
CANCER MORTALITY AMONG FRENCH ATOMIC ENERGY COMMISSION WORKERS

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Abstract : An analysis of the mortality of workers employed at the Commissariat à l'Energie Atomique (CEA) between 1946 and 1994 is presented. Standardized Mortality Ratios (SMR) are computed with reference to the French national population for the period 1968-1994. 51 286 workers are included in the study. 3 784 deaths occurred between 1968 and 1994. A healthy worker effect is observed for men (SMR=0.53 CI_{90%}=[0.52;0.55]) and for women (SMR=0.70 CI_{90%}=[0.64;0.76]). An excess is observed for male pleural cancers (SMR=1.54, CI_{90%}=[1.03;2.21]). An excess of breast cancer is observed among women, statistically significant for the 1980-1994 period (SMR=1.30, CI_{90%}=[1.04;1.61]). An excess is observed for malignant melanoma for both sexes (SMR=1.38, CI_{90%}=[0.95;1.96]), stronger for the 1990-1994 period (SMR=2.11, CI_{90%}=[1.25;3.34]). It diminishes with age.

The relation with occupational exposures will be examined in the on-going cohort study on French nuclear workers including retrospective exposures assessment.

1. INTRODUCTION

The study presented here is a descriptive study of cancer mortality among nuclear workers compared to the general population.

Numerous epidemiologic studies have examined the risk of cancer among nuclear workers. They focus primarily on the relation between external exposure to X and gamma rays and cancer mortality. The two most powerful studies, from a statistical point of view, are the combined analysis by Cardis et al. of 7 cohorts from the US, the UK, and Canada [1], and the UK study, [2]¹. Cardis's study brought out a significant relation between the X and gamma-ray doses received and the risk of death from leukemia, excluding chronic lymphocytic leukemia (CLL) and a significant dose-effect relation for multiple myelomas. Muirhead's study shows very similar results.

Authors studying nuclear workers have systematically observed a mortality rate lower than that of the general population, [2-20]. This is due to what is known as the Healthy Worker Effect: the working population has a better overall general health compared with the general population which includes people not working for healthy reasons. The size of this effect varies from one cohort to another. Excesses of some specific causes of cancer deaths have been found. The only cause being systematically in excess is pleural cancer, but it has been documented only rarely.

A cohort study of the workers at the Atomic Energy Commission (CEA) and at COGEMA, the uranium processing company, is underway in France. It will include about 35 000 individuals monitored for ionizing radiation exposure since 1950 and will provide a direct estimation of the risk of cancer associated with X- and gamma-rays in this population [21]. These data will also be analyzed as part of a combined study coordinated by the International Agency for Research on Cancer (IARC) [22], which will include roughly 500 000 workers.

¹ Ashmore et al's study [3] involves 206 620 workers for 2 861 093 person-years but 90 320 (1 247 553 person-years) belong to nuclear industry.

This article describes the mortality of CEA workers, whether they were exposed or not to ionizing radiation.

2. MATERIAL AND METHODS

2.1 Cohort Definition and Data Collection

The study population, called 'SETCEA'², includes all employees who spent more than one year at CEA between 1946 and 1994 whether or not they were exposed to ionising radiation. Identification data (date and place of birth, sex, hiring and departure dates) were provided to the CEA's Occupational Medicine Adviser from the personnel files. To obtain a list of employees who had died, we sent a mailing to the municipality of birth of each member of the cohort who left the firm, because deaths in France are reported to the department of vital records of the municipality in which a person was born. We then queried the national causes of death registry, which is administered by the French national health and medical research institute (INSERM). It includes all deaths in France since 1968. Due to the data included in the national file, matching was executed with the date of birth, the sex, and the date and place of death. The causes of death were coded according to the 9th revision of the International Classification of Diseases (ICD9) of the World Health Organization(1977).

2.2 Statistical Analysis

Follow-up began one year after recruitment in the company. The end of follow-up is defined as the date of death for those who have died, the study end-point (31.12.1994) for those alive at the end of the study, and the date of last contact for those whose vital status could not be ascertained at the end of the study (subjects lost to follow-up).

The mortality of CEA workers due to all causes was compared with that of the national population from 1947 to 1994. The mortality due to 30 specific causes was analysed only between 1968 through 1994, since the national file did not exist before. The national population was chosen as the reference because the workplaces were spread over the entire national territory.

Standardized Mortality Ratios (SMR) were computed as the ratio of the mortality observed in the cohort to that expected if the risk of death was the same as in the national population. The expected mortality was calculated in applying the national mortality rates for each calendar period, by sex and 5-year age groups, to the numbers of cohort members monitored during that period, by sex and age group. From 1947 to 1949 mortality rates were unavailable and replaced by the rates of 1950.

