Ministry of Health, Labour and Welfare Clinical Research Grant for
Work-related Injuries and Illness

Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers

(Epidemiological study on emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant)

Phase 2 (FY 2019 - FY 2023)

Third-Party Evaluation Committee Report

Chairperson Ginji Endo

March 2023

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Introduction

The Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers was initiated at the National Institute for Occupational Safety and Health, Japan in 2019, with the support of a clinical research grant from the Ministry of Health, Labour and Welfare (MHLW) for work-related injuries and illness.

This study aims to conduct a long-term follow-up investigation on approximately 20,000 emergency workers who were involved in the response to the Tokyo Electric Power Company's Fukushima Daiichi Nuclear Power Plant accident, which occurred in March 2011. The study seeks to elucidate the health effects of radiation exposure and other related factors throughout their lifetimes.

Based on the guidelines of the research grant, which stipulate the need to establish an independent committee (the third-party committee) comprising researchers with internationally recognized expertise, and to receive evaluation from an international standpoint, we formed a third-party committee in 2022. The committee consisted of experts recommended by relevant academic societies and was tasked with evaluating the study conducted from 2019 onwards. Committee meetings were held as follows.

At the committee meetings, the research team's progress reports were presented by the headquarters and co-investigators. These reports were thoroughly examined and discussed under the leadership of the committee chair, who was elected through mutual selection. The committee worked independently to compile this report, ensuring its originality and integrity.

Lastly, we sincerely thank Prof. Ginji Endo for serving as the Chairperson of the Third-Party Committee and Prof. Masayuki Tatemichi for his invaluable contributions as Deputy Chairperson in compiling this report. We are also grateful to all the committee members for their valuable and accurate opinions.

Date and time of the Third-Party Evaluation Committee meetings
The 1st meeting 13:30-17:30 on Monday, Nov. 28, 2022 at FUKURACIA Yaesu Tokyo
The 2nd meeting 13:30-17:30 on Wednesday, Dec. 7, 2022 at FUKURACIA Yaesu Tokyo
The 3rd meeting 13:30-17:30 on Monday, Feb. 20, 2023 at FUKURACIA Yaesu Tokyo

List of Third-Party Evaluation Committee Members

Hirotsugu Ueshima	Specially Appointed Professor, NCD Epidemiology Research Center, Shiga University of Medical Science
Ginji Endo*	Director, Osaka Occupational Health Service Center, Japan Industrial Safety & Health Association

Kazuyuki Omae	Professor Emeritus, Keio University
Michiaki Kai	Professor, Nippon Bunri University
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Kazuo Sakai	Director, Radiation Effects Association
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Masayuki Tatemichi**	Professor, Department of Preventive Medicine, Tokai University School of Medicine
Akizumi Tsutsumi	Professor, Department of Public Health, Kitasato University School of Medicine
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March 31, 2023

National Institute of Occupational Safety and Health, Japan
Director of the Research Center for Prevention from Radiation Hazards of Workers
“Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers ”
Toshiteru Okubo / Principal Investigator

Third-Party Evaluation Committee Report

Chapter I　Evaluation for the Second Phase Study

1. Securing of study participants, research implementation system, and health investigation results

In the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers (NEWS), the cumulative number of study participants reached 8,023 of the study population (n=19,812) in 6 years from the start of the study, and the cumulative number of workers who received health examinations reached 6,286, which should be highly evaluated as the effort of researchers.

The handover of operations associated with the transfer of the principal investigator of this study (Toshiteru Okubo) from the Radiation Effects Research Foundation (RERF) to the National Institute of Occupational Safety and Health, Japan (JNIOSH), began with the transfer of data collected in the first phase (paper documents, electromagnetic records, and electromagnetic recording media). The task must have required considerable effort and attention, particularly in ensuring privacy protection. Subsequently, the study made use of the experience gained from previous follow-up surveys conducted on A-bomb survivors at RERF to recruit participants through a postal survey and obtain their consent for the study. The study organization, including the researchers, made significant efforts that allowed the study to continue smoothly throughout the first and second phases.

The addresses and other personal information of the study participants are provided annually from the database created and maintained by the government with cooperation of Tokyo Electric Power Co., Ltd. (TEPCO). However, in this study, we also obtain individual information, such as address changes, through the epidemiological survey, resulting in a time lag in the information and causing difficulties in contacting the participants directly. For instance, it has been observed that on multiple occasions, after an individual has notified one organization of a change in address, another organization contacts the old address before the information is provided. Having multiple databases for the same individual is not desirable for the progress of this type of research, and database sharing is recommended.

The researchers made continuous efforts to recruit participants through various methods, in addition to the mail survey, and the results are evaluated positively. Although there was a decrease in the number of cooperating health examination institutions, the attempt to secure the number of examinees through new initiatives, such as the headquarters-sponsored intensive examinations, is commendable.

The accuracy of laboratory measurement has been improved recently, especially in the

nationwide laboratories. Therefore, we agree that the method of consolidating analytical work at a single laboratory, which has been conducted so far, may have diminished significance regarding general laboratory test items considering the advantages and disadvantages of workload and the time difference due to long-distance transportation. However, it is desirable that examination items specific to radiation hazards and diagnostic imaging should be consolidated under the supervision of the principal investigator and managed under the same conditions. Particularly for images, since differences due to the devices and radiologists cannot be ignored, it is preferable to manage and store them as electronic data (or film data) under the supervision of the principal investigator.

2. Scientific evaluation

1) Baseline survey

In the baseline survey, which included 6,031 participants as of December 31, 2022, the relationship between socioeconomic status, lifestyle habits, and the radiation exposure dose (mSv) during emergency operations was analyzed. To examine the causal relationship between the exposure dose and future disease incidence, mortality, etc., it is crucial to consider the presence of any differences in basic attributes in relation to radiation exposure doses, identify potential confounding factors, and understand methods of controlling them.

In this regard, it was revealed that the mean age in the group with the highest exposure dose (> 100 mSv) was younger by 2.8 years than the overall mean age (52.2 years). In the ≥ 100 mSv group, the percentage of TEPCO workers was significantly high at 85.2%, surpassing the overall percentage of 37%. The characteristic of younger age suggests a potential association with a lower prevalence of hypertension, diabetes, and cardiovascular disease, as indicated by the questionnaire, compared to the lower exposure dose groups. On the other hand, the characteristic of a higher proportion of TEPCO workers is likely to be associated with a high frequency of medical examinations and a higher detection rate of disease findings. Specifically, it appears to be related to a higher rate of reporting cataract and thyroid diseases as past medical history in the questionnaire.

Furthermore, the mean age in the group with a high exposure dose (50-99 mSv) was younger by 1.9 years than the overall mean age. At the same time, it appeared to be associated with a lower proportion of individuals with a college degree or higher education, a higher marriage rate, a higher prevalence of individuals engaged in leisure-time physical activities, a higher alcohol consumption rate, and a lower smoking rate.

The analysis based on the results of the baseline survey, including the analysis of other items, clearly demonstrates the need for thorough consideration in studying the causal relationship between exposure dose and the onset of diseases in the future.

2) Statistical power and analytical methods

According to the estimation of statistical power in the first phase, assuming a total of 7,200 study participants and using the calculation of 7,200 × 40 years = 288,000 person-years, it was determined that even with 40 years of follow-up, the study could not achieve a statistical power of 80% to detect a 10% increase in cancer incidence due to radiation exposure, based on the risk estimate from the epidemiological study of A-bomb survivors. Therefore, it was concluded that in order to detect the effects of radiation, it would be necessary to follow up with all participants (approximately 20,000 individuals) for over 40 years. Subsequently, in the second phase, the statistical power calculation was reassessed for different cancer types, including thyroid cancer, based on recommendations from the Third-Party Evaluation Committee.

The power calculation in the second phase showed that with a 40-year follow-up, the statistical power would be at most around 10% for any type of cancer. It was concluded that with an extension of the follow-up period from 20 years to 40 years and a doubling of the expected number of participants, the increase in statistical power would be only a few percent for cancers in any tissue, and no substantial improvement would be expected.

A number of assumptions are used in the power calculation, and changes in these assumptions can impact the results of the calculation. For the assumption of excess relative risk (ERR) of radiation at low doses, calculations of higher ERRs (from 2 to 10 fold) than previously reported have been reported. For overall cancer and thyroid cancer, it has been suggested that a ERR more than 5 times higher would be detectable. For thyroid cancer, the ERRs from the reported epidemiological survey of Chernobyl decontamination workers were used. The Chernobyl survey included screening of the thyroid gland, and the effects of its overdiagnosis and the effects of insufficient stable iodine intake may have biased the ERR estimates. The ERR value of 3.8 per Gy used in the calculation of statistical power for thyroid cancer is higher than the ERR estimated in the A-bomb studies. In studies of A-bomb survivors, the risk of thyroid cancer due to exposure in adulthood is barely detectable in analyses that exclude thyroid microcarcinoma (Furukawa et al. Int. J. Cancer: 132, 1222-1226 [2013]).

On the other hand, an analysis focusing on latent thyroid cancer and nodules revealed a significant correlation with radiation dose (Ezaki et al. https://doi.org/10.1269/jrr.32.SUPPLEMENT_193). When ultrasound screenings are performed, they can detect micro-cancers. This presents the potential to detect the presence or absence of radiation effects on thyroid cancer that were not previously included in the analysis as either micro-cancers or latent cancers. Reassessment of the statistical power is necessary. However, calculating the statistical power without considering the influence of confounding factors may lead to

overestimation. At the very least, for lung cancer, it is necessary to calculate the statistical power by taking into account the effect of smoking.

Among the emergency workers, there is a group that has been exposed to high levels of thyroid radiation due to inhalation of radioactive iodine. Therefore, it may be useful information for future epidemiological studies to estimate the thyroid dose and calculate the statistical power to detect not only thyroid cancer but also benign thyroid diseases that are suggested to have a high radiation sensitivity.

It is theoretically impossible to prove the absence of radiation effects through epidemiological studies. This power calculation conducted in this study demonstrated the challenges of verifying the risk estimation values reported in epidemiological studies of A-bomb survivors. However, despite the limitations in statistical power, this study stands out from large-scale epidemiological studies conducted internationally through its high-quality dosimetry measurements and comprehensive investigation of confounding factors. Leveraging the characteristics of this cohort, similar to the Japanese epidemiological study on low-dose radiation effects (J-EPISODE) (Kudo et al., Health Phys. 2022), it holds great significance to disseminate evidence-based information from a perspective of worker health management. This includes the message that improving lifestyle habits can lead to risk reduction, which goes beyond radiation risks. Further analysis in this regard is expected in the future.

Based on the detailed power calculation, it is unlikely that sufficient power can be obtained at present to detect the assumed effects of radiation, even with long-term follow-up for all participants. Therefore, it seems to be impossible to prove the absence of radiation effects from the emergency operations in this accident. Moreover, calculating a significant ERR large enough to indicate an effect, based on previous findings, is also unlikely. Therefore, careful consideration should be given to how the analysis results will be interpreted and communicated to society. One approach is to interpret the P-value according to its original meaning and explain that it represents the probability of observing the current values (or values more extreme than them) when it is true that there is no radiation effect (i.e., the null hypothesis is correct). Alternatively, a range of options should be considered, such as reporting the probability of observing a value when a socially acceptable value (e.g., ERR=X due to lack of exercise) is true. Nevertheless, it is important to acknowledge that interpreting and communicating these findings may be challenging. Given this situation, although it may extend beyond the role of analysis evaluation, it may be necessary to prepare knowledge about methods for risk communication in relation to the overall direction.

A significant role of the research team is to investigate the relationship between radiation exposure and the risk of developing cancer. However, unfortunately, the Analysis and

Evaluation Subcommittee (Shinji Yoshinaga) has pointed out the limited statistical power due to the small target population and sample size. Therefore, another important investigation is the relationship between radiation exposure and non-cancer diseases, specifically the deterministic effects expressed by prevalence. There are a large number of participants, and there are survey items that can be conducted on the entire population. If there is a causal relationship with radiation exposure, it is believed that a sufficient sample size can be obtained. Therefore, it is important to clarify the survey methods for individuals with non-cancer diseases and the measurement techniques, and conduct a fundamental examination to determine which indicators should be used to control the confounding bias in the analysis of the relationship between radiation exposure and non-cancer diseases.

The objective of the Clinical Investigation Subcommittee (II) is to identify the potential confounding factors in this population for future epidemiological studies that will examine the association between radiation exposure and the risk of cancer and non-cancer diseases. From this perspective, the following two objectives listed for this subcommittee's research are appropriate.

① To elucidate the health impacts of social factors including employment and living background, as well as health management conditions such as industrial health and healthcare environment, on emergency workers.

② To provide information that enables understanding of the social background of emergency workers, which is necessary for study evaluation, health examinations, and post-guidance.

As the outcomes in the second phase, significant associations were observed between educational background and systolic blood pressure, white blood cell count, HbA1c, γGTP, and other factors. Even after adjusting for age, an inverse association was observed between educational background and smoking rates and alcohol drinking habit. Similarly, a reverse association was observed between annual income and smoking rates. These results support the general hypothesis that higher education is associated with higher health literacy, indicating that these social factors can act as confounding factors in analyses with cancer and non-cancer diseases as endpoints. On the other hand, in other occupational populations, lower educational backgrounds are associated with more fieldwork and higher exposure doses in lower-income groups. However, in this study population, the group with the highest exposure dose (>100 mSv) has a higher proportion of TEPCO employees who have higher educational backgrounds and higher annual incomes. This opposite association compared to general radiation workers suggests the need to consider whether an individual is a TEPCO employee and the possibility of interaction between individual influencing factors when conducting disease endpoint analyses. In epidemiological analyses with cardiovascular

diseases as endpoints, besides strong risk factors associated with pathophysiology (such as smoking and heavy drinking), psychological stress is also known as a risk factor. Additionally, the effect related to disease onset is not necessarily linear, as moderate alcohol intake may even have a protective effect. It is recommended to evaluate whether the data collected until the second phase are sufficient for the analysis.

There was a relationship between the evacuation experience and the exposure dose in this study population. Although no in-depth analysis has been conducted on this aspect, it is likely that it simply reflects the fact that many employees of TEPCO and affiliated companies, who originally resided in the evacuation area and worked at the nuclear power plant, were involved in high-exposure operations during emergencies and inevitably had to evacuate. On the other hand, the evacuation experience may be associated with the level of social and psychological stress, as well as the living environment of the residence (urban vs. rural). Psychosocial stress and living environment in the residential area have been identified as confounding factors in previous epidemiological studies with cancer and non-cancer diseases. Therefore, it is necessary to seek more appropriate parameters that are related to evacuation experience.

Health literacy as a social factor includes exercise habits, eating habits, and the rate of regular health checkup. It seems necessary to confirm whether these factors are covered by this study.

3) Dose evaluation

In radioepidemiology, organ dose is an important indicator for studying the effects of radiation exposure. External exposure dose is estimated based on information from the individual monitor, allowing relatively accurate information to be obtained. However, in the estimation of internal exposure dose, indirect evaluation of organ dose is based on the information from whole-body counter (WBC) and analysis of nuclide concentration in the air. Therefore, it is necessary to evaluate the uncertainty of the estimated values corresponding to the organ dose levels.

In the first phase, an experiment was conducted to assess whether the effective dose specified by laws and regulations could be appropriately evaluated based on the indicated value of the personal dosimeter. A RANDO phantom was used to examine the dependence on the irradiation direction from the source, investigating both ROT (effective dose in rotating irradiation) and ISO (effective dose in isotropic irradiation). The results confirmed the validity of using the indicated value of the personal dosimeter. In the future, it will be necessary to evaluate organ doses using information such as the dose conversion factor of ICRP. Furthermore, it is expected to assess the accuracy of organ dose estimation in

situations where the irradiation direction from the source and gamma-ray energy information following an accident are uncertain.

In the second phase, a study was conducted to estimate the equivalent dose to the crystalline lens from β-rays using the indicated value of the personal dosimeter. The β/γ dose ratio was estimated through simulation, and an experiment was performed to assess the β-ray shielding effectiveness of a full-face mask. By calculating the correction factor to convert the indicated value of the personal dosimeter to the equivalent dose of β-rays for the crystalline lens, it became possible to accurately estimate the β-ray dose to the crystalline lens, which couldn't be directly measured by the personal dosimeter. However, when estimating the dose to the crystalline lens using this correction factor, it may be necessary to evaluate the uncertainty of the estimated dose (β-ray + γ-ray) for the crystalline lens, considering the uncertainty in the information used for the β/γ dose ratio.

