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BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018333
Article Type:	Protocol
Date Submitted by the Author:	21-Jun-2017
Complete List of Authors:	Ko, Seulki Chung, Hwan Hoon Cho, Sung Bum Jin, Young Woo ; Korea Institute of Radiological and Medical Sciences, National Radiation Emergency Medical Center Kim, Kwang Pyo Ha, Mina Bang, Ye Jin; Korea University College of Medicine, Department of Preventive Medicine Ha, Yae Won Lee, Won; Korea University, Department of Preventive Medicine, Korea University College of Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology
Keywords:	Cohort, Fluoroscopically guided procedures, Medical workers, Occupational exposure, Radiation

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

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Keywords: Cohort; Fluoroscopically guided procedures; Medical workers; Occupational exposure; Radiation.

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ABSTRACT

Introduction: Although fluoroscopically guided procedures involve a considerably high dose of radiation, only a few studies have investigated the effects of radiation on medical workers involved in interventional fluoroscopy procedures. Previous research remains at 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 ionizing radiation. Therefore, the objectives of this study are to conduct 1) baseline survey with the radiation medical workers who involve interventional fluoroscopy procedures, and 2) in-depth cross-sectional study to investigate the early clinical signs in relation to occupational radiation exposure.

Methods and analysis: Intervention medical workers in Korea will be enrolled by using a self-administered questionnaire survey, and the survey data will be linked with radiation dosimetry, cancer registry, and mortality data. After merging these data, the radiation organ dose, the lifetime attributable cancer risk, and the risk per unit dose will be estimated. A cross-sectional study will also be conducted with approximately 100 intervention radiology department workers, and this study will include the validation of badge dose, biodosimetry, blood tests, and clinical examinations, such as ultrasonography, thyroid scan, and lens opacity.

Ethics and dissemination: This study was reviewed and approved by the Institutional Review Board of Korea University. All participants will provide written informed consent prior to enrollment. 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 CDC to help with the development of appropriate research and management policies.

Strengths and limitations of this study:

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

INTRODUCTION

The radiation medical workers involved in interventional fluoroscopy procedures are exposed to radiation levels higher than those who perform conventional radiography.[1] However, this population is rarely studied as compared with other occupational fields or radiation epidemiology research. Therefore, epidemiologic studies have been suggested,[2] and an urgent need for implementing a culture of radiation protection has been called for with respect to interventional fluoroscopy procedures.[3] However, only a few studies have focused on investigating the medical workers who perform or assist interventional fluoroscopy procedures (table 1).

Previous studies on interventional medical workers have some limitations. No active cohort study has been conducted on interventional medical workers except for the US radiologic technologists (USRT) cohort.[4-6] Only the Multispecialty Occupational Health Group (MOHG) research 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 for health effects of occupational radiation exposure primarily focused on cancer and cardiovascular diseases.[9 10] Only Italian Cath lab study used detailed biomarkers and relevant clinical approaches.[11] Additionally, despite having a variety of medical specialties related to interventional radiologic procedures,[1] most studies have focused on the staff of interventional cardiology laboratory. 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-organized epidemiologic 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 utilization of diagnostic radiation procedures, the number of medical radiation workers has been increasing in Korea.[12] Interventional fluoroscopy procedures have also been widely used by several medical specialties, and the number of procedures performed is increasing;[13 14] 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 orthopedic surgeon who performing interventional radiologic procedures.[15] We recently reported the work practices and the radiation exposure dose among male radiology technologists assisting with the fluoroscopy guided interventional procedures.[16] 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 enrolling intervention medical workers in a baseline survey, and 2) an in-depth cross-sectional study to investigate the early clinical signs in relation to occupational radiation exposure.

METHODS AND ANALYSIS

Study design and population

The target population for this survey is all of the diagnostic radiation medical workers who perform or assist the interventional fluoroscopy procedures and are presently registered in the Korea Centers for Disease Control and Prevention (KCDC). As baseline, a cross-sectional study will be carried out with the support of various professional associations related with interventional radiology procedures. A cohort of interventional radiology medical workers will be formed with voluntary participation of those who belong to the relevant scientific societies, and they will be asked to complete the baseline questionnaire survey. After enrollment, we will combine the data from the questionnaires with dosimetry data supplied by the KCDC, and it will also be linked to secondary health data, including cancer registry and mortality data. 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. As for long-term outcomes, standardized mortality ratios (SMRs), standardized incidence ratios (SIRs) will be calculated with secondary data linkage, and the dose response relationship will be investigated through estimating excess relative risk (ERR) and excess absolute risk (EAR). We will conduct a cross-sectional in-depth study with staff in the interventional radiology department; it will include a detailed questionnaire survey, clinical examinations, badge monitoring program for validation of reported badge doses, biodosimetry, and a review of past health check-up records. The outline of the study design and data collection is presented in figure 1.

Baseline survey

For 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 enroll medical radiation workers to form a cohort. To enroll participants, we are conducting self-administered questionnaire survey via on-site visits and on the Internet via a web-based system (http://www.rhs.kr/intervention). We have been attending to the periodic meetings for occupational continuing education and various conferences for radiology workers to conduct the on-site surveys. We will conduct a subsequent supplementary survey via telephone to obtain information regarding the questionnaire items that are left blank or answered insufficiently.

To maximize the participation rate, we will undertake several efforts, such as periodic contacts with the executives and publicity team of the relevant professional societies, asking them to link to the website for the web survey, creating banner advertisements that advocate the study on their websites, directly sending e-mails to introduce the website to individual members, reminder calls as follow-ups to invitations, and raffle promotions to encourage participation in the on-site surveys.

All intervention medical workers registered in the target societies will be contacted and be invited to participate in the baseline survey. Previously, we conducted a survey for 15,501 medical radiation workers in 2012-2013,[17] which represented about 26% of the total diagnostic medical radiation workers in Korea. Although this particular study mainly focused on radiologic technologists, approximately 7% of diagnostic medical workers reported that they had been involved in radiation interventional fluoroscopy procedures. Therefore, we assume that the number of interventional medical workers is approximately 4,000. 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.

