

Mortality of Workers Exposed to Ionizing Radiation at the French National Electricity Company

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Background Exposure to ionizing radiation increases the risk of cancer in humans. Nuclear workers receive low doses over a relatively long period of time.

Methods A mortality study of a cohort of workers exposed to ionizing radiation at Electricité de France (EDF) was conducted. The cohort consisted of 22,395 individuals monitored for radiation exposure between 1961 and 1994, and followed-up for an average of 11.7 years.

Results Our study demonstrates a clear healthy worker effect (HWE) since mortality is less than half what is expected from National mortality statistics. The HWE is greater among workers who have spent most of their career in the nuclear sector. The analysis by cancer site shows no excess compared with the general population. No significant trend was observed according to level of exposure to ionizing radiation.

Conclusions The mortality of workers exposed to ionizing radiation at the French National Electricity company is very low compared to the French national mortality. Am. J. Ind. Med. 47:72–82, 2005. © 2004 Wiley-Liss, Inc.

KEY WORDS: cancer mortality; cohort study; occupational health; nuclear workers; ionizing radiation

INTRODUCTION

Exposure to ionizing radiation increases the risk of cancer in humans [BEIR, 1990]. An excess risk had been first

observed among the Hiroshima and Nagasaki atomic bomb survivors and among patients exposed for medical reasons, both populations having received relatively high doses [Boice et al., 1987; Preston et al., 1994]. Nuclear workers receive low doses and their exposure is generally protracted over a relatively long period. Large-scale epidemiological studies of their mortality in relation to the level of exposure to ionizing radiation have been conducted [Gilbert et al., 1993a; Cardis et al., 1995; Ashmore et al., 1998; Carpenter et al., 1998; Muirhead et al., 1999]. The International Agency for Research on Cancer (IARC) did a combined analysis of 96,000 workers from Canada, the United Kingdom, and the United States [Cardis et al., 1995]. The National Radiological Protection Board (NRPB) studied 125,000 workers in the UK National Registry of Nuclear Industry Workers [Muirhead et al., 1999]. These studies showed that the risk of leukemia death increased with the level of exposure.

Countries having published cohort studies of mortality related to radiation exposure among their nuclear workers are

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Canada, United Kingdom, United States, Spain, Japan, and Finland [Rinsky et al., 1981; Wilkinson et al., 1987; Beral et al., 1988; Wiggs et al., 1991; Fraser et al., 1993; Gilbert et al., 1993b; Gribbin et al., 1993; Wiggs et al., 1994; Artalejo et al., 1997; Frome et al., 1997; Ashmore et al., 1998; Muirhead et al., 1999; Omar et al., 1999; Ritz et al., 1999; Dupree-Ellis et al., 2000; McGeoghegan and Binks, 2000a,b, 2001; Iwasaki et al., 2003]. France derives 80% of its electricity from nuclear power. Electricité de France (EDF), the French National electricity company, is in charge of 19 nuclear power plants (NPP). This study presents the results of the first mortality study of the workers considered as potentially exposed to ionizing radiation at EDF. This cohort was set up as part of a research project conducted by IARC [Cardis et al., 1997].

POPULATION AND METHODS

Nuclear power production of electricity began at EDF in the early 1960s, and systematic dosimetric monitoring started in 1961. EDF owned and operated 19 NPP with pressurized water reactors and one with fast neutron reactor. Most of them were constructed during the 1980s. Two facilities were mixed with EDF and Commissariat à l'Énergie Atomique (Marcoule and Brennilis). Some EDF workers, previously working in other parts of the company, were transferred to the nuclear sector when its first plants were built, however most workers in EDF power plants were hired at the time of the French nuclear construction program. All EDF permanent staff benefit from an in-house health and pension management program. Pension benefits are acquired after 15 years of employment and are managed by a special department, which records the deaths of workers, both before and after retirement.

Study Population

The protocol of the IARC international study defined the study population for the EDF cohort [Cardis et al., 1997] as all EDF permanent staff who worked in the company for at least 1 year between 1961 and 1994, and whose exposure to ionizing radiation was monitored. Because assignment to work with ionizing radiation was not recorded, linkage of dosimetry records, personnel and pensions files were used to identify the cohort members.

The EDF dosimetric monitoring department, in collaboration with the occupational medicine department, retrospectively constructed from paper and computer records a dosimetric file that included the exposure of all workers (permanent, temporary, subcontractors) exposed between 1968 and 1996. To identify permanent workers exposed only between 1961 and 1968 and not after, we used paper archives from the nuclear plants operating at the time. Overall, 25,877 individuals were listed as having worn a dosimeter. After

eliminating duplicates, incomplete records, workers exposed only after 1994, this dosimetric file included 24,309 individuals.