Confidence intervals were calculated on the assumption that the number of deaths observed followed a Poisson distribution with mean equal to the number of deaths expected [23]. Statistical significance of excesses or deficits were tested for each cause of death at the 10% significance level (bilateral tests). Confidence intervals are expressed at 90%.

3. RESULTS

3.1 Cohort Description

As of May 1998, according to the CEA personnel file, 55 512 persons had worked at CEA for at least one year between 1946 and 1994. Out of those, 51 692 were sufficiently well identified (date and place of birth, sex, hiring and departure date, age at hiring known and older than 15 years) to enter the study. These individuals comprise the cohort whose mortality is studied here, called SETCEA1. Men made up 77.8% of the population.

From this cohort, 18 570 employees were still working on 31 December 1994, the end point of this study, and were thus alive on that date (Table 1) . Of the 33 122 individuals who left the firm and whose vital

² SETCEA: Suivi Epidémiologique des Travailleurs du CEA

status were sought, 25 694 were declared alive by birth townhalls, 3 867 had died and 3561 were lost to follow-up.

Thus, 44 264 workers of the cohort were still alive on 31 December 1994 which makes 85.6%, 7.5% had died, and 6.9% had been lost to follow-up. The latter were considered in the analysis until the date of their last contact, that is, the date they left the company.

The number of person-years included in the all causes mortality analysis (1947-1994) is 909 273.7 for the men and 242 642.0 for the women, for a total of 1 151 915.7.

The mean year of birth was 1940. The mean age at cohort entry was 30 years. The subjects were followed for a mean period of 22 years and worked in the company for a mean duration of 16.5 years. Some staff were hired at fairly advanced ages; these generally were scientific advisors with special contracts.

Table 1: SETCEA1 Cohort Description: CEA Staff Employed for More than One Year

	Men		Women		Total	
	n	%	n	%	n	%
Total number of subjects	40 212	100	11 480	100	51 692	100
Employed on 31/12/1994	13 877	34.5	4 693	40.8	18 570	35.9
Declared alive on 31/12/1994 by birth townhalls	20 074	49.9	5 620	49.0	25 694	49.7
Total presumed alive on 31/12/1994	33 951	84.4	10 313	89.8	44 264	85.6
Dead on 31/12/1994	3434	8.5	433	3.8	3 867	7.5
Lost to follow-up on 31/12/1994	2 827	7.1	734	6.4	3 561	6.9
Total person-years [1947-1994]	909 273.7		242 642.0		1 151 915.7	
Year of birth*	1939 ± 14 [1883;1975]		1944 ± 14 [1882 ;1973]		1940 ± 14 [1882 ;1975]	
Year hired*	1969 ± 11 [1946;1993]		1971 ± 11 [1946 ;1993]		1969 ± 11 [1946 ;1993]	
Year left CEA* (n=33 122)	1982 ± 9 [1947;1994]		1981 ± 10 [1947;1994]		1982 ± 9 [1947;1994]	
Year follow-up began (entered cohort)*	1970 ± 11 [1947;1994]		1972 ± 11.5 [1947;1994]		1970 ± 11 [1947;1994]	
Year follow-up ended (exited cohort)*	1992 ± 5 [1947;1994]		1992 ± 5 [1947;1994]		1992 ± 5 [1947;1994]	
Age at cohort entry*	30 ± 8 [16; 73]		28 ± 8 [18; 74]		30 ± 8 [16; 74]	
Duration of presence in the company *	17 ± 11 [1; 48]		15 ± 11 [1; 44]		16 ± 11 [1; 48]	
Duration of follow-up *	22 ± 11 [<1; 47]		20.5 ± 12 [<1; 47]		22 ± 11 [<1; 47]	

*mean ± standard deviation [min ; max], including lost-to-follow-up

3 783 workers died between 1968 and 1994 (table 2). INSERM found the cause of 3 609 of them (95.4%). The number of person-years included in the specific-cause mortality analysis (1968-1994) is 731 147.7 for the men and 211 669.7 for the women, for a total of 942 817.4.

