Radiation-Induced Cancers in DOE and Contractor Employees--Prospects for the Individual Ascertainment of Causation

Dale Hattis, Ph.D.

Research Associate Professor
Center for Technology, Environment, and Development (CENTED)
George Perkins Marsh Institute, Clark University
950 Main Street
Worcester, Mass 01610

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Executive Summary

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From the early 1940's to the present, hundreds of thousands of workers have participated ional efforts to develop and use nuclear technology for both military and civilian applications r the supervision of the Department of Energy and its predecessor agencies. This research ores the scientific bases for estimating the number of workers who are reasonably likely to e suffered serious adverse health effects as the result of their contributions to these efforts.

The analysis seeks to produce *central tendency* estimates of

- The overall amounts and distribution of officially measured radiation dosage in DOE and contractor employees (Section 2).
- The expected cancer risks likely to be associated with the exposures (Section 3). This analysis draws on expert consensus estimates (from Atomic Bomb survivors and other populations) of the potency of various forms of ionizing radiation to induce various cancers in people of different ages at different times after exposure. The same estimates are also used in combination with data on the age distribution of exposures in the worker population to estimate typical "doubling doses" for various types to tumors, considering the age distribution of the exposures assessed in Section 2.
- The prospects for individual "proof" of causation of the radiation-induced cancers (Section 4) with either current technology (Section 4.1) or new technology based on advances in molecular biology for discriminating among different kinds of DNA mutations, measuring past radiation dosage, and assessing individual susceptibility for radiation-induced DNA damage (Section 4.2).
- Possible effects of policies that change the threshold for recovery (Section 5). This section considers the implications of specific alternative settlement policies in addition to the traditional policy of compensating workers with greater than one doubling dose. The alternative policies correspond to lowering the threshold for recovery to between 7.5% and 50% of the official doubling doses.

Accumulated Radiation Dosage In DOE And Contractor Employees

This analysis brings together information from (1) the distribution of career total estimated radiation dosage for individual workers retiring in five recent years (1990-1994) from three major DOE facilities (2) annual summaries of aggregate DOE and contractor dosage reports, and (3) the excellent historical compilation of career total dosage by age and calendar year of dose delivery for workers included in a major epidemiological study of Hanford workers over the years from 1944-1989. The result is a set of estimates of how many workers are likely to have received various career total effective doses from exposures between 1944 and 1992. We also use approximate data on age-specific mortality to assess how much of this dose is likely to remain in workers who have survived to the present time, and in those who are likely to survive to various future years.

Through the good offices of Steve Zobel of the DOE we were able to obtain detailed data on the recorded career total radiation dosage* of nearly 19,000 workers retiring from three major facilities (Hanford, Savannah River, and Los Alamos) over the period from 1990-1994. These facilities were chosen to represent DOE offices and states with the greatest concentration of past radiation dosage and therefore likely compensation cases. Overall, the three DOE field offices that include the covered facilities report over half of the total collective radiation dose delivered to DOE and contractor employees between 1982 and 1992.

Data for the three facilities provided very similar distributions of past dosage among workers (Table ES-1). Combining the data, about two thirds of the aggregate dosage is carried by workers who received at least 10 rem (100 mSv), and also about two thirds of the dose is borne by workers retiring near the end of their normal work lives (Figure ES-1). The relative concentration of past dosage (and resulting risks) among a relatively small fraction of former career DOE/contractor workers is important for assessing the economic feasibility of measures to provide equitable relief in recognition of those risks.

In order to project the number and time distribution of likely cancers, we assembled data on the amount and time distribution of past exposures for DOE and contractor workers. To do this, we combined 1965-1992 information on DOE-wide aggregate exposures with detailed data on age-at-exposure and year of exposure from the Hanford facility on exposures occurring between 1944 and 1989 (Figure ES-2). It can be seen in Figure ES-3 (derived from the Hanford data) that most exposure occurs relatively evenly in the prime work years between the ages of about 27 and 55.

Overall, we project that the aggregate dosage received by DOE and contractor workers between 1944 and 1992 is about 640,000 person-rem. Given estimates of age-specific mortality rates for never-smokers, Table ES-2 shows how much of this dose is likely to persist in the surviving population to various times in the future. (The data for 1970 through 1990 in this table reflect the net effects of both accumulation and loss of exposure with mortality.) It can be seen that as of now (1995) about two thirds of all the dosage delivered in the 1944-1992 period is expected to occur in the population of surviving workers. Within 15 years from now (2010), however, only half of that remaining fraction (34% of the original dose delivered) will still be carried by living people. Ten years after that (2020), only 16% will remain, and by 2025 only 10% will

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* The request was for dosage in terms of the current DOE standard for expressing career dose--the lifetime committed dose. In theory this involves a different treatment of dosage from internal emissions from radionuclides than earlier standard forms for expressing dosage. The new "committed" doses are defined as the entire dosage that is expected to be delivered from work in a given year over the subsequent 50 years, if the worker survives for that period. My impression is that earlier conventions for expressing dose recorded only the external dose plus the portion of the internal dose that was expected to be delivered within a particular year. It is not completely clear how much recalculation of career committed doses from long past radionuclide exposures is reflected in the data we received.

Table ES-1

Distributions of Cumulative Radiation Exposures Among 1990-1994 Retirees from Savannah River, Los Alamos, and Hanford

	Hanford Retirees		Los Alamos Voluntary Early Retirees		Savannah River Retirees	
rem/person	% People with any dose over this dose	% Aggregate Dose over this dose	% People with any dose over this dose	% Aggregate Dose over this dose	% People with any dose over this dose	% Aggregate Dose over this dose
1	25.66	94.63	28.62	93.20	22.78	94.00
2	18.39	89.88	18.73	86.64	16.39	89.95
5	9.95	78.14	11.21	76.60	10.29	81.23
7.5	7.33	71.04	7.72	66.71	8.38	76.03
10	5.98	65.79	6.34	61.23	7.04	70.92
15	4.03	55.12	3.76	45.91	5.00	59.66
20	2.91	46.57	1.98	31.97	3.55	48.52
30	1.52	31.46	0.79	19.73	1.41	25.10
40	0.74	19.63	0.79	19.73	0.35	8.80
60	0.35	10.90	0.20	6.44	0.07	3.14
80	0.06	2.43	0.00	0.00	0.02	1.45
100	0.00	0.00	0.00	0.00	0.02	1.45

Figure ES-1

Total Cumulative Person-Rem in Hanford Retirees by Year of Age

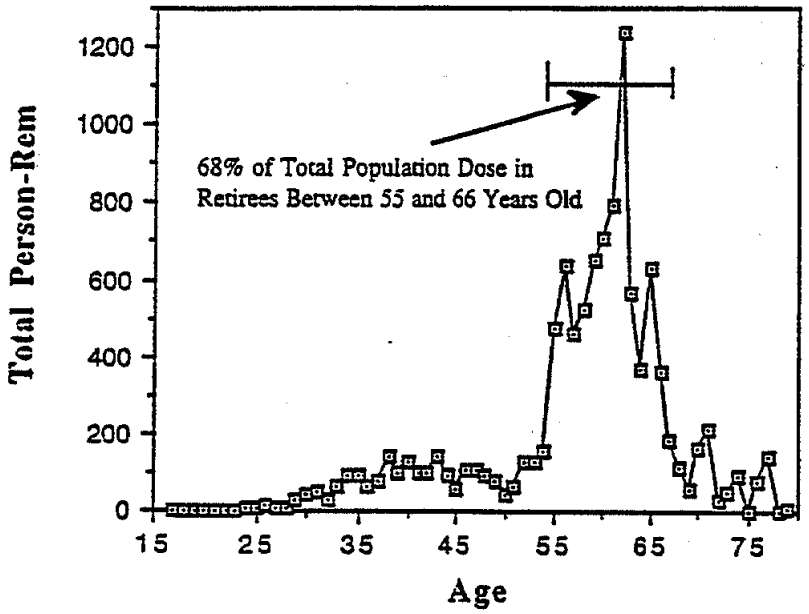

Figure ES-2

Collective Dose Delivered In Various Years to 37,009 Exposed Hanford Workers Who Were First Employed Between 1944 and 1978--Data of Buschbom and Gilbert, 1993

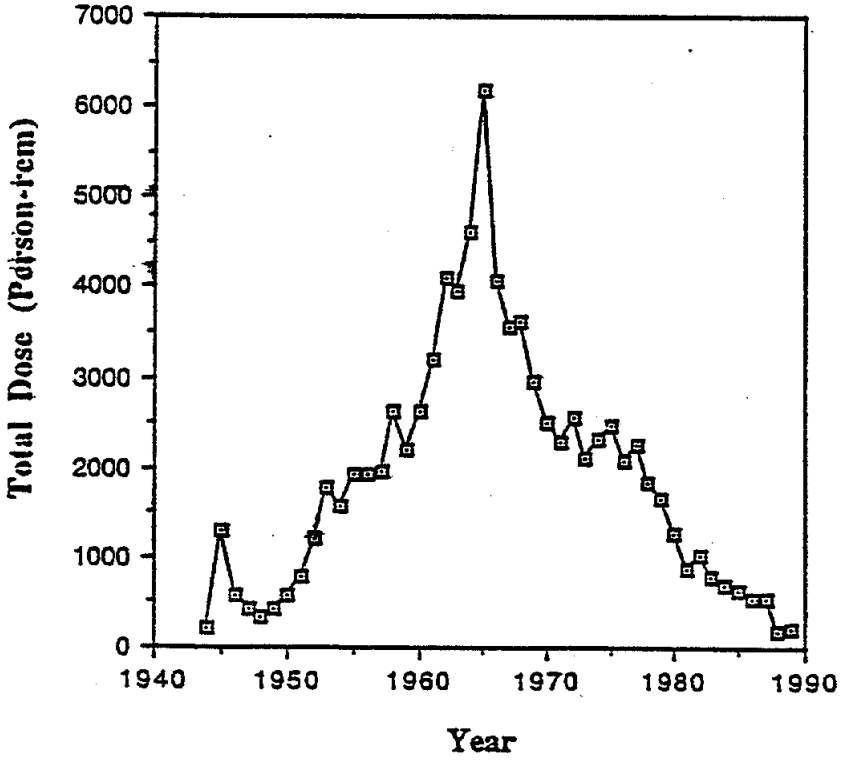

Figure ES-3

Age Distribution of % Total Cumulative Dosage Delivered to Hanford Workers, 1944-1989

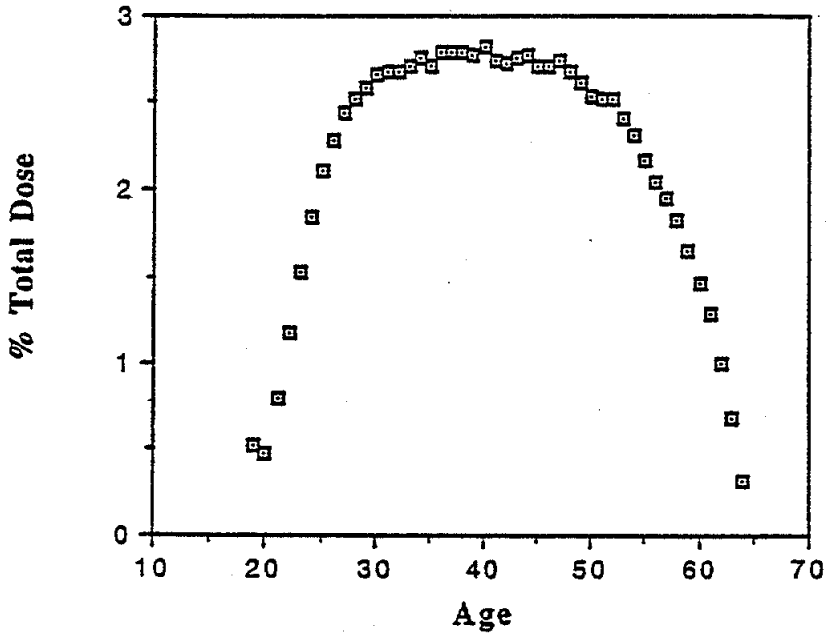

Table ES-2

Expected Changes in the "Inventory" of Collective Radiation Dosage in Surviving Workers, 1970-2025

	Dose Surviving to Year	% Dose Surviving
Total Delivered 1944-1992	640,000	100
1970	400,000	62
1975	460,000	72
1980	500,000	78
1985	500,000	78
1990	480,000	75
1995	420,000	66
2000	360,000	56
2005	290,000	45
2010	220,000	34
2015	160,000	24
2020	100,000	16
2025	63,000	10

remain. Clearly any policy measures that are considered necessary to deal with the effects of these exposures will need to be put into place in the immediate future in order to be effective.

Expected Cancer Cases and Deaths

The last two decades have seen important advances in our understanding of the fundamental mechanisms of carcinogenesis. We can now be very confident that with few known exceptions, tumors arise as a result of a series of changes or rearrangements of information coded in DNA within single cells or cell lines. The fundamental multiple mutation mechanism of radiation-induced carcinogenesis has strong implications for the likely relationship between delivered dose and incremental cancer risk at the limit of low dosage. Often the assumption of low dose linearity is presented in the context of its original use for cancer risk assessments over 20 years ago--as a "conservative" assumption--chosen in part for simplicity and in part because it was considered unlikely to understate risk. I think there is now a much stronger argument for its use, and that its status should be changed from a "conservative" assumption to a "central tendency" or "best estimate" assumption for carcinogens that act by primary genetic mechanisms. All recent national and international consensus summaries of radiation risks--which are the sources of the risk estimates presented below--use models that incorporate low dose linearity for all radiation-induced cancers, although there is still considerable uncertainty about appropriate low dose slopes for the dose response relationships for specific cancers in relation to specific types of radiation.

Our basic starting point for estimating likely cancer risks was a compilation of the most recent official EPA conclusions for ionizing radiation cancer potencies for exposure of the general population at low dose rates.* The EPA risk estimates were derived by taking the geometric mean of potency estimates from previous ICRP, NIH, and NRC risk models** applied to a stationary population with 1980 vital statistics, and then applying a downward adjustment of two-fold (the "Dose and Dose Rate Effectiveness Factor") for sites other than the breast to reflect an assumed lower efficiency/greater repair of DNA damage when radiation is delivered at low dose rates (relative to the high dose rates produced by the atomic bomb and some other sources of exposure). Combining these overall potency estimates with our earlier overall cumulative dose estimate of 640,000 person-rem, we arrive at an expectation that there will eventually be about 250 cancer deaths and 360 total cancer cases as the result of the occupational exposure of DOE and contractor employees to penetrating radiation.

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* Puskin, J. S., and Nelson, C. B. "Estimates of Radiogenic Cancer Risks" Health Physics 69:93-101 (July, 1995).

** National Institutes of Health. "Report of the National Institutes of Health Ad Hoc Working Group to Develop Radioepidemiolgical Tables." Washington. D.C.: U.S. Government Printing Office: NIH Publication 85-2748;, (1995); International Commission on Radiological Protection. 1990. "Recommendations of the International Commission on Radiological Protection." Oxford: Pergamon Press; ICRP Publication 60; Ann. ICRP 21 (1991).

A prudent policy planner will want to consider each of these estimates as the *lower* bound of an approximately 2-3 fold credible central range of likely overall cancer risk (250-500 cancer deaths; 360-1000 total cancer cases). This is because:

- With the possible exception of tritium exposures, long term exposures from absorbed radionuclides appear to be reflected incompletely in the past records of "penetrating" doses. DOE policies appear to have been changed to require reporting of "total effective dose equivalents" (including an estimate of internal dose for the current year) only since 1990. Most recently, the reporting definition has been changed again to "committed effective dose equivalents" which evidently include an estimate of the total dose that is expected to be delivered to workers over the next 50 years (if they survive) from radionuclide dosage absorbed in the current year. The pre-1990 data which comprise the great bulk of the cumulative dose delivered to workers, do not reflect these expanded definitions.

- Older methods of measuring even the penetrating dose were not sensitive to some forms of radiation (e.g., neutrons before 1972; low energy gamma radiation before 1957 at Hanford), although measurement of the predominant form of ionizing radiation--high energy gamma--was evidently fairly complete. Additionally, the monitoring was done primarily for compliance purposes and some workers who were thought to have relatively small exposures were not monitored. A study of 1943-1956 measurements of external dosage at Oak Ridge National Laboratory resulted in a 50% upward adjustment in the estimate of total collective dose for over 7000 workers at that facility during that time period (from a mean of 1.08 to 1.63 rem/worker). A similar analysis of dosage for nearly 8500 workers at the nearby Y-12 facility from 1947-1960 led to an overall 80% upward revision of their collective dose (from a mean of 0.5 to 0.9 rem/worker). On the other hand, a paper in press by Gilbert *et al.* points out that total penetrating dose as reported may tend to overstate the dosage delivered to various organs, depending on the geometry of the placement of the dosimeter and other factors. The overall upward bias was estimated at 1-27% for "deep dose", 41-75% for red bone marrow dose, and 6-33% for lung dose in various time periods between 1944 and 1989.

- Classical epidemiological methods have a bias toward underestimation of the slopes of dose response relationships where there is uncertainty in the estimation of individual dose. If estimates of these uncertainties are made, it is possible to correct for this bias, but such corrections are very unusual in epidemiology, and the international consensus estimates of radiation potency do not include an allowance for this effect. Additionally, there is some suggestion in the literature that the epidemiological results may tend to become more positive as additional time passes and longer lag periods are allowed in epidemiological analyses of relative risks.

- It is far from obvious that the two-fold Dose and Dose Rate Effectiveness Factor (DDREF) is appropriate (and uniform in magnitude) as applied to all cancers other than breast and leukemia. Surely if DNA repair saturation is the underlying mechanism, there is likely to be a different amount of high dose saturation (and therefore high-to-low dose change in dose response slope) for different tissues. The very fact that a uniform factor is applied indicates that specific data relevant for different cancer sites are probably not available, and the overall two-fold reduction in potency due to this factor carries considerable uncertainty.

- Competing sources of mortality (in particular, cardiovascular diseases) have been declining in recent decades, increasing the proportion of deaths due to cancer.

Therefore the use of stationary 1980 population distribution and death statistics is likely to understate future life expectancy and the numbers of people who will survive to older ages where there is a relatively high incidence of cancer. Additionally, improvements in the effectiveness of cancer treatment may well prolong the survival of patients with cancer and shift some cases from the "fatal" to "non-fatal" categories (hence I have broadened the range of "total cases" to three-fold, in comparison to the two-fold range applied to the base estimate of "cancer deaths").

Figure ES-4 presents the resulting time pattern of overall cancers (other than leukemia) expected to result from dosage delivered to DOE workers between 1944 and 1992; Figure ES-5 presents the same data projected in the form of a cumulative distribution for cancers occurring between 1965 and 2030. The peak year for the radiogenic cancers other than leukemia appears to be about 1995 or the next couple of years in the future. About 32% of the total cancers are expected to have occurred prior to 1990; about 44% will have occurred by the end of 1995; and two thirds are expected to happen by 2005.

Prospects For Individual "Proof" Of Causation Of The Radiation-Induced Cancers

Expected Compensation Under the Current "One Doubling Dose" Threshold for Recovery

In general a worker must show past exposure that exceeds the relevant cancer "doubling dose" in order to satisfy the usual "preponderance of evidence" test for legal causation. Figure ES-6 shows the estimated distribution of worker exposure in relation to the doubling doses for the most radiation sensitive cancer sites covered in the EPA radiation cancer potency estimates. It can be readily seen that although the past worker exposures may well have induced several hundred cancers, the numbers of workers who have past accumulated doses in excess of the officially recognized doubling doses are very small.

More detailed calculations indicate that if the doubling doses are as high as those calculated using a DDREF of 2--only about 1 % of total cases and 1.4% of total deaths would be compensated. 1% of total cases, of course, represents about 4 people out of the 360 cases in the lower bound of our range of estimates of radiogenic cancers in DOE and contractor employees. The outcome is markedly better, but still quite discouraging at half the calculated doubling doses (corresponding to a case in which the DDREF is set at 1). Under this assumption, about 4.2% of all cases and 5.4% of total fatal cases of the enumerated types could be eligible for compensation. 5.4% of all cases represents about 54 compensable cancers out of the 1,000 in our upper bound estimate of all occupationally caused radiogenic cancers in the DOE/contractor workers.

Figure ES-4

Projected Relative Rate of Occurrence (1995 = 1) of Radiogenic Cancer Cases (Except Leukemia) Induced in DOE Employees--1944-1992 Exposures

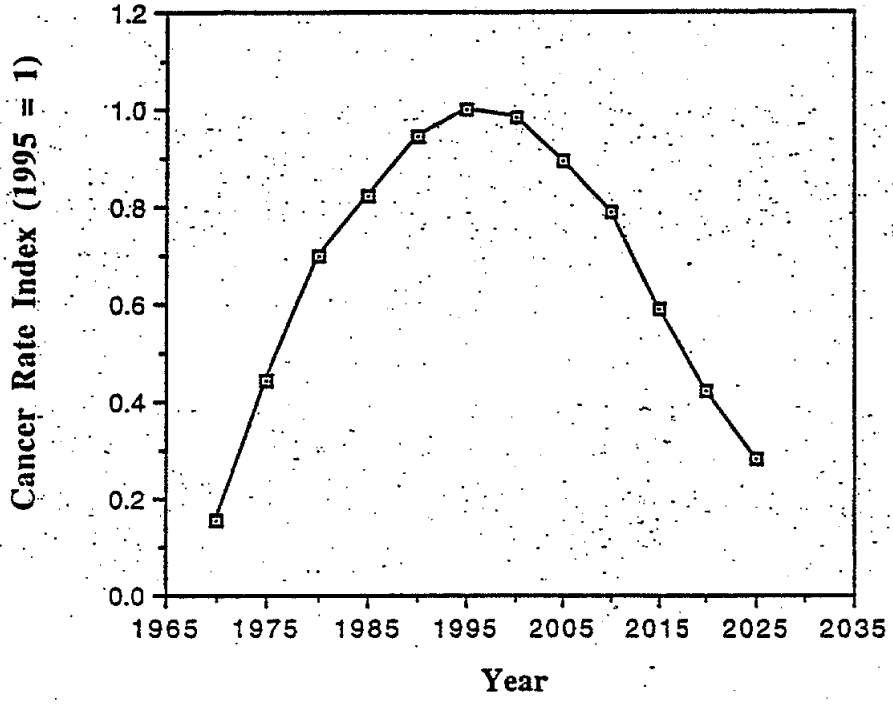


Figure ES-5

Cumulative % of All Radiogenic Cancers Except Leukemia Expected to Occur in Various Years