A personnel file consolidating all EDF employees working for the company in and after 1978 (approximately 230 150 individuals) enabled us to identify the permanent staff members employed at least 1 year between 1978 and 1994. Matching the dosimetric and personnel files identified 22,287 eligible workers. Matching the dosimetric file and archives of the plants functioning before 1978 and list of deaths recorded before 1978 by the pension department enabled us to identify the staff who left the company before 1978 (108 individuals). The cohort finally totaled 22,395 individuals, 763 of whom were women.

Each individual's date of birth was recorded. Job history (date, sites, place of employment, and job description) of the 22,287 workers identified in the personnel files was known. For the 108 workers who left the company before 1978, the employment period was determined from information in the archives. Employment dates were unknown or incomplete for 83 workers and replaced by the exposure period for duration of employment calculation.

Follow-Up, Vital Status, and Causes of Death

The overall follow-up period for all workers ran from 1961 to 1994. To determine vital status, internal EDF sources were validated using external National data. The reasons employment ended are included in the personnel department job files, which also contain the exact date of death for those who died while employed. The death and date of death of workers who died during retirement were ascertained through the EDF pension department. For workers who resigned or were dismissed, information on vital status was obtained by interrogating the city hall of the place of birth. Just before the end of the study, the national registry of the population born in France became accessible to epidemiologists (Répertoire National d'Identification des Personnes Physiques: RNIPP) allowing independent verification of the vital status. Among the 21,181 workers of the cohort born in France, 20,694 (98%) were identified in this registry; for the others, the identifiers were not complete enough or included errors. Comparison of in-house source and the RNIPP led to correction of vital status for 12 workers. Causes of death were obtained from the national causes of death register. Deaths are coded according to the International Classification of Diseases 8th revision before 1978 (ICD8) and 9th revision afterwards (ICD9).

Date of study entry was defined as the later of date of initial employment plus 1 year or date of the first dosimeter record. Study end-point was defined as the earlier of December 31, 1994, the date of death, and the last information date for workers lost to follow-up.

Confounding Factors

Age, sex, and calendar period are well-known confounders for cancer mortality and must be adjusted for. Additional confounders, such as socioeconomic status (SES) and geographic location, should also be examined [Kogevinas and Porta, 1997]. Information on SES was only partially available for the 108 workers who left the company before 1978. For all the workers included in the personnel job history file, all jobs and degrees obtained were coded at hiring and throughout their career. For the analyses presented here, the longest job held in six categories and the highest educational level in four categories were used.

To account for possible variations in cancer risk by geographic location, we attempted to estimate the location of exposure by reconstructing for each worker the geographical site of exposure for each year of exposure. For the 22,287 workers in the personnel files, we used their geographic job assignment. For the 108 workers who left the company before 1978, and for doses received by all members before 1968, we took as site of exposure, the nuclear plant where the exposure information was recorded. Workers were considered to have been exposed at the plant where they were exposed for the longest period. Sites were grouped by broad geographical region.

Exposure to Ionizing Radiation

In French Nuclear Power Plants described in Table III, workers were monitored for activation products; the most important isotope contributing to the dose being cobalt-60. The radiation exposure was, therefore, close to 100% mid-energy photons (100 keV to 3 MeV). Doses are controlled by restricting access to high dose rate areas and by the use of shielding materials. They were measured with film badges using Kodak type 2 films. Detection thresholds are unknown before 1968, and have been estimated to be either 0.1 or 0.2 mSv after. Dosimeters were issued monthly and worn on the chest. In case of missing dosimeters after 1983, daily dosimetry with electronic dosimeter was performed. Frequency of missing doses is unknown before 1968 and negligible after 1968. Doses below threshold are recorded as 0. A Rem counter-radiometer dosimeter was used for workers potentially exposed to neutrons (e.g., work in fuel handling reactor). Since 1980, internal contamination monitoring for activation products and transuranics were routinely monitored or in case of incident. For these, bioassay and anthropogammametry were carried out.

The study includes all workers who had a dosimetric monitoring whether they received or not doses above the dosimeter detection threshold. Based upon paper documents and computerized records, a file reconstructing the annual exposure of each worker for the 1968–1994 period has been made by the EDF dosimetry department, working with the

occupational medicine department. This file was used to define the population studied. Quantitative information on exposure before 1968 at EDF and on exposure before hiring was recorded in this file. For the period 1961–1968, information from the archives of plants in operation before 1968 was used. For those individuals whose dosimetry record contained information on cumulative exposure before 1968, we validated the reconstruction from the archives by comparing the sum of the reconstructed years with the cumulative dose indicated in the file. Some doses could not be reconstructed annually, some were received elsewhere than at EDF, other doses were received at EDF but the exact year was not indicated, all were considered as ‘transfer’ doses. While most information concerned gamma radiation, exposure to neutron radiation was also recorded and reconstructed on an annual basis from the dosimetric files. A dichotomous variable was constructed to indicate for each year whether the neutron dose represented more than 10% of the total external dose. Few workers had been internally contaminated, and the corresponding whole-body dose was known and validated by linking the dosimetry file with a file from the occupational medicine department that described nuclear incidents.

