

BMJ Open Occupational radiation exposure and its health effects on interventional medical workers: study protocol for a prospective cohort study

Seulki Ko,^{1,2} Hwan Hoon Chung,³ Sung Bum Cho,⁴ Young Woo Jin,⁵ Kwang Pyo Kim,⁶ Mina Ha,⁷ Ye Jin Bang,^{1,2} Yae Won Ha,¹ Won Jin Lee^{1,2}

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ABSTRACT

Introduction Although fluoroscopically guided procedures involve a considerably high dose of radiation, few studies have investigated the effects of radiation on medical workers involved in interventional fluoroscopy procedures. Previous research remains in the early stages and has not reached a level comparable with other occupational studies thus far. Furthermore, the study of radiation workers provides an opportunity to estimate health risks at low doses and dose rates of ionising radiation. Therefore, the objectives of this study are (1) to initiate a prospective cohort study by conducting a baseline survey among medical radiation workers who involve interventional fluoroscopy procedures and (2) to assess the effect of occupational radiation exposure and on the overall health status through an in-depth cross-sectional study.

Methods and analysis Interventional medical workers in Korea will be enrolled by using a self-administered questionnaire survey, and the survey data will be linked with radiation dosimetry data, National Health Insurance claims data, cancer registry and mortality data. After merging these data, the radiation organ dose, lifetime attributable risk due to cancer and the risk per unit dose will be estimated. For the cross-sectional study, approximately 100 interventional radiology department workers will be investigated for blood tests, clinical examinations such as ultrasonography (thyroid and carotid artery scan) and lens opacity, the validation of badge dose and biodosimetry.

Ethics and dissemination This study was reviewed and approved by the institutional review board of Korea University (KU-IRB-12-12-A-1). All participants will provide written informed consent prior to enrolment. The findings of the study will be disseminated through peer-reviewed scientific journals, conference presentations, and a report will be submitted to the relevant public health authorities in the Korea Centers for Disease Control and Prevention to help with the development of appropriate research and management policies.

INTRODUCTION

Medical radiation workers involved in interventional fluoroscopy procedures are exposed to higher radiation levels than those

Strengths and limitations of this study

- This study will provide comprehensive information on occupational radiation exposure and the health status of medical radiation workers involved in interventional fluoroscopy procedures.
- An in-depth cross-sectional study for interventional medical workers will provide a unique opportunity to investigate the overall health effects of radiation. A detailed questionnaire, laboratory and clinical examinations, badge monitoring and biodosimetry will be conducted to collect data.
- The major limitation of this study is the small number of participants for the in-depth cross-sectional study.

who perform conventional radiography.¹ However, this population is rarely studied as compared with other occupational fields or radiation epidemiology research. Therefore, epidemiological studies have been suggested,² and an urgent need for implementing a culture of radiation protection has been called for regarding interventional fluoroscopy procedures.³ However, only a few studies have focused on investigating medical workers who perform or assist in interventional fluoroscopy procedures (table 1).

Previous studies on interventional medical workers have some limitations.⁴⁻¹⁶ No cohort study with active follow-up has been conducted on interventional medical workers except for the US Radiologic Technologists (USRT) cohort.⁴⁻⁶ Only the Multispecialty Occupational Health Group (MOHG) study has attempted to investigate the long-term health effects of radiation on physicians performing interventional fluoroscopy procedures.^{7 8} Reported health outcomes have also focused on cataract development, whereas previous studies on the health effects of occupational radiation exposure primarily focused on



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For numbered affiliations see end of article.

Correspondence to
Dr Won Jin Lee;
leewj@korea.ac.kr

Table 1 Main epidemiological studies that focused on interventional medical radiation workers

Study	Country	Enrolled population	Endpoint	Reference
USRT study	USA	Radiological technologists who performed fluoroscopically guided interventional procedures	Mortality and incidence of cancer and circulatory disease	4–6
MOHG study	USA	Interventional cardiologists, radiologists and neuroradiologists	Mortality from cancer and non-cancer causes	7 8
SCAI study	USA	Interventional cardiologists and staff	Prevalence of orthopaedic injuries, cataracts and cancer	9
HCL study	Italy	Interventional cardiologists and staff	Surrogate endpoints (chromosome aberrations, telomere shortening, CIMT and olfactory ¹⁴ dysfunction)	10–12
OCLOC study	France	Interventional cardiologists	Cataract (lens opacities)	13
EURALOC study	European multinationals	Interventional cardiologists	Cataract (lens opacities)	14
RELID and SOLACI studies	International multinationals	Interventional cardiologists and staff	Cataract (lens opacities)	15 16

