer discovered by autopsy cases recognized the significant dose effect relationship in females 20 years old or over at the time of exposure, they did not recognize the effect in males (Epidemiology: 20: 181-187, 2009). In addition, INWORKS study of Richardson *et al.* observed the increase of thyroid cancer although the data is not significant (Epidemiology: 29: 31-41, 2018).

b. Radiation exposure and benign thyroid disease

On the other hand, various conclusions concerning the relationship between radiation exposure and benign thyroid disease are publicized, and the results of this survey are expected to bring valuable data. Although the survey of atomic bomb victims assuming tubercle and cyst as the end point found a significant dose effect relationship in the population that was 20 years old or less at the time of exposure, the risk to the population 20 years old or over was not significant in the situation of high dependency on age (Imaizumi *et al*. JAMA: 295: 1011-1022, 2006). Since the conclusion concerning autoimmune thyroid disease or autoantibody was divided, the survey results this time will add the valuable data.

One of the conclusive effects of radiation exposure is thyroid hypoparathyroidism. Clinical thyroid hypoparathyroidism is observed in the absorbed dose of 18 Gy or more in case of medical exposure. The possibility of the occurrence of subclinical (although a TSH rise is found, the thyroid hormone is within the reference value) thyroid hypoparathyroidism is pointed out even in lower doses. However, evidence for this is still poor (Note 2). Since this survey is participated in by the subjects whose thyroid equivalent dose exceeds 2 to 3 Sv, valuable data is considered to be provided.

Note 2. After the hydrogen bomb test in Bikini Atoll, Larson *et al.* observed subclinical thyroid hypoparathyroidism case in the inhabitants of Marshall Islands (JAMA: 247: 1571-1579, 1982). Since lower age inhabitants showed a higher thyroid absorbed dose, the age dependency of subclinical thyroid hypoparathyroidism was not clarified. On the other hand, the survey of the Marshall Islands inhabitants conducted by Takahashi *et al*. in the 1990s did not recognize the dose effect relationship to the thyroid function, and the relationship between a mild iodine deficiency and the thyroid tubercle was estimated

(Int J Epidemiol.28: 742-749, 1999).

c. Points to be surveyed selectively

(a) Thyroid cancer: The survey assuming thyroid cancer as the end point has limitations biologically and from the viewpoint of statistical power. However, the possibility that thyroid cancer is discovered in a frequency higher than the morbidity statistics thanks to the screening effect is considered. Therefore, the thyroid test should be conducted by setting a comparison control group in the same extraction rate including the low dose group in order to avoid the data being biased. Further, we would like to recommend comparing and examining after conducting thyroid biopsies for abnormal persons in the same criteria and completely integrating the criteria for non-operative follow-up observation (active surveillance) when a doubtful case was found. Although the medical examination rate of the thyroid test by the NEWS study so far is 12.2% (2,424 persons among 19,808 persons), the higher effective dose shows the higher examination rate of the ultrasonic test and the ratio of judgment B presents a trend of increase. The consultation guidelines for Japanese thyroid cancer recommends the active surveillance for thyroid cancer having low risk. However, since the subjects who are aware of high dose tend to desire surgery earlier than the active surveillance, careful response by clinical departments is requested.

(b) Benign thyroid disease: Since tubercle and cyst are discovered in high frequency, it is expected that useful data are brought. Although it is known that the ratio of Japanese having potential cancer is high, there is a possibility that the survey this time provides new knowledge concerning the natural history of adult thyroid tubercle. The subclinical thyroid hypoparathyroidism can be observed in the population with exposure to a high dose.

A certain amount of data should be summarized until the time 10 years after the start of the survey as a target.

(6) Survey of cataract

The definition of “prevalence rate of cataract” should be clarified, and whether the change this time is cataract or shows only the degradation of the crystalline lens should be clarified.

The method for selecting subjects should be clarified, and the inclusion of TEPCO’s non-emergency workers in the internal control population should also be taken into consideration. This enables the unification of the distribution of age and sexuality.

Since the radiation dose this time uses the effective dose, it is expected that the usage of the absorbed dose of crystalline lens prevents the deviation from the actual radiation dose.

The definition of cataract that stipulates the prevalence rate of cataracts should not be a unique one to this research, but should conform to the international definition, the guidelines of relevant academic societies, etc. and should be evaluated using the most general inspection method. If the

definition of cataract and its inspection method are reviewed in the relevant academic societies, etc. in the future, the results of the study of how the results of the EAS-1000 that is the standard of current cataract study and the simplified transillumination camera correlate should be assumed as the premise for promoting this research, and it will be preferable to install as many simplified transillumination cameras in medical examination facilities as possible. In addition, unification is preferable so that the method of filling in the observation sheet of the test is uniform, and the final evaluation determination is preferable to be universal but not personal determination. Therefore, the development of the system for automatically measuring the opacity of the crystalline lens is expected.

(7) Survey of psychological influence

This survey is to indirectly evaluate the disease and the exposure dose effect differing from other surveys. Therefore, we recommend proceeding with the research of the second period after clarifying the purpose and the arrival point of this survey.

The improvement of the follow-up accuracy is important to provide knowledge of the ranking among the countries of the world in the psychological influence evaluation. The acquisition of the outcome of suicide deaths, etc. asked in the question and answer is also recommended to be examined.

Since the especially important knowledge about depression and alcohol drinking behavior is considered to have been obtained, we ask you to continuously analyze so as to enable the comparison of frequency with the general population after the adjustment of age, etc. On the other hand, when comparing with the general population, the selection of subjects to be compared is also important, and it is necessary to minutely examine the confounding factors among the background factors including age. After that, we especially wish that a paper concerning the following knowledge is written at an early stage.

1. The frequency of “major depressive disorders (DSM-IV)” and “severe depression episodes without psychotic symptoms (ICD-10)” at the time of baseline (at the time of survey) compared with the data of the general population as well as the crisis rate before and after the disaster. We ask you to examine whether the comparison with the precedent research by Shigemura *et al.* provides a certain consideration point. In addition, we ask you to continuously examine the PTSD-related symptoms that seem to be analyzed concerning the period of entry.

2. Papers concerning stigma and relevant factors including discrimination and slander by the surrounding people, mental health, etc. while taking into consideration the abnormal situation after a nuclear disaster.

In addition, although “the usefulness of K6 in evaluation concerning depression is suggested” is described, since K6 is for measuring structural concepts differing from depression (psychological distress), this interpretation is not generally accepted. Although it is not incorrect that K6 evaluates an

aspect of the mental health degree itself, even if K6 is used in the long- and middle-term follow-up survey from now, the evaluation should be performed by separating it from the knowledge obtained from the research this time.

3. Research system

Since this is research to be performed over a long period of time, the main constituent of the research should not be transferred during the research period. For example, the training of structuring interviews was performed by making great effort. We wish to prevent the dissipation of the research resources including human resources and continue research utilizing these resources. A stable infrastructure system that copes with the changes in various social regions and enables the maintaining and continuation of this research throughout the lifetime of the subjects should be established.

Since the situation that the system for starting the second period was incomplete at the end of the first period was a big problem from the viewpoint of the continuation of the research, reexamination of the research continuation system is required. As a result, since the supervisory organization was not determined for two months from April to the beginning of June just after the first period had ended, all medical examinations and research were stopped. Specific problems concerning this are listed below:

・ Problems related to the continuous follow-up of survey subjects

The absence or change of the supervisory body was a great disturbance for maintaining the continuance of the conference and maintaining and developing the outcomes so far obtained, even if it is once every five years, because the tasks of inviting participants and reserving medical examinations were promoted by relying on a cooperative relationship with various external bodies. For example, we could not give clear reply to inquiries from research participants concerning the restart period because the consultation reservation system was stopped during this period, and it is feared that this disturbed the maintaining of the eagerness for participation.

・ Problems related to safety control of research resources

Since this research necessitates the safe accumulation of personal information requiring careful consideration for a long period of time, the establishment of a continuous control system including the construction of a network system is necessary. Therefore, the current method of public invitation of a supervisory body every five years is not suitable from the viewpoint of stably maintaining this.

・ Problems related to long term storage facility, etc. of biological specimens

Since the biological specimens collected in this research are presumed to be stored and maintained for a long period of time, the change of the supervisory body in charge greatly disturbs the maintaining of stable storage considering the labor, expense and time for changing and transferring the stored devices.

Chapter III　Summary

The evaluation by this committee concerning the research results of the five years in the first period of

the “Epidemiological Study of Health Effects in TEPCO Fukushima Daiichi Nuclear Emergency Workers” was described as above. We evaluate that the research was steadily promoted in the first period (2014 to 2018) in general, and also show the proposal by this committee concerning the ideal state of the five years of research in the second period. This research is now in progress, and although some contents may not immediately be incorporated in the research, this committee desires to cope with the tasks elastically by incorporating the results in a future research plan because this research will continue for a long period of time. In addition, we ask the Ministry of Labour, Health and Welfare to assist with the promotion of this research by proceeding with the evaluation of the research, so as to realize the contents of this research and taking actions for securing the research budget, etc. in the form following the above.

Industrial Disease Clinical Research Grants from
Japanese Ministry of Health, Labour and Welfare

Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant

General Research Report

(Excerpted Version)

Principal Investigator: Toshiteru Okubo

March 2019

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I. Comprehensive Research Report

General Research Report

Industrial Disease Clinical Research Grants

Comprehensive Research Report

Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant

Principal Investigator: Toshiteru Okubo, Radiation Effects Research Foundation (RERF), Consulting Researcher

Abstract

In the accident response work at the TEPCO Fukushima Daiichi Nuclear Power Plant, the radiation emergency exposure dose limit was raised from 100 mSv to 250 mSv for the period from March 14, 2011, to December 16 of the same year. During this period, 174 individuals among the approximately 20,000 people engaged in the work are estimated to have been exposed to doses exceeding the five-year normal work exposure limit of 100 mSv. This study aims to perform a lifelong follow-up of the entire emergency workforce of approximately 20,000 persons to investigate the relationship between their radiation exposure and health.

From the start of the appeal to the emergency workers living in Fukushima Prefecture in FY 2014, during the entire period until FY 2018, 19,808 emergency workers in the whole country responded as follows, 7,270 (36.7%) showed interest in participation, 3,334 (16.8%) declined participation, 6,976 (35.2%) returned no response, and 1,828 (9.2%) were addressees unknown at the address used.

The progress made in this study for each fiscal year was generally as follows: in FY 2014, we performed preparatory work for a country-wide launch of the survey by identifying challenges such as how to establish interview/health examination footholds, how to brief the outline of the survey, how to obtain informed consent, how to work with research partner institutions, and how to receive survey data. In FY 2015, we developed a network of 70 or so research partner institutions to establish clinical survey footholds all over the country. In FY 2016, we started a full-scale campaign to encourage emergency workers to participate in this study. The encouragement of TEPCO employees to take a health checkup was also started, which had been postponed due to the preparatory work for cooperation by TEPCO in this survey. Moreover, an information network system was developed, including application systems such as a "health questionnaire handling system" to be used by health checkup institutions and a "health checkup scheduling system" for making checkup appointments on the Web. We also started an integrated and standardized operation of the health examining methods and blood and urine sample tests at all research partner institutions. For the purpose of the cause-of-death/cancer incidence survey, we continued to undergo formalities to use demographic survey death certificates outside the intended purpose, and made preparations to collect information including causes of death. For FY 2017, we decided to place the focus on secondary campaign approaches. We newly started PR activities through posters and websites. In addition, we prepared flyers and asked for their inclusion in mail to be delivered to personal addresses on such occasions as the Current Status Survey, conducted as part of the MHLW long-term health management of the emergency workers. In FY 2018, health checkup appointment coordination tasks were outsourced.

Steadfast progress has also been made in clinical studies (by the Clinical Survey Subcommittee focusing on general health checkups, the Thyroid Cancer Survey Subcommittee, and the Psychological Impact Survey Subcommittee), exposure dose reconstruction by the Dose Assessment Subcommittee, and health effect-related surveys (by the Cause-of-Death/Cancer Incidence Survey Subcommittee and others). We, however, have not reached a definite conclusion because the encouragement of the study target population to participate is still in progress. To evaluate health effects, we should refrain from discussing causal relationships until various social factors are sufficiently evaluated as confounding factors lying in between.

Names, organizational affiliations, and titles of Co-Investigators

Makoto Akashi	National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Executive Officer	FY 2014 to present
Waka Oishi	Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	FY 2014 to present
Ryuji Okazaki	Department of Radiological Health Science, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health (UOEH)	Professor	FY 2014 to present
Kotaro Ozasa	Hiroshima Department of Epidemiology, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	FY 2014 to present
Fumiyoshi Kasagi	(Retired) Institute of Radiation Epidemiology, Radiation Effects Association (REA), Public Interest Incorporated Foundation	Institute Director	FY 2014 to 2017
Hiroaki Katayama	(Retired) Department of Information Technology, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Department Director	FY 2014 to 2017
Kazuaki Kawai	Department of Environmental Oncology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health (UOEH)	Professor	FY 2017 to present
Hiroko Kitamura	Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Deputy Office Head	FY 2017 to present
Eunjoo Kim	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Researcher	FY 2018 to present
Osamu Kurihara	Department of Radiation Measurement and Dose Assessment, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), National Research and Development Agency	Department Director	FY 2014 to present
Kazunori Kodama	Radiation Effects Research Foundation (RERF), Public Interest Incorporated Foundation	Principal Researcher	FY 2014 to 2017
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Nobuyuki Taniguchi	Department of Laboratory Medicine, Jichi Medical University	Professor	FY 2014 to present
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Megumi Miyagawa	Miyagawa Hospital, Medical Corporation Association Seiikai / Department of Endocrine and Metabolism, Toranomon Hospital, Federation of National Public Service Personnel Mutual Aid Associations	Staff Physician, Dept. of Internal Med (Part-Time)	FY 2014 to present
Takuma Momose	Nuclear Fuel Cycle Engineering Laboratories, Sector of Nuclear Fuel, Decommissioning and Waste Management Technology Development, Japan Atomic Energy Agency (JAEA), National Research and Development Agency	Deputy Director and Radiation Control Dept. Mgr.	FY 2014 to present
Shinji Yoshinaga	Division of Radiation Bio-Medical Informatics, Department of Environmetrics and Biometrics, Research Institute for Radiation Biology and Medicine, Hiroshima University	Professor	FY 2014 to present

A. Study objective

In the accident management work at the TEPCO Fukushima Daiichi Nuclear Power Plant, the radiation emergency exposure dose limit for workers was raised from the normal value of 100 mSv/5years to 250 mSv/5years for the period from March 14, 2011, to December 16 of the same year. It was estimated that 174 individuals among the approximately 20,000 people engaged in the work had been exposed to doses exceeding the five-year normal work exposure limit of 100 mSv during this period. This led to concerns over radiation-induced health disorders. Meanwhile, a majority of the workers experienced an exposure dose of less than 100 mSv. Therefore, it was required to conduct reliable epidemiological surveys with confounding factors such as lifestyle habits taken into consideration, in order to determine the presence or absence of diverse health effects, including the psychological impacts of low-dose exposures and to clarify their mechanisms. Besides, the need for such surveys was pointed out by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the International Atomic Energy Agency (IAEA). Thus, a survey for identifying the health effects of radiation exposure on emergency workers was planned as a national subsidized project. This study is a prospective cohort study on all of the approximately 20,000 persons registered in the Ministry of Health, Labour and Welfare (hereinafter "MLHW") Long-Term Health Management System (hereinafter referred to as the "Long-Term Health Management System") for Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant. This study aims to evaluate the relationships of radiation with cancer and other various results. Additionally, blood and other biological test samples shall be retained to help develop biological dosimetry and to prepare for studies on the action mechanisms of radiation effects, if results suggestive of radiation effects become apparent.

The promotion of this study is expected to compare the future incidence of disease among workers engaged in emergency work with that of the same disease among other groups of people, thereby helping to determine the relevance of the disease to emergency work.

B. Study methodology

1) Study target population and study design

This study is a prospective cohort study designed to perform lifelong follow-ups of the whole emergency workforce of approximately 20,000 persons. This study is based on this exhaustive survey and conducted assuming that diverse forms of individual studies, such as cohort, case-control, and nested case-control studies, will be planned for all or part of the study target population in the future.

2) Acquisition of existing materials and the study period

For this study, we are collecting all relevant existing materials, including exposure dose measurements taken during the emergency work and the results of health checkups done by the relevant enterprises in the past. Moreover, we shall also continuously obtain radiation exposure- and health-related information to be collected in the future by these related organizations from the survey target population. In this study, periodic address checks, clinical studies, interview surveys, and other activities shall be continuously performed to keep lifelong track of the whereabouts of the study target population and collect information on radiation exposures and its health effects. At the same time, materials and test samples shall be maintained for use in new individual studies to be planned in the future.

Where any study information related to this study has been obtained during the previous research grant-funded project conducted on the same target population as the present one before the start of this study, formalities shall be followed to take over such information for this study.

The first phase of the study period shall be five years (until the end of March 2019), during which time a group shall be developed that will form the basis for the cohort. While intended for lifelong follow-ups of the target population, this study shall be evaluated every five years by a third-party committee consisting of external experts.

3) Health effects to be evaluated

The health effects to be evaluated in this study fall within the following scope:

a) Malignant tumors (leukemia, thyroid cancer, etc.);
b) Non-cancerous diseases (circulatory system diseases, cataract, thyroid diseases, etc.);
c) Psychological impacts (PTSD, adaptation disorders, depression, etc.);
d) Biological indicators for evaluating the mechanisms of radiation health effects (immunosenescence indicators, chronic inflammatory indicators, etc.) and molecular biological indicators (single nucleotide polymorphism, genome sequence analysis, DNA adducts, etc.);
e) Health indicators that may be found necessary in the course of this study in addition to those in items a) to d) above; and
f) Health conditions that provide confounding factors necessary to evaluate the health indicators in items a) to e) above.

4) Analysis of test samples and the preservation of stored samples

To investigate the causes and backgrounds of the above-mentioned health effects, a long-term blood and urine sample storage plan shall be established to allow the biochemical analysis of biological changes before and after the detection of any health effects. For the first 11 months following the start of this study (from January 2016 to the end of November 2016), individual research partner institutions (hereinafter referred to

as "health checkup institutions") performed analyses and measurements by their usual clinical test methods; then, the obtained numerical results were collected by the Radiation Effects Research Foundation (RERF) (hereinafter abbreviated as "RERF"), which is the supervisory headquarters of this study. With a large number of institutions involved in analyses, however, long-term accuracy control is hard to maintain. Therefore, we decided to outsource all tests wholesale to Kotobiken Medical Laboratories, Inc. (hereinafter referred to as "Kotobiken") from December 2016 and onwards. Since then, blood and urine samples from research partner institutions all over the country have been collected and sent to Kotobiken's Biken Central Research Laboratory Tsukuba (hereinafter referred to as the "Central Research Laboratory") where they are aliquoted either as clinical test samples or as biological test samples for storage.

Serum, blood cell, and urine test sample aliquots for storage are frozen in cryogenic freezers, transferred while being kept at constant low temperature in dry ice to the RERF, and stored in the automated cryogenic handling and storage depository at the RERF. Among other things, we periodically check the required delivery time from the health checkup institutions to the Central Research Laboratory, the lead time for testing, and the lead time for cryogenic refrigeration storage. We also periodically monitor the temperature during transportation to the RERF.

Furthermore, each health checkup institution divides samples into two sets, one for in-house inspection and the other for normal submission to Kotobiken, whereby the samples undergo double-blind testing to verify the accuracy of clinical tests at Kotobiken.