Questionnaire

A questionnaire will be developed by reviewing previous cohort studies on radiation workers, adjusting the questionnaire items used during our previous survey of diagnostic radiologic medical workers,[18] and conducting a pilot study among interventional medical radiation workers. The enrollment questionnaire includes items on demographics, work history, work practices, experience of high-dose exposure, radiation exposure by personal medical examination, lifestyle, and past medical history. Demographic data includes 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 research participation.

Data linkage

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 date of birth, name, and workplace address. The national dose registry has the workers' name, gender, personal identification number, 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 health effects with long-term follow-up. For the follow-up, individual participant's data will be linked to the Korea Central Cancer Registry (KCCR) and National Vital Statistics Registry that have been available since 1999 and 1991, respectively. The Korean National Cancer

Center (KNCC) administers KCCR at the national level, and it has been reported that it features a high level of completeness (97.8% for 2014).[19] The registry data includes cancer code (International Classification of Diseases and Related Health Problems, 10th Revision – ICD-10) and International Classification of Diseases for Oncology, the 3rd Edition (ICD-O-3)), site, histological type, stage, diagnosis method, and the date of diagnosis. National Vital Statistics from Statistics Korea (http://kostat.go.kr) is also maintained with high level of completeness, and the registration rate was 99.7% in 2014.[20] Mortality data is classified by the underlying cause of death according to ICD-10.

To ascertain cancer incidence and the cause of death among study participants, individual personal identification numbers will be sent to the KNCC and Statistics Korea; upon our request, they will link these personal identification numbers to the 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 radiologic technologists previously.[18] We will continue to evaluate the association between the radiation dose and its health effects with long-term follow-up.

Calculation of radiation doses

The KCDC has been carrying out monitoring programs for all medical radiation workers involved in diagnostic radiology since 1996. It maintains a centralized national dose registry and operates a life-long 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.[21] Dose measurements have been collected quarterly by the five personnel monitoring centers 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 for each subject will be obtained as we reported previously.[22]

The method of organ dose estimation will be done using the methodology applied in the USRT study.[23] Briefly, the estimation of organ doses involves the use of measured badge dose reading and two ratios provided by the International Commission on Radiological Protection (ICRP):[24] (a) the organ absorbed dose per unit of air kerma free-in-air (Gy per Gy) and (b) the personal dose equivalent per unit of air kerma free-in air (Sv per Gy). The calculation of organ absorbed dose in this study will use the ICRP factors and the organ dose coefficients.[24] 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 (Gy), $H_p(d)$ is badge dose (Sv), and K_a is air kerma free-in-air (Gy).

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, thyroid shield, and goggle. The radiation doses were not documented for the 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, sex, and work place.[25]

Estimation of lifetime attributable cancer risk

Lifetime attributable cancer risk specifies the probability that an individual will develop or die from cancer attributable to radiation exposure.[26] 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.[27] The equation of LAR for an individual of sex *s*, exposed to dose *D* at age-at-exposure *e*, a specific cancer site at attained age *a*, is:

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

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 from the Statistics Korea for LAR of cancer mortality, while 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.[27]

In-depth cross-sectional survey

We will conduct a cross-sectional study for medical staff that work at the interventional radiology departments and are attending 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 are providing detailed information, advertising and recruiting volunteers who agree to participate by giving informed consent in advance. Approximately 100 workers, including radiologists, nurses, and radiology technologists have been enrolled to participate in the in-depth study. The study contents are a detailed questionnaire-based survey, clinical examinations, badge monitoring program, biodosimetry, and a review of the past health check-up records (table 4). Detailed questionnaire will give comprehensive information on the status of occupational radiation exposure and its health outcomes; clinical examinations and past heath check-up records could give us a clue about the health risks from radiation exposure by way of early warning signs. Using the badge monitoring program and biodosimetry, we will also investigate the validity of 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 the previous cohort studies on radiation workers to develop the basis of the baseline questionnaire, and a pilot study will be conducted with interventional radiology department staff of a hospital. While the baseline questionnaire we are developing enquires 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, lifestyle, 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 that of the baseline survey.

Clinical examination

On-site clinical examinations, including anthropometry, blood pressure measurement, sampling for blood analysis and biodosimetry, ophthalmologic examination, and ultrasonography examinations will be set up where Annual Joint Scientific Meeting will be held. All of the 100 registered participants will be contacted to schedule during the meeting, and they will be provided with information about the aims, contents, methods, and location of the on-site examination. All of the clinical examination procedures will be performed by trained medical personnel who will follow standardized 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.[11]

Anthropometrical profiles (i.e., height, weight, and waist circumference) will be measured as described by the Korea National Health and Nutrition Examination Survey (KNHANES) Health Examination Procedures Manual.[28] Body mass index (BMI) will be calculated as the ratio of body weight (kg) to height squared (m^2). Based on the standard protocol, systolic blood pressure and diastolic blood pressure 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 minutes 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

KNHANES protocol.[28] Blood will be drawn into several different tubes, such as an EDTA tube for complete blood count (CBC) test and for analyzing glycated hemoglobin A1c (HbA1c), a serum separation tube for analyzing blood lipid levels, high-sensitivity C-reactive protein (hs-CRP), homocysteine, thyroid function test (TFT), and a heparin tube for the biodosimetry sample. Detailed test items are listed on table 4. Serum separating tubes will be kept at room temperature for 30 minutes, and the blood will subsequently be centrifuged at 3000 rpm for 15 minutes. EDTA tubes and Heparin tubes will be mixed in a roller mixer for 10 minutes. All blood samples will be refrigerated at 4 °C and will be transported immediately to the accredited analytic laboratory (Seegene, Seoul, Korea).

Ophthalmologic examinations will be held to investigate lens opacities, including a visual acuity test and a slit lamp examination of the lens. All of the examinations will be conducted by a single ophthalmologist using the Slit Lamp 900BQ LED (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).[29] The LOCS classification also describes the localization of lens opacities (cortical, nuclear, posterior sub-capsular).

