

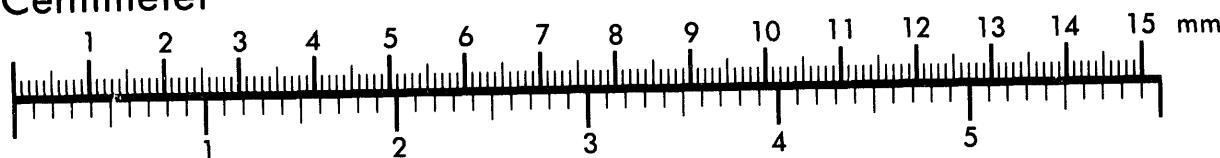


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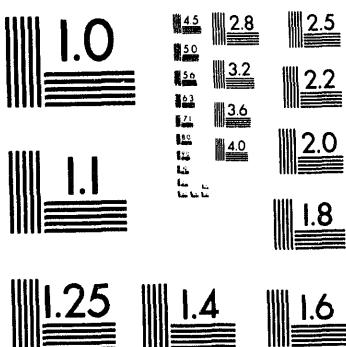
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SURVIVAL TIMES OF PRE-1950 U.S. WOMEN RADIUM DIAL WORKERS*

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Manuscript submitted to the
International Seminar on Health Effects of Internally Deposited Radionuclides:
Emphasis on Radium and Thorium
Heidelberg, Germany, April 18-21, 1994

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* Work supported by the U.S. Department of Energy, Assistant Secretary for Environment, Safety, and Health, Office of Epidemiology and Health Surveillance, under contract W-31-109-ENG-38.

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ABSTRACT

Survival times of U.S. women radium dial workers to the end of 1989 were examined by life table methods. Included were 1301 women first employed before 1930 and 1242 first employed in 1930-1949. Expected numbers of deaths were estimated from age- and time-specific death rates for U.S. white females. In the early group, 85 deaths from the well-known radium-induced cancers - bone sarcomas and head carcinomas - were observed, but only 724 deaths from all other causes were observed vs. 755 expected. Life shortening (\pm S.E.) of 1.8 ± 0.5 y compared to the general population of U.S. white females was calculated from the time distribution of all deaths in the pre-1930 group. In the 1930-1949 group, 350 deaths were observed vs. 343 expected and no bone sarcomas or head carcinomas occurred. Among women who survived at least 2 y after first measurement of body radium, a significant excess of observed vs. expected deaths was found only for radium intakes greater than 1.85 MBq of $^{226}\text{Ra} + ^{228}\text{Ra}$, and no trend of deaths or reduction of life expectancy was found with length of employment.

Introduction

Studies of women radium dial workers have shown that the most significant biological effects are bone sarcomas and carcinomas originating in the paranasal sinuses and the mastoid air cells (head carcinomas).¹⁻³ These malignancies and deleterious changes in bone structure⁴ are the only effects that have been convincingly correlated with radium body burden. These effects are apparently the result of direct irradiation from deposits of radium in the skeleton. However, other parts of the body receive some radiation from radium and its daughter products, and some dial workers were probably exposed to nontrivial amounts of external radiation and radon in the workplace,⁵ so other health effects may be present at incidences too small to have been established as related to radium dial work.

The purposes of this paper are to determine the average life shortening of women radium dial workers and to look for life shortening that may be ascribed to risks other than bone sarcomas and head carcinomas. This work is similar to that described in detail in a previous life table study of dial workers first employed before 1930,⁶ but it adds dial workers first employed in later years, extends the followup period from 1976 to the end of 1989, and uses revised estimates of systemic radium intake.

* Work supported by the U.S. Department of Energy, Assistant Secretary for Environment, Safety, and Health, Office of Epidemiology and Health Surveillance, under contract W-31-109-ENG-38.

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Methods and Materials

Dial Worker Populations

The target population comprised women employed in the U.S. radium dial painting industry before 1950 for whom year of birth and year of death or loss from the study were known. Subpopulations of women were defined by year of first employment in the industry (pre-1930 and 1930-1949) in order to increase homogeneity. Dial workers were identified by various methods,⁷ and followup was by personal contacts or by search of vital statistics files, including U.S. National Death Index (NDI) records through 1990. Ascertainment and follow up of target populations are each about 80% complete.⁷ Women who survived to age 85 were withdrawn from life tables at that age, because age- and year-specific U.S. mortality rates were not available for ages past 84. Table 1 summarizes followup data for the two cohorts.

