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Julie Lopes, Clémence Baudin, Frédéric Rousseau, Herve Roy, Philippe Lestaevel, et al.. Central nervous system tumours and occupational ionising radiation exposure: a nested case–control study among the ORICAMs cohort of healthcare workers in France. *BMJ Open*, 2024, 14 (6), pp.e084285. 10.1136/bmjopen-2024-084285 . hal-04618868

HAL Id: hal-04618868

<https://hal.science/hal-04618868>

Submitted on 20 Jun 2024


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BMJ Open Central nervous system tumours and occupational ionising radiation exposure: a nested case-control study among the ORICAMs cohort of healthcare workers in France

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To cite: Lopes J, Baudin C, Rousseau F, *et al*. Central nervous system tumours and occupational ionising radiation exposure: a nested case-control study among the ORICAMs cohort of healthcare workers in France. *BMJ Open* 2024;**14**:e084285. doi:10.1136/bmjopen-2024-084285

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2024-084285>).

Received 14 January 2024
Accepted 06 June 2024



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ABSTRACT

Objective This study aimed at investigating the relationship between occupational exposure to external ionising radiation and central nervous system (CNS) tumours mortality in healthcare workers working in France.

Design and setting The Occupational Radiation-Induced Cancer in Medical staff (ORICAMs) nested case-control study was conducted based on the dosimetric records of the national register of occupational dosimetry (Système d'information de la surveillance de l'exposition aux rayonnements ionisants).

Participants and methods 33 CNS tumour deaths occurred between 2002 and 2012 among the ORICAMs cohort composed of 164 015 healthcare workers. Each case was matched to five controls alive at the time of the corresponding case's death, based on sex, year of birth, date of enrolment in the cohort and duration of follow-up. All participants were badge monitored for external radiation exposure, expressed in H_p(10). Conditional logistic regression was used to analyse the dose-response relationship between radiation dose and CNS mortality.

Results Cases were exposed to a mean cumulative career radiation dose of 5.8±13.7 (max: 54.3) millisievert (mSv) compared with 4.1±15.2 (142.2) mSv for controls. No statistically significant association was found between CNS tumour mortality and cumulative whole-body career dose (OR=1.00, 95% CI 0.98 to 1.03), duration of exposure (OR=1.03; 95% CI 0.95 to 1.12) or age at first exposure (OR=0.98; 95% CI 0.91 to 1.06).

Conclusion We found no evidence of an association between external radiation exposure and CNS tumour risk in healthcare workers. Limitations of the study include low statistical power and short duration of follow-up.

INTRODUCTION

Ionising radiation plays a central role in medical diagnostic and therapeutic practices of modern societies. Technological advances such as diagnostic imaging, radiotherapy or fluoroscopy-guided interventional procedures have led to an exponential increase

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study relies on a national design and on the use of national registries to ensure thorough data collection.
- ⇒ Efforts were made to establish a nested case-control survey, where controls recruited into the cohort shared a certain number of characteristics with the cases, thereby reducing the impact of potential confounding factors linked to the choice of controls.
- ⇒ Study limitations include low statistical power and short duration of follow-up.
- ⇒ This study will integrate the international Brain cancer risk in pooled Case-control study of Medical workers project, which will address the same objectives with assessment of the dose to the brain, but using joint analyses of data from France, South Korea and the USA, which will provide sufficient power to identify low risks.

in the use of radiation for medical purposes. Thus, healthcare professionals currently represent the largest group of workers exposed to radiation, and their number increases rapidly worldwide to reach around 7.4 million.¹ While occupational exposure in the medical field figures in the low-dose range (0–100 mGy), it varies from practitioner to practitioner, according to medical specialty. Although health risks associated with exposure to high doses of ionising radiation are widely recognised,¹ whether protracted low-dose exposure to radiation increases the risk of cancer or non-cancer diseases remains uncertain. The Publication 147 from the International Commission on Radiological Protection (ICRP) defines low doses as radiation with low linear energy transfer <100 mGy to organs and tissues, and low-dose rates as radiation <5 mGy/hour.²