Ultrasonography examination consists of carotid artery and thyroid scan which 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, Seoul, Korea) and the ability to save Digital Imaging and Communications in Medicine (DICOM) images to be retrospectively evaluated. Carotid artery ultrasonography will be performed to measure carotid intima-media thickness (CIMT) as a useful indicator for refining cardiovascular disease assessment among high risk groups.[30] The CIMT will be measured at left, right near, and far walls of the common carotid artery, and internal carotid artery by automatic or semi-automatic measurement. Thyroid ultrasonography will detect thyroid nodules in both lobes, and the ultrasonography features of the nodules will be prospectively assessed in each patient during the examination. Subsequently, the nodules will be classified according to the Korean Thyroid Imaging Reporting and Data System (K-TIRADS)[31 32] to categorize thyroid nodules and stratify their malignancy risk.

Validity of badge dose

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 thermos-luminescent dosimeters (Panasonic TLD system) inside and outside of apron, and outside of thyroid shield, always correctly for one month with detailed description and close monitoring. Dose measurements will be collected by a fully accredited center (Orbitech, Seoul, Korea). Measured badge doses will be compared with the reported dose data from National dose Registry in order to assess the validity. Intraclass correlation coefficients[33] will be used as measures of validity.

Biodosemetry

Biodosimetry could be considered as an alternative method for estimating the absorbed dose, using a biomarker. Cytogenetic dosimetry analyzes 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.[34] We will score dicentric chromosomes as unstable aberrations because this has been considered the most reliable method for biodosimetry.[35] We will investigate reciprocal translocation recommended in the case of prolonged exposure for a stable aberration.[36] Blood samples for biodosemetry will be obtained during the on-site clinical examination. 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.[37] Metaphase cells will be prepared on a slide and 1, 2, and 4 whole chromosomes will be painted and scored for the analysis of translocation by fluorescence in situ hybridization. The absorbed dose for each individual will be calculated from the measured yield of dicentrics and translocations, using dose-response calibration curves constructed at Korea Institute of Radiological and Medical Sciences previously.[38 39]

Past medical examinations

Under Korean law concerning the health protection of medical radiation workers (Medical Service Act, Article 37), registered medical radiation workers are required to wear personal TLD and submit 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 WBC, RBC, hemoglobin, platelets, systolic and diastolic blood pressure. These data could helpful to examine the temporal trend of health effects from the occupational radiation exposure.

DISCUSSION

This article has described the study design and its procedures of a study on the Korean radiation medical workers performing interventional fluoroscopy procedures. The advantage of this study compared to the previous studies is that our study subjects are linked to individual information by way of a questionnaire, radiation dosimetry, cancer registry, and mortality data. All South Koreans are assigned a unique identification number at the time of their birth, and this number ensures accurate linkage to all national registry data. This allows the examination of associations between radiation exposure and its health effects. In-depth cross-sectional study examining a variety of health outcomes is another unique advantage of this study. The study participants will provide detailed information on their work practices by calendar year as well as on lifestyle factors. This allows for an in-depth exploration of occupational exposure and the working conditions. These workers will also provide a bio-sample (i.e., blood) which enhances our ability to investigate susceptibility and to assess exposure risk via surrogate biomarkers. Besides establishing scientific evidence of radiation-related health effects, this study will help improve the awareness of the importance of radiation protection and will help control the radiation risk from interventional procedures. However, this study has the limitation of having small number of participants for an in-depth cross-sectional study because of limited budget.

Previous studies for intervention medical workers also had some limitations. The majority of studies were of cross-sectional design that concentrated on cataract formation, and the radiation risks were rarely assessed by per unit of radiation dose. Compared to 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 knowledge base by providing evidence regarding the occupational radiation exposure and its health effects on interventional radiologic medical workers.

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

ETHICS AND DISSEMINATION

This study has been reviewed and approved by the Institutional Review Board of Korea University (KU-IRB-12-12-A-1) and funded by KCDC (2017E3600600). Informed written consent, including permission to collect personal information, and access to radiation dosimetry, cancer registry, and mortality data will be voluntarily obtained from each individual study participant before enrollment in the study. The participants of the baseline survey and in-depth study will receive a coupon for coffee (approximately worth 4 USD) and a gift card (approximately worth 90 USD), respectively.

The findings of the study will be shared with each 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 organization that is responsible for developing appropriate research and management policies.

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

Funding: This work was supported by the Korea Ministry of Health and Welfare and Center for Disease Control and Prevention grant number 2017E3600600 from 13 April, 2017 to 12 February, 2018

Conflict of interest: None

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Table 1 Main epidemiological studies focused on interventional medical radiation workers

Study	Country	Enrolled population	Endpoint	Reference
US radiology technologists (USRT) study	United States	Radiology technologists who performed fluoroscopically guided interventional procedures	Mortality and incidence of cancer and circulatory disease	5, 6
Multispecialty occupational health group (MOHG) study	United States	Interventional cardiologists, radiologists, neuroradiologists	Mortality from cancer and non-cancer causes	4, 7
Society for Cardiovascular Angiography and Interventions (SCAI) study	United States	Interventional cardiologists and staff	Prevalence of orthopedic injuries, cataracts and cancer	40
Healthy Cath Lab (HCL) Study	Italy	Interventional cardiologists and staff	Surrogate endpoints (chromosome aberrations, telomere shortening, carotid intima-media thickness, olfactory dysfunction)	11, 41, 42
Occupational Cataracts and Lens Opacities in interventional Cardiology (OCLOC) study	France	Interventional cardiologists	Cataract (Lens opacities)	43
European epidemiological study on radiation-induced lens opacities among interventional cardiologists (EURALOC) study	European multi-nations	Interventional cardiologists	Cataract (Lens opacities)	44
Retrospective Evaluation of Lens Injuries and Dose (RELID) study	International multi-nations	Interventional cardiologists and staff	Cataract (Lens opacities)	45

Table 2 Target societies in Korea for the baseline survey

Scientific societies	Member	Website
Korean Society of Interventional Radiology	Physician	www.intervention.or.kr
Korean Society of Interventional Cardiology	Physician	www.kvis.or.kr
Korean Society of Interventional Neuroradiology	Physician	www.ksin.or.kr
Korean Pancreatobiliary Association	Physician	www.kpba.kr
Korean Minimally Invasive Spine Surgery Society	Physician	http://komiss.org
Korean Pain Intervention Society	Physician	www.korsis.or.kr
Korean Society of Cardio-vascular Interventional Technology	Technologist	www.kscvit.or.kr
Korean Cardiovascular Technology Association	Technologist	-
Korean Radiology Nurses Association	Nurse	-