CIMT, carotid intima–media thickness; EURALOC, European epidemiological study on Radiation-Induced Lens Opacities among interventional Cardiologists; HCL, Healthy Cath Lab; MOHG, Multispecialty Occupational Health Group; OCLOC, Occupational Cataracts and Lens Opacities in interventional Cardiology; RELID, Retrospective Evaluation of Lens Injuries and Dose; SCAI, Society for Cardiovascular Angiography and Interventions; SOLACI, Latin American Society of Interventional Cardiology; USRT, US Radiologic Technologists.

cancer and cardiovascular diseases.^{17 18} Only the Italian Healthy Cath Lab study used detailed biomarkers and relevant clinical approaches.¹⁰ Additionally, despite the variety of medical specialties involved in interventional radiological procedures,¹ most studies have focused on the staff of interventional cardiology laboratories. Interventional cardiologists are probably the largest group and have the highest radiation exposure among interventional medical workers; however, a comprehensive approach is needed to understand the health effects of radiation exposure on the entire range of medical workers who are occupationally exposed owing to diverse interventional fluoroscopy procedures.

Therefore, additional well-organised epidemiological studies should be conducted to evaluate the precise risk of health outcomes, using measures expressed per unit of radiation dose. In particular, prospective cohort studies are necessary to determine the full extent of health risks among medical workers performing or assisting interventional fluoroscopy procedures.² In addition, in-depth studies that include detailed questionnaire survey, clinical examinations and exploration of significant biomarkers would be helpful to have a better understanding of occupational radiation exposure and its health effects.

According to the extended usage of diagnostic radiation procedures, the number of medical radiation workers has been increasing in Korea.¹⁹ Interventional fluoroscopy procedures have also been widely used by several medical specialties, and the number of procedures performed is increasing^{20 21}; however, this high-risk group among medical radiation workers has not been monitored or investigated separately in Korea. We found a case report of radiation-induced necrosis in orthopaedic surgeon

who performed interventional radiological procedures.²² We recently reported the work practices and the radiation exposure dose among male radiological technologists assisting with the fluoroscopy-guided interventional procedures.²³ However, there was no research on the health effects of medical radiation workers who perform or assist the interventional fluoroscopy procedures in Korea.

Therefore, we have launched a study about the effects of radiation on medical workers involved in interventional fluoroscopy procedures. The objectives of this study are to present the study design and protocol of (1) cohort construction by enrolment of interventional medical workers with a baseline survey and (2) an in-depth cross-sectional study to identify occupational radiation exposure and overall health status.

METHODS AND ANALYSIS

Study design and population

The target population for this survey is all of the diagnostic medical radiation workers who perform or assist in interventional fluoroscopy procedures and are presently registered in the Korea Centers for Disease Control and Prevention (KCDC), which operates a lifetime management system of occupational radiation doses. The KCDC collects information of all diagnostic medical radiation workers including basic demographic data, workplace and radiation dose as part of a government-managed registry. The registry includes physicians (radiologists and other specialists), dentists, dental hygienists, radiological technologists, nurses and medical assistants. However, there is no direct information to distinguish the medical

radiation workers who perform or assist in fluoroscopically guided procedures.

We will conduct two types of studies. First, as baseline, a cross-sectional study will be carried out with the support of various professional associations related to interventional radiological procedures. We will approach the study population through the professional societies and identify the target population based on the databases owned by each society. A cohort of interventional radiological workers will be set up with the voluntary participation of those who belong to the relevant professional societies, and they will be asked to complete the baseline questionnaire survey. We will compare between participants and the total membership of the societies regarding fluoroscopically guided procedures. After enrolment, we will combine the data from the questionnaires with dosimetry data supplied by the KCDC, which will also be linked to secondary health data, including the National Health Insurance (NHI) claim data, cancer registry and mortality data. The linked data will be annually updated to follow-up this cohort. We will estimate a lifetime attributable risk (LAR) of cancer for a given occupational exposure dose. Regarding long-term outcomes, standardised mortality ratios and incidence ratios will be calculated with secondary data linkage, and the dose–response relationship will be investigated by estimating excess relative risk (ERR) and excess absolute risk (EAR). Second, we will conduct an in-depth cross-sectional study with staff in the interventional radiology department. Because the first study yields crude exposure information only and requires a long follow-up period to detect the increased health risk, we build a small subcohort to detect potential clinical signs related to radiation health effects using an in-depth clinical study as a second study. This will include a detailed questionnaire survey, clinical examinations, a badge monitoring programme for validation of reported badge doses, biodosimetry and a review of past medical check-up records. The outline of the study design and data collection is presented in figure 1.