In the evaluation of internal exposure dose, as a result of obtaining detailed information beyond the effective dose through the MHLW, it becomes possible to estimate the dose contribution of individual radionuclides from the simple estimation based on combined dose of iodine and cesium. This improvement is expected to enhance the accuracy of estimating organ doses resulting from internal exposure. Building upon measurements obtained from WBC, a foundation has been established to estimate thyroid doses in workers in whom I-131 is not detected, using information such as the ratio of airborne concentrations of I-131 and Cs-137. Additionally, an estimation method using the furnace inventory has been developed to determine the contribution of short half-life radionuclides (such as I-132 and Te-132) to thyroid doses. While this method is effective for estimation of short half-life radionuclides, it is important to consider that the time of intake significantly affects the nuclide ratio and the chemical form greatly influences dose estimation. Therefore, evaluating the uncertainty of the estimation is inevitable. It is expected that the uncertainty of the dose estimation for a given dose level should be evaluated. Furthermore, after the initiation of stable iodine administration following the accident, the internal exposure to I-131 is suppressed. Thus, in the assessment of thyroid doses based on the I-131/Cs-137 ratio, it is essential to have information regarding the administration of stable iodine and the timing of its intake.

The accuracy of estimation should be further improved according to the level of organ doses, including thyroid dose, obtained through these estimation methods. Special attention should be given to the accuracy of estimating thyroid doses in workers whose effective dose exceeded 250 mSv.

Using the frequency of translocated chromosomes as an indicator, biological dose evaluation proves to be useful for validating the physically estimated organ dose. An nalysis is being conducted on 74 workers with an effective dose of ≥ 70 mSv. It is known that smoking

history and medical exposure history influence the biological dose estimation. Therefore, it is not possible to estimate the radiation dose from emergency operations solely on the frequency of translocation chromosomes. An assessment that takes into account the frequency of accumulated natural radiation associated with age, in addition to the number of CT scans and smoking history (number of cigarettes, etc.), is necessary to improve the accuracy. Gathering information (medical exposure and number of cigarettes) is essential for enhancing accuracy. It is expected that the uncertainty of the dose estimation, considering insufficient information and inter-individual variability, will be evaluated.

4) Investigation of cause of death

With regard to the investigation of the cause of death in 19,812 emergency workers in the nuclear power plant accident, it should be highly evaluated that the researchers were working hard to obtain consent and made efforts as much as possible for the subjects who can be followed up. Although only 3,646 (18.4%) of the study participants have given consent for the cause of death investigation, it is important to note that the process of obtaining consent was initiated midway through the study when it was initially deemed unnecessary. Given the current status of consent acquisition and even considering the potential number of participants who may provide consent in the future, analyzing the cause of death with such a sample size appears to be extremely challenging.

Solutions to address this issue will be addressed in the recommendations for the third phase.

5) Cancer morbidity investigation

The question of whether there is an increased incidence of cancer among emergency workers after the nuclear accident is a matter of significant public concern, highlighting the crucial importance of accurately understanding cancer morbidity. Consent for the use of the cancer registries has been obtained from 7,537 participants, and it is important to track cancer incidence by continually cross-checking with the national cancer registry.

However, the number of participants who have provided consent in this study falls short of half the total number of emergency workers. Consequently, the tracking of participants who have not given consent poses a challenge, and recommendations are proposed to address this issue.

Furthermore, cancer cases prior to 2015 will be supplemented by regional cancer registries. Considering the latency period from radiation exposure to cancer onset, it is likely that the number of cases during this period is relatively low. Nevertheless, for the sake of ensuring data integrity, it is deemed valuable to investigate cancer incidence in all 47 prefectures, even if conducted gradually, covering several prefectures at a time.

6) Thyroid cancer investigation

The first research topic is to utilize the data of comprehensive examination of those who were required to undergo the detailed examination in the " Study on Thyroid Survey and Others in Workers of TEPCO Fukushima Daiichi Nuclear Power Plant " project, funded by the MHLW in the 2013 fiscal year (Principal Investigator: Tomotaka Sobue, hereinafter referred to as the previous research team). As reported in the 2020 report, data was obtained from 627 individuals out of the total 2,064 participants who consented to their data being used for the NEWS study. Among them, 531 individuals (274 in the exposure group and 257 in the control group) underwent thyroid ultrasound examinations during the baseline survey. If there is a possibility of acquiring additional data from the previous research team, apart from the 627 individuals, it is recommended to continue efforts to obtain it.

The second research topic involves investigating the implementation method for conducting thyroid ultrasound examinations on approximately 20,000 emergency workers as part of the NEWS study. This topic aims to integrate data from the previous research team, as well as data from newly conducted thyroid ultrasound examinations in the NEWS study, including consent for the examinations and data on examination accuracy control. The high rates of consent obtained for the thyroid examinations are commendable, with 4,633 individuals (77.1%) of 6,006 participants in the baseline survey, and 1,101 individuals (83.0%) out of 1,326 in the first follow-up survey agreeing to participate. Additionally, training sessions have been conducted for examiners to ensure accuracy control in thyroid ultrasonography, and certified technicians have been trained. Furthermore, a thyroid ultrasonography information system has been established, through which image data and findings are transmitted to Jichi Medical University for central assessment by the Accuracy Control Committee. These achievements have been highly evaluated as they have led to the establishment of a framework for advancing thyroid ultrasonography while maintaining accuracy.

Both research topics are progressing smoothly. In the third phase, the following points and continue the investigation accordingly are expected.

Since the definition of the longitudinal study population has not been clearly stated, it is necessary to include it in the report. The subcommittee report for the fiscal year 2019 stated, “According to the guidelines of the MHLW, individuals whose effective dose exceeds 100 mSv during emergency operations should undergo thyroid tests once every 3 to 5 years.” However, the actual longitudinal survey population consists mostly of individuals with an effective dose below 100 mSv. Therefore, it is unclear how the longitudinal survey population was determined.

The data analysis is progressing smoothly. There is a slight tendency for a higher incidence rate of thyroid cancer in the population with an effective dose of 50 mSv or higher. On the

other hand, the prevalence rates of nodules, cysts, and hypothyroidism increase with age at the time of examination, but no association was observed between the effective dose and these conditions. The association between thyroid cancer and radiation dose is subject to confounding factors and bias, necessitating further detailed analysis. There are biases in the examination supply system, such as a higher rate of visits to collaborating medical institutions that are unable to perform ultrasound examinations in the low-dose group. Additionally, there is a trend of higher examination consent rates in the high-dose group. In fact, the population with higher effective doses has undergone a greater number of ultrasound examinations.

Regarding the quality control of ultrasound examinations, central assessments of primary examination images are being conducted. The central assessment rates for the participants with a dose of > 50 mSv were 66.7-72.9% in the baseline survey, compared to 47.1-50.7% in the participants with a dose of < 10 mSv. In the follow-up survey, the rates were 93.3-100% and 79.3-85.7% respectively. It is necessary to examine whether there are any systematic differences between local assessments and central assessments through a sample survey. Furthermore, accuracy control has not been implemented for image diagnosis and decisions on needle biopsy in the secondary examination. Therefore, there is a concern that compliance with the guidelines for active surveillance of micro cancers with a major axis length of less than 10 mm may vary between facilities that regularly observe a large number of thyroid cancer cases and local facilities with a smaller number of cases. It is important to be cautious about the regional variations in compliance with active surveillance guidelines, as they can be a confounding factor in the detection rate.

In conclusion, the study is progressing smoothly. However, there are factors that could introduce bias, and it is necessary to analyze their impact.

7) Cataract investigation

Cataract is characterized by the clouding of the crystalline lens, with aging being the primary and most significant risk factor. However, radiation also has a noticeable impact. Cataract can be effectively treated through surgery, allowing for the restoration of visual acuity. There is a tendency to perform surgery when cataracts are diagnosed at an early stage or with mild symptoms, which makes studying the onset mechanism and epidemiology challenging. Therefore, investigating the influence of radiation is crucial as it may provide valuable insights into the study of cataract onset mechanisms.

In this study, a significant number of screenings were conducted, examining in detail vacuoles and other changes detected through transillumination. There is a trend of early cataract surgery in recent years. Simply studying clear changes in the crystalline lens, such as

cortical cataracts, is insufficient for monitoring the progression. By detecting vacuoles, which represent early changes, using a transillumination camera, it was discovered that vacuoles can be present and detected even in individuals aged 30-40, and that visual acuity is often good despite the presence of vacuoles. These findings, obtained through the world's first large-scale study, are highly valuable.

In previous studies, the Lens Opacities Classification System (LOCS) and similar classification systems were used, which requireda high level of examiner subjectivity. Therefore, the utilization of transillumination cameras, which excel in detecting early cataract changes like the presence of vacuoles, along with the ophthalmologists' diligent research into the causes when adequate transillumination cannot be attained, are highly commendable. Nonetheless, detecting changes in vacuoles can be challenging with slit-lamp microscopy, and if this method is only available procedure, there may be difficulties in comparing and reconciling the findings of both examinations.

According to a questionnaire survey conducted among TEPCO employees, it was found that there was a higher prevalence of cataracts among individuals exposed to high radiation doses. However, it is important to consider that the accessibility for high-dose individuals to seek medical examination might have influenced the results. Additionally, there is a possibility that participants misunderstood Stage 1, which includes vacuoles detected through transillumination, as cataracts and responded accordingly. Therefore, it is crucial to clearly distinguish between the early changes in the crystalline lens and the definition of cataracts.

Human observation alone makes it challenging to standardize the results of the transillumination camera and slit lamp examination, hence the desire for AI implementation. Fortunately, the automatic detection of vacuoles has been successfully implemented. This automated method has demonstrated impressive results, achieving a sensitivity of 90% and specificity of 96%. These findings pave the way for standardization and deserve high praise.

8) Psychological impact investigation

Further analysis should be conducted to explore the dose as an exposure factor, and continuous investigation and observation of psychosocial effects, including behavior, is necessary.

When conducting analyses, it is important to adjust for major confounders, including age and educational background. Adequate consideration of confounding factors from a literature perspective, such as identifying confounding factors within the general population, is crucial when adjusting for confounders in the analysis of each event.

For life events that serve as exacerbating factors of anxiety and mood disorders, it has been reported that the following were frequently experienced within the past year: "Work-related events (promotion, reassignment, and work-related conflicts)," " illness or injury,"

"discrimination against TEPCO employees," "experience of evacuation," "family separation or living apart," as well as other personal events (marriage, divorce, relocation, traffic accidents, etc.) and family issues (illness, death, etc.). It is important to analyze which of these specific factors served as aggravating factors.

9) Health management database

The establishment of a health management database for emergency workers contributes to ongoing Personal Health Record (PHR) and the maintenance and promotion of the health of users. This idea is preferable. Long-term health surveys are expected to make significant contributions to enhancing the health of aging study participants. It may also be used as a valuable means of follow-up of study participants. In addition, it is expected to become a tool to improve the self-care of participants.

Effective feedback of information to encourage continuous participation in the study is an important issue, and health interventions using health examination data have shown numerous successes so far. Therefore, it is desirable to make further efforts to consolidate knowledge of healthcare apps. Also, health intervention may modify the outcome toward radiation effects. Therefore, it is necessary to provide detailed descriptions of how changes in lifestyle and health status resulting from these interventions are assumed to be associated with modifications to radiation damage.

Chapter II　Suggestions for the Third Phase Study

1) Research management structure

The Research Center for Prevention from Radiation Hazards of Workers at the National Institute of Occupational Safety and Health, which serves as the study headquarters, is responsible for overseeing and directing this epidemiological study, which is planned to have a follow-up of 5 years in the second phase and 30 years in the subsequent phases. The materials provided for the Third-Party Committee indicate that there are four researchers affiliated with this center, while the website mentions two researchers. However, all of them are non-regular researchers without salary increases or bonuses. It can be inferred that the study has been sustained so far through individual efforts. Nevertheless, the current composition of having only non-regular researchers in the organization is unusual and precarious, and it is not stable or attractive for both the current researchers and young researchers who may consider participating in the study in the future. If MHLW, which has been directing and sponsoring the implementation of this epidemiological study, and the Japan Organization of Occupational Health and Safety, the contract organization, recognize this study as academically significant for Japan both domestically and internationally, we propose transforming the Research Center for Prevention from Radiation Hazards of Workers into a resilient organization capable of continuing the research for the next 30 years.

Furthermore, concerns have been raised by the subcommittee about the difficulties in ensuring a study environment, stating that " we are not dedicated research institutions or personnel." Therefore, a comprehensive examination is necessary regarding the organizational structure for the implementation of the study in the third phase.

In the midst of these circumstances, there is a lack of clear division of roles between the study headquarters and each subcommittee. Although it is stated that "the final selection and examination of confounding factors in the assessment of major health effects, such as radiation exposure, will be conducted by the control of headquarters for the survey in the third phase, the positioning of the study headquarters remains a challenge. It is unclear whether the study headquarters can assume the role of the control headquarters, or if the study headquarters and each subcommittee should jointly establish and take charge of the control headquarters.

2) Follow-up of the cohort and subcommittee and study organization

Unfortunately, the number of responses and the number of new participants in the postal survey are not sufficient, and it is also not expected to see a substantial increase in the future. While we are planning to　continue recruiting new participants in the third phase, the more

important and demanding focus should be on the tracking, retention, and dropout prevention of the current study participants, numbering over 6,000. Even if the participation rate is only around 30%, a high follow-up rate will greatly enhance the reliability of the study data. To improve the follow-up rate and gain a proper understanding of the cohort's characteristics, it is necessary to understand the socioeconomic characteristics of not only the current study participants but also all emergency workers. Emergency workers belong to thousands of companies, and so, they should have diverse socioeconomic backgrounds. Additionally, various health support programs, such as cancer screenings, provided by the government and workplaces, overlap and compete depending on radiation exposure levels and other conditions. Furthermore, with participants retiring in the future, the responsibility for conducting health examinations is transitioning from workplaces to local communities. In this context, the "Expert Review Committee on the Vision of the Epidemiological Study of Emergency Workers at TEPCO Fukushima Daiichi Nuclear Power Plant", which was responsible for preparing start of this research project, has determined that cancer screenings should be included in the health examinations. However, it is currently not feasible due to budget constraints. It is necessary to evaluate the significance of conducting cancer screening every 5 years. Moreover, the incidence of cancer, particularly in the thyroid and prostate glands, has significantly increased, warranting examination of potential overdiagnosis. To ensure the long-term continuity of the cohort, it is advisable to consider integrating various initiatives at this opportunity.

The MHLW has its own database, which the NEWS study utilizes, while relevant companies have their own records. Handling them separately in each organization is inefficient. It is deemed essential to aggregate or cross-reference the data in the NEWS study.

Amid limited human and financial resources, it is important to allocate resources to necessary studies and prioritize them, while also streamlining low-priority studies. For example, the following items can be considered.

Clinical Investigation Subcommittee (I): The study that resembles the Life Span Study (LSS) cohort of A-bomb survivors is intriguing, but surpassing the LSS, except for the different radiation exposure scenario, is deemed difficult. It is anticipated that the study may not surpass NIPPON DATA and other studies in terms of population representativeness and the number of participants. We kindly request a reassessment of the significance of continuing this survey in the planning of research plan for the next 5-year term.

Clinical Investigation Subcommittee (II): The primary significance is believed to lie in the identification and assessment of necessary confounding factors. However, has this objective remained unachieved in the first and second phases?

Storage of biological samples: Blood and urine samples are stored for future research, and

blood samples are specifically stored for human genome/gene analysis. We would appreciate a consideration of the possibility to narrow down the participants and samples for blood and urine storage by clearly defining the research objectives in the thrid phase.

Taking these points into account, we kindly request the research team to thoroughly deliberate and design the implementation framework for the third phase, including the decision on potential discontinuation.

Data on confounding factors have been collected in the questionnaires in the first and second phases, and it is expected that the amount of information neccesary in the third phase will be relatively small. It is important for the central headquarters to discuss the future direction of these subcommittees. In the future, it is crucial to have the participation of researchers with high expertise in epidemiology and statistics, exceeding the current level of expertise within the team. Therefore, the supply of highly specialized researchers, particularly for the "Clinical Investigation Subcommittee (II)", is considered necessary.

Would it be worth considering the promotion of utilizing Rosai Hospital, an institution within the same organization, as the designated facility for conducting the headquarters-sponsored centralized health examinations? For instance, we could explore the possibility of establishing a specialized Research Center for Health and Employment Support, which could serve as a central point of contact. This center could be set up in multiple Rosai Hospitals, known for their proactive approach in connecting patients with society.

One of the challenges that long-term cohort studies face is the potential disruption of temporal continuity of results due to the improved performance of diagnostic instruments and laboratory measurement techniques. Variations resulting from the improvement of device performance, which may not pose a significant problem in actual clinical practice, can have a substantial impact on this epidemiological study that focuses on subclinical effects. Therefore, it is a challenging issue to address. How about considering implementation of a system to continuously monitor this problem?