Statistical Analysis

An external analysis was conducted to describe the mortality of the workers and to compare it with that of the French population. We obtained from INSERM, the numbers of deaths by sex, 5-year age group and periods of 5 years. The size of the French population for the corresponding sex, age and period was obtained from Institut National de la Statistique et des Etudes Economiques (INSEE). Mortality rates were calculated for specific cancer sites and non-cancer causes of death. In each stratum s defined by sex, age group, and calendar period, the number of person-years at risk n_s was multiplied by the French mortality rate λ_s^* for the same stratum, to obtain the expected number of deaths e_s . The standardized mortality ratio (SMR) was calculated as the ratio between the sum of observed deaths o_s in each stratum ($O = \sum o_s$) and the sum of the expected deaths ($E = \sum e_s$). The person-years before 1968 were not taken into account because we had no access to National rates for all the specific causes of death. The SMRs for all causes and all cancers were estimated according to levels of the following factors: sex, year of study entry, age at study entry, SES, and special exposure. In order to study the ‘healthy worker effect’ (HWE), we estimated SMRs for all causes and all cancers according to different time-dependent factors: calendar period, age group, time since hiring, and duration of employment [Gilbert, 1982; Howe et al., 1988; Goldberg and Luce, 2001]. To assess whether this effect was greater among the EDF workers who had spent their entire career in the nuclear sector than among those who changed sectors, SMRs were also calculated as a function of fraction of time

spent in the nuclear sector (total exposure duration divided by total employment duration). Poisson regression and relative risk (RR) model were used to estimate SMRs (and their confidence interval (CI)) by each category j for each of these factors [Callas et al., 1994]. Number of observed deaths o_{sj} in each stratum s and category j is assumed to follow a Poisson distribution with mean $n_{sj}\lambda_s^* \exp(\beta_j)$, where n_{sj} represents person-years in category j [Breslow and Day, 1987]. For unordered categories, homogeneity was tested by a likelihood ratio test comparing the model assuming $SMR_j = \exp(\beta)$ to the one assuming $SMR_j = \exp(\beta_j)$. For ordinal categories, trend was tested by a score test on the parameter β in the model where o_{sj} follows a Poisson distribution with a mean $n_{sj}\lambda_s^* \exp(\beta_j)$. The SMRs were also calculated for specific causes of deaths. The 90% CIs were calculated using Byar's approximation [Breslow and Day, 1987].

Using an internal analysis and adjusting for confounding factors, we then examined the relations between mortality and cumulative radiation dose. Person-years at risk and deaths were stratified according to age group, calendar period, sex, SES based on job held longest, exposure to neutrons and cumulative dose categories (<10, 10–50, 50–100, ≥ 100 mSv). To take account of a minimal latent period, cumulative dose was lagged by 2 years for leukemia and by 10 years for other causes of death. Trend test was performed as in external analysis, with j being the dose category and assuming that o_{sj} follows a Poisson distribution with mean $n_{sj}\lambda_s \exp(\beta x_{sj})$, where λ_s is the internal background rate in stratum s , and x_{sj} the mean dose in stratum s , and dose category j . This test is equivalent to Mantel's trend test [Breslow and Day, 1987]. Our main aim was to determine whether mortality increased according to level of exposure, while controlling for the principal confounding factors, we therefore performed one-sided tests. Because there were so few deaths, the excess RR model could not be used [Gilbert, 1983; Thomas, 1983]. Nonetheless, to enable comparisons with the literature, we estimated the RR for a cumulative dose of 100 mSv by the maximum likelihood estimates of the parameter β determined in the RR model described above, with 90% likelihood-based CIs. The small number of deaths led us to combine some cancer sites. Moreover, we took into account the cancers listed as a contributing cause of death in addition to those mentioned as the main cause of death: this added only two cancers. This analysis was performed for the population exposed primarily to gamma radiation, defined by excluding individuals with internal contamination or neutron exposure.