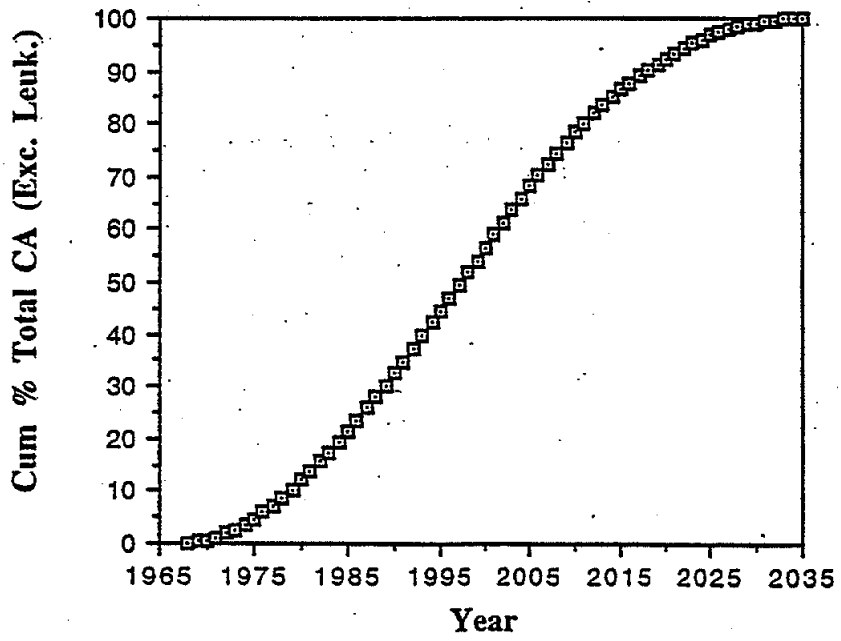
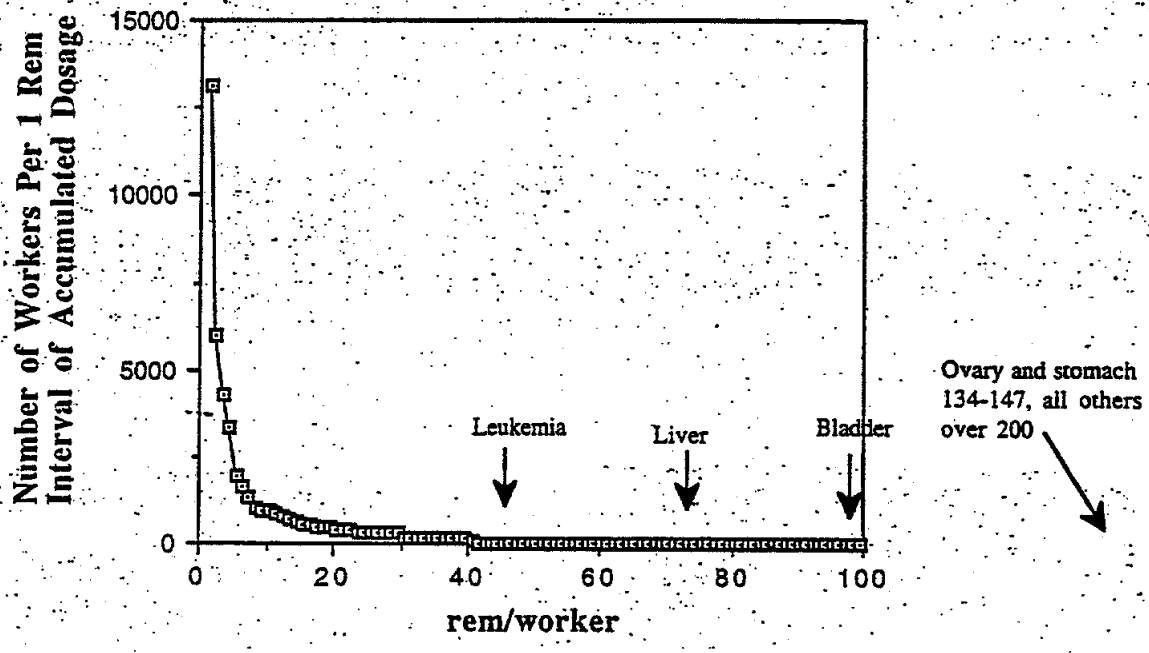


Figure ES-6

Estimated Distribution of Career Doses
For Former DOE and Contractor Workers
with 1-100 Total Rem of Exposure



Estimated Distribution of Career Doses
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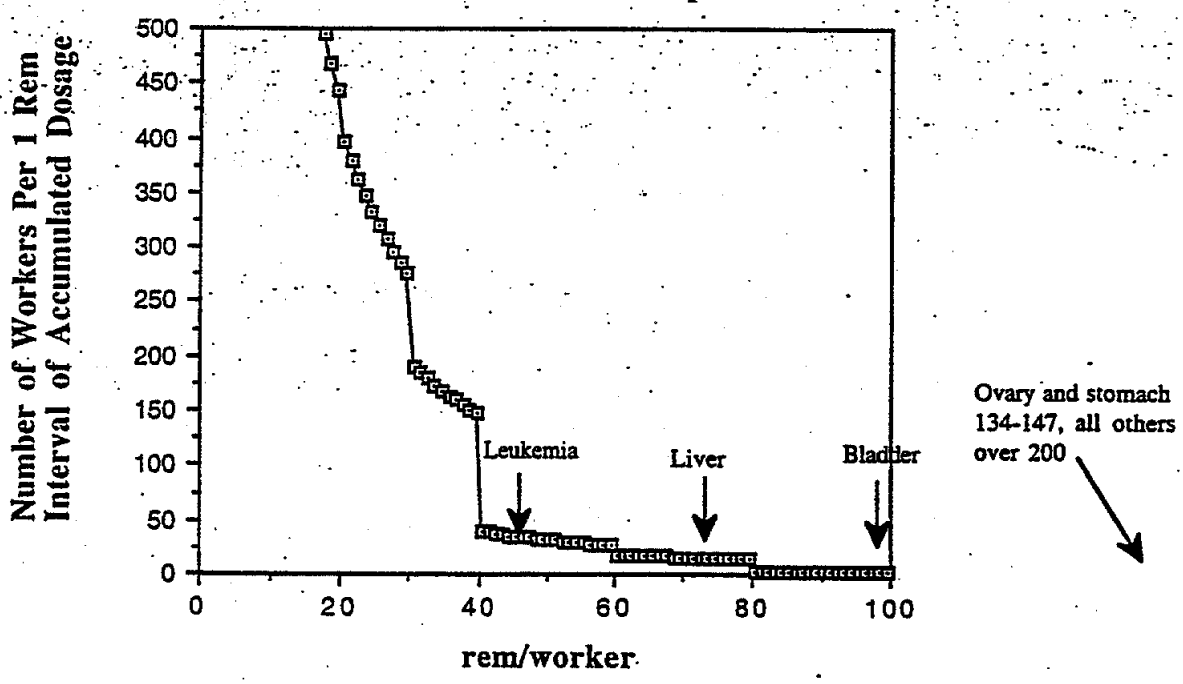

These estimates do not include allowances for brain cancers and multiple myelomas. If brain cancers were to be as susceptible to induction by internal radiation exposure as estimated by one researcher--a doubling dose of 25 rem--then 35% of induced brain cancers would be compensable under a 1 doubling dose requirement, and 62% would be compensable under a 1/2 doubling dose requirement. If the threshold for recovery were one tenth of a doubling dose, 87% would be compensable.

Potential Effects of New Molecular Biological Techniques on the Compensability of Radiogenic Cancers

The last two decades have seen dramatic advances in the molecular biological tools available for (1) analysis of changes in genetic information and (2) understanding the significance of specific changes in particular genes for carcinogenesis. Specifically, these advances in molecular biology have yielded information of four kinds that conceivably could have a bearing on the dilemma described above:

- Category 1 innovations essentially have the potential to make possible much more fine scale radiation cancer epidemiology by subdividing tumors observed at particular anatomical sites (and histological types) into categories of molecular pathology. By molecular pathology I mean (A) the specific series of genes that have been altered or impaired to produce a particular cancer and (B) the specific changes in DNA sequence that have occurred in those genes, or the changes in the location of specific sequences in the genome that has altered the activity of the cancer genes. This category of innovations has the potential to effectively lower the doubling dose for types of genetic changes that are established to be preferentially produced by specific kinds of radiation/radionuclide exposure. P53 in particular is an important gene on the pathway to many cancers that has been the subject of a large amount of DNA sequence analysis in individual tumors. About 37% of all tumors carry a defined change in this gene. The specific type of change that has occurred in individual tumors may provide a clue to causation.

- Category 2 innovations are techniques to improve radiation dosimetry for past exposures (e.g., "FISH"/"Chromosome painting"). These techniques are likely to be useful in disclosing risks to individual workers who for one reason or another were not adequately monitored, and who received total career doses of at least 5-10 rem. Unfortunately, it is difficult to see how these techniques by themselves will be very helpful in improving the fairness of workers compensation results in the light of the calculations in Section 2. The status of the affected workers' legal cases would only improve if the new procedures revealed that they had received career total accumulated dosage that exceeded the levels in Tables 15-18 (or Appendix Tables A1-A4). Unless there is a substantial amount of historically unrecorded dosage due to poorly monitored neutron exposures, etc., this seems likely only in a vanishingly small proportion of cases.

- Category 3 innovations are improvements in the assessment of differences in individual susceptibility to cancer risk from different types of agents. The recent literature contains a great deal of information on the variability in genetic and non-

genetic factors that are likely to alter susceptibility to different classes of carcinogens. If person were known to have a special sensitivity to radiation-induced cancers (say, because of less efficient repair of radiation-induced DNA damage), it is possible that their effective doubling dose for the resulting radiation-induced cancers would be reduced. The recent publication of data on the gene responsible for Ataxia Telangiectasia is a further case in point. This gene is important in detecting radiation induced damage to DNA and inhibiting cell replication until repair enzymes can remove the damage, and impaired forms of the gene are relatively common. One copy of a mutant form of this gene is carried by about 1% of all people. These heterozygotes are more sensitive to radiation-induced cell killing and mutagenesis. Current preliminary epidemiology studies suggest that the heterozygotes have a threefold increase in their relative risk of cancer in general, and a five-fold increased risk of breast cancer (the breast is a relatively radiosensitive site in humans). If these findings are confirmed, they would suggest larger relative increases in the risk due to specific identifiable causes (such as radiation) and correspondingly lower doubling doses, because the overall increases in incidence are relative to a background incidence that is related to multiple carcinogenic agents.

- Category 4 innovations represent improvements in the recognition of non-agent-specific individual differences in susceptibility to carcinogenesis--such as germ line mutations in genes that contribute to the genetic pathway to cancer in specific tissues (e.g., the retinoblastoma gene.) Although such mutations could be expected to increase the absolute risk due to both radiation and other exposures in affected people, there is no a priori reason to expect a specific change in relative risk, and therefore doubling doses would be essentially unchanged on average.

Section 4.2 analyzes in some detail the most promising single category of innovation--measurement of mutational spectra associated with radiation and other exposures as seen in specific genes that are likely to be part of the molecular pathogenic pathway for specific cancers. Radiation tends to cause a somewhat (3-5 fold) enhanced frequency of deletion mutations when compared to other agents. In addition, there has been one report of a dramatic (over 100 fold) increase in the frequency of one specific change at a particular DNA base among lung cancers in highly exposed uranium miners.

In order for p53 sequence analysis for deletions and insertions to push a particular case beyond the preponderance-of-evidence threshold, the tumor must:

A) Occur in a person who is between the original doubling dose for the tumor and the revised doubling dose for tumors bearing p53 deletions or insertions

B) Carry a p53 mutation (The p53 analysis is potentially more helpful for cancers other than leukemias in part because leukemias rarely carry p53 mutations.)

C) Carry a deletion mutation in p53 given the assumed 5 X multiplicative enrichment of deletions in radiation-induced mutations (limited of course, by the upper bound of 100%).

As deduced earlier, only approximately 1%-4% of the total radiation induced tumors might be compensable under a preponderance of evidence test without any p53 sequence analysis (with

the 4% figure derived from the elimination of the DDREF). With the same baseline assumptions, if there is a 5 fold enrichment of deletion and insertion p53 mutations in radiation-induced tumors, then an additional 1.6-3.4% of the total radiation-induced tumors might be able to pass the preponderance of evidence threshold with the p53 sequence analysis. Based on our earlier estimate that a total of about 360-1000 extra cancers might have been initiated in DOE and contractor employees by exposures over the 1944-92 period, then the number of potential beneficiaries from the p53 technology in this group might be approximately 5-30, spread out over the next couple of decades. Therefore, marvelous as the new technology is for understanding the molecular basis for some tumors, there is no near term prospect that, by itself, it will solve the problem of under compensation of radiation-induced tumors.

Estimated Effects Of Policies That Change The Threshold For Recovery

Finally I consider the likely effects of changes in the probability of causation threshold for recovery for the numbers and types of radiation-induced cancers (and "background" cancers) that would be eligible for compensation. The overall policy-relevant findings from these calculations are summarized in Figure ES-7 and Tables ES-3 and ES-4. Basically, there is a tradeoff between the percentage of true radiogenic cancers compensated and the total expenditures made for both "true" cases and indistinguishable "false positive" cases. If a policy decision were made that it is desirable to compensate an equal number of cancer cases to those caused, this would be achieved by setting the threshold for compensability at about 10% of the doubling doses. At 7.5% of the doubling doses, the cases compensated would be about 60% greater than the cases caused. If the threshold is set at a higher level than 10% of the doubling doses, the percentage of true radiogenic cancers compensated declines rapidly.

From a microeconomic and social efficiency perspective, the present system (which requires that for workers to recover financially, they must receive at least the doubling dose for their specific cancers) will fail to internalize the true social costs of operating DOE nuclear facilities because only about 1% of the radiation-caused cancer is likely to receive compensation. If the goal were to internalize social costs by ensuring that roughly as many cancers receive compensation as are caused by workplace exposure to radiation, this could be done by paying full compensation to all workers who get radiogenic cancer and are exposed to about one-tenth the doubling dose for their specific cancer. Referring to Figure ES-7, Table ES-3 and Table ES-4, by allowing all workers who can demonstrate that they received one-tenth the doubling dose, or greater, the system would compensate about 25% of the radiogenic cancer cases (and 25% of deaths), rather than the 1% of cases (and 1.4% of deaths) who develop cancer after 1991 and who could be

Figure ES-7

Tradeoff Between Compensating True Radiogenic Cancers and Equalizing the Cases Compensated to Cases Caused

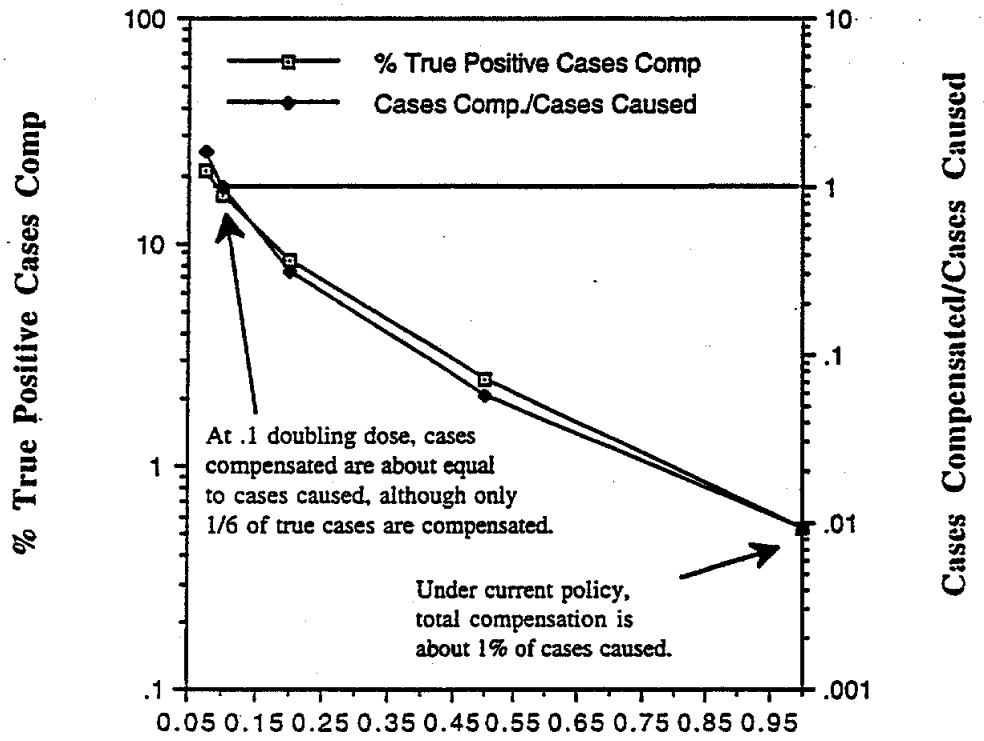

Table ES-3

Final Tradeoffs Between Compensating "True" Radiogenic Cancers and the Overall Ratio of Cases Compensated to Cases Caused

A. Conclusions Based on Total Cancer Cases

Threshold for Compensation (Fraction of a Doubling Dose)	% True Radiogenic Cancers Compensated, 1991+	Ratio of Total Cases to True Positive Cases	Ratio, Cases Compensated/Cases Caused
1	0.527	1.74	0.0092
0.5	2.43	2.35	0.057
0.2	8.40	3.75	0.32
0.1	16.4	6.04	0.99
0.075	21.2	7.54	1.60

B. Conclusions Based on Total Cancer Deaths

Threshold for Compensation (Fraction of a Doubling Dose)	% True Radiogenic Cancers Compensated, 1991+	Ratio of Total Cases to True Positive Cases	Ratio, Cases Compensated/Cases Caused
1	0.721	1.73	0.0125
0.5	3.08	2.33	0.072
0.2	9.58	3.65	0.35
0.1	17.3	5.80	1.01
0.075	21.7	7.20	1.57

Table ES-4

Central Projections of Absolute Numbers of Cases and Deaths That Would Be Eligible for Compensation Under Different Scenarios

A. Conclusions Based on Total Cancer Cases

Threshold for Compensation (Fraction of a Doubling Dose)	1991-2000	2001-2010	2011-2035	Total 1991+*
1	2.8 (1-5-4.2)	2.8 (1-5-4.2)	0.6 (0.3-0.9)	6 (3-9)
0.5	15 (8-22)	17 (9-25)	7 (4-10)	39 (21-57)
0.2	74 (39-109)	78 (41-114)	63 (33-92)	210 (113-320)
0.1	230 (122-340)	230 123-340)	210 (111-310)	670 (360-990)
0.075	380 (200-560)	370 (200-540)	340 (178-490)	1080 (570-1600)

B. Conclusions Based on Total Cancer Deaths

Threshold for Compensation (Fraction of a Doubling Dose)	1991-2000	2001-2010	2011-2035	Total 1991+*
1	2.2 (1.4-2.9)	2.2 (1.4-2.9)	0.4 (0.2-0.5)	5 (3-6)
0.5	11 (7-14)	12 (8-16)	4 (3-6)	27 (18-36)
0.2	47 (31-62)	49 (33-65)	35 (24-47)	131 (87-175)
0.1	135 (90-180)	131 (88-175)	111 (74-147)	380 (250-500)
0.075	210 (143-280)	200 (135-270)	170 (114-230)	590 (390-780)

* Totals may not add due to rounding.

compensated under the current system. The estimates for cancer cases and cancer deaths (from all causes) in DOE facilities that could be compensated is 670 and 385, respectively. Note that under this option, about 75% of post-1991 radiogenic cancer cases will never be compensated. Thus this option makes a significant tilt towards fairness to workers, but in no way compensates most cancer in workers. The numbers of radiogenic cancer cases and deaths that are expected to appear after 1991 are 460 and 255, respectively. The actual numbers of radiogenic cancer cases and deaths which get compensated under this option is 25% of these numbers, namely 111 and 65. Table ES-5 summarizes our findings.

Table ES-5

Expected Consequences of Adopting 10% of a Doubling Dose as the Threshold for Recovery

CANCER IN DOE WORKERS	OCCURRING SINCE 1944	OCCURRING SINCE 1991	NUMBER COMPENSATED
True Radiogenic Cases	680 (360-1000)	460 (240-680)	111 (60-165)
True Radiogenic Deaths	375 (250-500)	255 (170-340)	65 (43-87)
All Cancer Cases			670 (355-985)
All Cancer Deaths			380 (250-500)

1. Introduction

From the early 1940's to the present, hundreds of thousands of workers have participated in national efforts to develop and use nuclear technology for both military and civilian applications under the supervision of the Department of Energy and its predecessor agencies. This research explores the scientific bases for estimating the number of workers who are reasonably likely to have suffered serious adverse health effects as the result of their contributions to these efforts.

Although DOE and its contractors took extensive precautions to minimize worker radiation exposures, a significant amount of radiation dosage was received by the worker population as a whole. Current understanding of radiation biology and carcinogenesis indicates that some cancers have resulted from these exposures, and that additional cancers will continue to occur in the future. Unfortunately, with the exception of some worker subgroups,[1] the precise numbers of induced cancers have generally been difficult to unequivocally measure directly in the population as a whole[2] because of (1) the high background of cancers from other sources, (2) the relatively small proportion of workers exposed at very high dose levels, and (3) other imperfections in long term occupational epidemiology, such as the relatively short period of follow-up in some cases, the "healthy worker effect",[3] and difficulties in accurate ascertainment of individual occupational dose.[4]

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[1]Lubin, J. H., Boice, J. D. Jr., Edling, C., Hornung, R. W., Howe, G., Kunz, E., Kusiak, R. A., Morrison, H. I., Radford, E. P., Samet, J. M., Tirmarche, M., Woodward, A., Xiang, Y. S., and Pierce, D. A. Radon and Lung Cancer Risk: A Joint Analysis of 11 Underground Miners Studies U. S. Department of Health and Human Services, NIH Publication No. 94-3644 (1994; Frome, E. L., Cragle, D. L., and McLain, R. W. "Poisson Regression Analysis of the Mortality Among a Cohort of World War II Nuclear Industry Workers," Radiation Res.: 123:138-152 (1990); Wilkinson, G. S., Tietjen, G. L., Wiggs, L. D., Galke, W. A., Acquavella, J. F., Reyes, M., Voelz, G. L., and Waxweiler, R. J., "Mortality Among Plutonium and Other Radiation Workers at a Plutonium Weapons Facility," Am. J. Epidemiol. 125:231-250 (1987); Checkoway, H., Pearce, N., Crawford-Brown, D. J., and Cragle, D. J. "Radiation Doses and Cause-Specific Mortality Among Workers at a Nuclear Materials Fabrication Plant," Am J. Epidemiol. 127:255-266 (1988); Wing, S., Shy, C. M., Wood, J. L., Wolf, S., Cragle, D. L., and Frome, E. L. "Mortality Among Workers at Oak Ridge National Laboratory," JAMA 265:1397-1402; Alexander, V., "Brain Tumor Risk Among United States Nuclear Workers," Occupational Medicine: State of the Art Reviews 6:695-714 (1991).

[2]Cardis, E., Gilbert, E. S., Carpenter, L., Howe, G., Kato, I., Armstrong, B. K., Beral, V., Cowper, G., Douglas, A., Fix, J., Fry, S. A., Kaldor, J., Lave, C., Salmon, L., Smith, P. G., Voelz, G. L., and Wiggs, L. D. "Effects of Low Doses and Low Dose Rates of External Ionizing Radiation: Cancer Mortality Among Nuclear Industry Workers in Three Countries," Radiat. Res. 142:117-132 (1995); Gilbert, E. S., Fry, S. A., Wiggs, L. D., Voelz, G. L., Cragle, D. L., and Petersen, G. R. "Analyses of Combined Mortality Data on Workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant," Radiat. Res. 120:19-35 (1989); Dupree, E. A., Watkins, J. P., Ingle, J. N., Wallace, P. W., West, C. M., and Tankersley, W. G. "Uranium Dust Exposure and Lung Cancer Risk in Fur Uranioum Processing Operations, Epidemiology 6:370-375 (July, 1995).

[3]Steenland, K., and Stayner, L. "The Importance of Employment Status in Occupational Cohort Mortality Studies," Epidemiology 2:418-423 (1991).

[4]Gilbert, E. S., Fix, J. J., and Baumgartner, W. V. "An Approach to Evaluating Bias and Uncertainty in Estimates of External Dose Obtained from Personal Dosimeters," Health Physics, (1995, in press); Gilbert, E. S., and Fix, J. J. "Accounting for Bias in Dose Estimates in Analyses of Data from Nuclear Worker Mortality Studies," Health Physics 68:650-660 (1995); Watkins, J. P., Cragle, D. L., Frome, E. L., West, C. M., Crawford-Brown, D. J., and

The analysis below seeks to produce *central tendency* estimates of

- The overall amounts and distribution of officially measured radiation dosage in DOE and contractor employees (Section 2). For this analysis we bring together information from (1) the distribution of career total estimated radiation dosage for individual workers retiring in five recent years (1990-1994) from three major DOE facilities[5] (2) annual summaries of aggregate DOE and contractor dosage reports,[6] and (3) the excellent historical compilation of career total dosage by age and calendar year of dose delivery for workers included in a major epidemiological study of Hanford workers over the years from 1944-1989.[7] The result is a set of estimates of how many workers are likely to have received various career total effective doses from exposures between 1944 and 1992. We also use approximate data on age-specific mortality to assess how much of this dose is likely to remain in workers who have survived to the present time, and in those who are likely to survive to various future years.