As stated in the report of the Analysis and Evaluation Subcommittee (Shinji Yoshinaga), it has been reported that the original population size of this cohort is not sufficiently powered to examine the risk of cancer. Therefore, in such circumstances, it is necessary and feasible to consider methods for controlling confounding factors through continuous analysis within the future research framework. This includes measures such as the standardization of radiation dose surveys, standardization of health check-up data, and prevention of increase in the rate of follow-up loss among the participants. To achieve this, it is crucial to establish an organization capable of maintaining a long-term research system and to establish a foundation for the continuity of the study.

It is requested that the study headquarters and the subcommittees engage in discussions

and make a determination regarding the adequacy of obtaining sufficient information on social factors from the research results in the first and second phases. Additionally, they should consider whether it is necessary to obtain further information on potential new confounding factors in the future.

Social factors addressed within the Clinical Investigation Subcommittee (II) hold significant importance as information on confounding factors for analyzing health effects, including cancer. However, it is requested that the design of the third phase be determined after careful examination within the research team to ascertain the possibility of discovering additional important information beyond what has been revealed in the first and second phases. Furthermore, attention should be given to ensuring a conducive research environment for this subcommittee.

In the analysis conducted by this subcommittee, the confounding effect of alcohol consumption on systolic blood pressure was not examined in the context of the relationship between educational background and blood results. Similarly, the confounding effect of smoking was not considered in relation to white blood cell count. It is speculated that the results would have been different from what was reported if the amount of alcohol intake and the amount of smoking were also adjusted using analysis of covariance. This aspect may be due to the absence of dedicated research institutions and researchers, as mentioned by the investigator themselves.

It is essential to thoroughly examine whether it is possible to select appropriate confounding factors in the final evaluation of major health effects, such as radiation exposure.

The issues are listed as individual suggestions.

① Further investigation is needed to explore methods for controlling confounding factors and correcting bias in the identification of non-cancer diseases. Additionally, it is anticipated that there are differences in the opportunities and quality of health examinations between TEPCO workers and other workers. Therefore, it is important to analyze the factors that may impact the occurrence and prevalence of non-cancer diseases attributed to the differences between TEPCO workers and non-TEPCO workers. We look forward to future surveys and analyses that leverage the extensive experience of RERF.

② The postal survey (pilot survey) indicates that there is a potential increase in the number of participants willing to cooperate with this study after retirement, suggesting the importance of continuing the postal survey in the thrid phase.

③ The assessment of whether there is a risk of cardiovascular disease in the dose range below 500 mSv, particularly below 100 mSv, is a significant challenge in the field of radiation protection. Due to limited statistical power, significant results cannot

be expected in epidemiological surveys that rely on stochastic effects as endpoints. However, it would be an intriguing analysis if early changes in arteriosclerosis, such as calcification of the aortic arch and abdominal aorta, as well as variations in carotid intima media thickness (IMT), can be quantitatively evaluated. Therefore, it is crucial to prioritize the development of tools for the quantitative evaluation of XP and ultrasound image data for the third phase.

④ It is anticipated that in the future, a pooled analysis can be conducted between this study, which utilizes the dose of emergency radiation exposure after the Fukushima Nuclear Power Plant accident, and the epidemiological study of radiation workers conducted by the Radiation Effects Association using the radiation dose during planned radiation exposure. To ensure a smooth pooled analysis, it is important to confirm that there are no discrepancies in the questionnaire regarding confounding factors between both surveys. This aspect should also be verified in the third phase.

3) Statistical power and analytical methods

The statistical power calculation has indicated the difficulty in verifying the currently estimated risk values from epidemiological studies of A-bomb survivors. However, it is necessary to examine the power calculation specifically for thyroid cancer. In studies of A-bomb survivors, the risk of thyroid cancer from adult exposure is scarcely detected in analyses that exclude patients with micro-cancer (Furukawa et al. Int. J. Cancer: 132, 1222-1226 [2013]). On the other hand, a significant correlation with dose has been reported in analyses focusing on the endpoint of latent thyroid cancer and nodules (Ezaki et al. https://doi.org/10.1269/jrr.32. SUPPLEMENT_193). Since ultrasonography can detect micro-cancers, it has the potential to detect the presence or absence of a radiation effect on thyroid cancer that has not been included as an analysis target, either as micro-cancer or latent cancer. Therefore, a reconsideration of the power calculation is necessary.

This study should aim to investigate not only the current risk estimates but also the underlying reasons for the difficulty in estimating risks. By quantitatively elucidating confounding factors such as lifestyle habits, it has the potential to contribute to understanding the reality of radiation risks. Among the confounding factors, it is necessary to quantitatively evaluate and analyze smoking and drinking. In terms of analysis evaluation, considering the limitations and characteristics of NEWS study, it is important to acquire data necessary for investigating the occurrence of radiation effects and to conduct appropriate statistical analysis that includes confounding factors. This will ensure that the study estimates the magnitude of radiation risks.

4) Dose evaluation

The accuracy of dose estimation has been improved through research that addresses the respective dose evaluation challenges of external and internal exposure. However, due to limitations in physically measuring emergency workers' exposure, the biological dose evaluation through chromosomal aberration frequency measurement becomes crucial complementary data. History of medical exposure should be taken into consideration when analyzing chromosomal aberration. Additionally, medical exposure history serves as important information for biological dose surveys. In order to further advance the biological dose evaluation using chromosomal aberration frequency, it is recommended to also examine the estimation of medical exposure history. Some emergency workers were advised to take stable iodine preparations to avoid excessive intake of radioactive iodine. Since this factor affects the evaluation of thyroid dose, it should be taken into account when evaluating the intake of radioactive iodine through estimation, rather than relying solely on direct measurement.

5) Investigation of cause of death

This study is highly significant in investigating the radiation hazards in an unprecedented nuclear power plant accident that will be remembered in human history. It has garnered significant attention worldwide, and as a research endeavor, it is essential to analyze the entire dataset regarding deaths and causes of death as expected hard outcomes. Epidemiological studies require long-term follow-up, and ethical guidelines for research have evolved over time, with the possibility of future changes in the future. It would be a loss for humanity if the understanding of radiation hazards is compromised by biased data resulting from unpredictable guideline changes, especially considering the substantial research funding drawn from taxpayers. Obtaining informed consent is not possible due to the occurrence of fatalities. Currently, there is a focus on returning the study's findings to the public. Therefore, to establish a review committee that includes perspectives from scientific ethics, legal experts involved in research, and the general public. This committee would reconsider matters regarding the consent of study participants, exploring possibilities such as whether it is unnecessary or opt-out options are viable.

6) Cancer morbidity investigation

To track cancer incidence, data up to 2015 were collected and matched with the regional cancer registry, while data from 2016 onwards were matched with the national cancer registry. The regional cancer registry is responsible for managing cancer incidence up until 2015 in all 47 prefectures, and as of 2023, it is believed that the data is largely complete. Conducting

the investigation once is deemed sufficient, and there is no need for future implementations. It is considered feasible to gradually carry out the investigation.

The low rate of obtaining consent has been a bottleneck for the national cancer registry. However, there is a possibility that consent is not set as a mandatory condition in Article 17 of the Act on Promotion of Cancer Registry. This article stipulates the provision of national cancer registry information by the MHLW for "research studies on cancer necessary for planning or implementing national cancer control measures."

While it is essential to avoid the misuse of consent exemption for ethical reasons, it is worth considering the applicability of consent exemption under the mentioned article in consultation with the responsible section in the MHLW. This consideration takes into account the social importance of the study and the fact that it represents the sole opportunity to learn from the Fukushima Nuclear Power Plant accident, acknowledging its irreplaceable nature.

7) Thyroid cancer investigation

The report indicating a significantly higher standardized incidence ratio (SIR) of thyroid cancer can be understood in light of existing findings. If the morbidity used to calculate the expected value is based on the clinical incidence of thyroid cancer, the expected value will be calculated to be smaller. As mentioned in the report's comment, over-detection by screening may inflate the observed value, resulting in an overestimation of the SIR. In order for the SIR to be scientifically valid, expected values should be calculated based on the thyroid cancer morbidity, including early-stage thyroid cancer that does not exhibit clinical symptoms in the general population undergoing screening. However, the International Agency for Research on Cancer (IARC) recommends against thyroid screening for the general population following a nuclear accident*. In other words, it is not advisable to recruit non-exposed individuals who have not participated in disaster prevention activities and conduct thyroid cancer screening anew. Therefore, if information on the thyroid cancer morbidity in the general population is found through existing thyroid screening, it is recommended to recalculate the SIR using that information. If no existing information is available, the change in morbidity according to radiation dose will be examined within the study population recruited until the second phase, considering a low-dose exposure group (criteria for group classification are subject to discussion) as a control group. However, it is important to appropriately adjust the confounding factors (candidates) in the final model. This includes factors such as the screening rate and frequency of examinations by the same individual, differences in image assessment accuracy between central and local assessments, and whether there are any dose-related differences in adherence to guidelines from academic societies recommending active surveillance instead of immediate surgery for micro-cancers,

as pointed out in Chapter I, as these factors can influence the detection rate.

* IARC TECHNICAL PUBLICATIO NO.46, THYROID HEALTH MONITORING AFTER NUCLEAR ACCIDENTS, 2018.

8) Cataract investigation

In the last year of the second phase, it is desirable to verify the comparison and consistency of findings between transillumination and slit lamp examinations for Vacuoles, which represent the early stage of posterior subcapsular opacity, as they are prone to bias caused by medical examination.

In the third phase, the following aspects are expected. Firstly, in analyzing the relationship between radiation dose and cataracts, it is important to clarify the definitions of "cataract" and "changes in the crystalline lens." It may be preferable to use terms such as "Stage 1" or "Stage 2 and above" instead of "changes in the crystalline lens" or "cataract" to minimize subjectivity. Secondly, as cataract surgeries are often performed at an early stage nowadays, it is necessary to clearly define the endpoints when evaluating the long-term effects of radiation. Considering that the radiation effects in this case might be very small and may not be classified as cataract but rather as Stage 1, it is recommended to perform analyses with endpoints placed solely in Stage 1, as well as analyses considering cataracts including Stage 2 and above. However, it should be noted that TEPCO employees, who undergo frequent screenings, may have a higher detection rate for cataracts and changes in the crystalline lens. While aging is the primary risk factor for cataract development, it is advisable to consider other risk factors besides age. If radiation dose is a concern, it is necessary to take into account occupational radiation exposure in addition to medical radiation exposure. Lastly, it is acknowledged that there is a potential for bias in evaluations based on human observations, and therefore, further utilization of AI is encouraged.

9) Psychological impact investigation

As we continue with the further analysis using radiation dose as an exposure factor, it is crucial to conduct ongoing and detailed investigations of the psychological and social impacts, including behavior.

In the follow-up survey, the events such as retirement, unemployment, and the presence of isolation or loneliness are planned to be measured. It is important to always verify the chronological sequence of these events and, during the evaluation, carefully examine the interrelationships among the factors and be cautious about the possibility of reverse causality.

Therefore, in order to achieve the initial objective of elucidating the mid- and long-term mental health of emergency workers, it is recommended to continue conducting thorough

follow-up surveys and analyses. It is speculated that the influence of events occurring during follow-up on the association between exposure factors and outcomes is not straightforward, thus necessitating investigation and analysis to clearly understand the interrelationships among the factors.

10) Health management database

If behavior change is expected to observe through the use of a database, it will be insufficient to have information merely on the deviation of health examination data from reference values. It is important to incorporate thoughtful measures, such as utilizing algorithms derived from reliable sources like NIPPON Data, to provide evidence-based risk assessments.

Considering the purpose of constructing a database for the lifelong and comprehensive monitoring of overall health status, it is necessary to conduct ongoing discussions and considerations for sustainable business continuity, including financial support.

Chapter Ⅲ Evaluation of the Second Phase Study and Suggestions for the Third Phase Study [Summary]

The NEWS is conducted utilizing information provided from the government-created and maintained database in collaboration with TEPCO, while also inviting participants. As a result, the cumulative number of study participants reached 8,023 over a period of 6 years since the study began, and the cumulative number of workers who received health examinations reached 6,286, highlighting the importance of recognizing the participants' understanding and the efforts made by the researchers.

The characteristics were observed in attributes such as affiliated company, age, educational background, and marriage rate as well as in the prevalence of hypertension, diabetes, and cardiovascular diseases when observed by exposure dose group in the baseline survey. It was indicated that potential confounding factors should be identified among these characteristics, and after understanding methods to control for confounding, the causal relationship between exposure dose and disease onset should be investigated.

The calculation of statistical power in the second phase demonstrated that, over a 40 years of follow-up, the maximum statistical power for detecting any type of cancer was approximately 10%. However, it is crucial to elucidate the survey methodology for patients with non-cancer diseases and the measurement techniques used. This investigation should aim to determine which indicators can be used to control confounding in the analysis of the relationship between radiation exposure dose and non-cancerous diseases, as well as whether bias can be corrected. Despite the low statistical power, the significance lies in the ability to disseminate evidence-based information from the perspective of worker health management, emphasizing that lifestyle improvements, rather than radiation risks, contribute to risk reduction, considering the high quality of dose measurement and thorough investigation of confounding factors.

In the second phase, significant associations were observed between educational background and variables such as systolic blood pressure, white blood cell count, HbA1c, and γ GTP. Even after adjusting for age, an inverse association was observed between educational background and smoking as well as drinking habit. Additionally, a similar inverse association was found between annual income and smoking. These results support the general hypothesis that higher education is associated with higher health literacy, indicating that these social factors can be confounders in epidemiological studies focusing on cancer and non-cancer diseases as endpoints.

In the second phase, the crystalline lens equivalent dose from β-rays was estimated based on the indicated value of the personal dosimeter. The β / γ dose ratio was estimated through simulation, and an experiment was conducted to assess the β-ray shielding performance

using a full-face mask. As a result of this experiment, a correction factor was calculated to convert the indicated value of the personal dosimeter to the crystalline lens equivalent dose from β-rays, enabling the accurate estimation of β-ray doses to the crystalline lens that could not be directly measured by the dosimeter. Regarding the evaluation of internal exposure dose, it became possible to estimate the dose contribution of each nuclide by utilizing the effective dose as the combined dose of iodine and cesium. This improvement enhances the accuracy of estimating organ doses resulting from internal exposure. Using information obtained from WBC, a foundation was established for estimating thyroid doses in workers where I-131 was not detected. This estimation was based on factors such as the ratio of air concentrations between I-131 and Cs-137. Additionally, an estimation method was developed using the inventory ratio inside the reactor to determine the contribution from short half-life nuclides (e.g., I-132 and Te-132) to thyroid dose. This method proves effective for estimating doses from short half-life nuclides.

The biological dose evaluation, using the frequency of translocated chromosomes as an index, serves as a validation of the accuracy of physically estimated organ doses. Currently, an analysis is being conducted on 74 workers with an effective dose ≥70 mSv.

It is commendable that researchers have made diligent efforts to obtain consent and have made considerable efforts to follow up with the participants who can be traced in the investigation of the cause of death. However, even considering the number of participants expected to provide consent in the future, analyzing the cause of death may still be challenging due to the limited sample size.

The question of whether the cancer incidence increases in radiation workers after the nuclear accident is a matter of significant social concern. Thus, needless to say, it is very important to grasp the accurate cancer morbidity. Consent for the use of the cancer registry has been obtained from 7,537 workers, and it is crucial to track cancer incidence by continuously cross-referencing with the national cancer registry. However, since consent has been obtained from less than half of all emergency workers, tracking individuals without consent remains a challenge.

In the thyroid cancer investigation, the first research topic focuses on utilizing the data from the previous research project led by Prof Tomotaka Sobue(as mentioned earlier). As reported in the 2020 report, data from 627 individuals who consented to the use of their data for the NEWS study were obtained out of the total 2,064 participants. If there is a possibility of acquiring additional data from the previous research team beyond the 627 individuals, continued efforts should be made to obtain it. The second research topic involves the integration and collection of data from the previous research project, as well as the newly conducted thyroid ultrasound examinations in the NEWS study, consent for

these examinations, and accuracy control of the examinations. An information system for thyroid ultrasound examinations was established, whereby image data and findings were sent to Jichi Medical University for central assessment by the accuracy control committee. This system allows for the implementation of thyroid ultrasound examinations while maintaining accuracy, and it is highly regarded as an achievement.

In the cataract investigation, a considerable number of individuals underwent thorough examinations, specifically analyzing vacuoles and others detected through the transillumination method. This detailed examination allows for accurate assessment. Notably, there is a growing trend of early cataract surgery, and the detection of vacuoles, an early change, through transillumination cameras has been observed. The results have revealed that vacuoles can be detected even in individuals aged 30-40 years, and the presence of vacuoles does not necessarily indicate poor visual acuity. These findings, obtained through the world's first large-scale study, hold significant value. Therefore, this can be evaluated with the results of the world's first large-scale study. The use of the conventional LOCS and similar classification systems for comparing and ensuring the consistency of examination findings has been a challenge. It is necessary to clearly distinguish between early changes in the crystalline lens and the definition of cataract.