Table 2: SETCEA1 Cohort Description between 1968 and 1994

	Men	Women	Total
Died between 1968 and 1994	3 359	424	3 783
Causes of death identified [1968-1994]	3 205	404	3 609
Percentage of identified causes of death	95.4	95.3	95.4
Total person-years [1968-1994]	731 147.7	211 669.7	942 817.4

3.2 Mortality – All Ages

All cause mortality for men employed at CEA was half that of the national population, thereby indicating a substantial “healthy worker effect” (table 3). Mortality from cancer was also significantly lower than in

the general population (SMR = 0.61, CI_{90%}=[0.58; 0.64]). For most of the sites analysed separately SMRs showed significant mortality deficits (table 3). We note an excess of pleural cancer (SMR = 1.54, CI_{90%}=[1.03; 2.21]) and of malignant melanoma (SMR = 1.36 CI_{90%}=[0.89; 1.99]) on the borderline of statistical significance.

A “healthy worker effect” was also present among women, although not quite as strongly (table 4). There was no significant excess or deficit at any site. Nonetheless, we noted two sites with an excess on the borderline of significance: brain (SMR = 1.58, CI_{90%}=[0.83; 2.76]) and breast (SMR = 1.18, CI_{90%}=[0.96; 1.45]) cancers. The latter accounted for one third of all cancer deaths among women.

Table 3: Standardized Mortality Ratios (SMR) by Cause of Death³ for the 40 212 Men in the Cohort

	ICD9	Obs	Exp	SMR	90%	CI
n=40 212						
All causes [1947-1994]		3434	6827.83	0.50	0.49	0.52
n=39 906 alive on 01.01.1968						
All causes [1968-1994]		3359	6329.87	0.53*	0.52	0.55
All cancers	140 to 208	1322	2172.93	0.61*	0.58	0.64
Specific malignancies						
Mouth, oral cavity and pharynx	140 to 149	79	205.90	0.38*	0.32	0.46
Oesophagus	150	59	156.52	0.38*	0.30	0.47
Stomach cancer	151	62	97.34	0.64*	0.51	0.79
Small intestine, colon, and rectum	152 to 154 +159.0	124	175.24	0.71*	0.61	0.82
Liver and the gallbladder	155+156	56	72.11	0.78*	0.61	0.97
Pancreas	157	59	77.63	0.76*	0.61	0.94
Peritoneum and other digestive organs	158+159-159.0	28	31.40	0.89	0.63	1.22
Nose, sinus, and middle ear	160	15	53.32	0.28*	0.17	0.43
Larynx	161	41	125.70	0.33*	0.25	0.42
Lung	162	336	529.50	0.63*	0.58	0.69
Pleura	163	21	13.65	1.54*	1.03	2.21
Bone	170	11	15.69	0.70	0.39	1.16
Melanoma	172	19	14.02	1.36	0.89	1.99
Other skin cancers	173	0	4.99	-	-	-
Prostate	185	71	95.20	0.75*	0.61	0.91
Other genital organs	186-187	6	8.72	0.69	0.30	1.35
Bladder	188	46	58.99	0.78*	0.60	1.00
Kidney	189	33	45.90	0.72*	0.53	0.96
Brain	191	36	41.70	0.86	0.64	1.14
Thyroid gland	193	4	4.95	0.81	0.28	1.84
Lymphosarcoma and reticulosarcoma	200	9	9.13	0.99	0.51	1.72
Hodgkin's disease	201	10	11.52	0.87	0.47	1.47
Non-Hodgkin lymphoma	202	16	29.57	0.54*	0.34	0.82
Multiple myeloma	203	18	17.21	1.05	0.68	1.55
Leukemia	204 to 208	45	55.71	0.81	0.62	1.03
Lymphoma and leukemia	200 to 208	98	123.14	0.80*	0.67	0.94
Other cancers		118	221.31	0.53*	0.46	0.62
All known causes except Cancer		1883	4156.94	0.45*	0.44	0.47

* : SMR>1 or SMR<1 with a statistical significance of 5% (unilateral test)

underlined : excesses with a magnitude of more than 15%

³ 9th International Classification of Diseases

Table 4: Standardized Mortality Ratios (SMR) by Cause of Death for the 11 480 Women in the Cohort