Table 3 Items collected in the baseline survey questionnaire

Domains (No. of questions)	Items
Demographics (4)	Date of birth, gender, name, workplace address
Work history (4)	Job title, specialty, years since beginning work, 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, use of shielding devices
Experience of high radiation exposure (2)	Exposure to >5 mSv a quarter, low WBC count
Personal medical examination (6)	CT scan, fluoroscopy, nuclear medicine imaging, PET-CT scan, interventional radiography, radiation therapy
Lifestyle (2)	Smoking, alcohol consumption
Medical history (9)	Cataract, eye irritation, anemia, hypertension, dyslipidemia, cancer, thyroid disease, neck/back pain, skin disease

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, use of shielding devices (by decade[a])
	Experience of high radiation exposure	Exposure to >5 mSv a quarter, low WBC count, radiation work in other job
	Management of radiation exposure	Regular health check-up, knowledge of dose limits and personal dose. risk perception items
	Personal medical examination	X-ray (by site[b]), mammography, dental radiography, CT (by site[c]), fluoroscopy (by site[d]), interventional radiography, PET-CT, nuclear medicine imaging, radiation therapy, MRI
	Lifestyle	Smoking, alcohol consumption, physical exercise, night shifts
	Medical history	Cataract, skin diseases, thyroid diseases, neck/ back pain, cardiovascular diseases, cancer, etc. medication history, family history of cataract, cardiovascular diseases and cancer
Clinical examination	Anthropometry	Height, weight, waist circumference
	Blood pressure	Systolic and diastolic blood pressure
	Blood analysis	Hematologic disease WBC, Differential count, RBC, Hemoglobin (Hb), Hematocrit (Hct), MCV, MCH, MCHC, RDW, Platelet, MPV, PDW, Reticulocyte count Diabetes glycated hemoglobin A1c (HbA1c) Dyslipidemia total cholesterol, Triglyceride (TG), High density lipoprotein (HDL) cholesterol, Low density lipoprotein (LDL) cholesterol Thyroid disease thyroid-stimulating hormone (TSH), Thyroid hormones triiodothyronine (T3), Thyroxine

		(T4), free T4
		Cardiovascular risk factors
		homocysteine, hs-CRP
	Ophthalmologic examination	Visual acuity Lens opacities
	Ultrasonography examinations	Thyroid nodule Common carotid artery and internal carotid artery intima-media thickness
Badge monitoring	Dosimetry	Inside/outside of lead apron at chest, outside of thyroid shield
	Work diary	Interventional procedures (type, frequency, time)
Biodosimetry	Stable and unstable chromosomal aberrations	Dicentric analysis Translocation
Past health check-up records	Hematology Blood pressure	WBC, differential count, RBC, Hb, platelet Systolic and diastolic blood pressure

[a]1980-1989, 1990-1999, 2000-2009 and 2010-present; [b]head & neck, chest, abdomen and extremity; [c]head & neck, chest, abdomen, pelvis and extremity; [d]stomach, intestine, hepatobiliary, kidney and others

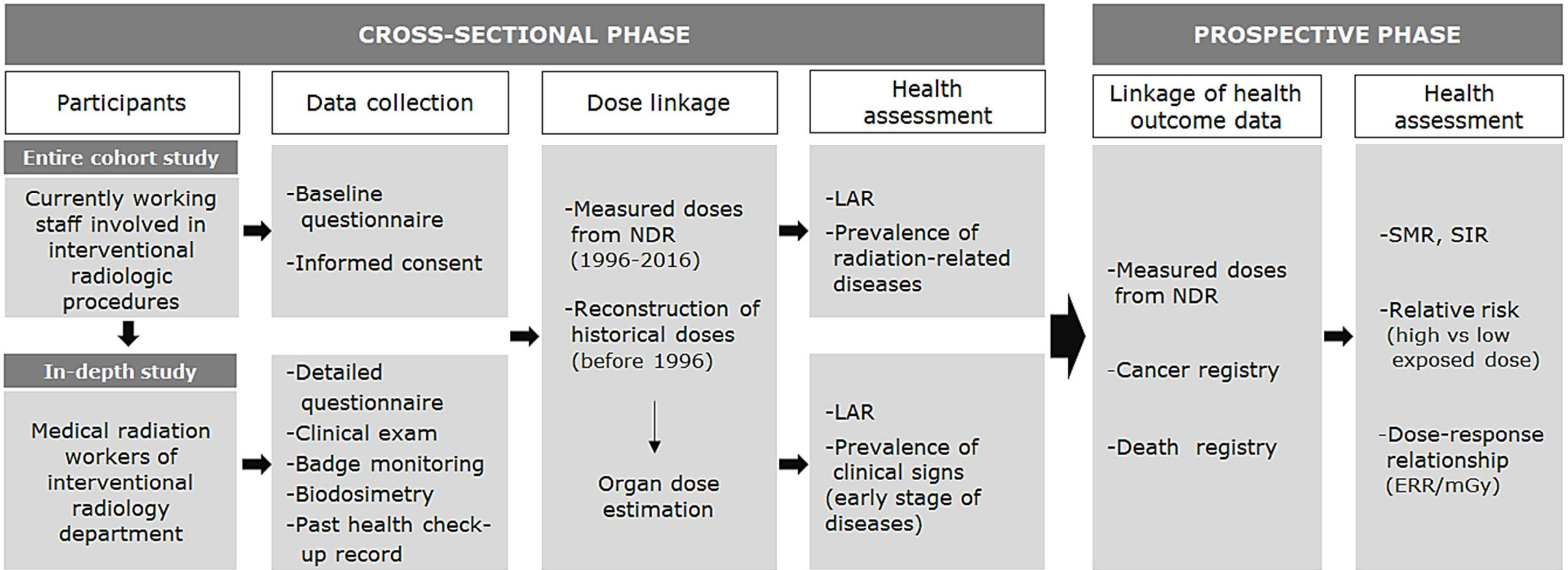

Figure 1 Study design and population

NDR, national dose registry; LAR, lifetime attributable risk; SMR, standardized mortality ratio; SIR, standardized incidence ratio; ERR, excess relative risk

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page/ Table/ Figure
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6, Figure 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7 Table 2
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11, Table 3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12-16, Table 4
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	NA
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17-18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018333.R1
Article Type:	Protocol
Date Submitted by the Author:	25-Aug-2017

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Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology
Keywords:	Cohort, Fluoroscopically guided procedures, Medical workers, Occupational exposure, Radiation

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

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Keywords: Cohort; Fluoroscopically guided procedures; Medical workers; Occupational exposure; Radiation.