Baseline survey

For the baseline survey, we work closely with the professional societies for workers who are involved in medical radiation intervention procedures (table 2). With endorsement from these professional societies, we will enrol medical radiation workers to set up a cohort. To enrol participants, we are conducting a self-administered questionnaire survey via visit in person or a web-based system (<http://www.rhs.kr/intervention>). The survey method will be different depending on the preference of each scientific society. With their cooperation, we will conduct an in-person survey at the periodic meetings for professional education and various conferences organised by the scientific societies. However, if only the web-based survey is allowed, we will promote the survey on the websites of the societies and via personal email. We will conduct a subsequent supplementary survey via telephone to obtain information regarding the questionnaire items that are left blank or answered insufficiently.

To maximise the participation rate, we will take several approaches, such as periodic contacts with the executives and publicity team of the relevant professional societies, asking them to link their website to the web survey, creating banner advertisements that promote the study on their websites, directly sending emails to introduce the web survey to individual members, reminder calls as follow-ups to invitations, raffle promotions to encourage participation in the in-person surveys and sending a statement from the KCDC for official cooperation to the related societies.

All intervention medical workers registered in the target societies will be contacted and invited to participate in the baseline survey. Previously, we conducted a survey of 15501 medical radiation workers in 2012–2013,²⁴ which represented about 26% of the total diagnostic medical radiation workers in Korea. Although this particular study mainly focused on radiological technologists, approximately 7% of diagnostic medical workers

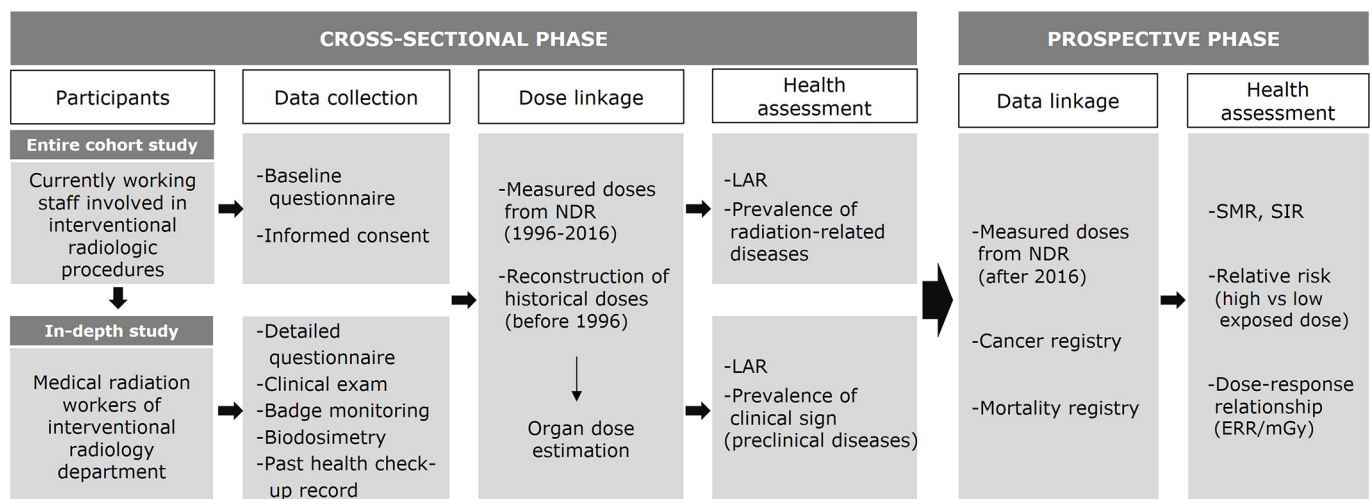


Figure 1 Study design and population. ERR, excess relative risk; LAR, lifetime attributable risk; NDR, National Dose Registry; SIR, standardised incidence ratio; SMR, standardised mortality ratio.

Table 2 Target societies in Korea for the baseline survey

Scientific societies	Member	Website	Specialty
Korean Society of Interventional Radiology	Physicians	http://www.intervention.or.kr	Interventional radiology
Korean Society of Interventional Cardiology	Physicians	http://www.kvis.or.kr	Interventional cardiology
Korean Society of Interventional Neuroradiology	Physicians	http://www.ksin.or.kr	Interventional neurology and neurosurgery
Korean Pancreatobiliary Association	Physicians	http://www.kpba.kr	Gastroenterology
Korean Orthopaedic Association	Physicians	http://www.koa.or.kr	Orthopaedic surgery
Korean Minimally Invasive Spine Surgery Society	Physicians	http://komiss.org	Orthopaedic surgery
Korean Pain Intervention Society	Physicians	http://www.korsis.or.kr	Pain and rehabilitation
Korean Society of Cardiovascular Interventional Technology	Technologists	http://www.kscvit.or.kr	Interventional radiology
Korean Cardiovascular Technology Association	Technologists	http://www.cta.or.kr	Interventional cardiology
Korean Radiology Nurses Association	Nurses	–	Interventional procedures

reported that they had been involved in radiation interventional fluoroscopy procedures. Therefore, we assume that the number of interventional medical workers is approximately 4000. This study is designed to possibly recruit all of the radiation medical intervention workers who are presently working; however, a sample size calculation is not appropriate at this time because there is no clear information to distinguish the medical radiation workers who perform or assist in fluoroscopically guided procedures and the main purpose of this study is to identify the possible target population at this stage.