	ICD9	Obs	Exp	SMR	90%	CI
n=11 480						
All causes [1947-1994]		433	656.70	0.66*	0,61	0,71
n=11 380 alive on 01.01.1968						
All causes [1968-1994]		424	606.28	0.70*	0.64	0.76
All cancers	140 to 208	199	218.05	0.91*	0.81	1.03
Specific malignancies						
Mouth, oral cavity, and pharynx	140 to 149	3	3.51	0.86	0.23	2.20
Oesophagus	150	0	2.41	-	-	-
Stomach	151	8	7.56	1.06	0.53	1.91
Small intestine, colon, and rectum	152 to 154+159.0	14	22.94	0.61*	0.37	0.95
Liver and the gallbladder	155+156	4	5.28	0.76	0.26	1.73
Pancreas	157	6	7.23	0.83	0.36	1.63
Peritoneum and other digestive organs	158+159-159,0	4	3.53	1.13	0.39	2.59
Nose, sinus, and middle ear	160	0	0.84	-	-	-
Larynx	161	1	1.01	0.99	0.04	4.65
Lung	162	8	11.66	0.69	0.34	1.24
Pleura	163	0	0.90	-	-	-
Bone	170	0	1.24	-	-	-
Melanoma	172	4	2.61	1.53	0.52	3.50
Other skin cancers	173	1	0.52	1.92	0.08	9.03
Breast	174	68	57.41	1.18	0.96	1.45
Uterine	179+180 to 182	15	18.67	0.80	0.50	1.24
Cervix uteri	180	4	6.56	0.61	0.21	1.39
Other genital organs	183-184	20	17.47	1.14	0,76	1.66
Bladder	188	0	2.02	-	-	-
Kidney	189	3	3.97	0.76	0.20	1.95
Brain	191	9	5.68	1.58	0.83	2.76
Thyroid gland	193	0	1.20	-	-	-
Lymphosarcoma and reticulosarcoma	200	2	1.07	1.86	0.32	5.84
Hodgkin's disease	201	1	1.53	0.65	0.03	3.08
Non-Hodgkin lymphoma	202	6	3.99	1.50	0.65	2.96
Multiple myeloma	203	3	2.64	1.14	0.31	2.93
Leukemia	204 to 208	6	8.43	0.71	0.31	1.40
Lymphoma and leukemia	200 to 208	18	17.67	1.02	0.65	1.48
Other cancers		13	22.73	0.57	0.21	1.09
All cancers except breast cancer		131	160.64	0.82*	0.70	0.94
All known causes except cancer		205	388.23	0.53*	0.47	0.59

* : SMR>1 or SMR<1 with a statistical significance of 5% (unilateral test)

underlined : excesses with a magnitude of more than 15%

3.3 Mortality for specific cancer sites by age and calendar period

For the sites for which a significant or nearly significant excess was found, we examined the distribution of deaths observed and expected by calendar period from 68 through 94, and their distribution by age group.

For pleural cancer, the excess deaths actually occurred after 1985; the excess reached significance only for the 1990-1994 period ($SMR_{1990-1994} = 1.93$, $CI_{90\%}=[1.08; 3.19]$), table 5). It involved those older than 55 years (table 6).

For breast cancer among women employees, the excess deaths began in the 1980s and continued through 1994, (table 5). For the period 1980-1994, there is a significant 30% excess ($SMR_{1980-1994} = 1.30$, $CI_{90\%}=[1.04; 1.61]$). These excesses focus on the groups aged 45-54 years and 75-84 years ($SMR_{45-54 \text{ years}} = 1.29$, $CI_{90\%}=[0.91; 1.77]$ and $SMR_{75-84 \text{ years}} = 2.35$, $CI_{90\%}=[0.93; 4.93]$), (table 6).

The mortality from melanoma is greater than expected only for the 1990-1994 period ($SMR_{1990-1994} = 2.11$, $CI_{90\%}=[1.25; 3.34]$). The excess diminishes with age (from $SMR_{35-44 \text{ years}} = 1.86$ to $SMR_{65-74 \text{ years}} = 1.31$ and $SMR_{+74 \text{ years}} = 0$). For persons younger than 75 years, the excess borders the statistical significance ($SMR_{15-74 \text{ years}} = 1.45$ $CI_{90\%}=[0.99; 2.05]$).

Table 5: Standardized Mortality Ratios (SMR) by Calendar Period 1968-1994

	Observed	Expected	SMR	90%	CI
Pleural cancer, men					
68-74	1	0.72	1.40	0.06	6.60
75-79	2	1.13	1.78	0.31	5.57
80-84	1	2.18	0.46	0.02	2.16
85-89	6	3.92	1.53	0.67	3.01
90-94	11	5.71	1.93	1.08	3.19
68-94	21	13.65	1.54	1.03	2.21
Breast cancer, women					
68-74	3	5.33	0.56	0.15	1.45
75-79	6	6.71	0.89	0.39	1.76
80-84	15	10.37	1.45	0.89	2.23
85-89	18	15.04	1.20	0.77	1.77
90-94	26	19.97	1.30	0.91	1.81
68-94	68	57.41	1.18	0.96	1.45
80-94	59	45.38	1.30	1.04	1.61
Melanoma, both sexes					
68-74	3	1.17	2.57	0.70	6.63
75-79	0	1.77	0.00	-	-
80-84	3	3.13	0.96	0.26	2.47
85-89	4	4.39	0.91	0.31	2.08
90-94	13	6.17	2.11	1.25	3.34
68-94	23	16.63	1.38	0.95	1.96