5) Evaluation of radiation exposure

a) Information on personal exposure doses during emergency work shall be provided through the MHLW "Long-Term Health Management System for Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant." Based on this information, this study reexamines the exposure dose for all the study target individuals. We shall receive the provision of primary materials necessary for exposure dose reconstruction from TEPCO and other parties that have been responsible for emergency work radiation control. At the same time, we shall strive to obtain detailed information on stable-iodine intake status and actual work conditions in order to improve the accuracy of exposure dose reconstruction.

b) Information on personal exposure doses due to engagement in nuclear radiation work before and after employment for emergency work shall be provided from the Radiation Effects Association (REA) Radiation Dose Registration Center.

c) To make dose estimations based on medical exposure, which are is the main kind of radiation exposure other than from radiation work, we shall, with the consent of each target individual concerned, inquire to treatment-providing institutions for information on high radiation dose treatments and examinations, such as therapeutic radiation exposure and abdomen CT examinations. Information on daily life exposure shall be obtained through interviews with target individuals.

d) Organ-specific exposure doses shall be estimated by calculation.

e) Biological dosimetry shall be performed using tests such as blood chromosome tests.

f) Information shall be collected on radiation-related disease risk factors other than radiation (confounding factors). Psychological impact risk factors shall be collected and evaluated through self-completed or interview-based questionnaire surveys. Attention shall also be paid to factors such as histories of occupational exposure to hazardous substances.

6) Follow-up of the target population and collection of result indicators

We shall select one to several institutions per prefecture as footholds for making direct contact with target individuals spread over across the country, to explain to them about this study, obtain their consent, conduct health checkups, and carry out other functions. We shall consign research-related tasks to these institutions.

In addition, we shall strive to track causes of death based on demographic surveys and obtain cancer incidence information through the National Cancer Register.

While paying attention to consistency with regular health checkups conducted as a responsibility of proprietors, we shall conduct regular health checkups to collect clinical data and shall perform questionnaire surveys, health examinations and checks, biological test sampling, and so forth. We shall also receive the provision of health checkup data held by proprietors.

7) Research system

As regards research organizations, the Operational Committee and Study Groups consisting of Working-Group Investigators shall convene for their respective meetings to facilitate efficient execution of this study. Each year, The Study Groups shall hold one or more Study Group Meetings with full member attendance, to discuss study methodology, research outcomes, and future research policy, and other issues.

a) Operational Committee: Supervises this Research Project as a whole. This Committee deliberates on all important matters for the execution of this study, including Research Proposals, research ethics, research organizations, storage and use of materials and test samples, allocation of research budget, research publication, and third-party review.

b) Analysis/Evaluation Subcommittee: Performs statistical analysis and evaluation of survey results.

c) Centralized control of epidemiological data and application thereof to studies

No change can be made to the basic data stored in the data server, except for the addition of new data and corrections made to existing data. Direct manipulation of the basic data is limited to authorized personnel only. Therefore, investigators cannot make access to basic data. For all studies, the only available data is the research-use database that contains necessary items created based on the Research Proposal and extracted from the basic data.

d) Clinical Study (Health Checkup) Subcommittee: Plans, conducts, and manages clinical studies (health checkups). This Subcommittee considers the details of the outsourcing of health checkups and performs information gathering and other responsibilities. The Subcommittee also standardizes clinical tests, interviews, health examinations, blood sampling, and preparation and transportation of test samples for storage to ensure proper accuracy control.

e) Cataract Working Group: Conducts and manages cataract surveys and evaluates obtained data and analysis results.

f) Thyroid Cancer Survey Subcommittee: Conducts and manages thyroid cancer surveys and evaluates obtained data and analysis results.

g) Psychological Impact Survey Subcommittee: Conducts and manages psychological impact surveys and evaluates obtained data and analysis results. Of the data on the target population of the previous study conducted with the MHLW Grant-in-Aid for Scientific Research before the start of this study, those on the target population of this study (person-specific raw data) shall be taken over as existing materials for this study (the same applies to e) and f) above).

h) Cause-of-Death/Cancer Incidence Survey Subcommittee: Checks whether the study target individuals are alive or dead based on the information from the periodic status surveys (including inquiries for certificates of residence) on the study target population recorded in the MHLW "Long-Term Health Management System for Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant." Regarding deceased individuals, information, including causes of death, shall be periodically collected through the formalities to use demographic survey death certificates outside the intended purpose. This Subcommittee performs periodic collation with the National Cancer Register to collect cancer incidence information, including survivors.

i) Dose Assessment Subcommittee: Based on the exposure doses measured, with a focus on external exposure doses, during the emergency work, this Subcommittee collects various information before and after the work to reconstruct exposure doses. The Subcommittee comparatively examines internal exposure doses through verification of measurement data and reconstruction of intake scenarios, and also performs chromosome analysis-based evaluation to achieve a multi-faceted reconstruction of personal exposure doses. More specifically, the Subcommittee performs dose assessment, factoring in uncertainty, mainly through simulation-based or otherwise driven verification of internal exposure measurement data and reconstruction of intake scenarios based on personal behavior records, with stable iodine tablets and other modifiers taken into consideration. For this purpose, the Subcommittee shall develop an exposure information control/dose calculation system that is able to store existing exposure and behavior record information and perform dose calculation. The existing exposure information shall include REA's records referenced for past nuclear workers and the inquiries for the results of prefectural resident health surveys conducted on Fukushima Prefecture residents to assess the effect of environmental exposure. For study target individuals deemed as exposed to a dose of more than 70 mSv, the Subcommittee shall assess their exposure doses based on the analysis of translocated chromosome frequencies (nearly free of secular variations).

j) Radiobiological Study Working Group: Plans and conducts radiobiological studies using biological test samples obtained from health checkups.

(Ethical considerations)

The Research Proposal for this study was reviewed and approved by the RERF Ethics Committee. The individual studies planned by the Co-Investigators shall be classified by study theme to undergo ethics review by their respective affiliated institutions as necessary. This study shall be conducted in compliance with the "Ethical Guidelines for Medical and Health Research Involving Human Subjects" and the "Ethical Guidelines for Medical and Health Research Involving Human Subjects."

a) Handling of materials and test samples

Information on the study target population shall be strictly protected and controlled in accordance with nationally prescribed standards (the Personal Information Protection Act, the "Ethical Guidelines for Medical and Health Research Involving Human Subjects," etc.) The materials and test samples for this study shall be provided to the RERF as personally identifiable information by related parties, including the MHLW and other agencies possessing materials and test samples, health checkup institutions engaged in health checkups and surveys, and Joint-Researchers engaged in individual studies, and shall be centrally stored associated with individual target individuals. If required for research purposes, only the required items shall be provided to the Research Director after being anonymized at the RERF in accordance with the approved Research Proposal. All correspondence

tables for merging shall be securely retained by a specific administrator designated by the RERF. Materials and test samples shall be stored in a lockable room. Personally identifiable materials shall be stored in a lockable storage cabinet installed in that room. Electronic data shall be stored in a dedicated server installed in a lockable room and shall be manipulated by authorized personnel only. In principle, electronic data shall be auto-backed up on a separate server as a precaution against unexpected failure. Additionally, copies of magnetically recorded data shall be created at regular intervals and stored in a bank safe as a precaution against critical situations where all computers have become unusable. In principle, all data and materials shall be retained until the end of the study period (tentatively set as 30 years). Each biological test sample (such as blood and urine) shall be pre-treated for storage, then aliquoted into more than one tube for storage, labeled with a suitably anonymized ID for merging, and stored in a storage vault at −80°C. Materials and test samples shall be disposed of as follows: primary materials (including personal identification materials), anonymized materials for research purposes, and anonymized correspondence tables shall be disposed of separately by kind; more specifically, printed materials shall be disposed of by shredding whereas electromagnetic data shall be disposed of after physical initialization. Biological test samples shall be disposed of by their respective suitable methods (specific details of which shall be given in individual Research Protocols). Requests from target individuals for disposal of their materials and test samples during the study period shall be accepted in accordance with prescribed formalities: the pertinent materials and test samples shall be disposed of by transparent methods, and the results shall be appropriately explained to the requesters and retained for record.

b) Explanations to target individuals and acquisition of their consent

In this Research Proposal, after the explanation of the meaning, purpose, entity, and method of this study, target individuals shall be informed that their participation in this study is at their discretion. After the explanation of the benefits and disadvantages of their cooperation in this study and the rights of the participants, their consent to the items given below shall be obtained. Where informed consent (hereinafter abbreviated as "IC") is difficult to obtain from a target individual due to reasons such as old age or poor health condition, IC obtained from their proxy may be acceptable.

(i) Receiving information provided from agencies possessing existing materials;

(ii) Clinical studies including health checkups; and

(iii) Receiving requests for participation in individual Research Proposals to be planned in the future.

c) Benefits and risks of this study for the target population

In surveys conducted using methods such as interviews, self-completed questionnaires, or other similar methods, or in analyses of existing materials and obtained test samples, there are no benefits or risks to the target population. In cases such as tests/biological test sampling involving physical invasion, minor physical risks may occur depending on the type/level of the test. When informing target individuals of the answers to a questionnaire survey or the results of a test or a biological test sample analysis, we shall give priority to providing them with benefits such as easier health management. As regards procedural manuals for addressing expected adverse events during health checkups, the manuals of individual research partner institutions shall be used *mutatis mutandis* or shall be prepared beforehand by the responsible investigator. Should any such event occur, the research partner institution concerned and the responsible investigator shall immediately provide appropriate treatment for recovery and prevent the spread of damage. Should any such event occur, the research partner institution concerned or the responsible investigator shall immediately provide its details to the Principal Investigator. The Principal Investigator shall report the information to the head of the Supervising Research Institution and shall make contact with the members of the Operational Committee of this study, and likewise with the research partner institutions engaged in the health checkup concerned and necessary investigators. Then, the Operational Committee shall convene as soon as reasonably possible for reporting on the event concerned and response thereto, and consider the subsequent measures to be taken. The head of the Supervising Research Institution shall ask the Ethics Committee for their views on the event concerned and take necessary measures accordingly. For individual Research Proposals, specific instructions shall be provided in the corresponding Research Protocols.

d) Release of research outcome

When this study Group presents its research outcome at an academic conference or gets it published in a specialist academic journal, it goes without saying that the normal standards and operational regulations practiced in the WG Investigators' affiliated research institutions must be complied with. This study, however, has attracted much public attention. Hence, the contents to be presented or published by the WG Investigators shall not be left at their exclusive discretion, but shall be carefully examined for relevance with the contents of the presentations and publications by the Study Group as a whole, including those made in the past to ensure the overall consistency. The formalities to follow are described in the following paragraphs separately for presentations at academic conferences and submissions to journals.

Presentations at academic conferences

Prior to submitting an application for presenting at a conference, the Lead Presenter shall, as usual, obtain approval from all members of his/her affiliated Subcommittee or Working Group and all Co-Presenters. Then, the Lead Presenter shall follow the formalities specified by his/her affiliated institution to obtain approval for presenting. After the completion of the internal formalities, a summary of the draft presentation shall be submitted to the Research Secretariat of the RERF, which is the Supervising Research Institution. On the basis of the content of the draft presentation, the Principal Investigator shall determine whether to seek comments from other relevant WG Investigators. The Principal Investigator shall inform the Principal Presenter of the approval after the addition of necessary corrections.

At the same time, the Principal Investigator shall communicate the summary of the conference presentation to the Office for Radiation Protection of Workers, Industrial Health Division, Industrial Safety and Health Department, Labour Standards Bureau, MHLW.

Submissions to academic journals

Prior to submitting a paper to an academic journal, the Lead Author shall, as usual, obtain approval from all members of his/her affiliated Subcommittee or Working Group and all Co-Authors. Then, the Lead Author shall follow the formalities specified by his/her affiliated institution to make arrangement for internal peer review. After the completion of the internal formalities of his/her affiliated organization, the Lead Author shall submit the abstract of the paper to the RERF Research Secretariat. The Principal Investigator shall determine whether to seek comments. Should any other relevant WG Investigator find peer review necessary, the Principal Investigator shall make a request for peer review and add necessary corrections before informing the Principal Presenter of the approval.

At the same time, the Principal Investigator shall submit the abstract of the paper for submission to the Office for Radiation Protection of Workers, Industrial Health Division, Industrial Safety and Health Department, Labour Standards Bureau, MHLW.

e) The status of progress made in this study shall be reported once a year to the MHLW, from which this study was commissioned. Reports shall be made to the head of the RERF and Science Advisory Committee as necessary. In addition, the study shall be reviewed by the Ethics Committee as appropriate. After reaching a certain stage, this study shall undergo an international third-party review.

f) Conflicts of interest

A review for conflicts of interest regarding this study shall be performed by the RERF Conflict of Interest Prevention Committee to ensure that no financial benefit from the Principal Investigator and the Co-Investigators will occur in excess of the prescribed standard.

g) Methods of information disclosure

The outline of this study and other information thereon shall be posted on the homepage for the external audience on the website of this study. A newsletter explaining the status of progress made in this study shall be sent out to the target individuals of this study once a year or so. Whenever a request for perusal is received from any study target individual, the Research Protocol shall be disclosed without delay.

h) Handling of consultation requests from study target individuals

Any request for consultation from a study target individual shall first be received by the RC in charge thereof. After checking with the Principal Investigator or an appropriate Co-Investigator or a Research Collaborator, the RC shall reply to the study target individual.

i) Economic costs on study target individuals and compensations therefor

The health checkup cost shall be covered by the grant for this Research Project. Hence, no cost will occur to any participant. As regards the cost of traveling to the research partner institutions where participants undergo health checkups, the most economical amount for traveling by the normal route shall be paid. Honoraria shall be paid as appropriate for the cost and time spent on participation in this study.

[Study results]

Outline of progress made in the study for the individual years

1) FY 2014

In FY 2014, the initial year of the study period, a preliminary survey of emergency workers living in Fukushima Prefecture was conducted to identify challenges such as how to establish interview/health examination footholds, how to brief the outline of the survey, how to obtain consent to this study, how to work with partner institutions, and how to receive survey data. Then, preparations were made for a country-wide launch, including the standardization of the methodology for full-scale surveys and the selection of the survey results compilation method.

2) FY 2015

In FY 2015, focus was placed on the development of a clinical survey implementation system and the encouragement of the study target population to participate in this study. Each Subcommittee started specific planning of a Research Proposal and made the preparations necessary to start their study, such as the establishment of a research support organization. As a clinical survey implementation system, a network of research partner institutions was established consisting of 70 institutions listed in Table 1 (increased to 77 institutions as of the end of

Oct. 2018 through subsequent partnership expansion efforts) with NFIHO member institutions at the core. Next, each institution was requested to appoint an RC in charge of this study, so that RC meeting could convene and hold training workshops on, e.g., the approach to surveys as an effort to standardize surveys.

We assisted the Thyroid Cancer Survey Subcommittee and the Psychological Impact Survey Subcommittee with holding a training workshop for health checkup institution personnel in charge of the structured interview and the primary ultrasound screening of the thyroid.

We signed an outsourcing agreement with the RERF and the Radiation Effects Association (hereinafter abbreviated as "REA"), respectively, and considered outsourcing for FY 2015 the extraction of exposure dose records on the emergency workers and the verification of the consistency of exposure dose records.

3) FY 2016

In FY 2016, the focus was placed on the development of the clinical survey implementation system and the encouragement of the study target population to participate in this study. Assistance was provided for each Subcommittee to start their study full scale.

As an effort to further develop the clinical survey implementation system, a preliminary meeting was held for the persons in charge of this epidemiological study (Research Coordinators, hereinafter abbreviated as "RCs"), who were mainly nursing professionals, and each appointed by their respective health checkup institutions. An inquiry handling system for handling various inquiries from research partner (health checkup) institutions and a health checkup scheduling system for making checkup appointments on the Web were introduced as application systems for the information network system. We were finally ready to start centralized sample testing, which had been a pending matter since the start of this Research Project. On December 1, we started a long-term integrated and standardized operation of health examining methods practiced at all the health checkup institutions.

As an effort to encourage the study target population to participate in this study, a second letter was sent out to those who in FY2015 had expressed by letter their intention to participate, but had failed to be accepted by the institution of their preference to take health checkup at. Encouragement of TEPCO employees to take health checkups was started, which had been postponed during their internal discussions on the details of their framework for cooperation in this study. In September, the first issue of "NEWS Health Checkup News" was issued as a newsletter for informing all emergency workers of the progress made in this study.

In accordance with the Agreement with the REA for "Preliminary Survey Work for Extracting Records of Exposure Doses Experienced by Emergency Workers," REA-held personal information was checked against the information on the participants of this study on a person-by-person basis to identify potential problems. More specifically, we conducted a preliminary survey for improving the actual working accuracy of identification with emergency workers, using the exposure dose record consistency verification method developed in FY 2015.

4) FY 2017

We strove to develop a partnership with the health checkup institutions with NFIHO member institutions at the core. Despite our efforts, however, blank prefectures still remained (Akita, Yamanashi, Nara, Yamaguchi, Tokushima, and Kagawa). Another challenge was low checkup participation rates due to poor transportation access in some prefectures. We redoubled our efforts for further expansion of the network of research partner institutions.

Hosting of meetings

a) Hosting of the RC Meeting

After explanations were made on the questionnaire for use in health checkups and the standard operating procedures for interviews and other related tasks, a question-and-answer session was held.

b) Thyroid Ultrasound Scan Training Workshop

Based on the anatomical and physiological explanations on the thyroid, ultrasound scan techniques for various diseases were explained. Then, hands-on training was provided through ultrasound scan group learning for disease/case exercises. This training workshop is held as necessary on such occasions as the replacement of the person in charge at any institution or the participation of a new member.

c) Practical training workshop on structured interviews related to psychological impact surveys

Lectures and computer-based role-playing training were provided for the trainees to learn the standard testing method of the WHO Structured Interview. This training workshop is also held as the need arises and has been held an average of once or twice per year.

In accordance with the outsourcing agreement with REA, the information of 1,414 individuals each with an identity matching an emergency worker having given written consent was provided from the database of the "Radiation Exposure Dose Registration System for Workers Engaged in Decontamination Work."

5) FY 2018

FY 2018 saw the fruition of the activities up to the previous fiscal year into a functioning comprehensive health examination framework, including tests on individuals having consented to participation in this study.

What was newly started in FY 2018 was the outsourcing of health checkup appointment coordination tasks, which had been a pending matter since the start of this Research Proposal. This relieves institutions assigned with a large number of target individuals from the burden of making contact with prospective examinees for the adjustment of the health checkup schedule. Whether to use this proxy service is left at the discretion of each institution, because situations may significantly vary depending on the health checkup institution.

The events held as regular activities of the Headquarters for FY 2018 are as follows: the eighth meeting of the Operational Committee in Tokyo on September 6 (Thu), 2018; the 5th session of the Study Group Meeting scheduled to convene in Tokyo on March 12 (Tue), 2019; and the 5th session of the RC Meeting in Tokyo on June 28 (Thu), 2018. Besides, an extra session of RC Meeting was held on June 8 (Fri), 2018 (Hiroshima) as a workshop for persons in charge from the following three newly joined institutions: General foundational juridical person Japan Occupational Hygiene Association (JOHA) Takaido Higashi Health Checkup Clinic, General foundational juridical person Japan Occupational Hygiene Association (JOHA) Nagano Prefectural Branch, and General foundational juridical person Association for Preventive Medicine of Japan (APMJ) Western Japan Division.

As regards PR activities, posters and flyers were revised, and web pages were upgraded in addition to the issuance of RC News and a newsletter (NEWS Health Checkup News) as regular activities.