RESULTS

Description of the Study Population

Table I summarizes the size and characteristics of the cohort. Among the 22,395 workers followed-up during an

TABLE I. Characteristics of the Study Population; EDF Workers Exposed to Ionizing Radiation in France

Characteristics	N = 22,395
Sex: n (%)	
Men	21,632 (96.6)
Women	763 (3.4)
Age in years: median (range)	
At first employment	23.5 (14.7–55.6)
At study entry	27.6 (17.7–69.5)
At study end	39.4 (19.7–88.0)
At death	44.2 (22.1–73.5)
Duration in years: median (range)	
Employment	14.1 (1–43)
Exposure	10.0 (1–33)
Follow-up	11.7 (1–33.5)
Vital status on January 1, 1995: n (%)	
Died	387 (1.7)
Alive	22,001 (98.2)
Lost to follow-up	7 (0.0)
SES based on highest job (%)	
Professional	3,368 (15)
Intermediate	158 (0.7)
Skilled non-manual	1,538 (7)
Skilled manual	16,945 (75)
Partly skilled	180 (0.8)
Unskilled workers	126 (0.6)
Unknown	80 (0.3)

average of 11.7 years, 387 (1.7%) deaths have been observed. Only seven subjects were lost to follow-up. Women comprised 3.4% of the workers. Cause of death was ascertained for 94% (364) of the deaths. Nine of the 23 deaths with unknown cause occurred abroad. Of the 364 ascertained causes of death, 116 are cancers, and 6 of these are leukemia. The cohort is composed of 75% of skilled manuals, mainly technicians and qualified industrial workers. Figure 1 shows the number of workers at EDF according to hiring year; the median year of entry was 1983.

The total collective dose received by cohort members can be divided into 396.6 Sv of gamma radiation, 4.94 Sv of neutron radiation (for 1934 workers), and 0.06 Sv of internal whole-body contamination (for 20 workers). Table II summarizes the distribution of the total collective dose according to sex, age at exposure, and period of exposure; most of the collective dose was received by men under age 35 and during the 1985–94 period. Figure 2 describes the distribution of the cumulative dose received at EDF. The median cumulative dose was 5.5 mSv (range: 0–608); 1,499 (7%) individuals had a cumulative dose equal to 0, and 88 (0.4%) a cumulative dose greater than 200 mSv. Table III lists the NPP operated by EDF with the starting date of monitoring considered to begin 2 years before their start-up, and the number

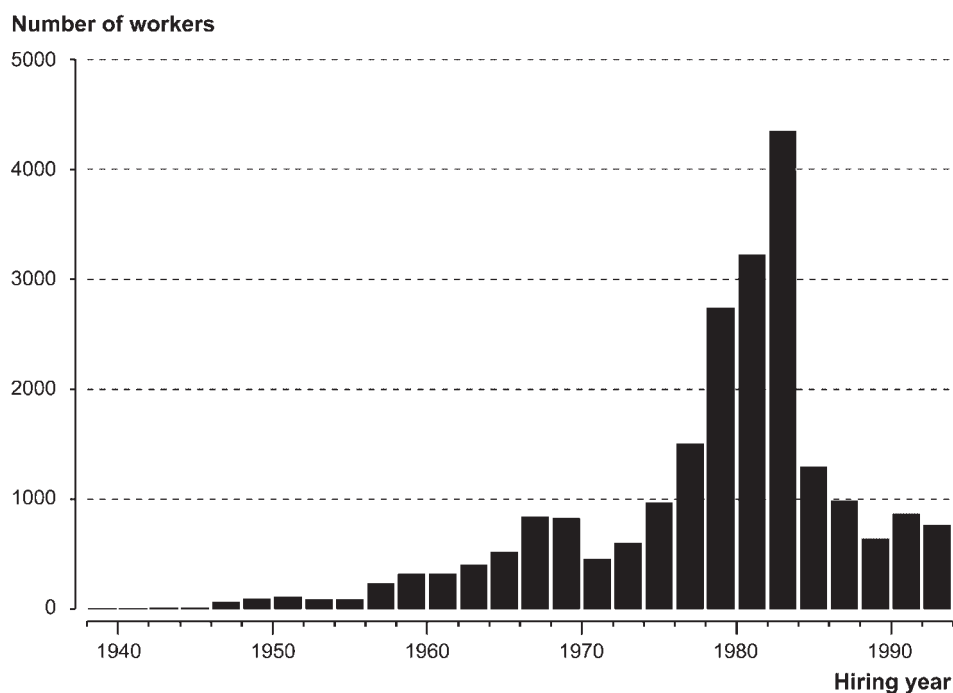


FIGURE 1. Distribution of hiring years; EDF workers exposed to ionizing radiation in France.

of workers assigned. The site is unknown for 1,293 workers. The site was an operational unit (research unit, for example) that was not part of a NPP and was thus not identified for 1991 workers.