- The expected cancer risks likely to be associated with the exposures (Section 3). This analysis draws on expert consensus estimates[8] (from Atomic Bomb survivors and other populations) of the potency of various forms of ionizing radiation to induce various cancers in people of different ages at different times after exposure. The same estimates are also used in combination with data on the age distribution of exposures in the worker population to estimate typical "doubling doses" for various types to tumors.

- The prospects for individual "proof" of causation of the radiation-induced cancers (Section 4) with either current technology (Section 4.1), new technology based on advances in molecular biology for discriminating among different kinds of DNA mutations,[9] measuring past radiation dosage, and assessing individual susceptibility

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Tankersley, W. G. "Adjusting External Doses from the ORNL and Y-12 Facilities for the Oak Ridge Nuclear Facilities Mortality Study," Report by Oak Ridge Associated Universities in collaboration with the University of North Carolina School of Public Health, ORISE 94/G-34 (1994); Watkins, J. P., Reagan, J. L., Cragle, D. L., Frome, E. L., West, C. M., Crawford-Brown, D. J., and Tankersley, W. G., "Data Collection, Validation, and Description for the Oak Ridge Nuclear Facilities Mortality Study," Report by Oak Ridge Associated Universities in collaboration with the University of North Carolina School of Public Health, ORISE 93/J-42 (1993); Checkoway, H., and Crawford-Brown, D., "Metabolic Modeling of Organ-Specific Doses to Carcinogens as Illustrated with Alpha-Radiation Emitting Radionuclides, J. Chron. Dis. 40(Suppl. 2):191S-200S (1987).

[5]These data were graciously assembled by the individual facilities in response to the good offices of Steve Zobel of the DOE headquarters.

[6]Smith, M. H., Hui, T. E., Strom, D. J., Millet, W. H., and Scholes, V. A. 25th Annual Report--Radiation Exposures for DOE and DOE Contractor Employees--1992, U. S. Department of Energy, Draft, December, 1994.

[7]Buschbom, R. L., and Gilbert, E.S. Summary of Recorded External Radiation Doses for Hanford Workers 1944-1989, Report to the U.S. Department of Energy by Batelle Pacific Northwest Laboratory, PNL-8909/AD-902, 1993.

[8]Committee on the Biological Effects of Ionizing Radiations, National Research Council, Health Effects of Exposure to Low Levels of Ionizing Radiation, BEIR V, National Academy Press, Washington, D.C., 1990; Puskin, J. S., and Nelson, C. B. "Estimates of Radiogenic Cancer Risks" Health Physics 69:93-101 (July, 1995).

[9]We can now be very confident that cancer is fundamentally a genetic disease. The last two decades have seen dramatic advances in the molecular biological tools available for (1) analysis of changes in genetic information and (2) understanding the significance of specific changes in particular genes for carcinogenesis. Such changes include both "point mutations" (changes at particular places in the DNA code) and rearrangements of information represented by the transfer of large sections of chromosomes in recombination events. Point mutations have been studied by extracting specific genes from tumors and other cells, copying the genes many times, and determining the detailed sequence of DNA bases in those genes. One specific cancer related gene that has been extensively studied in this way is p53 (Greenblatt, M. S., Bennett, W. P., Hollstein, M., and Harris, C. C. "Mutations in the p53 Tumor Suppressor Gene: Clues to Cancer Etiology and Molecular Pathogenesis." Cancer Research 54:4855-4878, 1994.)

for radiation-induced DNA damage (Section 4.2), and/or new Bayesian evaluation of likely past dosage in workers presenting with cancers, based on the uncertainties in individual dosimetry among other factors (Section 4.3). The "doubling doses" calculated in Section 3 are important because in order to show that a particular cancer was caused by occupational radiation exposure by a "preponderance of the evidence" (the usual test for legal recovery) a worker must generally show personal occupational exposure above the doubling dose for that tumor. Only a tiny proportion of former workers with radiation-induced cancers will have received doses high enough to qualify by this standard. The newer molecular biological techniques have promise to both better document individual worker exposures and to identify specific kinds of mutations in individual cancers that are somewhat more likely to have been caused by radiation than by other DNA damaging agents. However it is likely that only a small minority of the radiation-induced cancers will be moved across the "more likely than not" boundary by these techniques.

- Possible effects of policies that change the threshold for recovery (Section 5). This section considers the implications of specific alternative settlement policies in addition to the traditional policy of compensating workers with greater than one doubling dose. The alternative policies correspond to lowering the threshold for recovery to between 7.5% and 50% of the official doubling doses.

The analysis focuses on "central tendency" estimates--estimates that are based on assumptions that are neither deliberately biased high or biased low. Nevertheless, it should be understood that the estimates cannot be perfectly precise. The uncertainties in both past dosimetry/reporting and dose response relationships mean that the narrowest credible ranges for estimates of aggregate cancer cases, and other relevant factors, will include values at least two-fold higher and lower than the stated "central tendency" values.

Persistent chromosome rearrangements suitable for assessment of past radiation doses have been studied by both conventional cytogenetic and chromosome banding studies, and newer techniques that are referred to under the "Fluorescence In Situ Hybridization (FISH)" or "Chromosome Painting" rubrics (Brenner, D.J. and Sachs, R.K. "Chromosomal 'Fingerprints' of Prior Exposure to Densely Ionizing Radiation," Radiation Research 140:134-142. 1994; Tucker, J. D., Ramsey, M. J., Lee, D. A., and Minkler, J. L. "Validation of Chromosome Painting as a Biodosimeter in Human Peripheral Lymphocytes Following Acute Exposure to Ionizing Radiation In Vitro," International Journal of Radiation Biology 64(1):27-37, 1993; Lucas, J. N., Poggensee, M., and Straume, T. "The Persistence of Chromosome Translocations in a Radiation Worker Accidentally Exposed to Tritium," Cytogenetics & Cell Genetics 60(3-4):255-256, 1992.)

2. Magnitude and Distribution of Past Radiation Dosage in DOE and Contractor Employees

2.1 The Distribution of Cumulative Career Total Dosage in Recent Retirees from Hanford, Los Alamos, and Savannah River

The distribution of career total dosage among workers is a key determinant of the efficiency of any system for discriminating between cancers that are and are not likely to have been caused in part by occupational radiation. Other things being equal, if a large fraction of all dosage (and resulting risk) is concentrated among a relatively few workers, then both assessment and compensation resources can be targeted toward those few with relatively high chances of occupational causation, with relatively little loss of "sensitivity" in addressing the needs of rare individuals who by bad luck developed cancer attributable to relatively low-dose occupational exposures. On the other hand, if the aggregate past dosage is widely dispersed among a large population, then in order to deal appropriately with a meaningful percentage of the "true positive" cases, more substantial costs will need to be incurred in evaluating and compensating larger numbers of cancers of non occupational origin that are indistinguishable from those whose causal pathway includes a contribution from occupational radiation exposures.

Through the good offices of Steve Zobel of the DOE we were able to obtain detailed data on the recorded career total radiation dosage[10] of workers retiring from three major facilities over the period from 1990-1994. These facilities were chosen because they represent DOE offices and states with relatively higher concentrations of past radiation dosage, and therefore are likely to have a significant percentage of eventual compensation cases (Table 1). Overall, the three DOE field offices that include the covered facilities report over half of the total collective radiation dose delivered to DOE and contractor employees between 1982 and 1992. Originally, we had also sought data for Rocky Flats, but because of needs to process data for large numbers of recent personnel changes, the Rocky Flats facility was unable to supply the requested data in time for this report.

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[10]The request was for dosage in terms of the current DOE standard for expressing career dose--the lifetime committed dose. In theory this involves a different treatment of dosage from internal emissions from radionuclides than earlier standard forms for expressing dosage. The new "committed" doses are defined as the entire dosage that is expected to be delivered from work in a given year over the subsequent 50 years, if the worker survives for that period. My impression is that earlier conventions for expressing dose recorded only the external dose plus the portion of the internal dose that was expected to be delivered within a particular year. It is not completely clear how much recalculation of career committed doses from long past radionuclide exposures is reflected in the data we received. The responsible person from one facility (Los Alamos) was unable to supply us fully recalculated information from all retirees; but was able to supply these data for participants in their Voluntary Early Retirement program, and these are the data reflected in our tables. We expect to receive a limited representative sample of data for 100 retirees from this facility in the future.

Table 1

Summary of Collective Dose Reported by Different DOE Field Organizations

Field Organization	Total person-rem, 1982-1992	% All DOE person-rem
Albuquerque (Includes Los Alamos)	8591	13.4
Chicago	4146	6.5
Idaho	3752	5.9
Nevada	216	0.3
Oak Ridge	3741	5.8
Pittsburgh	1305	2.0
Richland (Includes Hanford)	16636	26.0
Rocky Flats	11089	17.3
San Francisco	1493	2.3
Savannah River	10978	17.2
Schenectady N.R. Office	2056	3.2
Total	64003	100

Source: Table 4.7 of the DOE overall annual radiation report.[11]

For two of the three facilities (Hanford and Savannah River), extensive data were available from all retirees. For Los Alamos, the data come from a substantial subset of retirees who participated in a voluntary early retirement program. Table 2 provides an overview of the ages, and overall dosage recorded in the three data sets. It can be seen that the only important difference among the groups is that the Los Alamos voluntary early retirees have a greater average age—in other respects the data appear very comparable to one another.

The same basic consistency among the data sets is seen in the distributional breakout (Table 3 and Figure 1). In Table 3 I have assessed for each facility (1) the percentages of retirees with career total doses above each level, and (2) the percentage of the total population dose that was received by workers above each dose cutoff. Overall, combining all three populations, about two thirds of the aggregate dosage is carried by workers who received at least 10 rem (100 mSv) (Table

[11]Smith et al., cited earlier as note 6.

Table 2

Overall Summary Statistics for the Data on Cumulative Career Total Exposures for 1990-1994 Retirees from Savannah River, Los Alamos, and Hanford

	Ave age	Total person-rem	Ave rem/person with non-zero dose	Total number of retirees	Number with any non-zero dose
Savannah River	40.9	12,202	2.24	7,333	5,444
Los Alamos Voluntary Early Retirees	57.6	1,104	2.19	830	505
Hanford	38.6	10,964	2.25	10,709	4,883
Total	40.3	24,271	2.24	18,872	10,832

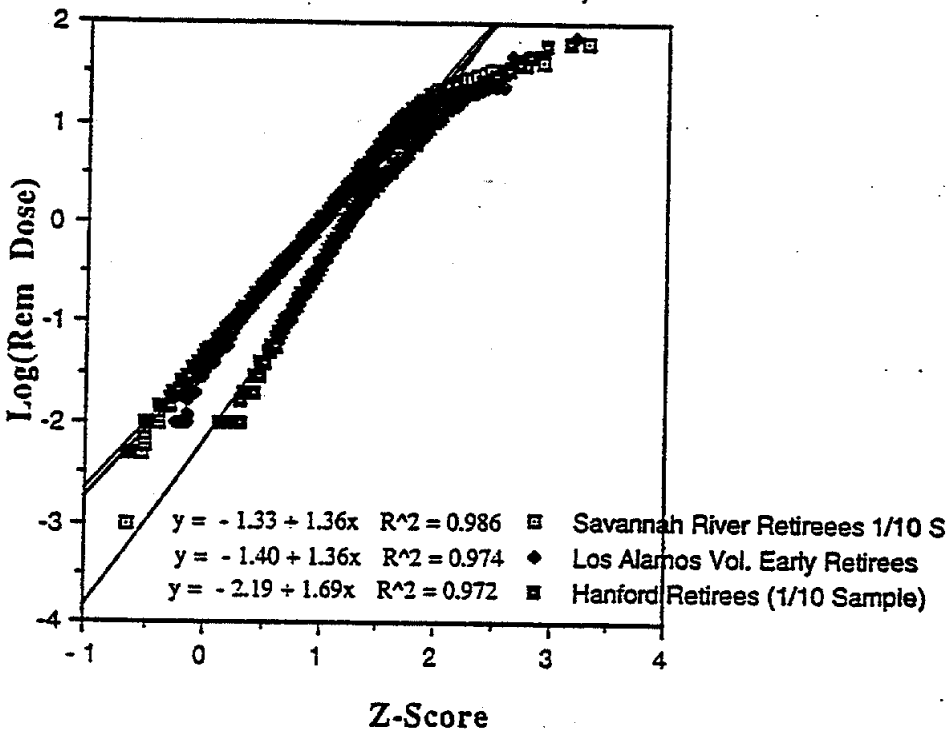
Table 3

Distributions of Cumulative Radiation Exposures Among 1990-1994 Retirees from Savannah River, Los Alamos, and Hanford

	Hanford Retirees		Los Alamos Voluntary Early Retirees		Savannah River Retirees	
rem/person	% People with any dose over this dose	% Aggregate Dose over this dose	% People with any dose over this dose	% Aggregate Dose over this dose	% People with any dose over this dose	% Aggregate Dose over this dose
1	25.66	94.63	28.62	93.20	22.78	94.00
2	18.39	89.88	18.73	86.64	16.39	89.95
5	9.95	78.14	11.21	76.60	10.29	81.23
7.5	7.33	71.04	7.72	66.71	8.38	76.03
10	5.98	65.79	6.34	61.23	7.04	70.92
15	4.03	55.12	3.76	45.91	5.00	59.66
20	2.91	46.57	1.98	31.97	3.55	48.52
30	1.52	31.46	0.79	19.73	1.41	25.10
40	0.74	19.63	0.79	19.73	0.35	8.80
60	0.35	10.90	0.20	6.44	0.07	3.14
80	0.06	2.43	0.00	0.00	0.02	1.45
100	0.00	0.00	0.00	0.00	0.02	1.45

Figure 1

Probability Plots of the Cumulative Dose Distribution for All Retiring Workers (Including Those with 0 Dose)



4). (Table 4 also incorporates important information on the overall aggregate population dose likely to be borne by workers and former workers surviving to 1995. I will show the formal derivation of these estimates in the subsections below).

The aggregate dose is also substantially concentrated among a relatively narrow range of ages. Figure 2 indicates that two thirds of the dose is borne by workers retiring near the end of their normal work lives. The workers with substantial dosage are, by and large, not temporary employees, but people who have worked for many years directly or indirectly on DOE projects. Figure 3 shows the growth in average rem/person as a function of age at retirement in the Hanford retirees.

Table 5 summarizes the Hanford retiree data broken down by the year that employment ended. These data indicate that relatively large numbers of older workers with substantial dosage have retired in the most recent year covered (1994).

Table 4

Estimated Absolute Numbers of Current and Former Workers At Various Career Dose Levels as of 1995

rem/person	% People with any dose over this dose	% Aggregate dose over this dose	Estimated absolute numbers of current and former workers surviving to 1995
1	24.35	94.25	46,000
2	17.40	89.76	33,000
5	10.18	79.62	19,000
7.5	7.87	73.35	15,000
10	6.53	68.16	12,000
15	4.51	56.97	8,500
20	3.19	46.87	6,000
30	1.43	27.72	2,700
40	0.54	14.20	1,000
60	0.20	6.79	380
80	0.04	1.82	70
100	0.01	0.73	17

Figure 2

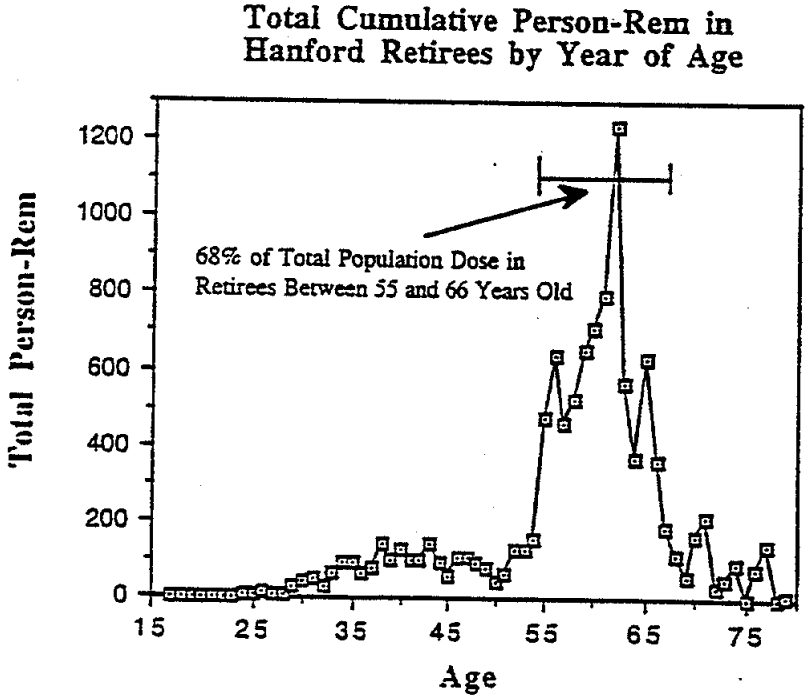


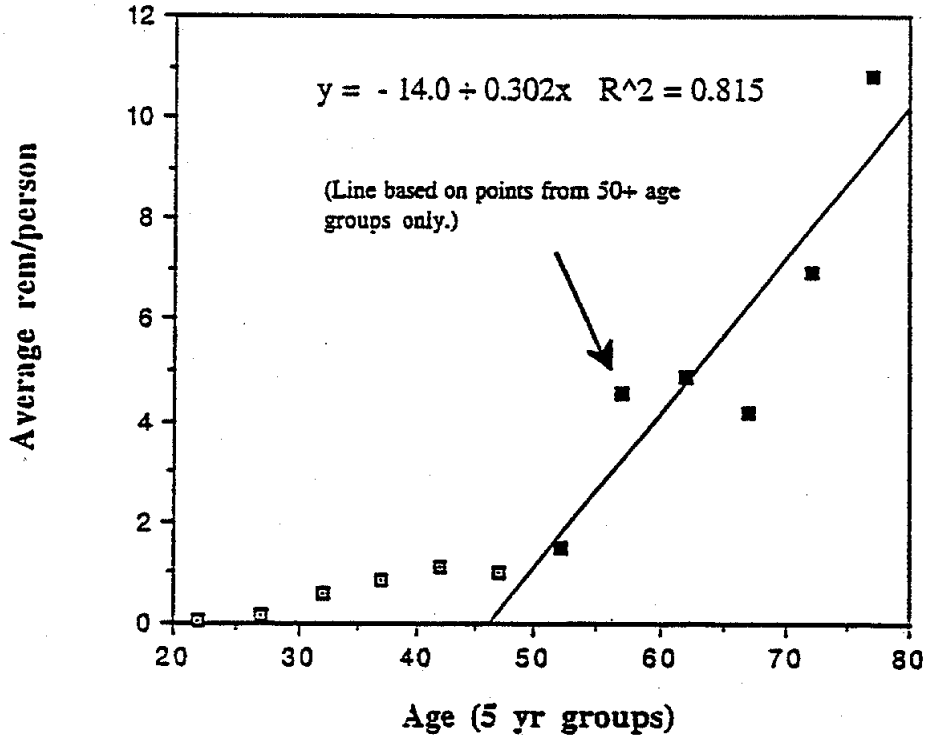
Table 5

Hanford Summary by Year of Retirement

End Employment	Ave age	Ave age of workers with dose	Total person-rem	Total N	N with non-zero dose	% with non-zero dose
1990-1994	38.6	46.3	10964	10709	4883	45.6
1990	36.7	42.1	731	1109	282	25.4
1991	37.8	43.2	1425	1361	758	55.7
1992	37.1	43.5	1261	1470	660	44.9
1993	37.6	44.3	1804	2359	1120	47.5
1994	40.3	50.0	5744	4410	2063	46.8

Figure 3

Rate of Increase in Average Career Rem/Person in Older Age Groups--Hanford Retirees



2.2 Estimation of the Aggregate Dosage Delivered to DOE and Contractor Employees

Data are readily available for radiation exposures for the period 1965-1992 from the latest draft DOE annual radiation report.[12] However because some cancers appear several decades after the initiating exposure, it is desirable to build as complete a picture as possible of the history the dosage delivered to DOE and contractor workers extending back to World War II. To do this, I will first describe the relevant DOE-wide data, and then combine it with a more extensive data set for Hanford workers giving information back to 1944, with important details on the age distribution of the workers who received the dosage. The age distribution information in turn allows us to assess (1) how much of the dosage is borne by workers who can be expected to survive to various years in the present and the future, and (2) the time distribution of the cancers likely to result eventually.

2.2.1 Data from the DOE-Wide Annual Compilation of Current Dosimetry Measurements for 1965-1992

The annual radiation report includes in its Table 4.7 a summary of collective DOE-wide dosage for 1982-1992. For 1965-1981, I calculated dosage from the distributional information provided in Table 4.2 of the report.

Figures 4-12 show lognormal probability plots of official DOE exposure data for every third year from 1965-1992 from DOE's ongoing personal monitoring program for radiation exposures(the 1989 data are not shown because there were only two usable data points). In this kind of plot, the basic hypothesis is that the data are lognormally distributed. That is, the logarithms of the exposures have a normal gaussian distribution. Such a distribution is expected when the causes of variability in exposures among employees are multiplicative. The correspondence of the points to the line allows a rapid appraisal of whether the data are reasonably accurately described by the lognormal hypothesis. In practice, many exposure distributions for environmental agents are approximately lognormal.[13] The correspondence to a lognormal distribution is seen by comparing the data points to the fitted line. The slope of the fitted line is an estimate of the standard deviation of the logarithms (base 10) of the exposures; the intercept of the fitted line is an estimate of the median of the distribution of the $\log_{10}$ of the exposures. The estimated "geometric standard deviation" of the distribution is simply the antilog of this slope.

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[12]Smith et al., cited earlier as note 6.

[13]Hattis, D. and Burmaster, D. E. "Assessment of Variability and Uncertainty Distributions for Practical Risk Analyses" Risk Analysis, Vol. 14, pp. 713-730, October 1994.

