LA-UR -- 83 - 85

Conf-830101--3

LA-UR--83-85

DE83 005058

TITLE: MORTALITY STUDY OF LOS ALAMOS WORKERS WITH HIGHER EXPOSURES TO PLUTONIUM

AUTHOR(S): G. L. Voelz
G. S. Wilkinson
J. W. Healy
J. F. McInr
G. L. Tietj

SUBMITTED TO: 16th Mid Year Topical Meeting
Epidemiology Applied to Health Physics
January 9-13, 1983
Albuquerque, New Mexico

MASTER

Los Alamos Los Alamos National Laboratory
Los Alamos, New Mexico 87545

MORTALITY STUDY OF LOS ALAMOS WORKERS WITH HIGHER EXPOSURES TO PLUTONIUM

G. L. Voelz, G. S. Wilkinson, J. W. Healy, J. F. McInroy,
and G. L. Tietjen
Los Alamos National Laboratory
P. O. Box 1663
Los Alamos, NM 87545

ABSTRACT

A group of white male workers with the highest internal depositions of plutonium at the Los Alamos National Laboratory was selected in 1974 for a study of mortality. This group of 224 persons includes all those with an estimated deposition (in 1974) of 10 nanocuries or more of plutonium, principally ^{239}Pu but also in some cases ^{238}Pu. Follow-up of these workers is 100% complete through 1980. Smoking histories were obtained on all persons. Exposure histories for external radiation and plutonium were reviewed for each subject. Standardized mortality ratios (SMR) were calculated using rates for white males in the United States population, adjusted for age and year of death. SMRs are low for all causes of death (56; 95% CI 40,75) or for all malignant neoplasms (54; 95% CI 23,106). Cancers of interest for plutonium exposures, including cancers of bone, lung, liver, and bone marrow/lymphatic systems, were infrequent or absent. The absence of a detectable excess of cancer deaths is consistent with the low calculated risk to these workers using current radiation risk coefficients. An alternate theory that suggests much higher risk of lung cancer due to synergistic effects of smoking and inhaled insoluble plutonium particles is not supported by this study.

Introduction

Health risks from exposures to ionizing radiation and internal depositions of radionuclides are derived primarily from human exposure data. Experimental animal data have great value for basic information regarding effects of total dose, dose rate, dose distribution, and internal deposition behavior of radionuclides, but are not definitive for human health risk coefficients. In this paper, human data on 224 persons exposed to plutonium are updated and evaluated in order to contribute to our understanding of current health risks from plutonium exposures.

The data on plutonium-exposed persons has reached an important stage because the length of time since first exposures is long enough to permit a significant fraction of late effects, namely cancer, to have occurred. The exposures in humans, although low compared to experimental animal exposures, occurred mostly 25 years or more ago and thus extend well beyond any long-term experiments in animals. The findings should be indicative of what can be expected from lifetime exposures to plutonium.

Methods

A mortality study of all Los Alamos workers with the higher depositions of plutonium since the beginning of the Los Alamos project was begun in 1974. A cohort of these workers, each with an internal plutonium deposition of 10 nanocuries (nCi) or more, was formed by searching Los Alamos health physics records as of January 1, 1974. The plutonium deposition estimates were calculated by the PUQFUA computer code[1] using plutonium excretion values in urine. This search identified 241 Los Alamos workers (224 white males and 17 white females) who had internal depositions of 10 or more nanocuries of plutonium.

The PUQFUA computer code was revised sometime after the 1974 selection of the group. The revision, PUQFUA 2, resulted in more accurate estimates of plutonium depositions by employing more elaborate consistency criteria between urine sample results. These changes resulted in a large number of plutonium deposition estimates, initially in excess of 10 nCi, to be reduced to less than 10 nCi. All persons, however, were retained in the study, only their plutonium deposition estimates were revised to the new calculations.

An initial study of mortality in this group through June 1976 was reported earlier[2,3]. The present report extends the study through April 1980.

Mortality status was obtained on each individual as of April 1980 by a Social Security Administration records search and subsequent procurement of all death certificates. A health questionnaire was completed by living persons in the group. Follow-up on the group is 100 percent complete with data from all living subjects and next-of-kin for deceased persons.