Continuing from the preceding fiscal year, we, in accordance with the outsourcing agreement with the REA, it was requested that the REA provide the dose record information of an additional 4,560 target individuals having submitted written consent addressed to the name of the Chairperson of the REA. The extraction of the list of appropriate target individuals is underway for delivery in March 2019.

Establishment of a partnership with institutions willing to conduct health examinations

When this study started in 2014, the residential locations of approximately 20,000 emergency workers, who became the interest of this study, had already been spread across all 47 prefectures of Japan. Hence, it was critically important to establish a country-wide research implementation organization to make contact with each of these study target individuals and investigate their health condition. So, we called out for research cooperation to related medical institutions across the country, with a focus on the member institutions of the National Federation of Industrial Health Organizations (hereinafter abbreviated as "NFIHO") organized by health checkup institutions specializing in industrial health services for workers. As a result, 70 facilities (66 NFIHO member institutions and other four facilities) expressed their intention of research cooperation. After some subsequent shuffling in and out, the current number stands at 77 facilities (See Table 1). As regards the outsourcing of health checkup work to these health checkup institutions, the items to be checked/tested in the health checkup/test, and associated matters such as cost and results reporting method were agreed upon in accordance with individual agreements with the NFIHO and partner institutions. The RERF entered into a package-deal agreement with the NFIHO to outsource all health checkup-related formalities, billing of costs and expenses, and other clerical tasks to the NFIHO.

These 70-odd health checkup institutions are expected to make periodic contact with each target individual over the coming 30 years or more, to obtain their written consent and continuously provide services, such as questionnaire form filling, history taking and health checkups, in accordance with an established formula. Many emergency workers are, however, frequent job-hoppers whose residential location frequently changes accordingly. When it comes to surveying such target individuals with high mobility between health checkup institutions, it is essential to standardize health checkup techniques and maintain test accuracy among health checkup institutions. Most health checkup institutions can only manage to spare their tightly limited time available in between their primary duties, such as thorough medical screening, for health checkup tasks. Moreover, the amount or proportion of time required for research cooperation significantly varies among the institutions. In other words, it was considered difficult to expect uniform levels of cooperation and work accuracy from all the health checkup institutions on a long-term basis. Introduced as a strategic solution to this problem was the concept of each institution appointing a person in charge of this epidemiological study to develop a cooperation framework under them to suit institutional circumstances. This person is called an RC. We requested each institution appoint an RC in charge of this study primarily from among their nursing staff.

We requested the institutions engage mainly RCs in history taking, written-consent acquisition, psychological survey interviews, and the overall coordination of research-related tasks, including reporting of health checkup results and dispatching of collected samples. To standardize these tasks and improve the efficiency thereof, we issued the "Guidebook for the Health Checkup Institutions" and have hosted an RC Meeting once a year, with full attendance of all RCs, to have the discussions necessary for coordination. At the same time, we have also been issuing a periodical newsletter (RC News) to communicate and share the latest information.

The "Guidebook for the Health Checkup Institutions" issued to each RC is carefully designed to allow standardization down

to detailed procedures. The resulting standardized techniques are supposed to be passed on from a preceding RC to a succeeding RC. In some cases, however, this intergenerational succession of techniques was impossible due to unusual circumstances, such as the replacement of the RC due to illness. As a precaution against such cases, the Headquarters implemented a framework for providing RCs with on-the-job training. This is indispensable support for RCs from newly joined research partner institutions. More specifically, RCs are invited to the Headquarters Secretariat to be briefed on the outline of this study, while observing demonstrations of actual work, and to undergo on-the-job training in the health checkup workflow, system operations, and other tasks.

Acquisition of basic and related information (long-term health management system, causes of death, and REA's doses)

We, as this study Group, continued with the continuous health survey of the target population to analyze and evaluate changes therein. At the same time, we obtained the following relevant information from related organizations and made the obtained radiation exposure information available for use in this study to investigate its relevance:

(i) Provision of information, including the latest address and dose information, biological effects information, and detailed exposure work-related information, through the long-term health management system

We were provided with the following information from the MHLW-developed database for the long-term health management of emergency workers, including the latest address information based on the annual current status survey:

• Worker information file;
• Work/exposure dose information file;
• Daily work/exposure dose information file;
• General health checkup information file;
• Ionizing radiation/emergency health checkup information file;
• Other test information file;
• Exposure work-related information relevant to Notification No. 1109-1 "Matters Concerning Submission of Exposure Work-Related Information on Designated Emergency Workers (Request)," issued on November 9, 2015, by the Industrial Safety and Health Department, Labour Standards Bureau, MHLW;
• Company Code List;
• Emergency Worker List;
• Cataract patient identification numbers;
• FY 2016 Cataract Examination Results, etc. (TEPCO).

(ii) Radiation Effects Association (REA)

REA's Radiation Dose Registration Center (hereinafter referred to as "Central Registration Center") has a register of those engaged in emergency work, to record the names of nuclear facilities they worked at and the exposure doses they experienced. In other words, the REA investigates the types, characteristics, and other aspects of personal dosimeters and other instruments in current or former use at nuclear power and associated facilities in Japan. Additionally, taking into consideration the reality of personal dose control and related practices at nuclear power business operators, the REA maintains long-term records of exposure doses experienced by individual workers. Accordingly, it was planned to obtain the exposure doses experienced by emergency workers during the work. For those with a history of nuclear work before and after the emergency work, it was planned to receive the provision of such exposure doses and other information. To realize this, we must first undergo formalities to obtain consent to the provision of exposure dose records of emergency workers from the corporate participants in the Radiation Exposure Dose Registration System for Workers Engaged in Decontamination Work. This is no more than the prerequisite for us to obtain the consent of individual emergency workers to the use of their information. Under these conditions, the RERF first concluded an outsourcing agreement with the REA for the implementation of tasks to be described later.

The external doses indicated by pocket dosimeters worn by almost all workers during the emergency work are available, along with the effective whole-body doses calculated based thereon, from the above-mentioned MHLW Long-Term Health Management Database. Then, as a project for FY 2015, we considered how to verify the consistency of the long-term health management system data with REA's exposure dose records. After this, in the FY 2016 Commissioned Project "Preliminary Survey Work for Extracting Records of Exposure Doses Experienced by Emergency Workers," we ran checks against REA's records and identified potential problems for each individual. In the FY 2017 "Commissioned Work Including the Extraction of Exposure Dose Records of the Emergency Workers," with these challenges taken into consideration, identity collation was performed of individuals having submitted a written consent. Then, we received the provision of information of 1,414 individuals, each with an identity matching an emergency worker. In FY 2018, we outsourced the identity collation of the remaining 4,560 individuals having submitted written consent, and will receive delivery of the results in March 2019.

(iii) Cause-of-death data from the MHLW

We requested that the MHLW extract and provide the necessary contents of diagnosed death certificates and death receipts from MHLW-possessed questionnaire-based information, so that we could produce demographic statistics for FY 2017 onwards to perform statistical analysis of the personal information of target individuals, such as their time of

death and cause of death, and determine the relevance between radiation and deaths due to specific diseases. We were then provided with such information on Japanese nationals who died during the period from March 2011 to December 2016. From now on, the name, sex, and birth date of each emergency worker whose death is confirmed shall be collated with the demographic statistics to collect the cause-of-death information of those deceased. Moreover, we intend to use the Cancer Registration System to receive the provision of information on cancer incidence among the target population.

3) Information processing system and information control

This study includes in its scope more than 5,000 enterprises to which the survey target individuals belonged at the time of the emergency work. In addition, the residential locations of the target individuals are spread across all prefectures. Accordingly, health checkups and other investigatory tasks, such as history taking, are consigned to more than 70 research partner institutions located across the country. There is a clinical testing body that undertakes the analysis of all the samples for analysis. There is also a proxy service provider for checkup appointment scheduling. Because a wide range of data is handled by such a large research organization stretched all over the country throughout the rest of the target population's life, an information system is required for assistance in all practical aspects of study implementation, including management and analysis of collected data suitable to conduct continuous surveys. Therefore, by outsourcing to specialist contractors, we built a dedicated basic database for this study, a network system connecting all the footholds, and various application systems, and outsourced the operation and support of these systems. While more than one organization is involved here, there are preparatory tasks to be completed for each checkup examinee ahead of the health checkup date. Such tasks include: making health checkup appointments; dispatching consent forms and questionnaire forms; calculating the travel fares to and from the health checkup institutions; and procuring materials and equipment including blood collection tubes necessary for the collection and transportation of blood or urine samples. On top of these, cases are not rare where changes occur in the middle. This system is intended to handle personally identifiable information and, as such, must provide a high level of maintainability of its information management function. Furthermore, there are many Co-Investigators and Research Collaborators involved. Some of them have to collect their target individuals' data from six joint research institutions located in different locations. In addition, some of the data to be provided may have to undergo collation with certain basic data items before acceptance. In a system with such a cross-sectionally complicated structure that assumes changes over time, study information must be sent and received by a secure method. Moreover, this structure may be changed as time elapses. Hence, the information processing system must flexibly accommodate changes that may occur.

Immediately after the start of this study, consultation started on the basic concept of system development. In FY 2015, the fundamental part of the dedicated information network system featuring robust confidentiality was completed, followed by the completion of the application systems, such as a transmission and reception system, an inquiry handling system, a health checkup scheduling system in FY 2016. On December 1, 2016, the current system became operational.

As explained in the next Section, all basic data obtained through this study will be stored in the data server installed in the supervising institution. This data server has the function of automatically creating backup copies as a precaution against unexpected failure. In addition, all possible measures have been taken to protect the basic data: for example, backup copies periodically created are stored in external storage. Although the data server is maintained by the System, there are many connections to the network, and the risk of hacking attacks from outside is correspondingly high. Hence, all possible measures are taken to ensure security.

All the health checkup institutions must submit test data obtained through health checkups to the RERF. Therefore, all institutions have dedicated terminals installed that are connected via mobile routers to the dedicated network. To log in to this system, the operator must use an ID and password issued to a pre-registered user.

Considering the diverse specialties of the personnel using the System, efforts were made to enhance the usability of the information network system as much as possible. One of these efforts is the development of application systems such as the "inquiry handling system" for handling various inquiries from health checkup institutions, and the "health checkup scheduling system" for making checkup appointments on the Web. Accordingly, the RC Meeting provided explanation on the standard method of data exchange through the dedicated system, as well as how to apply the information available from the health checkup scheduling system to the billing of costs and expenses. In the FY 2018 session of the RC Meeting, discussions were had on matters such as better approaches to deal with individual study participants.

Establishment and management of the tasks of the Supervising Research Institution

In the RERF (Hiroshima) Clinical Research Department as the Supervising Research Institution, the "Nuclear Emergency Workers Health Study Office" (hereinafter abbreviated as "NEWS") was organized to provide a secretariat function and establish a research support framework for carrying out the following tasks:

(i) Request for the internal review of the Research Protocol

The Basic Research Proposal part of the "Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant" was approved as Research Protocol (RP6-15) in accordance with the research review and approval rules of the RERF.

This study was reviewed for ethical aspects as follows: the 204th Joint Session of the RERF Human Investigation Committee (HIC) and Ethics Committee for Genetic Research (ECGR) was held on December 11, 2014, to review the method of obtaining the list of target individuals from the MHLW long-term health management database, and also to review the content of the letter sent to inform the survey target population of 20,000 persons about this study. Then on January 21, 2015, the 205th Joint Session reviewed the fundamental part of the Research Protocol and the content of the letter of consent to participation in the preliminary survey before sending it to the target individuals living in Fukushima Prefecture. On January 23, 2015, approval was granted. Since then until today, information letters to the survey target population, the consent form and written explanation thereof, and other documents have been reviewed and approved for additions and modifications as follows:

• December 11, 2014 (204th HIC/ECGR);
• January 21, 2015 (205th HIC/ECGR) / Approved on January 23, 2015;
• May 21, 2015 (208th HIC full board review) / Approved on June 11, 2015;
• July 29, 2015 (210th HIC expedited review);
• August 26, 2015 (212th HIC/ECGR expedited review) / Approved on September 11, 2015;
• July 13, 2016 (FY 2016 5th IRB expedited review) / Approved on July 19, 2016;
• August 15, 2016(FY 2016 7th IRB expedited review) / Approved on August 16, 2016;
• October 12, 2016(FY 2016 10th expedited review) / Approved on November 2, 2016;
• May 18, 2017 (IRB full board review) / Approved on July 11, 2017;
• September 4, 2017 / September 14, 2017; and
• April 18, 2018 (full board review) / April 23, 2018.

(ii) Application to MHLW for Research Grant Delivery and Project Performance Report to MHLW

• Application for Continued Research and Formal Application for Grant Delivery

[Background of application for a research grant for the initial year]

On July 31, 2014, the Worker's Compensation Administration Division, Worker's Compensation Department, Labour Standards Bureau, MHLW, issued a notice of open application for the FY 2014 Industrial Disease Clinical Research Grants to invite applications for grant for an Epidemiological Study on Health Effects on Radiation Workers as an area of radiation effects studies. The Notice said that the amount for the initial year would be approximately ¥100 million, the research budget per year would range from ¥300 million to ¥500 million, and the grant period would be extended by five years at a time. One of the requirements for research proposals for the application was for them to build on the recommendations by the "Report of the Expert Meeting on Epidemiological Studies Targeting Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant (June 4, 2014)." It was additionally required for the implementation of the study to ensure continuity from an existing study funded by MHLW Grant-In-Aid, and cooperation with the co-authoring investigators of that study. Furthermore, as regards the post-adoption research system, it was suggested to consult with the MHLW as a method of guaranteed research outcomes.

On August 29, 2014, Toshiteru Okubo (then RERF Chairman) was the representative of the Supervising Research Institution and submitted, as the Principal Investigator of this study the Research Protocol for the study theme "Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant" in accordance with the applicable Guidelines for Open Application. On October 21 of the same year, as the result of a hearing and a review, Okubo was notified of the standard amount to be granted from the National Treasury (¥89,440,000). The study period of the initial accounting year was from October 15, 2014, to March 31, 2015. As a result of subsequent consultation with the MHLW, a research organization was established, followed by submission of the Application for Research Grant Delivery with a due date of November 14 of the same year.

Then from the second year onwards, an Application for Continued Research has been filed to undergo an interim evaluation as required. Every year up until FY 2018, the fifth year, an annual Research Implementation Plan has been continually presented.

• Preparation and distribution of the Research Reports

The Annual Research Reports for the years from FY 2014 to FY 2017 each consist of a Comprehensive Research Report and Working-Group Research Reports. The manuscripts were submitted from the WG Investigators and then compiled by the Secretariat for outsourced proofreading and printing. The total number of pages of the Annual Research Reports in book form for FY 2014, FY 2015, FY 2016, and FY 2017 were 97, 172, 213, and 229, respectively. These were submitted to the MHLW at the end of March of every fiscal year and distributed to the WG Investigators, all the research-partner health checkup

institutions across the country, public libraries, and other audiences.

(iii) Hosting of Meetings based on the Research Operations Framework

• Hosting of Meetings of the Operational Committee

An Operational Committee consisting of key Co-Investigators was established as the decision-making body of this study Group to deliberate on, among other agenda, the Research Proposal and issues concerning the implementation of this study.

1st meeting of Operational Committee: December 9 (Tue.), 2014, Tokyo;
2nd meeting of Operational Committee: January 8 (Thu.), 2015, Tokyo;
3rd meeting of Operational Committee: April 30 (Thu.), 2015, Tokyo;
4th meeting of Operational Committee: August 17 (Mon.), 2015, Tokyo;
5th meeting of Operational Committee: December 15 (Wed.), 2015, Tokyo;
6th meeting of Operational Committee: November 1 (Tue.), 2016, Tokyo;
7th meeting of Operational Committee: August 30 (Wed.), 2017, Tokyo; and
8th meeting of Operational Committee: September 6 (Thu.), 2018, Tokyo.

• Hosting of Study Group Meetings

A Study Group Meeting was held once a year to provide each Study Group with an opportunity to report on their study. All the Co-Investigators and Research Collaborators were convened so they could be updated on the status of activities at the headquarters of the Supervising Research Institution and the status of progress made by each of the other Subcommittees.

1st session of Study Group Meeting: November 14 (Fri.), 2014, Tokyo;
2nd session of Study Group Meeting: March 12 (Sat.), 2016, Kitakyushu;
3rd session of Study Group Meeting: March 9 (Thu.), 2017, Tokyo;
4th session of Study Group Meeting: March 15 (Thu.), 2018, Tokyo; and
5th session of Study Group Meeting: March 12 (Tue.), 2019, Tokyo.

• Research Coordinator (RC) Meeting

Each of the 77 research-partner health checkup institutions across the country has appointed one or more RCs, whose specialty is basically medical or public health nursing. At their respective institutions, these RCs have the function of making adjustments with the Appointment Scheduling Department, the Test Department, the Information Processing Department, and the Administrative and Accounting Department to facilitate smooth execution of health checkups for this study. To conduct health checkups with the same level of quality across the country, the RC Meeting convened once each year as follows in order to share important information and handle various issues, such as improvement requests and opinions received from individual institutions:

1st session of RC Meeting: March 14 (Sat.), 2015, Tokyo;
2nd session of RC Meeting: August 18 (Tue.), 2015, Tokyo;
3rd session of RC Meeting: June 18 (Sat.), 2016, Tokyo;
4th session of RC Meeting: June 21 (Wed.), 2017, Tokyo; and
5th session of RC Meeting: June 28 (Thu.), 2018, Tokyo.

In FY 2017 and FY 2018, the RERF (Hiroshima) provided an orientation for the following newly joined research-partner health checkup institutions in order to explain to them the outline of this study and the health checkup workflow, as well as to demonstrate how to use health checkup-related systems:

May 26 (Fri.), 2017, Hiroshima

General foundational juridical person Kimitsu Health Center;

Seirei Sakura Citizen Hospital, Social welfare juridical person Seirei Social Welfare Community; and

Medical juridical person Sugai Clinic;

June 8 (Fri.), 2018, Hiroshima

General foundational juridical person Japan Occupational Hygiene Association (JOHA) Takaido Higashi Health Checkup Clinic;

General foundational juridical person Japan Occupational Hygiene Association (JOHA) Nagano Prefectural Branch; and

General foundational juridical person Association for Preventive Medicine of Japan (APMJ) Western Japan Division.

In addition, "RC News" was issued as necessary to share information, including the status of progress made in this study, with the health checkup institutions. Meanwhile, annual updates were made to the basic information of the RC contacts of all the health checkup institutions once a year.

(iv) Operation of remote conferences with individual Subcommittees (WG Investigators/Research Collaborators) and implementation of adopted resolutions

In cooperation with the Co-Investigators of the respective Subcommittees in accordance with Research Proposals, the target individuals necessary for the studies under the Subcommittees were identified followed by the provision of the following clerical assistance including the preparation of various information letters, address printing thereof, and dispatch thereof:

• Clinical Survey Subcommittee

A system was established for ensuring the accuracy of clinical investigations to perform various information transaction tasks, including: the process from the printing of the "Questionnaire Form on Health and Lifestyle Habits" to data

entry; various inquiries to health checkup institutions; collation of the questionnaire and test results with the consent information; preparation and transmission of hepatitis virus test/thyroid function test results reports; sample transportation; receipt of test results; and control of stored test samples.

• Thyroid Cancer Survey Subcommittee

Qualification registration tasks for participants in the Thyroid Ultrasound Technician Training Workshop and issuance of the Workshop Handbook: A skill evaluation-and-registration system was introduced to improve and control the accuracy of the thyroid ultrasound technicians engaged in the Study concerned. The Secretariat took on this technician registration work and issued copies of the Health Handbook to the technicians from research-partner health checkup institutions involved in the Training Workshop.