Figure 4

1965--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

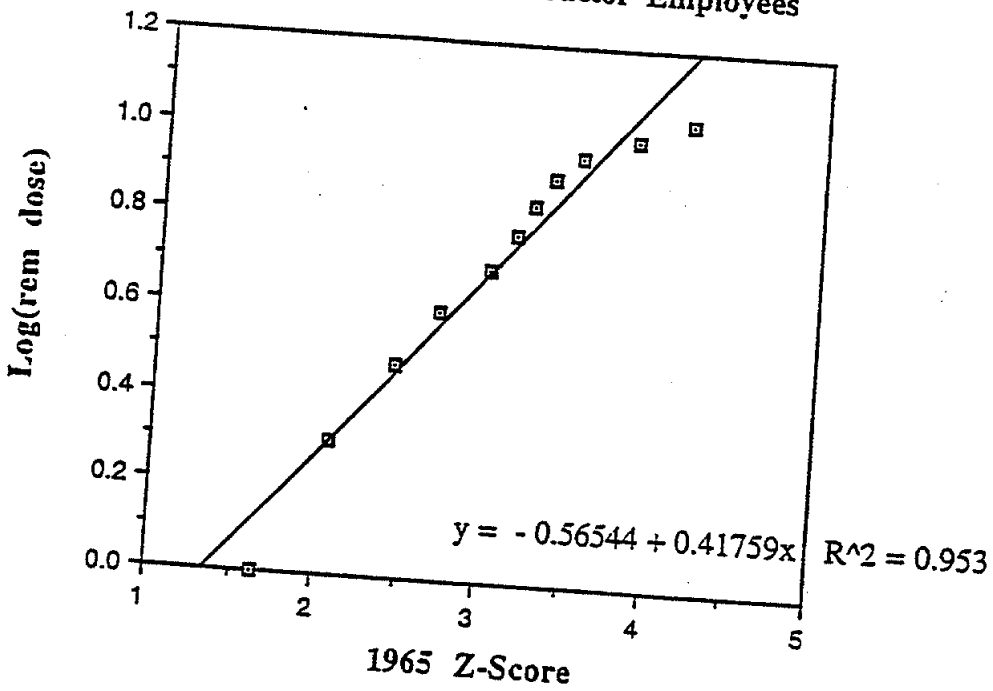


Figure 5

1968--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

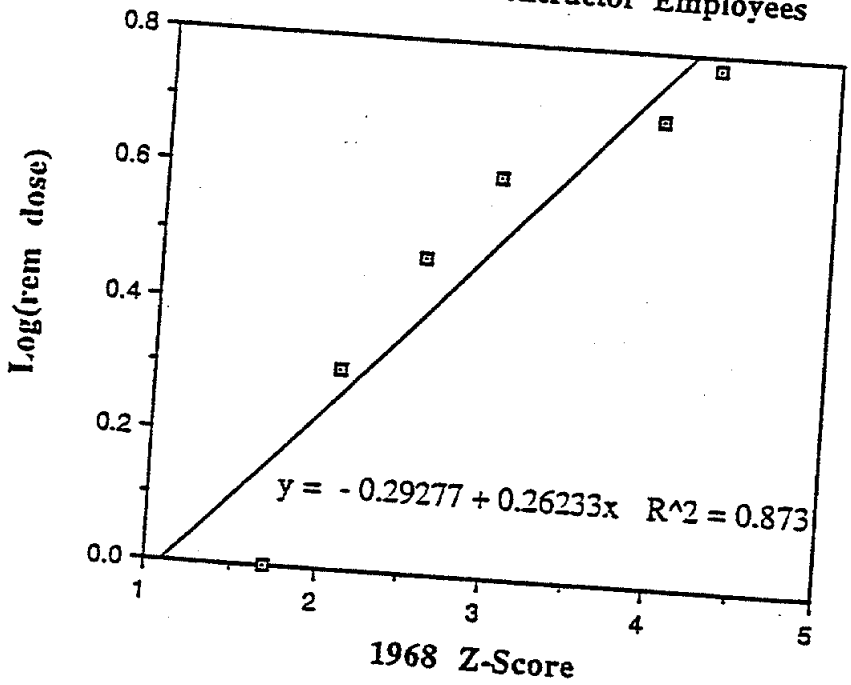


Figure 6

1971--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

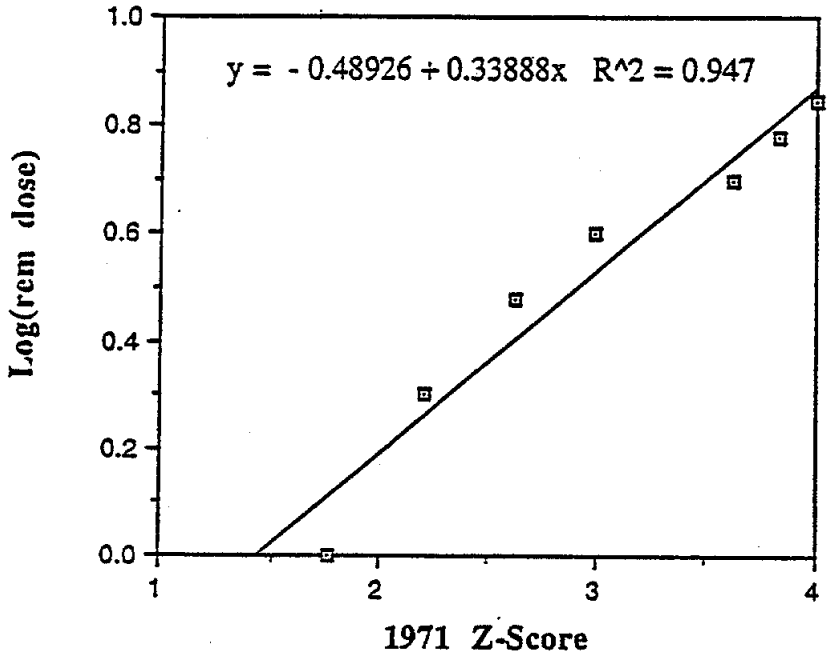


Figure 7

1974--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

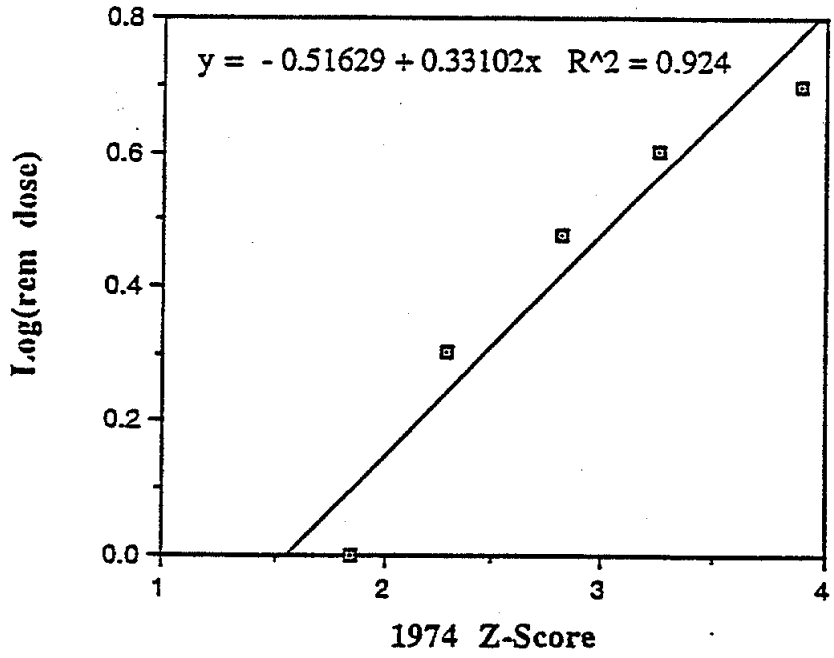


Figure 8

1977--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

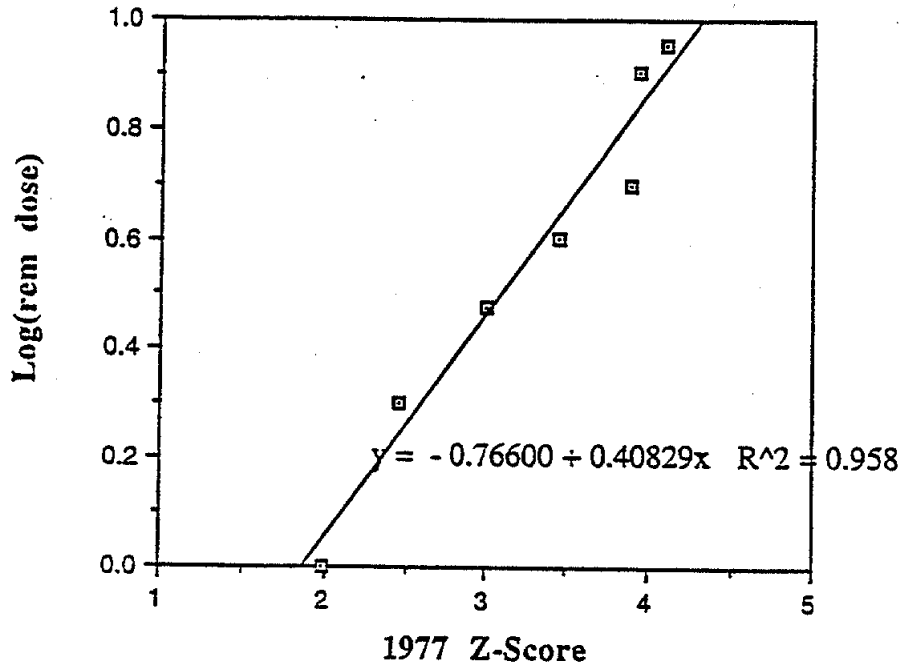


Figure 9

1980--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

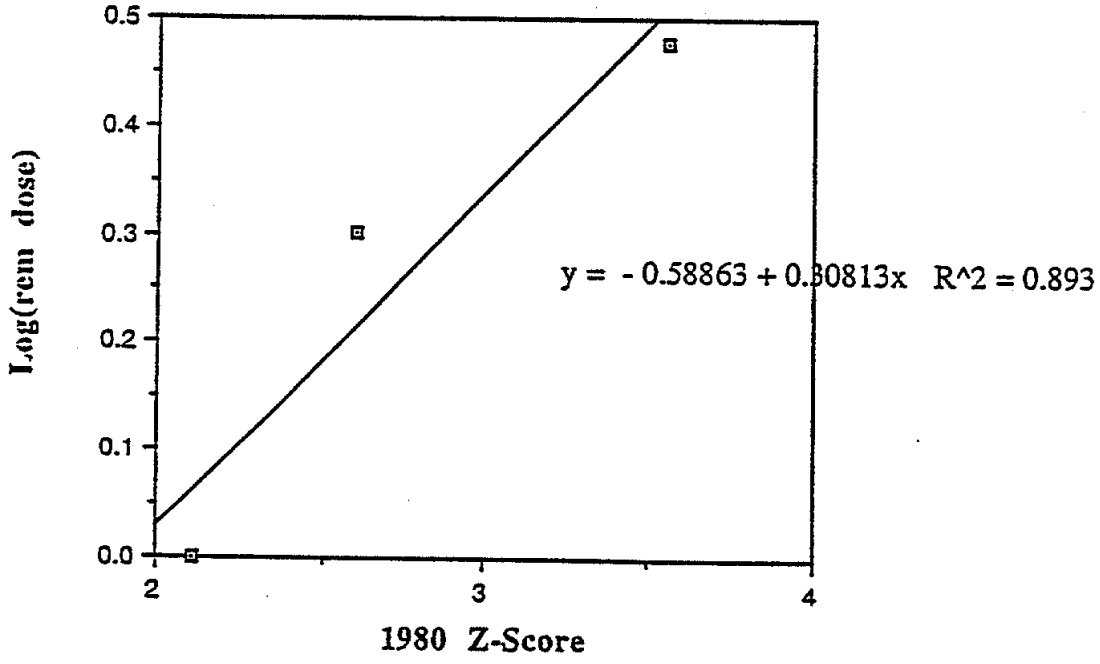


Figure 10

1983--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

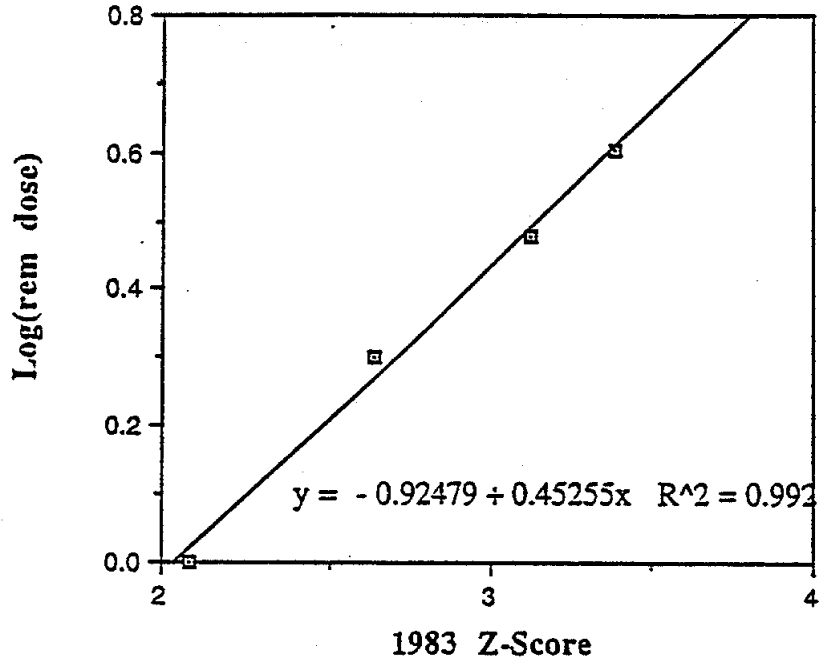


Figure 11

1986--Lognormal Plot of Penetrating Ionizing Radiation Exposures for DOE and Contractor Employees

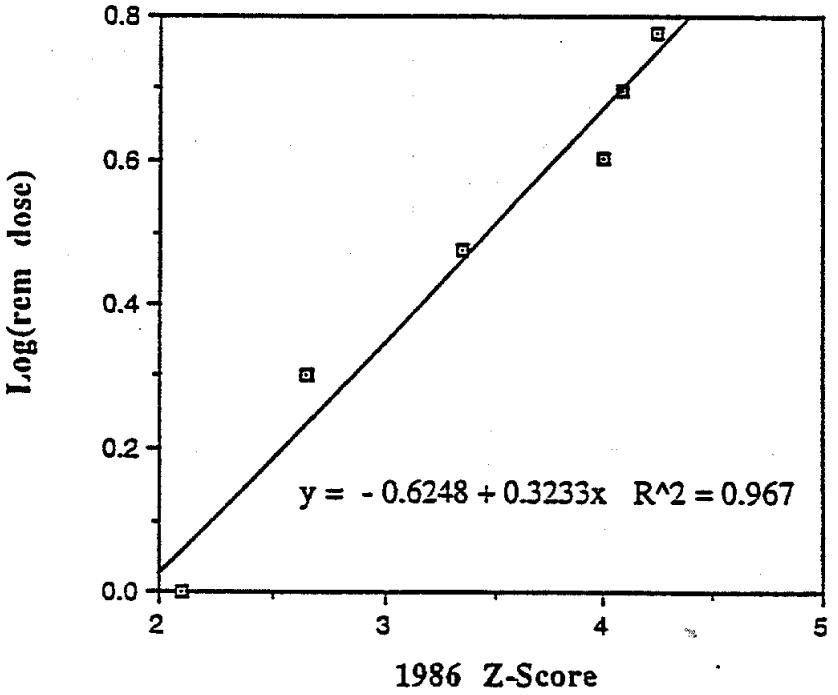
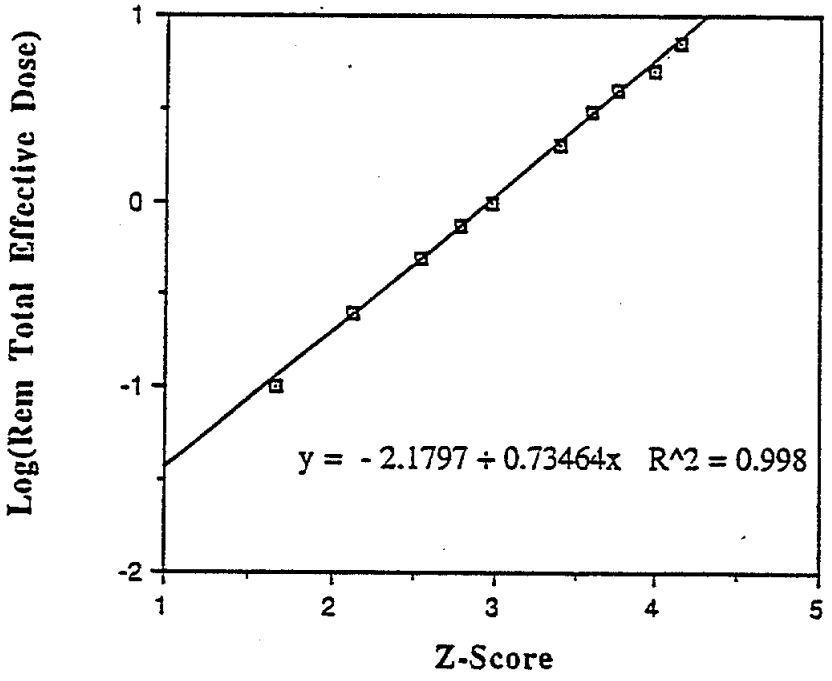


Figure 12

1992--Lognormal Plot of Total Equivalent Exposures for DOE and Contractor Employees



Figures 4-12 indicate that for these data sets, with the possible exception of 1992, the fit is reasonable, but there are systematic tendencies to depart from the expected lognormal distribution in particular ways. For all of the graphs through 1986 the slope of a line drawn between the first two points (corresponding to 1 rem and 2 rem) is steeper than the line for the overall population distribution. A steeper line corresponds to more variability. This is an indication that if one were to use the simple regression lines in these figures to estimate the full distribution of worker exposures, that would very likely overestimate the exposures experienced by lower- exposed workers (below 1 rem per year). To reduce this problem, I have estimated exposures in the below 1 rem region by using the steeper lines drawn between the 1 and 2 rem data points. For the region above 2 rem, I have further pruned the data used by eliminating data points based on fewer than 10 workers in any one year (out of approximately 100,000 per year total monitored).[14]

Table 6 summarizes estimates of total collective person-rem delivered for 1965-1992. For the years 1982-1992 I have taken the collective dose estimates directly from data summarized in

[14]This does not mean that I have eliminated the exposures accrued by the highest exposed workers. Only that in determining the overall slope and intercept of the lognormal regression line I have not given equal weight to the relatively unreliable data based on very small numbers of workers at the highest end of the distribution of exposures.

Table 6
Estimates of Total Collective Dose Delivered to DOE and Contractor Workers, 1965-1992

Year	Total collective person-rem*
1965	3.13×10^4
1966	2.79×10^4
1967	2.45×10^4
1968	2.11×10^4
1969	2.03×10^4
1970	1.95×10^4
1971	1.87×10^4
1972	1.70×10^4
1973	1.53×10^4
1974	1.36×10^4
1975	1.39×10^4
1976	1.41×10^4
1977	1.44×10^4
1978	1.35×10^4
1979	1.25×10^4
1980	1.16×10^4
1981	1.04×10^4
1982	7.88×10^3
1983	8.16×10^3
1984	8.42×10^3
1985	8.68×10^3
1986	8.26×10^3
1987	6.35×10^3
1988	3.93×10^3
1989	3.38×10^3
1990	3.33×10^3
1991	2.94×10^3
1992	2.68×10^3
Sum, 1965-92	3.64×10^5

* Data for 1982-1992 taken from Table 4.7 of the draft 1992 Annual Radiation Exposure Report; data for 1965-1981 calculated by distributional analyses based on data in Table 4.2 of that report (see Figures 4-12).

Table 4.7 of the annual dosimetry report; for years before 1982, the analysis is based on the distributional analysis (Figures 4-12).

One other point related to dosimetry is worth mentioning here. The data for 1965-1986 reflect only "penetrating" radiation, whereas the 1992 data shown reflect total equivalent dosage (including contributions from internal radionuclides and other sources that are not fully reflected in the earlier data for "penetrating" ionizing radiation.) A very limited comparison of data at the high end of the exposure distribution (1-2 rem) for 1992 suggests that there may be about a two-fold difference between the two dose metrics for the most highly exposed people. A discussion with a knowledgeable DOE health physicist[15] indicates that the ratio between total exposures and the monitored "penetrating" doses is likely to be much less than 2 for the bulk of employees with smaller exposures.

2.2.2 Data on Hanford Exposures for 1944-1989

As part of a long term mortality study, Buschbom and Gilbert (1993)[16] have extensively documented the exposures of 44,156 workers first employed at the facility between 1944 and 1978. The collective dose delivered in various years to the 37,012 workers with at least one annual dose record are presented in Table 7 and Figure 13. The data show a pronounced peak of collective exposure in the middle-1960's. Over 90% of the recorded exposure occurred between 1952-1982; 58% occurred between 1958-1972.

These Hanford data also include a detailed characterization of the ages at which the radiation dose was delivered. It can be seen in Figure 14 that most exposure occurs relatively evenly in the prime work years between the ages of about 27 and 55.

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[15]B. Brooks, Office of Epidemiology and Health Surveillance, personal communication, April, 1995.
[16]See above, note 7.

Table 7

Annual Recorded Dosage Delivered to Hanford Workers, 1944-1989

Year	Workers Monitored	Total Dose (person-rem)	% Total Dose in Year
1944	3495	207.2	0.24
1945	5826	1309.8	1.50
1946	4195	583.8	0.67
1947	5349	420.1	0.48
1948	6923	329.1	0.38
1949	6665	436.2	0.50
1950	6499	584	0.67
1951	8090	770.4	0.88
1952	8457	1193.5	1.36
1953	8108	1772.9	2.03
1954	8337	1566.4	1.79
1955	9055	1918.3	2.19
1956	9406	1943.5	2.22
1957	9463	1951.2	2.23
1958	8848	2613.3	2.99
1959	8115	2211.3	2.53
1960	8308	2629.9	3.00
1961	8398	3204.8	3.66
1962	8404	4098.9	4.68
1963	8669	3948.8	4.51
1964	8969	4605.8	5.26
1965	8878	6182.4	7.06
1966	8660	4062	4.64
1967	8731	3556.7	4.06
1968	8634	3629.4	4.15
1969	8315	2961	3.38
1970	7967	2496.8	2.85
1971	7618	2293.3	2.62
1972	6981	2579.7	2.95
1973	7000	2120.9	2.42
1974	7919	2317.2	2.65
1975	8432	2487.1	2.84
1976	9577	2082.5	2.38
1977	10778	2254.8	2.58
1978	11818	1828.8	2.09
1979	10775	1657.9	1.89
1980	9666	1254.1	1.43
1981	8934	873.9	1.00
1982	8446	1030.7	1.18
1983	8175	771	0.88
1984	7972	685.4	0.78
1985	7699	642.7	0.73
1986	7387	530.1	0.61
1987	6983	533.2	0.61
1988	6406	169.1	0.19
1989	5700	222.6	0.25
Total	369030	87,522	

Figure 13

Collective Dose Delivered In Various Years to 37,009 Exposed Hanford Workers Who Were First Employed Between 1944 and 1978--Data of Buschbom and Gilbert, 1993

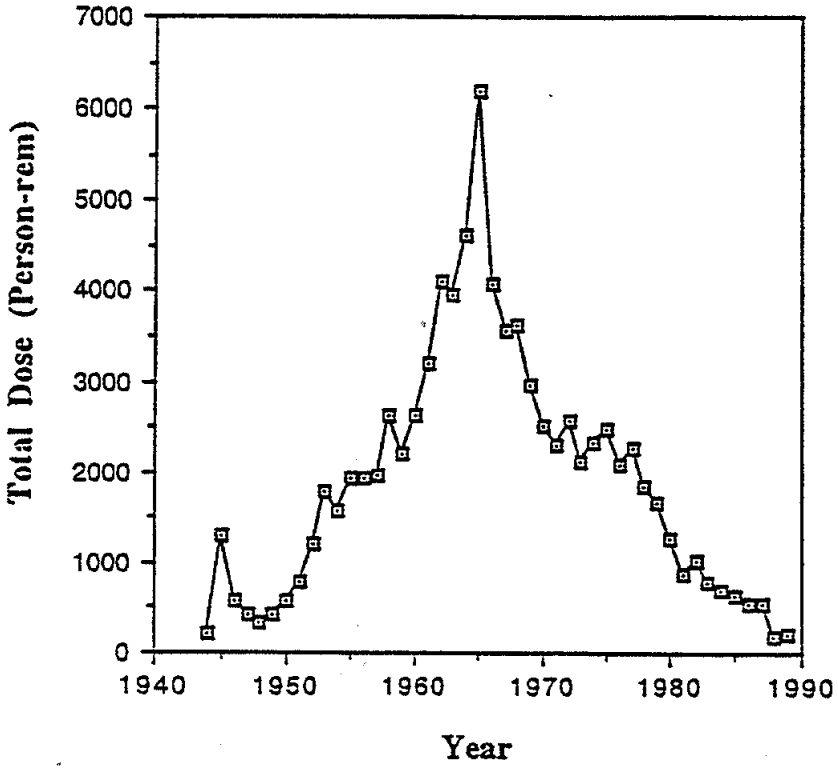
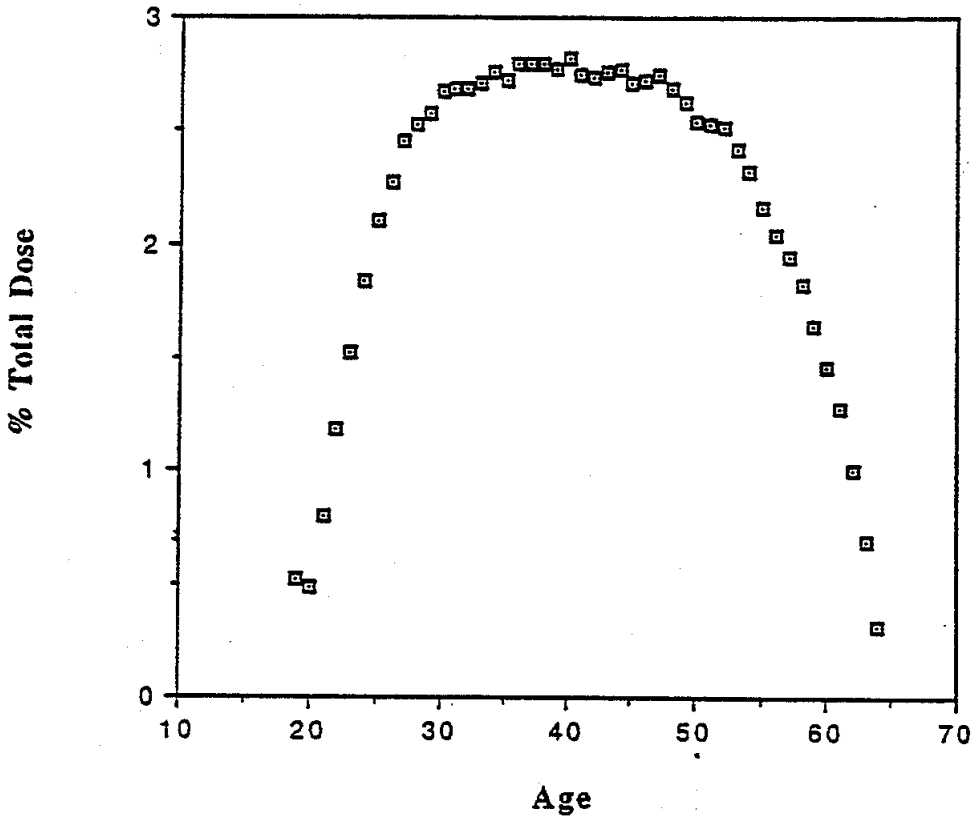


Figure 14

Age Distribution of % Total Cumulative Dosage Delivered to Hanford Workers, 1944-1989



2.2.3 Estimates of Aggregate Radiation Doses Delivered for DOE and Contractor Employees as a Whole, By Year and Age, 1944-1992

Assuming that the dose delivered in the studied Hanford population has been a roughly consistent fraction of overall DOE exposures over the years, the Hanford data can be used to make an approximate projection of the overall DOE-wide collective dose delivered between 1944 and 1992. We first note that between 1965 and 1989, the studied Hanford workers received about 14% of the total DOE-wide collective dose:

Hanford 1965-1989 person-rem	DOE 1965-1989 person-rem	%Hanford/DOE
49,200	355,000	13.9

The result is similar if the analysis is restricted to the period between 1965-1978, when all eligible Hanford hires should be included in the study group:

Hanford 1965-1978 person-rem	DOE 1965-1978 person-rem	%Hanford/DOE
40,900	265,000	15.4

If we assume this same relationship holds approximately for the 1944-1964 period, we project

Recorded Hanford 1944-1964 person-rem	Estimated DOE 1944-1964 person-rem
38,300	276,000

This leads to a projection that DOE and contractor workers as a whole probably received about 640,000 person-rem between 1944 and 1992.