Questionnaire

A questionnaire will be developed by reviewing previous cohort studies among radiation workers, adjusting the questionnaire items used for our previous survey of diagnostic radiological medical workers²⁵ and conducting a pilot study among interventional medical radiation workers. The enrolment questionnaire includes items on demographics, work history, work practices, experience of high-dose exposure, radiation exposure by personal medical examination, health-related behaviours and medical history. The demographic data include the date of birth, gender, name and workplace address. Table 3 lists the information to be collected via the questionnaire survey. In addition, an informed consent form will be developed based on the Privacy Act in Korea; it will include items regarding the collection and use of personal information, identifying information and sensitive information, in addition to sharing of personal information with third parties and consent to participate in a research study.

Validation of self-reported medical radiation exposure and medical history

The medical radiation exposures, health-related behaviours and medical history included in the questionnaire will be validated through the NHI claim data. It is collected and managed by the National Health Insurance

Service (NHIS), the only public health insurance scheme in Korea, which covers the entire Korean population and includes eligibility data, the national health screening data and the healthcare usage data.²⁶ We can use information on health-related behaviours from the national health screening data and information on medical radiation exposure and radiation-associated diseases from the healthcare usage data.

Table 3 Items collected in the baseline survey questionnaire

Domains (no of questions)	Items
Demographics (4)	Date of birth, gender, name and workplace address
Work history (4)	Job title, specialty, years since beginning work and total duration of work
Work practices (7)	Proportion of interventional procedures for the recent year, working days per month, working hours per week, name of the main procedure performed, badge wearing, wearing of protective equipment and use of shielding devices
Experience of high radiation exposure (2)	Exposure to >5 milliSievert a quarter and low WCC
Personal medical examination (6)	CT scan, fluoroscopy, nuclear medicine imaging, PET-CT scan, interventional radiography and radiation therapy
Lifestyle (2)	Smoking and alcohol consumption
Medical history (9)	Cataract, eye irritation, anaemia, hypertension, dyslipidaemia, cancer, thyroid disease, neck/back pain and skin disease

PET, positron emission tomography; WCC, white cell count.

Data linkage and follow-up

After the completion of the survey, participants' data will be linked with dosimetry data from the National Dose Registry managed by KCDC by means of participant's name, gender, date of birth and workplace address. The National Dose Registry contains the workers' name, gender, date of birth, personal identification number, workplace address, job title, quarterly measured dose data and the beginning and end of the period of measurement.

We will continue to evaluate the association between the radiation dose and its overall health effects with a long-term follow-up. Participants will be passively followed by linking the NHI claims data, Korea Central Cancer Registry (KCCR) and National Vital Statistics Registry that have been available since 2002, 1999 and 1991, respectively. We will use the healthcare usage data and the national health screening data in the NHI claim data to identify non-cancer diseases such as cataracts, cardiovascular diseases and thyroid diseases related to radiation exposure as well as other risk factors such as body mass index (BMI). The KCCR is the national level registry and maintains a high level of completeness (97.8% in 2014).²⁷ The registry data include cancer code (International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) and International Classification of Diseases for Oncology, Third Edition (ICD-O-3)), site, histological type, stage, diagnosis method and the date of diagnosis. The National Vital Statistics from Statistics Korea (<http://kostat.go.kr>) has also maintained a high level of completeness; the registration rate was 99.7% in 2014.²⁸ Mortality data are classified by the underlying cause of death according to the ICD-10.

To ascertain cancer incidence and the cause of death among study participants, personal identification numbers will be sent to the NHIS, Korean National Cancer Center and Statistics Korea; on our request, they will link these personal identification numbers to the NHI claims data, cancer registry data and mortality data. This linkage method is highly specific because of the uniqueness of the personal identification number of an individual in Korea, and we have successfully linked these data for radiological technologists previously.²⁵ All the data linkage processes will be conducted only when informed consent is obtained.