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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 ionizing 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: Intervention 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 intervention 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. All participants will provide written informed consent prior to enrollment. 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.

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.

INTRODUCTION

Medical radiation medical workers involved in interventional fluoroscopy procedures are exposed to higher radiation levels than those who perform conventional radiography.[1] However, this population is rarely studied as compared to other occupational fields or radiation epidemiology research. Therefore, epidemiologic 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 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 radiologic 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-organized epidemiologic 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 utilization 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 orthopedic surgeon who performing interventional radiologic procedures.[22] We recently reported the work practices and the radiation exposure dose among male radiology 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 enrollment of intervention 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 medical radiation workers including basic demographic data, work place, and radiation dose as part of a government-managed registry. The registry includes physicians (radiologists and other specialists), dentists, dental hygienists, radiologic technologists, nurses, and medical assistants. 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 radiology procedures. A cohort of interventional radiology 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 enrollment, 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 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, standardized mortality ratios (SMRs), and standardized incidence ratios (SIRs) 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 to assess detailed occupational radiation exposure and overall health status. This will include a detailed questionnaire survey, clinical examinations, a badge monitoring program 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 enroll medical radiation workers to set up a cohort. To enroll 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 organized by the scientific societies. However, if only the web-based survey is allowed, we will promote the survey on the web sites of the societies and via personal e-mail. We will conduct a subsequent supplementary survey via telephone to obtain information regarding the questionnaire items that are left blank or answered insufficiently.

To maximize 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 e-mails 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 be invited to participate in the baseline survey. Previously, we conducted a survey of 15,501 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 radiologic technologists, approximately 7% of diagnostic medical workers reported that they had been involved in radiation interventional fluoroscopy procedures. Therefore, we assume that the number of interventional medical workers is approximately 4,000. 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 radiologic medical workers,[25] and conducting a pilot study among interventional medical radiation workers. The enrollment questionnaire includes items on demographics, work history, work practices, experience of high-dose exposure, radiation exposure by personal medical examination, health-related behaviors, and medical history. The demographic data includes 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 behaviors, and medical history included in the questionnaire will be validated through the national health insurance 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 health care utilization data.[26] We can use information on health-related behaviors from the national health screening data and information on medical radiation exposure and radiation-associated diseases from the health care utilization data.

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 date of birth, name, 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 long-term follow-up. Participants will be passively followed by linking the national health insurance 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 health care utilization data in the national health insurance claim data to identify non-cancer diseases related to radiation exposure. The KCCR is the national level registry, and maintains a high level of completeness (97.8% in 2014).[27] The registry data includes cancer code (International Classification of Diseases and Related Health Problems, 10th Revision – [ICD-10]) and International Classification of Diseases for Oncology, 3rd 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 is 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; upon our request, they will link these personal identification numbers to the national health insurance 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 radiologic 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 programs for all medical radiation workers involved in diagnostic radiology since 1996. It maintains a centralized national dose registry and operates a life-long 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 centers 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 United States Radiologic Technologists (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] (a) the organ absorbed dose per unit of air kerma free-in-air (Gy per Gy) and (b) the personal dose equivalent per unit of air kerma free-in air (Sv per Gy). 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 (Gy), $H_p(d)$ is badge dose (Sv), and K_a is air kerma free-in-air (Gy).

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, sex, and work place.[33]

Estimation of lifetime attributable risk of cancer

The lifetime attributable risk 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

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

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 radiologic 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 Cardio-vascular 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 program, 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 heath check-up records could give us a clue about the health risks of radiation exposure regarding early warning signs. Using the badge monitoring program 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 behaviors, 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 standardized 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 (i.e., height, weight, and waist circumference) will be measured as described by the Korea National Health and Nutrition Examination Survey (KNHANES) Health Examination Procedures Manual.[36] Body mass index (BMI) will be calculated as the ratio of body weight (kg) to height squared (m^2). Based on the standard protocol, systolic and diastolic blood pressure 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 minutes 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 complete blood count (CBC) test and for analyzing glycated hemoglobin, a serum separation tube for analyzing 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 minutes, and the blood will subsequently be centrifuged at 3000 rpm for 15 minutes. EDTA tubes and heparin tubes will be mixed in a roller mixer for 10 minutes. 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 localization of lens opacities (cortical, nuclear, posterior sub-capsular).

Ultrasonography examination consisting of carotid artery and thyroid scans will be performed by a single radiologist, using high-resolution B-mode ultrasonography (E-CUBE i7; Alpinion, Seoul, Korea) that has a linear 8-17 MHz transducer (L8-17; Alpinion, Seoul, Korea) and the ability to save Digital Imaging and Communications in Medicine (DICOM) images to be retrospectively evaluated. Carotid 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 semi-automatic 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 (K-TIRADS)[39 40] to categorize 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 thermo-luminescent dosimeters (Panasonic TLD system) inside and outside of the apron, and outside of the thyroid shield, always correctly for one month while keeping a working diary. Dose measurements will be collected by a fully accredited center (Orbitech Co., Ltd, 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 coefficients[41] 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 analyzes 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 hybridization. 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 WBC, RBC, hemoglobin, platelets, systolic and diastolic blood pressure. 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 standard deviations and categorical variables as frequencies and percentages. The student`s t-test and the chi-square tests will be used to test for 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 analyze binary variables for the abnormality of clinical exams to ascertain whether occupational characteristics and radiation exposure are associated. Models will be adjusted for potential confounding factors, and the odds ratios and their 95% confidence intervals 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 to previous studies is that our study participants are linked to individual information by way of a questionnaire, radiation dosimetry, the national health insurance 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 pre-clinical 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.