However, increased risk of cancer and non-cancer mortality associated with low-dose exposure among nuclear workers has been reported.³ Recent studies have also shown adverse effects following cumulative low-dose ionising radiation exposure among healthcare workers, such as cataract⁴ and lung cancer.⁵ Some case reports have suggested a potential link between the incidence of brain cancer in healthcare workers and occupational radiation exposure,^{6,7} and increased mortality from brain tumours has been reported among technologists who had performed fluoroscopically guided procedures.⁸ These results have not been observed in studies on interventional radiologists.⁹

However, these studies present some limitations such as a lack of dosimetry assessment,⁹ a former exposure that poorly reflects the current one^{5,10} or a low statistical power related to small cohort size.¹¹

In this context, a case-control study nested within the Occupational Radiation-Induced CAncer in Medical staff (ORICAMs) cohort was set up to assess the association between protracted exposure to ionising radiation and the risk of central nervous system (CNS) tumour and to estimate the dose-response relationship in healthcare workers with current ionising radiation exposure in France.

METHODS

Study population

This case-control study nested within the ORICAMs cohort has been described in detail elsewhere.¹² Briefly, ORICAMs is a nationwide French cohort of 164015 healthcare workers who have at least one dosimetric record in the national register of occupational dosimetry (Système d'information de la surveillance de l'exposition aux rayonnements ionisants (SISERI)) between 2002 and 2012 in France. Set up in 2011 by the French Institute for Radiation Protection and Nuclear Safety (IRSN) in France, the ORICAMs study aims to investigate the risk of radiation-induced cancer or non-cancer mortality among occupationally exposed medical workers. Follow-up is still ongoing, but the present study focuses on an initial assessment of causes of death, for which vital status and medical causes of death, if any, were obtained via national data repositories for deaths occurring up to 31 December 2013. Vital statuses and medical causes of death were respectively obtained from the French National Register of Identification of Physical Persons (RNIPP) and from the French National Institute of Health and Medical Research (CépiDc).

Selection of cases and controls

Every death occurring in the cohort between 2002 and 2013 with a CNS tumour cause—International Classification of Diseases, 10th revision (ICD-10, 2014) codes C70-C72, D32-D33, D42-D43—was selected as a case.

Five controls alive at the time of the case's death were assigned to each case, matched on sex, year of birth (± 1

year), date of entry into the ORICAMs cohort (ie, date of first exposure ranked in a 5-year class from 1967 to 2011) and duration of follow-up (ie, the time between the date of first exposure and the date of the case's death).

Exposure and confounders

Monthly or quarterly dose monitoring (depending on workers' exposure levels) is carried out by external dosimetry using thermoluminescence, radiophotoluminescence or optically stimulated luminescence dosimeters worn at chest level, under the lead apron where applicable. Dosimetric information or exposure measurements are regularly sent to the SISERI system by persons appointed within companies using a secured internet access, with a strictly defined protocol and transmission formats.¹³ Individual dose equivalents of external radiation in soft tissue at a depth of 10 mm ($H_p(10)$, expressed in millisievert (mSv)), were estimated from badges with a recording threshold of 0.05 mSv, and considered hereafter as the whole-body exposure.

Information on occupation, medical service of occupational activity, age and sex were collected via the SISERI database. Furthermore, medical records from occupational medicine departments were analysed not only to confirm information provided by SISERI but also to provide additional information on the body mass index (BMI), smoking status, alcohol intake and history of other malignancies when available.

Statistical analysis

Descriptive analyses of the study population were carried out using standard statistics: mean, SD, Student's t-test for continuous variables or frequency, percentage, χ^2 and Fisher tests for categorical variables. Then, ORs were calculated to investigate associations between exposure to ionising radiation and the risk of death from a CNS tumour, using conditional logistic regression models. Exposure to ionising radiation was considered in two different ways: duration of exposure (in years) and cumulative career dose (in mSv). First, univariate analyses were performed to test the effect of each potential risk or confounding factor (ie, radiation exposure, age at first exposure in years, profession or physicians' medical specialty) on CNS tumour mortality. Then, several multivariate models were tested to assess the association between ionising radiation exposure (duration of exposure or cumulative dose over career) and CNS tumour mortality, adjusted for several combinations of the profession variable (model 1: physicians vs all others; radiologic technologists vs all others; nurses vs all others) or physicians' medical specialty (model 2: conventional radiologists vs all others; interventional cardiologist and radiologist vs all others; nuclear physicist vs all others) as potential confounders.