Calculation of radiation doses

The KCDC has been carrying out monitoring programme for all medical radiation workers involved in diagnostic radiology since 1996. It maintains a centralised National Dose Registry and operates a lifelong follow-up management system for radiation dose in accordance with the Rules for Safety Management of Diagnostic Radiation and the Rules for Safety Management of Diagnostic Radiation Emitting Generators.²⁹ Dose measurements have been collected quarterly by five personnel monitoring centres designated by the KCDC. The data for radiation dosimetry are available starting from 1996. To discover the occupational radiation exposure, individual doses

recorded over the periods involved will be combined and annual effective doses and cumulative doses for each participant will be obtained as we reported previously.³⁰

The organ dose estimation will be performed using the methodology applied in the USRT study.³¹ Briefly, the estimation of organ doses involves the use of measured badge dose and two ratios provided by the International Commission on Radiological Protection (ICRP):³² (1) the organ absorbed dose per unit of air kerma free-in-air (Gray per Gray) and (2) the personal dose equivalent per unit of air kerma free-in-air (Sievert per Gray). The calculation of organ absorbed dose in this study will use the ICRP factors and the organ dose coefficients.³² The equation is,

$$D_T = H_p(d) \left[\frac{D_T/K_a}{H_p(d)/K_a} \right]$$

where D_T is organ dose (Gray), $H_p(d)$ is badge dose (Sievert) and K_a is air kerma free-in-air (Gray).

To adjust for the use of protective aprons and placement of the badge relative to the apron, we will apply the attenuation factor of protective device for apron. The radiation doses were not documented for individuals who were working before 1996; therefore, we will estimate their historical occupational exposed doses, by applying our previous methods, using a dose reconstruction model that includes predictors, such as age, gender and workplace.³³

Estimation of LAR of cancer

The LAR of cancer specifies the probability that an individual will develop or die from cancer due to radiation exposure.³⁴ For a given dose, LAR is the additional cumulated probability of having a specific cancer up to the maximum age of 89 years. We will calculate LAR based on the methods applied in the WHO report as follows.³⁵ For an individual of sex s , exposed to dose D at age-at-exposure e and a specific cancer site at attained age a , the LAR is estimated as follows:

$$\text{LAR}(D, e, s) = \int_{e+L}^{a_{\max}} M(D, e, a, s) \frac{S_{aj}(a, s)}{S_{aj}(e, s)} da$$

To calculate LAR, a risk model is needed which can be either an ERR model or an EAR model, or a mixture of the two; $M(D, e, a, s)$ is the risk model in the equation. $S_{aj}(a, s)$ is the probability of cancer-free survival until age a for the radiation-unexposed population; the ratio of $S_{aj}(a, s)/S_{aj}(e, s)$ is the conditional probability of an individual being alive and cancer-free at age-at-exposure e to reach at least an attained age a . L is the minimum latency period depending on the cancer site. Survival functions ($S(a, s)$ or $S(e, s)$) will be calculated based on the age-specific all-cause mortality rates derived from Statistics Korea for LAR of cancer mortality, while the adjusted survival functions ($S_{aj}(a, s)$ or $S_{aj}(e, s)$) will be applied for LAR of cancer incidence, which are derived on the basis of all-cause mortality and the difference between all-cancer incidence and all-cancer mortality.³⁵

In-depth cross-sectional survey

We will conduct a cross-sectional study for medical staff who work in the interventional radiology departments and will attend the 2017 Annual Joint Scientific Meeting of the Korean Society of Interventional Radiology, Korean Society of Cardiovascular Interventional Technology and Korean Radiology Nurses Association. These societies will provide detailed information, advertise and recruit volunteers who agree to participate by giving informed consent in advance. We aim to recruit approximately 100 workers, including 50 radiologists and 50 nurses and radiological technologists. The Korean Society of Interventional Radiology, the main collaborator of this project, is trying to recruit participants nationwide, through local branches of the society approaching whole list of 200 members with advance registration. The Korean Society of Cardiovascular Interventional Technology and Korean Radiology Nurses Association will select participants among the attendees of the Annual Joint Meeting.

The study contents are a detailed questionnaire-based survey, laboratory and clinical examinations, badge monitoring programme, biodosimetry and a review of the past health check-up records (table 4). A detailed questionnaire will give comprehensive information on the status of occupational radiation exposure and health status; clinical examinations and past health check-up records could give us a clue about the health risks of radiation exposure regarding early warning signs. Using the badge monitoring programme and biodosimetry, we will investigate the validity of the reported badge dose and the correlation between physical dosimetry and biodosimetry.