2.3 Expected Loss of the Inventory of Cumulative 1944-1992 Dose with Past and Expected Future Mortality, 1970-2025

As a prelude to the calculation of the times of appearance of the cancers resulting from radiation exposure, it is of interest to know how the "inventory" of overall accumulated radiation dosage changes over the years. Inventory accumulates as more dosage is received by the worker population, but it is also lost as the workers who received some of the radiation die. (The mortality is of course from all causes, not just the small number of radiation-induced cancers).

General mortality is a strong function of age. Therefore, using the age-at exposure information from the Hanford study (Figure 14) I created a year-of-exposure by age-at-exposure matrix. For single years in each dimension I then applied the general mortality rates listed in Table

8.[17] These mortality rates were derived from non-smoker data for the mid-1960's. I chose to apply non-smoker mortality rates as a very approximate recognition of the fact that worker populations have lower mortality than the general population.

Given these assumptions, Table 9 shows the expected changes in the "inventory" of cumulative radiation exposure in surviving current and former workers over time through the year 2025. (The data for 1970 through 1990 in this table reflect the net effects of both accumulation and loss of exposure with mortality.) It can be seen that as of now (1995) about two thirds of all the dosage delivered in the 1944-1992 period is expected to occur in the population of surviving workers. Within 15 years from now (2010), however, only half of that remaining fraction (34% of the original dose delivered) will still be carried by living people. Ten years after that (2020), only 16% will remain, and by 2025 only 10% will remain. Clearly any policy measures that are considered necessary to deal with the effects of these exposures will need to be put into place in the immediate future in order to be effective.

[17]Most of the data come originally from Lew, E. A., and Garfinkel, L. "Differences in mortality and longevity by sex, smoking habits and health status." Trans. Soc. Actuaries 39: 107-130 (1987). The data were extended to additional ages and otherwise adapted in Silver, K., Harris, D., and Attfield, M. "Methodology for Quantitative Assessment of Risks From Chronic Respiratory Damage: Lung Function Decline and Associated Mortality from Coal Dust." M. I. T. Center for Technology, Policy and Industrial Development, Report No. CTPID 90-9, (1991).

Table 8

Assumed Mortality Rates as a Function Of Age

Age	Non-Smoker Mortality Risk Per Year	% of Starting Population Alive at End of Year
20	0.00158	99.842
21	0.00166	99.676
22	0.0017	99.507
23	0.00169	99.339
24	0.00166	99.174
25	0.0016	99.015
26	0.00155	98.862
27	0.00153	98.710
28	0.00156	98.556
29	0.00162	98.397
30	0.00169	98.230
31	0.00171	98.062
32	0.00172	97.894
33	0.00172	97.726
34	0.00175	97.555
35	0.00173	97.387
36	0.00157	97.234
37	0.00167	97.071
38	0.00170	96.906
39	0.00178	96.734
40	0.00187	96.552
41	0.00198	96.362
42	0.00211	96.159
43	0.00222	95.945
44	0.00236	95.718
45	0.00253	95.476
46	0.00272	95.216
47	0.00296	94.934
48	0.00330	94.622
49	0.00367	94.274
50	0.00408	93.889
51	0.00454	93.463
52	0.00505	92.991
53	0.00568	92.463
54	0.00636	91.875
55	0.00709	91.224
56	0.00786	90.506
57	0.00874	89.716
58	0.00974	88.842
59	0.01082	87.881
60	0.01200	86.827
61	0.01323	85.678
62	0.0145	84.435
63	0.0222	82.559
64	0.0174	81.121
65	0.0189	79.585
66	0.0212	77.897
67	0.0234	76.076
68	0.0256	74.123
69	0.0279	72.053
70	0.0302	69.877
71	0.0312	67.697
72	0.0322	65.518

Table 8, Continued

Age	Non-Smoker Mortality Risk Per Year	% of Starting Population Alive at End of Year
73	0.0338	63.302
74	0.0353	61.065
75	0.0368	58.818
76	0.0411	56.400
77	0.0454	53.839
78	0.0495	51.171
79	0.0537	48.425
80	0.0578	45.626
81*	0.222	35.499
82	0.387	21.768
83	0.556	9.653
84	0.728	2.624
85	0.98	0.053

*Data for ages over 80 were adjusted upward to produce complete essentially mortality by age 86.

Table 9

Expected Changes in the "Inventory" of Collective Radiation Dosage in Surviving Workers, 1970-2025

	Dose Surviving to Year	% Dose Surviving
Total Delivered 1944-1992	640,000	100
1970	400,000	62
1975	460,000	72
1980	500,000	78
1985	500,000	78
1990	480,000	75
1995	420,000	66
2000	360,000	56
2005	290,000	45
2010	220,000	34
2015	160,000	24
2020	100,000	16
2025	63,000	10

3. Doubling Doses for Radiation-Induced Cancer, and Expected Lifetime Excess Cancer Risk in Current and Former DOE and Contractor Workers

3.1 Basic Dose Response Relationships for Radiation-Induced Cancer--Why Do We Expect Low Dose Linearity?

Often the assumption of low dose linearity is presented in the context of its original use for cancer risk assessments over 20 years ago--as a "conservative" assumption--chosen in part for simplicity and in part because it was considered unlikely to understate risk. I think there is now a much stronger argument for its use, and that its status should be changed from a "conservative" assumption to a "central tendency" or "best estimate" assumption for carcinogens that act by primary genetic mechanisms. Ionizing radiation is a paradigmatic case in point.[18] Although there are still some remaining adherents to older "threshold" theories,[19] and even some who advance "hormesis" theories (under which low doses of radiation are proposed to have positive net benefit, rather than harm),[20] I believe that our mechanistic understanding of carcinogenesis had progressed to the point where such possibilities are highly doubtful. All recent national and international consensus summaries of radiation risks--which are the sources of the risk estimates presented below--use models that incorporate low dose linearity for all radiation-induced cancers. (As will

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[18]Hattis, D., and Smith, J., "What's Wrong with Quantitative Risk Assessment." in Quantitative Risk Assessment, J. M. Humber and R. F. Almeder, eds., Biomedical Ethics Reviews: 1986, Humana Press, Clifton, New Jersey, 1987, pp. 57-105.

[19]For example Raabe has used projections of the time distribution of bone sarcomas induced by very high doses of radionuclides to advance the notion that cancers produced at low dose rates should occur only at times longer than the normal lifespan, creating a "quasi-threshold". [Raabe, O. G., Rosenblatt L. S., and Schlenker, R. A. "Interspecies Scaling Of Risk For Radiation-Induced Bone Cancer. Int J Radiat Biol 57: 1047-1061 (1990); White R. G., Raabe, O. G., Culbertson, M. R., Parks, N. J., Samuels, S. J., and Rosenblatt, L. S. "Bone Sarcoma Characteristics And Distribution In Beagles Fed Strontium-90." Radiation Research; 136: 178-189 (1993).] Similar arguments have been advanced in the field of chemical carcinogenesis based on similar observations of a power law dependence of time to tumor on dose rates of various nitrosamine carcinogens [Druckery, H. "Quantitative aspects in chemical carcinogenesis. In Potential Carcinogenic Hazards from Drugs, (Truhaut, R., ed.) New York: Springer-Verlag, 1967); Peto, R., Gray, R., Brantom, P., and Grasso. P. "Nitrosamine Carcinogenesis in 5120 Rodents: Chronic Administration of Sixteen Different Concentrations of NDEA, NDMA, NPYR, and NPIP in the Water of 4440 Inbred Rats, with Parallel Studies on NDEA Alone of the Effect of Age on Starting (2, 6, or 20 weeks) and of Species (Rats, Mice, or Hamsters)." IARC Sci. Publ. 57: 627-655 (1986)]. Travis and colleagues have analyzed the latter data and shown that the power law dependence of dose rate is not incompatible with the Moolgavkar two-stage carcinogenesis theory--indeed it appears that the value of the time power is closely related to the power of dose seen in the relationship between carcinogen dose and the apparent rate of proliferation of relevant initiated cells. [Travis, C. C., and Birkner, P. D. "Druckery slope controlled by mitotic rate of enzymatically-altered foci." J Theor Biol 149: 217-227 (1991); Travis, C. C., McClain, T. W., and Birkner, P. D. "Diethylnitrosamine-induced hepatocarcinogenesis in rats: a theoretical study." Toxicol Appl Pharmacol: 109: 289-304 (1991).] Such proliferative stimulation would not be expected to extend to very low dosage, linearizing any effect of this process on tumor risk at low doses.

[20] Mine, M., Okumura, Y., Ichimaru, M., Nakamura, T., and Kondo, S. "Apparently Beneficial Effect Of Low To Intermediate Doses Of A-Bomb Radiation On Human Lifespan." Int J Radiat Biol. 58: 1035-1044 (1990); Balaram, P., and Mani, K. S. "Low dose radiation--a curse or a boon?" Natl Med J India: 7: 169-172 (1994).

be seen, however, there is considerable remaining uncertainty about appropriate low dose slopes for the dose response relationships for specific cancers in relation to specific types of radiation).

The last two decades have seen important advances in our understanding of the fundamental mechanisms of carcinogenesis. We can now be very confident that with few known exceptions, tumors arise as a result of a series of changes or rearrangements of information coded in DNA within single cells or cell lines[21]. These changes can be induced either by DNA-reactive chemicals, radiation, some viruses, or the free-radical byproducts of the normal use of oxygen in the body. With the identification of "oncogenes," and tumor suppressor genes, we are now getting some detailed molecular characterization of what some of the resulting DNA changes are.[22]

The fundamental multiple mutation mechanism of radiation-induced carcinogenesis has strong implications for the likely relationship between delivered dose and incremental cancer risk. Basically, all pharmacokinetic process, such as DNA repair, must proceed linearly at relatively low dose rates where there is negligible saturation of the enzymes involved.[23] Because of this, and because the mutations induced by radiation add to other mutations that cause an appreciable "background" cancer risk in the exposed human population, the basic expectation is that incremental risk is a linear function of dose at low dose rates–although in some cases changes in the efficiency of DNA repair and other processes at higher dose rates may yield an steeper increase in risk as a function of dose at those higher dose rates.

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[21]Vogel, F. and A. G. Motulsky (1979) Human Genetics--Problems and Approaches Springer-Verlag, New York. pp. 326-329; Fialkow, P. J. (1977) "Clonal origin and stem cell evolution of human tumors," In Genetics of Human Cancer (Mulvihill, J.J., et al., eds.) 439. Raven, New York; Knudson, A. G. (1973) "Mutation and Human Cancer," Adv. Cancer Res. 17, 317-352; Knudson, A. G. (1977). "Genetics and Etiology of Human Cancer," Adv. Hum. Genet. 8, 1-66.

[22]Weinberg, R. A. "The molecular basis of oncogenes and tumor suppressor genes." Ann N Y Acad Sci 758:331-338 (1995); Weinberg, R. A. "Oncogenes and tumor suppressor genes." CA Cancer J Clin 44: 160-170 (1994); Yunis, J. J. (1983) "The chromosomal basis of human neoplasia," Science 221, 227-236; Hoel, D. G. (1985) "Epidemiology and the Inference of Cancer Mechanisms. Natl. Cancer Inst. Monogr. 67, 199-203; Fischinger P. J., and V. T. DeVita, Jr. (1984), "Governance of science at the National Cancer Institute: Perceptions and opportunities in oncogene research," Cancer Res 44, 4693-4696; Modali, R., and S. S. Yang, (1986), "Specificity of Aflatoxin B1 Banding on Human Proto-Oncogene Nucleotide Sequence." In Monitoring of Occupational Genotoxicants Alan R. Liss, Inc.

[23]The basic reason for this is that at low doses the rates of the transport and transformation processes that lead to DNA damage and repair directly depend on the number of collisions between molecules of an "input" chemical (or activated intermediate or DNA adduct) and a resident cellular reactant (or hole in a membrane or repair enzyme molecule). At low doses the number of resident cellular reactant molecules does not change appreciably as a function of the concentration of the "input". Therefore the number of relevant collisions and the rates of the reactions and side reactions in the causal sequence at low dosage must be direct linear functions of the amounts of input chemical and its activated derivatives. Some finite fraction of the ultimate DNA lesions must escape repair before the next cell replication so long as the cells affected have a non-zero turnover rate, there are a finite number of repair enzyme molecules, and the repair molecules operate at a finite rate. [Hanis. D., "Pharmacokinetic Principles for Dose Rate Extrapolation of Carcinogenic Risk from Genetically Active Agents." Risk Analysis, Vol. 10, pp. 303-316, 1990.]

3.2 Estimates of the Potency of Low Dose Rate Radiation Exposures for Inducing Cancers of Various Types

A variety of national and international expert committees have used the latest estimates of dose and cancer incidence for the Japanese atomic bomb survivors and various medical radiation treatments to arrive at consensus estimates of the potency of different forms of ionizing radiation for causing different cancers. The results differ somewhat depending on:

- Risk modeling approaches--"absolute" vs "relative" risk models;[24] assumptions about minimal latency periods for different cancers, and approaches for analyzing the distribution of cancer occurrence as a function of the age at exposure; and the elapsed time since exposure occurred.

- Conventions for aggregating cancer sites--for example data can be analyzed as all digestive system cancers (e.g, BEIR V) or by esophagus, stomach, intestine, colon, etc.

- The choice of whether to incorporate a "dose and dose rate effectiveness factor" (DDREF)--a reduction of the potency estimated from studies done after exposure at high dose rates (e.g., atomic bomb survivors) to reflect a greater efficiency of DNA repair, etc. when dose is administered over a prolonged period, as is typically expected for long term cumulative worker exposures. Conventionally, this is given a value of 2, applied uniformly to all sites except those (such has breast) where the primary data come from populations exposed to relatively low doses or dose rates (acute exposures below about 10 rem).

Table 10 shows the most recent official EPA conclusions for ionizing radiation cancer potencies for exposure of the general population at low dose rates.[25] The EPA mortality estimates were derived by taking the geometric mean of potency estimates from previous ICRP, NIH, and NRC risk models[26] applied to a stationary population with 1980 vital statistics, and then applying a downward adjustment of two-fold for sites other than the breast. The morbidity estimates (numbers of cases, rather than deaths) were derived by dividing the mortality rates by the lethality fractions shown in Table 11 for various sites. For background, Table 12 compares the indicated distribution of radiogenic cancers among cancer sites with the general population distribution of cancer morbidity and mortality among sites.[27]

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[24]Absolute risk models analyze results in terms of the raw numbers of excess cancers that occur as a function of exposure level; relative risk models analyze the multiplicative increase in some baseline risk as a function of exposure.

[25]Puskin, J. S., and Nelson, C. B. "Estimates of Radiogenic Cancer Risks" Health Physics 69:93-101 (July, 1995).

[26]National Institutes of Health, "Report of the National Institutes of Health Ad Hoc Working Group to Develop Radioepidemiolgical Tables." Washington. D.C.: U.S. Government Printing Office; NIH Publication 85-2748;, (1995); International Commission on Radiological Protection, 1990. "Recommendations of the International Commission on Radiological Protection." Oxford: Pergamon Press; ICRP Publication 60; Ann. ICRP 21 (1991).

[27]The general population mortality data for various sites are from 1990 and 1991 U.S. vital statistics compilations. Morbidity estimates are for 1995 from the American Cancer Society, "Cancer Facts and Figures--1995", American Cancer Society, Inc., Atlanta. 1995.

Table 10

Official EPA Estimates of Low Dose Rate Cancer Risks for Ionizing Radiation Exposure to the General Population (Puskin and Nelson, 1995)

	Mortality (10^{-4} per Gy)	Morbidity (10^{-4} per Gy)	% Radiogenic Ca Deaths	% Radiogenic Cancer Cases
Colon/Intestine	98.2	178.5	19.3	23.5
Lung	71.6	75.4	14.1	9.9
Leukemia (Acute and Non-Lymphocytic--approx. 2/3 of all leukemias)	49.6	50.1	9.7	6.6
Breast	46.2	92.5	9.1	12.2
Stomach	44.4	49.3	8.7	6.5
Bladder	24.9	49.7	4.9	6.5
Ovary	16.6	23.7	3.3	3.1
Liver	15.0	15.8	2.9	2.1
Esophagus	9.0	9.5	1.8	1.2
Kidney	5.5	8.4	1.1	1.1
Thyroid	3.2	32.1	0.6	4.2
Skin (presumably based on fatal cancers only, overall morbidity for nonfatal cancers would be about 500 times greater)	1.0	1.0	0.2	0.1
Bone	0.9	1.3	0.2	0.2
Remainder	123.1	173.4	24.2	22.8
Total	509.1*	760.6*	100.0	100.0

* These overall estimates are for the general population (all ages included). For occupational exposures (assumed to be delivered at a uniform rate between age 18 and 65 years) the mortality and morbidity incidence rates are given as 394 and 567 X 10^{-4} per Gray respectiveiy.

Table 11

Estimated Lethality Fractions for Different Cancer Sites (ICRP 1991[28], as Quoted by Puskin and Nelson, 1995)

Cancer site	Lethality fraction
Esophagus	0.95
Stomach	0.90
Colon/Intestine	0.55
Liver	0.95
Lung	0.95
Bone	0.70
Skin	0.002 (for all skin cancers, not just fatal types)
Breast	0.50
Ovary	0.70
Bladder	0.50
Kidney	0.65
Thyroid	0.10
Leukemia (acute)	0.99
Remainder	0.71

[28]International Commission on Radiological Protection. 1990. Recommendations of the International Commission on Radiological Protection. Oxford: Pergamon Press: ICRP Publication 60; Ann. ICRP 21 (1991), Tables B-19 and B-20.

Table 12

Comparison of the Distribution of Cancer Mortality and Morbidity Among Sites for Radiogenic vs General U.S. "Background" Cancers

	Estimated Total U.S. Deaths, 1995	Estimated Total U.S. Cases, 1995	Estimated % U.S. Deaths from All Causes	% Radiogenic Ca Deaths
Colon/Intestine	56420	142800	2.58	19.3
Lung	157400	169900	7.19	14.1
Leukemia (Acute and Non-Lymphocytic--approx. 2/3 of all leukemias)	12445	12571	0.57	9.7
Breast	46240	183400	2.11	9.1
Stomach	14700	22800	0.67	8.7
Bladder	11200	50500	0.51	4.9
Ovary	14500	26600	0.66	3.3
Liver	14200	18500	0.65	2.9
Esophagus	10900	12100	0.50	1.8
Kidney	11700	28800	0.53	1.1
Thyroid	1120	13900	0.05	0.6
Skin	6420	Not estimated	0.29	0.2
Bone	1280	2070	0.06	0.2
Remainder	188475	568059	8.61	24.2
Total	547000	1252000	25.00	100.0

Overall, radiation exposures are expected to be more potent in inducing cancers in younger people than in older people. Table 13 shows EPA relative risk coefficients (per Gray) for exposures in various occupational age ranges for the sites where they have used relative risk models (for some other sites, absolute risk models were used).

Table 13

EPA Relative Risk Coefficients[29] (Per Gray = 100 Rad) for Exposure at Various Ages

	20-29	30-39	40+
Esophagus	0.252	0.289	0.326
Stomach	1.905	0.288	0.252
Colon	0.281	0.428	0.090
Liver	1.345	1.345	1.345
Lung	0.045	0.134	0.179
Leukemia (Ave 3-20 yrs after exposure)	3.268	2.341	1.458
Bladder	1.074	1.054	0.964
Kidney	0.391	0.391	0.391
Residual	0.174	0.175	0.185

As noted in the footnote to Table 10, the general observation of lower potency at older ages at exposure for most sites (but not all sites--see, for example, lung) reduces the expected number of total cancers per unit of low dose occupational exposure, relative to general population exposure, by about 20% --from about 510 deaths and 760 cases per million person rem for the general population to 390 deaths and 570 cancer cases per million person rem for workers.[30] Combining these overall potency estimates with our earlier overall cumulative dose estimate of 640,000 person-rem, we arrive at an expectation that there will eventually be about 250 cancer deaths and 360 total cancer cases (the 250 fatalities plus 100 cancer cases who survive) as the result of the occupational exposure of DOE and contractor employees to penetrating radiation.

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[29]For example, exposure of 20-29 year olds to 1 Gray is expected to increase their relative risk (after a 10 year lag) by 25% for cancer of the esophagus, by 190% over baseline (to nearly 3 times the basal level) for cancer of the stomach.

[30]Mettler and Upton give similar worker risk estimates of 400 fatal cancers and 480 total cancers per million person-rem based on reference 28 above [Mettler, F. A., and Upton, A. C. "Medical Effects of Ionizing Radiation" 2nd Edition, Philadelphia: W.B. Saunders Company, 1995, p. 85.