Table 1. Cohorts of U.S. women radium dial workers by year of first employment.

	<1930	1930-1949
Total number	1301	1242
Mean year at entry	1922	1942
Mean age at entry	20.0	24.5
Mean years worked	3.1	4.3
Followup years	65,846	53,174
Withdrawn while living		
At end of study	242	846
At age 85	239	35
Lost to study	11	11
Total deaths	809	350
Bone sarcomas	64	0
Head carcinomas	24	0

Radium Exposures

The luminous paints used in the early days of the U.S. dial industry contained various proportions of ^{226}Ra (half-life 1600 y) and ^{228}Ra (half-life 5.75 y) as activators, but little or no ^{228}Ra was used after 1926.

Of the total study population of 2543 women, radium body contents of 1518 were determined by measurement of gamma rays and/or exhaled radon. The systemic intake, the quantity of radium that entered the blood during the period of exposure,⁶ was calculated for each woman by use of a detailed model of radium retention.^{8,9} Because this measure of internal exposure is time invariant and does not specify a critical organ, it seems more appropriate for a study of life shortening than another frequently used parameter, the average skeletal dose. In the present analysis, I have simply used the sum of the systemic intakes of ^{226}Ra and ^{228}Ra in order to indicate the level of radium intake by means of a single parameter.

Calculations

Life table methods were used to record the time sequence of deaths and withdrawal from the study and to estimate survival probabilities and survival times.^{10,11} Person-years of followup were counted by methods described by Monson.¹² The year of entry was the year of first employment in the radium dial industry or two years after the first measurement of radium burden. Events were assumed to occur on the average at mid-year, because the dates of start of employment and withdrawal while living were usually known only by calendar year. However, those still living after the common closing date of followup, December 31, 1989, were withdrawn at the end of 1989. Events were entered into the life tables by calendar year intervals, but only 0.5 y of followup could be counted in the year of entry, so the next interval started at 0.5 y after entry, the next at 1.5 y after entry, and so forth. Expected numbers of deaths were calculated by multiplying age- and time-specific U.S. mortality rates for white females by age- and time-specific years of followup.

The primary quantities calculated for each interval were the observed and expected probabilities that a person alive at the start of the interval would survive to the end of the interval.⁶ The net survival probabilities and survival times that would have been observed in the absence of the known radium-related tumors were estimated by methods described by Chiang.¹¹ In the present paper, statistically significant differences are defined as a P-value of less than 0.05 by the Mantel-Haenszel chi-square test¹³ for expected and observed numbers of deaths and as 1.96 times the standard error (S.E.) for expected and observed average years of survival.

Results

Entry at First Employment

Table 2 shows the numbers of persons under observation and deaths among the 1301 radium dial workers in the pre-1930 cohort as a function of time after start of work. The ratios of observed numbers of deaths from all causes to the expected numbers diminished from highly significant excesses in the first 19.5 y after entry to slightly less than unity after about 50 y. Also shown are the time distributions of deaths of persons who died with bone sarcoma or head carcinoma or both. The bone cancers began to appear earlier and were much more numerous than the head cancers, but both types of radium-related tumors had a wide range of occurrence times and occurred as late as the interval 59.5-69.5 y, in which three cases of bone sarcoma and one case of head carcinoma were diagnosed. The numbers of deaths from other causes were not significantly different from the expected numbers.

The average years of survival of the pre-1930 cohort from various times after start of work to 69.5 y after entry are compared with the expected numbers in Table 3. From 0 to 69.5 y, the difference between expected and observed years of life was 1.8 y, more than three times the standard error of the calculated years of survival, but most of the loss occurred during the first 30 y after start of work. With corrections for the radium-related tumors, the same calculations showed no loss of years of life when risk of death from bone or head cancer was removed.

Table 2. Deaths in pre-1930 cohort by time after start of work.