OR and 95% CI for CNS tumour mortality in relation with exposure variables were provided after adjustment.

A lag of 5 years was used for radiation exposure in the analyses: this latency period is based on the principle of

a minimum delay between the initiation of the tumour process linked to exposure to a given factor and the onset of cancer.¹⁴

Analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed test of significance with an α level of 0.05 was used to determine statistical significance of the OR.

Patient and public involvement

This study was based solely on national registers. No involvement of participants was required. A general written information note concerning the implementation of the study has been disseminated via the occupational health departments of each healthcare workers (the participants) included in the study. Following this information note, workers could express their opposition to the research if they so wished. As this retrospective study was based on data already collected for other purposes, workers' consent was not required. All data in this study were fully anonymised before we had access to them. This article will be distributed to the persons concerned in compliance with the distribution rules.

RESULTS

A total of 33 cases were identified within the 164015 workers of the ORICAMs cohort as having died from CNS tumour between 2002 and 2013. For each case, 5 controls were selected for a total of 166, 2 of which were selected twice.

Characteristics of the cases and the controls are presented in table 1. Cases were predominantly men (63%) with a mean age of 54 years at the time of death. In average, they were first exposed at 37 years old and had been employed for 13 years. Controls were similar in terms of age, sex, age at first exposure (matching variables), but their mean cumulative dose was slightly lower than that of the cases, although not significantly: 4.1 and 5.8 mSv ($p=0.54$) for controls and cases, respectively.

The most frequent profession for cases and controls was physician (46% and 32%, respectively), with the most frequent medical specialty being conventional radiology for controls (36%) and cardiology/interventional radiology (20%), surgery (20%), conventional radiology (20%) and other medical specialties (20%) for cases. Information on potential confounding factors (BMI, smoking status, alcohol status and medical history) could only be collected from occupational medical records for 21% of cases and 15% of controls, making it impossible to include this information in the analyses. 88% of deaths

Table 1 Characteristic of cases and controls

Characteristic	Cases, n=33	Controls, n=160	P value*
Age (years)	54±12 (24–72)	54±12 (23–73)	0.81
Sex			1.00
Men	20 (63%)	95 (63%)	
Women	13 (37%)	65 (37%)	
Profession			0.07
Physicians	15 (46%)	52 (32%)	
Anaesthesiologist	2 (13%)	7 (13%)	
Interventional cardiologist and radiologist	3 (20%)	6 (12%)	
Nuclear physician	1 (7%)	2 (4%)	
Surgeon	3 (20%)	14 (27%)	
Conventional radiologist	3 (20%)	19 (36%)	
Other medical specialties†	3 (20%)	4 (8%)	
Radiologic technologists	7 (21%)	17 (11%)	
Nurses	4 (12%)	48 (30%)	
Others‡	7 (21%)	43 (27%)	
Age at first exposure (years)	37±12 (22–64)	37±12 (19–67)	0.93
Exposure duration (years)	13±10 (0–31)	12±9 (0–37)	0.73
Education duration (years)	8±4.0 (3–11)	7±4 (3–11)	0.23
Cumulative career dose (mSv)	5.8±13.7 (0.0–54.3)	4.1±15.2 (0.0–142.2)	0.54

Results are presented as mean±SD (range) or n (%).

*Student's t-test evaluating the difference in mean values between case and control groups or χ^2 test of independence for categorical variables at alpha 5% risk.

†Other specialties: stomatologist (n=1), rheumatologist (n=1), nephrologist (n=1), gastroenterologist (n=1), missing data (n=5).

‡Others: hospital assistant (n=20), technician (n=10), dentist (n=1), missing data (n=19).

**Table 2** Causes of death of cases according to ICD-10

Codes	Causes of death	N (%)
C71	Malignant neoplasm of brain	29 (88)
C71.0	Cerebrum, except lobes and ventricles	7 (21)
C71.1	Frontal lobe	3 (9)
C71.2	Temporal lobe	3 (9)
C71.8	Overlapping lesion of brain	2 (6)
C71.9	Brain, unspecified	13 (40)
D43	Neoplasm of uncertain or unknown behaviour of brain and CNS	4 (12)
D43.0	Brain, supratentorial	1 (3)
D43.2	Brain, unspecified	2 (6)
D43.4	Neoplasm of uncertain or unknown behaviour of spinal cord	1 (3)

CNS, central nervous system; ICD-10, International Classification of Diseases 10th revision.

were due to malignant neoplasms of the brain (ICD-10: C70), while the remaining 12% were due to neoplasms of uncertain or unknown behaviour of the brain and CNS (ICD-10: D43) (table 2). The most frequent cause of death was malignant brain tumour, unspecified (C71.9).