Detailed questionnaire

A detailed questionnaire will be developed for the in-depth survey. We are reviewing previous cohort studies on radiation workers as a basis for developing the detailed questionnaire, and a pilot study will be conducted among the staff of the interventional radiology department of a hospital. While the baseline questionnaire we are developing inquires about the current radiation exposure, the detailed questionnaire consists of questions relating to work practices by calendar period in order to obtain comprehensive work-related information. The questionnaire includes information on demographics, work history, work practices, experience of high radiation exposure, management of radiation exposure, personal medical examination, health-related behaviours and medical history (table 4). The survey will be conducted during September of 2017 via the postal mail, together with a respondent-friendly description of the survey and the questionnaire. An informed consent form for the in-depth survey is prepared in the same way as that of the baseline survey.

Clinical examination

On-site clinical examinations, including anthropometry, blood pressure measurement, sampling for blood analysis and biodosimetry, ophthalmic examination and

ultrasonography examinations, will be set up at the venue of the Annual Joint Scientific Meeting. All of the 100 registered participants will be contacted to schedule the examination during the meeting, and they will be provided with information regarding the aims, contents, methods and location of the temporal examination suite. All of the clinical examination procedures will be performed by trained medical personnel who will follow standardised protocols and use calibrated equipment. Based on the clinical and subclinical findings from these clinical examinations, potential radiation health risks could be detected, and this might increase our understanding of the initial damage from radiation exposure and allow us to infer long-term health outcomes.¹⁰

Anthropometrical profiles (ie, height, weight and waist circumference) will be measured as described by the Korea National Health and Nutrition Examination Survey (KNHANES), a health examination procedures manual.³⁶ BMI will be calculated as the ratio of body weight (kilogram) to height squared (squared metre). Based on the standard protocol, systolic and diastolic blood pressures will be measured by trained nurses using a sphygmomanometer (JPN1 model; Omron, Kyoto, Japan) on the right arm of the seated subject after at least 5 min of rest.

Venous blood samples will be obtained from the antecubital vein by trained nurses to perform blood analysis and biodosimetry, and samples will be processed according to the KNHANES protocol.³⁶ Blood will be drawn into several different tubes, such as an EDTA tube for testing complete blood count (CBC) and for analysing glycated haemoglobin; a serum separation tube for analysing blood lipid levels, high-sensitivity C reactive protein, homocysteine and thyroid function test; and a heparin tube for the biodosimetry sample. Detailed test items are listed in table 4. Serum separating tubes will be kept at room temperature for 30 min, and the blood will subsequently be centrifuged at 3000 revolutions per minute for 15 min. EDTA tubes and heparin tubes will be mixed in a roller mixer for 10 min. All blood samples will be refrigerated at 4°C and will be transported immediately to the accredited analytic laboratory (Seegene, Seoul, Korea).

Ophthalmic examinations will be conducted to investigate lens opacities, including a visual acuity test and a slit-lamp examination of the lens. A single ophthalmologist will conduct all of the examinations using the slit-lamp BQ 900 (Haag-Streit AG, Koeniz, Switzerland). The diagnosis and grading of cataracts will be done according to the Lens Opacities Classification System (LOCS) III from early (stage 1) to severe (stage 5).³⁷ The LOCS classification also describes the localisation of lens opacities (cortical, nuclear and posterior subcapsular).

Ultrasonography examination consisting of carotid artery and thyroid scans will be performed by a single radiologist, using a high-resolution B-mode ultrasonography (E-CUBE i7; Alpinion, Seoul, Korea) that has a linear 8–17 MHz transducer (L8-17; Alpinion) and the ability to save digital imaging and communications in medicine images to be retrospectively evaluated. Carotid

Table 4 Items investigated with in-depth survey among the medical staff of intervention radiology department

Survey contents	Components	Detailed item	
Detailed questionnaire	Demographics	Same as baseline survey questionnaire	
	Work history	Same as baseline survey questionnaire	
	Work practices	Frequency of interventional procedures, badge wearing, wearing of protective equipment and use of shielding devices (by decade*)	
	Experience of high radiation exposure	Exposure to >5 milliSievert a quarter, low WCC and radiation work in other job	
	Management of radiation exposure	Regular health check-up, knowledge of dose limits and personal dose and risk perception items	
	Personal medical examination	X-ray (by site†), mammography, dental radiography, CT (by site‡), fluoroscopy (by site§), interventional radiography, PET-CT, nuclear medicine imaging, radiation therapy and MRI	
	Lifestyle	Smoking, alcohol consumption, physical exercise and night shifts	
Clinical examination	Medical history	Cataract, skin diseases, thyroid diseases, neck/back pain, cardiovascular diseases, cancer and so on Medication history, family history of cataract, cardiovascular diseases and cancer	
	Anthropometry	Height, weight and waist circumference	
	Blood pressure	Systolic and diastolic blood pressure	
	Blood analysis		For haematologic disease WCC, differential count, RBC, Hb, Hct, MCV, MCH, MCHC, RDW, platelet, MPV, PDW and reticulocyte count
			For diabetes HbA1c
			For dyslipidaemia Total cholesterol, TG, HDL cholesterol and LDL cholesterol
			For thyroid disease TSH, thyroid hormones T3, T4 and free T4
	For cardiovascular risk factors Homocysteine, hs-CRP		
	Ophthalmological examination	Visual acuity Lens opacities	
	Ultrasonography examination	Thyroid gland Common and internal carotid artery CIMT	
Badge monitoring	Dosimetry Work diary	Inside/outside of lead apron at chest and outside of thyroid shield Interventional procedures (type, frequency and time)	
Biodosimetry	Stable and unstable chromosomal aberrations	Dicentric assay 1,2,4-FISH translocation assay	
Past health check-up records	Haematology	WCC, differential count, RBC, Hb and platelet	
	Blood pressure	Systolic and diastolic blood pressure	