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 to 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 radiologic 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

This study has been reviewed and approved by the Institutional Review Board of Korea University (KU-IRB-12-12-A-1) and is funded by the KCDC (2017E3600600). Informed written consent, including permission to collect personal information, and access to radiation dosimetry, national health insurance claims data, cancer registry, and mortality data will be voluntarily obtained from each study participant before enrollment in the study. The participants of the baseline survey and in-depth study will receive a coupon for coffee (approximately worth 4 USD) and a gift card (approximately worth 90 USD), 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 organization that is responsible for developing appropriate research and management policies.

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

Funding: This work was supported by the Korea Ministry of Health and Welfare and Center for Disease Control and Prevention grant number 2017E3600600 from 13 April 2017 to 12 February 2018

Conflict of interest: None

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

Study	Country	Enrolled population	Endpoint	Reference
US radiology technologists (USRT) study	United States	Radiology technologists who performed fluoroscopically-guided interventional procedures	Mortality and incidence of cancer and circulatory disease	4, 5, 6
Multispecialty occupational health group (MOHG) study	United States	Interventional cardiologists, radiologists, neuroradiologists	Mortality from cancer and non-cancer causes	7, 8
Society for Cardiovascular Angiography and Interventions (SCAI) study	United States	Interventional cardiologists and staff	Prevalence of orthopedic injuries, cataracts and cancer	9
Healthy Cath Lab (HCL) Study	Italy	Interventional cardiologists and staff	Surrogate endpoints (chromosome aberrations, telomere shortening, carotid intima-media thickness, olfactory dysfunction)	10, 11, 12
Occupational Cataracts and Lens Opacities in interventional Cardiology (OCLOC) study	France	Interventional cardiologists	Cataract (lens opacities)	13
European epidemiological study on radiation-induced lens opacities among interventional cardiologists (EURALOC) study	European multi-nations	Interventional cardiologists	Cataract (lens opacities)	14
Retrospective Evaluation of Lens Injuries and Dose (RELID) and Latin American Society of	International multi-nations	Interventional cardiologists and staff	Cataract (lens opacities)	15, 16

Interventional Cardiology (SOLACI) study	

Table 2 Target societies in Korea for the baseline survey

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

Table 3 Items collected in the baseline survey questionnaire

Domains (No. of questions)	Items
Demographics (4)	Date of birth, gender, name, workplace address
Work history (4)	Job title, specialty, years since beginning work, 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, use of shielding devices
Experience of high radiation exposure (2)	Exposure to >5 mSv a quarter, low WBC count
Personal medical examination (6)	CT scan, fluoroscopy, nuclear medicine imaging, PET-CT scan, interventional radiography, radiation therapy
Lifestyle (2)	Smoking, alcohol consumption
Medical history (9)	Cataract, eye irritation, anemia, hypertension, dyslipidemia, cancer, thyroid disease, neck/back pain, skin disease

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, use of shielding devices (by decade[a])
	Experience of high radiation exposure	Exposure to >5 mSv a quarter, low WBC count, radiation work in other job
	Management of radiation exposure	Regular health check-up, knowledge of dose limits and personal dose. risk perception items
	Personal medical examination	X-ray (by site[b]), mammography, dental radiography, CT (by site[c]), fluoroscopy (by site[d]), interventional radiography, PET-CT, nuclear medicine imaging, radiation therapy, MRI
	Lifestyle	Smoking, alcohol consumption, physical exercise, night shifts
	Medical history	Cataract, skin diseases, thyroid diseases, neck/ back pain, cardiovascular diseases, cancer, etc. medication history, family history of cataract, cardiovascular diseases and cancer
Clinical examination	Anthropometry	Height, weight, waist circumference
	Blood pressure	Systolic and diastolic blood pressure
	Blood analysis	Hematologic disease WBC, Differential count, RBC, Hemoglobin (Hb), Hematocrit (Hct), MCV, MCH, MCHC, RDW, Platelet, MPV, PDW, Reticulocyte count Diabetes glycated hemoglobin A1c (HbA1c) Dyslipidemia total cholesterol, Triglyceride (TG), High density lipoprotein (HDL) cholesterol, Low density lipoprotein (LDL) cholesterol Thyroid disease

		thyroid-stimulating hormone (TSH), Thyroid hormones triiodothyronine (T3), Thyroxine (T4), free T4
		Cardiovascular risk factors
		homocysteine, hs-CRP
	Ophthalmologic examination	Visual acuity Lens opacities
	Ultrasonography examinations	Thyroid gland Common carotid artery and internal carotid artery intima-media thickness
Badge monitoring	Dosimetry	Inside/outside of lead apron at chest, outside of thyroid shield
	Work diary	Interventional procedures (type, frequency, time)
Biodosimetry	Stable and unstable chromosomal aberrations	Dicentric analysis Translocation
Past health check-up records	Hematology Blood pressure	WBC, differential count, RBC, Hb, platelet Systolic and diastolic blood pressure

[a]1980-1989, 1990-1999, 2000-2009 and 2010-present; [b]head & neck, chest, abdomen and extremity; [c]head & neck, chest, abdomen, pelvis and extremity; [d]stomach, intestine, hepatobiliary, kidney and others

Figure Legend

Figure 1 Study design and population

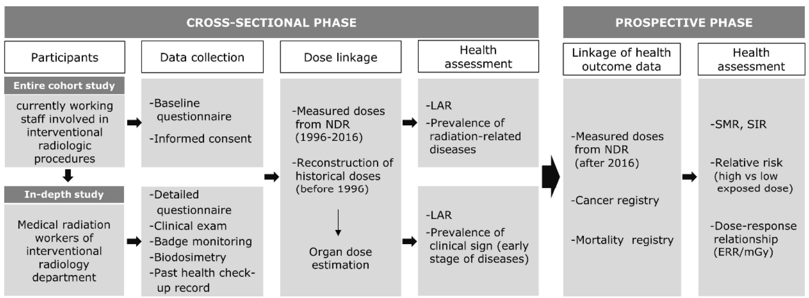

Figure 1 Study design and population
NDR, national dose registry; LAR, lifetime attributable risk; SMR, standardized mortality ratio; SIR, standardized incidence ratio; ERR, excess relative risk