Among cases, physicians had the highest average cumulative dose over the course of their career (9.6±17.4 mSv, n=15), particularly in nuclear medicine departments (54.3±NA mSv, n=1) (table 3). Among controls, the highest average cumulative dose was seen in nurses (5.1±23.1 mSv, n=48) and radiologic technologists (5.1±12.6 mSv, n=17). Cumulative career doses by sex are shown in online supplemental table S1.

The ORs for CNS tumour death were non-significantly higher in physicians (OR=2.29; 95% CI 0.83 to 6.33) and in radiologic technologists (OR=2.59; 95% CI 0.90 to 7.48) when compared with all other professions (table 4).

Among physicians, this upward trend seemed partly due to the not statistically significant increased OR among interventional cardiologists and radiologists (OR=2.35; 95% CI 0.59 to 9.45). No statistically significant association was found between the CNS tumour mortality and cumulative career dose (OR=1.00, 95% CI 0.98 to 1.03), exposure duration (OR=1.03; 95% CI 0.95 to 1.12) or age at first exposure (OR=0.98; 95% CI 0.91 to 1.06) (table 4). Furthermore, the ORs by medical department revealed no significant differences.

Multivariate analyses showed similar results with ORs for CNS tumours death remaining non-significant for exposure variables (cumulative career dose or exposure duration) after inclusion of the different versions of the profession variable (table 5).

DISCUSSION

The analyses of this case-control study nested in the ORICAMs cohort did not show increased risk of CNS tumour death in relation to cumulative career whole-body dose in healthcare workers employed in France between 2002 and 2012 and potentially exposed to ionising radiation. Other covariates, such as profession, medical specialty or medical department, were also tested as factors of interest, without showing significant results.

Several studies have discussed a potential link between the incidence of brain cancer in interventional cardiologists and occupational exposure to ionising radiation.^{7 15 16} However, the suspected increased risk was based on a few case reports and small retrospective cohort studies, without comparison with unexposed control subjects. Recent reviews and meta-analyses^{9 17 18} did not conclude to an excess risk of death by CNS tumours in medical workers, but studies lack of specific analyses on interventional cardiologists. Overall, our results are consistent with other recent international medical worker

Table 3 Cumulative average career doses (in mSv) for cases and controls, according to the profession

	Cases (n=33)		Controls (n=160)		P value
	N	Mean±SD (range)	N	Mean±SD (range)	
Physicians	15	9.6±17.4 (0.0–54.3)	52	4.3±10.4 (0.0–48.8)	0.53
Anaesthesiologists	2	0.23±0.32 (0.0–0.45)	7	2.6±6.9 (0.0–18.5)	
Interventional cardiologist and radiologist	3	17.2±14.9 (8.5–34.3)	6	1.3±2.9 (0.0–7.1)	
Nuclear physicians	1	54.3±NA (54.3–54.3)	2	17.4±24.2 (0.3–34.5)	
Surgeons	3	12.3±21.4 (0.0–37.0)	14	0.5±1.2 (0.0–4.0)	
Conventional radiologist	3	0.0±0.0 (0.0–0.0)	19	8.5±14.3 (0.0–48.8)	
Other specialties*	3	0.4±0.4 (0.0–0.8)	4	0.2±0.2 (0.0–0.3)	
Radiologic technologists	7	6.5±13.9 (0.0–37.9)	17	5.1±12.6 (0.0–50.1)	0.71
Nurses	4	0.0±0.0 (0.0–0.0)	48	5.1±23.1 (0.0–142.2)	0.14
Others†	7	0.2±0.3 (0.0–0.7)	43	2.4±8.5 (0.0–53.1)	0.15

*Other specialties: stomatologist, rheumatologist, nephrologist, gastroenterologist, missing data.
†Others: hospital assistant, technician, dentist, missing data.