*1980–1989, 1990–1999, 2000–2009 and 2010–present.

†Head and neck, chest, abdomen and extremity.

‡Head and neck, chest, abdomen, pelvis and extremity.

§Stomach, intestine, hepatobiliary, kidney and others.

CIMT, carotid intima–media thickness; FISH, fluorescent in situ hybridisation; Hb, haemoglobin; HbA1c, glycated haemoglobin; Hct, haematocrit; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; PDW, platelet distribution width; PET, positron emission tomography; RBC, red blood cell; RDW, red cell distribution width; T3, tri-iodothyronine; T4, thyroxine; TG, triglyceride; TSH, thyroid-stimulating hormone; WCC, white cell count.

artery ultrasonography will be performed to measure carotid intima–media thickness (CIMT), which is a useful indicator for refining cardiovascular disease assessment among high-risk groups.³⁸ The CIMT will be measured

at near and far walls on both the left and right sides of the common carotid artery and internal carotid artery by automatic or semiautomatic measurement. Thyroid ultrasonography will detect thyroid nodules in both lobes,

and the ultrasonography features of the nodules will be prospectively assessed in each participant during the examination. Subsequently, the nodules will be classified according to the Korean Thyroid Imaging Reporting and Data System^{39 40} to categorise thyroid nodules and stratify their malignancy risk.

Validity of badge dose

The validity of the badge doses reported from the National Dose Registry is important in evaluating occupational radiation exposure assessment and in estimating organ doses. To monitor the exact radiation exposure dose among interventional radiologists, study participants will wear three personal thermoluminescent dosimeters (Panasonic TLD system) inside and outside of the apron, and outside of the thyroid shield, always correctly for 1 month while keeping a working diary. Dose measurements will be collected by a fully accredited centre (Orbitech, Seoul, Korea). Measured badge doses will be compared with the reported dose data from the National Dose Registry in order to assess their validity. Intraclass correlation coefficients⁴¹ will be used as measures of validity.

Biodosimetry

Biodosimetry could be considered as an alternative method for estimating the absorbed dose, using a biomarker. Cytogenetic dosimetry analyses radiation-induced chromosome aberrations that are classified as unstable or stable aberrations, and this could evaluate individual radiation-related health risks represented by genomic instability.⁴² We will score dicentric chromosomes as unstable aberrations because this has been considered the most reliable method for biodosimetry.⁴³ We will investigate reciprocal translocation as recommended in the case of prolonged exposure for a stable aberration.⁴⁴ Blood samples for biodosimetry will be obtained during the clinical examination for the in-depth study. The samples will be collected in a heparin tube and will be processed for culturing within 24 hours after collection and delivery. The process of culturing, harvesting, staining and scoring for the analysis of dicentric chromosomes by solid Giemsa staining will be performed in accordance with the International Atomic Energy Agency recommendations.⁴⁵ Metaphase cells will be prepared on a slide and 1, 2 and 4 whole chromosomes will be stained and scored for the analysis of translocation by fluorescence in situ hybridisation. The absorbed dose for each individual will be calculated from the measured yield of dicentrics and translocations, using dose–response calibration curves previously constructed at the Korea Institute of Radiological and Medical Sciences.^{46 47}

Past medical examinations

Under the Korean law regarding the health protection of medical radiation workers (Medical Service Act, Article 37), registered medical radiation workers are required to wear personal thermoluminescent dosimeters and

report their annual health check-up records, including the results of CBC test. We will ask participants to provide their previous health check-up data by filling out a structured form included in the in-depth questionnaire. The items include white cell count, red blood cells, haemoglobin, platelets, systolic and diastolic blood pressure and will be collected by requesting the electronic records of medical examination results. These data could be helpful in assessing the temporal trend of health effects from occupational radiation exposure.