Findings

The findings in this study are important because the study group includes persons with highest plutonium exposures that occurred mostly in the late 1940s thru the 1950s. The length of time since initial deposition of plutonium is now considerably longer than the latent period for cancer, usually considered to be 10 years for the cancers of interest here. Thus, deaths from cancer in the group should be reflecting the effect of many years of plutonium deposition in these individuals. In the 241 subjects of the study, there were 43 deaths among the 224 male subjects and 3 deaths among the 17 females. The data on females is limited by small numbers. No cancer deaths were present in the females. Plutonium depositions in the female workers of this group average about 9 nCi (range <1 to 23 nCi), which is about one-half of the 19 nCi average deposition in males. Cumulative external radiation to the females averaged 0.58 rem (range 0 to 4.2 rem), much less than the male average of about 7 rem (range 0 to 180 rem). Because of the limited number of females in the study, no further analysis is presented.

The mortality data and some characteristics of the cohort of 224 white, male plutonium workers are presented in Table I. The average year of entry into the study, 1947, was determined by the time of the subjects' first recorded urine test for plutonium exposure or their first presumed accidental exposure. Most subjects did not receive their current or final deposition of plutonium until later. As will be shown later, the average effective time for plutonium deposition in the group is estimated to be about 1954. The average age at entry into the study was 31 years; the average effective time of plutonium deposition was at age 38. The average age of the living persons in 1980, the study cut-off time, was 64 years.

Expected number of deaths, age- and calendar-year adjusted, are based on United States white male rates and generated by Monson's computer program.[4] The results for broad categories of deaths are shown in Table I. The standardized mortality ratio (SMR) for all causes of death and for all diseases of the circulatory system, 56 and 45 respectively, were significantly less than expected as shown by the upper limit of the 95% confidence interval (CI) being less than 100. The SMRs for all malignant neoplasms and all respiratory diseases were low, 54 and 46 respectively, but not significantly low based on the 95% CI.

TABLE I

THIRTY-THREE YEAR MORTALITY IN 224 WHITE MALE PLUTONIUM WORKERS

	Observed Number	Expected Number	SMR	95% CI for SMR
All causes of death	43	77.1	56	40-75
All malignant neoplasms	8	14.9	54	23-106
All diseases of circulatory system	18	40.0	45	27-71
All respiratory disease	2	4.4	46	5-165
All external causes	8	7.6	105	45-206

Average year of entry: 1947.4

Average age of entry: 30.9

Total person-years of survival: 6930

The low mortality ratios found in this study are most likely explained by selection biases relative to the general United States population. These include the healthy worker effect for employed populations, plus additional selection factors for members in this group of required security clearances and military selection for some of the earliest workers. Nevertheless, the SMRs reported here are about as low as any reported in studies of industrial groups. In context our data suggest no excess of mortality due to any cause in these workers with the highest plutonium exposures at Los Alamos.

The cancer deaths observed in the study are listed in Table II. The cancer sites of greatest interest after plutonium exposure, based on radiobiological experiments in animals, are in bone, liver, and lung. No malignancies of bone and liver are present, and only one lung cancer appeared while five were expected.

Smoking histories were obtained by health questionnaires from the living persons in the study; interviews with the next-of-kin were conducted for the

TABLE II

THIRTY-THREE YEAR CANCER MORTALITY IN 224 WHITE MALE PLUTONIUM WORKERS

	Observed Number	Expected Number	SMR	95% CI for SMR
All digestive system	4	4.17	96	26-246
Stomach (2)				
Large intestine (1)				
Rectum (1)				
All respiratory system	1	5.04	20	0-110
Lung (1)				
Buccal cavity and Pharynx	1	0.50	200	3-1110
Bladder	1	0.43	233	3-1294
All lymphopoietic	1	1.5	67	1-370
All Cancers	8	14.9	54	23-106

deceased. One individual wished not to give his smoking history, but data was obtained on all others. A smoker was defined as a person who continued to smoke cigarettes after January 1975. Cigar and pipe smoking data was disregarded. By these definitions, 82 workers (37 percent of the group) were smokers and had an average smoking history of 39 pack-years. A pack-year is the equivalent of smoking one pack of cigarettes per day for 1 year. There were 66 ex-smokers (29 percent of the group), who had a 29 pack-year average smoking history. The remainder were nonsmokers except for the one unknown. These smoking data are the basis for determining individuals who are at risk from smoking plus plutonium deposition.