Table 4 Univariate logistic regression analyses for central nervous system tumours death in relation with exposure variables, professions, physicians' medical specialties or medical departments

		Case n=33	Controls n=160	OR	95% CI	P value
Exposure variables	Cumulative career dose (mSv)	33	157	1.00	0.98 to 1.03	0.69
	Exposure duration (years)	33	160	1.03	0.95 to 1.12	0.52
	Age at first exposure (years)	33	160	0.98	0.91 to 1.06	0.62
Profession	All other workers*	18	108	1.00	Ref	0.11
	Physician	15	52	2.29	0.83 to 6.33	
	All other workers*	26	143	1.00	Ref	0.08
	Radiologic technologist	7	17	2.59	0.90 to 7.48	
	All other workers*	29	114	1.00	Ref	0.05
Physician specialty	Nurse	4	46	0.31	0.09 to 1.01	
	All other workers*	30	141	1.00	Ref	0.59
	Conventional radiologist	3	19	0.70	0.19 to 2.63	
	All other workers*	30	154	1.00	Ref	0.23
	Interventional cardiologist and radiologist	3	6	2.35	0.59 to 9.45	
	All other workers*	32	158	1.00	Ref	0.59
Medical department	Nuclear physicist	1	2	1.94	0.17 to 21.69	
	All departments*	29	128	1.00	Ref	0.29
	Diagnostic and conventional radiology	4	32	0.55	0.18 to 1.67	
	All departments*	29	141	1.00	Ref	0.96
	Cardiology and interventional radiology	4	19	1.03	0.31 to 3.38	
	All departments*	31	153	1.00	Ref	0.74
	Nuclear medicine	2	7	1.31	0.27 to 6.32	

*All other types of professions/specialties/departments except the one studied.

studies where radiation was not significantly associated with brain tumours. A recent study carried out in the USA did not show any significant association between cumulative absorbed dose to the brain of medical radiation workers (mean=18.9 mGy, max=1.08 Gy) and risk of death by brain cancers (Excess Relative Risk (ERR) at 100 mGy=0.20, 95% CI -0.30 to 0.71; n=165).⁵ In addition, similar results between cumulative absorbed dose to the brain (mean=12 mGy, max 290 mGy) and brain cancer mortality (ERR per 100 mGy=0.1, 95% CI -0.3 to 1.5; n=195) were reported in the US radiologic technologist study.¹⁹ However, the latter studies were conducted only on radiological technologists¹⁰ and assessed risks due to exposures received between the 50s and the 90s^{5 10} that do not necessarily reflect the drastic increase in the use of ionising radiation, particularly in interventional cardiology and radiology since the 2000s. Moreover, older dose estimates may be associated with greater uncertainties than contemporary estimates, because these estimates may rely on dose reconstructions which are not necessarily based on dosimetric monitoring.

The present study took the advantages of a nested case-control survey, where controls recruited into the cohort share a certain number of characteristics with the cases, thereby reducing the impact of potential confounding

factors linked to the choice of controls. Cases and controls were similar regarding the matching criteria (sex, year of birth, duration of follow-up and date of entry into the ORICAMs cohort), but may be different on the variables of interest. In addition, the selection of a limited number of workers using this case-control design made it possible to reconstruct their occupational exposure more precisely and to attempt to retrieve information on other risk factors for the disease studied from the occupational health records, a task that would be impossible to carry out for a large cohort. Nevertheless, despite the rigorous data collection carried out, occupational medical records did not allow to retrieve information on potential risk factors (socioprofessional data, lifestyle information and compliance with radiation protection measures) for all the workers—except information about profession and medical department of employment—to be included in the multivariate analyses. Furthermore, to date, there are no firmly established environmental risk factors for CNS tumours other than ionising radiation.²⁰ It has been suggested that a few non-modifiable (male sex, older age, Caucasian ethnicity, taller height, certain rare syndromes) and a few other suggested risk factors (immune-related conditions, history of epilepsy) may be associated with an increased risk of death from CNS tumour.²¹ This

**Table 5** Multivariate logistic regression analyses for CNS tumours death in relation with exposure variables adjusted for profession or physicians' medical specialties