External Analysis

Table IV presents SMRs when expected number of deaths is greater than 5. We observed a very strong HWE: all-cause mortality was half that of the French population ($SMR = 0.48$; 90% CI: 0.44–0.52). The result was similar when we looked only at deaths from all cancers

TABLE II. Collective Dose by Sex, Age at Exposure, and Calendar Period of Exposure; EDF Workers Exposed to Ionizing Radiation in France

Characteristics	Collective dose (Sv)
Sex	
Men	399.5
Women	2.1
Age at exposure in years	
<35	245.3
35–49	150.7
50+	5.6
Period of exposure	
1961–1974	44.7
1975–1984	111.7
1985–1994	245.2
Total	401.6

($SMR = 0.58$; 90% CI: 0.49–0.68) or from tobacco-related cancers ($SMR = 0.50$; 90% CI: 0.39–0.63). Mortality was also half that of the French population for circulatory diseases and for external causes. Particularly low mortality was observed for cirrhososes, and there were no observed deaths from respiratory diseases. We observed a significant deficit of cancers of mouth and pharynx, esophagus, and lung. The highest SMRs were observed for cancer of the pancreas and for brain tumors, but they are not significantly above 1. We note that the brain tumors include malignant and six benign and unspecified tumors. Overall, six deaths from leukemia were observed, and the SMR was 0.76 (90% CI: 0.33–1.49). After exclusion of one death due to chronic lymphoid leukemia, the SMR was 0.70 (90% CI: 0.27–1.46). Table V describes all-cause and all-cancer mortality ratios according to various characteristics. The number of observed deaths among women being small (8), the SMR is not significantly different from 1. No heterogeneity in mortality was detected according to the year of study entry or to the calendar period. All-cause SMRs increased significantly with age at study entry and attained age. All-cause and all-cancer SMRs decreased significantly as SES rose. No significant variations in mortality ratios were observed with time since hiring or duration of employment. All-cause mortality ratios were significantly higher in the population exposed primarily to gamma radiation, a population defined by excluding those with internal contamination and/or substantial neutron exposure. This result was, however, not observed for all-cancer mortality. Exposure before employment did not modify mortality results. All-cause and all-cancer mortality

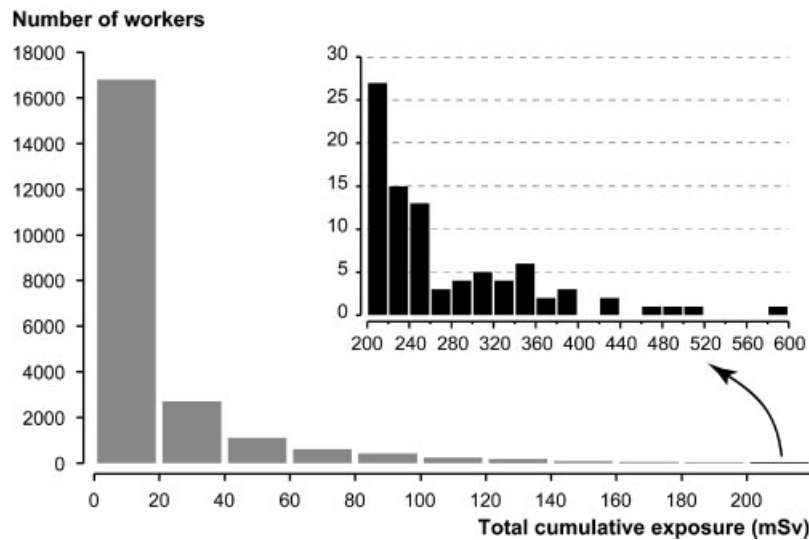


FIGURE 2. Distribution of total cumulative radiation doses; EDF workers exposed to ionizing radiation in France.

TABLE III. Description of Nuclear Power Plants Included in the Study; EDF Workers Exposed to Ionizing Radiation in France

Nuclear power plant	Start of monitoring ^a	Number of workers ^b
Northwest		
Gravelines	1978	1,627
Flamanville	1983	641
Paluel	1982	1,278
Penly	1988	539
Brennilis	1965	128
Northeast		
Cattenom	1984	1,017
Fessenheim	1975	700
Nogent	1985	603
Chooz	1962	485
Center		
Bellevalle	1985	648
Chinon	1961	2,001
Dampierre	1978	1,181
Saint-Laurent	1963	1,316
Civaux	>1994	0
Southwest		
Le Blayais	1979	1,232
Golfech	1988	435
Southeast		
Bugey	1968	1,802
Cruas-Meyssse	1981	1,059
Saint-Alban	1983	617
Tricastin	1978	1,196
Creys-Malville	1983	587
Marcoule	1962	19

^aTwo years before start-up on average.

^bFor definition of the workers included in the study, see text.

ratios were both significantly lower for the workers who had spent more than 30% of their EDF career in the nuclear sector.

Internal Analysis

Table VI summarizes the internal comparison analysis. It presents for each dose category the number of observed deaths by cause and the number of death expected under the null hypothesis that exposure to radiation does not modify mortality. The *P*-values according to a one-sided trend test and the RR estimate per cumulative dose of 100 mSv are displayed.