In my opinion a prudent policy planner will want to consider these estimates as the lower bounds of an approximately 2-3 fold credible central range of likely overall cancer risk (250-500 cancer deaths; 360-1000 total cancer cases). This is because:

- With the possible exception of tritium exposures, long term exposures from absorbed radionuclides appear to be reflected incompletely in the past records of "penetrating" doses. DOE policies appear to have been changed to require reporting of "total effective dose equivalents" (including an estimate of internal dose for the current year) only since 1990. Most recently, the reporting definition has been changed again to "committed effective dose equivalents" which evidently include an estimate of the total dose that is expected to be delivered to workers over the next 50 years (if they survive) from radionuclide dosage absorbed in the current year. The pre-1990 data which comprise the great bulk of the cumulative dose delivered to workers, do not reflect these expanded definitions.

- Older methods of measuring even the penetrating dose were not sensitive to some forms of radiation (e.g., neutrons before 1972; low energy gamma radiation before 1957 at Hanford), although measurement of the predominant form of ionizing radiation--high energy gamma--was evidently fairly complete.[31] Additionally, the monitoring was done primarily for compliance purposes and some workers who were thought to have relatively small exposures were not monitored. A study of 1943-1956 measurements of external dosage at Oak Ridge National Laboratory resulted in a 50% upward adjustment in the estimate of total collective dose for over 7000 workers at that facility during that time period (from a mean of 1.08 to 1.63 rem/worker). A similar analysis of dosage for nearly 8500 workers at the nearby Y-12 facility from 1947-1960 led to an overall 80% upward revision of their collective dose (from a mean of 0.5 to 0.9 rem/worker).[32] On the other hand, a paper in press by Gilbert et al.[33] points out that total penetrating dose as reported may tend to overstate the dosage delivered to various organs, depending on the geometry of the placement of the dosimeter and other factors. The overall upward bias was estimated at 1-27% for "deep dose", 41-75% for red bone marrow dose, and 6-33% for lung dose in various time periods between 1944 and 1989.

- Classical epidemiological methods have a bias toward underestimation of the slopes of dose response relationships where there is uncertainty in the estimation of individual dose.[34,35] If estimates of these uncertainties are made, it is possible to correct for this bias, but such corrections are very unusual in epidemiology, and the international consensus estimates of radiation potency do not include an allowance for this effect.[36]

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[31]Gilbert, E. S., and Fix, J. J. "Accounting for Bias in Dose Estimates in Analyses of Data from Nuclear Worker Mortality Studies." Health Physics 68: 650-660 (1995).

[32]Watkins, J. P., Cragle, D. L., Frome, E. L., West, C. M., Crawford-Brown, D. J., and Tankersley, W. G. "Adjusting External Doses from the ORNL and Y-12 Facilities for the Oak Ridge Nuclear Facilities Mortality Study," Oak Ridge Institute for Science and Education, Report No. ORISE 94/G-34, 1994,

[33]Gilbert, E. S., Fix, J. J., and Baumgarner, W. V. "An Approach to Evaluating Bias and Uncertainty in Estimates of External Dose from Personal Dosimeters" Health Physics, 1995 in press.

[34]Copeland, K.T., Checkoway, H., McMichael, A. J., and Holbrook, R. H. "Bias due to misclassification in the estimation of relative risk. Akm . J. Epidemiol, 105:488-495 (1987).

[35]Shy, C. M., Kleinbaum, D. G., and Morgenstern, H. "The effect of misclassification of exposure status in epidemiological studies of air pollution health effects. Bull. N.Y. Acad Med. 54:1155-1165 (1978).

[36]Additionally, there is some suggestion in the literature that the epidemiological results may tend to become more positive as additional time passes and longer lag periods are allowed in epidemiological analyses of relative risks.

- It is far from obvious that the two-fold Dose and Dose Rate Effectiveness Factor is appropriate (and uniform in magnitude) as applied to all cancers other than breast and leukemia. Surely if DNA repair saturation is the underlying mechanism, there is likely to be a different amount of high dose saturation (and therefore high-to-low dose change in dose response slope) for different tissues. The very fact that a uniform factor is applied indicates that specific data relevant for different cancer sites are probably not available, and the overall two-fold reduction in potency due to this factor carries considerable uncertainty.

- Competing sources of mortality (in particular, cardiovascular diseases) have been declining in recent decades, increasing the proportion of deaths due to cancer. Therefore the use of stationary 1980 population distribution and death statistics is likely to understate future life expectancy and the numbers of people who will survive to older ages where there is a relatively high incidence of cancer. Additionally, improvements in the effectiveness of cancer treatment may well prolong the survival of patients with cancer and shift some cases from the "fatal" to "non-fatal" categories (hence I have broadened the range of "total cases" to three-fold, in comparison to the two-fold range applied to the base estimate of "cancer deaths").

3.3 How Many Radiation-Induced Cancers of Various Types Should Be Expected When?

For most cancer sites other than leukemia, the EPA assumes that there will be a constant increase in relative risk over baseline after a 10 year lag period. [For the relevant leukemias, the time pattern is more complex--depending on both age at exposure and time after exposure (Figure 15).]

To calculate the expected time pattern for the occurrence of cancers other than leukemia for the DOE and contractor workers I started with a generic baseline relative risk assumption derived

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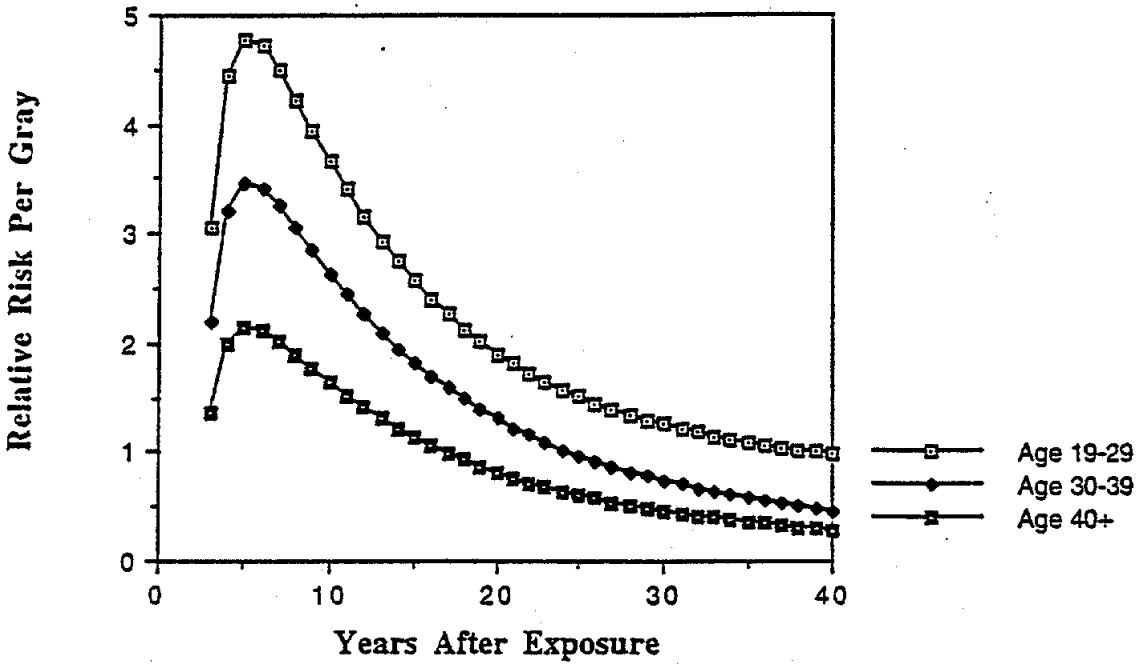
For example, although the most recent analysis of worker mortality does not show an overall excess of cancer in relation to 10-year lagged dose when leukemias are separated out, there is a trend in the data toward more positive results with longer lag periods:

Lags for dose (years)	All Cancers Excluding Leukemia--Excess Relative Risk/100 Rem	90% Confidence Limits
0	-0.21	(-0.4,0.1)
5	-0.13	(-0.4,0.2)
10	-0.07	(-0.3,0.3)
15	-0.04	(-0.5,0.5)
20	+0.14	(-0.5,0.9)

Source: Cardis, E., Gilbert, E. S., Carpenter, L., Howe, G., Kato, I., Armstrong, B. K., Beral, V., Cowper, G., Douglas, A., Fix, J., Fry, S. A., Kaldor, J., Lave, C., Salmon, L., Smith, P. G., Voelz, G. L., and Wiggs, L. D. "Effects of Low Doses and Low Dose Rates of External Ionizing Radiation: Cancer Mortality Among Nuclear Industry Workers in Three Countries," Radiat. Res. 142:117-132 (1995).

Figure 15

Overall Time Since Exposure Relationship --Relative Risk for Chronic Granulocytic Leukemia + Acute Leukemia



from age-specific cancer data for males[37] for 5 sites (Figure 16). With the exception of very young and very old ages, these cancers on average increase with about the fourth power of age. (In the framework of multistage cancer modeling, this would be compatible with a typical 5-stage mutation process from normal stem cells through fully developed tumors).

Every 5 years beginning with 1970, I then used the age-at-exposure vs year of exposure matrices developed in Section 2 to calculate the age distribution of the surviving dosage that had

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[37]Male data were used because 95% of the total radiation dosage was received by male workers. The sources of the data were:

Lung (never-smokers only)--Garfinkel. L. "Time Trends in Lung Cancer Mortality Among Nonsmokers and a Note on Passive Smoking." JNCI 66:1061-1066 (1981).

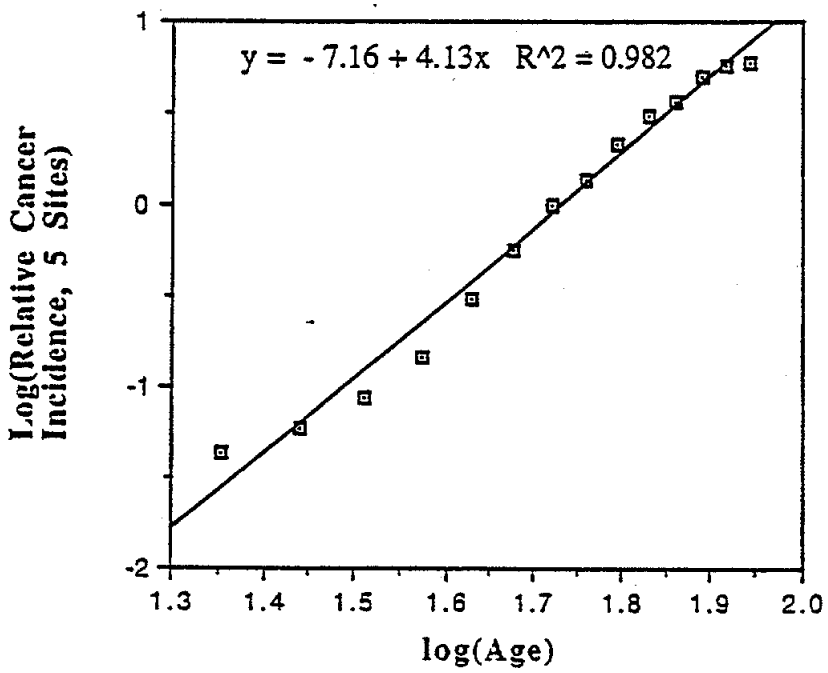
Larynx (from the Third National Cancer Survey, All Areas Combined, 1969-71) Austin. D. F. "Larynx" in Cancer Epidemiology and Prevention, D. Schottenfeld and J. E. Fraumeni, eds., W. B. Saunders Co., Philadelphia. 1982. p. 557.

Liver (from the Third National Cancer Survey, All Areas Combined, 1969-71) Falk. H. "Liver" in Cancer Epidemiology and Prevention, D. Schottenfeld and J. E. Fraumeni, eds., W. B. Saunders Co., Philadelphia. 1982. p. 670.

Bladder and Kidney (from the Third National Cancer Survey, All Areas Combined. 1969-71) Austin. D. F. "Urinary Tract" in Cancer Epidemiology and Prevention, D. Schottenfeld and J. E. Fraumeni. eds., W. B. Saunders Co., Philadelphia, 1982. p. 926.

Figure 16

Power-Law Increase in Cancer Incidence With Age (Based on Morbidity Data for Larynx, Liver, Kidney, Bladder, and Lung)



been received at least 10 years previously. For each year of the age distribution I then multiplied the total surviving 10-year old dose by the baseline cancer risk to arrive at an index of the number of cancers that would be expected to occur in that year to workers of that age. Figure 17 presents the resulting time pattern of overall cancers (other than leukemia) expected to result from dosage delivered to DOE workers between 1944 and 1992; Figure 18 presents the same data projected in the form of a cumulative distribution for cancers occurring between 1965 and 2030. The peak year for the radiogenic cancers other than leukemia appears to be about 1995 or the next couple of years in the future. About 32% of the total cancers are expected to have occurred prior to 1990; about 44% will have occurred by the end of 1995; and two thirds are expected to happen by 2005.

Table 14 shows the expected age distribution of the non-leukemia cancers occurring in different years. The aging of the workers leads to a progressive increase in the age distribution of the people expected to develop the radiogenic cancers.

Figure 17

Projected Relative Rate of Occurrence (1995 = 1) of Radiogenic Cancer Cases (Except Leukemia) Induced in DOE Employees--1944-1992 Exposures

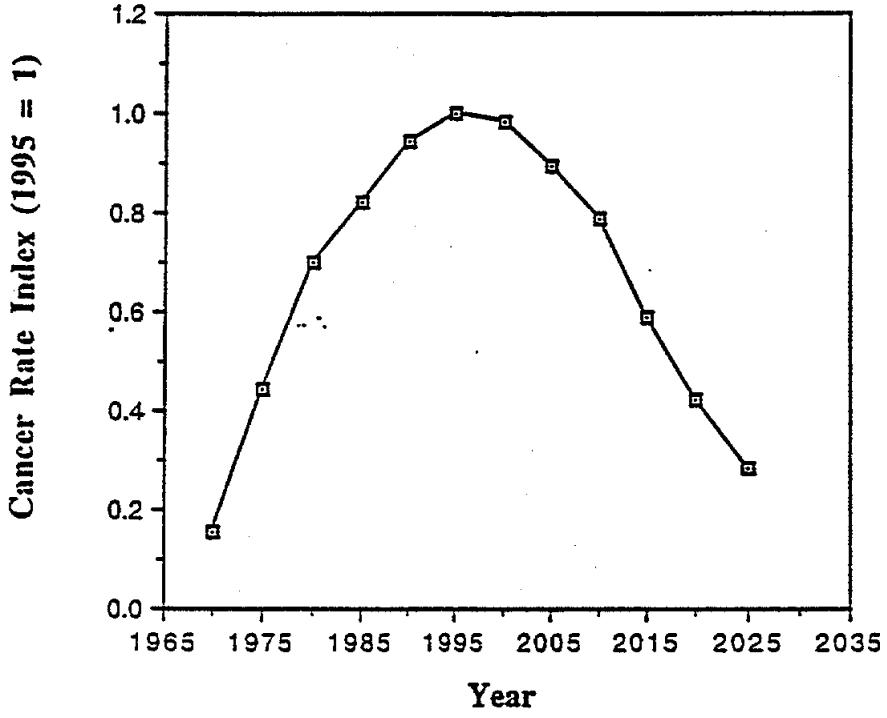


Figure 18

Cumulative % of All Radiogenic Cancers Except Leukemia Expected to Occur in Various Years

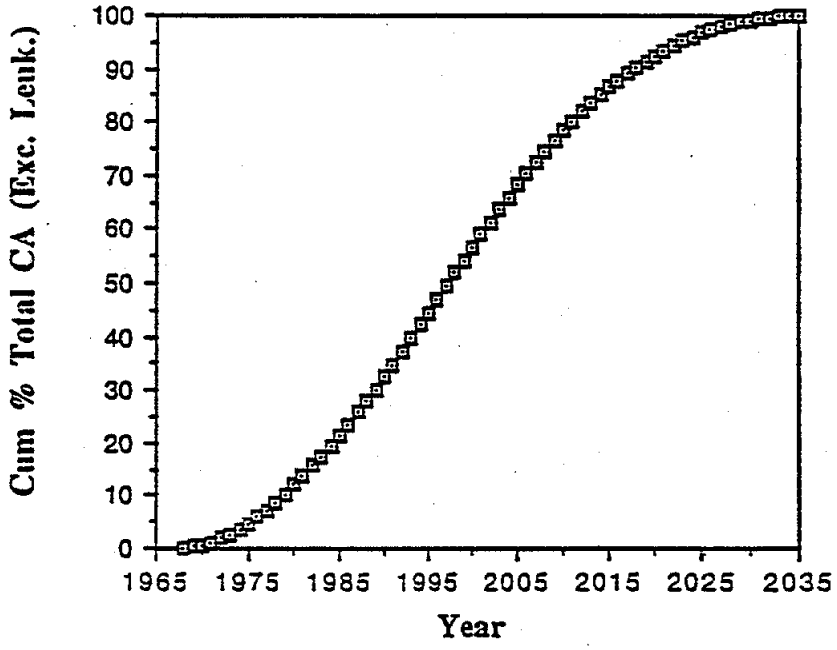


Table 14
Expected Age Distribution of Background Cancers and Radiation-Induced Cancers Other Than Leukemia in Various Years

	% Total Cancers in Each Age Group						
Background Cancers	29-39	40-49	50-59	60-69	70-79	80-85	All
	1.8	6.0	15.8	29.9	37.1	9.5	100.0
Radiation-induced cancers in various years							
1985	0.2	3.7	15.9	34.1	36.1	9.9	100.0
1990	0.2	2.6	13.7	32.8	38.2	12.5	100.0
1995	0.1	1.8	11.1	31.3	40.6	15.0	100.0
2000	0.1	1.3	8.5	29.2	43.3	17.7	100.0
2005	0.0	0.8	6.2	25.8	46.3	20.8	100.0
2010	0.0	0.4	4.2	20.8	46.9	27.7	100.0
2015	0.0	0.1	2.9	18.0	49.4	29.6	100.0
2020	0.0	0.0	1.6	15.2	48.7	34.4	100.0
2025	0.0	0.0	1.6	12.5	48.3	37.7	100.0

More complex calculations needed to describe the expected time pattern of the leukemias. Clearly, a larger proportion of the leukemias should be expected to occur sooner after exposure than will be the case for the other cancers whose expected time pattern is depicted in Figures 17 and 18. For purposes of the potential compensability calculations in Section 4, I have simply assumed that (1) essentially all the leukemias that will result from 1944-1992 exposures occur by the year 2010, and (2) the leukemias that might otherwised occur after 2010 (under the time pattern for other cancers) should be added to the calculated number of leukemias that have already occured prior to 1991.

I have also not attempted to separately describe in detail the time patterns of expected morbidity vs mortality from cancers. The mortality curve will of course be shifted a few years into the future relative to the morbidity curve. For planning purposes, and to avoid complications arising from the changing success of cancer treatment in prolonging life, I recommend that the time patterns in Figure 17 and 18 be regarded as morbidity (cases) rather than mortality.

3.4 Calculation of Doubling Doses for Various Cancer Sites, Considering the Age Distribution of the Exposures

3.4.1 The Implications of the "Preponderance of the Evidence" Test for Causation, Applied on an Individual Basis

Over the years various national and international expert committees have assessed the epidemiological evidence relating specific kinds and amounts of ionizing radiation exposure to the excess risk of various kinds of cancer in people exposed at various ages. The National Council on Radiation Protection and Measurements (NCRP)[38] has provided a simple and convenient formula that utilizes these relationships to calculate the probability that a specific cancer was caused by a specific radiation exposure:

$$PC = \frac{AD}{B + AD} X\,100 \qquad (1)$$

where PC is the probability of causation in percent, "A is the lifetime radiation risk coefficient for the individual (taking account of age, sex, time since exposure, etc.), B is the appropriate baseline lifetime malignancy rate for the individual, and D is the radiation dose[39] received by the individual."

The usual standard of proof for causation/work-relatedness in tort law and workers' compensation is a "preponderance of the evidence". In this context, therefore, "proof" means that it must be just barely "more likely than not" that the worker's cancer was caused by his or her exposure. This translates into a Probability of Causation (PC in the above formula) of just over 50%. Based on the formula clearly in order for PC to exceed 50%, AD must be larger than B—or in other words the dose D received by the worker must exceed the "doubling dose" (the dose that just doubles the background risk) given by B/A.

3.4.2 "Doubling Doses" for Induction of Various Cancers by Ionizing Radiation Delivered at Various Ages

Table 15 shows calculated "doubling doses" as defined in the previous section, based on the age specific EPA risk coefficients discussed earlier for sites where EPA has used relative risk

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[38]National Council on Radiation Protection and Measurements, "The Probability That a Particular Malignancy May Have Been Caused by a Specified Irradiation," NCRP Statement No. 7, Issued September 30, 1992, 4 pp.

[39]Or doses, if the individual has been exposed more than once or continuously over some period such as a working lifetime.

Table 15

Doubling Doses for Selected Cancer Sites for Low Dose Rate Ionizing Radiation Exposure, Calculated From EPA Age Specific Risk Coefficients Incorporating a Dose and Dose Rate Effectiveness Factor of 2

Males	Risk Coefficients by Age Group (1/Gy)			Resulting Doubling Doses (rem) by Age Group		
	20-29	30-39	40+	20-29	30-39	40+
Esophagus	0.2517	0.2892	0.3258	397	346	307
Stomach	1.9051	0.2881	0.2524	52	347	396
Colon	0.2809	0.4275	0.0899	356	234	1112
Liver	1.3449	1.3449	1.3449	74	74	74
Lung	0.0453	0.1342	0.1794	2208	745	557
Leukemia (Ave 3-20 yrs after exposure)	3.2681	2.3407	1.4575	31	43	69
Bladder	1.0736	1.0544	0.9639	93	95	104
Kidney	0.3911	0.3911	0.3911	256	256	256
Residual	0.1735	0.1754	0.1847	576	570	541

models.[40] It should be recalled that these risk coefficients incorporate the potency reduction (and corresponding reduction of the calculated probability of causation) embodied in the "Dose and Dose Rate Effectivness Factor (DDREF) of 2. To calculate doubling doses without this factor, the numbers in Table 15 should be divided by 2. A couple of other caveats are also in order:

- EPA has not chosen to list separately all the specific sites (and tumor types within sites) where radiation-induced cancers may occur--only, I believe, those where the consensus documents they used as their sources provided comparable estimates of potency. Attachment A provides another view of the basic cancer potency information based on more aggregated cancer sites, derived principally from the BEIR V report. The aggregation for example, treats all digestive system cancers as a group, leading to an overall estimated doubling dose of slightly over 100 rem for men. The BEIR V risk estimates do not incorporate a DDREF (although there is language in the report favorable to the use of a 2-fold correction for low dose rates) and appear to indicate an increasing relative risk with age for respiratory cancer, among other differences with the EPA conclusions.

- Further analysis of some data has led other researchers to somewhat different conclusions about particular cancer sites. In particular, Alexander[41] has studied combined epidemiological data from 10 U.S. worker populations, and concluded that the combined data indicate a modest but significant excess relative risk for brain cancer (142 observed vs 123.3 expected). He reports that the overall 15% excess for workers with a mean radiation dose of about 3.4 rem translates into an average relative risk per rem of about 4%. This would imply that brain cancer is among the most radiogenic cancers, with a doubling dose of about 25 rem. Based on the fraction of expected brain cancer deaths to total deaths given in the Alexander report, the absolute risk of brain cancer per Gray would be about 2.7×10^{-2}--far larger than any of the other cancer sites (see Table 10 above). This absolute risk estimate would also lead to an expectation of about 170 additional fatal cancers for the DOE/contractor worker population exposed to about 6.4×10^5 person rems as of 1992.

- There probably should also be some allowance for radiogenic multiple myelomas. These immune system cancers have been found to be significantly in excess in the latest compilation of worker mortality results (Cardis et al., 1995, op. cit., note 36) (the p value for the trend with dose was .037).