	Variables	OR	95% CI	P value
Model 1	Cumulative career dose (mSv)	1.01	0.98 to 1.03	0.67
	Profession			
	All other workers*	1.00	Ref	0.14
	Physician	2.25	0.82 to 6.21	
	Cumulative career dose (mSv)	1.00	0.98 to 1.03	0.73
	Profession			
	All other workers*	1.00	Ref	0.07
	Radiologic technologist	2.67	0.93 to 7.70	
	Cumulative career dose (mSv)	1.01	0.98 to 1.03	0.48
	Profession			
All other workers*	1.00	Ref	0.03	
Nurse	0.27	0.08 to 0.90		
Model 2	Cumulative career dose (mSv)	1.00	0.98 to 1.03	0.67
	Physician specialty			
	All other workers*	1.00	Ref	0.63
	Conventional radiologist	0.72	0.19 to 2.71	
	Cumulative career dose (mSv)	1.00	0.98 to 1.03	0.71
	Physician specialty			
	All other workers*	1.00	Ref	0.23
	Interventional cardiologist and radiologist	2.34	0.58 to 9.39	
	Cumulative career dose (mSv)	1.00	0.98 to 1.03	0.73
	Physician specialty			
All other workers*	1.00	Ref	0.68	
Nuclear physicist	1.67	0.15 to 18.84		
Model 1	Exposure duration (mSv)	1.03	0.95 to 1.11	0.46
	Profession			
	All other workers*	1.00	Ref	0.11
	Physician	2.34	0.84 to 6.45	
	Exposure duration (mSv)	1.02	0.95 to 1.10	0.60
	Profession			
	All other workers*	1.00	Ref	0.08
	Radiologic technologist	2.54	0.88 to 7.33	
	Exposure duration (mSv)	1.02	0.94 to 1.09	0.68
	Profession			
All other workers*	1.00	Ref	0.04	
Nurse	0.29	0.09 to 0.96		
Model 2	Exposure duration (mSv)	1.02	0.95 to 1.11	0.49
	Physician specialty			
	All other workers*	1.00	Ref	0.57
	Conventional radiologist	0.67	0.18 to 2.58	
	Exposure duration (mSv)	1.02	0.94 to 1.10	0.61
	Physician specialty			
All other workers*	1.00	Ref	0.26	
Interventional cardiologist and radiologist	2.26	0.55 to 9.24		

Continued

Table 5 Continued

Variables	OR	95% CI	P value
Exposure duration (mSv)	1.03	0.95 to 1.12	0.44
Physician specialty			
All other workers*	1.00	Ref	0.49
Nuclear physicist	2.40	0.19 to 29.17	

Significant values in bold.
 *All other professions/medical specialties except the one studied.

information was not available for our study, but as these risk factors are not fully established, we may assume that our analyses are unlikely to suffer from confounding bias.

Another strength of our study is that it takes into account the recent exposure of workers (inclusion period 2002–2012),¹² which allows us to consider the impact of the considerable increase of interventional cardiology procedures observed in the last thirty decades and nuclear medicine procedures since the 2000s, that are associated with relative high doses of radiation. However, as the age at the end of follow-up is still young, 54 years on average, the ability of our study to detect an association between radiation exposure and CNS tumour mortality is limited. In France, the median ages at diagnosis and death due to brain cancer in 2018 were 63 and 66 for men and 67 and 68 for women, respectively.²² However, the cohort study from which this case–control study was built included all healthcare professionals in France (over 200 000 individuals) with sufficient dosimetric and administrative information to carry out the study. No exclusions were made. An extended follow-up of the cohort will improve the statistical power of the analyses, as the number of deaths will increase. An extension of the follow-up to 2021 is underway, which has identified over 2300 additional deaths in the cohort for which causes of death are currently being collected. It is estimated that 50 new cases of brain tumour deaths will be included in this case–control analysis.

A latency period of 5 years was considered, meaning that exposures in the 5 years preceding the death of the case were not taken into account in the calculation of cumulative dose, for both cases and controls. Among other things, this excludes biases potentially linked to changes in the attitude of cases following diagnosis of their cancer, which is estimated in the 5 years prior to death for this type of cancer.²³

At last, our study relies on a national design and on the use of national registries to ensure thorough data collection. The definition of cases was based on a national mortality registry provided by the CépiDc, which produces the database of medical causes of deaths in France. Causes are coded following the CIM-10 classification, ensuring high reliability. However, due to the absence of a national cancer registry in France, we were unable to study the incidence of brain tumours, but only mortality. However, the incidence of this cancer

is close to its mortality, due to its poor prognosis, then we would expect the incidence results to be similar to those we got for mortality. Analyses by tumour subtype were not possible, as we did not get any histological data concerning the cases of CNS tumours. While we performed the main analysis including both CNS malignant tumours and uncertain or unknown behaviour neoplasms, the sensitivity analysis restricted to malignant CNS tumours alone showed similar results.