There was no significant relation between the dose of radiation and the risk of death for any of the cause of death considered. The estimated RR for a cumulative dose of 100 mSv is significantly less than 1 for external causes. No RR estimate is significantly greater than 1; for the overall population, the RR for all cancers deaths excluding leukemia is 0.85 (90% CI: 0.38–1.61) and the RR for leukemia deaths excluding chronic lymphoid leukemia is 1.68 (90% CI: 0.16–7.22). We note that in the three dose categories where leukemia are observed (i.e., for doses below 100 mSv), the ratio of observed to expected cases increases with dose. The conclusion of the internal analysis was not modified when the analysis includes workers exposed to internal contamination or to neutrons. The conclusion was not modified when the analysis was not stratified on SES, or was stratified on SES based on education instead of job, or was additionally stratified on region or duration of employment.

DISCUSSION

Our study of 22,395 nuclear workers followed-up for an average of 11.7 years demonstrates a clear HWE since its

TABLE IV. Observed (O) and Expected (E) Number of Deaths Among EDF Workers Exposed to Ionizing Radiation in France, Standardized Mortality Ratio (SMR) and 90% Confidence Intervals by Cancer Site

Causes of death ^a	ICD9	O	E	SMR	[90% CI]
All cancers	140 to 208	116	200.5	0.58	[0.49 0.68]
Smoking related	140 to 150 + 157 + 161 + 162 + 188 + 189.1	51	102.5	0.50	[0.39 0.63]
Mouth and pharynx	140 to 149	4	21.0	0.19	[0.06 0.44]
Esophagus	150	5	13.3	0.38	[0.15 0.79]
Stomach	151	3	7.2	0.41	[0.11 1.07]
Colon	153	8	8.3	0.97	[0.48 1.75]
Liver	155.0 + 155.1	3	5.0	0.60	[0.16 1.54]
Pancreas	157	11	6.6	1.66	[0.93 2.74]
Nasal cavity	160	0	6.6	0.00	[0.00 0.34]
Larynx	161	8	10.5	0.76	[0.38 1.38]
Lung	162	23	47.5	0.48	[0.33 0.69]
Brain and CNS	191 to 192 + 238	16	10.3	1.56	[0.98 2.37]
Ill-defined and secondary	195 to 199	8	13.8	0.58	[0.29 1.04]
Non-Hodgkin lymphoma	200 + 202	5	5.6	0.89	[0.35 1.88]
Multiple myeloma	203	0	1.3	0.00	[0.00 1.81]
All leukemia	204 to 208	6	7.9	0.76	[0.33 1.49]
Leukemia except CLL	(204 to 208)–(204.1 + 204.9)	5	7.2	0.70	[0.27 1.46]
All non-cancers	(000 to 999)–(140 to 208)	271	603.8	0.45	[0.40 0.50]
Circulatory diseases	390 to 459	61	120.8	0.50	[0.40 0.62]
Respiratory diseases	460 to 479 + 487.1 to 519.9	0	15.1	0.00	[0.00 0.15]
Cirrhosis	571.2 + 571.5 + 571.6	8	36.7	0.22	[0.11 0.39]
External causes	800 to 999	132	251.8	0.52	[0.45 0.61]
All deaths	000 to 999	387	804.2	0.48	[0.44 0.52]

^aResults for specific cause when expected number are greater than 5 (except for multiple myeloma).

mortality is less than half what is expected from National mortality statistics. The HWE is greater among workers who have spent most of their career in the nuclear sector. The analysis by cancer site shows no excess compared with the general population. No significant trend was observed according to level of exposure to ionizing radiation.

The cohort is composed of a stable population, followed-up very effectively since only seven individuals were lost to follow-up. Vital status was ascertained by two independent sources: in-house EDF files and archives, and the National registry (RNIPP). Vital status could thus be determined with certainty, even for workers born or who had died abroad. The cohort is very young since the median age at end of study is 39.4 years old. The information is missing for only 0.3% for job category and for 2% for educational level. The method to identify geographical site of exposure does not guarantee that the exposure occurred in the regions considered; however, most EDF workers have stable assignments to nuclear sites and even more stable regions of work. The identification of the geographical site may nevertheless be a problem for the highly mobile minority of workers who participated in the opening of the first plants and then moved to build others.