Table 6: Standardized Mortality Ratios (SMR) by 10 year age group between 1968 and 1994

Pleural cancer men					
age	Observed	Expected	SMR	90%	CI
15-24	0	0.00	0.00	-	-
25-34	1	0.09	10.58	0.42	49.89
35-44	0	0.83	0.00	-	-
45-54	2	3.20	0.63	0.11	1.96
55-64	8	5.17	1.55	0.77	2.79
65-74	7	3.26	2.15	1.01	4.02
75-84	3	1.01	2.96	0.80	7.63
85-	0	0.07	0.00	-	-
total	21	13.65	1.54	1.03	2.21
Breast cancer women					
15-24	0	0.01	0.00	-	-
25-34	2	1.38	1.44	0.25	4.53
35-44	9	8.97	1.00	0.52	1.75
45-54	27	20.99	1.29	0.91	1.77
55-64	17	16.88	1.01	0.64	1.51
65-74	7	6.78	1.03	0.49	1.94
75-84	5	2.13	2.35	0.93	4.93
85-	1	0.27	3.70	0.15	17.47
total	68	57.41	1.18	0.96	1.45
Melanoma, both sexes					
15-24	0	0.03	0.00	-	-
25-34	0	0.85	0.00	-	-
35-44	5	2.69	1.86	0.73	3.90
45-54	8	5.17	1.55	0.77	2.79
55-64	7	4.87	1.44	0.68	2.69
65-74	3	2.29	1.31	0.36	3.37
75-84	0	0.66	0.00	-	-
85-	0	0.06	0.00	-	-
total	23	16.63	1.38	0.95	1.96
younger than 75 years	23	15.91	1.45	0.99	2.05

4. DISCUSSION

4.1 About Cohort follow-up

The percentage of subjects lost to follow-up is 6.9% (4% of the total person-years). The loss of these individuals is mainly due to the incompleteness of the personnel file cleanup when the study first began. The dates they left the company appear to be relatively random. For women, the main reason for loss to follow-up was a change in the patronymic name. Thus, their loss in the cohort should not primarily due to health problems. Comparing people lost of follow-up with the rest of the cohort reveals that they were born 4 years earlier, on average, and had been hired 4 years later. They also stayed at the company for 4 years less than the rest of the cohort. These differences may indicate that they constitute a different population, including, for example, more non-permanent staff. If this turns out to be the case, it would suggest that the analysis presented here under-estimates the impact of the mortality of non-permanent employees in the overall CEA employee mortality. No information currently available validates this hypothesis. The impact on mortality might work in both directions: overestimation of mortality if the subjects lost to follow-up were individuals with research training contracts (doctoral students), because they would thus come from a high socioeconomic category, or underestimation of mortality if they are short-term workers without a permanent contract, and thus more likely to belong to a lower socioeconomic category. It is also possible that these subjects had part-time contracts with CEA (for staff

training, for example), because the personnel file lists all persons paid by CEA during the study period. Removing these subjects from the cohort might therefore be justified.

In order to evaluate the impact of those individuals who were lost to follow-up we excluded them from the analysis: results were very close. Furthermore, an extension of the study is currently underway with only 4% of people lost to follow up. Results are totally consistent with the present study.

The number of deaths for which the cause could not be found is relatively low (4.5%). These missing causes of death cannot in any case call into issue the excesses observed above, because they would be added to the number observed.

4.2 About results

The comparison of our population with the national population shows that the former had a substantially reduced overall mortality ($SMR_{men} = 0.53$, $CI_{90\%}=[0.52; 0.55]$), ($SMR_{women} = 0.70$, $CI_{90\%}=[0.64; 0.76]$), a reflection of the *healthy worker effect*, which is standard among occupational cohorts. This lower mortality results from the fact that a population of workers is, on average, in better health than the overall population, which contains people who do not work because of health problems. This effect is particularly great at the time of hiring [24]. The SMR was on the same order as that described for CEA and COGEMA workers in previous studies [25], [26]. Mortality from cancer was also lower than among the general population ($SMR_{men}= 0.61$, $CI_{90\%}=[0.58; 0.64]$, $SMR_{women}=0.91$, $CI_{90\%}=[0.81; 1.03]$).

Results on the mortality all causes and all cancers are closer to literature for women than they are for men (table 7).