In the psychological impact investigation, it is important to conduct further analysis using radiation dose as an exposure factor, while adjusting for major confounding factors, including age and educational background. It is crucial to thoroughly examine the confounding factors from a literature perspective, considering "What factors may act as confounders in the general population?" when adjusting for confounders during the analysis of each event.

The idea of establishing a health management database for emergency workers and conducting lifelong comprehensive health surveys (Personal Health Record or PHR), as well as contributing to the maintenance and improvement of users' health throughout their lives through its utilization, is considered favorable. Long-term health surveys are expected to play a significant role in enhancing the health of study participants as they age. It may also be used as a useful means of follow-up for participants. Moreover, there is an expectation that it will serve as a tool to enhance the self-care of the participants.

Suggestions for the Third Phase Study

Research Center for Prevention from Radiation Hazards of Workers at the National Institute of Occupational Safety and Health, serving as the study headquarters, oversees and directs this epidemiological study, which is planned to have a follow-up period of 5 years in the second phase and 30 years in subsequent phases. As all researchers are non-regular staff and the organization tasked with continuing the survey for the next 30 years is deemed

vulnerable, it is suggested that the MHLW, which provides guidance and sponsorship for this epidemiological study, and the Japan Organization of Occupational Health and Safety, the contracted agency, transform this center into a resilient organization capable of enduring the 30-year follow-up period. Furthermore, since the subcommittees are not exclusively dedicated to this study, securing a conducive research environment becomes challenging, necessitating substantial improvement in the implementation structure for the third phase.

The most important and demanding aspect is the tracking, retention, and prevention of dropouts among the current cohort of over 6,000 participants. In order to improve the follow-up rate and gain a proper understanding of the cohort's characteristics, it is necessary to comprehend the socioeconomic backgrounds of not only the study participants but also all emergency workers. Emergency workers belong to numerous companies, numbering in the thousands, and exhibit diverse socioeconomic profiles. In addition, various support programs offered by the government and workplaces, such as health examinations, are overlapping and competing with each other depending on factors such as radiation exposure dose.

Amid limited human and financial resources, it is important to allocate resources to necessary studies and sort out low-priority studies through streamlining by integrating projects.

The main issues are listed as individual suggestions.

① Further examination is needed to explore ways to control confounding factors and correct bias in non-cancer disease identification.

② It is desirable to continue the postal survey in the third phase due to the retirement of participants.

③ It is considered important to develop tools for the quantitative evaluation of image data from XP and ultrasonography for the third phase.

④ In order to conduct a pooled analysis between this study and the epidemiological study of radiation workers conducted by the Radiation Effects Association, it is important to ensure consistency in the questionnaire on confounding factors between both studies.

⑤ Quantitative evaluation and analysis of confounding factors such as lifestyle habits including smoking and drinking are necessary.

⑥ The evaluation of biological dose by measuring the frequency of chromosomal aberration is important as complementary data for dose assessment.

⑦ It is recommended to establish a review committee to discuss the feasibility of investigating the causes of death among all emergency workers.

⑧ It is worth considering the applicability of consent exemption for cancer incidence

survey.

⑨ In the thyroid cancer survey, confounding factors (candidates) should be appropriately adjusted in the final model.

⑩ It is desirable to compare the findings of vacuoles, which indicate the early stage of cataracts, using transillumination and slit-lamp microscopy.

⑪ In the psychological impact survey, it is necessary to continue conducting ongoing observations and investigations into psychosocial effects, including behavior, while further analyzing the dose as an exposure factor.

⑫ Efforts should be made in the health management database to provide evidence-based risk assessment, and it is necessary to consider various aspects, including financial support, for the establishment of a lifelong database.

Attachment

Research management structure

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Hokuto Hoshi	Clinical Investigation (II)	The Hoshi General Hospital
Kotaro Ozasa	Cause of death/ cancer morbidity	Health Management Center, Kyoto Prefectural University of Medicine
Tomotaka Sobue	Thyroid cancer survey	Division of Environmental Medicine and Population Sciences, Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine
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Headquarters and Sub-Investigation Committee Reports

1. Epidemiological Survey Headquarters

Principal Investigator: Toshiteru Okubo

In the operations for responding to the accident at TEPCO Fukushima Daiichi Nuclear Power Plant, the emergency radiation exposure dose limit for emergency workers was increased from 100 mSv to 250 mSv from March 14 to December 16 in 2011. It is estimated that 19,812 workers were engaged in the operations during this period and 174 workers were exposed to more than 100 mSv, which is the 5-year dose limit for normal work. The dose in the rest of the workers was less than 100 mSv, and the total dose was less than 10 mSv in the majority. The purpose of this study is to follow up the health effects of emergency operations in all of these emergency workers throughout their lifetime.

We have been asking the target subjects of 19,812 workers to participate in the study since the start of this study in 2014. The results until December 31, 2022 were as follows: 8,023 (40.5%) agreed to participate in the study; 3,843 (19.4%) refused participation; 4,992 (25.2%) did not respond; 1,734 (8.8%) with unknown addresses; 757 (3.8%) died; and 463 (2.3%) for others. Of the participants, 1,345 answered that they would only cooperate with the study such as questionnaires but not undergo health examinations provided by the study. Of those who wished to undergo health examinations, 6,286 (31.7%) underwent health examinations planned by the study group. A total of 419 workers wished to undergo health examinations but did not because of personal reasons or lack of nearby cooperating institutions.

The places of residence of study participants are distributed nationwide, and there is no other way than establishing study cooperating institutions in each prefecture to promote the health survey of all subjects. Thus, we asked at least one medical institution that mainly conducts health examinations for workers in each prefecture to cooperate in the study and asked healthcare professionals who were in charge of health examinations such as public health nurses of the contract institutions to become study collaborators. The number of cooperating institutions has been decreasing and there are currently about 60 institutions.

At the time of health examinations at each medical institution, blood and urine samples are collected and laboratory tests are performed. There were considerable differences in the test accuracy between institutions at the start of the study. Therefore, all samples collected in various places in Japan were sent to a laboratory in Tsukuba City, Ibaraki Prefecture for centralized analysis. In addition, a portion of blood and urine was dispensed for storage and frozen at -80℃ so that past biochemical changes can be investigated if any health abnormality is observed in emergency workers in the future.

A health examination with multiple items which is performed at the first time of participation in the study is called a "baseline health examination," and the second and subsequent examinations are called "Lx health examination." The above number of those undergone the baseline health examination does not include L1 health examinations.

To date, the numbers of subjects who have undergone the L1 health examination (the first follow-up examination after the baseline examination) by fiscal year were, 7 in 2019, 1,130 in 2020, 1,014 in 2021, and 1,116 in 2022 (including subjects to undergo health examinations), with a total of 3,267. Since the baseline health examination was conducted over a long period of 5 years, it is expected that some more workers will undergo the health examination in the future. However, it may be necessary to consider making another effort to encourage them to continue the examination. In FY 2022, those who wished to have a health examination since the beginning of the study in 2014 but were waiting for it accounted for only 5.2% of all workers who wished to participate in the study.

As for the relationship between the exposure dose and age at the time of emergency operations, the mean age in the group with exposure dose of < 5 mSv was the highest at 53.4 years (SD11.0). The mean age was the lowest at 49.6 years (SD10.7) in the ≥ 100 mSv group. The marriage rate was the highest at 88.7% in the ≥ 100 mSv group and the lowest at 78.8% in the 10 - < 20 mSv group. As for the educational background, the percentage of university graduates or higher was the highest at 41.0% in the < 5 mSv group and the lowest at 21.7% in the ≥ 100 mSv group. The percentage of high school graduates was the lowest at 39.8% in the < 5 mSv group and the highest at 70.8% in the ≥ 100 mSv group. When comparing the percentage of people assigned to control the nuclear reactor by exposure dose, the percentage was the highest at 56.6% in the ≥ 100 mSv group, followed by 43.7% in the 50 - < 100 mSv group, and the lowest at 13.5% in the < 5 mSv group.

During the 10-month emergency operation period when the exposure limit was increased, the percentage of those who worked for ≥ 7 months was the highest at 69.2% in the 50 - < 100 mSv group, followed by 68.9% in the ≥ 100 mSv group. On the other hand, the < 5 mSv group showed a relatively low percentage of 6.9%. In the < 5 mSv group, the percentage of those who worked for 1 - 3 months was the highest at 75.2%.

In this study, "multi-item health examinations" equivalent to comprehensive medical examinations are conducted once every 5 years and "basic health examinations" equivalent to statutory regular health examinations are conducted every year for the participants. The first round of the multi-item health examination is called the baseline health examination considering the start of this cohort study. After explaining the purpose of the study to the first examinees, we asked them to give consent to the use of the health examination results and to give their own hand-written signatures of their agreement. Then, we asked them to

complete a detailed questionnaire about their previous health history.

Among the questions related to past illness, the subjects with thyroid diseases and cataract tended to be significantly more in the high-dose group. The percentages of hypertension and dyslipidemia tended to be higher in the groups with higher exposure dose, but no relationship with the exposure dose was observed in the subjects with a history of cancer or cardiovascular disease.

Next, the relationships of the health examination results to the contents of operations and the exposure dose are described. We examined the relationships of the exposure dose and the contents of operations in the baseline examinees with (1) peripheral blood test values, (2) parameters related to the so-called metabolic syndrome such as liver function tests, glucose metabolism, lipid metabolism, blood pressure, and obesity, (3) renal function parameters, and (4) C-reactive protein, prostate-specific antigen, and pepsinogen I/II ratio. As a result, statistically significant differences between groups by exposure dose were observed in hematocrit, neutrophils, eosinophils, platelet count, alkaline phosphatase, leucine aminopeptidase, gamma-GTP, systolic blood pressure, abdominal circumference, calcium, and inorganic phosphorus. Also, statistically significant differences between groups by operation were observed in hemoglobin, hematocrit, mean corpuscular hemoglobin concentration, white blood cells, total bilirubin, lactate dehydrogenase, alkaline phosphatase, leucine aminopeptidase, gamma-GTP, total cholesterol, HDL cholesterol, triglyceride, systolic blood pressure, abdominal circumference, creatinine, uric acid, chloride, calcium, and pepsinogen I/II ratio. However, all these statistical differences were incidental and were not considered significant when observed by dose or operation.

The above report is the result of investigating the diagnosis results only once, and it cannot deny that the result may be different if the long-term observation is continued.

The objective of this study is to observe the health effects of radiation exposure due to repain operations of the nuclear power plant accident. According to past studies, the biggest concern is the increase in the incidence of cancer. However, the subjects are limited to those who engaged in emergency operations immediately after the accident at the Fukushima Nuclear Power Plant, and the total number is limited. When the observation target is limited to cancer, the statistical power is not sufficient. If we make all cancers the study target, we have to follow up for at least 40 years to detect a significant increase. It is also meaningful to study the safety thresholds for future nuclear operations to ensure that no significant increases are observed. However, instead of limiting the target disease to cancer, simultaneous monitoring for more prevalent cardiovascular diseases should also be considered. Also, attention should be directed to variables that are measured simultaneously in all target subjects as continuous variables, such as blood pressure and many biochemical changes.

2. The Clinical Investigation Subcommittee (I)

Subcommittee Chair, Co-Investigator: Waka Ohishi
Co-Investigator: Hiroko Kitamura

1. Evolution of Research Objectives

   1) In the first phase of the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers from fiscal years (FYs) 2014 to 2018, the Clinical Investigation Subcommittee (Chair: Toshiteru Okubo) was established at the Radiation Effects Research Foundation (referred to as "RERF") as the lead institute. The subcommittee conducted initiatives to encourage participation in the study and health examinations among emergency workers, as well as implementing nationwide health examinations. In the second phase starting from FY 2019, with the relocation of the lead institute from RERF to the National Institute of Occupational Safety and Health (referred to as "JNIOSH"), the research headquarter also transitioned to JNIOSH. Therefore, in FYs 2019-2020, the Subcommittee I transferred the work of this epidemiological study to JNIOSH and provided support to the research headquarter at JNIOSH.

   2) In FY 2019, our objectives were to transfer tasks related to this epidemiological study to JNIOSH, assist and support tasks related to health examinations, and plan and execute the transfer of paper documents, electronic records, and electronic storage media related to epidemiological study collected and preserved in the first phase at RERF to JNIOSH.

   3) In FY 2020, the objective was to plan and execute the transportation of biological samples related to this epidemiological study collected and preserved in the first phase at RERF to JNIOSH. Also, we aimed to conduct a pilot mail survey targeting non-responders to the invitation to participate in this epidemiological study (those who did not respond to previous invitations for study participation or health examinations), and transfer the survey operation to JNIOSH in FY2021.

   4) In FY 2021 onward, with the assumption that the relationship between individual exposure dose and the prevalence and incidence of non-cancer diseases such as lifestyle diseases will be examined in the future, we aim to create an algorithm for identifying individuals with non-cancer diseases.

2. Summary of study results (major outcomes since the start of the study)

< Publication of papers >

・ Kitamura H, Okubo T, Kodama K; Nuclear Emergency Workers Study Group. Epidemiological study of health effects in Fukushima nuclear emergency workers -study

design and progress report. Radiat Prot Dosimetry, 2018,182: 40-48.

- Kitamura H, Ohishi W, Kodama K, Ohkubo T. Epidemiological study of health effects in Fukushima Emergency Workers: Progress report on the Health Examination Study, 2016-2019. Environmental Advances 9 (2022) 100275.

< Presentation at academic conferences >

- Waka Ohishi: Epidemiological study of emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant: Overview of Clinical (Health Examination) Study based on Experience in the RERF Adult Health Study. The 2nd Epidemiological Study Conference for emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant (Mar. 11, 2016)
- Kitamura H, Kodama K, Okubo T. Epidemiological study of health effects in Fukushima nuclear emergency workers—Study design and progress report. UNSCEAR Technical Events in Japan to Present the Highlights of UNSCEAR Reports on Levels and Effects of Radiation Exposure due to the Fukushima Accident. (2016.11.14-11.15)
- Kitamura H, Okubo T, Kodama K. Epidemiological study of health effects in Fukushima nuclear emergency workers (Nuclear Emergency Workers Study: NEWS)--Study design and progress report. 15th Coordination and Planning Meeting of the WHO REMPAN Collaborating Centers. (2017.7.3-7.5)
- Hiroko Kitamura: Epidemiological study of emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant: Report on trends of study participants and the initiatives to encourage the participation in the study. The 4th Epidemiological Study Conference for emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant (Mar. 14, 2018)
- Kitamura H, Okubo T. Baseline Survey of the Epidemiological Study of Health Effects in Fukushima Emergency Workers. WHO REMPAN Webinar "Public Health consequences of Fukushima nuclear disaster: 10 years towards recovery". (2021.3.23)
- Hiroko Kitamura, Waka Ohishi, Kazunori Kodama, Hitomi Fujise, Shoko Kawanami, Toshiteru Okubo. Epidemiological study of emergency workers at TEPCO Fukushima Daiichi Nuclear Power Plant - Summary of the results of health examination in the 1st phase -. The 94th Annual Meeting of Japan Society for Occupational Health. (May 18-21, 2021)
- Hitomi Fujise, Hiroko Kitamura, Misa Imaizumi, Michiko Yamada, Waka Ohishi, Toshiteru Okubo. Epidemiological study of health effects of radiation workers - Mail survey. The 31st National Council of Japan Society for Occupational Health. (Dec. 3-5, 2021)

< Results from FY 2019 to 2020: Succession of research work from RERF to JNIOSH >

- We created an attachment to the research plan regarding the method and procedure for

transferring epidemiological research-related materials and biological samples that had been collected during the first phase and stored at RERF to JNIOSH, obtained the approval from the IRB, and carried out the work.

-- Transfer of documents: It was approved by the IRB on March 6, 2020, and the transfer of paper documents, electromagnetic records, and electronic storage media from RERF to JNIOSH was completed by the end of March 2020.

-- Transfer of biological samples: It was approved by the IRB on November 20, 2020, and the transfer of samples from RERF to JNIOSH was completed on December 2, 2020.

< Results in FY 2020: A pilot mail survey to encourage the participation in this epidemiological study among non-respondents >

・ In preparation for full-scale implementation of the mail survey since FY 2021, a pilot study was conducted with the following objective: (1) to understand the characteristics of mail survey respondents, (2) to try and evaluate measures to improve response rates, (3) to link mail survey respondents to study participation and health examinations, and (4) to confirm whether there are any areas that need improvement in the questionnaire for the mail survey.

-- The response rate to the mail survey of the 913 individuals who have never responded to previous mail invitations for study participation or health examination was 18.0% (164 individuals).