1) Issuance of system login IDs and passwords for the "Thyroid Ultrasound Scan Information System" for the Accuracy Control Committee and health checkup institutions

2) Uploading of past scan test data to the "Thyroid Ultrasound Scan Information System"

3) Tasks for ensuring the continuity from the existing Study:

• Ethics review of the Research Protocol for transferring the information collected during FY 2013 Health and Labour Sciences Research Grant Special Research Proposal "Research on Thyroid Gland Examinations, etc., of Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant" for use in this study; receipt and storage of information in accordance with the review results; dispatch of documents for obtaining consent for personal data use to target individuals; sorting and organization of return mail; and handling of the data sampling request from the Subcommittee.

• In accordance with the plan for collecting TEPCO-held thyroid-related information, a consent acquisition form and a reminder were sent to target individuals, followed by the receipt and storage of thyroid-related information from TEPCO and by the provision of anonymized personal data to the Subcommittee.

• Dose Assessment Subcommittee

A sealed letter requesting dose information was sent to the emergency workers considered to be target individuals of the Fukushima Health Management Survey, followed by the entry and compilation of received data, and by the handling of inquiries from the target individuals who received the letter. After the completion of data compilation, anonymized data for research and the aggregate results will be provided to the Subcommittee.

• Cause-of-Death/Cancer Incidence Survey Subcommittee

1) Provision of data, including the number of checkup examinees, for annual reports.

2) Retention of the death certificate-based and death receipt-based information for FY2011 to FY2015 that was received through the application filed in FY 2017 to the MHLW for approval of using demographic survey information outside the intended purpose.

3) Selection of the contractor for the development of a system for extracting the cause-of-death data on the target individuals of the relevant Study; and preparation of the reference materials for bidders.

4) In FY 2018, an application for approval of a change in the procedures for using demographic survey information outside the intended purpose was filed to the MHLW to suit the purpose of rational system development; and the approval was granted.

• Psychological Impact Survey Subcommittee

1) Outsourcing of the preparation and printing of psychological impact study questionnaire forms, optical answer sheets, and envelopes.

2) Dispatch of questionnaires and answer sheets to the health checkup institutions.

3) Control of answer sheets received from the target population (by means of personal identification numbers), request for computerization of information scanned from optical answer sheets, and acceptance of data

4) Provision of data linking structured interview results with consent information and relevant factors to the Subcommittee, besides anonymized information scanned from optical answer sheets

• Cataract Working Group: Printing of the checkup cards for use at ophthalmological clinics all over the country cooperating in the cataract study; collection and organization of consent forms, findings/evaluation results, and bills and other reply documents from clinics; data transmission of the Subcommittee; and checking of cataract examination bills and forwarding thereof to the Study Group.

(v) Management of personally identifiable information on target individuals (printed materials and electronic information)

Printed materials, such as participation intention survey sheets, consent forms, and questionnaire sheets, are received by the Secretariat via health checkup institutions and checked for content. Printed materials containing any imperfections and/or inaccuracies are completed or corrected by checking with the relevant parties, and the resulting final information is entered into the System. After this, the printed materials are filed in person-specific master files for retention in storage.

• Acceptance and checking of health checkup results (printed media), such as questionnaire answer sheets and consent forms, from the health checkup institutions

• Entry of information from participation intention questionnaires, other questionnaires, consent forms, and other printed media into the System

• Collation of the name and residential location data of target individuals with the results of the Current Status Survey

• Data updating authorized by the authority of the master update system administrator

(vi) Framework building and health checkup support tasks for research-partner health checkup institutions

To provide a safe margin of health checkup capacity for target individuals, efforts were made to increase the number of partner health checkup institutions, mainly from among NFIHO member institutions, in blank prefectures with no research-partner health checkup institutions or in prefectures with an excessive number of target individuals. As a result, the number increased from the original 70 to 77 in FY 2018.

The "Guidebook for the Health Checkup Institutions" was compiled to standardize health checkups at the research-partner health checkup institutions. The Guidebook consists of the "Guide for epidemiological research partner institutions" and the operator's manual for each system, in addition to the "Standard Operating Procedure for Clerical Work Processing for the Epidemiological Study Project" based on the contractual relationship with the NFIHO. Whenever any revision is made to files, copies of new files are distributed to the health checkup institutions, and the corresponding electronic files are also revised. Accordingly, a framework was established for health checkup institutions to download these documents from the "file transmission and reception system" whenever required to.

Requests were made for improvements on the part of the research-partner health checkup institutions, such as health checkup quota enhancement and System usage enhancement. At the same time, proposals and adjustments were made to solve various issues. One such example is the health checkup appointment scheduling proxy service that became operational in FY 2018. In the case of ordinary health checkups, contacts for appointments come in from the checkup examinees' side. In the case of this study, however, contacts must be made by the health checkup institutions. Phone calls very often end up going unanswered, cumulatively causing a heavy burden on the health checkup institutions. Accordingly, for the sake of some health checkup institutions hoping to be relieved of this burden, it was decided to outsource this task to specialist contractors. This decision led to the smooth processing of backlogs of appointment scheduling jobs. Other health checkup support tasks are as follows:

• Liaison tasks: various types of notification, requests for provision of missing data/materials, handling of various inquiries (questions, complaints, etc., received from target individuals before, during, or after their health checkup are eventually entered by each health checkup institution into the "Inquiry Handling System" and then responded to by the Secretariat.)

• Courier tasks: calculation of honoraria/travel expenses payable to target individuals; preparation and dispatch of receipts, etc.; dispatch of health checkup-use materials such as consent forms

• Receipt of health checkup results: receipt and check of data by collation with consent information; and inquiries in case of imperfections or inaccuracies

• Preparation and updating of the Guidelines for TEPCO's Alternative Health Checkup: An explanatory document was prepared, which contained the health checkup schedule, the test items to be added depending on the age, type of work engaged in, etc., and the methods of reporting.

• "RC News" was issued as necessary to share information, including the status of progress made in this study, with the health checkup institutions. The basic information of the RC contacts of all the health checkup institutions was condensed into a list and updated once a year.

• Adjustments were made with institutions preferred by target individuals to determine the number of health checkups acceptable for each institution. For institutions with an excessive number of health checkup appointments, the backlog of examinees was split and diverted to other institutions.

• Hepatitis virus test/thyroid function test results reports are prepared and then transferred via a file exchange system for inclusion in the checkup results to be sent from the health checkup institutions to checkup examinees.

(vii) Framework building for centralized testing and the main functions of the Secretariat

As explained above in "Research Methodology (4) Analysis of test samples and preservation of stored samples," the prerequisite for the centralization of testing tasks to Kotobiken was a method of adjusting test results deliveries to the health checkup institutions and the RERF. At first, complaints were received from the health checkup institutions saying, for example, that they could not make evaluations due to the discrepancy between their reference ranges for clinical test evaluation and those reported by Kotobiken. It was agreed that Kotobiken should match their reference range to that of each institution. At the same time, it was agreed that Kotobiken should be provided with data formatted to suit the system on the part of each health checkup institution. Since when all test samples began to be centrally sent to Kotobiken, a sample delivery form for the health checkup scheduling system has been used in collation work to ensure that the current day's batches of samples are processed without fail. Leasing centrifuge machines to some health checkup institutions not equipped with their own has also started. Following the centralization of tests, it has become an important task to prevent various problems such as hemolysis, missing samples, and reports of panic values: In practice, incidents and accidents in testing tasks have been dealt with in accordance with a troubleshooting manual and recurrence prevention measures

have been verified.

One of the tests thus standardized is thyroid ultrasound scanning. On account of understaffing, some health checkup institutions failed to cooperate in standard thyroid ultrasound scanning, posing a problem for the future.

(viii) Publicity activities targeted at emergency workers

The following PR activities were deployed to call out for participation and cooperation in this study:

• Phone calls requesting for cooperation (In FY-2016 calls were made to confirm the receipt of the application form for participation and to request cooperation; In FY-2018 calls were made to encourage high-dose target individuals to take health checkup.)

• Development and updating of the website (which accepts consent forms and applications for health checkup; at the same time, however, the task of asking for a signature on the consent form still persists.)

• Preparation and distribution of posters and flyers

• Production and delivery of NEWS Health Checkup News

• Re-dispatch of information to alternative addresses of persons unknown at the address used

• Preparation and dispatch of additional letters requesting cooperation from non-respondents

• Production of listing advertisements, landing pages, PR videos, and banner advertisements

• Open house at RERF facilities as a publicity activity of this study

(ix) Encouragement of in-house (TEPCO) alternative health checkup; and *ex post facto* support

• Every spring since 2017, TEPCO has set up consultation booths during the regular in-house health checkup to handle inquiries from their employees regarding matters such as application for participation.

• Extraction of the names of target individuals by status, such as prospective health checkup examinee, participation refuser, or person unknown at the address used, from TEPCO's alternative health checkup

• The categorical attributes of prospective examinees of TEPCO's alternative health checkup, such as current departmental affiliation or decontamination work history, were checked with TEPCO so that they would be flagged in the health checkup scheduling system to allow the viewing of the additional test items required to be made known to health checkup institutions.

• Data extraction tasks were outsourced to reflect health checkup results in TEPCO's in-house health management system.

(x) RERF internal formalities and accounting paperwork

The appropriate and effective use and reporting of the expenses for this grant-funded Study is one of the responsibilities of the Headquarters Secretariat. The main tasks involved are as listed below:

• The purposes of expenditures for research implementation; and awareness-raising for efficient use of human resources

► Preparation of written justifications required to complete formalities for commodity purchasing, outsourcing, staff recruitment, etc.

► Negotiations for effective allocation of human resources to related in-house departments

► Explanations at Review Commission, etc., and presentation to Board Members

• Outsourcing agreement: order placement; preparation of bid specifications; request for estimation; request for a legal check of written agreement and correction thereof; and retention of the written agreement

• Scrutinizing and inquiring about outsourced service performance reports from the NFIHO

• Scrutinizing and inquiring about health checkup participation rate reports from research-partner health checkup institutions;

• Accounting-related documentation, including documentation for allocating shares of expenses to each Study Group

• Checking test data report results received and amounts billed from Kotobiken

• Checking health checkup participation rate reports from health checkup institutions all over the country and preparing requests for payment

• Reminding health checkup institutions of submission of month-end due data not delivered yet

• Order placement for health checkup-use materials, such as consent forms and questionnaire forms; requisitioning and inventory control of other items such as consumables, furniture and fixtures, etc.

• Receipt and payment bookkeeping and other accounting tasks

• Internal formalities such as requisitioning payment of postage, courier service bills, phone bills;

• Handling of inquiries from MHLW Workers' Compensation Administration Division, and other related tasks

• Dealing with internal audit, MHLW accounting audit, and on-site investigation by the Board of Audit of Japan

[Summaries of Studies by Individual Subcommittees]

Clinical Survey Subcommittee (Clinical I)

Throughout the year, the Clinical Survey Subcommittee obtained informed consent from voluntary study participants, provided them with health checkups for grasping their health condition as the baseline data for follow-up studies, and conducted clinical studies including the storage of biological test samples.

Questionnaire survey of health and lifestyle habits, various test results, and the status of acquisition of consent to

cooperation in this study

Written consent consisted of the following items: 1) study objective, 2) study period; 3) study target population; 4) health effects to be studied; 5) test items; 6) participation cost; 7) access to and disclosure of Research Proposal; 8) protection of personally identifiable information; 9) freedom to opt in and out of this study; 10) benefits and disadvantages of participation in this study; 11) reporting of health checkup results and publication of research outcomes; 12) Intellectual property rights generated from this study; and 13) conflicts of interest arising from this study. So far, the consent rate for each of these items has been 99.9% or more.

The age-adjusted proportion of obese individuals (BMI 25 Kg/m^2 or more) among the past health checkup examinees was 35.6%, showing a slightly higher propensity to obesity than shown by the male obesity rate in the National Health and Nutrition Survey. The age-adjusted average systolic blood pressure was 123.6 mmHg and lower than among the general public.

The proportion of habitual smokers was 33.9% and slightly higher. The proportion of individuals with a habit of drinking alcohol once a month or more was 84.2%, which is a proportion considerably higher than among the general public. Thus, an overview of the health conditions among the target individuals having taken health checkup during the 5-year first phase of this study revealed that they showed some anomalies, such as higher values for several items as compared with the ordinary individuals.

Clinical Survey Subcommittee (Clinical II)

For Clinical Survey Subcommittee II to evaluate the health effects on the emergency workers, social factors, such as employment and daily-life background, and health control conditions, such as industrial health or medical services accessibility environment must be taken into consideration as confounding and other factors for the evaluation of the effect of radiation exposure. Accordingly, it was decided to examine in detail the worksite conditions and social factors specific to these engaged workers during the period from the time of the emergency work until now, and to question significant ones on the occasion of the clinical survey. The methods for this purpose were considered.

The survey results so far showed no significant differences in health conditions between the types of work engaged in. The "Other" types of work engaged in, however, accounted for the highest proportion of 45.5% among the target population. Hence, it is planned to consider making a finer segmentation of the "'Other types of work engaged in" on the questionnaire.

In the evaluation of the long-term health effects after engagement in emergency work, social factors must not be ignored, as they provide confounding factors. The long-term effect factors to be covered may include: nationality, area of residence, income, educational level, and serious social experience encountered, among others. The important factors from a short-term perspective include the time and period of engagement in the emergency work, and the status as an employee.

Cataract Working Group

For the current TEPCO employees exposed to a dose of 50 mSv or more (approximately 700 persons), a joint cataract study has been conducted every year at three locations, the Fukushima Nuclear Power Plant (Daiichi and Daini), Kashiwazaki-Kariwa, and Tokyo Headquarters, as a joint survey with the Department of Ophthalmology of Keio University School of Medicine.

For this study, 3,685 individuals exposed to 20 mSv or more were selected as the target individuals of the cataract study. With cooperation from 71 ophthalmological clinics across the country, the cataract study was started in FY 2018. The diagnostic criteria for cataract vary depending on the ophthalmologist. Hence, a Cataract Determination Manual based on the WHO's Criteria was prepared for use in a training workshop held for ophthalmologists from the partner facilities. In addition, naked-eye determination alone cannot provide sufficient consistency and reproducibility of diagnosis. Therefore, a simplified transillumination camera was built to enable objective and quantitative evaluation, and was put into use for the eye checkup of TEPCO employees. In FY 2018, capturing retroillumination images of lenses was started, with one unit installed in an ophthalmological clinic in Fukushima with a large population of target individuals. From the next fiscal year and onwards, all facilities will each be installed with a camera.

In response to a letter of request in FY 2018, replies have been received as of now from 996 individuals, 703 of whom expressed their willingness to undergo a checkup. Of these people, 217 individuals have completed their checkups.

Thyroid Cancer Survey Subcommittee

As a result of the thyroid ultrasound scanning conducted in the survey prior to this study, 425 individuals' worth of information was received (275 cases in 2014; 333 for in 2015; and 372 for 2016; 980 in total) to continue with the analysis. Then, this study considered the thyroid ultrasound scanning methodology for the whole emergency workforce, prepared the "Guide to Thyroid Ultrasound Scanning," and held eight sessions of Thyroid Ultrasound Scanning Training Workshops for engineers on ultrasound scanning procedures, image diagnosis methods, and post-test workflow.

By the end of 2017, the number of certified technicians

reached 107 individuals, while that of certified facilities reached 49. As of the end of October 2018, 2,424 cases of determination have been completed at Jichi Medical University (final determinations: 1,076 A1 cases (44.4%), 966 A2 cases (39.9%), 382 B cases (15.8%), zero C cases (0.0%)). As regards the secondary screening, replies of consent to consignment were received from 130 facilities. As of December 2018, 157 reports on checkup examinees have been received. The guidelines for the secondary thyroid scanning and after shall be the same as those for the primary scanning. It shall be sufficiently explained that thyroid scanning will result in the need of detailed screening for a certain proportion of the target individuals, a certain proportion of whom will be found in need of treatment.

Psychological Impact Survey Subcommittee

For the evaluation of psychological impact evaluation in this Survey, a questionnaire survey and an interview survey were used side by side.

A questionnaire prepared in FY 2014 was used to investigate the relevance between the mental health level of nuclear emergency workers and major stress-related factors. A request for cooperation in the questionnaire survey was made to health checkup examinees. To those who consented, copies of the questionnaire form were issued with a request for a reply by mail. The 3,000 individuals who sent back their answers by January 31, 2018, showed no apparent differences in mental health levels from those from the previous study. These mental health levels and PTSD symptoms (evaluated based on IES-R scores) showed a significant relevance with stress-related factors, including stigmas, life events, social assistance with daily life, some stress-coping behaviors, the sense of self-esteem, and the level of satisfaction with work and home life. It was also suggested that the support from superiors had significance in the case of long-term emergency work.

For the interview survey, use was made of the depression module of the computer-assisted personal interviewing (CAPI) in the WHO's Comprehensive International Diagnostic Interview (CIDI). From among the 1,380 individuals interviewed by the end of January 2018, six persons (0.4%) (most recent one month), 30 (2.2%) (most recent 12 months), and 93 (6.7%) (lifelong) were determined to have "major depression disorders" as per the DSM-IV, while four persons (0.3%) (most recent one month), 19 (1.4%) (most recent 12 months), and 52 (3.8%) (lifelong) were determined to have "severe depressive episodes without psychotic symptoms" as per the ICD-10. Additionally, the evaluation results as per K6 (evaluation scale for depression and anxiety disorders) from the questionnaire survey conducted at the same time showed a moderate level of relevancy to the results of this structured interview method, thereby suggesting the effectiveness of K6 in depression-related evaluations.

A phenomenon is known that certain environmental factors negatively stigmatize certain groups as objects of discrimination, character assassination, slander, and blame-shifting. The FY 2016 and FY 2018 surveys on 1,572 and 3,000 individuals suggested the relevance of such stigmas with their age (especially thirty-somethings), educational background (high school graduates), long work period, mental health (psychological distress/post-traumatic stress symptoms), and insomnia symptoms. The stigma scale showed a correlation with psychological distress/post-traumatic stress symptoms and insomnia. Drinking habits, with which no correlation had been found, showed correlation with more than half of the questions asked.

Cause-of-Death/Cancer Incidence Survey Subcommittee

Of the health checkup examinees, 90% or more expressed their consent regarding the collection of cause-of-death data and cancer incidence data. Reportedly, of the survey target population, 269 individuals died. For a cause-of-death survey, an application for collation with Demographic Statistics Information was filed to the MHLW, followed by receipt of approval dated November 2, 2017. Following the receipt of the provision of country-wide data based on death receipts, a method of collation with the list of target individuals began to be considered. The challenge to cancer incidence data collection is how to collect target individuals' addresses as of the time of their cancer diagnosis.

Radiobiological Study Working Group

When the effects of low-dose exposures were evaluated based on radio-adaptive responses, mice exposed to 3 Gy after 0.02-Gy pre-exposure showed a p53-dependent extension of life as compared with those exposed only to 3 Gy. This difference, along with others, including one observed in a miRNA expression analysis, revealed that large individual differences exist among radio-carcinogenic miRNAs. Additionally, EML4-ALK fusion genes frequently detected in thyroid papillary carcinoma in atomic bomb survivors are detected dependent on the increase in exposure dose (0, 0.2, 1, and 5 Gy), and hence may provide a useful diagnostic biomarker. When urinary 8-hydroxydeoxyguanosine (8-OHdG) samples taken from workers were measured to evaluate radiation-induced oxidative stress, slightly higher values were obtained, suggesting the need to investigate the effects of low-dose exposures.