Table 7: SMR for All Cause and All Cancer reported in cohorts of Nuclear Industry Workers

		Follow-up period	Size of population	All Causes		All Causes except cancers		All Cancers	
				SMR	Obs	SMR	Obs	SMR	Obs
CEA	This study	47-94	51 286	0.55	3783	0.46	2088	0.64	1521
CEA ^a	This study	47-94	39 906	0.53	3359	0.49	2038	0.61	1322
CEA-DTECH ^a	[26]	47-94	356	0.46	44	0.33	22	0.77	22
Sellafield	[7]	47-92	14 319	0.98	3854	0.99	2817	0.95	1037
AEA	[5]	46-86	39 718	0.78	5509	0.77	4003	0.80	1506
AWE	[27]	51-82	22 552	0.77	3115	0.75	2250	0.82	865
Sell+AEA+AWE	[8]	46-88	75 006	0.81	13505	0.80	9760	0.84	3745
NRRW	[2]	47-88	124 743	0.82	12765	0.79	8 840	0.82	3598
AECL ^a	[9]	56-85	8 977	0.77	878	0.75	651	0.87	227
NDRC	[3]	51-87	206 620	0.59	5420	0.56	3788	0.69	1632
Hanford	[4]	45-86	44 154	0.82	9452	0.81	7257	0.86	2195
ORNL (X10) ^a	[10]	43-84	8 313	0.74	1524	0.47	1178	0.79	346
Oak Ridge Y12	[11]	47-74	7 664	0.88	1861	0.84	1358	1.00	503
Oak Ridge ^r	[12]	42-84	98 471	0.98	26319	0.99	20516	0.95	5803
Los Alamos ^a	[6]	43-77	15 727	0.63	3196	0.62	2464	0.64	732
Portsmouth	[13]	52-77	24 545	0.89	4762	0.79	3424	0.94	977
Rocky Flats	[14]	52-79	5 413	0.62	409	0.60	314	0.71	95
UNC ^a	[15]	56-78	3 512	0.82	219	0.81	168	0.85	51
Mound ^a	[16]	43-84	4 402	0.93	987	0.92	774	1.00	213
LLNL (SIR)	[17]	69-80		N.A.	N.A.	N.A.	N.A.	1.09	137
Savannah River ^a	[18]	52-80	9 860	0.75	1091	0.76	875	0.74	216
Savannah River ^{a,b}	[18]	52-80	2 745	0.64	294	0.62	228	0.68	66
Linde ^a	[19]	43-79	995	1.18	429	1.21	355	1.06	74
CIEMAT	[20]	54-92	4 122	0.65	318	0.61	217	0.77	101
Rocketdyne	[28]	50-93	4 563	0.68	844	0.79	248	0.65	596

^a men only

^b day laborers excluded

N.A.: Not Available

Examining the results by specific cancer causes for published cohorts of nuclear workers reveals no overall consistency. The disparities may result from the choice of the reference population for calculating expected deaths. Gilbert [4], for example, used the entire US national population as a reference for Hanford, which is in the Pacific Northwest of the US. Adjustment for socioeconomic or occupational category may also have an effect in some cases [2] [5] [27].

No excess was found in our study for leukemia and lymphoma. This result is similar to most of those observed in the other worker cohorts (table 8). For myeloma, on the other hand, the SMR, although not significant, is slightly higher among CEA workers ($SMR=1.06$, $n=21$) than in other studies.

For pleural cancer, for which a significant excess was found among CEA workers, an excess was also found in other studies [7];[8]; [2]. It should nonetheless be noted that this has been studied only rarely. This excess suggests possible asbestos exposure. Actually, of the deaths coded "pleural cancer" in France, 80% correspond to pleural mesothelioma [29], a disease specific to asbestos exposure. The individuals concerned are more than 55 years old, and the excess began to appear around 1985. It is thus possible that this excess will continue as our population ages and reaches the end of the latency period after exposure (10 to 30 years).

An excess on the borderline of statistical significance appeared for two sites among women: cancer of the brain (SMR = 1.58, CI_{90%}=[0.83; 2.76], n=9) and the breast (SMR = 1.18, CI_{90%}=[0.96; 1.45], n=68). For the brain cancer excess, we must nonetheless note that the number of deaths observed is low and that death certificates are not very accurate for this disorder, as they frequently include primary and secondary cancers.

The excess of breast cancers had previously been observed in CEA and COGEMA workers [25]. Our detailed analysis showed that the excess deaths began during the 1980s. A nationwide campaign to make doctors more aware of this disease took place during the same period and might have resulted in a higher screening rate. The maximum excess affected women in the 45-54 year-old age group.