338x190mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page/ Table/ Figure
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6, Figure 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7 Table 2
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11, Table 3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12-16, Table 4
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	NA
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17-18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018333.R2
Article Type:	Protocol
Date Submitted by the Author:	30-Sep-2017
Complete List of Authors:	Ko, Seulki; Korea University College of Medicine and School of Medicine, Department of Preventive Medicine; Korea University Graduate School of Public Health Chung, Hwan Hoon; Korea University Ansan Hospital, Department of Radiology Cho, Sung Bum; Korea University Anam Hospital, Department of Radiology Jin, Young Woo ; Korea Institute of Radiological and Medical Sciences, National Radiation Emergency Medical Center Kim, Kwang Pyo; Kyung Hee University - Global Campus Ha, Mina; Dankook University College of Medicine Bang, Ye Jin; Korea University College of Medicine and School of Medicine, Department of Preventive Medicine; Korea University Graduate School of Public Health Ha, Yae Won; Korea University College of Medicine and School of Medicine, Department of Preventive Medicine Lee, Won; Korea University, Department of Preventive Medicine, Korea University College of Medicine; Korea University Graduate School of Public Health
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology
Keywords:	Cohort, Fluoroscopically guided procedures, Medical workers, Occupational exposure, Radiation

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

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Keywords: Cohort; Fluoroscopically guided procedures; Medical workers; Occupational exposure; Radiation.

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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 ionizing 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: Intervention 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 intervention 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. All participants will provide written informed consent prior to enrollment. 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.

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.

INTRODUCTION

Medical radiation medical workers involved in interventional fluoroscopy procedures are exposed to higher radiation levels than those who perform conventional radiography.[1] However, this population is rarely studied as compared to other occupational fields or radiation epidemiology research. Therefore, epidemiologic 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 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 radiologic 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-organized epidemiologic 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 utilization 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 orthopedic surgeon who performing interventional radiologic procedures.[22] We recently reported the work practices and the radiation exposure dose among male radiology 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 enrollment of intervention 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, work place, and radiation dose as part of a government-managed registry. The registry includes physicians (radiologists and other specialists), dentists, dental hygienists, radiologic 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 radiology 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 radiology 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 enrollment, 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, standardized mortality ratios (SMRs), and standardized incidence ratios (SIRs) 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 sub-cohort 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 program 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 enroll medical radiation workers to set up a cohort. To enroll 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 organized by the scientific societies. However, if only the web-based survey is allowed, we will promote the survey on the web sites of the societies and via personal e-mail. We will conduct a subsequent supplementary survey via telephone to obtain information regarding the questionnaire items that are left blank or answered insufficiently.

To maximize 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 e-mails 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 be invited to participate in the baseline survey. Previously, we conducted a survey of 15,501 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 radiologic technologists, approximately 7% of diagnostic medical workers reported that they had been involved in radiation interventional fluoroscopy procedures. Therefore, we assume that the number of interventional medical workers is approximately 4,000. 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 radiologic medical workers,[25] and conducting a pilot study among interventional medical radiation workers. The enrollment questionnaire includes items on demographics, work history, work practices, experience of high-dose exposure, radiation exposure by personal medical examination, health-related behaviors, and medical history. The demographic data includes 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 behaviors, 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 health care utilization data.[26] We can use information on health-related behaviors from the national health screening data and information on medical radiation exposure and radiation-associated diseases from the health care utilization data.

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 date of birth, name, 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 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 health care utilization 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. The KCCR is the national level registry, and maintains a high level of completeness (97.8% in 2014).[27] The registry data includes cancer code (International Classification of Diseases and Related Health Problems, 10th Revision – [ICD-10]) and International Classification of Diseases for Oncology, 3rd 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 is 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; upon 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 radiologic 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 programs for all medical radiation workers involved in diagnostic radiology since 1996. It maintains a centralized national dose registry and operates a life-long 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 centers 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 United States Radiologic Technologists (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] (a) the organ absorbed dose per unit of air kerma free-in-air (Gy per Gy) and (b) the personal dose equivalent per unit of air kerma free-in air (Sv per Gy). 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 (Gy), $H_p(d)$ is badge dose (Sv), and K_a is air kerma free-in-air (Gy).

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, sex, and work place.[33]

Estimation of lifetime attributable risk of cancer

The lifetime attributable risk 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

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

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 radiologic 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 Cardio-vascular 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 program, 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 heath check-up records could give us a clue about the health risks of radiation exposure regarding early warning signs. Using the badge monitoring program 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 behaviors, 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 standardized 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 (i.e., height, weight, and waist circumference) will be measured as described by the Korea National Health and Nutrition Examination Survey (KNHANES) Health Examination Procedures Manual.[36] Body mass index (BMI) will be calculated as the ratio of body weight (kg) to height squared (m^2). Based on the standard protocol, systolic and diastolic blood pressure 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 minutes 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 complete blood count (CBC) test and for analyzing glycated hemoglobin, a serum separation tube for analyzing 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 minutes, and the blood will subsequently be centrifuged at 3000 rpm for 15 minutes. EDTA tubes and heparin tubes will be mixed in a roller mixer for 10 minutes. 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 localization of lens opacities (cortical, nuclear, posterior sub-capsular).

Ultrasonography examination consisting of carotid artery and thyroid scans will be performed by a single radiologist, using high-resolution B-mode ultrasonography (E-CUBE i7; Alpinion, Seoul, Korea) that has a linear 8-17 MHz transducer (L8-17; Alpinion, Seoul, Korea) and the ability to save Digital Imaging and Communications in Medicine (DICOM) images to be retrospectively evaluated. Carotid 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 semi-automatic 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 (K-TIRADS)[39 40] to categorize 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 thermo-luminescent dosimeters (Panasonic TLD system) inside and outside of the apron, and outside of the thyroid shield, always correctly for one month while keeping a working diary. Dose measurements will be collected by a fully accredited center (Orbitech Co., Ltd, 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 coefficients[41] 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 analyzes 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 hybridization. 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 WBC, RBC, hemoglobin, 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 standard deviations and categorical variables as frequencies and percentages. The Student`s t-test and the chi-square tests will be used to test for 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 analyze binary variables for the abnormality of clinical exams to ascertain whether occupational characteristics and radiation exposure are associated. Models will be adjusted for potential confounding factors, and the odds ratios and their 95% confidence intervals 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 to 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 pre-clinical 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 ophthalmologic 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 maximize the participant rate in this limited situation, we will set up the dark conditions enough to dilate the pupil during the ophthalmologic 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 to 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 radiologic 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

This study has been reviewed and approved by the Institutional Review Board of Korea University (KU-IRB-12-12-A-1) and is funded by the KCDC (2017E3600600). 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 enrollment in the study. The participants of the baseline survey and in-depth study will receive a coupon for coffee (approximately worth 4 USD) and a gift card (approximately worth 90 USD), 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 organization that is responsible for developing appropriate research and management policies.