Description of Radiation Exposures

A summary of plutonium and external radiation exposure of the 224 workers is given in Table III. The current plutonium depositions, estimated by the latest PUQFUA 2 computer program, range from < 1 to 243 nCi. The average deposition for all, living and dead, is about 19 nCi; median value is about 9. The predominant radionuclide is ^{239}Pu in most persons, except for 9 individuals in which the major exposure is ^{238}Pu. For simplicity, the activity of ^{239}Pu and ^{238}Pu have been combined in this study. The principal mode of exposure is inhalation of plutonium particulates. In only a few instances have contaminated wounds been the principal exposure route. External radiations have contributed modest doses (less than 10 rem lifetime total) to all but 37 individuals, who have exposures ranging from 10 rem to over 100 rem for one person. A truly exceptional exposure occurred to another individual who died as a result of acute external radiation from a criticality accident.

In Table III is given the total and average plutonium exposure calculated in nCi-years. A nCi-year is defined as the exposure resulting from 1 nCi being present in the body for a period of one year. The total nCi-years here is derived by summing the estimated deposition for each year from initial exposure through 1980. The estimates are taken from annual PUQFUA estimates of deposition based on urine excretion data. In effect, the nCi-year estimates take into account the amount of plutonium in the body and length of time of deposition for each intake.

TABLE III

PLUTONIUM AND EXTERNAL RADIATION EXPOSURE OF 224
LOS ALAMOS PLUTONIUM WORKERS (1980)

	Living	Dead
Number of Workers	181	43
Average Pu deposition (nCi)	21	12
Median deposition (nCi)	9.6	8.7
Average nCi-year exposure	544	238
Total nCi-year exposure[a]	98 437	10 251
Average external radiation (rem)	7.7	4.3[b]

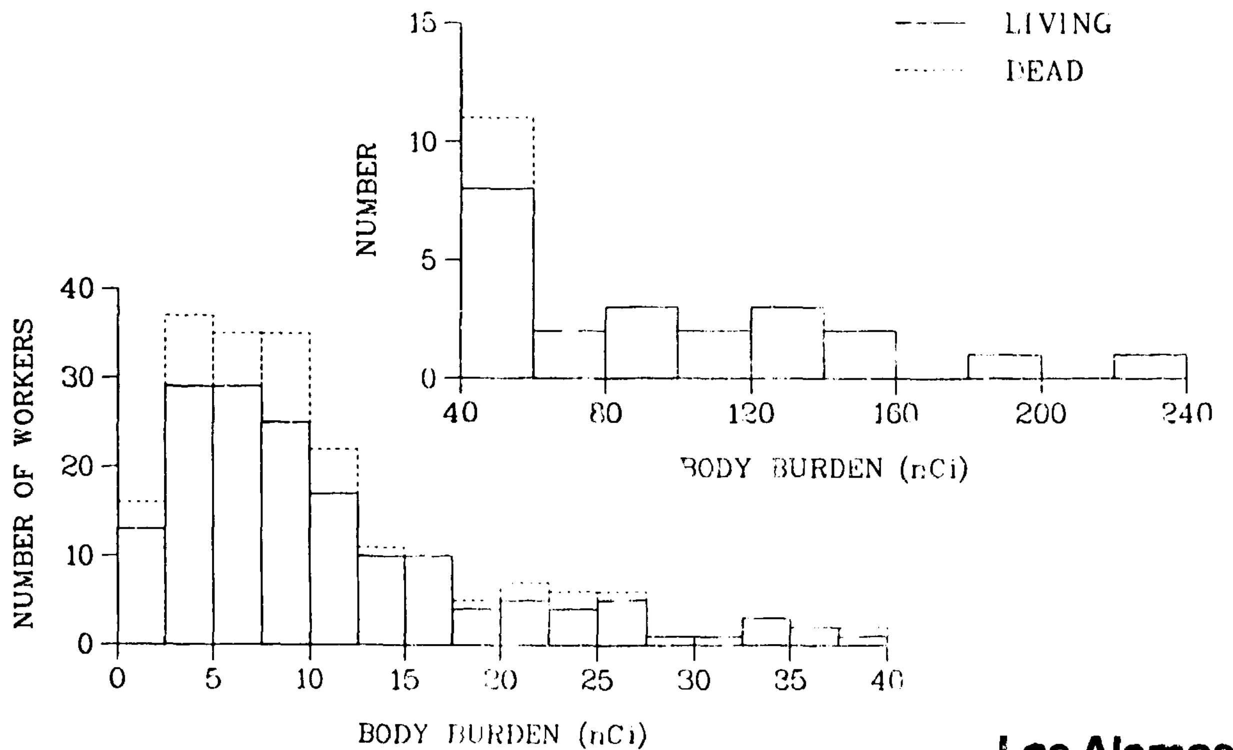
[a]Summed thru 1980 or date of death.
[b]One exposure resulting in acute radiation death omitted from average.