In published cohort on nuclear workers, an SMR above one was found for breast cancer among the British AWE cohort [27], which had a non-significant SMR of 1.1 (44 cases observed, table 8). In the British AEA cohort, an excess number of breast cancers was found only among workers not monitored for exposure to ionizing radiation [5]. These two cohorts together form a population quite comparable to that of CEA. A non significant SMR of 1.21 was also found in Oak Ridge, Y12 facility [Loomis and Wolf, 1996] (11 cases observed) (table 8).

The link between breast cancer and chronic exposure to low doses of ionizing radiation has not been demonstrated, although a dose-effect relation has not been ruled out among radiology technicians [30] [31]. An excess of mortality or incidence in relation to the general population have been shown among airline cabin crew personnel [32] and among workers at the French national utility company (Electricité-de-France, Gaz-de-France [33]. Industrial sectors where an excess of deaths from breast cancer have been noted are primarily the pharmaceutical industry and the "beauty and cosmetics" sector [34] [35]. Suspected occupational risk factors are styrene, some solvents, and metals [36].

The main risk factors for breast cancer are early menstruation, late menopause, having a first child late (or never having children), and a family history of breast cancer (mother, sister, daughter). The number of children and breast feeding are protective factors. Selection bias might therefore be present, since the working population and even more CEA population (mostly made of medium and high socio-economic categories) may have some of these risk factors in higher proportions than the general population. This bias may suffice to explain the excess observed.

The incidence of breast cancer (34 000 new cases in France in 1995 and 11 000 deaths) [37] justifies conducting analytic studies including all known and suspected risk factors to explain excesses observed and prevent them.

Table 8: Synthesis of SMR for Some Cancer Sites reported in cohorts of Nuclear Industry Workers

Cohort		lymphoma and leukemia		myeloma		leukemia		pleurum		skin		melanom a		breast		brain	
		SMR	Obs	SMR	Obs	SMR	Obs	SMR	obs	SMR	obs	SMR	obs	SMR	obs	SMR	obs
CEA	This study.	0.82	116	1.06	21	0.80	51	1.44	21	1.08	24	1.38	23	1.18	68	0.95	45
CEA ^a	This study	0.80	98	1.05	18	0.81	45	1.54	21	1.00	19	1.36	19	N.A.	N.A.	0.86	36
Sellafield	[7]	0.85	61	0.87	11	0.71	20	3.51	14	N.A.	N.A.	1.02	8	0.79	29	0.84	24
AEA	[5]	0.98	124	0.76	15	1.19	60	N.A.	N.A.	0.73	14	N.A.	N.A.	0.95	84	0.65	32
AWE	[27]	0.82	54	0.87	9	0.74	20	N.A.	N.A.	0.53	5	N.A.	N.A.	1.10	44	0.75	19
Sell+AEA+AWE	[8]	0.93	273	0.86	42	1.00	116	1.35	17	0.68	30	N.A.	N.A.	0.94	178	0.77	109
NRRW	[2]	0.88	275	0.74	40	0.88	275	1.93	42	0.90	46	1.11	43	0.71	41	0.90	144
AECL ^a	[9]	0.68	15	0.56	2	0.60	6	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.05	10
NDRC ^a	[3]	0.78	190	0.72	22	0.79	82	N.A.	N.A.	0.54	26	0.59	25	0.87	158	0.69	72
Hanford	[4]	0.93	220	0.91	32	0.84	80	N.A.	N.A.	0.80	36	N.A.	N.A.	0.92	102	0.86	61
ORNL (X10) ^a	[10]	1.08	47	N.A.	N.A.	1.63	28	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.04	15
Oak Ridge Y12	[11]	0.83	40	N.A.	N.A.	0.60	11	N.A.	N.A.	1.07	11	N.A.	N.A.	1.21	11	1.29	20
Oak Ridge	[12]	0.94	529	N.A.	N.A.	0.95	214	N.A.	N.A.	0.99	102	N.A.	N.A.	0.86	263	1.03	181
Los Alamos ^a	[6]	0.95	105	N.A.	N.A.	1.01	44	N.A.	N.A.	1.03	24	N.A.	N.A.	N.A.	N.A.	0.68	23
Portsmouth	[13]	0.85	84	N.A.	N.A.	0.94	39	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Rocky Flats ^a	[14]	0.64	9	N.A.	N.A.	0.75	4	N.A.	N.A.	1.02	3	N.A.	N.A.	N.A.	N.A.	1.19	6
UNC ^a	[15]	0.81	4	N.A.	N.A.	0.84	2	N.A.	N.A.	2.35	3	N.A.	N.A.	N.A.	N.A.	2.23	5
Mound ^a	[16]	0.85	18	N.A.	N.A.	0.82	7	N.A.	N.A.	0.95	4	N.A.	N.A.	N.A.	N.A.	0.59	4
LLNL (SIR)	[17]	0.63	9	-	0	0.80	3	N.A.	N.A.	3.57	31	3.52	29	0.68	8	1.19	5
Savannah River ^a	[18]	0.95	32	N.A.	N.A.	1.46	18	N.A.	N.A.	0.66	5	N.A.	N.A.	N.A.	N.A.	0.55	7
Savannah River ^{a,b}	[18]	0.77	8	N.A.	N.A.	1.05	4	N.A.	N.A.	0.92	2	N.A.	N.A.	N.A.	N.A.	1.06	4
Linde ^a	[19]	0.89	6	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
CIEMAT	[20]	1.10	8	N.A.	N.A.	1.01	4	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.52	7
Rocketdyne	[28]	1.01	30	N.A.	N.A.	1.60	18	N.A.	N.A.	0.86	6	N.A.	N.A.	N.A.	N.A.	1.19	11