It is noteworthy that our analyses relied on individual cumulative $H_p(10)$ doses, as the result of dosimetric reconstruction from personal whole-body dosimeter records worn on the chest under the apron. Nevertheless, estimates may be subject to uncertainties, as some healthcare professionals do not systematically wear their personal dosimeters, despite the fact that it is mandatory.^{24 25} Furthermore, the workers wear their badge under the apron. That could reflect only partially the dose received by the unprotected head. Consequently, future studies would benefit from reconstructing the doses received by the brain, taking into account the uncertainties associated with precisely wearing the dosimeter.

To overcome several previously mentioned limitations, the ORICAMs cohort will integrate the international Brain cancer risk in joint COhort of MEDical workers study. This project aims to carry out a joint case–control study nested in three national cohorts of healthcare professionals exposed to ionising radiation in France, South Korea and the USA. The project is being carried out in partnership with the IRSN, the Barcelona Institute for Global Health, Seoul University and the National Cancer Institute. A dosimetric reconstruction will be performed to estimate cumulative brain doses, considering uncertainties related to collection methods and badge types in each cohort. This study will also improve the statistical power of our analyses by greatly increasing the number of cases.

In conclusion, the ORICAMs case–control study did not show any significant increased risk of CNS tumour death linked to protracted occupational exposure to ionising radiation. This study benefits from a national level design including all medical workers specialties and available individual dosimetry data. An extension of the follow-up and an estimate of the dose absorbed to the brain, as well as a joint analysis with other cohorts of the same type, will enable to better characterise the risks for medical professionals exposed to ionising radiation.

Acknowledgements The authors would like to thank all members of the ORICAMS cohort and the medical departments of hospital and clinics that kindly provided information on cases and controls.

Contributors CB, KL and M-OB conceptualised and designed the study. HR, SC-L, FR and PL provided the dataset. JL and CB conducted the statistics. JL drafted the manuscript. All authors participated in the drafting and revision of the manuscript, approved the final version and agree to be responsible for the content and integrity of the manuscript. CB and MOB are responsible for the overall content as the guarantors of this paper.

Funding This study is part of the Brain cancer risk in joint COhort of MEDical workers study, which received funding from the French Agency for Food, Environmental and Occupational Health Safety.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The study protocol received ethical approval (N°912327) from the French National Data Protection Commission (CNIL) to ensure that the research project was conducted in compliance with CNIL's policies and procedures for the protection of human research participants and data. An information note regarding the implementation of the study has been disseminated via the occupational health departments of each healthcare workers included in the study. Upon receipt of this note, workers could express their opposition to the research if desired. This retrospective study being based on data already collected for other purposes, workers' consent was not required. The study data were fully pseudonymised before analysis.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. The data cannot be shared publicly as they are subject to the authorisation of an ethical committee. Proposals for possible collaborations for further analyses of the data should be addressed to M-OB (marie-odile.bernier@irsn.fr) and will be reviewed by the Institute for Radiological Protection and Nuclear Safety committee.