The distribution of plutonium exposures is shown in Fig. 1. The distribution, showing the living and dead, does not suggest any undue number of deaths in persons with the higher depositions.

Eight of the 43 deaths have had post-mortem tissue samples taken for plutonium analyses. A few results on these cases are shown in Table IV. The data indicate that the urine estimates ranged from 58 to 180 percent of the tissue values extrapolated to total tissue deposition. The PUQFUA estimates of internal deposition from urine excretion were within 15 percent of the tissue estimates on average.

The data show the wide variability in lung retention as expected. An interesting finding in these cases was that, although the amount of plutonium in the lung was highly variable, the lung contained an average of 51 percent of the total activity in the tissues of the body. In light of the long time periods since exposure, over 30 years in several of these cases, this finding suggests biological retention in man is much longer than the 500 days used in current dosimetric models. This subject will be explored in greater detail in a future paper. For our purposes, the tissue data indicate that on average the plutonium in lung acts as a highly insoluble particulate over many years. The current PUQFUA calculation makes an estimate of plutonium deposition that appears to account adequately for the lung burden as an internal source.

DISTRIBUTION OF PLUTONIUM DEPOSITION IN 224 LOS ALAMOS WORKERS



Los Alamos

Fig. 1

Cancer Risk Estimation

Calculation of the risk of excess cancers predicted by current risk models is of interest for purposes of comparing with the results of this mortality study. Such calculations are made using the lifetime risk approach of the UNSCEAR 1977 report[5] and the annual risk estimation by the BEIR III procedure.[6] In both instances, the dose estimates were made using group average values (Table III) rather than individual plutonium depositions. The internal distribution of plutonium activity was taken to be 50 percent in lung, 40 percent in bone, and 10 percent in liver. The basis for the lung estimate was discussed above. The distribution between bone and liver was also derived from human tissue data.[7]

Dose rates per year were calculated for lung, bone, and liver using depositions of plutonium estimated for the living and dead. The ICRP method[6] was used for calculating doses to bone surfaces. This calls for all of the plutonium to be deposited on bone surfaces and retained there indefinitely. The total weight of endosteal cells is taken as 120 grams with 25 percent of the alpha energy absorbed in these cells.