-- In order to improve the response rate for future mail surveys, several measures were considered, including sending a notice letter one week before the survey materials, including a ballpoint pen with the materials, presenting Quo cards to respondents at a later date, and sending a reminder postcard 10 days before the deadline.

-- Approximately 99% of the 164 respondents to the mail survey answered an optional questionnaire, and 62.3% selected "wished to participate or cooperate in the study" as the reason for cooperating in the survey.

-- Among the respondents to the optional questionnaire, 46.6% selected "I want to have a health examination of NEWS" and 15.5% selected "I want to know a little more about it."

✓ Based on the above, it was considered that the mail survey of non-respondents to encourage the participation in this epidemiological study is a method that contributes to improving the rate of participation in the study and health examination.

✓ The mail survey operations were handed over to JNIOSH in FY 2021.

< Results in FY 2021: Establishment of a process for identifying individuals with non-cancer diseases (pilot study) >

・ In this epidemiological study, the relationship between individual exposure dose and the prevalence and incidence of non-cancer diseases such as lifestyle diseases is expected to be investigated in the future. To achieve this objective, it is necessary to establish a process to more surely identify individuals with non-cancer diseases to be followed up.

Therefore, in the fiscal year 2021, a pilot study was conducted with the aim of identifying patients with hypertension and B/C type hepatitis, using the baseline survey data of all subjects undergoing health examinations in this epidemiological study. The survey aimed to (1) identify patients with the respective diseases and (2) compare them with those who were self-reported in the self-administered questionnaire. An algorithm was developed to extract patients with the respective diseases, and the usefulness of the algorithm was evaluated by dividing it into two types: (1) prioritizing self-reported information and (2) prioritizing objective information.

-- The results showed that the algorithm prioritizing objective information may be more reliable in identifying people with hypertension and hepatitis B/C. However, because objective information such as blood pressure measurements and hepatitis virus marker values can be affected by therapeutic interventions in all diseases, it was suggested that combining information from a self-completed questionnaire (health and lifestyle questionnaire) on past and current history of illness, drug information, etc., is important for a more accurate identification of people with the relevant diseases.

✓ Creating an algorithm to identify patients with non-cancer diseases is useful as a process, but the reliability of self-reported information is limited. Therefore, it is crucial to carefully examine the contents of the data and select and combine appropriate objective information to improve the accuracy of identifying patients with the targeted diseases.

< Objectives of the third phase >

We will proceed with creation of an algorithm to identify patients mainly with non-cancer diseases and precancerous lesions which are suggested to be related to radiation exposure in atomic bomb survivors. At the same time, we will consider the method for evaluating the objective accuracy and reliability of necessary objective information (imaging tests, etc.) for the algorithm.

3. The Clinical Investigation Subcommittee (II)

Subcommittee Chair, Co-Investigator: Hokuto Hoshi

In investigating the long-term health effects of radiation exposure in emergency workers involved in the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers (NEWS), the Subcommittee II conducted a study to clarify confounding factors such as employment and living background of emergency workers, social factors such as industrial health and medical treatment environment, etc., and their health effects as well as to understand the social background of the subjects required for medical examination and subsequent guidance.

At the Third-Party Committee meeting in 2019, it was pointed out that "the handling of confounding factors is crucial to this study, and it should be clarified that the responsible department is the research headquarters." In response to this, it has been confirmed that the department responsible for handling confounding factors is the research headquarter at the National Institute of Occupational Safety and Health (JNIOSH). Therefore, the research headquarters will select and review confounding factors in the final evaluation of major health effects such as radiation exposure. On the other hand, the Subcommittee II is intended to provide information on the social factors of emergency workers and their actual conditions. The results of this sub-study (Subcommittee II) will contribute to the research as reference information for the entire study.

This sub-study has been continuously conducted from the start of the first phase of the NEWS study, and the following contents and results are presented.

The first phase

(1) Literature research on employment and living background, etc. at the time of emergency operations (FY 2015)
(2) Interview survey with business operators involved in the operations (FY 2015-2016)
(3) Summary of the above surveys and consideration of the method for classifying emergency workers based on the survey (FY 2017)
(4) Pilot of a prototype questionnaire based on the above discussion (FY 2018)

The second phase

(5) Examination of the health effects of social factors by the existing questions (education background, etc.) (FY 2019)
(6) Examination of the significance of the new questions (experience of evacuation, annual income, etc.) as social factors (FY 2020)

(7) Examination of the relationship between the new questions (experience of evacuation, annual income, etc.) and exposure dose (FY 2021)
(8) Examination of the relationship between the new questions (experience of evacuation, annual income, etc.) and BMI/blood pressure (FY 2022)

In addition, we are continuously conducting on-site surveys to confirm whether there are any events that could potentially affect clinical studies, such as trends in disease onset among emergency workers.

In the study described in (1), we conducted a literature review of the employment and living conditions of emergency workers mainly using press materials. However, there were many unclear points.

In the study described in (2), we surveyed emergency operation personnel from 12 companies with a large number of emergency workers through interviews and written responses.

Based on these results, in the study described in (3), we classified emergency workers into the following four categories [1]-[4] based on their employment and living backgrounds.

[1] Temporal classification

(1) Super emergency operation period (around March 2011)
(2) Operation environment preparation period (around April to June 2011)
(3) Late emergency operation period (around July to October 2011)
(4) Decommissioning work period (November 2011 to present)

[2] Employment pattern classification

(1) Long-term employment/long-term low-dose pattern
(2) Long-term employment/temporary high dose pattern
(3) Short-term employment/planned period pattern
(4) Short-term employment/dose limited pattern

[3] Personal background classification

(1) Locally recruited
(2) Unaccompanied assignment
(3) Short-term worker

[4] Employment status classification

(1)	Still working and working on 1F at least once a week
(2)	Other workers
(3)	Retired

Since some of them can be classified from the data obtained in the NEWS study, it is considered that the following two points should be newly confirmed in the clinical research.

(1)	Presence/absence of disaster-affected/evacuation life due to earthquake/nuclear accident
(2)	Employment status when engaged in emergency operations

We asked questions about the presence or absence of experience of evacuation, period of evacuation, and state of returning home for the above item (1) and about the employment status (no fixed term, fixed term, etc.,), presence or absence of specialist job, and annual income at the time of emergency operation engagement (2011) for the above item (2) by the questionnaire. We prepared an actual questionnaire and tested them in the study (4), and the questions were included in the first follow-up survey.

"Evacuation experience" asked in this question refers to the fact that the respondents needed to evacuate as residents due to the Great East Japan earthquake and the Fukushima Daiichi Nuclear Power Plant accident in 2011. It was not about the evacuation under the operational instruction by TEPCO, etc.

In the "baseline survey," the first clinical survey, questions were also asked about social factors such as education background of emergency workers, contents of emergency operations, etc. We first examined the relationship between the education background and clinical survey results in order to examine the evaluation method for the effects of social factors in the future (study (5)). As a result, the following were found.

(1)	The education level greatly varies depending on the age of the target population at the time of the earthquake. This seems to be an effect of the background of the times when respondents were students.
(2)	The contents of emergency operations greatly vary depending on education background. For example, those with junior high school as the education background were engaged in construction work more than others.
(3)	Differences in education background were considered to be related to some blood

test results, medical history, and blood pressure (systolic blood pressure) in particular. (There was statistically significant difference in education background among all pairs of junior high school graduates, high school graduates, university graduates, and graduate school graduates ($p < .001$), and blood pressure was higher in those with lower education background.)

(4) Although the influence of age and lifestyle is considered to be great, a certain trend was observed even after adjusting for age (particularly for systolic blood pressure), suggesting that education background may cause differences as an independent factor.

(5) However, education background is complicated in the first place and greatly varies depending on employment and living background and the background of the times. Therefore, it seems to be problematic to use it as a certain social factor in this study, and other social factors that are evaluable from a perspective of natural science were necessary.

(6) Many of the responses to the contents of emergency operations were "others," suggesting that it was inadequate to estimate the radiation exposure from the results of this question. Other detailed dose evaluations were considered necessary to grasp the individual doses.

In this study, the relationship between education background and blood pressure, etc. was not examined by adjusting for information on lifestyle. If necessary for the study in the future, the relationship between education background and clinical survey results will be re-examined after taking account of lifestyle factors.

In the study (6), we examined the validity of the questions (experience of evacuation and employment status at the time of emergency operations, etc.) newly asked in the first follow-up survey based on the results of 383 subjects that we could summarize at the time of preparation of the research report in FY 2020. As a result, the following were found.

(1) About 1/5 of the emergency workers may have experienced evacuation, and the higher percentage of the workers seem to have experienced evacuation soon after the earthquake (accident). (The percentage of subjects, who had experienced evacuation life, started emergency operation engagement was 34% in March, 29% in April, and 12-13% in May and after in 2011.)

(2) Annual income is said to be a representative indicator of social factors that are quantitative and easy to evaluate, but its significance greatly varies depending on age, and therefore it is necessary to further investigate the evaluation method.

(Young people are mainly at the level of lower incomes. As the age rises, the income increases. But it decreases again in older people.)

According to these results, we decided that the significance of social factors would be evaluated in the future, particularly based on the response results of evacuation experience and annual income at the time of emergency operations.

In the study described in (7), the relationship between the experience of evacuation and annual income at the time of emergency operations and cumulative exposure dose during emergency operations was examined based on the results of 1,294 subjects in the first follow-up survey aggregated at the time of preparation of the research report in FY 2021. As a result, the following were found.

In the subjects of this study, the cumulative exposure dose during emergency operations correlates with the annual income at the time of emergency operations and the presence/absence of experience of evacuation. (The exposure dose is higher in the subjects with relatively high income and experience of evacuation. (See Table 1))

Table 1 The distribution of cumulative radiation exposure by annual income and experience of evacuation at the time of emergency operations (From the FY 2021 annual report)

		Cumulative exposure dose for emergency operations (mSV)									
		<5.0		<20.0		<50.0		50.0≤		n	Percentage of the total
Annual income (10,000 yen)	<200	44	(53.0%)	28	(33.7%)	11	(13.3%)	0	(0.0%)	83	6.5%
	<400	79	(44.9%)	67	(38.1%)	27	(15.3%)	3	(1.7%)	176	13.8%
	<600	149	(47.2%)	103	(32.6%)	44	(13.9%)	20	(6.3%)	316	24.8%
	<800	171	(52.1%)	97	(29.6%)	42	(12.8%)	18	(5.5%)	328	25.8%
	800≤	195	(52.7%)	88	(23.8%)	54	(14.6%)	33	(8.9%)	370	29.1%
	Total	638	(50.1%)	383	(30.1%)	178	(14.0%)	74	(5.8%)	1,273	
Period of evacuation life experience	None	576	(56.5%)	293	(28.8%)	116	(11.4%)	34	(3.3%)	1,019	78.7%
	Up to half a year	32	(30.2%)	39	(36.8%)	22	(20.8%)	13	(12.3%)	106	8.2%
	Half a year or longer	38	(22.5%)	60	(35.5%)	44	(26.0%)	27	(16.0%)	169	13.1%
	Total	646	(49.9%)	392	(30.3%)	182	(14.1%)	74	(5.7%)	1,294	

No certain trend was observed between age and cumulative exposure dose during emergency operations.

Many subjects with relatively high annual income at the time of emergency operations had high cumulative exposure dose at the time of emergency operations. This seems to be a result of the fact that the career employee subjects such as the employees of TEPCO and those in the managerial position continued to be involved in the site for a long period of time.

Also, the cumulative exposure dose at the time of emergency operations was higher in those with experience of evacuation, suggesting that the local residents were more frequently involved in the operations at the Fukushima Daiichi Nuclear Power Plant from the early stage. (Many of the workers dispatched from other places seem to have left the Fukushima Daiichi Nuclear Power Plant after completion of the outsourced operations.)

Based on these results, we consider that the annual income at the time of emergency operations and the presence/absence of evacuation experience are factors that may be relevant to the cumulative exposure dose at the time of emergency operations and need to be examined in the evaluation of long-term health effects that will be revealed in the clinical survey in the future.

In the remaining second phase, we will review the previous study results among all subjects in the first follow-up survey and examine the relationship between the annual income, etc. at the time of emergency operations, evacuation experience, contents of emergency operations (including exposure dose), and the results of health examinations, etc.

In addition, regarding the method of asking questions about social factors, it is planned to examine how we should ask questions in the survey in the next phase.

In the future research, we are thinking of conducting a literature survey on socioeconomic factors and health effects related to evacuation experience.

In the third phase, while clarifying how social factors unique to the study population such as annual income and evacuation experience at the time of emergency operations are related to the contents of emergency operations, we will promote the examination of whether these social factors have effects on health. We will examine the actual evaluation method for those required to be evaluated as confounding factors considering the independence from other factors in the health effect evaluation in the NEWS study. In addition, an on-site survey will be conducted continuously to monitor the health status of emergency workers for any signs of change.

Survey on social factors, such as annual income, during emergency operations are based solely on the responses obtained from the questionnaire. We did not obtain information from official sources, so it is important to exercise caution with respect to the accuracy and objectivity of the information. However, we selected these factors for the survey in order

to achieve the objective of this study, which is to clarify the social background of the study participants. Additionally, the NEWS study does not focus on socioeconomic factors per se. Furthermore, there is no established consensus on what kind of socioeconomic information is required to be obtained for the long-term health effect evaluation. Therefore, it is currently unclear what kind of questions or surveys can adjust for socioeconomic factors appropriately in the long-term health effect evaluation. We will continue to investigate these matters in future studies and examine the socioeconomic information necessary to achieve the study objectives of the NEWS study.

Our hospital is located at a site where we can reach Fukushima Daiichi Nuclear Power Plant, and we are one of medical institutions where clinical surveys (health examination) are conducted. We have been continuously conducting this sub-study by utilizing these factors since the beginning of the NEWS study. However, as a general medical institution and not an organization solely dedicated to research, it is challenging to establish an adequate research environment. If the necessity for the study increases in the future, we believe that it will be necessary to reevaluate the research organization of this sub-study.

4. The Analysis and Evaluation Subcommittee

Subcommittee Chair, Co-Investigator: Shinji Yoshinaga

1. Study Objective

The primary objective of this subcommittee is to perform statistical analyses or evaluations of accumulated study data in cooperation with other subcommittees.

2. Initiatives for study topics

Since data for sufficient analysis have not been accumulated in this phase, among the items pointed out by the Third-Party Committee in the first phase, we recalculated the statistical power to detect radiation exposure effects for each type of cancer including thyroid cancer as particularly related to the analysis and evaluation.

3. Summary of research results (outcome)

Among approximately 6,000 participants who have participated in the study as of October 2021, the statistical power was calculated using a sample of 5,887 participants, after excluding women, individuals with unknown sex, and those with unknown radiation doses. In the calculations, we assumed the long-term follow-up and calculated the statistical power to detect the trend of increased risk according to the dose received during the emergency work period for the incidence of major cancers by site (gastric cancer, colon cancer, lung cancer,

prostate cancer, leukemia, and thyroid cancer) reported in previous studies, in addition to all solid cancers combined.

The data we used included demographic information of the study participants, such as year of birth, sex, and radiation dose (effective dose), as well as the national all-cause mortality rates based on publicly available vital statistics and cancer incidence data based on national cancer registry. The excess relative risk of cancer according to radiation dose was primarily based on estimates reported in the Life Span Study of atomic bomb survivors. However, for thyroid cancer, since no radiation-related increase was shown in atomic bomb survivors exposed in adulthood or most of the other epidemiological studies, a conservative assumption was made, and estimates reported by Kesminiene et al. (2012) for Chernobyl clean-up workers were used.

The calculation procedure involved first calculating the baseline cancer incidence, which is the number of cancers that would occur regardless of radiation exposure. Based on a model that assumes cancer increases linearly with radiation dose, the amount of increase due to radiation was calculated. Finally, the statistical power for a one-sided test was calculated based on the trend where the ratio of the baseline number and the expected total number (baseline plus radiation-induced number) increases with radiation dose increase.

For the calculation, we used the following assumptions: The 2018 mortality or cancer incidence rate remained constant subsequently; the survey began for all study participants in 2016; and the radiation-induced cancer risk remained constant regardless of ages. The minimum latency period from radiation exposure to cancer development was not considered. It was assumed that the following effects are negligible: The effects of confounding factors related to smoking or other lifestyle habits, etc., the effects of medical exposure, occupational exposure due to ordinary radiation operations, and environmental exposure. Since the estimated dose for each organ/tissue of the study subjects is not available, the effective dose was assumed to be equivalent to the dose of each organ/tissue.

As a result, under the assumption the baseline incidence continued for 40 years at the same level, the predicted incidence, which was calculated by adding the baseline and excessive amount due to radiation exposure, and the statistical power in the case of a follow-up period of 40 years are shown in Table 1. The statistical power was 10% for all solid tumors and below 10% for other cancers by site.