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

Funding: This work was supported by the Korea Ministry of Health and Welfare and Center for Disease Control and Prevention grant number 2017E3600600 from 13 April 2017 to 12

February 2018

Conflict of interest: None

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

Study	Country	Enrolled population	Endpoint	Reference
US radiology technologists (USRT) study	United States	Radiology technologists who performed fluoroscopically-guided interventional procedures	Mortality and incidence of cancer and circulatory disease	4, 5, 6
Multispecialty occupational health group (MOHG) study	United States	Interventional cardiologists, radiologists, neuroradiologists	Mortality from cancer and non-cancer causes	7, 8
Society for Cardiovascular Angiography and Interventions (SCAI) study	United States	Interventional cardiologists and staff	Prevalence of orthopedic injuries, cataracts and cancer	9
Healthy Cath Lab (HCL) Study	Italy	Interventional cardiologists and staff	Surrogate endpoints (chromosome aberrations, telomere shortening, carotid intima-media thickness, olfactory dysfunction)	10, 11, 12
Occupational Cataracts and Lens Opacities in interventional Cardiology (OCLOC) study	France	Interventional cardiologists	Cataract (lens opacities)	13
European epidemiological study on radiation-induced lens opacities among interventional cardiologists (EURALOC) study	European multi-nations	Interventional cardiologists	Cataract (lens opacities)	14
Retrospective Evaluation of Lens Injuries and Dose (RELID) and Latin American Society of	International multi-nations	Interventional cardiologists and staff	Cataract (lens opacities)	15, 16

Interventional Cardiology
(SOLACI) study

Table 2 Target societies in Korea for the baseline survey

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

Table 3 Items collected in the baseline survey questionnaire

Domains (No. of questions)	Items
Demographics (4)	Date of birth, gender, name, workplace address
Work history (4)	Job title, specialty, years since beginning work, 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, use of shielding devices
Experience of high radiation exposure (2)	Exposure to >5 mSv a quarter, low WBC count
Personal medical examination (6)	CT scan, fluoroscopy, nuclear medicine imaging, PET-CT scan, interventional radiography, radiation therapy
Lifestyle (2)	Smoking, alcohol consumption
Medical history (9)	Cataract, eye irritation, anemia, hypertension, dyslipidemia, cancer, thyroid disease, neck/back pain, skin disease

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, use of shielding devices (by decade[a])
	Experience of high radiation exposure	Exposure to >5 mSv a quarter, low WBC count, radiation work in other job
	Management of radiation exposure	Regular health check-up, knowledge of dose limits and personal dose. risk perception items
	Personal medical examination	X-ray (by site[b]), mammography, dental radiography, CT (by site[c]), fluoroscopy (by site[d]), interventional radiography, PET-CT, nuclear medicine imaging, radiation therapy, MRI
	Lifestyle	Smoking, alcohol consumption, physical exercise, night shifts
	Medical history	Cataract, skin diseases, thyroid diseases, neck/ back pain, cardiovascular diseases, cancer, etc. medication history, family history of cataract, cardiovascular diseases and cancer
Clinical examination	Anthropometry	Height, weight, waist circumference
	Blood pressure	Systolic and diastolic blood pressure
	Blood analysis	Hematologic disease WBC, Differential count, RBC, Hemoglobin (Hb), Hematocrit (Hct), MCV, MCH, MCHC, RDW, Platelet, MPV, PDW, Reticulocyte count Diabetes glycated hemoglobin A1c (HbA1c) Dyslipidemia total cholesterol, Triglyceride (TG), High density lipoprotein (HDL) cholesterol, Low density lipoprotein (LDL) cholesterol Thyroid disease

		thyroid-stimulating hormone (TSH), Thyroid hormones triiodothyronine (T3), Thyroxine (T4), free T4
		Cardiovascular risk factors
		homocysteine, hs-CRP
	Ophthalmologic examination	Visual acuity Lens opacities
	Ultrasonography examinations	Thyroid gland Common carotid artery and internal carotid artery intima-media thickness
Badge monitoring	Dosimetry	Inside/outside of lead apron at chest, outside of thyroid shield
	Work diary	Interventional procedures (type, frequency, time)
Biodosimetry	Stable and unstable chromosomal aberrations	Dicentric analysis Translocation
Past health check-up records	Hematology Blood pressure	WBC, differential count, RBC, Hb, platelet Systolic and diastolic blood pressure

[a]1980-1989, 1990-1999, 2000-2009 and 2010-present; [b]head & neck, chest, abdomen and extremity; [c]head & neck, chest, abdomen, pelvis and extremity; [d]stomach, intestine, hepatobiliary, kidney and others

Figure Legend

Figure 1 Study design and population

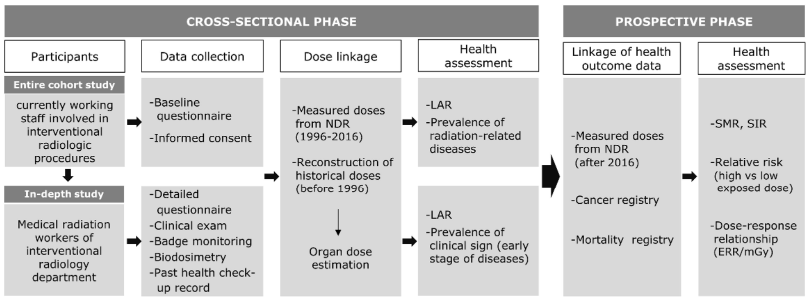

Figure 1 Study design and population
NDR, national dose registry; LAR, lifetime attributable risk; SMR, standardized mortality ratio; SIR, standardized incidence ratio; ERR, excess relative risk

338x190mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page/ Table/ Figure
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6, Figure 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7 Table 2
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11, Table 3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12-16, Table 4
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	NA
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Section	Item	Recommendation	Page
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17-18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.