TABLE IV

PLUTONIUM IN TISSUES COMPARED TO URINE EXCRETION ANALYSIS

No.	Tissue Analysis in nCi Lung	Other	Total Tissue Deposition	Urine (PUQFUA) Estimate	Tissue: Urine Ratio
1	2.4	20.1	22.5	21	1.07
2	1.6	7.4	9.0	10	0.90
3	3.9	6.1	10.0	8	1.25
4	36.5	10.3	46.8	26	1.8
5	10.4	8.2	18.6	18	1.03
6	30.6	24.3	54.9	49	1.12
7	1.4	1.3	2.7	4	0.58
8	5.2	9.4	14.6	24	0.61
Average	11.5	10.9	22.4	20	1.12
%	51.4%	48.6%			

TABLE V

CALCULATED DOSES (RADS) AND DOSE RATES (RADS/YEAR) FROM PLUTONIUM

	Living		Dead	
	Dose	Dose Rate	Dose	Dose Rate
Lung	4738	1.01	493	0.6
Bone Surface	7897	1.69	822	1.0
Liver	527	0.112	5	0.066

Total doses were also calculated using the average integrated exposure in nCi-years. The calculated dose rates and total doses for the lung, bone surfaces, and liver are given in Table V.

Coefficients for risk of developing excess cancers were taken from the UNSCEAR[5] and BEIR III[6] reports. The coefficients used are summarized in Table VI.

The UNSCEAR approach estimates lifetime risks as the product of the total dose and the risk coefficient. Excess cancer estimates using this approach are given in Table VII. These estimates are for doses estimated through 1980. Additional risk will develop in the survivors with time as additional doses from the internal depositions occur.

TABLE VI

RISK COEFFICIENTS USED

	UNSCEAR	BEIR
	Cancers/rad per million	Cancers/year/rad per million persons
Lung	40-180	22-45
Bone	20-50	1
Liver	100	13

TABLE VII

LIFETIME CANCER RISK FROM DOSES THROUGH 1980 BASED ON UNSCEAR RISK COEFFICIENTS

Organ	Number of Cancer Cases Predicted		
	Living	Dead	Total
Lung	0.2-0.9	0.02-0.09	0.2-1
Bone	0.2-0.4	0.02-0.04	0.2-0.4
Liver	0.05	0.006	0.06

The BEIR method requires the use of a life table and summing the risk for each year for the survivors. As an approximation, the annual risk was summed over an average time of exposure to the group to obtain the risk of cancer as of 1980. The years of exposure are obtained by dividing the total nCi-years by the total nCi deposition in the group. This gives 25.8 years for the living and 19.1 years for the deceased. A 10-year latent period was assumed. Results of the BEIR risk calculation is given in Table VIII.

The BEIR estimate in Table VIII shows the risk of lung cancer to be greater than for bone or liver cancer. The estimate of 0.6 to 1.2 excess lung cancers is sufficiently low, however, that in a group this size we cannot expect to identify a risk of this magnitude.

TABLE VIII

ESTIMATED CANCER INCIDENCE TO 1980 BASED ON BEIR III RISK COEFFICIENTS

Organ	Number of Cancer Deaths Predicted		
	Living	Dead	Total
Lung	0.55-1.1	0.026-0.052	0.6-1.2
Bone	0.042	0.0019	0.04
Liver	0.036	0.0017	0.04

A major uncertainty in both the above calculations results from the method of dose estimation. We assumed that the quantity in the body and each organ was invariant during the full time of exposure. This is obviously a simplifying assumption that gives only an approximate answer. The resultant risk estimates are well below the level detectable by epidemiologic methods in a group this size.

Both methods identify lung cancer as a principal risk. The risk of lung cancer has been cited also by Gofman,[9] who has developed an unproven theory on the elevated risk in smokers inhaling insoluble plutonium. Calculation of the risk of excess lung cancers in this group was performed using Gofman's method. The previously cited tissue data, showing long retention times in the lung, establishes the study subjects as having inhaled insoluble plutonium particulates. His "lung cancer dose" is age dependent. Application to this group was made by assuming average group exposure to occur at age 38 and to continue for 26 years until the age of 64 years. A latent period of 10 years was assumed. For purposes of these dose estimates, the plutonium depositions estimated as of 1969 were used. The total plutonium deposition in the 82 smokers is estimated to be 1475 nCi, an average of 18 nCi per person.

The "lung cancer dose" at age 38, using Gofman's age corrections, is 0.125 microgramsof ^{239}Pu deposited. This converts to 7.7 nCi of ^{239}Pu. For each of the 82 smokers, the lung deposition was estimated to be 50 percent of their total deposition. The total excess lung cancers for the group calculates to be 96 cancers. If no individual is permitted to have more than one lung cancer, the estimate is 48 cancers.