^a men only

^b day laborers excluded

N.A.: Not available

The excess of melanoma (23 cases, SMR = 1.38, $CI_{90\%}=[0.95;1.96]$), approaching significance, touches the age groups from 35 to 74 years. It is nearly significant for people younger than 75 years (SMR = 1.45, $CI_{90\%}=[0.99;2.05]$) After 35 years, the SMR diminishes with age. Finally, the excess is primarily concentrated in the calendar period 1990-94 (13 cases, SMR = 2.11, $p<0.01$). Actions to prevent and increase awareness of this disease should be planned.

An association between skin cancers and ionizing radiation has been demonstrated among the Hiroshima and Nagasaki survivors and among radiologists at the beginning of the 20th century. A study of Chinese radiologists and radiology technicians suggests the possibility of a link between chronic exposure to ionizing radiation and skin cancers [31]. Finally, an excess of melanomas and other skin cancers has been shown in some cohorts of nuclear industry workers: an excess in relation to the general population among the workers at Lawrence Livermore National Laboratory [38] and those at the Mound nuclear site [16], and a dose-effect relation in the UK combined study [8]. Their link with low-dose exposure to ionizing radiation remains to be proven. A case-control study at Los Alamos National Laboratory [39], a laboratory of the same type as Lawrence Livermore, found melanoma to be associated with educational level. The principal risk factors for this disease are exposure to ultra-violet rays and genetic factors. In order to cover other risk factors, case-control studies should be set up. Efforts should also be made to distinguish melanoma from other types of skin cancers, for which lethality is lower and suspected risk factors different. This justifies the necessity of setting up incidence analyses.

5. CONCLUSION

This descriptive study has highlighted the principal characteristics of the mortality of CEA employees between 1968 and 1994. For the men, the comparison with the general male population shows a general and an all cancer reduction in mortality greater than that observed in most cohorts of nuclear industry workers. The all cause and all cancer mortality rates among women are also lower than the comparable national rates for the same period (1968-1994), but to a lesser extent. These results are closer to those observed in the literature about nuclear industry workers.

A statistically significant excess of pleural cancers was observed among men (SMR = 1.54, $CI_{90\%}=[1.03; 2.21]$). An excess of breast cancers near the significant level was observed among women (SMR = 1.18, $CI_{90\%}=[0.96;1.45]$). Finally, a nearly significant excess of melanomas was observed among subjects aged less than 75 years (SMR = 1.45, $CI_{90\%}=[0.99;2.05]$),).

The purely descriptive nature of this analysis does not allow us to uncover any causal factors for these disorders. Three extensions of the study are under consideration. The first is the constitution of a cohort of individuals within the CEA-COGEMA group who are monitored for external exposure to ionizing radiation. This will allow an analysis of the relation between exposure to X- and gamma rays and cancer mortality. Moreover, the data will be combined with those from 17 other countries as part of the international survey coordinated by IARC [22]. The identification of exposures besides X- and gamma rays should also help refine the interpretation of the results.

As a further extension, we may set up case-control studies nested within the CEA cohort for specific diseases. This would allow us to take more risk factors into account. The diseases that deserve further study are, in particular, melanoma and breast cancer. Finally, for the diseases poorly described by death certificates (brain cancer, among others) and for less lethal disorders (breast, skin, and thyroid cancers, as well as leukemia), this study of the mortality within the CEA-COGEMA group should be extended over the long term to a study of their morbidity.

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