In general, workers will not have all their dosage delivered within the age ranges specified in Table 15. Table 16 shows the expected percentages of dose surviving to various calendar years that is likely to have been delivered in those age ranges. Table 17 then uses these age distributions of delivered dosage for various years to calculate the doubling dosage that are likely to be applicable to "typical" workers who receive their personal dosage delivered in the time pattern for

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[40] Thyroid, skin, and bone are not included because EPA chose to use absolute risk models for these sites. I believe it does little harm to exclude them from these calculations at this time because I have little reason to believe that the effective doubling doses for these sites would significantly alter the picture of compensability inferred from the remaining sites.

[41] Alexander, V., "Brain Tumor Risk Among United States Nuclear Workers." Occupational Medicine: State of the Art Reviews 6:695-714 (1991).

Table 16

Percentage Distribution of the Past Dosage Surviving to Different Calendar Years that is Likely to Have Been Delivered to Workers in Different Age Ranges

	Dose Surviving to Year	% Dose Surviving	% Dose Delivered to Workers in Specific Age Ranges ≤ 29	30-39	40+
Total Delivered 1944-1992	640,000	100	18.3	27.4	54.3
1995	420,000	66	25.2	34.3	40.5
2000	360,000	56	28.5	36.5	35.1
2005	290,000	45	32.6	38.4	29.0
2010	220,000	34	37.8	39.3	22.9
2015	160,000	24	44.0	38.3	17.7
2020	100,000	16	50.5	36.7	12.8

Table 17

Expected Future Changes in Typical Doubling Doses for Different Cancer Sites, Given the Changing Age Pattern of Dosage Delivered Derived in Table 16

		Doubling Doses for Dose Surviving To Various Years					
Cancer Site	Age Dist. as Delivered	1995	2000	2005	2010	2015	2020
Esophagus	331	339	343	348	353	358	364
Stomach	177	147	136	124	112	101	91
Colon	460	394	374	355	339	330	322
Liver	74	74	74	74	74	74	74
Lung	702	769	802	845	901	970	1051
Leukemia (Ave 3-20 yrs after exposure)	49	45	44	42	(not calc)	(not calc)	(not calc)
Bladder	99	98	97	97	96	96	95
Kidney	256	256	256	256	256	256	256
Residual	555	560	561	563	566	568	569

all dosage derived in Table 16. Finally, Table 18 analyzes the cumulative total cancer deaths and cancer cases in order of increasing 1995 doubling dose. This table will be the starting point for our analysis of the consequences of the current compensation system, and possible alternatives. It can be seen that the majority of expected radiogenic cancers will develop at sites that have expected doubling doses of a few hundred rem or (if the DDREF is set at 1) at least 170 rem.

Table 18
Analysis of the Distribution of Cancer Cases and Cancer Deaths, In Ascending Order of Typical 1995 Expected Doubling Doses

	% Radiogenic Ca Deaths	% Radiogenic Cancer Cases	Doubling Dose (1995)	Cum % Radiogenic Ca Deaths	Cum % Radiogenic Cancer Cases
Leukemia (Acute and Non-Lymphocytic--approx. 2/3 of all leukemias)	10.9	7.6	45	11.1	8.0
Liver	3.3	2.4	74	14.4	10.6
Bladder	5.5	7.6	98	19.9	18.6
Ovary	0.7	0.6	134	20.6	19.2
Stomach	9.8	7.5	147	30.5	27.1
Kidney	1.2	1.3	256	31.7	28.5
Colon/Intestine	21.6	27.2	339	53.6	57.1
Esophagus	2.0	1.4	339	55.6	58.7
Breast	1.0	1.3	456	56.6	60.0
Remainder	27.1	26.4	560	84.0	87.9
Lung	15.8	11.5	769	100.0	100.0
Thyroid	0.7	4.9	not calc		
Skin	0.2	0.2	not calc		
Bone	0.2	0.2	not calc		
Total	100.0	100.0			

4. Prospects for Individual "Proof" of Causation for Radiation-Induced Cancers in the Population of Former DOE/Contractor Workers

4.1 Fraction of Cancers that Could be Compensable Under the Usual "More Likely Than Not" Test

Given the estimates of doubling doses in Tables 17 and 18 in the previous section, the estimated distribution of cumulative dosage in workers surviving to 1995 and various years in the future (Tables 4 and 9 of Section 2), what percentage of DOE and contractor employees who might be expected to develop cancer as the result of their DOE exposures will be in a position to "prove" causation on the basis of their own personal documented dosages? Table 19A shows the proportions of affected workers who would be expected to exceed the doubling doses for the tumors in question, and the overall percentage of radiogenic cancers expected to appear in various periods that would be expected to be compensable. Table 19B shows a similar treatment under the assumption that the threshold of compensation might be set at half of the doubling dose (omitting the effect of the DDREF). 20A and 20B are similar except that for this table the analysis is confined to fatal cancers only.

It can be readily seen that very few workers with radiogenic cancers could be expected to be compensated under the 1 doubling dose standard, if the doubling doses are as high as those calculated using a DDREF of 2--about 1 % of total cases and 1.4% of total deaths would be compensated. 1% of total cases, of course, represents about 4 people out of the 360 cases in the lower bound of our range of estimates of radiogenic cancers in DOE and contractor employees.

The outcome is markedly better, but still quite discouraging at half the calculated doubling doses (corresponding to a case in which the DDREF is set at 1). Under this assumption, about 4.2% of all cases and 5.4% of total fatal cases of the enumerated types could be eligible for compensation. 5.4% of all cases represents about 54 compensable cancers out of the 1,000 in our upper bound estimate of all occupationally caused radiogenic cancers in the DOE/contractor workers.

These tables do not include allowances for brain cancers and multiple myelomas. If brain cancers were to be as susceptible to induction as estimated by Alexander (see above)--a doubling dose of 25 rem--then 35% of induced brain cancers would be compensable under a 1 doubling dose requirement, and 62% would be compensable under a 1/2 doubling dose requirement.*

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* Under progressively less demanding thresholds. the fractions compensable under .2. .1. and .075 doubling dose thresholds would be about 80%. 87%. and 90%. respectively.

Table 19

Percentage of Total Radiogenic Cancer Cases Occurring in Different Time Periods That Would Be Eligible for Compensation

A. Requirement for 1 Doubling Dose--% Cases Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	0.453	0.210	0.215	0.000	0.879
Liver	0.020	0.015	0.013	0.013	0.061
Bladder	0.020	0.015	0.014	0.015	0.063
Ovary	0.000	0.000	0.000	0.000	0.000
Stomach	0.000	0.000	0.000	0.017	0.017
Kidney	0.000	0.000	0.000	0.000	0.000
Colon/Intestine	0.000	0.000	0.000	0.000	0.000
Esophagus	0.000	0.000	0.000	0.000	0.000
Breast	0.000	0.000	0.000	0.000	0.000
Remainder	0.000	0.000	0.000	0.000	0.000
Lung	0.000	0.000	0.000	0.000	0.000
Total	0.49	0.24	0.24	0.045	**1.02**

B. Requirement for 1/2 Doubling Dose--% Cases Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	1.29	0.597	0.728	0.000	2.61
Liver	0.18	0.136	0.088	0.122	0.53
Bladder	0.24	0.179	0.165	0.152	0.74
Ovary	0.01	0.005	0.006	0.003	0.02
Stomach	0.03	0.020	0.094	0.139	0.28
Kidney	0.00	0.000	0.000	0.000	0.00
Colon/Intestine	0.00	0.000	0.000	0.000	0.00
Esophagus	0.00	0.000	0.000	0.000	0.00
Breast	0.00	0.000	0.000	0.000	0.00
Remainder	0.00	0.000	0.000	0.000	0.00
Lung	0.00	0.000	0.000	0.000	0.00
Total	1.74	0.94	1.08	0.42	**4.18**

Table 20

Percentage of Total Radiogenic Cancer Deaths Occurring in Different Time Periods That Would Be Eligible for Compensation

A. Requirement for 1 Doubling Dose--% Deaths Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	0.639	0.301	0.309	0.000	1.25
Liver	0.027	0.020	0.018	0.018	0.083
Bladder	0.014	0.011	0.010	0.011	0.045
Ovary	0.000	0.000	0.000	0.000	0.000
Stomach	0.000	0.000	0.000	0.023	0.023
Kidney	0.000	0.000	0.000	0.000	0.000
Colon/Intestine	0.000	0.000	0.000	0.000	0.000
Esophagus	0.000	0.000	0.000	0.000	0.000
Breast	0.000	0.000	0.000	0.000	0.000
Remainder	0.000	0.000	0.000	0.000	0.000
Lung	0.000	0.000	0.000	0.000	0.000
Total	0.68	0.33	0.34	0.052	**1.40**

B. Requirement for 1/2 Doubling Dose--% Deaths Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	1.81	0.855	1.044	0.000	3.71
Liver	0.24	0.187	0.120	0.167	0.72
Bladder	0.17	0.130	0.119	0.110	0.53
Ovary	0.01	0.006	0.007	0.003	0.02
Stomach	0.03	0.026	0.122	0.182	0.36
Kidney	0.00	0.000	0.000	0.000	0.00
Colon/Intestine	0.00	0.000	0.000	0.000	0.00
Esophagus	0.00	0.000	0.000	0.000	0.00
Breast	0.00	0.000	0.000	0.000	0.00
Remainder	0.00	0.000	0.000	0.000	0.00
Lung	0.00	0.000	0.000	0.000	0.00
Total	2.27	1.20	1.41	0.46	**5.35**

In the section immediately below, we will consider possible "technical fixes" for this problem--possible new molecular biological technology on the horizon that could help better quantify past dosage and distinguish cancers that are more vs less likely to have been caused by ionizing radiation.

4.2 Analysis of Recent Innovations in the Molecular Biology of Cancer, and Potential Implications for the Legal Determination of Cancer Causation

4.2.1 Four Categories of Improved Information Resulting from Recent Scientific and Technical Advances

The last two decades have seen dramatic advances in the molecular biological tools available for (1) analysis of changes in genetic information[42] and (2) understanding the significance of specific changes in particular genes for carcinogenesis. Specifically, these advances in molecular biology have yielded information of four kinds that conceivably could have a bearing on the dilemma described in the previous section:

- Category 1 innovations essentially have the potential to make possible much more fine scale radiation cancer epidemiology by subdividing tumors observed at particular anatomical sites (and histological types) into categories of molecular pathology. By molecular pathology I mean (A) the specific series of genes that have been altered or impaired to produce a particular cancer and (B) the specific changes in DNA sequence that have occurred in those genes, or the changes in the location of specific sequences in the genome that has altered the activity of the cancer genes. This category of innovations has the potential to effectively lower the doubling dose for types of genetic changes that are established to be preferentially produced by specific kinds of radiation/radionuclide exposure.

- Category 2 innovations are techniques to improve radiation dosimetry for past exposures (e.g., "FISH"/"Chromosome painting"--see note 42 above for citations). These techniques are likely to be useful in disclosing risks to individual workers who for one reason or another were not adequately monitored, and who received total

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[42]Such changes include both "point mutations" (changes at particular places in the DNA code) and rearrangements of information represented by the transfer of large sections of chromosomes in recombination events. Point mutations have been studied by extracting specific genes from tumors and other cells, copying the genes many times, and determining the detailed sequence of DNA bases in those genes. One specific cancer related gene that has been extensively studied in this way is p53 (Greenblatt, M. S., Bennett, W. P., Hollstein, M., and Harris, C. C. "Mutations in the p53 Tumor Suppressor Gene: Clues to Cancer Etiology and Molecular Pathogenesis," Cancer Research 54:4855-4878, 1994.) Persistent chromosome rearrangements suitable for assessment of past radiation doses have been studied by both conventional cytogenetic and chromosome banding studies, and newer techniques that are referred to under the "Fluorescence In Situ Hybridization (FISH)" or "Chromosome Painting" rubrics (Brenner, D.J. and Sachs, R.K. "Chromosomal 'Fingerprints' of Prior Exposure to Densely Ionizing Radiation." Radiation Research 140:134-142, 1994; Tucker, J. D., Ramsey, M. J., Lee, D. A., and Minkler, J. L. "Validation of Chromosome Painting as a Biodosimeter in Human Peripheral Lymphocytes Following Acute Exposure to Ionizing Radiation In Vitro," International Journal of Radiation Biology 64(1):27-37, 1993; Lucas, J. N., Poggensee, M., and Straume, T. "The Persistence of Chromosome Translocations in a Radiation Worker Accidentally Exposed to Tritium." Cytogenetics & Cell Genetics 60(3-4):255-256, 1992.)

career doses of at least 5-10 rem.[43] Unfortunately, it is difficult to see how these techniques by themselves will be very helpful in improving the fairness of workers compensation results in the light of the calculations in Section 2. The status of the affected workers' legal cases would only improve if the new procedures revealed that they had received career total accumulated dosage that exceeded the levels in Tables 15-18 (or Appendix Tables A1-A4). Unless there is a substantial amount of historically unrecorded dosage due to poorly monitored neutron exposures, etc., this seems likely only in a vanishingly small proportion of cases.

- Category 3 innovations are improvements in the assessment of differences in individual susceptibility to cancer risk from different types of agents. The recent literature contains a great deal of information on the variability in genetic and non-genetic factors that are likely to alter susceptibility to different classes of carcinogens.[44] If person were known to have a special sensitivity to radiation-induced cancers (say, because of less efficient repair of radiation-induced DNA damage), it is possible that their effective doubling dose for the resulting radiation-induced cancers would be reduced. The recent publication of data on the gene responsible for Ataxia Telangiectasia is a further case in point.[45] This gene is important in detecting radiation induced damage to DNA and inhibiting cell replication until repair enzymes can remove the damage, and impaired forms of the gene are relatively common. One copy of a mutant form of this gene is carried by about 1% of all people. These heterozygotes are more sensitive to radiation-induced cell killing and mutagenesis. Current preliminary epidemiology studies suggest that the heterozygotes have a threefold increase in their relative risk of cancer in general, and a five-fold increased risk of breast cancer (the breast is a relatively radiosensitive site in humans).[46] If these findings are confirmed, they would suggest larger relative increases in the risk due to specific identifiable causes (such as radiation) and correspondingly lower doubling doses, because the overall increases in incidence are relative to a background incidence that is related to multiple carcinogenic agents.

- Category 4 innovations represent improvements in the recognition of non-agent-specific individual differences in susceptibility to carcinogenesis--such as germ line mutations in genes that contribute to the genetic pathway to cancer in specific tissues (e.g., the retinoblastoma gene.) Although such mutations could be expected to increase the absolute risk due to both radiation and other exposures in affected people.

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[43]Straume, T., and Lucas, J. N. "Validation Studies for Monitoring of Workers Using Molecular Cytogenetics." in Biomarkers and Occupational Health: Progress and Perspectives, Mortimer L. Mendelsohn, John P. Peeters, and Mary J. Normandy, eds., Joseph Henry Press, Washington, DC, 1995, pp. 174-193. These authors report that "many Department of Energy (DOE) radiation workers were exposed to neutrons during the 1940s through the 1960s when neutron dosimetry was in its infancy. Aslo, many individuals have received substantial radiation exposures in connection with accidents, nuclear weapons testing, human experimentation, the atom bombs dropped on Hiroshima and Nagasaki, and various medical radiological procedures."

[44]Hattis, D., and Barlow, K. "New Estimates Of Variability In Parameters Putatively Related To Individual Cancer Risk" Report to the Ministry of Health, Government of Canada, by the Center for Technology, Environment, and Development, Clark University, March, 1995.

[45]Nowak, R., "Discovery of AT Gene Sparks Biomedical Research Bonanza." Science 268:1700-1701, (June 23, 1995).

[46]Savitsky, K., Bar-Shira, A., Gilad, S., Rotman, G., Ziv, Y., Vanagaite, L., Tagle, D. A., Smith, S., Uziel, T., Sfez, S., Ashkenazi, M., Pecker, L., Frydman, M., Harnik, R., Patanjali, S. R., Simmons, A., Clines, G. A., Sartiel, A., Gatti, R. A., Chessa, L., Sanal, O., Lavin, M. F., Jaspers, N. G. J., Taylor, A. M. R., Arlett, C. F., Miki, T., Weissman, S. M., Lovett, M., Collins, F. S., and Shiloh, Y. "A Single Ataxia Telangiectasia Gene with a Product Similar to PI-3 Kinase." Science 268:1749-1753 (June, 23, 1995).

there is no a priori reason to expect a specific change in relative risk, and therefore doubling doses would be essentially unchanged on average.

4.2.2 Analysis of the Potential of "Category 1" Innovations--Approaches for Subclassifying Tumors According to Specific Putatively Causal Somatic Mutations

Categories of DNA Damage and Repair Processes, and Implications for Mutational Spectra

It is well known that cancers come in a variety of types. Following the diagnostic categories developed for cancer treatment by physicians, epidemiologists have traditionally used anatomical sites of origin of cancers, and histological types, to classify cancers to deduce possible relationships with exposures. The new molecular biological techniques of Category 1 essentially allow us to distinguish cancers further, by the types of DNA mutations found in specific genes that are likely to have contributed to the development of the cancer.[47] These finer subcategories resulting from "molecular pathology" furnish epidemiologists with a set of categories that may eventually prove even more useful than anatomy and histology for developing relationships with specific putative causal agents.

Part of the promise of the molecular pathology categories is that they allow researchers to bring to bear fundamental information about the ways specific kinds of mutations are produced in sorting out which cancers are likely to have been caused by which agents.[48] For example:

- The DNA bases cytosine and 5-methylcytosine spontaneously deaminate (lose an amino group) at a slow rate at normal body temperature. This converts the parent bases to uracil and thymine respectively, which tend to pair with the "wrong" base on the opposite DNA strand. If these changes are not detected and repaired before the next time the DNA is copied the altered bases therefore give rise to G:C to A:T "transitions".[49] These changes occur most frequently at CpG dinucleotides, which are

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[47]One such gene, which has been found to be altered in about 37% of all cancers studied is P53--a gene that in its normal state helps suppress the development of cancer in part by recognizing the presence of extensive DNA damage and blocking cell replication until most of the damage is repaired. Mutations in this gene will be covered in some detail below, but other genes in multiple pathways to cancer may eventually be subject to similar molecular analysis.

[48]Greenblatt, M. S., Bennett, W. P., Hollstein, M., and Harris, C. C. "Mutations in the p53 Tumor Suppressor Gene: Clues to Cancer Etiology and Molecular Pathogenesis," Cancer Research 54:4855-4878, 1994.

[49]The four DNA bases are divided into two chemical families. Adenine (A) and guanine (G) are purines, whereas thymine (T) and cytosine (C) are pyrimidines. Normally adenine pairs with thymine on the complementary DNA strand of the double-helix, and guanine pairs with cytosine. If a mutation causes one purine base to be substituted for the other purine base (and the corresponding pyridines to be exchanged on the opposite strand), this is designated as a "transition". By contrast, if the mutation consists of the substitution of a purine for a pyrimidene (or vice versa) on a particular strand, this is designated as a "transversion". Both of these are simple single-base substitution mutations. Other kinds of mutations either eliminate one or more bases ("deletions") or add one or more bases ("insertions"). If a deletion or insertion does not delete or insert a an integral multiple of 3 bases (e.g., 3, 6, 9, etc.).

frequently methylated. Therefore the proportion of such transitions at CpG dinucleotides is taken as a marker for the relative contribution of spontaneous deamination to the cancers of particular kinds.

- Other types of transitions (not at CpG dinucleotides) tend to result from small DNA adducts--especially methyl groups at the O^6 position of guanine, which often give rise to mistakes in pairing.

- By contrast, bulky adducts--such as those derived from polycyclic aromatic hydrocarbons, other carcinogens in cigarette smoke [the tobacco-specific nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone], and aflatoxin--tend to give rise to transversions. The explanation for this is that these bulky adducts tend to block passage of the normal copying enzyme, and when this happens adenine is preferentially inserted into the complementary DNA strand. When this happens opposite a guanine (guanine is most frequently modified by bulky adducts in this way), a G:C to T:A transversion results.

- Ultraviolet light tends to join together two adjacent thymidine bases, causing CC to TT tandem transitions.

- Ionizing radiation gives rise to unusual recombination events (both within and between DNA strands) and tends to be associated with an increased frequency of deletions and other large chromosomal changes. The degree of enrichment of deletions will be assessed as part of the quantitative analysis below. Otherwise, deletions and insertions are associated mechanistically with slippage of the DNA copying enzymes and mistaken within-strand pairing at repetitive sequences in the DNA.

Beyond these relatively well understood mechanisms that tend to give rise to different proportions of mutations within the broad families of DNA changes, there is a more mysterious and occasionally spectacular concentration of mutations induced by specific agents at particular places, "hotspots," in the DNA sequence. "Hotspots" have been repeatedly observed ever since the first detailed genetic maps of mutation frequencies were made based on observations in bacterial viruses.

In the context of radiation, an extreme case of a hotspot has been reported by a single group of investigators in a group of Colorado Plateau uranium miners exposed to large amounts of radon (and possibly other agents). Taylor et al.[50] studied the P53 sequence in the lung tumors of 52 miners who developed large-cell or squamous-cell cancers. 29 miners (56%) were found to have a mutation in their P53 protein, and of those, 16 (55%) were identical G to T transversions at the second base of codon 249. G to T transversions in general are not uncommon in other lung cancers, but out of 337 lung cancer cases not associated with radon in an updated version of a P53 mutation data base, there was only one other case of a G to T transversion at this specific place in

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then the mutation is a "frameshift" mutation because the 3-base reading frame of the DNA code has been disrupted and all amino acids coded for by DNA translated after the point of the mutation will generally be changed.

[50]Taylor, J. A., Watson, M. A., Devereux, T. R., Michels, R. Y., Saccomanno, G., and Anderson, M. "P53 Mutation Hotspot in Radon-Associated Lung Cancer." Lancet, Vol. 343, pp. 86-87 (1994).

the gene. Examining the whole database of documented P53 mutations for cancers at all sites, this specific mutation was seen only six other times among 2472 cases at sites other than the lung.

Making the simplifying assumption that we can label all 29 cancers with P53 mutations studied as "radon lung cancers" (in reality some fraction are likely not to have been related to the radon exposure) the indicated enrichment of this mutation in this population of P53 mutants is therefore

$$\frac{16 \text{ codon 249 AGG to ATG / 29 "radon" cancers with P53 mutations}}{1 \text{ codon 249 AGG to ATG / 337 non - radon lung cancers}} = 186 \text{ fold} \qquad (2)$$

If we were to modestly reduce the 29 P53 "radon" mutants to reflect the proportion likely to have been actually caused by the radon progeny, considering the average dose in the group (about 1600 working level months), the calculated enrichment would be slightly larger.[51] Moreover a further adjustment could be made considering that there was undoubtedly some radon exposure history in the 337 putatively "non-radon" lung cancers. The net result of this could indicate that this mutation is for all practical purposes specific for radon exposure--*if* on further study with a couple other high radon exposed groups, similar results are replicated.

There is unfortunately one other smaller study,[52] of less-exposed uranium miners from New Mexico in which the mutation was not found among 7 workers found to have P53 mutations. The average exposure of the 7 workers bearing these mutations was 215 WLM. Because this dose is less than the estimated doubling dose for radon-induced lung cancer for smokers (see Table A3, Appendix A), it is possible that only a minority of the 7 lung cancers covered in this report were actually causally related to radon.

One other aspect of the findings in the Taylor et al. (1994) paper that gives me pause is that in order to be confident that this mutation to be truly related to radon, I would like to see a dose response relationship--an increasing frequency of the mutation in workers with higher exposures. This unfortunately is not apparent in the data (Table 21).

It should be noted that at the very high doses seen in this population, the most highly exposed workers do not show proportional increases in the frequency of lung cancer in general as a function of dose (the dose response relationship appears to approach a saturation level, possibly in part due to high dose killing of cells that might otherwise be capable of carcinogenic

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[51] If we were use the radon potency estimates in Table A3 (see Appendix A) the correction would be very small, as nearly all lung cancers would be expected to be caused by radon exposure at the indicated levels.