Interval (y)	Women at Start	Deaths		Bone Sarc.	Head Carc.	Other Deaths	
		No.	SMR ^a			No.	SMR ^a
0.0-	1301	57	144 ^b	8	0	49	124
9.5-	1244	64	143 ^b	16	1	47	105
19.5-	1180	66	123	15	3	48	90
29.5-	1113	89	105	8	8	74	87
39.5-	1024	162	108	8	4	150	100
49.5-	850	222	97	6	7	211	93
59.5-	580	149	97	3	1	145	94
69.5-	17	0	0	0	0	0	0
0.0-71.5	1301	809	107	64	24	724 ^c	96

^a SMR = (observed/expected) x 100.

^b P < 0.01 (Mantel-Haenszel chi-square).

^c Three women had both bone sarcoma and head carcinoma.

Table 3. Mean survival times (y) from T to 69.5 y after start of work for women first employed before 1930.

T (y after start)	All Causes of Death			No Radium Tumors		
	Exp'd	Obs'd	S.E.	Exp'd	Obs'd	S.E.
0.0	54.3	52.5	0.5	54.3	54.4	0.5
9.5	46.3	45.2	0.5	46.4	46.9	0.4
19.5	37.9	37.3	0.4	37.9	38.5	0.4
29.5	29.5	29.3	0.3	29.5	30.0	0.3
39.5	21.4	21.3	0.3	21.5	21.7	0.3
49.5	14.2	14.3	0.2	14.2	14.5	0.2
59.5	7.62	7.67	0.16	7.62	7.73	0.16

The time distributions of deaths and mean years of life after start of work of women in the 1930-1949 cohort are shown in Table 4. Except for fewer than expected deaths during the first 9.5 y after start of work, differences between observed and expected numbers of deaths or years of survival were not significant at the 5% level.

Table 4. Deaths and mean survival times (y) after start of work for women first employed 1930-1949.

Interval (y)	Women at Start	Death		Survival (T to 54.5 y)			
		No.	SMR ^a	T	Exp'd	Obs'd	S.E.
0.0-	1242	13	57 ^b	0.0	48.0	47.8	0.3
9.5-	1229	42	125	9.5	39.3	38.8	0.3
19.5-	1183	69	115	19.5	30.2	29.9	0.3
29.5-	1111	105	106	29.5	21.6	21.4	0.2
39.5-	991	111	99	39.5	13.2	13.2	0.2
49.5-	104	10	68	49.5	4.67	4.68	0.11
0.0-59.5	1242	350	102				

^a SMR = (observed/expected) x 100.

^b P < 0.05.

Entry at First Measurement Plus Two Years

Subgroups based on radium dose and duration of employment were examined for evidence of life shortening due to early deaths from causes other than the known radium-related tumors. Unfortunately, valid analyses of this type could not be done with entry at first employment, because measurements of radium burden were not made for all of the radium dial workers, and the proportion of deaths is higher among the unmeasured than among the measured, because intensive efforts to determine the radium content of all the workers did not begin until about 1955 and few of those who died earlier were measured.⁶ To avoid cases that may have been selected for measurement because of symptoms of acute illness, we counted only deaths and person-years that occurred at least 2 y after first measurement and not before 1957 (1955 + 2 y). These criteria reduced the number of measured persons acceptable for comparison with radium dose by less than 10%. Because good estimates of duration of employment were available only for women whose radium burden had been measured, the populations for analysis by duration were identical to those for analysis by radium dose.

Table 5 shows followup results for the pre-1930 cohort by systemic radium intake and by duration of employment. Thirteen women died with bone sarcoma and 12 with head carcinoma 2 y or more after their radium burdens were determined; all had systemic intakes of $^{226}\text{Ra} + ^{228}\text{Ra}$ greater than 1.85 MBq (50 mCi). In both dose groups with intake less than 1.85 MBq, the average survival time was greater than expected and the number of deaths less than expected. For systemic intakes above 1.85 MBq, deaths from all causes were significantly higher than expected. The difference between expected and observed years of life to 29.5 years after entry was 2.8 ± 0.9 y. No trend with increasing radium burden was found in the ratio of observed to expected net deaths (deaths without bone or head tumor), and no trend with increasing duration of employment was found in net deaths, deaths from all causes, or survival times.

Differences between observed and expected numbers of deaths or mean years of survival in the 1930-1949 cohort were not statistically significant when analyzed by radium intake or duration of employment (Table 6).