Table 1 Baseline Incidence, Expeted Total Incidence, and Statistical Power after 40-year Follow-up

	All solid tumors	Stomach cancer	Colon cancer	Lung cancer	Prostate cancer	Leukemia	Thyroid cancer
Baseline incidence	2,225	371.5	228.6	349.5	401.3	30.1	17.6
Expected Total incidence	2,236	373	231	352	405	30.5	18.6
Statistical power	10.3%	6.7%	8.3%	7.1%	8.2%	6.5%	9.9%

The statistical power gradually increases with the increase in the number of years of follow-up and the number of participants. However, even if the number of participants was about 18,000, equivalent to 3 times the current number of participants, the statistical power was calculated to be about 15-16% for all solid tumors and thyroid cancer and about 10% for other cancers. Also, we calculated the statistical power by increasing the value of the excess relative risk per unit dose assuming an increase in cancer risk due to radiation exposure. However, it was suggested that a high statistical power would not be ensured unless the estimated value of the excess relative risk per unit dose was approximately 5 or 10 times higher.

Since we assumed high risk estimates for thyroid cancer, the results should be carefully interpreted. Also, thyroid cancer includes a group with a very high dose in thyroid due to internal exposure here, and therefore it is considered more important for the calculation considering the internal exposure. In addition, although we used a different calculation method for the statistical power this time from the statistical power for all solid tumors calculated in FY 2018, the results were mostly consistent.

The results of this statistical power calculation suggest that it is difficult to detect the increased cancer risk of radiation exposure in this study unless the risk of cancer due to radiation is significantly higher than values obtained from the current findings. However, even if it is difficult to detect cancer risks related with radiation exposure, it is important to continuously monitor the health effects of radiation in the only study population and disseminate information on these results.

4. Objectives of the third phase

In cooperation with other subcommittees such as the Cause of Death/Cancer Morbidity Subcommittee and the Thyroid Cancer Investigation Subcommittee, we will evaluate the potential effects of confounding factors and various biases and examine the handling of these factors in the analysis. Also, we will start an analysis of the relationship between radiation exposure and health effects using the accumulated data.

5. The Radiation Dose Evaluation Subcommittee

Subcommittee Chair, Co-Investigator: Makoto Akashi
Co-Investigator: Osamu Kurihara
Co-Investigator: Yumiko Suto
Co-Investigator: Norio Tsujimura
Co-Investigator: Takumaro Momose

Study objectives

The Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers has been carried out on the workers who were engaged in emergency operations just after the accident at TEPCO Fukushima Daiichi Nuclear Power Plant. In this study subcommittee, we examined the existing radiation exposure dose from the derivation process and evaluated the conversion factor to the dose of the target organs of the study and uncertainty of radiation exposure dose aiming at refining the exposure dose of emergency workers used in this epidemiological study. The biological dose was estimated using stable chromosome aberration in some emergency workers and compared with the physical dose.

Initiatives for study topics

In the first phase of this research project (FY 2014-2018), our main focus was on examining the re-evaluation method for physical dose and establishing a system for implementing biological dose estimation. In the second phase of the project, we verified the personal dose data of about 20,000 emergency workers provided by the Ministry of Health, Labour and Welfare through the National Institute of Occupational Safety and Health, Japan (JNIOSH), which served as the lead institute. We also established the conversion factor from the value indicated by the personal dosimeter used at the time of the accident to the dose in each organ (absorbed dose), and attempted to estimate the biological dose based on the frequency of chromosomal translocation, which is a stable chromosome aberration, using blood samples provided by participants in this study project. Furthermore, throughout the first and second phases of the study project, we examined the analytical method for I-129 (physical half-life: About 15.7 million years) contained in urine samples of about 230 emergency workers collected at the time of the accident.

Summary of research results

(1) Accuracy verification of direct thyroid measurements in high dose emergency workers
We conducted numerical simulations at the National Institute of Radiological Sciences (present National Institutes for Quantum Science and Technology) to assess the accuracy of the direct thyroid measurements at the time of the accident for six high-dose

(≥ 250 mSv) emergency workers who have been followed-up since immediately after the accident. The simulations incorporated a numerical phantom prepared from individual cervical MRI images and a detector model. Such a measurement is a method for quantifying the residual amount of gamma rays released from radioactive iodine (mainly I-131) remaining in the thyroid using a radiation detector put close to the front of the patient's neck. The use of a physical phantom to determine the detection efficiency of the detector can introduce errors in the evaluation of the residual amount of radioactive iodine in the thyroid due to morphological differences between the phantom and the participant being measured. The results of the study confirmed that this measurement error was within ± 20% considering the uncertainty of the position of the detector. On the other hand, differences in individual thyroid volume were found to be significant during the process of creating a numeric phantom, suggesting that it is an important modifier when discussing the thyroid absorbed dose.

(2) Evaluation of effective dose and organ dose based on the values of electronic personal dosimeter

It has been confirmed that the electronic personal dosimeter (ZP-1460) used at the time of accident appropriately evaluated the effective dose based on the response test at high dose rate (> 100 mSv/h) and rotating/isotropic irradiation tests conducted on a human body-shaped phantom. Additionally, the conversion factor was established from personal dosimeter values to effective doses or organ doses (red bone marrow, colon, lung, thyroid, crystalline lens) for the major gamma rays emitted by the nuclide that was present in the immediate aftermath of the accident. In the meanwhile, for beta rays not measured by the same personal dosimeter, in addition to the experimental evaluation of the attenuation rate by protective gears such as a full-face mask, we evaluated the beta ray dose when the radionuclide that existed immediately after the accident was present on the ground surface as radioactive fallout by calculation simulation, taking into account the radioactivity ratio of each nuclide and its change in time. The beta ray dose greatly changes according to the height from the ground surface. The ratio of the 3 mm dose equivalent from beta rays, at the eye height of emergency workers, to the 1 cm dose equivalent from gamma rays, the value of the personal dosimeter, was evaluated to be about 0.25 at maximum. However, the ratio is expected to be substantially lower considering the absorption of beta rays due to the actual surface unevenness and the protective effect of the full-face mask.

(3) Verification and analysis of existing radiation exposure dose data

We thoroughly examined several datasets related to the personal exposure dose of approximately 20,000 emergency workers provided by JNIOSH, and constructed a relational database that maintains the relationship between these datasets. F71 contains published definitive values of emergency dose, F72 contains monthly dose values during the emergency operation period, including external exposure dose (effective dose, eye lens dose, and skin dose) and internal exposure dose (committed effective dose), and F73 contains personal dosimeter data (indicated value) measured for each operation. and they form a hierarchy. Additionally, there is TEC, which records internal exposure dose data (measurement of residual amount of the detected nuclide in the body, date of measurement, date of intake, method of measurement, etc.) of emergency workers from TEPCO and cooperating companies collected by TEPCO.

When the dose data of F71-73 was checked, the emergency dose in F71 almost matched the total value of the monthly emergency dose in F72, but the monthly dose in F72 and the total value of the indicated values of the personal dosimeter during the emergency operation in F73 did not match. This was because additional doses, such as the stay dose in the anti-seismic buildings and travel dose from J village to the Fukushima Daiichi Nuclear Power Plant, were separately added to the indicated value of the personal dosimeter in F72. We confirmed that these doses were evaluated individually based on the length of stay and number of transfers. Furthermore, F72 contained external exposure doses, including effective dose (1 cm dose equivalent), eye lens dose (3 mm dose equivalent), and skin dose (70 μm dose equivalent), and the values were mostly the same. This was probably because the personal dosimeter did not have sensitivity to beta rays as described above. Additionally, there was little data available for the internal exposure dose (committed effective dose) of F72, and the record level (2 mSv) was applied for TEPCO employees.

The data on internal exposure dose in TEC was categorized into about 20 evaluation methods based on various conditions such as the type of measuring equipment used, the method of estimation when I-131 is not detected, the presence of additional measurements, and individual evaluations. Verification calculations of the internal exposure doses were performed using residual measurements in the body, dates of measurement, and dates of intake. Results showed that internal exposure doses were reproducible for those who detected I-131. When I-131, which greatly contributes to the internal exposure dose, was not detected, one of the two methods was adopted to obtain a lower internal exposure dose: (1) estimating the intake of I-131 by applying the ratio of the concentration of radioactive substances of I-131 and Cs-137 in the air obtained from daily dust sampling

at the Fukushima Daiichi Nuclear Plant to the intake of Cs-137 calculated from the in vitro measurement; or (2) estimating assuming that the lowest detection limit of I-131 in the in vitro measurement remained in the body at the time of measurement. However, for (1), since the sampling was performed only for a short time, the data were missing in the first week after the accident, and the ratio of radioactivity in the environment did not necessarily coincide with the ratio of intake after inhalation, the uncertainty is large, and for (2), overestimation is expected. Therefore, we extracted the emergency workers in whom both I-131 and Cs-137 were detected, classified them into each fixed period during March and April 2011 when exposure to I-131 was remarkable, calculated the distribution of the ratio of intake based on the results of the in vitro measurement of each subject, and proposed a method in which the measure of central tendency is applied to the persons in whom I-131 was not detected. As a result, a natural distribution of internal exposure dose (committed effective dose) was obtained, in which the number of affected individuals increased as the dose decreased. Also, based on the results, organ doses due to internal exposure to thyroid, lung, colon, and bone surfaces were calculated.

(4) Biological dose estimation based on chromosome analysis

The degree of injury of chromosomes in peripheral blood lymphocytes was measured to observe comprehensive dose throughout the life in both occupational and non-occupational exposure.

In this study, we conducted biological dose estimation using the frequency of translocation chromosomes, a form of stable chromosome aberration, as an indicator. By the baseline survey (62 participants who underwent blood sampling in FY 2018), we confirmed a positive correlation between the biological estimated dose and the external exposure dose measured by personal dosimeters and also revealed that the history of smoking and medical exposure of participants was involved in the biological estimated dose. In addition, the frequency of stable chromosome aberrations increased with aging, suggesting the need for reinforcing the calibration curve using blood samples from participants of different ages. Analysis of biological dose estimates for emergency workers (blood samples collected from 54 participants in FY 2020) with external exposure dose > 70 mSv is currently ongoing.

(5) Research on analysis of urinary iodine-129

Urine samples were collected from 517 emergency workers who underwent in vitro measurements at the Japan Atomic Energy Agency at the time of the accident. Of them, the samples of 230 workers are still stored. If I-129 can be detected in these urine samples,

the amount of I-131 in urine at the time of collection can be evaluated from the iodine isotope ratio (I-131/I-129) in the environment, and it may help in evaluating the internal exposure dose of individuals without detection of I-131. However, the measurement of I-129 requires the use of an accelerator mass spectrometry (AMS). Thus, we have been developing an analysis method for that purpose. Iodine isolation in urine was attempted using ion exchange resin or CL resin, and iodine recovery rate was evaluated using simulated urine samples. Actual urine samples will be analyzed using AMS in the next fiscal year.

Objectives of the third phase

In the third phase, we will further strengthen cooperation with other study subcommittees and JNIOSH, the lead research institute, build the dose database requested by each study subcommittee, and make efforts to contribute to creation of study outcomes of the entire epidemiological study aiming at further refining the dose evaluation, and evaluating the exposure dose and its uncertainty considering individual behavioral information.

6. The Cause of Death/Cancer Morbidity Investigation Subcommittee

Subcommittee Chair, Co-Investigator: Kotaro Ozasa

1. Study objectives

The survey on the cause of death/cancer morbidity aims to track and confirm the survival or death status of participants in the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers and collect information on the cause of death and cancer morbidity.

2. Initiatives for study topics

In order to achieve the study objectives, informed consent for the follow-up items below has been obtained (there are missing numbers in the items because they are excerpted from the informed consent form).

(1) To be provided with documents related to the status of emergency operations, exposure dose, and the results of statutory health examinations owned by TEPCO, contractors, and the companies to which the participants were affiliated during the emergency operations. (4) To check the residence records in accordance with the statutory procedures in order to obtain information such as the address after moving in the future, name after change due to marriage, etc., and information necessary for checking and tracking survival or death. (5) To be provided with the information on cancer morbidity from the local cancer registry of

prefectures where the participants live or the national cancer registry of the National Cancer Center. (6) To be provided with the past and future results of statutory health examinations of the participants engaged in radiation operations from medical institutions. (7) To be provided with the results of the detailed examination and related medical information owned by the medical institution where the participants underwent the thyroid test (hematologic test, ultrasonography, cytology, etc.). (9) In the case of death in the future, to be provided with the information on death in the Vital Statistics (based on the death certificate) from the Ministry of Health, Labour and Welfare through the statutory procedure and check it with the information of the participant (name, date of birth, address, etc.) to investigate the cause of death.

Since this practice is mainly carried out at the time of health examinations, it has been conducted at the headquarters. In order to determine the starting time for the follow up which is required for the calculation of the follow-up person-years, it is necessary to determine the time at which the emergency operations started and the time at which the workers were withdrawn from the emergency operations. The current status survey and contact at the time of making an appointment for health examination should be used to obtain follow-up information such as address, and information regarding death or survival, etc. In order to obtain outcome information (cause of death/development of cancer), information on the cause of death in the Vital Statistics has been obtained since 2011, and information of the national cancer registry has been obtained since 2016. In the former, there are issues related to individual identification, and in the latter, there is a problem that it is limited to explicit consenters, primarily consisting of participants who underwent health examinations.

3. Summary of study results

A total of 6,221 participants underwent a baseline health examination from the beginning of the survey to October 31, 2022. Of them, consent was acquired from 6,141 (99%) for (1), 6,083 (98%) for (4), 6,149 (99%) for (5), 6,160 (99%) for (6), and 6,165 (99%) for (7). Those who gave consent to (9) that was added after FY 2020 were 197 (63%) of 314 who attended the baseline health examination during this period. The total number of participants who gave consent including via postal mail and on the website and the percentage of the 19,812 emergency workers were 7,815 (39%) for (1), 7,657 (39%) for (4), 7,750 (39%) for (5), 7,794 (39%) for (6), 7,785 (39%) for (7), and 4,103 (21%) for (9).

As for the follow-up of death/cause of death, the information on death in the Vital Statistics for the generations relevant to the participants in this study between 2011 and the end of 2019 was issued according to the Statistics Act. When this information was collated with 4,103 participants who gave consent to the above item (9), only one death was identified.

The small number of identified deaths was considered due to the short follow-up period after consent was obtained. Since the layout of the cause of death data in the Vital Statistics was changed in 2017, the collation software is currently being updated. For these reasons, the standardized mortality ratio was not calculated.

In order to follow up cancer morbidity, for 7,537 participants (7,526 men, 10 women, and one person of unknown sex, up to the time of collation) who gave consent to the above mentioned item (5), we applied for the use of the information of neoplasms (ICD-10: C00-D48) diagnosed between 2016 and 2018 to the national cancer registry and obtained the information. Of the participants, 140 men and <10 women had the first primary solid cancer (C00-C80) (in the case of less than 10 patients, the number is shown <10 because the number is not disclosed, and the same applies hereinafter). Table 1 shows the number of cancer cases with the major sites in men. Leukemia and lymphoma were observed in <10 men and no women, and cancer in situ of the colon and rectum (D010-D012) was observed in 16 men and no women. Benign neoplasm (D10-D36) was observed in <10 men and no women, and neoplasms of uncertain or unknown behavior (D37-D48 including polycythemia vera and myelodysplastic syndrome that are considered to have borderline characteristics) were observed in <10 men and no women. There were <10 men and no women with the second or higher primary cancer.

The standardized incidence ratio (SIR) was obtained based on the incidence rates by calendar year and by age in Japan during the same period as the standard rate, of which information was published by the National Cancer Center (Table 1). First, the SIR for total solid cancer was significantly higher. The point estimates for the SIR were 1.1 or higher (10% or higher than the reference population) for cancers of the stomach, liver, gallbladder, pancreas, prostate, kidney, urinary tract, and thyroid gland, and cancer in situ of the colon and rectum, and others, with statistically significantly higher values for cancers of the prostate and thyroid gland, and cancer in situ of the colon and rectum. On the other hand, the point estimate for the SIR was ≤0.9 in colorectal and lung cancers. The point estimates for the SIR for cancers in other sites and leukemias/lymphomas ranged between 0.9 and 1.1. These results indicate that SIR is high for cancers for which screening tests are performed in health examination and human dry dock (comprehensive health examinations), which is consistent with the high SIR for cancer in situ. On the other hand, SIR for clinically detected and unscreened cancers was generally not deviated from the national level. Therefore, it was considered that the high SIR of cancer was likely to be due to excessive detection by health examinations in this study and voluntary health examinations. It will be necessary to examine how many of them were found in the health examination of this epidemiological study.