Dose Assessment Subcommittee

Several years of whole-body counter measurement confirmed that the change in the in-vivo residual amount of radioactive Cs is similar to that of the biokinetic model

presented by the International Committee of Radiation Protection (ICRP). The thyroid measurements taken immediately after the accident were verified to have a sufficiently high measurement accuracy, even with the subjects' locational uncertainty taken into consideration; on the other hand, it was suggested that the individual differences in the shape of the thyroid need to be reflected in internal exposure dose evaluations.

As regards the analysis method for I-129, the iodine separation procedure was optimized, thereby providing the prospects for analysis of the actual urine test sample. This Subcommittee established a tricolor FISH-based retrospective dosimetry technique, contributing to the preparation of ISO procedural manual "ISO/FDIS 24006" as a P-member of the International Standards Organization (ISO) Working Group 18. Additionally, an automated image analysis software platform was developed for the technique. In FY 2018, from 62 individuals who took health checkups at health checkup institutions in Fukushima Prefecture from October to December, blood samples were experimentally taken with their consent and are currently under chromosome analysis.

For the review of the dose assessment for the whole emergency workforce, a database for storing the information necessary therefor is under development and construction, but will take some time before completion.

D. Discussions

The results of the encouragement to participate in this study are as follows for the period from the start of the Study to October 31, 2018: of the study target population of 19,808 individuals, 7,270 (36.7%) showed interest in participation (6,656 agreed to take health checkup; 614 agreed to participate in other studies); 3,334 (16.8%) declined participation; 6,976 (35.2%) returned no response; 1,828 (9.2%) were addressees unknown at the address used; 254 (1.3%) were deceased; and 146 (0.7%) were unaccountable for due to other reasons. In light of the Study objectives, this situation cannot be said to be satisfactory. To increase the future study target population, it is necessary to reduce non-respondents and to urge participation refusers to reconsider participating in the study. For this purpose, we will repetitively send out letters encouraging participation in this study and make approaches to specific target groups. At the same time, we will take all measures imaginable for encouraging participation in this study, including PR activities using websites, posters, and other information dissemination methods that automatically attract the attention of the target audience regardless of their awareness.

Recently, individuals kept waiting are increasing despite their expressed intention to participate in this study; this must be dealt with urgently. Various possible causes are beginning to be identified, including: insufficient response capacity of the health checkup institutions; or geographical difficulties for emergency workers living too far from research partner institutions to take a health checkup. First and foremost, partnerships with additional partner institutions must be established in areas with a fast-growing waiting list. A change should be made from the current strategies for solicitation of cooperation.

This report evaluated the baseline health conditions of the January 2016-to-October 2018 health checkup examinees, who accounted for the majority of the follow-up population of this study. As a result, characteristic results were obtained. Obesity is known to have relevance to various lifestyle-related illnesses, such as diabetes, hypertension, dyslipidemia, and hyperuricemia. The proportion of obese individuals among the male checkup examinees after age adjustment by the same reference population as in the National Health and Nutrition Survey was 35.6% and slightly higher than in the results of the National Health and Nutrition Survey. It is considered necessary, from now onwards, that obesity-related test items and disease occurrences be monitored with close attention. The average systolic blood pressure among the male checkup examinees after age-adjustment by the National Health and Nutrition Survey was 123.6 mmHg, while the proportion of individuals with a systolic blood pressure of 140 mm Hg or more was 14.7%: both indicators were low.

The male prevalence of atrial fibrillation increased with age when compared with an epidemiological survey by the Japanese Circulation Society. Considering that this study is a long-term follow-up study, we believe that considerations should be given to collecting and retaining cardiogram records, centralizing determinations, and actively using archived materials for comparative determination, besides the collection of determinations and findings at each research partner institution.

Blood biochemical tests detected no items with extreme bias. Biochemical tests found that the proportion of individuals with an age-adjusted total cholesterol level of 240 mg/dL or more among the male checkup examinees was 14.8% and their average value of non-HDL-cholesterol was 146.2 mg/dL: both values were slightly high, suggestive of the effects of the high proportion of obese individuals. It is considered necessary that dyslipidemia-related test items and diseases be evaluated with caution.

The UNSCEAR pointed out in its report the possibility of future increases in the occurrences of hypothyroidism. Of the male checkup examinees during the period from January 2016 to October 2018, 368 persons (7.0%) showed thyroid functional disorders. Those with high TSH levels were, however, 78 persons (1.6%). We consider it necessary to keep a close eye on future trends in the prevalence and incidence of hypothyroidism.

The results of cancer checkups, including fecal occult blood tests, showed no anomalies. The total cancer incidence and prevalence among the health checkup examinees were 195 persons and 3.8%, respectively. Eight individuals suffering two types of cancer were observed along with another suffering three types of cancer. The breakdown of the total incidence was approximately as follows: 35 individuals with gastric cancer; 39 with colon cancer; 18 with lung cancer; 15 with thyroid cancer; and 30 with prostatic cancer.

The current age-adjusted proportion of smokers among the male checkup examinees was 32.9%, slightly higher than the results of the National Health and Nutrition Survey. The proportion of individuals with a habit of drinking alcohol once a month or more among the health checkup examinees was 84.2%, which is considerably higher than the total proportion of 42.1% among male adults (with the following drinking frequencies all combined: every day; 5 to 6 days/week; 3 to 4 days/week; 1 to 2 days/week; 1 to 3 days/month as per Comprehensive Survey of Living Conditions 2016). It was considered necessary to observe with close attention the occurrences of diseases known to be affected by alcohol consumption, including lifestyle-related illnesses.

E. Conclusions

The approaches made to the survey target population resulted in the acquisition of consent to participation in this study from 7,270 persons, or 36.7% of the target population, as of October 31, 2018. To increase the future study target population, it is necessary to reduce the 6,976 non-respondents and to urge the 3,334 participation refusers to reconsider participating in this study. From the next fiscal year onwards, we would like to encourage participation in this study, using new tools, and continue our efforts to further expand the cohort size while moving this epidemiological study forward.

Fortunately, a majority of the checkup examinees expressed their intention to participate in the research: 98.5% or more of the health checkup examinees consented to cooperate for all items of the study. For storage of biological test samples, 99% or more consented to the storage of their blood and urine samples; and 98.5% consented to the storage of their blood samples for use in future human genome and genetic analysis research. Moreover, in the statistical results obtained this time, there were no items indicating particularly significant health anomalies in the group. Therefore, it was concluded that this group had no bias in the baseline health conditions and hence constituted a desirable group as a study target population. It is, however, necessary, from now onwards, to watch with strong interest some recognized tendencies, including higher proportions of individuals with obesity, hyperlipidemia, a current smoking habit, and a drinking habit.

F. Research publications

1. Papers published in academic journals

Toshiteru Okubo: Epidemiological Survey: From the Experiences of Hiroshima and Nagasaki to Fukushima: Journal of Clinical and Experimental Medicine, 239(10):995-1000, 2011.

Toshiteru Okubo: Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant: Occupational Health Management, 27(3): 39-46, 2016.

Toshiteru Okubo: "Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant" - Progress Report: Health Development, 20(3):83-93, 2016.

Toshiteru Okubo: "Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant": UPDATE, 27 (1): 29-30, 2016.

Toshiteru Okubo: RERF Epidemiological Study of Health Effects in Fukushima Emergency Workers: UPDATE, 27(1): 29-30, 2016.

Hiroko Kitamura, Toshiteru Okubo, Kazunori Kodama, Nuclear Emergency Workers Study Group: Epidemiological study of health effects in Fukushima nuclear emergency workers–study design and progress report: Radiation protection dosimetry, ncy136, https://doi.org/10.1093/rpd/ncy136, 2018.

2. Conference presentations

Kazunori Kodama: Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant: Application of the Know-how Developed through the Survey of Radiation Health Effects of Atomic Bomb Explosions: Second Conference on Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant, 11 March, 2016, Kitakyushu.

Waka Oishi: Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant: An Outline of the Clinical (Health Checkup) Study based on the Experience from the RERF Adult Health Study: The Second Conference on Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant, 11March, 2016, Kitakyushu.

Hiroko Kitamura, Kazunori Kodama, Toshiteru Okubo: Epidemiological study of health effects in Fukushima nuclear emergency workers–study design and progress report: The UNSCEAR Meeting in Tokyo, Fukushima Follow-up Project (FFUP), 15 November, 2016, Tokyo.

Toshiteru Okubo: Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear

Power Plant: The 63rd Conference of the Japanese Society of Occupational Medicine and Traumatology, 17 November, 2017, Kitakyushu.

Hiroko Kitamura, Toshiteru Okubo, and Kazunori Kodama: Epidemiological study of health effects in Fukushima nuclear emergency workers (Nuclear Emergency Workers Study; NEWS)-study design and progress: The 15th Coordination Meeting of the WHO Radiation Emergency Medical Preparedness and Assistance Network (REMPAN). 4 July, 2017, Geneva, Switzerland.

Toshiteru Okubo: Epidemiological Survey of Emergency Workers Engaged in Accident Response Work at TEPCO Fukushima Daiichi Nuclear Power Plant: Industrial Medicine Workshop, Okayama Prefectural Medical Association, 2018, Okayama.

Hiroko Kitamura: Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant: Change in Study Participants: Fourth Conference on Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant, 14 March, 2018, Kitakyushu.

G. Intellectual property rights acquired

None

II. Working-Group Research Reports (by Individual Subcommittees)

Industrial Disease Clinical Research Grants
Working-Group Research Report

Epidemiological Study Targeting Nuclear Emergency Workers at the TEPCO Fukushima Daiichi Nuclear Power Plant

Approaches to the Study Target Population: Characteristic analysis of the Study Target Population

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Co-Investigator: Hiroko Kitamura, Sub-Chief Researcher, Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF)

Abstract

This report looks back on the approaches made to the study target population during the first cycle of this study (the five years from its start) and summarizes the characteristics of the study participants. Calls to engage individual study target persons in this study were made primarily by mail. At the same time, various PR activities were also promoted without narrowing it down to any specific audience. The results of the approaches made are as follows, as of October 31, 2018: Of the study target population of 19,808 individuals, 7,270 (36.7%) showed interest in participation (6,656 agreed to take a health checkup; 614 agreed to cooperate otherwise in the study); 3,334 (16.8%) declined participation; 6,976 (35.2%) returned no response; 1,828 (9.2%) were addressees unknown at the address used; 254 (1.3%) were deceased; and 146 (0.7%) were unaccountable for due to other reasons.

* Those "unaccountable for due to other reasons" were individuals currently not regarded as study participants due to reasons including their intention still being checked or their consent to study participation being inconsistent.

In order to increase the number of study participants in the future, it is necessary to reduce that of non-respondents and to encourage participation refusers to reconsider participating in the study. For this purpose, consideration is underway to send by mail calls for participation in this study, and to make approaches to specific target groups. At the same time, all measures imaginable to encourage participation in this study will be taken, including PR activities using a website, posters, and other information dissemination methods that automatically attract the attention of the target audience regardless of their awareness.

In addition, recently, those kept waiting for a health checkup are increasing despite their expressed intention to participate in this study. This problem should also be dealt with urgently. Various possible causes are beginning to be identified, including: insufficient response capacity of the health checkup institutions (hereinafter referred to as "health checkup institutions"); or geographical difficulties for the emergency workers living too far from research partner institutions to take a health checkup. First and foremost, partnerships with additional health checkup institutions must be established in areas with a fast-growing waiting list. A change should be made from the current strategies for soliciting cooperation.

A. Study objective

This study is a prospective cohort study that performs lifelong follow-up of the emergency workers (hereinafter referred to as "study target population (or individuals)") spread across the country. The first cycle of this study (the five years from its start) aimed to obtain as many study participants as possible from the study target population of 19,808 individuals in order to lay down the foundation for the framework for the lifelong follow-up survey.

The objective of this study is to investigate the radiation exposure effects in the human body among this study target population. Hence, a long-term prospective follow-up survey is required. For most of the study target population herein, the radiation exposure levels experienced were, however, equal to or below the radiation exposure threshold said to cause known health effects. With a target population of the size herein, therefore, the diseases with radiation effects confirmed by previous surveys on atomic bomb survivors and others would only occur intermittently. Therefore, the success of this study depends on the maximization of the population to be observed in a long-term epidemiological survey, because this study explores an exposure region with no known risks to verify the existence of effects to which the so-called "No-Threshold Hypothesis" (,) applies. In other words, a longer-term observation than in conventional epidemiological surveys is the prerequisite. Based on such an awareness of the issue, this

report presents a wide range of efforts made to increase the number of study participants during the first cycle of this study (the five years from its start), examines the effectiveness of each effort, and considers measures to take in the future.

The promotion of this study is expected to help determine the relevance of diseases to radiation exposure and the emergency work through a comparison of the future frequency of occurrence of diseases among the emergency workers with that of the same diseases among those other than the emergency workers.

B. Study methodology

Types of approaches

During their engagement in the emergency work, the study target individuals belonged either to Tokyo Electric Power Co., Ltd. (then and now Tokyo Electric Power Company Holdings, Incorporated, hereinafter abbreviated as "TEPCO") or to one of the companies outsourced with the emergency work from TEPCO. Hence, these companies would supposedly provide the most effective channels for encouraging participation in this study. However, most of the study target individuals, and especially those engaged in contingent work under construction-related companies, had already changed their organizational affiliation from that at the time of the emergency work, because this study started more than three years after the end of the emergency work period. Besides, it was one of the fundamental policies in this study to provide study-related explanations strictly on an individual-by-individual basis and limit the study target individuals to those with expressed consent to participation, rather than call out for participation in this study through their affiliated companies. Therefore, though there was some cooperation received from the companies in calling out for participation in this study, all applications for participation in this study were accepted in principle on an individual-by-individual basis.

The most basic method of making approaches is sending by mail calls for participation in this study. Phones and other modes of personal communication were used to answer inquiries about the formalities for participation, or to provide additional explanations. As the methods of calling out for intentional non-responders or those who had been unreachable by mail due to the change in whereabouts, PR methods intended for a broad unspecified audience were employed. Specific examples included preparation of posters and enclosure of flyers in multi-purpose mail correspondences. The latter included requests for their enclosure in the envelope of the questionnaire for the Current Status Survey conducted under the MHLW once a year as part of the long-term health management provided to the emergency workers.

A website for this study was created to provide information on the progress made in the study to the general public besides the study target population. Moreover, a newsletter has been published once a year. These media were also used to make approaches to non-participants. The website includes a screen designed to accept individual access from study target individuals, so that study target individuals with their personal identification number registered and their password set can submit a completed consent form, notify the change in their whereabouts or phone number, and apply for a health checkup. These approaches made during the five-year first phase of this study have been summarized into a list (Table 1).

Approaches tailored to the characteristics of target individuals

While the study target individuals in this study differ diversely in work-related characteristics, such as occupation or work history, the difference most worthy of note for this study is the difference in radiation work experience. The target individuals with prior engagement in radiation work have a history of radiation exposure and hence are expected to differ in cumulative exposure dose from those temporarily engaged in radiation work for the emergency work. The study target population includes a large number of workers who were temporarily employed to deal with the emergency caused by the nuclear reactor explosion accident. Many of these workers are assumed to have been employed on temporary contract terms. Consequently, the study target population consists of individuals with various combinations of differences in prior radiation work experience, labor contracts, and other conditions, among other characteristics.

When it comes to investigating the effects of radiation exposure due to the emergency work, the availability of past exposure histories based on the Radiation Work Passports issued by the Radiation Dose Registration Center of the Radiation Effects Association (REA) would allow a more accurate study than one based exclusively on the exposure doses during the emergency work. The emergency workers herein have all been registered at the Center and issued a Radiation Work Passport. Hence, their exposure doses during the emergency work are all available in theory. The knowledge of the exposure levels they experienced earlier than that would allow for a more accurate analysis of their exposure doses and health conditions.

In addition to the above-mentioned combination of labor contracts and other conditions, companies differed in their willingness to cooperate in this study. Hence, a decision was made to encourage participation in this study individually on a company-by-company basis. A typical example is provided by TEPCO. Considering that the accident-struck power plant belongs to TEPCO in the first place, it may be a matter of course

that among all the companies concerned, TEPCO has the most significant number of participants, though the number includes those collectively deemed as its affiliated individuals, namely, professional engineers urgently mobilized to deal with the accident and other external experts involved voluntarily as individuals, such as academic experts and industrial doctors. TEPCO has a positive stance regarding cooperation in the study. For example, TEPCO decided to deem the time spent by its employees for the health checkup for this study as part of the time worked by them, thereby providing a condition most conducive to target individuals' participation. Additionally, the company decided to regard the health study conducted in this study as an alternative to the regular health checkup compulsory for workers under the Occupational Safety and Health Act. This means the exemption of the regular health checkup of the pertinent year, which resulted, among the target individuals, in a higher motivation to take health checkups, namely, a higher willingness to participate in the study.

Although their cooperation may not have been comparable in content to that of TEPCO, many of the other companies encouraged their employees to participate in this study. This encouragement, however, applies only to those who were their employees at the time they encouraged participation. In the case of companies such as construction companies, such encouragement was impossible because the majority of their on-site workers had been contingency workers and had already left their positions when the letter of request for participation in this study was sent.

Because of the above circumstances, the results of approaches made to engage target individuals in the study are reported here separately for those with affiliation with TEPCO and those without.

Table 1

	FY 2014						FY 2015												FY 2016												FY 2017												FY 2018								
	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
(i) Requests for participation (by mail)				• Preliminary							• Non-TEPCO																																									
(ii) Encouragement to take health checkups (by mail or otherwise)				• Preliminary							• Non-TEPCO													• TEPCO																										• Participation pending	• Re-dispatch to	• Individual support	• Approaches by age	• Individual support
(iii) Acquisition of consent (by mail, via website, or otherwise)																															• TEPCO	• TEPCO	• Non-respondents		• Website opened				• Checkup refusers				• TEPCO	• TEPCO							
(iv) Corporate explanatory meetings (principal contractors and subcontractors)										•	•																																							
(v) Approaches from related personnel of principal contractors											•	•																					•																	
(vi) TEPCO's EPICON Booth																															•	•											•	•							
(vii) Enclosure of epidemiological study-related information in envelopes of mail from NFIHO																					•						•						•													•				
(viii) Phone calls												•	•																																			• High dose				
(ix) Individual approaches to NIRS health checkup examinees																																																•				

(i) Requests for participation (by mail)
(ii) Encouragement to take health checkups (by mail or otherwise)
(iii) Acquisition of consent (mail/website)

In FY 2014, a letter of request for participation in the preliminary survey was sent to target individuals living in Fukushima Prefecture. In FY 2015, a letter of request for participation in the survey was sent to non-TEPCO-affiliated target individuals all over the country.
In FY 2014, target individuals living in Fukushima Prefecture were requested to participate in the preliminary survey, and a written encouragement to take health checkup was sent out by mail. Written encouragements to take health checkups have been sent by mail to non-TEPCO-affiliated target individuals all over the country since FY 2015 and TEPCO-affiliated target individuals since FY 2016. Dispatches by mail are made all the time, including those made upon individual request. At the same time, broadcast mailing is also conducted per a plan factoring in different types of addressees such as "non-respondents," "addressees unknown," and "non-participants in the preliminary survey."
In September 2017, accepting written consent via the website was started. In FY 2017, correspondence was sent by mail to reluctant target individuals, such as "non-respondents" and "checkup refusers," in an attempt to obtain their consent to cooperate in the study. TEPCO's EPICON Booths in FY 2017 and 2018 were intended for non-respondents, who were then-current employees relatively shy of the health checkup, and hence the main focus was placed on obtaining their consent for cooperation in the study.