Discussion

Significantly more deaths than expected or significant differences between expected and observed average years of life were found only when deaths with bone sarcoma or head carcinoma were included. However, the pre-1930 workers did have appreciably more net deaths than expected in the first 20 years after employment (Table 2), probably because of workers who suffered serious bone necroses and blood dyscrasias soon after the start of dial work.¹ A rather strong "healthy worker effect"¹⁴ in the first few years after employment and more deaths than expected during the next 20-30 y were seen in the 1930-1949 cohort (Table 4). The otherwise unremarkable SMRs of "other deaths" in Table 2 and all deaths in Table 4 are rather surprising in view of the debilitating effect of radium on bone structure² and reports of more deaths than expected from multiple myeloma in the pre-1930 cohort^{7,15} and from cancers of the breast, colon, lung and stomach in both cohorts.⁷ A possible explanation is that the excess deaths from these causes were not numerous enough to counteract a "healthy worker effect" on the more common causes of death.

Table 5. Followup of pre-1930 cohort by systemic radium intake and by duration of employment, with entry at first measurement plus 2 y.

	226Ra + 228Ra (MBq)			Weeks of Employment			
	<0.185	0.185-	≥1.85	Total	0-49	50-499	≥500
Number of women	356	237	123	716	358	303	55
Mean year of entry	1967	1964	1962	1965	1966	1964	1967
Deaths observed	163	106	74	343	156	162	25
SMR	92	87	135 ^a	97	89	108	92
Mean years survival to 29.5 y after entry							
Observed	20.7	21.4	18.4	20.6	21.2	19.8	21.3
Expected	20.1	20.9	21.2	20.5	20.5	20.5	20.6
S.E.	0.5	0.7	0.9	0.4	0.5	0.6	1.4
Deaths with							
Bone sarcoma	0	0	13	13	1	12	0
Head carcinoma	0	0	12	12	3	7	2
Other deaths observed	163	106	51 ^b	320	152	145 ^b	23
SMR	92	87	93	91	87	97	84

^a P < 0.025.

^b Two women in these subgroups had both bone sarcoma and head carcinoma.

Table 6. Followup of 1930-1949 cohort by systemic radium intake and by duration of employment, with entry at first measurement plus 2 y.

	226Ra + 228Ra (MBq)		Total	Weeks of Employment		
	<0.0185	0.0185-0.52		0-49	50-499	≥500
Number of women	362	324	686	238	363	85
Mean year of entry	1976	1974	1975	1977	1973	1972
Deaths observed	55	46	101	28	54	19
SMR	95	86	91	82	94	95
Mean years survival to 24.5 y after entry						
Observed	21.0	21.6	21.3	21.2	21.4	20.2
Expected	21.0	21.3	21.2	21.0	21.3	20.5
S.E.	0.5	0.4	0.3	0.9	0.4	0.9

The finding that the average survival time of women in the pre-1930 cohort was 1.8 ± 0.5 y less than expected during 69.5 y after start of work (Table 3) agrees with results in a previous study in which a loss of 1.8 ± 0.5 y was observed during 59.5 y.⁶ However, the previous study found a very significant excess of deaths from all causes (SMR = 115, P < 0.005) in pre-1930 women dial workers, whereas the present study found an SMR of 107 (Table 2) and P = 0.056. Data in Table 2 indicate that the difference may be ascribed to better than expected survival in the cohort after the close of the previous study in 1976. No trend with increasing radium burden was found in the ratios of observed to expected net deaths of women in the pre-1930 cohort (Table 5), whereas 24 observed vs. 16.9 expected net deaths (P = 0.11) in the dose range 1.85-18.5 MBq (50-499 mCi) were reported in the previous study. However, the previous study did not require survival for 2 y after

measurement, so some of the excess deaths in that work may have been an artifact of selecting seriously ill subjects for measurement because of symptoms.

Acknowledgements

The author thanks R.R. Monson for providing a computer tape of abstracted U.S. death rates and a program for calculating survival rates. I also thank H.F. Lucas and T.J. Kotek for program modifications and K.L. Haugen for editing assistance. With the help of Mr. Kotek, followup data on the dial workers were obtained from data files of the Argonne radium study.

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