Table 1 Number of cancer cases by site and standardized incidence ratio (SIR) in men, 2016-2018

ICD code	Site	Number of patients	Expected number	SIR (95% CI)
C00-C80	All solid cancer	140	108.3	1.29 (1.09, 1.53)
C16	Stomach	19	16.6	1.14 (0.69, 1,79)
C18-C20	Colon and rectum	19	22.0	0.86 (0.52, 1.35)
C22-C25	Liver/gallbladder/pancreas	14	11.3	1.23 (0.67, 2.07)
C34	Lung	10	14.5	0.69 (0.33, 1.27)
C61	Prostate	26	13.8	1.89 (1.23, 2.78)
C64-C68	Kidney/urinary tract	15	8.5	1.77 (0.99, 2.91)
C73	Thyroid gland	16	2.0	8.01 (4.58, 12.9)
C00-C80 other than the above	Other sites	21	19.6	1.07 (0.66, 1.64)
C81-C96	Leukemia/lymphoma	<10	-*	0.91 (0.36, 1.87)
D010-D012	Cancer in situ (colon and rectum)	16	8.7	1.84 (1.05, 2.98)
D00-D09 other than the above	Cancer in situ (other sites except for colon or rectum)	<10	-*	1.24 (0.50, 2.56)

*Not described because the observed number of patients was <10.

3. Objectives of the third phase

Our goal is to obtain the results regarding cancer development within 15 years and death within 30 years. To achieve this, we need to confirm the person-years of follow-up, especially for confirming the beginning of follow-up. For this purpose, it is necessary to confirm the participants' situation of engagement in operation and therefore, collaboration with the Dose Evaluation Subcommittee will be necessary. In order to obtain follow-up information on address, survival/death, etc., it is necessary to overcome the problem of missing information on death during the current status survey or contact when making an appointment for health examinations. It is necessary to conduct a resident record survey within the record retention period of deleted records at municipality offices. In any case, it is essential to conduct a simultaneous survival confirmation survey with confirmation of date of death at a certain time point.

It is unrealistic to obtain consent from all participants (19,812) to investigate the cause of death. Significant bias may occur in the analysis of only participants with consent who mainly underwent health examinations. Not only to avoid but also to evaluate such bias, it is

necessary to collect information on the cause of death in all participants including those not receiving health examinations. Therefore, we need to establish a system to make information on death and cause of death available for all participants.

It is unrealistic in practice to collect the information on cancer incidence until the end of 2015 from local cancer registries in 47 prefectures because of a problem of transfer of cancer registry information between prefectures due to the difference in the patient's address and the location of medical institutions providing medical care/submitting notification and a problem of data quality due to differences in registry accuracy. Since the period from the nuclear power plant accident to 2016 is approximately 5 years, it is not considered to be problematic to evaluate the radiation risk of solid cancers. However, for diseases such as leukemia that increase in a short period after radiation exposure, other measures such as the use of information on death should be considered.

The Analysis and Evaluation Subcommittee will discuss radiation risk analysis, but there are challenges to determining person-years of follow-up, as well as challenges in the Radiation Dose Evaluation Subcommittee regarding dose evaluation during emergency operations and non-emergency situations, and how to combine and accumulate them. There are also several radiation risk analysis-specific problems to consider, such as handling the exposure dose during emergency operations and doses during other period as time-dependent variables. Additionally, there is a challenge in handling risk factors other than radiation that are obtained from questionnaire surveys, as they may act as confounding factors. While these risk factors can be collected from the participants in health examinations, it may be difficult to obtain them from non-participants. Therefore, multiple imputation and other methods are required. Furthermore, there is a problem how to deal with cancers that are excessively detected by health examinations in this study, as well as in voluntary health examinations. Generally, if there is no relationship between health examinations and exposure doses, over-detection of cancer by health examination only affects an increase in the baseline incidence rate and does not affect radiation risk estimation. However, if participants exposed to higher doses tend to undergo health examinations more frequently, the estimation of radiation risk would be affected. In either case, the Analysis and Evaluation Subcommittee is thought to conduct a large part of the above analyses.

7. The Thyroid Cancer Investigation Subcommittee

Subcommittee Chair, Co-Investigator: Tomotaka Sobue
Co-Investigator: Nobuyuki Taniguchi
Co-Investigator: Megumi Miyagawa

Study Objectives

The objectives of this study are: [Topic A] to collect and analyze the data of diagnostic examination of those who were required to undergo the detailed examination in the "Study on Thyroid Survey and Others in Workers of TEPCO Fukushima Daiichi Nuclear Power Plant" of the Health Labour Sciences Research Grant 2013 Special Research Project (Chief Investigator: Tomotaka Sobue; hereinafter referred to as the old study group) and the data of previous thyroid ultrasonography in the exposure group and [Topic B] to examine the method of implementing thyroid ultrasonography in the target population of about 20,000 emergency workers and collect and analyze the examination data.

Through these objectives, we aim to collect information on the health condition of emergency workers and provide more detailed and accurate information on measures for a nuclear power plant in an emergency. It is also expected that this study will provide information to help the health management of the people engaged in occupations with the potential exposure to radiation, such as nuclear power plant workers and emergency workers.

Initiatives for study topics

In this study, the following were conducted in response to Chapter II "the Suggestions for the Study in the Second Phase" in the report of the Third-Party Committee in the first phase in 2019.

1. Key points to be investigated: In the case of thyroid cancer, thyroid tests should be performed by setting a control group with the same extraction rate including the low-dose group.

■ Response: To make the extraction rate the same for the low-dose group and the high-dose group, health examinations will be encouraged to further increase the number of examinees in the low-dose group. However, in the IARC expert report, thyroid screening for the low-dose group is not recommended as the potential harms outweigh the benefits. Therefore, it is not ethically appropriate to encourage them to undergo examinations. Since the low-dose group originally has a larger population of participants, even if the examination rate is lower, the number of examinees is still considerably higher than that of the high-dose group. To address potential biases related to examination motivation, we will conduct stratified analysis using indicators such as past thyroid ultrasonography

examination history, presence or absence of findings, family history, and other factors related to health check-up attendance.

2. Key points to be investigated: We would like to recommend that those with an abnormality should undergo thyroid biopsy based on the same criteria and those with suspected results should undergo active surveillance by thoroughly unifying the criteria to compare the results.

■ Response: We have obtained consent from 127 specialized medical institutions nationwide to perform secondary examinations, and if abnormalities are detected by ultrasound, we refer or recommend patients to see physicians based on the same criteria. However, regarding individual cases such as tests and treatment options at each specialized medical institution, we will only receive the results. We believe it is inappropriate to intervene in clinical decision-making.

3. Key points to be investigated: In benign thyroid diseases, nodules and cysts are frequently detected, and useful data are can be gathered as a result. The Japanese population is known to have a high risk of latent cancer. This survey may provide new insights regarding the natural history of thyroid nodules in adults. Subclinical hypothyroidism may be observed in the group exposed to high doses.

■ Response: Thyroid cancer, hypothyroidism (including latent one), nodules, and cysts are considered primary diseases and were mainly investigated. We developed diagnostic criteria and conducted a comprehensive examination using ultrasonography, blood tests, information from secondary examination from medical institutions, cancer registry data, and questionnaires.

These initiatives allowed us to collect detailed data and comprehensively examine the primary diseases, including thyroid cancer.

Summary of study results

1. [Topic A]

Concerning the data of the old study group, we obtained data for 627 out of 2,064 participants from the National Institute of Occupational Safety and Health and checked the data of 531 participants who underwent thyroid ultrasonography (274 in the exposure group, 257 in the control group). In the future, we plan to effectively utilize the data of the old study group in conjunction with the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers.

To gather information on past thyroid ultrasonography, we included questions about past thyroid diseases and ultrasonography history, obtained consent to contact medical institutions, and collected the information through questionnaires and consent forms. This fiscal year, we counted the number of ultrasonography exams performed after emergency operations.

2. [Topic B]

The Quality Control Committee has been established at Jichi Medical University. This Committee is engaged in the development of technicians involved in thyroid ultrasonography, central review of ultrasonography findings, and referral of those requiring the secondary examination to specialized medical institutions. We provide the training seminars for beginners and experienced technicians twice a year and try to improve skills and knowledge of thyroid ultrasonography. Also, we certify technicians and health examination institutions that meet certain criteria as certified technicians and certified institutions. As of December 2022, there are 113 certified technicians and 40 certified institutions. In addition, we have been conducting a central review for all participants since April 2017 and sending the results to each health examination institution. Regarding those requiring the secondary examination, we aim to obtain more accurate information by referring them to specialized medical institutions and collecting the results. Through these initiatives, the examinations are conducted while improving and maintaining the accuracy of thyroid ultrasonography of each health examination institution.

As of the end of October 2022, out of 6,203 participants in the baseline survey, 4,779 (77.0%) consented to undergo thyroid ultrasonography, and out of 2,540 participants in the longitudinal survey, 1,920 (75.6%) consented to it. In both surveys, the percentage of participants who visited medical institutions where ultrasonography was not available was higher in the low-dose group, and the percentage of participants who consented to the examination tended to be higher in the high-dose group. Overall, the non-consent rate was low at 0.5%.

Regarding the implementation rate of the central review, in the baseline survey, 3,284 participants (16.6% of the 19,808 emergency workers and 52.9% of the 6,203 examinees of health examinations) underwent the central review. In the longitudinal survey, 1,916 participants (9.7% of the 19,808 emergency workers and 75.4% of the 2,540 examinees of health examinations) underwent the central review. There was a tendency toward a higher rate of the central review by ultrasonography in the high-dose group.

Regarding the final diagnosis of thyroid ultrasonography, the percentage of B diagnosis (requiring secondary examination) was 15.5% in the baseline survey and 16.8% in the longitudinal survey, and there were no cases of C diagnosis. Both the baseline and longitudinal

surveys showed that the percentage of B diagnosis tended to increase with age, and no clear increase in the percentage of B diagnosis was observed in the high-dose group.

Regarding the receipt rate of the secondary examination results in participants assessed as B/C, in the baseline survey, 39.2% of participants assessed as B received the secondary examination results and 74 (37.2%) of them underwent cytology. The results of cytology were confirmed in 72 participants. Cytology results were confirmed in 14.2% (72/508) of participants assessed as B, and of those, 5 were diagnosed with cancer or were suspected of having cancer. In the longitudinal survey, 45.0% of participants assessed as B received the secondary examination results, and 29 (20.0%) of them underwent cytology. The results of cytology were confirmed by 23 participants. Cytology results were confirmed by 7.1% (23/322) of participants assessed as B, and of those, 2 were diagnosed with cancer or were suspected of having cancer.

The diagnostic criteria for the cumulative incidence of thyroid cancer were 1) definite diagnosis based on information from medical institutions or cancer registry, 2) malignancy confirmed by cytology, or 3) suspicion based on the patient's history of thyroid cancer as reported in a questionnaire. The study analyzed 6,199 health examination examinees, excluding 4 participants with a history of thyroid cancer before the earthquake. The cumulative incidence of thyroid cancer after the earthquake was 30 (7 definitive and 23 suspected cases), with a cumulative incidence of 0.5%. The same rate was observed in participants who underwent central review of ultrasonography. Age of the participants diagnosed with thyroid cancer were mostly in their 30s to 50s at the time of the earthquake (many of the participants were in their 30s to 50s). The incidence tended to be higher in those who were exposed to an effective dose of 50 mSv or higher. Furthermore, 20% of the patients were diagnosed within 5 years after the earthquake, 60% were diagnosed between 5 and 10 years, and 20% were diagnosed 10 years or more after the earthquake. Finally, we examined the number of thyroid ultrasonography tests after emergency operations as a factor related to the diagnosis of thyroid cancer. The results showed that participants with higher radiation exposure had more frequent ultrasonography tests and a higher chance of being diagnosed with thyroid cancer.

The diagnostic criteria for hypothyroidism were defined as a TSH level above the reference range and a Free T4 level below the upper limit of reference range, or self-reported treatment for hypothyroidism or current use of thyroid hormone medication as reported in the questionnaire (except being treated for thyroid diseases other than hypothyroidism, a history of thyroid surgery, or a history of neck radiotherapy). Participants who underwent a thyroid blood test were tabulated. Among 6,192 participants who underwent the baseline survey, the prevalence of hypothyroidism was 3.5%. The prevalence tended to increase as

the age at the time of examination increased, but there was no clear association between the effective dose level and prevalence.

The diagnosis of nodules was based on the presence of a nodule or cystic nodule with a largest diameter of ≥ 5.1 mm on the primary examination (ultrasonography). Among the 3,284 baseline survey participants who underwent central review of ultrasonography, the prevalence of nodules was 15.2%. The prevalence tended to increase with age at the time of examination, but there was no clear association between the effective dose level and prevalence.

Cysts were diagnosed using the same criteria as nodules, with a largest diameter of ≥ 5.1 mm on the primary examination (ultrasonography). Among the 3,284 baseline survey participants who underwent central review, the prevalence of cysts was 11.3%, and the prevalence tended to increase with age at the time of examination. However, no clear association was found between the effective dose level and cyst prevalence.

Objectives of the third phase

The objective of the third phase is to confirm whether or not important data are missing and establish a system for long-term observation by updating the health examination and analyzing all currently available data, with a focus on the results of ultrasonography and the primary endpoint. In order to increase the rate of acquisition of secondary examination results, it is important to establish a system for tracking whether or not participants have undergone secondary examination and take measures to increase the rate of result acquisition. Additionally, while reducing the burden on health examination institutions associated with ultrasonography and introduction of secondary examinations, we will establish a system to determine the incidence of thyroid cancer by cross-checking with the national cancer registry in cooperation with the Cause of Death/Cancer Morbidity Investigation Subcommittee, and then select examination participants and analyze the results based on re-evaluation of the dose of thyroid radiation in cooperation with the Dose Evaluation Subcommittee.

8. The Cataract Investigation Subcommittee

Subcommittee Chair, Co-Investigator: Hiroshi Sasaki

Study objectives

The crystalline lens is one of the tissues in the human body that is highly sensitive to radiation, and it has been reported that cataract is caused by exposure to the low-dose radiation even lower than the threshold previously considered. The Cataract Investigation Subcommittee is intended to conduct a cataract survey in emergency workers and clarify

the relationship between radiation exposure and the onset of cataracts through long-term follow-up observation.

Initiatives for study topics

The Cataract Subcommittee conducts two surveys in parallel. One survey has been conducted every year since 2013 for current TEPCO employees with an effective dose of > 50 mSv. The screening is conducted at 3 sites: Fukushima Daiichi and Daini Nuclear Power Plants, Kashiwazaki Kariwa Nuclear Power Plant, and Tokyo Head Office. The diagnosis of cataracts was made by the combination of diagnosis by slit lamp microscopy by ophthalmologists and diagnostic imaging by using two cameras (anterior eye segment analyzer EAS-1000 (NIDEK) and simple retroillumination camera (LOVEOX)), and both were performed under mydriasis. The other is a nationwide survey of participants across in Japan, conducted at ophthalmic clinics. This study began in 2018 and was designed to have one course every three years. The 1st course was conducted between FY 2018 and FY 2020, and the 2nd course is being conducted between FY 2021 and FY 2023. We are in the 2nd year of the 2nd course. The survey is conducted at 71 ophthalmic clinics in Japan with the cooperation of Japanese Society for Cataract Research and Japan Ophthalmologists Association. The diagnosis of cataracts was made by ophthalmologists under mydriasis, and a simple retroillumination camera is also installed at some clinics to take images of crystalline lenses. The final assessment of the test results (findings and lens images) diagnosed in the two surveys was made by the Quality Control Committee of Kanazawa Medical University.

Cataracts were evaluated based on the classification by Merriam & Focht (1962), which is a diagnostic criterion of radiation cataract, using a six-type categorization system. It included 3 main types (cortical, nuclear, posterior subcapsular) that lead to a deterioration of visual functions, 2 subtypes (Retrodots [RD] and Waterclefts [WC]), and minute opacities that are considered to be an initial change in radiation cataracts (Vacuoles [VC]). Localization (presence or absence of central posterior subcapsular) was also evaluated for VC (see Figure 1). Ophthalmologists performing diagnoses were provided with a diagnostic manual for the 6 types of cataracts and used a table of findings for entering descriptions to ensure consistent evaluation. In general ophthalmic practice, macroscopic diagnosis by an ophthalmologist with slit-lamp microscopy is the standard, but we believe that retroillumination images with a crystalline lens camera are also essential for follow-up of such minute opacities. We have also developed an automated crystalline lens opacity measurement system that uses deep learning-based image recognition processes to detect cataracts based on retroillumination images. We are currently working on creating a universal evaluation for the final judgment.