(iv) Corporate explanatory meetings (principal contractors and subcontractors)

In July FY 2015, an explanatory meeting was held for TEPCO and 15 principal contractors. In August, explanatory meetings for subcontractors were held in Tokyo, J Village, and Kashiwazaki, with the attendance of 533 individuals.

(v) Approaches from related personnel of principal contractors

Contacts were made with the persons in charge of radiation control or safety and health at 14 principal contractors. The persons in charge at virtually ten contractors encouraged their in-house non-responding target individuals to reply.

(vi) TEPCO's EPICON Booth

In FY 2017, the TEPCO's Headquarters, the Fukushima Daiichi NPP, and the Kashiwazaki-Kariwa NPP each set up an EPICON Booth in sync with TEPCO's spring in-house health checkup. In FY 2018, the Headquarters, the Fukushima Daiichi and Daini NPPs, and the Kashiwazaki-Kariwa NPP did the same. For FY 2019, it is planned to identify the departmental affiliations of non-respondents and pay visits to establishments other than those installed with an EPICON Booth.

(vii) Enclosure of epidemiological study-related information in envelopes of mail from NFIHO

Since FY 2016, the NFIHO has, as requested, been enclosing information on this epidemiological study in the envelopes of the current status questionnaires or booklets they issue.

(viii) Phone calls

In FY 2015, the tasks of making phone-calls for confirming the receipt of the letter concerning the intention to participate and soliciting the submission of the "letter of consent to participation" were outsourced. In FY 2018, phone contact was made with non-respondents identified from among those registered in the database as target individuals exposed to a dose of 100 mSv or more during the emergency work. Consideration is underway to contact by phone in stages those exposed to doses below 100 mSv. Following the increase in the number of health checkup institutions, phone calls were made to encourage the switching of preferred health checkup institutions.

(ix) Individual approaches to NIRS health checkup examinees

Those registered in the database as workers exposed to a dose of 250 mSv or more during the emergency work undergo health checkup once a half year at the NIRS as exceptions. These occasions were used as opportunities to meet target individuals directly and encourage them to participate in this study.

Individual approaches

1) Approaches made to target individuals unaffiliated with TEPCO

The initial contact with target individuals unaffiliated with TEPCO was made through the "Notice of Study Commencement" sent by mail to their personal addresses in January 2015. Then, after an explanatory meeting held to ask the managing supervisors of the major principal contractors for cooperation in this study, the "Questionnaire on the Intention to Participate in Health Checkups" was sent by mail to the personal addresses of non-TEPCO-affiliated target individuals from July to August 2015. To positive respondents to the Questionnaire on the Intention to Participate in Health Checkups, the "Application Form for Participation" was sent by mail in order of receipt of their responses. In August 2016, the "Application Form for Participation" was sent by mail to non-respondents. In September, to the non-respondents to the "Questionnaire on the Intention to Participate in Health Checkups," the "Questionnaire on Readiness to Participate in Health Checkups" was sent by mail in order to urge them to take a health checkup.

2) Approaches made to major related companies

In June 2017, 14 major principal contractors belonging to the Fukushima Daiichi Nuclear Power Plant Safety and Health Promotion Council (group of collaborative companies) were requested, through the liaison person of TEPCO's Radiological Health and Safety Center, to appoint a liaison person in charge of communications related to this study with the Research Secretariat. Following the receipt of replies from 10 companies informing the names of their liaison persons, a request for cooperation in this study was made to each company through their liaison person. Although they differed in the content of actual cooperation, eight companies encouraged their affiliated non-respondents to reply. Calls for a change of mind about participation in health checkups were first made in December 2017 to the negative respondents to the "Questionnaire on the Intention to Participate in Health Checkups," and then in January 2018 to the negative respondents to the "Questionnaire on Readiness to Participate in Health Checkups." At the same time, the "Form of Consent to Cooperation in the Study" and the "Questionnaire on Readiness to Participate in Health Checkups" were sent by mail in order to uncover hidden study target individuals who had an intention to cooperate in the study though were not ready to take a health checkup at the moment.

(All the materials sent by mail to make the above approaches are found in the FY 2017 Study Report.)

3) Approaches made to target individuals affiliated with TEPCO

The encouragement of TEPCO-affiliated target individuals to participate in the study remained on hold until the end of TEPCO's internal discussions on their cooperation in this study, and lagged behind the first contact with non-TEPCO-affiliated target individuals by more than one year. The first contact with the former was made through the "Questionnaire on Readiness to Participate in Health Checkups" sent by mail to their personal addresses in August 2016. In November, with cooperation from the company, the "Questionnaire on Readiness to Participate in Health Checkups" was redistributed by in-house mail to the non-respondents to the same Questionnaire sent by mail in August.

In April to May 2017, with cooperation from the company, consultation booths for urging participation in this study were set up at the regular health checkup venues on the premises of their Headquarters, the Fukushima Daiichi Nuclear Power Plant, and the Kashiwazaki-Kariwa Nuclear Power Plant, each with a relatively large number of non-respondents, in order to provide face-to-face consultation regarding participation in this study, including encouragement for submission of the "Form of Consent to Cooperation in the Study" and the "Questionnaire on Readiness to Participate in Health Checkups."

In September of the same year, with cooperation from the company, the "Form of Consent to Cooperation in the Study" and the "Questionnaire on Readiness to Participate in Health Checkups" were distributed by their in-house mail to non-respondents other than those affiliated with the Headquarters, the Fukushima Daiichi Nuclear Power Plant, and the Kashiwazaki-Kariwa Nuclear Power Plant. In January 2018, a decision made was to make calls for a change of mind about cooperation in this study and participation in health checkups to the known negative respondents to the "Questionnaire on Readiness to Participate in Health Checkups." Then, the "Form of Consent to Cooperation in the Study" and the "Questionnaire on Readiness to Participate in Health Checkups" were mailed.

Results of PR activities

In September 2016, the first issue of "NEWS Health Checkup News" was published for such purposes as the provision of information to all the emergency workers falling within the scope of this study. In September 2017, the second issue was published. A decision was made to publish subsequent issues periodically once a year. The coverage of NEWS Health Checkup News included the number of study participants, the trends in the number of health checkup examinees, explanations on the health checkup items in this study, information on the partner health checkup institutions across the country, and health-related topics.

In the descending order of the number of their health checkup examinees, research partner institutions are asked to provide photographs full of local color for use on the cover page of NEWS Health Checkup News.

In September 2017, a website for this study was opened for

the publicity of this study *per se,* and also as the access gate for target individuals to submit their application for participation in this study. Figure 1 shows the trend in the number of views of the website per day for the website since its opening (Figure 1). The number of viewers per day temporarily shot up immediately after the opening, but soon started to drop gradually down to 10 or fewer persons per day three months after. In March 2018, however, a listing advertisement* was introduced as one of the methods of guiding target individuals to the website for this study. Then, following the start of a banner advertisement campaign in March 2018, the number of viewers of the website increased to the order of several hundred per day. After the end of the banner advertisement campaign, the number remained at approximately 10 to 30 persons per day. Hence, it seemed evident that the website owed the increase in the number of its viewers to the effect of the banner advertisements. After that, the number of visits has remained at an average level. Accordingly, the cumulative number of visitors has been slightly but steadily increasing as time elapses (Figure 2).

* Listing advertisement is an advertising technique that displays advertisements associated with keywords searched by internet search engine users on the search results page. Though intended for commercial purposes, this technique was adopted this time in expectation that listed adverts would guide study target individuals among an indefinitely large number of internet users to the website for this study, and help prompt them to apply for participation in this study from the website.

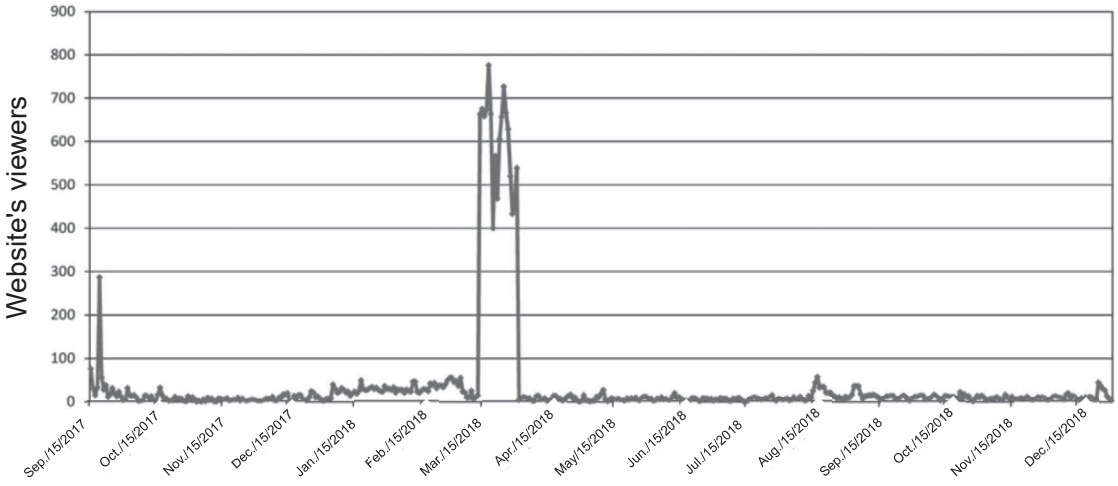


Figure 1. Trend in the number of viewers per day after the opening of the website

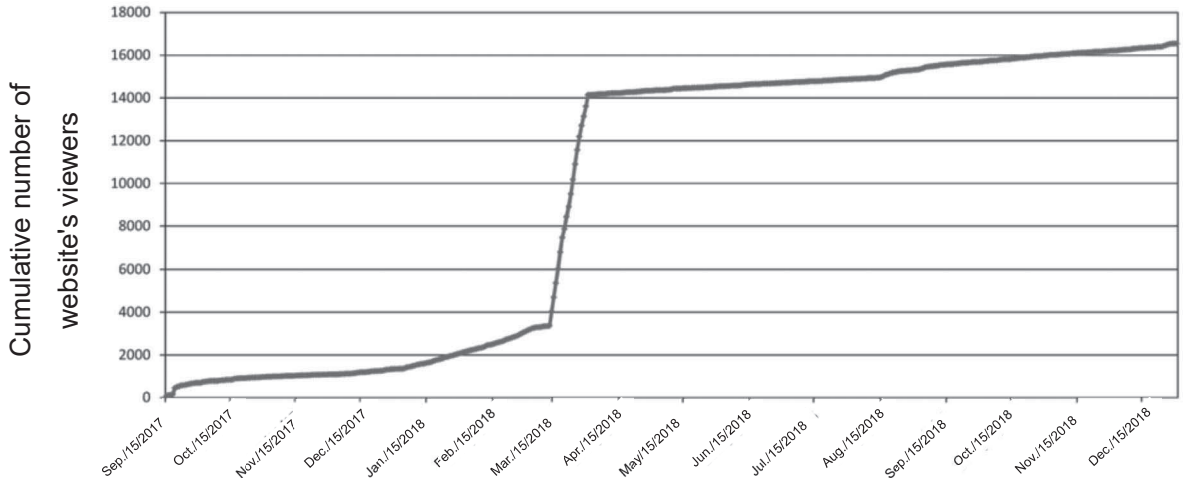


Figure 2. Trend in the cumulative number of viewers for the website

Table 2: Proportions of participants and others in this study by age

	Age group total	Study participants (%)	Participation refusers (%)	Non-respondents (%)	Addressees unknown (%)	Deceased (%)	Others (%)
20-29-yrs old	592	130 (21.9%)	112 (18.9%)	250 (42.2%)	97 (16.3%)	1 (0.1%)	2 (0.3%)
30-39-yrs old	2752	807 (29.3%)	379 (13.8%)	1094 (39.8%)	437 (15.8%)	11 (0.3%)	24 (0.9%)
40-49-yrs old	5221	1923 (36.8%)	820 (15.7%)	1963 (37.7%)	461 (8.8%)	26 (0.4%)	28 (0.5%)
50-59-yrs old	5759	2320 (40.2%)	978 (17.0%)	1908 (33.3%)	449 (7.7%)	60 (1.0%)	44 (0.8%)
60-69-yrs old	4781	1857 (38.8%)	905 (18.9%)	1520 (31.9%)	340 (7.1%)	124 (2.5%)	35 (0.7%)
70-yrs old or over	696	233 (33.5%)	140 (20.1%)	241 (34.9%)	44 (6.3%)	32 (4.5%)	6 (0.9%)
Unknown	7						7
Total	19808	7270	3334	6976	1828	254	146

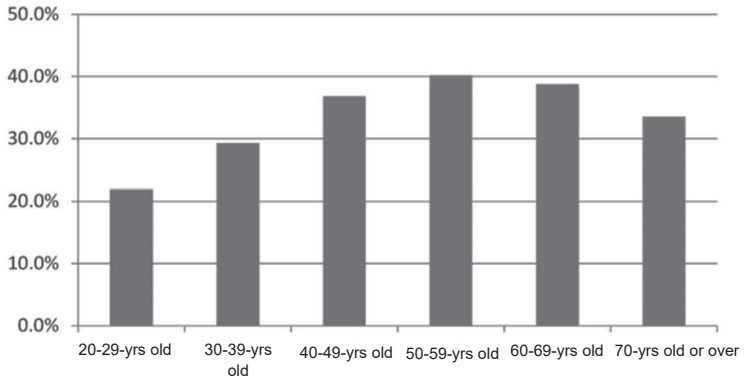


Figure 3. Comparison of the proportions of study participants (by age)

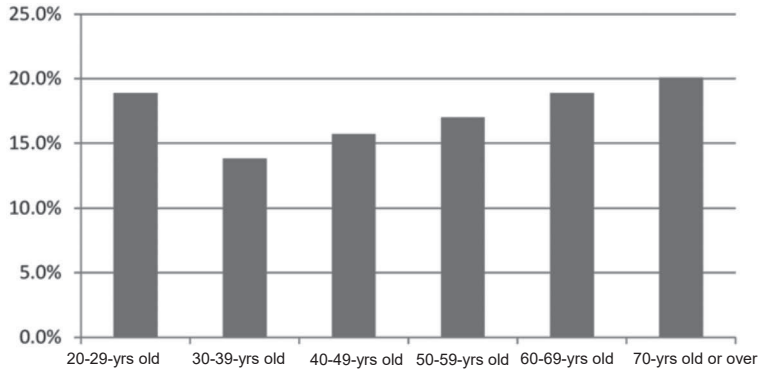


Figure 4. Comparison of the proportions of participation refusers (by age)

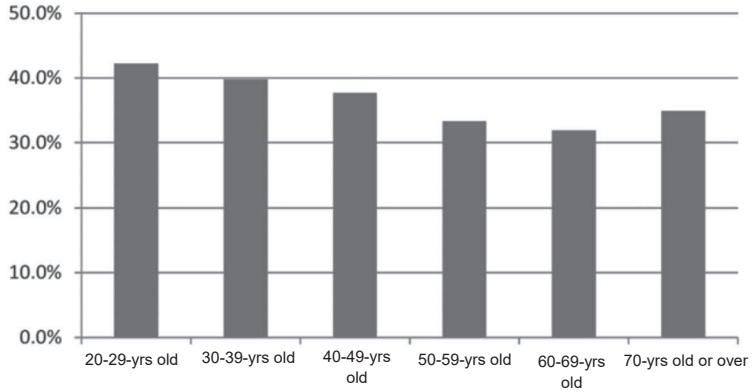
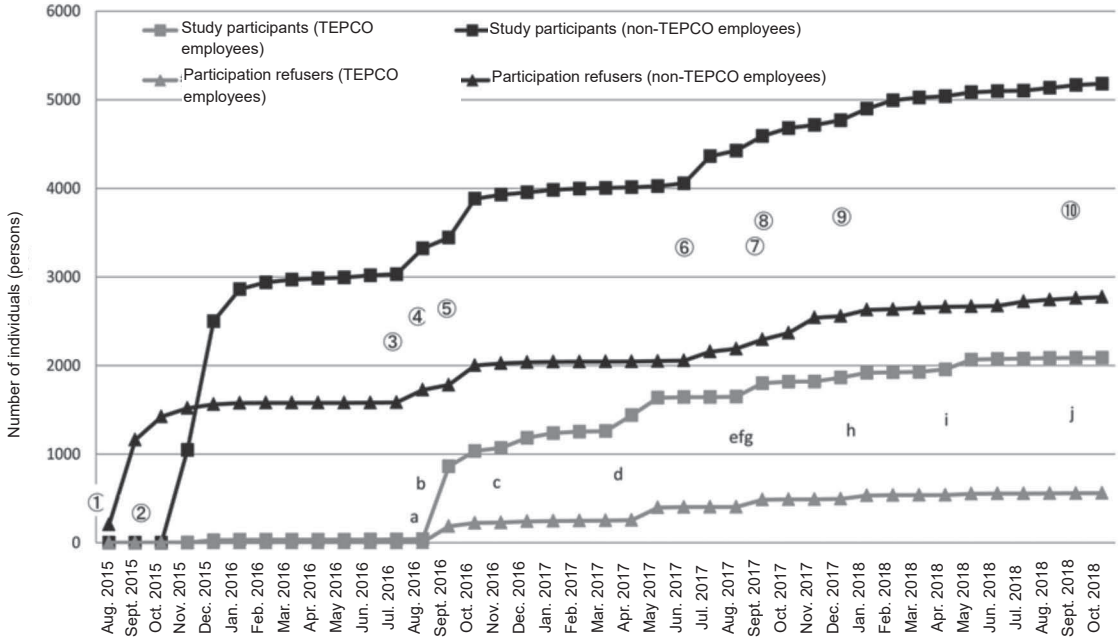


Figure 5. Comparison of the proportions of non-respondents (by age)



Non-TEPCO employees
(1): The Questionnaire on the Intention to Participate in Health Checkups was sent by mail.
(2): The Form of Application for Participation was sent by mail to the positive respondents to the Questionnaire on the Intention to Participate in Health Checkups.
(3): The Questionnaire on Readiness to Participate in Health Checkups was resent to non-respondents to (2).
(4): The first issue of NEWS Health Checkup News was sent by mail.
(5): The Questionnaire on Readiness to Participate in Health Checkups was resent to non-respondents to (1).
(6): The major principal contractors encouraged the workers under their charge to return a reply.
(7): The second issue of NEWS Health Checkup News was sent by mail.
(8): The NEWS website was opened.
(9): Written encouragement for a change of mind about cooperation in this study was sent by mail along with a consent form and the Questionnaire on Readiness to Participate in Health Checkups to those who had refused to participate in more than one health checkup.
(10): As regards addressees unknown, the Questionnaires on the Intention/Readiness were sent to those whose whereabouts had been located.

TEPCO employees
a: The Questionnaire on Readiness to Participate in Health Checkups was sent by mail.
b: The first issue of NEWS Health Checkup News was sent by mail.
c: The Questionnaire on Readiness to Participate in Health Checkups was sent by in-house mail to non-respondents to (a).
d: Consultation booths were set up on the premises of the Headquarters, the Fukushima Daiichi NPP, and the Kashiwazaki-Kariwa NPP.
e: The second issue of NEWS Health Checkup News was sent by mail.
f: The NEWS Website was opened.
g: The Form of Consent to Cooperation in the Study and the Questionnaire on Readiness to Participate in Health Checkups were sent by in-house mail to the non-respondents to (a) at establishments other than the Headquarters, the Fukushima Daiichi NPP, and the Kashiwazaki-Kariwa NPP.
h: Written encouragement for a change of mind about cooperation in this study was sent by mail along with a consent form and the Questionnaire on Readiness to Participate in Health Checkups to those who had refused to participate in more than one health checkup.
i: Written correspondences were sent by TEPCO's in-house mail, and consultation booths were set up on the venues of TEPCO's regular health checkup.
j: As regards addressees unknown, the Questionnaires on the Intention/Readiness were sent to those whose whereabouts had been located.