The history of exposure in these indivduals indicates that nearly all of the deposited plutonium resulted from inhalation exposures. It would be valid to assume under such exposure circumstances that initially all the current plutonium depositions were made in the lung. Under this assumption, the total number of "lung cancer doses" is 192. Limiting cancer cases to one per person reduces the estimate to 65 cancers.

Gofman's method includes a calculation of the number of cases that can be expected to occur at different ages of exposure and different periods of time afterwards. Assuming the exposures occurred at age 38, 19.7 percent of the excess cancers would have developed by age 64. Taking 19.7 per cent of the 48 and 65 cancers estimated by limiting cancers to no more than one person suggests that 9 to 13 excess lung cancers should have occurred by 1980.

No lung cancer deaths have occurred in this group of 82 smokers. The one lung cancer death that occurred in the 224 workers was an ex-smoker, who quit smoking cigarettes in 1924. His tissue analysis for plutonium and urine excretion estimate is listed as No. 2 in Table IV.

The data from this study do not support the risk estimates proposed by Gofman. An excess of lung cancer as predicted by his theory, if valid, should have been evident in this study group.

Conclusions

This study of 224 white male, plutonium-exposed workers indicates no excess mortality from all causes of death, all malignant neoplasms, respiratory diseases, or diseases of the circulatory system. For the cancers of particular interest after plutonium exposure, no bone or liver cancer deaths occurred; only one lung cancer death was observed versus an expected five cases based on United States general population experience. The median exposure to plutonium in the group is about 9 nCi, or roughly 25 percent of the permissible lifetime exposure (40 nCi) for workers. The average exposure time for the group was 26 years for the living and 19 years for deceased. Conventional radiation risk estimates from the UNSCEAR and BEIR reports suggest that lung cancer is of principal interest here; the risk of extra lung cancers in this group, using such risk coefficients, is about one extra case by 1980 in addition to the five expected. The data show no suggestion of excess lung cancers to date. A theory by J. Gofman on increased risk of lung cancer from inhaled insoluble plutonium particles in smokers predicts 9 to 13 excess cancers in the smokers of this group by 1980. Such high risk estimates of lung cancer after plutonium exposure are not supported by this study.

References

(1) J. N. P. Lawrence, "A History of PUQFUA, Plutonium Body Burden (Q) from Urine Assays," Los Alamos Report LA-7403-H, October, 1978.

(2) G. L. Voelz, J. H. Stebbings, L. H. Hempelmann, L. K. Haxton, and D. A. York, "Studies of Persons Exposed to Plutonium," pp. 353-366 in Late Biological Effects of Ionizing Radiation, Vol. 1, International Atomic Energy Agency, Vienna, 1978.

(3) G. L. Voelz, J. H. Stebbings, Jr., J. W. Healy, and L. H. Hempelmann, "Studies of Health Risks to Persons Exposed to Plutonium," pp. 419-430 in The Medical Basis for Radiation Accident Preparedness, Eds., K. F. Hubner and S. A. Fry, Elsevier North Holland, Inc., New York, 1980.

(4) R. R. Monson, "Analysis of Relative Survival and Proportional Mortality," Comput. Biomed. Res., 7, 325, 1974.

(5) United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and Effects of Ionizing Radiation, United Nations, New York, 1977.

(6) Committee on the Biological Effects of Ionizing Radiations, The Effect on Populations of Exposure to Low Levels of Ionizing Radiation: 1980, National Academy Press, Washington, DC 1980.

(7) R. G. Thomas, J. W. Healy, and J. F. McInroy, "Plutonium Partitioning Among Internal Organs," Submitted to Health Physics for publication, December, 1982.

(8) International Commission on Radiological Protection, "Limits for Intakes of Radionuclides by Workers," ICRP Publication 30, Annals of the ICRP, 2, 3/4, 1979.

(9) J. W. Gofman, Radiation and Human Health, Sierra Club Books, San Francisco, 1981.