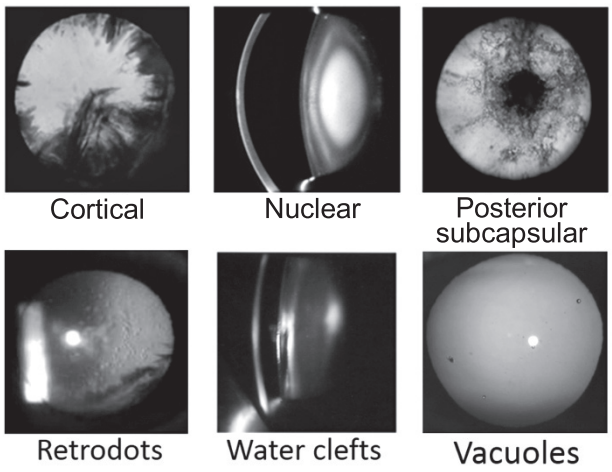

Figure 1. Types of cataracts to be examined in this study

Summary of study results

The survey of the TEPCO employees, which was suspended in 2020 and 2021 due to the influence of the COVID-19 pandemic, has resumed from FY 2022. In addition, image analysis of past screening data has been initiated. First, data of participants who provided consent to this study are being tabulated and extracted to investigate the prevalence of the 5 types of cataracts and VC (minute opacities). We also plan to investigate the 7-year follow-up of the same participants.

In the nationwide survey, 497 participants (mean age: 54.2 ± 10.0 years) were enrolled in the 1st course. Of these, 26.4% had clear eyes (no cataracts) without minute opacities such as VC. Those with an initial change in radiation cataract, including VC and cataracts, accounted for 73.0%, and 0.6% had intraocular lenses after cataract surgery. Of the 363 subjects diagnosed with cataracts, 90.1% had corrected visual acuity of > 1.0, 7.9% had visual acuity of 0.7-0.9, and 2.1% had visual acuity of < 0.6. These results indicated that nearly 90% of the study participants, 8 to 10 years post-accident, did not have cataracts or had changes in their crystalline lenses but still had good visual acuity (see Figure 2). The prevalence of VC in the central posterior subcapsular of crystalline lenses was 8.3% in the 30s and 12.7% in the 40s. It is particularly important to track changes in posterior subcapsular VC in people in their 30s and 40s. One hypothesis for the current threshold dose set by the ICRP is that all minute opacities progress to visual impaired cataracts at least 20 years after radiation exposure. Observing young participants could help verify this hypothesis, but since the 20-year period may also cause age-related cataracts, a careful examination is necessary. Currently, the 2nd course is ongoing. Approximately 7,000 participants who provided consent and cooperation in the Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers (NEWS)The target subjects of the 2nd course were approximately 7,000 for whom we obtained

consent to /cooperation in the NEWS study, and the guide letters of screening were sent to them. 3,504 subjects answered that they wished to undergo the screening. Of these participants, approximately 2,500 were eligible for screening. 1,474 of them were screened in 2021 and 2022, and the remaining 1,000 are scheduled for screening in 2023.

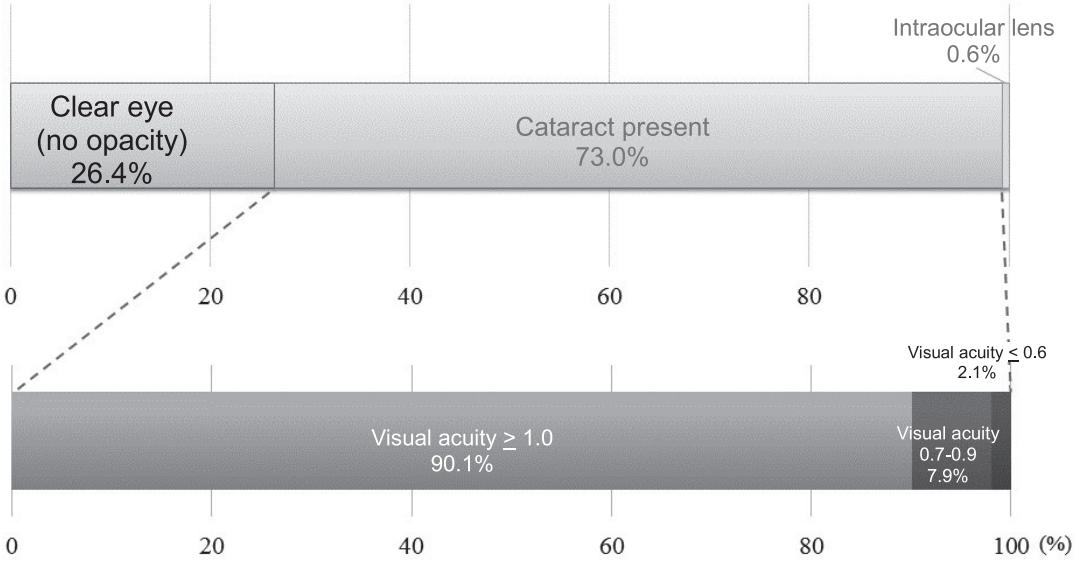

Figure 2. Results of 1st course

Multicenter studies such as nationwide surveys require a large amount of data analysis and follow-up based on image data. To enable objective evaluation, it is urgently necessary to establish an automatic analysis system for crystalline lens opacities. With regards to the model for VC detection, we have improved its accuracy by analyzing a large number of images from TEPCO screening. Moreover, we are increasing the versatility of the model to make it useful in wider range of screenings as a model specialized in radiation cataract.

Objectives of the third phase

The cataract survey will continue in the third phase of the NEWS study, as in the current phase. The nationwide survey will start the 3rd course. We will install simple retroillumination cameras in many facilities, and we will also consider transferring cameras between facilities in prefectures with a small number of participants to take as many crystalline lens images as possible. In addition to conducting a detailed examination of these cataract survey results, it is necessary to examine the relationship between cataract survey results and exposure dose in past data analysis.

9. The Psychological Impact Subcommittee

Subcommittee Chair, Co-Investigator: Hisashi Eguchi
Co-Investigator: Kosuke Mafune

We examined the psychological effects of emergency workers by using the questionnaire and interview in the "Study on the assessment of psychological effects on radiation operation workers" (first phase survey for 5 years from 2014 and second 5-year phase from 2019). We reduced variation by interviewers in the interview survey through construction of a survey implementation system that enables us to cope with a large number of subjects.

[Questionnaire survey]

Of the 5,249 responses returned by October 31, 2022, the questionnaire survey included 4,735 subjects who provided consent to participate in the study and whose data were collated with the attribute information. Only the initial survey of each subject was analyzed in this report. In the questionnaire survey, we used 4 scales as outcome indices: Psychological stress (K6), alcohol-related problems (AUDIT), insomnia symptoms (AIS), and post-traumatic stress disorder (PTSD) symptoms (IES-R). As exposure variables, we also asked the subjects to answer the beginning of the emergency work at TEPCO Fukushima Daiichi Nuclear Power Plant, duration of the work, and type of emergency operations. The following 9 scales were used as adjustment variables assumed to be associated with mental health: Defamation or discrimination associated with emergency operations (stigma), life events in the past 1 year from the time of the survey, social support at 2 time points: At present and at the time of emergency operations, stress coping (BSCP), sense of coherence (SOC3-UTHS), resilience (CD-RISC2), self-efficacy, self-esteem, and life/job satisfaction. The prevalence of psychological stress (K6) and insomnia symptoms (AIS) did not markedly differ from previous studies in Japanese workers. Psychological stress, insomnia symptoms, alcohol-related problems, and PTSD symptoms were found to be significantly associated with stress-related factors such as stigma, life events, social support, part of stress coping, self-esteem, and work/life satisfaction. In particular, stigma showed the same strong association as in the previous studies. It was also suggested that social support in emergency operations is important as a protective factor for the mental health of workers even taking into account the influence of stigma and life events. In particular, social support by the superiors at the time of emergency operations was considered to be an important protective factor when the period of emergency work extended longer than 30 days.

[Interview survey]

In the interview survey, we analyzed 3,504 subjects (3,489 men, 3 women, and 12 unknown)

who underwent the health examination survey by October 31, 2022 and provided valid responses in the interview survey. In order to reduce evaluation variability of interviewers, we adopted a structured interview and used the Computer-Assisted Personal Interviewing (CAPI) of the World Health Organization Composite International Diagnostic Interview (WHO-CIDI). In this study, we used only the depression module from WHO-CIDI to evaluate the prevalence of depression and used 2 criteria, American Psychiatric Association's DSM-IV-TR and WHO's ICD-10, to evaluate the depression findings during the past 1 month, last 12 months, and lifetime from the time of survey. The prevalence of "major depressive disorder" (296.xx) in DSM-IV-TR was 0.2% (n=8) in the last 1 month, 1.9% (n=66) in the last 12 months, and 6.9% (n=242) in the lifetime. The prevalence of "severe depressive episodes without psychotic symptoms" (F32.2, F33.2) in ICD-10 was observed to be 0.1% (n=5) in the last 1 month, 1.1% (n=37) in the last 12 months, and 3.3% (n=117) in the lifetime. In the large-scale preceding study in Japan, the prevalence according to the criteria of DSM-IV-TR and ICD-10 was 4.3% and 2.3% in the lifetime, 2.2% and 0.9% in the last 12 months, and 0.3% and 0.1% in the last 1 month, respectively. Although it was comparable to this study over the last 1 year, the lifetime prevalence was slightly higher in this study. It should be noted that since only the depression module of the CIDI was excerpted and used in this study, there was an issue that the age at relapse could not be adequately estimated. In FY 2022, the age calculation method was improved and accordingly, the estimation of the time of relapse was improved. As previously reported, incidence of depression after disaster was significantly higher in those with history of depression before disaster. As a result, it was suggested that the strength of the association was underestimated before the program was improved. In addition, based on ICD-10, the lifetime prevalence and incidence after the disaster were significantly higher in the exposure group with an effective dose of > 100 mSv.

[Implementation system for interview survey]

In this study, in order to examine the relationship between emergency operations and mental health, we emphasize the combination of a valid interview method that can identify the time of onset of symptoms. We examined the existing structured interviews in FY 2014 and 2015 and decided to adopt the depression module of the CAPI of WHO-CIDI. In addition, we have been continuously providing training programs to develop the interviewers so that the interview survey can be conducted at the study cooperation institutions in throughout Japan. In FY 2020, due to the influence of the COVID-19 pandemic, it became difficult to continue structured interviews at the time of health examinations conducted at the study cooperation institutions. From the latter half of FY 2021, a centralized health survey trial was conducted,

which enabled us to interview a larger number of participants at one time. Thus, in order to establish a system to ensure sufficient accuracy of the survey and to conduct the survey nationwide, we outsourced the implementation of structured interviews to an institution specialized in this survey, which allowed us to conduct high-quality surveys in a stable manner. They provide periodic training for interviewers who can continuously conduct the survey. Outsourcing of a large-scale survey can also contribute to reducing the burden of study cooperation institutions that cannot allocate dedicated staff for the interview survey. In FY 2022, we provided the education and training specified by WHO-CIDI and further improved the sustainability of structured interview surveys to increase the number of interviewers who can respond to the actual survey in the metroporitan region and secure the quality.

10. The Health Management Database Subcommittee

Subcommittee Chair, Co-Investigator: Akira Ogami

◆ Background and Objectives of the Subcommittee's Establishment

The overall objective of this Epidemiological Study of Health Effects in Fukushima Nuclear Emergency Workers is to conduct detailed health checkups over the lifetime to investigate health effect of radiation over the long term in a comprehensive manner. The health data collected in this study are expected to contribute to the maintenance and improvement of the health of emergency workers through health guidance to study participants. However, there is currently no established protocol for providing health guidance and explaining the results to health examination participants who expressed their intention to undergo the examination. Therefore, we have decided to establish a subcommittee from the second phase of the study to develop an effective feedback system for the summarized health management database of the operation workers and to study how to lead it to continuous and effective use.

◆ What have been conducted in this study

(1) Survey of the actual status of acceptance criteria in medical institutions conducting health examinations for this epidemiological study (2020-2021)

We obtained the notifications of health examination results from 45 medical institutions nationwide participating in this epidemiological study and compared with the reference values of each test item listed in there (reference values that give some alert as presence of findings).

(2) Creation of a risk matrix for health assessment based on health examination data (2020-2021)

With the aim of conducting a comprehensive "health assessment" using health

examination data, we attempted to create a risk matrix based on the anonymous health examination data of participants who underwent multiple-item health examination and basic health examination in the epidemiological study regarding the health effects of radiation workers that was conducted up until 2020.

① In multiple-item and basic health examinations, health examination items were classified by system into 10 groups (obesity/emaciation, blood pressure, liver function, glucose tolerance, lipids, renal function, inflammation, anemia or polycythemia, ECG, and chest X-ray), and the reference values were set for health examination items in each group based on the frequency distribution of test values.

② The risk items were classified into 3 groups: "Low risk group," "medium risk group," and "high risk group" according to the reference values, and the risk levels were determined by the reference values set among the 10 risk items.

(3) Longitudinal examination of the DATABASE using risk matrix: Risk Distribution when Applied to Basic and Multiple-item Health Examination Data (From 2021)

The risk assessment obtained from the risk matrix in (2) was applied to the data of 885 participants who underwent basic health examinations in FY 2019 and 1,564 participants who underwent basic health examinations in FY 2020 and were registered in an online community. Participants who had data for both years were defined as 'continued participants', and their risk assessment and analysis of changes in data were conducted for each year.

Regarding the annual changes in 2019 and 2020, we evaluated the following items as numerical values: (1) obesity/emaciation (BMI), (2) blood pressure (systolic blood pressure: BP-s) (diastolic blood pressure: BP-d), (3) hepatic function (AST/GOT, ALT/GPT, γ-GTP), (4) glucose tolerance (BS), (5) lipids (HDL, LDL, TG), and (6) inflammation (WBC). We calculated the increase/decrease from 2019 to 2020 as delta for each individual and tabulated it by risk group in 2020. As a result, in terms of obesity/emaciation, the high risk group in 2020 showed an average increase in BMI of 0.20 kg/m^2 compared to the previous year, while the medium risk group showed almost no change at -0.03 kg/m^2, and the low risk group decreased by -0.20 kg/m^2. Similarly, the high risk group showed a positive increasing trend in blood pressure, hepatic function, and triglycerides from the previous year.

(4) Development and production of health examination DB app (from 2020)

Regarding the system for feedback of health examination results, we formulated design guidelines for the following items, and at the same time, prepared draft specifications.

A. System operating environment requirement definition, security requirement definition

B1. Establishment of operation flow
B2. Design of a function of sending and receiving emails
B3. System functional configuration design
B4. Formulation of types of information to be processed
C1. Design of content/forms of history taking
C2. Specifications/functions of data import
C3. Import specifications/functions for past health examination data
D1. Health examination results format specifications/processing function design
D2. Development of individual data assessment techniques and expression methods

For an overview of the application, registrants enter through the login screen. After logging in, they move to the authentication screen. For the first-time authentication, they enter a confirmation key to proceed to the menu screen. To view health examination data, they click on the corresponding tab to access the health examination item screen. Clicking on any item displays the data graph screen, which allows registrants to check their own data transitions. The 'Assessment Based on Health Examination Data' tab on the menu screen uses the 'Risk Matrix for Health Examination Data' to provide a new way of assessing health based on risk items identified during the examination. Medical descriptions of test items are also prepared as content. On this screen, 10 risk items are displayed using colors to indicate low (blue), medium (yellow), and high (red) risk. The background colors are shown as overall assessment, and they are presented in a similar way by using colors.

◆ Goals for the remaining one year of the second phase

The plan for the remaining year is to conduct a pilot application demonstration, verify the operability and security, and revise it towards full-scale operation. We will also conduct verification of the validity of the risk matrix.

◆ Objectives for the third Phase

We will actually use the app and disclose the results of health examinations to the participants who expressed their intention to undergo health examinations, and we will continue to verify the validity of the risk matrix based on the analysis results of longitudinal basic health examination data. Thus, we aim to contribute to the maintenance and promotion of health of emergency workers through health guidance for study participants.

◆ What hindered the progress of the study

The number of entries of examinees undergoing health examination increases or decreases depending on the year of health examination, and there is still room for improvement in the accuracy of data from various health examination institutions. These are the issues that seem to be hindering the progress of the study.

◆ Proposal for future improvements

In this study, we will examine new decision logic for detecting abnormalities in health examination items based on data from previous examinations, including questionnaires. We anticipate that in the future, we will be able to explore areas not typically covered in conventional health examinations. Therefore, it is important to present a step-by-step plan to health examination participants regarding what analysis results will be provided based on the health examinations, as well as what information will be obtained in the future.

Also, it is necessary to construct the implementation system of a health examination app after obtaining "consent to participation" based on a full understanding after giving an explanation. Thus, it is considered necessary to improve data management, system maintenance, service response, etc. as a study infrastructure.