Figure 6: Trends in the numbers of study participants and participation refusers per month

C. Study results

1) Trends in study participants, participation refusers, non-respondents, addressees unknown, and others

At the beginning of this study, calls for participation in this study were made on the assumption that "participating in this study = taking health checkups." Many among the study target population are, however, active workers, who were heard to opine, e.g., that they cannot afford the time to take health examinations conducted for this study, or that they do not feel the need because they take in-house health checkups. Hence, the members of the Operational Committee of this study agreed to include in the number of study participants, the study target individuals with an expressed intention to "cooperate in the study though not ready to take a health checkup at the moment." The total numbers since April 2017 are based on the expanded definition of study participants. Additionally, though currently still small in number but expected to increase in the future, deceased individuals were classified into a new category separate from the above four categories. A decision made was to classify the following individuals into the "Others" category: 99 persons ineligible as target individuals of an epidemiological study, such as those living abroad or those whose whereabouts was unknown from the beginning; those who replied unclearly about their intention as to participation or failed to respond to inquiries about inconsistencies between some items in the written consent received prior from them; and those otherwise ineligible.

The response status as the results achieved through the

approaches made to target individuals during the period from the initial approach by mail in 2015, the first year of the first phase, to the end of October 2018, the fifth year is shown in Table 2 by ten year-bracketed age as of the initial year for each of the six categories. Of the statistical target population of 19,808 individuals in (Table 2), 7,270 persons (36.7%) showed interest in participation, 3,334 (16.8%) declined participation, 6,976 (35.2%) returned no response, 1,828 (9.2%) were addressees unknown at the address used, 254 (1.3%) were deceased, and 146 (0.7%) were unaccountable for due to other reasons. A look at the proportion of study participants by age group reveals that the proportion of participants increased with age among those in their twenties to forties, and showed a slight drop after the peak marked in the 50- to 59-years-old age bracket.

The proportion of non-respondents was highest among younger individuals while approximately flat among those in their fifties and older. The proportion of participation refusers was high among both the younger and older age groups while a little low among the intermediate-age group (Figures 3 to 5).

Figure 6 shows the number of replies per month since the start of calls for participation in this study, along with other statistical data, for those with affiliation with TEPCO and those without. The figure shows the points of time at which major approaches were made. The number of study participants increased over time as a result of the approaches made to encourage participation in this study, including encouragement to reply by mail, by in-house mail, or via the major principal contractors. As explained above, calls for participation were made separately for TEPCO employees and those of other companies, so the figure shows the separate trends for the former and the latter (Figure 6).

Table 3 shows the proportions of study participants for TEPCO employees and non-TEPCO employees. The proportion of participants in this study strikingly differs between the two categories. Only 29.3% of non-TEPCO employees expressed their intention to participate, whereas 58.5% of TEPCO employees did so. Moreover, the proportion of non-respondents was lower among TEPCO employees (Table 3).

Table 3: Proportions of participants and others in this study among TEPCO employees and non-TEPCO employees

	Total by affiliation	Study participants (%)	Participation refusers (%)	Non-respondents (%)	Addressees unknown (%)	Deceased (%)	Others (%)
Non-TEPCO employees	16662	5182(31.1%)	2774(16.6%)	6540(39.3%)	1785(10.7%)	253(1.5%)	128(0.8%)
TEPCO employees	3146	2088(66.3%)	560(17.8%)	436(13.9%)	43(1.3%)	1(0.0%)	18(0.6%)
Total	19808	7270	3334	6976	1828	254	146

Table 4: Proportions of participants and others in this study by dose

	Total by dose	Study participants (%)	Participation refusers (%)	Non-respondents (%)	Addressees unknown (%)	Deceased (%)	Others (%)
Below 5 mSv	9336	3284 (35.2%)	1721 (18.4%)	3326 (35.6%)	776 (8.3%)	119 (1.3%)	110 (1.2%)
5 mSv or more to below 10 mSv	2854	1003 (35.1%)	426 (14.9%)	1071 (38.1%)	314 (11.0%)	31 (1.1%)	9 (0.3%)
10 mSv or more to below 20 mSv	3265	1095 (33.5%)	507 (15.5%)	1243 (38.1%)	367 (11.2%)	47 (1.4%)	6 (0.2%)
20 mSv or more to below 50 mSv	2816	1119 (39.7%)	427 (15.2%)	950 (33.7%)	275 (9.8%)	40 (1.4%)	5 (0.2%)
50 mSv or more to below 100 mSv	881	505 (57.3%)	147 (16.7%)	184 (20.9%)	32 (3.6%)	7 (0.8%)	6 (0.7%)
100 mSv or more to below 150 mSv	139	111 (79.9%)	21 (15.1%)	6 (4.3%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
150 mSv or more	37	29 (78.4%)	6 (16.2%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

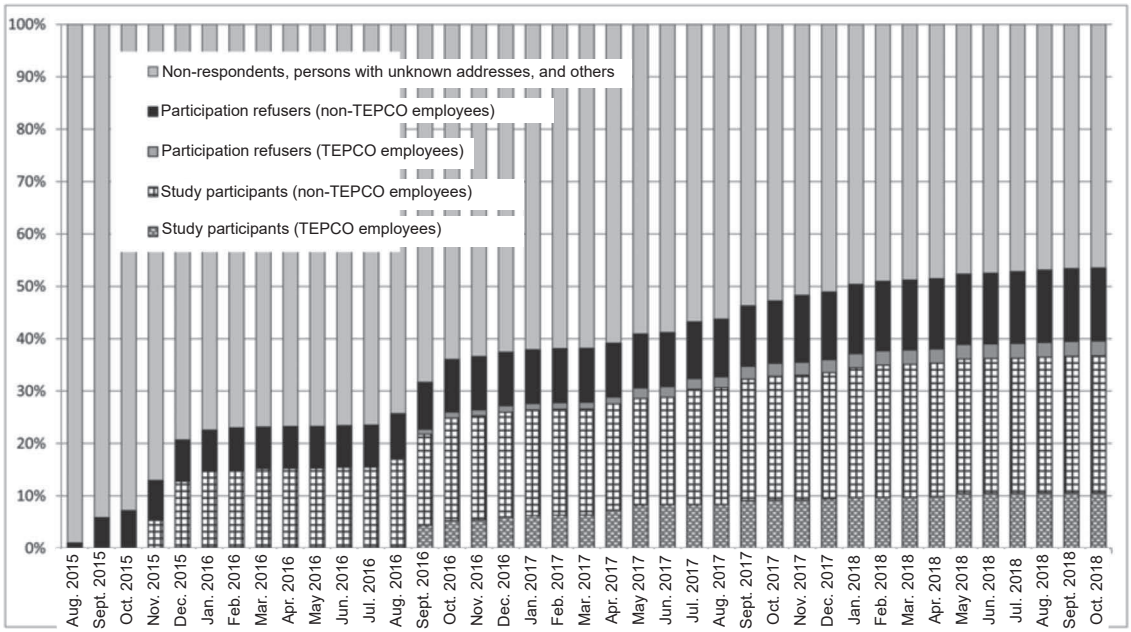


Figure 7. Trends in monthly participation in this study (TEPCO employees vs. others)

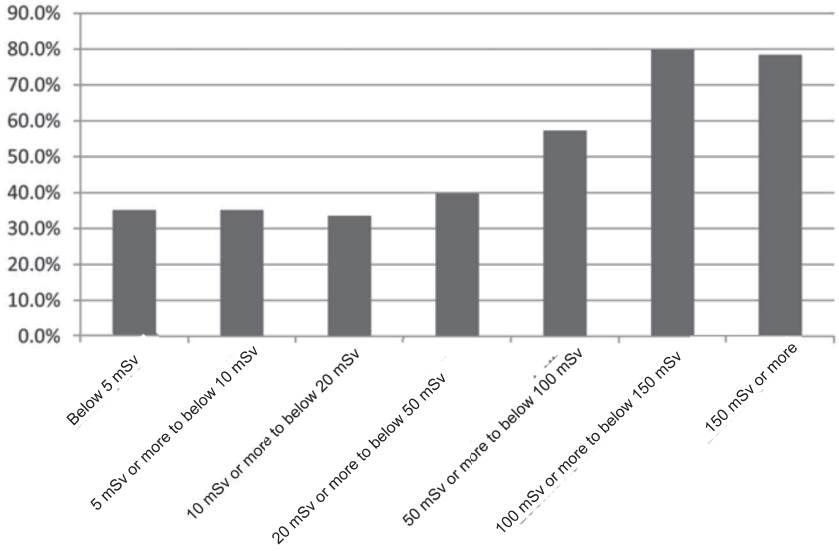


Figure 8. Comparison of the proportions of study participants by dose

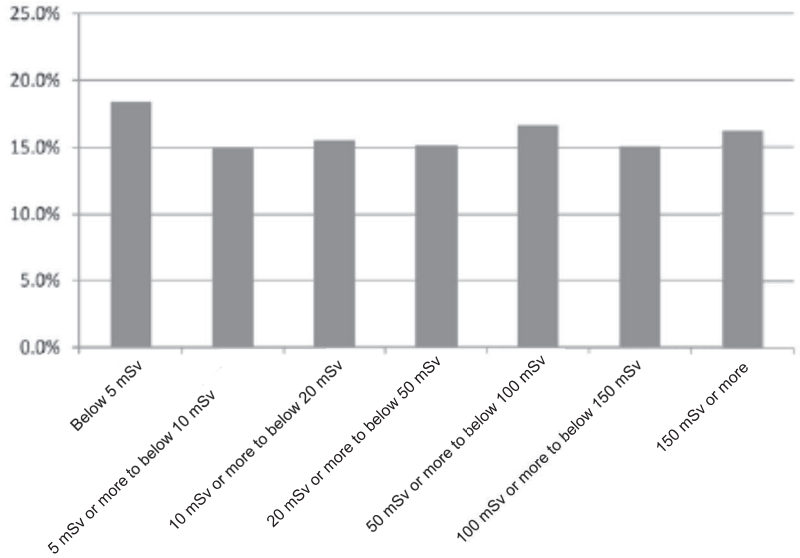


Figure 9. Comparison of the proportions of participation refusers by dose

2) Breakdown of the study participants by exposure dose level

With doses classified into seven categories (below 5 mSv; 5 mSv or more to below 10 mSv; 10 mSv or more to below 20 mSv; 20 mSv or more to below 50 mSv; 50 mSv or more to below 100 mSv; 100 mSv or more to below 150 mSv; and 150 mSv or more), this report examines the status of participants in this study by dose category. The proportions of study participants were as follows: 35.2% for those with exposure dose of less than 5 mSv; 35.1% for those with 5 mSv or more to below 10 mSv; 33.5% for those with 10 mSv or more to below 20 mSv; 39.7% for those with 20 mSv or more to below 50 mSv; 57.3% for those with 50 mSv or more to below 100 mSv; 79.9% for those with 100 mSv or more to below 150 mSv; and 78.4% for those with 150 mSv or more. This calculation excluded 480 individuals with no dose information available (Table 4).

The proportion of study participants showed differences among the dose categories. In the dose categories of 100 mSv or more to below 150 mSv and 150 mSv or more, the proportion of study participants tended to be notably higher than in the other dose categories (Figure 8). The group exposed to less than 5 mSv tended to show a higher proportion of participation refusers than other groups (Figure 9). The proportion of non-respondents also showed differences among the dose categories. The proportion was lower in 100 mSv or more to below 150 mSv and 150 mSv or more.

3) Exposure status by company

Table 5 shows the exposure status in two categories, TEPCO and other companies. In the dose categories of 50 mSv or more to below 100 mSv, 100 mSv or more to below 150 mSv, and 150 mSv or more, TEPCO employees accounted for a larger proportion with the increase in dose.

4) Study participation consent status among the study participants

Of the written consent obtained from 5,016 individuals by the end of December 2017, those of 4,622 individuals were obtained at the time of health checkups. Among the target individuals with an expressed intention to "cooperate in the study though not ready to take a health checkup at the moment," 394 persons presented written consent. Regarding their intention to cooperate in this study, the following seven questions were asked: (1) Do you consent to receive information on the work situations and exposure dose measurements during the emergency work and the results of statutory medical examinations from TEPCO, the principal contractor, the company, or any other entity affiliated with you at the time of the emergency work? (hereinafter "receipt of information on work situations and exposure dose measurements during the emergency work and the results of statutory medical examinations from the then affiliated entity"); (2) Do you consent to receive exposure dose-related information, including information predating the nuclear power plant accident, stored in the Radiation Dose Registration Center of the Radiation Effects Association (REA)? (hereinafter "receipt of exposure dose, including dose predating the nuclear power plant accident"); (3) Do you consent to receive information on your medical radiation exposure dose from the medical institution, health insurance society, or any other entity through which you have taken a radiological examination or treatment? (hereinafter "receipt of information on medical radiation exposure doses from examinations and treatments at medical institutions"); (4) Do you consent to have your identity checked by certificate of residence in accordance with procedures under the law, in order to allow acquisition of the information necessary to confirm and trace your whereabouts after a future change of residence, check any change in your name due to reasons such as marriage, and ascertain your survival or death? (hereinafter "identity check by certificate of residence in accordance with procedures under the law"); (5) Do you consent to receive cancer incidence information from the regional cancer register of the prefecture of your residence, or the National Cancer Register of the National Cancer Center? (hereinafter "receipt of cancer incidence information from the regional cancer register or the National Cancer Register"); (6) Do you consent to receive past and future results of statutory medical examinations for occupationally radiation-exposed personnel from the health checkup institution? (hereinafter "receipt of past and future results of statutory medical examinations from the health checkup institution"); (7) Do you consent to receive the results of thorough screening and other related diagnostic information from the medical institution at which you have taken a thyroid checkup (such as blood test, ultrasound test, or cytological diagnosis)? Your prior consent shall be obtained specifically regarding the content of reference, the medical institution to be referred to, and other relevant issues. (If you have never taken any of these tests, please answer the question assuming that you will in the future.) (hereinafter "receipt of the provision of the results of thorough screening and other related diagnostic information from the medical institution at which you underwent thyroid scanning."). The consent rates fell within the range of 97.0% to 98.3% (Table 6).

Table 5: Breakdown of TEPCO employees and non-TEPCO employees by dose

	Below 5 mSv	5 mSv or more to below 10 mSv	10 mSv or more to below 20 mSv	20 mSv or more to below 50 mSv	50 mSv or more to below 100 mSv	100 mSv or more to below 150 mSv	150 mSv or more	Unknown	Total
Non-TEPCO employees	8219	2481	2753	2290	408	46	9	456	16662
TEPCO employees	1117	373	512	526	473	93	28	24	3146
Total	9336	2854	3265	2816	881	139	37	480	19808

Table 6: Consenter ratio for each question in the informed consent questionnaire

	Consenters		Non-consenters		Non-responders
	No. of persons	Ratio	No. of persons	Ratio	No. of persons
1) Receipt of information on work situations and exposure dose measurements during the emergency work and the results of statutory medical examinations from the then affiliated entity	6259	96.5%	221	3.4%	3
2) Receipt of exposure dose information, including information predating the nuclear power plant accident	6222	96.0%	257	4.0%	4
3) Receipt of information on medical radiation exposure doses from examinations and treatments at medical institutions	6248	96.4%	231	3.6%	4
4) Identity check by certificate of residence in accordance with procedures under the law	6164	95.1%	316	4.9%	3
5) Receipt of cancer incidence information from the regional cancer register or the National Cancer Register	6220	95.9%	259	4.0%	4
6) Receipt of past and future results of statutory medical examinations from the health checkup institution	6257	96.5%	221	3.4%	5
7) Receipt of the results of thorough screening and other related diagnostic information from the medical institution at which you underwent thyroid scanning	6252	96.4%	226	3.5%	5

5) Views of those responsible at the companies concerned

When developing a plan for future approaches, it is important to hear the opinions of those in direct contact with the emergency workers on site, such as those responsible at the companies concerned. So far, opinions including the following have been heard, providing explanation about the current situation, comments on the sluggish increase in the number of study participants, and proposals for improvements:

"Our workers and we have received documents on studies titled similarly to yours from other institutions similarly named to yours. Our workers may have failed to reply to some of these documents, assuming they were all the same."

"As is common with residential practices in Fukushima, many of our workers have changed their residential locations (living alone near the power plant away from their families). Some of the information letters and other correspondence addressed to them may not have reached them directly."

"These workers frequently move between companies. They are highly likely to leave their current company every time their contract term nears the end and the work completes."

"In the construction industry, it is a common practice to employ workers with required skills only for a period need. Hence, they move to another site as soon as their contracted work period is over. On construction sites in general, you often bump into workers moving between different sites almost on a daily basis. Unlike manufacturing workers or research professionals, few construction workers remain at one place to work on one job for a long time."

"Back then shortly after the Fukushima Daiichi Nuclear Power Plant accident, we invited workers with required skills from all over the country to help us with the emergency work. After the emergency work was completed, they went back to their normal jobs."

"We expect our workers to be very reluctant to cooperate because it has been quite a long time since the emergency work ended."

"The Radiation Control Department has lost communication with the target individuals. Although they may still be with the company, they are dispersed among other departments or types of jobs across the country. If they are no longer radiation workers, the Radiation Control Department has no control over them."

Opinions heard from subcontractors include the following:

"We have no channel to communicate with the radiation control department of the principal contractor responsible for the then emergency workers, and hence have no control over the workers."

"We are not a radiation work specialist company in the first place. Many of the target individuals belong to departments completely unrelated to radiation. Since the completion of the emergency work, they have been working back in their original departments. We have lost our interest in and information about the nuclear power plant accident or radiation."

"The majority of the target individuals, who do not belong to a large company, cannot afford the time to take health checkups between tasks."

"Currently, most companies use buses for the collective commute of their workers to and from the Fukushima Daiichi Nuclear Power Plant. It is difficult for individual workers to leave for a health checkup in the middle of their work hours."

"Assuming that many of the target individuals are working on TEPCO's sites, we propose that you should conduct health checkups at the Fukushima Daiichi, Fukushima Daini, and

Kashiwazaki-Kariwa Power Plants."

D. Discussions

As the aim of the first cycle, continuous efforts were pursued to collect a sufficient number of study participants to establish a cohort. As of October 31, 2018, the number of study participants was 7,270 persons and accounted for only about 37% of the study target population of 19,808 people.

Comparison by age reveals the characteristics of the 20- to 29-year-old age group. This age group showed a high proportion of both non-respondents and participation refusers, and hence accounted for a small part of the study participants. Even if they were aware of the delivered mail, many of these target individuals might have thrown them away without returning a reply or even bothering to unseal the envelope. Moreover, those in this age group have relatively less health anxiety and hence have a lower motivation to feel like taking health checkups. What characterized those in their thirties was that they showed the highest proportion of non-respondents only next to their 20- to 29-year-old counterparts, but have the lowest proportion of participation refusers among all the age groups. The fact may be that, like those in their twenties, many of these study target individuals did not read or unseal the delivered mail. Still, the above characteristics suggest that they might have decided not to participate depending on whether they are married or have children. Those in their forties showed a relatively higher proportion of non-respondents. Meanwhile, they also showed a relatively low proportion of participation refusers and maintained the proportion of study participants in the 30-to-39% range. Those in their fifties had, as their characteristics, a relatively lower proportion of non-respondents and the highest proportion of study participants among all the age groups. Considering that those in their forties and fifties account for the large part of the study target population, a high proportion of study participants in these age groups is critically important to secure a cohort. Among the study participants, there were 336 target individuals with an expressed intention to "cooperate in the study though not ready to take health checkup at the moment." Of these people, 108 were in their forties, and 98 were in their fifties. Although busy and in the prime of life, many of those in their forties and fifties probably participated in this study with the understanding of its meaning and purpose. Those in their sixties and seventies showed a relatively low proportion of non-respondents, and the former in particular included the smallest number of non-respondents among all the age groups. In both age groups, however, the proportion of participation refusers was high and exceeded 20%. Some of these people may have refused to participate in this study because they were still active workers in the latter half of their fifties or sixties at the time of their expressed intention to refuse participation, and could not afford the time to take part and take health checkups. Therefore, consideration is underway for activities to encourage participation refusers in their sixties and seventies to reconsider taking health checkups in this study as one of their health management methods after retirement.