The exposure history is reliable and based on dosimetric monitoring. Some limitations of the monitoring data should, however, be mentioned. Based on the information collected through questionnaires and by contact with experts, a study of errors in recorded doses was carried out within the International Collaborative Study of Cancer Risk among Radiation Workers in the Nuclear Industry to identify and quantify sources of bias and uncertainties in dose estimates [Cardis et al., 1997]. Errors in dosimeter response, radiation fields, and calibration practices were quantified, and correction factors were derived for each model of dosimeter in use in participating facilities. These factors took into account the results of experiments carried out on the energy and geometry response of a representative sample of dosimeters used historically and the estimated predominant conditions of exposure in different types of facilities. The two types of dosimeters in use at EDF (Sn and Pb film badges) have similar response than dosimeters used in the UK, which have been studied in details. It has been estimated that the measurement of doses in terms of Hp(10) could be underestimated as a maximum by 10% [Thierry-Chef et al., 2002]. For the 1968–1994 period, the archives contained information about a

TABLE V. Person-Years (PY), Observed Number of Deaths (O) Among EDF Workers Exposed to Ionizing Radiation in France, Standardized Mortality Ratios (SMR) According to Cause of Death and Workers' Characteristics

Characteristics	PY	All causes			All cancers		
		O	SMR	P ^a	O	SMR	P ^a
Sex							
Men	251589	379	0.47		113	0.57	
Women	7023	8	0.86	0.12	3	0.97	0.41
Year of study entry							
1961–1972	51679	158	0.56		67	0.69	
1973–1977	25198	36	0.42		13	0.56	
1978–1982	90138	103	0.45		24	0.52	
1983–1987	70960	74	0.46		9	0.33	
1988–1994	20637	16	0.35	0.18	3	0.39	0.17
Calendar year							
1968–1972	7908	7	0.33		2	0.63	
1973–1977	12637	17	0.43		4	0.49	
1978–1982	30131	57	0.65		17	0.88	
1983–1987	68926	86	0.46		20	0.47	
1988–1994	139009	220	0.47	0.17 (t)	73	0.57	0.45 (t)
Age at study entry (year)							
<40	241301	277	0.44		72	0.53	
40+	17311	110	0.64	<0.001	44	0.67	0.22
Attained age (year)							
<40	184439	139	0.40		18	0.51	
40–60	69846	193	0.53		68	0.53	
60+	4327	55	0.59	0.006 (t)	30	0.76	0.25 (t)
SES based on job							
High	60922	69	0.31		22	0.35	
Moderate	192705	272	0.50		77	0.62	
Low	3465	17	1.00		6	0.91	
Unknown	1519	29	1.28	<0.001	11	1.41	0.002
Time since hiring (year)							
<5	51501	44	0.49		4	0.48	
5–10	71296	62	0.44		10	0.55	
10+	135815	281	0.49	0.77 (t)	102	0.58	0.91 (t)
Duration of employment (year)							
<5	52693	54	0.55		9	0.81	
5–10	71503	70	0.46		11	0.51	
10+	134415	263	0.47	0.42 (t)	96	0.57	0.56 (t)
Radiation type							
Gamma	231680	363	0.49		109	0.58	
gamma, neutron, IC	26932	24	0.34	0.06	7	0.48	0.61
% Career in nuclear sector							
<30%	33718	110	0.59		40	0.61	
≥30%	223265	246	0.42		65	0.51	
Unknown	1629	31	1.17	<0.001	11	1.24	0.04

^aP-value of test for heterogeneity or for trend (t) if specified.

TABLE VI. Observed (O) and Expected (E) Number of Deaths by Cumulative Doses: Internal Analysis Among Population Primarily Exposed to Gamma Rays; EDF Workers Exposed to Ionizing Radiation in France

Causes of death	Cumulative dose (mSv) ^a				P-value trend test	RR by 100 mSv	[90% CI]
	< 10	10–49	50–99	100			
	O/E	O/E	O/E	O/E			
All cancers	92/88.0	12/15.9	5/4.9	2/2.1	0.70	0.80	[0.36 1.50]
All cancers except leukemia	88/84.3	11/15.1	5/4.6	2/2.0	0.64	0.85	[0.38 1.61]
Cancers							
Digestive	34/31.4	3/6.0	1/1.8	2/0.8	0.46	1.11	[0.36 2.56]
Respiratory	22/23.0	5/4.9	3/1.5	0/0.6	0.49	1.01	[0.25 2.74]
Genito-urinary	6/6.5	2/1.0	0/0.3	0/0.2	0.67	0.43	[0.00 4.11]
Brain, central nervous system	14/12.7	0/1.7	1/0.4	0/0.2	0.64	0.59	[0.01 3.89]
Lymphatic tissues	4/4.3	1/0.5	0/0.2	0/0.0	0.55	0.55	[0.01 16.7]
Leukemia	2/3.2	2/1.2	1/0.4	0/0.2	0.39	1.36	[0.12 5.94]
Leukemia except CLL	1/2.5	2/1.0	1/0.3	0/0.2	0.31	1.68	[0.16 7.22]
Non-cancers							
Circulatory disease	50/50.4	6/7.1	2/1.8	2/0.7	0.14	1.70	[0.66 3.53]
External causes	110/108.1	11/9.7	0/2.3	0/0.9	0.94	0.21	[0.03 0.88]
Unknown causes ^b	25/25.3	3/2.8	1/0.8	0/0.2	0.54	0.97	[0.07 4.54]
All causes	314/307.5	36/40.0	9/11.0	4/4.5	0.83	0.76	[0.45 1.20]
Person-years	216,614	13,365	2,959	1,275			

^aA lag time of 2 years is assumed for leukemia, and 10 years for other causes.