Statistical analyses

All collected variables will be tabulated using summary statistics stratified by job title for continuous variables as mean values with SD and categorical variables as frequencies and percentages. The Student's t-test and the χ^2 test will be used to test for the significance of the differences between two groups. The prevalence of clinical signs or diseases will be stratified by the job titles. Logistic regression analysis will be used to analyse binary variables for the abnormality of clinical examinations to ascertain whether occupational characteristics and radiation exposure are associated. Models will be adjusted for potential confounding factors, and the ORs and their 95% CIs will be reported. Analysis of the long-term health effects through the follow-up will be conducted in parallel with the entire cohort.

DISCUSSION

This article has described the study design and protocol of a study on Korean medical radiation workers performing interventional fluoroscopy procedures. The advantage of this study compared with previous studies is that our study participants are linked to individual information by way of a questionnaire, radiation dosimetry, the NHI claims data, cancer registry and mortality data. All South Koreans are assigned a unique identification number at birth, and this number ensures accurate linkage to all national registry data. This allows investigating associations between radiation exposure and its health effects. The inclusion of an in-depth cross-sectional study examining a variety of preclinical health conditions is another unique advantage of this study. The study participants will provide detailed information on their work practices by calendar year. This allows for an in-depth exploration of occupational exposure and working conditions. We will collect participants' blood samples which enhance our ability to investigate radiation susceptibility and to assess exposure risk via surrogate biomarkers. Besides establishing scientific evidence of radiation-related health effects, this study will help to improve the awareness of the importance of radiation protection and to control the radiation exposure risk from interventional procedures. However, this study has the limitation of having a small number of participants for the in-depth cross-sectional study because of a limited budget. Further assessment by an international collaborative study would be necessary to

overcome the limitation of small sample size. In addition, although the conditions of the ophthalmological examination may be less than perfect, examinations taking place at the venue of the Annual Joint Scientific meeting should be as quick and comfortable as possible. Therefore, to maximise the participant rate in this limited situation, we will set up the dark conditions enough to dilate the pupil during the ophthalmological examination without application of mydriatics.

Previous studies for intervention medical workers also had some limitations. The majority of studies were of a cross-sectional design and concentrated on cataract/lens opacities; radiation risk was rarely assessed per unit of radiation dose. Compared with the previous studies, this study is rather unique because it collects comprehensive information to evaluate the health effects of low-dose radiation exposure. Therefore, this study will make important contributions to the literature by providing evidence regarding the occupational radiation exposure and its health effects on interventional medical radiological workers.

In summary, we will conduct a study regarding the health effects of radiation exposure on medical workers performing or assisting in interventional fluoroscopy procedures in Korea. This study features comprehensive information on the health outcomes, and the in-depth survey provides unique opportunities to investigate work-related factors and radiation exposure status of the interventional medical workers. This study will give further understanding of work practices and the association between protracted occupational radiation exposure and the health of interventional medical workers.

Ethics and dissemination

Informed written consent, including permission to collect personal information, and access to radiation dosimetry, NHI claims data, cancer registry and mortality data will be voluntarily obtained from each study participant before enrolment in the study. The participants of the baseline survey and in-depth study will receive a coupon for coffee (approximately worth US\$4) and a gift card (approximately worth US\$90), respectively.

The findings of the study will be shared with each professional society first and will be disseminated to their members through the society's website and its educational meetings. The main results of the study will also be disseminated through peer-reviewed scientific journals, and national and international academic conferences. We will also provide a full report to the KCDC, the organisation that is responsible for developing appropriate research and management policies.

Author affiliations

¹Department of Preventive Medicine, Korea University College of Medicine, Seoul, South Korea

²Graduate School of Public Health, Korea University, Seoul, South Korea

³Department of Radiology, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, South Korea

⁴Department of Radiology, Korea University Anam Hospital, Korea University College of Medicine, Seoul, South Korea

⁵National Radiation Emergency Medical Center, Korea Institute of Radiological and Medical Sciences, Seoul, South Korea

⁶Department of Nuclear Engineering, Kyung Hee University, Yongin, South Korea

⁷Department of Preventive Medicine, Dankook University College of Medicine, Cheonan, South Korea

Contributors SK and WJL: study concept and design, study coordination and drafting the manuscript. HHC and SBC: study design, planning of clinical examinations and revising the manuscript. YWJ: biodosimetry and revising the manuscript. KPK: badge monitoring and revising the manuscript. MH: study design, questionnaire and revising the manuscript. YJB and YWH: conducting field study, badge monitoring and revising the manuscript. All authors: approved and critically reviewed the final version of the manuscript.

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