Comparison by dose reveals that TEPCO employees accounted for a progressively higher proportion in the higher dose categories. This is probably because the proportion of TEPCO employees was higher among the study participants than that of non-TEPCO employees (Figure 10).

When giving encouragement to reply, the major principal contractors showed differences in their reaction. More specifically, some companies encouraged only their own employees to do so while others extended their encouragements to the employees of their subcontractors as well. These companies also showed differences in how they encouraged and collected replies in-house. For example, some companies used their in-house email or other internal communication methods to encourage replying to sealed letters received from the Research Secretariat, others delivered necessary forms via in-house mail, or they internally collected completed forms for submission. The actual reply ratio to the number of non-respondents widely varied from 7.8% to 57.8% between the companies that directly encouraged individual works to reply. However, all these companies found it difficult to keep track of the whereabouts of workers who had already resigned or retired.

In order to increase the number of study participants, it is necessary to reduce the current approximately 7,000 non-respondents and to encourage participation 3,334 refusers to reconsider participating in the study. So far, the primary method of encouraging participation in this study has been mail. No sealed letter, however, can communicate its content without being actively unsealed and read by the recipient. Chances are not high that non-respondents and participation refusers will take positive action. In this sense, it is necessary to disseminate passive information and encouragement for participation in a form that can be seen and heard unconsciously. The website would provide an effective method for this purpose.

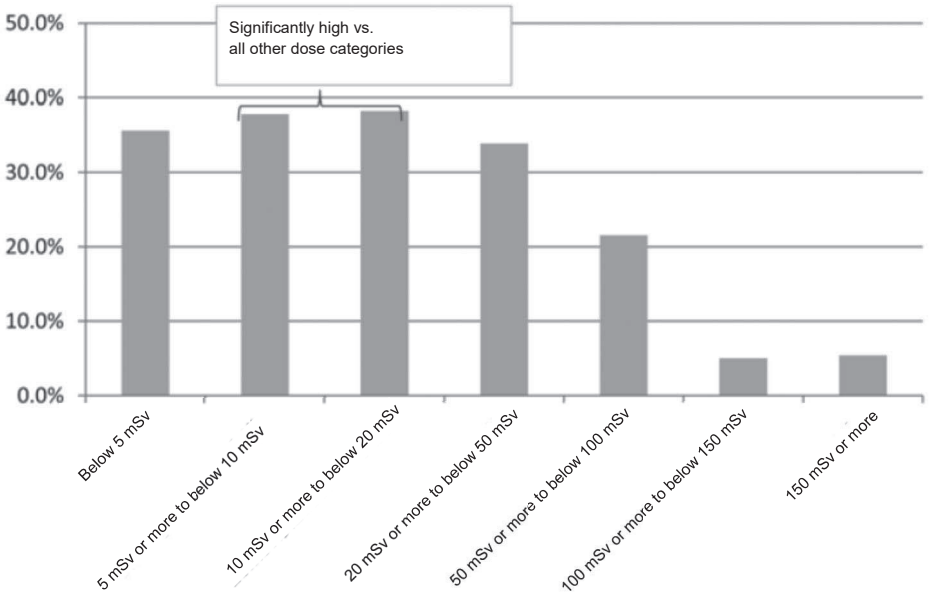


Figure 10. Comparison of the proportions of non-respondents by dose

E. Conclusions

This report described the characteristics of the relationship between the proportion of study participants and the classification criteria, such as age group, business entity type, and exposure dose level. Not covered herein were many confounding factors associated with the proportion of study participants at the time of response. Such factors include the most critical, current employment status besides the number of days engaged in the emergency work, the content of the work engaged in, the presence of subjective symptoms or suffered diseases during or after the work period, and the family situations. Therefore, there is no denying the possibility that a factor or factors other than the above-described characteristics related to the proportion of participants might have had a strong influence on the results. Hence, it is still too early to say something conclusive at this point. The characteristics presented herein should be regarded strictly as no more than superficially observable events without discussing any causal relationships until those confounding social factors are sufficiently investigated, so that the proportional contribution of each factor can be analyzed independently from those of others.

F. Research publications

1. Papers published in academic journals

None

2. Conference presentations

None

G. Intellectual property rights acquired

None

Industrial Disease Clinical Research Grants
Working-Group Research Report

Statistical Detection Power in the Follow-Up Study on the Number of the emergency workers

Principal Investigator: Toshiteru Okubo, Radiation Effects Research Foundation (RERF), Consulting Researcher
Research Collaborator: Kyoji Furukawa, Biostatistics Center, School of Medicine, Kurume University, Professor
Co-Investigator: Hiroko Kitamura, Sub-Chief Researcher, Hiroshima Clinical Research Department, Radiation Effects Research Foundation (RERF)

Abstract

A solid cancer incidence model was used to estimate statistical detection power. A 40-year-or longer follow-up study on the entire target population (of approx. 20,000 persons) would allow detection of a 10% increase in solid cancer incidence risk, with a statistical detection power of 80%. Assuming that the proportion of health checkup participants remains in the current range of 35 to 40%, sufficient detection power cannot be expected without assuming a risk considerably higher than the above value. Additionally, in cases that presuppose the involvement of multiple factors or require the correction of confounding factors, the required number of samples will increase accordingly. On the other hand, if the disease model aimed to observe not stochastic events but changes in analog quantities of all samples, a smaller sample size would allow detection.

For this epidemiological survey, it matters most to call out for all members of the given group to participate in this study, and then to continue observation of target individuals steadily with their consent.

A. Study objective

In the accident response work at the TEPCO Fukushima Daiichi Nuclear Power Plant, the radiation emergency exposure dose limit was raised from 100 mSv to 250 mSv for the period from March 14, 2011, to December 16 of the same year. During this period, 174 individuals among the approximately 20,000 people engaged in the work are estimated to have been exposed to doses exceeding the five-year normal work exposure limit of 100 mSv. This study aims to perform lifelong follow-ups of the entire emergency workforce of approximately 20,000 persons to investigate the relationship between their radiation exposure and health. In other words, a specific group will undergo long-term observation to look out for occurrences of health anomalies. The health anomalies to observe herein are not restrictively predefined from the beginning. The scope of this study covers occurrences of cancer, which is usually the principal concerns as radiation effects, and many other diseases, including psychological impacts. The occurrence of these target diseases involves not only radiation exposure but also many factors. These factors fall broadly into two categories: the first relates to the mechanism of the occurrence of the target diseases while the second indirectly relates to the occurrence of the target diseases. When there is only one primary factor, analysis is relatively easy. With more than one primary factor, the disease model will become complicated, making analysis difficult in most cases. The secondary factors are called confounding factors, and show behaviors that make it challenging to discern the causal relationships induced by the primary factors. As a result, corrections become necessary before analyzing the effects of the primary factors. This report aims to estimate statistical detection power: hence, it limits the disease model exclusively to the most straightforward factor, i.e., the cancer incidence, and does not take into consideration the effects of secondary factors, i.e., confounding factors.

The number of diseases or deaths observed to occur due to the involvement of hypothetical factors will be larger than that in the standard group. What an epidemiological survey aims to do is to determine whether the increase exceeds the range of commonly observed random variation. Putting it differently, when an observed increase exceeds the reference range, the conclusion will be that "a significant increase occurred." This determination result depends on the size of the observation group. This determination result depends on the size of the observation group, proportionally to which smaller variations will allow the detection of significant differences. It follows then that more minute changes can be detected with the increase in the size of the observation group. The objective of this study is to estimate the number of years of continuous observation required to detect significant increases from the currently available size of the observation group in this study.

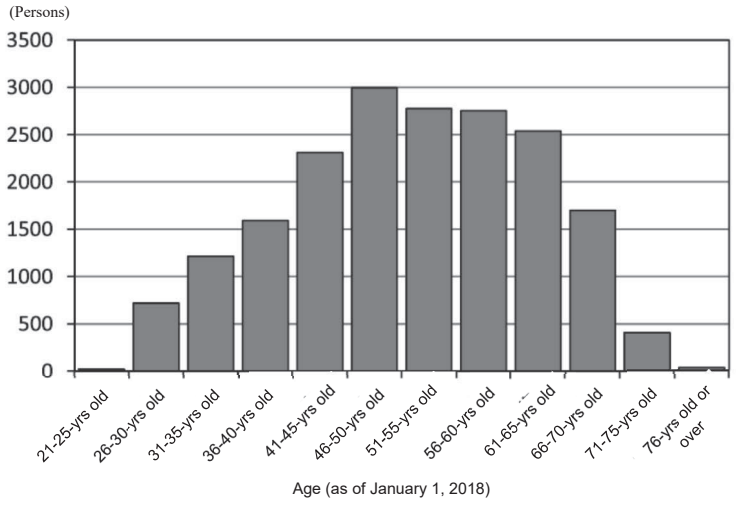


Figure 1. Age distribution

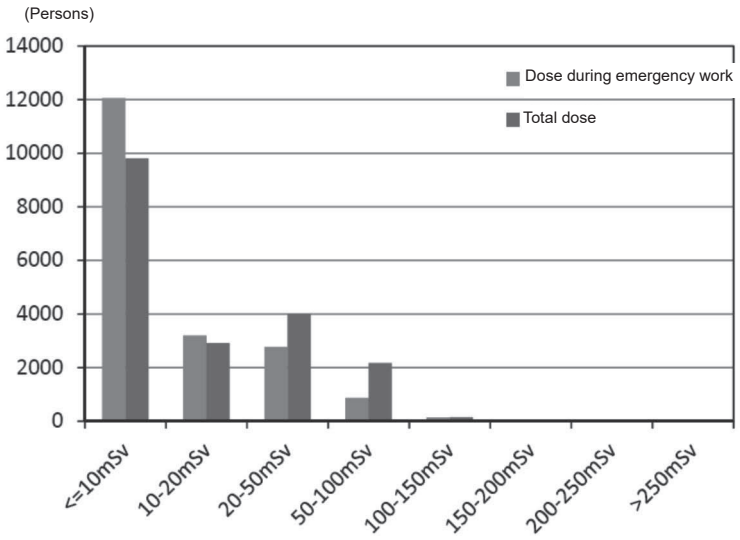


Figure 2. Dose distribution

B. Study methodology

The setting of the criterion for determining whether an increase in an observation result is random or significant is arbitrary. There are, however, standard criteria defined empirically. The usual practice is to determine an increase as significant if the increase occurs only at a rate less than 5% (five times per 100 times) or 1% for the distribution of a standard group (called "p-value"). In other words, these criteria determine an event as non-random (a significant increase) if it occurs only five times or once out of 100 times. Conversely, the rate at which the same determination criteria can determine the distribution of the observation group correctly as such is called detection power.

In order to evaluate the frequency of the occurrence of a disease with respect to the size of the observation group in an epidemiological survey of the emergency workers, the investigator must select a target disease of interest and calculate the expected number of occurrences. While this is the study hypothesis *per se*, this report aims to estimate the size, and hence takes up the incidence of all cancers for which both the incidence and mortality rates in Japan are available, as well as risks that have been estimated in the life span study of the atomic bomb survivors.

The size of the current target group is evidently too small for a cross-sectional comparison of a one-year track record. Thus, it is decided to think in terms of cumulative total numbers and consider how many years of continuous observation and how many occurrences of the disease it will take to allow the

determination. In order to calculate the expected number of occurrences of the target disease, the age-specific numbers of individuals in the observation group over time during the observation period will be necessary, along with the age-specific ratios of incidence of the disease concerned for each year. Because both the age-specific populations and incidence rates for each year in the future are unknown at this moment, there is no choice but to simulate these values. In the simulation performed this time, the age-specific populations were estimated using a demographic model that assumed that the current age-specific populations would decrease every year at the rate of the current age-specific number of deaths. Then, the expected number of cases was estimated on the assumption that the current age-specific cancer incidence rates would continue in the future.

Finally, the magnitudes of the increase in the risk for this group per radiation exposure of 100 mSv were expressed by relative risk (RR) levels and estimated for the following three levels: 1.1 (10% increase), 1.075 (7.5% increase), and 1.05 (5% increase). As for exposure doses, the simulation used both the "dose during emergency work" during the emergency work period and the "total dose" consisting of the dose during the emergency work and the dose recorded thereafter.

C. Study results

The data for the calculation was provided by the 19,084 individuals whose doses during the emergency work and total doses are both registered in the MLHW long-term health management system database. Figure 1 shows the age distribution of the 19,084 individuals as of January 1, 2018, while Figure 2 shows the distribution of the dose during emergency work and that of the total dose. In the 20-50 mSv and 50-100 mSv ranges, the total dose applies to a larger number of individuals than the dose during emergency work. One of the likely reasons is that many of these individuals have been engaged in some sort of radiation work after the emergency work period; another likely reason is that exposure due to engagement in radiation work is controlled not to exceed the dose prescribed under the Guidelines for Maintaining and Promoting the Health of Emergency Workers at Nuclear Power Facilities and the Ordinance on Prevention of Ionizing Radiation Hazards.

Figure 3 shows age-specific mortality rates for all causes of death (2014), cancer incidence rates (2011), and cancer mortality rates (2014) per population of 100,000 people in Japan. This report assumes that these rates will remain unchanged in the future. Figure 4 shows the cumulative expected number of occurrences of solid cancer for each follow-up period; a rapid increase will continue until approximately 40 years later, after which the increase will gradually slow down with the decrease in the remaining population.

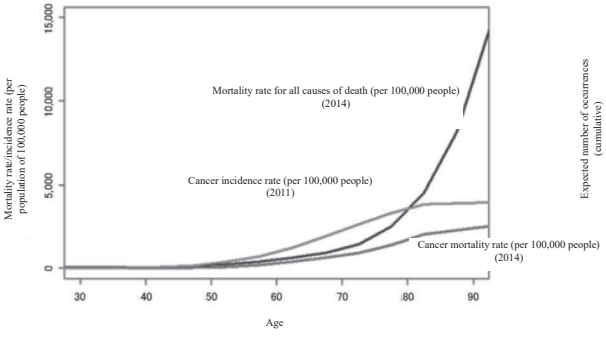


Figure 3. Mortality rate/incidence rate in Japan

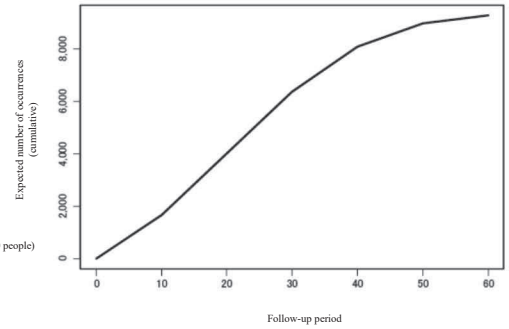


Figure 4. Expected number of occurrences of cancer (cumulative)

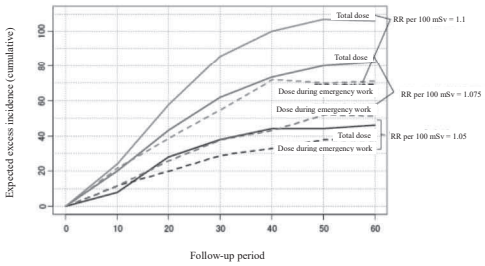


Figure 5. Expected excess incidence (cumulative)

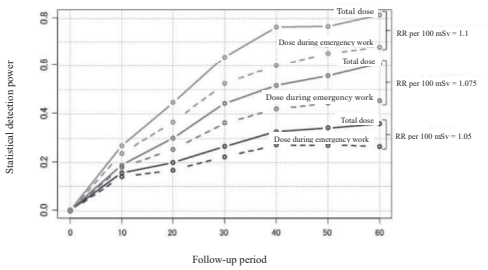


Figure 6. Statistical detection power

Figure 5 shows the expected cumulative excess incidence of cancer (cumulative number of occurrences of cancer induced by radiation exposure) when assuming the three relative risks (RR) levels of 1.1, 1.075, and 1.05 per 100 mSv to separately follow up the target population until 60 years later for the dose during emergency work and the total dose. The expected excess incidence increases with the increases in relative risk (RR) and exposure dose. Figure 6 shows the increases in statistical detection power for when assuming relative risk (RR) levels of 1.1, 1.075, and 1.05 per 100 mSv. Even when assuming the relative risk level as a 10% risk increase per 100 mSv (RR=1.1), which is higher than the average percentage observed among atomic bomb survivors (RR per 100 mSv = approx. 1.051), the total dose-based calculation predicted that the usually intended statistical detection power of 80% would not be achieved until 60 years later. A simulation of a 60-year-long follow-up study based on the doses during the emergency work predicted the statistical detection power would not reach 70%.

D. Discussions

This report has examined no more than a cancer incidence model that assumes that the disease occurs or not and stochastically develops; hence, it differs from ones that deal with events observable as analog quantities commonly among all subjects, such as height, weight, blood pressure, or blood biochemical test values. Moreover, this report assumed that only one factor contributes to the development of the disease. In real workplaces, however, there are almost no diseases to which only one factor contributes. If what needs to be done here is to determine whether or not the disease is a prescribed industrial disease to be covered by industrial accident compensation insurance (on-duty vs. off-duty), the issue will be whether or not the contribution ratio was 50% or more. Of course, this is purely theoretical, and contribution ratios are extremely difficult to calculate precisely. In reality, there are always confounding factors involved. In cases where their correction is necessary, it must be borne in mind that the sample size must be increased to accommodate the correction.

E. Conclusions

On the assumption that there would be a follow-up study on solid cancer incidence, this report estimated statistical detection power. If the radiation exposure-induced cancer incidence excess risk were considerably overestimated (10% increase for 100 mSv), a forty-year or longer follow-up of the entire target population (approximately 20,000 individuals) would allow the detection of solid cancer incidence risk with a statistical detection power of 80%. Accordingly, supposing that the percentage of health checkup participants remains at the current level of 35 to 40%, sufficient detection power cannot be expected without assuming a considerably higher risk than the above value. In practice, however, cancer hardly develops due to a single factor, and the stochastic contributions of its factors would take various values. Hence, an assumption of the involvement of more than one contributory factor will completely change the sample size estimation. In cases that require the correction of confounding factors, the required number of samples will increase accordingly. Moreover, if the disease model is intended to observe not a stochastic event but the change in the continuous quantity of all samples, successful detection may be possible even with a small sample size. Thus, the sample size simulation results presented herein must be understood as derived from the assumptions of a simplified model. For this epidemiological survey, it matters most to call out for all members of the given group to participate in this study and then to continue observation of target individuals steadily with their consent.

F. Research publications

1. Papers published in academic journals

None

2. Conference presentations

None

G. Intellectual property rights acquired

None

■ References

1) Preston DL, Ron E, Tokuoka S, et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. Radiat Res, 168: 1-64, 2007.

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