^bNo causes and undetermined causes.

“career cumulative dose,” but the sum of the reconstructed annual doses described in the method section differed from that career dose for almost half of the workers, often because of delays in sending dosimetric film for development. Applying a protocol designed by a group of dosimetry expert to correct these anomalies reduced the collective dose by less than 0.8%. Some dose records may have been lost for the 1961–1968 period, however for nearly all workers whose pre-1968 exposure was reconstructed from archives, this information was consistent with the dose for prior exposure recorded in the 1968–1994 dosimetric file. Information about neutron exposure was not recorded separately from gamma exposure until 1976, an annual neutron exposure indicator could thus not be constructed. Natural or other non-occupational radiation exposures were not taken into account into the analysis. No information was available on periodic medical examinations during employment, thus it was not considered in the study. In the present study, exposure to other carcinogens, such as electromagnetic fields, chlorinated solvents, mineral fibers, and benzene. . . , have not been taken into account [Guenel et al., 2002].

The HWE is often observed in occupational cohorts, including studies of workers in the nuclear sector [Wilkinson et al., 1987; Beral et al., 1988; Wing et al., 1991; Fraser et al., 1993; Gilbert et al., 1993b; Gribbin et al., 1993; Wiggs et al.,

1994; Artalejo et al., 1997; Ashmore et al., 1998; Muirhead et al., 1999; Ritz et al., 1999; McGeoghegan and Binks, 2000a,b, 2001; Iwasaki et al., 2003], other studies of EDF workers [Marshall et al., 1999; Marchand et al., 2003], and study of French Atomic Energy Commission (CEA) workers [Telle-Lamberton et al., 2004]. However, our study shows a specially important HWE. It may be moreover slightly over-estimated due to removal of 2687 person-years of follow-up before 1968, period where only one death was observed. Table V shows that the all-cause SMR is lower in workers who spent more that 30% of their career in the nuclear sector. These findings tend to confirm a selection phenomenon among workers in this sector, as well as the possible exclusion from it of workers who develop any disease symptoms [Howe et al., 1988]. This phenomenon was also reported in a recent study of the health status of EDF workers in nuclear plants, which did not consider exposure to ionizing radiation [Gros et al., 2002]. Table V shows that this HWE is not decreasing with calendar period. The very particular status of this company, in particular its special health insurance, may have a protective effect on workers’ health, throughout their careers. This strong HWE should not be interpreted as an evidence of a protecting effect of ionizing radiation: the SMR for leukemia is higher than the SMR for all cancers, that is higher than the SMR for all causes.

Moreover, the internal analysis showed no evidence of a significant decrease in risk with level of exposure for any of the causes studied, except for external causes. We note a borderline significant excess of brain tumors, which is not related to the level of gamma exposure; 15 cases among the 16 have a cumulative dose below 10 mSv. An excess of brain tumor risk has been already reported in workers of the nuclear sector (monitored or not) compared to other EDF workers [Gros et al., 2002]. A non-significant excess was reported in a study of EDF workers occupationally exposed to magnetic field [Kheifets et al., 1999].

The internal analysis lacked statistical power and yielded no significant results. The sensibility of the results was studied by including and excluding in turn the doses before hiring by EDF and the workers who were exposed not only to gamma rays and then by exploring different analytical approaches. The risk estimates obtained are close to those obtained by the IARC '3-country' study, based on 96,000 workers, and those obtained by the UK study of the "National Registry of Radiation Workers (NRRW)," based on 125,000 workers; both studies however used the excess RR model [Cardis et al., 1995; Muirhead et al., 1999]. We estimated a RR of death from all cancers excluding leukemias per 100 mSv of 0.85, while estimate of the IARC study was 0.99 and estimate of the NRRW study, 1.01. We estimated a RR of death from leukemia excluding chronic lymphoid leukemia per 100 mSv of 1.68, while the IARC study estimate was 1.22 and NRRW study estimate was 1.26. However, the CIs in our study are very wide.

In summary, our study shows an important HWE. Its statistical power is too small for a precise analysis of the relation between exposure and mortality, but it shows consistent results with the literature. The population of this cohort is still very young (median age at study end is 39.4 years) but is composed of stable workers, carefully followed, with low and precisely known exposure. The aging of the population will allow promising repetition of this analysis in the future. Moreover, this cohort is a part of a larger study conducted by the International Agency for Research on Cancer that seeks to pool data for workers from 15 countries in order to estimate as precisely as possible the dose-effect relation between exposure to gamma radiation and cancer risk.

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