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REFERENCES

- 1 UNSCEAR. Effects of ionizing radiation, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 2006 report, volume I. United Nations. 2008.
- 2 Harrison JD, Balonov M, Bochud F, et al. The use of dose quantities in radiological protection: ICRP publication 147 Ann ICRP 50(1) 2021. *J Radiol Prot* 2021;41:410–22.
- 3 Gillies M, Richardson DB, Cardis E, et al. Mortality from circulatory diseases and other non-cancer outcomes among nuclear workers in France, the United Kingdom and the United States (INWORKS). *Radiat Res* 2017;188:276–90.
- 4 Della Vecchia E, Modenese A, Loney T, et al. Risk of cataract in health care workers exposed to ionizing radiation: a systematic review. *Med Lav* 2020;111:269–84.
- 5 Boice JD, Cohen SS, Mumma MT, et al. Mortality among medical radiation workers in the United States, 1965–2016. *Int J Radiat Biol* 2023;99:183–207.
- 6 Rajaraman P, Doody MM, Yu CL, et al. Cancer risks in US Radiologic Technologists working with Fluoroscopically guided Interventional procedures, 1994–2008. *AJR Am J Roentgenol* 2016;206:1101–8.
- 7 Roguin A, Goldstein J, Bar O. Brain tumours among Interventional Cardiologists: a cause for alarm? Report of four new cases from two cities and a review of the literature. *EuroIntervention* 2012;7:1081–6.
- 8 Rajaraman P, Doody MM, Yu CL, et al. Cancer risks in U.S. Radiologic Technologists working with Fluoroscopically guided Interventional procedures, 1994–2008. *AJR Am J Roentgenol* 2016;206:1101–8.
- 9 Bhatti P, Doody MM, Rajaraman P, et al. Novel breast cancer risk Alleles and interaction with ionizing radiation among U.S. Radiologic Technologists. *Radiat Res* 2010;173:214–24.
- 10 Kitahara CM, Linet MS, Balter S, et al. Occupational radiation exposure and deaths from malignant intracranial neoplasms of the brain and central nervous system in U.S. Radiologic Technologists, 1983–2012. *AJR Am J Roentgenol* 2017;208:1278–84.
- 11 Lee WJ, Ko S, Bang YJ, et al. Mortality among diagnostic medical radiation workers in South Korea, 1996–2015. *Occup Environ Med* 2018;75:739–41.
- 12 Lopes J, Baudin C, Feuarterd J, et al. Cohort profile: Oricams, a French cohort of medical workers exposed to low-dose ionizing radiation. *PLOS ONE* 2023;18:e0286910.
- 13 Rapport IRSN. Rapport IRSN / 2023-00387. La radioprotection des travailleurs exposition professionnelle aux rayonnements ionisants en France: Bilan 2022. 2023.
- 14 National Research Council. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2. Washington, DC: The National Academies Press, 2006. Available: <https://doi.org/10.17226/11340>
- 15 Picano E, Vano E, Domenici L, et al. Cancer and non-cancer brain and eye effects of chronic low-dose ionizing radiation exposure. *BMC Cancer* 2012;12:157.
- 16 Roguin A, Goldstein J, Bar O, et al. Brain and neck tumors among physicians performing Interventional procedures. *Am J Cardiol* 2013;111:1368–72.
- 17 Chartier H, Fassier P, Leuraud K, et al. Occupational low-dose irradiation and cancer risk among medical radiation workers. *Occup Med (Chic Ill)* 2020;70:476–84.
- 18 Lopes J, Baudin C, Leuraud K, et al. Ionizing radiation exposure during adulthood and risk of developing central nervous system tumors: systematic review and meta-analysis. *Sci Rep* 2022;12:16209.
- 19 Kitahara CM, Linet MS, Balter S, et al. Occupational radiation exposure and deaths from malignant intracranial Neoplasms of the brain and CNS in US Radiologic Technologists, 1983–2012. *AJR Am J Roentgenol* 2017;208:1278–84.
- 20 International Agency for Research on Cancer. List of classifications by cancer sites with sufficient or limited evidence in humans, IARC monographs volumes 1–135A. 2023. 2023.
- 21 Bondy ML, Scheurer ME, Malmer B, et al. Brain tumor epidemiology: consensus from the brain tumor epidemiology consortium (BTEC). *Cancer* 2008;113:1953–68.
- 22 Defossez G, Le Guyader-Peyrou S, Uhry Z, et al. Estimations Nationales de L'Incidence et de la Mortalité par cancer en France Métropolitaine Entre 1990 et 2018. Étude À Partir des Registres des cancers Du Réseau Francim. Volume 1 - Tumeurs Solides. 2019.
- 23 Ostrom QT, Cioffi G, Gittleman H, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2012–2016. *Neuro Oncol* 2019;21:v1–100.
- 24 Jacob S, Boveda S, Bar O, et al. Interventional Cardiologists and risk of radiation-induced cataract: results of a French multicenter observational study. *Int J Cardiol* 2013;167:1843–7.
- 25 Rapport ASN. Rapport de l'ASN sur l'État de la Sûreté Nucléaire et de la Radioprotection en France en 2022. 2022.