[52] Vahakangas, K. H., Samet, J. M., Metcalf, R. A., Welsh, J. A., Bennett, W. P., Lane, D. P., and Harris, C. C. "Mutations of p53 and ras Genes in Radon-Associated Lung Cancer From Uranium Miners." Lancet. Vol. 339. pp. 576-580 (1992).

Table 21

Frequency of the Putative Radon-Related P53 Mutations as a Function of Estimated Radon Doses

Dose Range (WLM)	Number of P53 Mutants Studied	Number of Codon 249 AGG to ATG Changes Found	% of Mutant P53s with Codon 249 AGG to ATG
0-52 (including 6 controls)	8	1	12
100 to 1000	9	5	56
1000 to 2000	8	5	62
2000+	9	5	56

transformation; possibly in part due to competing risks from other causes in the highest exposure groups and in part due to notorious inaccuracies in the individual worker dosimetry in this study.)

The take-home lesson from this example therefore is that there is some promise that some radiation-induced mutations will be found to be very much more frequent in groups exposed to specific kinds/sources of radiation than in background tumors related to other environmental factors. For the workers whose cancers bear such mutations, there is a reasonable long term hope that this kind of information could dramatically increase the assessed probability that their cancer was caused by their radiation exposure. The radon information even in its present state of development is probably sufficient to sustain more-likely-than-not determinations. However the vagaries of the available information are such that even in this best case (radon, in the light of the Taylor et al. study) there is room for some doubt that the basic relationship will be eventually validated in further studies. And finding other examples of radiation "hot spots" in the P53 gene and other cancer-related genes will require a sustained molecular epidemiological effort with only a modest prospect of short term benefit for the workers whose tumors are studied. The section immediately following outlines the mathematical theory that can be used to adjust probability-of-causation estimates in the light of information on the preferential causation of some types of mutations by specific kinds of ionizing radiation.

Mathematical Theory

Imagine that in unexposed people, the lifetime risk of a particular cancer is R_b, and the proportion of those cancers with P53 mutations of a particular type is P_b. Now suppose that large

well-controlled epidemiological studies have found that people exposed to a dose of radiation d have a lifetime risk of those cancers of R(D), where

$$R(D) = R_b + q_1 D \quad (3)$$

The doubling dose defined earlier, D_{2x}, where the probability of radiation-induced causation is at the borderline of the conventional more-likely-than-not ("preponderance of the evidence") criterion of tort law and most workers' compensation system, is of course given by

$$D_{2x} = \frac{R_b}{q_1} \quad (4)$$

Now let us suppose that radiation is much better at causing one kind of DNA change (e.g., deletions) than another (e.g., point mutations). We can break down the total cancer risk, R(D) into these two components:

$$R(D)_{total} = R(D)_{deletions} + R(D)_{point\ mutations}$$
$$= R_{background\ deletions} + q_{1\ induced\ deletions} D + R_{background\ point\ mutations} + q_{1\ induced\ point\ mutations} D \quad (5)$$

Because, by hypothesis, radiation is better at inducing deletions than point mutations, the q_1 for deletions must be larger in relation to the corresponding background for deletions than the q_1 for point mutations is in relation to the background for point mutations. Therefore, in terms of the doubling doses for cancers with each type of genetic change,

$$D_{2x\ cancers\ with\ deletions} = \frac{R_{background\ deletions}}{q_{1\ induced\ deletions}} < D_{2x\ cancers\ with\ point\ mutations} = \frac{R_{background\ point\ mutations}}{q_{1\ induced\ point\ mutations}} \quad (6)$$

The magnitude of the reduction of the doubling dose for the cancers with deletions (or any other type of mutation) depends on just how much enrichment there is of the deletions in the radiation-induced cancers/mutations relative to the background cancers/mutations. If we believe the Taylor et al. (1994) observations reported earlier (see equation 2 above), this enrichment could be as much as a couple of hundred fold in favorable cases. Below we will examine the less favorable case of deletion mutations based on available information from a number of different sources.

Data on the Enrichment of Deletions in Radiation-Induced Mutations

Tables 22-24 show data from three *in vitro* (cell culture) system on the enrichment of deletions in radiation-exposed cells with specific selectable mutations relative to similar mutations arising spontaneously or in cultures exposed to other mutagenic agents. Each of these data sets is

Table 22

HPRT Mutations Studied by Jostes et al. (1994)[53] in CHO (Chinese Hamster Ovary) Cells: (percentages in parentheses)

Agent	Whole Gene Deletions	"Alterations"*	No Detected Change	Total	Relative Enrichment of Whole Gene Deletions
None (Spontaneous)	5 (16%)	3 (10%)	23 (74%)	31	1.0 (defined)
.25-.3 Gy radon	14 (52%)	4 (15%)	9 (33%)	27	3.2
.76 Gy radon	11 (44%)	8 (32%)	6 (24%)	25	2.7
3.0 Gy x-rays	16 (47%)	7 (21%)	11 (32%)	34	2.9
All ionizing radiation groups	41 (48%)	19 (22%)	26 (30%)	86	3.0

Table 23

APRT Mutations Reported by Lehman et al. (1994)[54] in CHO (Chinese Hamster Ovary) Cells (Percentages in Parentheses)

Agent	Transitions and Transversions	Deletions	Insertions	Total	Relative Enrichment of Deletions
None (Spontaneous)	28 (93%)	2 (7%)	0	30	1.0 (defined)
Ultraviolet Light	32 (94%)	1 (2%)	1 (2%)	34	0.9
Ionizing Radiation	**11 (69%)**	**5 (31%)**	**0**	**16**	**4.7**
Benzopyrene Diol Epoxide	19 (90%)	1 (5%)	1 (5%)	21	0.7

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[53]Jones. R. F., Fleck, E. W., Morgan. T. L., Stiegler, G. L., and Cross. F. T. "Southern Blot and Polymerase Chain Reaction Exon Analyses of HPRT⁻ Mutations Induced by Radon and Radon Progeny," Mutation Research, Vol 137, pp. 271-379, 1994.

* According to the authors, these are "rearrangements within the gene or loss of fewer than 8 exons."

[54]Lehman, T. A., Greenblatt, M., Bennett, W. P., and Harris, C.C. "Mutational Spectrum of the p53 Tumor Suppressor Gene: Clues to Cancer Etiology and Molecular Pathogenesis." Drug Metabolism Reviews, Vol. 26. pp. 221-235. 1994.

Table 24

HPRT Mutations Studied by Nelson et al. (1994)[55] in TK6 cells (Human B Lymphoblastoid Cell Line)

Agent	Complete Gene Deletions	Other Deletions	Total, All Deletions	Total Mutants Studied	Relative Enrichment of Complete Deletions
None (Spontaneous)	7 (9%)	41 (53%)	48 (62%)	78	
X-Rays (200 cGy)	41 (35%)	45 (39%)	86 (74%)	116	3.9

based on a limited sample size, and the results vary depending in part on the kinds of deletions and other mutations that are effectively detected in the various authors' assay system, the background frequencies of different mutations in the different systems, etc. Overall, however, it can be said that complete gene deletions often seem to be enhanced in radiation-exposed cultures, and there is some evidence that smaller deletions are enhanced relative to other mutations in some cases. The most favorable case for the latter conclusion is seen in Table 23, where (based on a very limited sample) deletion mutations are enhanced nearly 5-fold relative to spontaneous mutations and mutations induced by other agents.

Table 25 is a large compilation of data from over 2800 P53 mutations found in human tumors and cell lines derived from human tumors. The first column of data--the % of tumors of various types that have been found to contain p53 mutations--comes from Table 2 of Greenblatt et al.[48] The other information was extracted from the latest available version of a data base (last updated June, 1994) available from the European Molecular Biology Laboratory over the internet.[56] Table 26 analyzes the subset of this information that involves lung cancers--comparing the frequency of deletions and insertions in lung cancers that were and were not associated with radon. It can be seen that if all the lung cancers are included (Table 26A) there appears to be about a 3-fold enrichment of deletions and insertions in radon-associated lung cancers compared to other

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[55]Nelson, S. L., Giver, C. R., and Grosovsky, A. J. "Spectrum of X-ray-induced Mutations in the Human HPRT Gene," Carcinogenesis, Vol. 15, pp. 495-502, 1994.

[56]Hollstein, M., Rice, K., Greenblatt, M. S., Soussi, T., Fuchs, R., Sorlie, T., Hovig, E., Smith-Sorensen, B., Montesano, R., and Harris, C. C. "Database of P53 Gene Somatic Mutations in Human Tumors and Cell Lines." Nucleic Acids Research, Vol. 22, pp. 3551-3555, 1994. The database can be obtained by sending an Email message to NetServ@EBLAC.UK and including the line Get P53:(filename). A list of the filenames can be obtained by sending the message "help p53".

Table 25

Frequency of Deletions and Other Selected Mutation Types Observed in P53 Genes in Human Cancers and Cell Lines Derived from Human Cancers

Type of Tumor	% of Tumors with P53 Mutations	Number of Mutations Studied	% Deletions	% Deletions + Insertions	% CpG Transitions
All Tumors	**37**	**2847**	**8.2**	**10.4**	**24.5**
Breast	**22**	**274**	**14.6**	**15.0**	**22.3**
Respiratory system		**401**	**6.0**	**7.2**	**7.5**
Larynx		26	7.7	11.5	7.7
All Lung Cancer	**56**	**375**	**5.9**	**6.9**	**7.5**
All Non-Radon LC		337	5.0	5.6	8.0
Adenocarcinoma		40	2.5	7.5	17.5
Carcinoid		5	0.0	0.0	0.0
Large cell		12	8.3	16.7	0.0
non-SCLC		98	5.1	5.1	8.2
SCC or Adeno/SCC		55	16.4	18.2	7.3
SCLC		92	2.2	3.3	9.8
Metastasis		2	0.0	0.0	50.0
Lung not otherwise specified		25	4.0	4.0	16.0
nonsmoker		8	0.0	0.0	12.5
All Radon LC		38	13.2	18.4	2.6
radon, not otherwise specified		29	10.3	17.2	3.4
radon--CIS		1	0.0	0.0	0.0
radon--non SCLC		3	33.3	33.3	0.0
radon--SCC/SCLC		5	20.0	20.0	0.0
All Digestive System		**855**	**7.0**	**8.8**	**30.2**
Esophagus	45	98	11.2	13.3	19.4
Stomach	41	107	10.3	15.0	36.4
Heparocellular carcinoma	29	240	7.9	8.3	8.8
Pancreas	44	64	4.7	7.8	28.1
Colon	50	343	4.7	6.1	46.6
Anal		3	0.0	0.0	33.3

Table 25, Continued

Frequency of Deletions and Other Selected Mutation Types Observed in P53 Genes in Human Cancers and Cell Lines Derived from Human Cancers

Type of Tumor	% of Tumors with P53 Mutations	Number of Mutations Studied	% Deletions	% Deletions + Insertions	% CpG Transitions
All Leukemia/ Lymphoma	**12**	**289**	**7.3**	**11.1**	**30.8**
Leukemias and Related Neoplasms		**167**	**9.0**	**14.4**	**29.3**
ALCL		1	0.0	0.0	0.0
ALL		24	8.3	16.7	33.3
B-ALL		7	28.6	28.6	57.1
pre-B		3	0.0	0.0	0.0
B-CLL		16	0.0	18.8	12.5
T-ALL		2	0.0	0.0	0.0
T-leukemia		1	0.0	0.0	0.0
T-lymphoma		2	0.0	0.0	50.0
TFL		10	20.0	20.0	20.0
CML		23	8.7	13.0	26.1
CTCL		1	0.0	0.0	100.0
PTCL		1	0.0	0.0	0.0
Richter		3	0.0	0.0	33.3
Eryth		1	0.0	0.0	0.0
FL		3	0.0	0.0	0.0
HCL		1	0.0	100.0	0.0
Myeloid + myeloprolif		18	22.2	22.2	22.2
AML		22	4.5	9.1	40.9
ATL		15	13.3	13.3	40.0
Lymphoid		1	0.0	0.0	100.0
MDS		12	0.0	8.3	33.3
Other Blood and Lymph Tissues		**122**	**4.9**	**6.6**	**32.8**
B-Lymphoma		18	11.1	11.1	22.2
Burkitt's Lymphoma		51	7.8	9.8	37.3
Hodgkin's		5	0.0	0.0	40.0
Non-Hodgkins' Lymphoma		22	0.0	0.0	40.9
Multiple Myeloma	9	8	0.0	0.0	25.0
Not specified		18	0.0	5.6	22.2

Table 25, Continued

Frequency of Deletions and Other Selected Mutation Types Observed in P53 Genes in Human Cancers and Cell Lines Derived from Human Cancers

Type of Tumor	% of Tumors with P53 Mutations	Number of Mutations Studied	% Deletions	% Deletions + Insertions	% CpG Transitions
All Other Tumors		**1028**	**8.7**	**11.7**	**25.3**
All Nervous System		**170**	**8.8**	**12.9**	**35.9**
Brain astrocytoma	25 (all brain)	53	9.4	15.1	37.7
Brain--glial cell (glioma, glioblastoma)	25 (all brain)	96	8.3	11.5	37.5
Brain--other or not stated	25 (all brain)	17	11.8	11.8	29.4
Neuroblastoma	1	3	0.0	0.0	0.0
Neuroepithelioma		1	0.0	100.0	0.0
All Female Reproductive System (Except Breast)		**257**	**8.9**	**10.5**	**26.8**
Cervix	7	25	12.0	12.0	28.0
Ovary	44	170	8.2	9.4	23.5
Uterine		56	10.7	14.3	37.5
Vulva		6	0.0	0.0	16.7
All Sarcomas	**31**	**90**	**10.0**	**14.4**	**24.4**
Chondrosarcoma		2	0.0	0.0	50.0
Leiomyosarcoma		2	0.0	0.0	50.0
Ewing's Sarcoma		21	9.5	14.3	23.8
Liposarcoma		4	0.0	0.0	0.0
Sarcoma--MFH		5	0.0	0.0	40.0
NFS		1	0.0	0.0	100.0
Osteosarcoma		33	15.2	24.2	18.2
Rhabdosarcoma		3	33.3	33.3	0.0
Soft tissue sarcoma		1	0.0	0.0	0.0
Sarcoma--nos		18	5.6	5.6	33.3
All Skin	**44**	**123**	**4.9**	**8.1**	**24.4**
Basal		55	1.8	7.3	27.3
Bowens		8	0.0	0.0	12.5
Melanoma	9	6	0.0	0.0	16.7
Squamous Cell Carcinoma		17	11.8	11.8	5.9
Xeroderma Pigmentosum		27	0.0	3.7	40.7
Skin, NOS		10	30.0	30.0	10.0

Table 25, Continued

Frequency of Deletions and Other Selected Mutation Types Observed in P53 Genes in Human Cancers and Cell Lines Derived from Human Cancers

Type of Tumor	% of Tumors with P53 Mutations	Number of Mutations Studied	% Deletions	% Deletions + Insertions	% CpG Transitions
Miscellaneous		**388**	**9.3**	**12.4**	**20.1**
Adrenal cortex	23	4	0.0	0.0	25.0
Angiosarcoma		2	0.0	0.0	0.0
Bladder	34	109	4.6	7.3	17.4
Buccal cavity & Pharynx ("Head and Neck" - Larynx)		143	13.3	18.2	14.0
Carcinoid	11	1	0.0	0.0	0.0
Cholangio		13	0.0	0.0	53.8
Endometrial	22	1	0.0	100.0	0.0
Eye (melanoma)		2	0.0	0.0	0.0
Kidney--Wilms'		2	0.0	0.0	0.0
Mesothelioma	22	4	0.0	0.0	50.0
Parathyroid	8	1	0.0	0.0	0.0
Prostate	30	29	13.8	13.8	31.0
Renal	19	9	22.2	22.2	22.2
Testis	0	2	50.0	50.0	0.0
Thyroid	13	48	8.3	10.4	33.3
Unknown--metastases		8	12.5	12.5	0.0
Urothelial		10	0.0	0.0	20.0

Table 26
Enrichment of Insertions and Deletions in Radon-Associated Lung Cancers

A. Analysis Based on All Studied P53 Mutations

Agent	Deletions	Insertions	Total Mutations	Relative Enrichment of Deletions	Relative Enrichment of Deletions + Insertions
Non-Radon Lung Cancers	17 (5%)	2 (0.6%)	337	1.0 (defined)	1.0 (defined)
Radon-Associated Lung Cancers	5 (13%)	2 (5%)	38	2.6	3.3

B. Analysis After Excluding Radon-Specific Codon 249 Transversions

Agent	Deletions	Insertions	Total Mutations	Relative Enrichment of Deletions	Relative Enrichment of Deletions + Insertions
Non-Radon Lung Cancers	17 (5%)	2 (0.6%)	336	1.0 (defined)	1.0 (defined)
Radon-Associated Lung Cancers	5 (23%)	2 (9%)	22	4.5	5.6

lung cancers. If the lung cancers with radon-specific transversions are excluded from both the radon and non-radon groups (Table 26B), the apparent enrichment is increased to about 5-fold.

Because of the small sample size of radon-associated lung cancers studied, these estimates of deletion/insertion enrichment carry considerable uncertainty. This uncertainty is likely to be reduced in the future, however, as additional data become available. For our purposes here, they at least allow some tentative calculations of how many workers' compensation cases for different radiation-induced tumors might be improved by examining their tumor p53 sequences for insertions or deletions. To do this I assume:

- A maximum five-fold effective reduction in the doubling dose for deletions and insertions for all tumors and all types of ionizing radiation,
- No difference in the frequency of p53 mutations for radiation-induced tumors compared to the "background" tumors described in the p53 database (Table 25),

- the distributions of radiation dosage among DOE and contractor workers previously developed in Section 2 (this includes an allocation of 95% of all dosage to male employees)

- the doubling doses given in Tables 17 and 18, and

Based on these assumptions, Tables 27 and 28 describe the approximate percentages of radiation-induced tumors of various kinds that might be able to satisfy a "more likely than not" criterion of causation, with and without the aid of P53 sequence analyses, based on deletion/insertion findings. Table 27, in parallel with Table 19A assumes a five-fold effective reduction in doubling dose from the original EPA doubling dose estimates (incorporating the DDREF of 2). Table 28 assumes that the 5-fold reduction in doubling dose occurs in combination with elimination of the DDREF--meaning that the calculations for qualifying tumors in this table are based on a 10-fold reduction in doubling doses from their original values in Tables 17 and 18.

In order for P53 sequence analysis to push a particular case beyond the preponderance-of-evidence threshold, the tumor must:

A) Occur in a person who is between the original doubling dose for the tumor (column 3) and the revised doubling dose for tumors bearing p53 deletions or insertions (column 4). The expected percentage of each type of radiation induced tumor occurring in this dose interval is the difference between columns 5 and 6.

B) Carry a p53 mutation (column 7) (The p53 analysis is potentially more helpful for cancers other than leukemias in part because leukemias rarely carry p53 mutations.)

C) Carry a deletion mutation in p53 (column 9) given the assumed 5 X multiplicative enrichment of deletions in radiation-induced mutations (limited of course, by the upper bound of 100%).

As deduced earlier, the bottom lines of column 11 in these tables indicate that only approximately 1%-4% of the total radiation induced tumors might be compensable under a preponderance of evidence test without any p53 sequence analysis (with the 4% figure derived from the elimination of the DDREF in Table 28). With the same baseline assumptions, if there is a 5 fold enrichment of deletion and insertion p53 mutations in radiation-induced tumors, then an additional 1.6-3.4% of the total radiation-induced tumors might be able to pass the preponderance of evidence threshold with the p53 sequence analysis. Based on our earlier estimate that a total of about 360-1000 extra cancers might have been initiated in DOE and contractor employees by exposures over the 1944-92 period, then the number of potential beneficiaries from the p53 technology in this group might be approximately 5-30, spread out over the next couple of decades.

A further factor that is not included in these calculations is the issue of background radiation exposure. Tests such as those described above have some modest promise for distinguishing radiation-induced mutations from other mutations, but there is little hope of

Table 27

Potential Increases in Compensable Radiation-Induced Cancers That Might Result from Analysis of P53 Insertion and Deletetion Mutations in Individual Tumors--Based on EPA Doubling Dose Assumptions, DDREF = 2

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Cancer Site	Approx % Total Radiation-Induced Tumors (Cases)	Original 1995 Doubling Doses (Rem)	1995 Doubling Doses with 5X Reduction	Percentage of Total Dose Above Original Doubling Doses	Percentage of Total Dose Above 5X Reduced Doubling Doses	% Tumors in Category with p53 Mutations	Baseline % p53 Mutant Genes With p53 Insertions or Deletions	% Radiation-Induced Tumors with Insertions or Deletions	Expected % Radiation-Induced Tumors in Category With p53 Insertions or Deletions	% Total Radiation Induced Tumors Compensable in Base Case Without P53 Analysis	Addied % Total Radiation Induced Tumors Compensable With P53 Analysis
Leukemia	7.6	45	9.0	11.4	71	12	14.4	72	8.6	0.870	0.395
Liver	2.4	74	14.9	2.5	57	29	8.3	42	12.0	0.061	0.158
Bladder	7.6	98	19.6	0.8	48	34	7.3	37	12.4	0.061	0.439
Ovary	0.6	139	28	0.0	30	44	9.4	47	20.7	0.000	0.039
Stomach	7.5	177	35	0.0	18.8	41	15	75	30.8	0.000	0.434
Kidney	1.3	256	51	0.0	9.1	19	22.2	100	19.0	0.000	0.022
Colon/Intestine	27.2	460	92	0.0	1.0	50	6.1	31	15.3	0.000	0.042
Esophagus	1.4	339	68	0.0	3.9	45	13.3	67	29.9	0.000	0.017
Breast	1.3	523	105	0.0	0.0	22	15	75	16.5	0.000	0.000
Remainder	31.6	555	111	0.0	0.0	30	12	61	18.4	0.000	0.000
Lung	11.5	702	140	0.0	0.0	56	6.9	35	19.3	0.000	0.000
All Sites Combined	100.0			0.99	12.5					0.99	1.55

Table 28

Potential Increases in Compensable Radiation-Induced Cancers That Might Result from Analysis of P53 Insertion and Deletetion Mutations in Individual Tumors--Based on 1/2 EPA Dobuling Dose Assumptions, DDREF = 1

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Cancer Site	Approx % Total Radiation-Induced Tumors (Cases)	1995 Doubling Doses (Rem) for DDREF = 1 (1/2 official values)	1995 Doubling Doses with 5X Reduction	Percentage of Total Dose Above Original Doubling Doses	Percentage of Total Dose Above 5X Reduced Doubling Doses	% Tumors in Category with p53 Mutations	Baseline % p53 Mutant Genes With p53 Insertions or Deletions	% Radiation-Induced Tumors with Insertions or Deletions	Expected % Radiation-Induced Tumors in Category With p53 Insertions or Deletions	% Total Radiation Induced Tumors Compensable in Base Case Without P53 Analysis	Addied % Total Radiation Induced Tumors Compensable With P53 Analysis
Leukemia	7.6	23	4.5	32	81	12	14.4	72	8.6	2.47	0.32
Liver	2.4	37	7.4	23	73	29	8.3	42	12.0	0.56	0.14
Bladder	7.6	49	9.8	9.8	69	34	7.3	37	12.4	0.74	0.55
Ovary	0.6	70	14	3.6	59	44	9.4	47	20.7	0.02	0.07
Stomach	7.5	89	18	1.1	51	41	15	75	30.8	0.08	1.15
Kidney	1.3	128	26	0.0	34	19	22.2	100	19.0	0.00	0.08
Colon/Intestine	27.2	230	46	0.0	10.2	50	6.1	31	15.3	0.00	0.42
Esophagus	1.4	170	34	0.0	21	45	13.3	67	29.9	0.00	0.09
Breast	1.3	261	52	0.0	8.7	22	15	75	16.5	0.00	0.02
Remainder	31.6	278	56	0.0	7.8	30	12	61	18.4	0.00	0.45
Lung	11.5	351	70	0.0	3.3	56	6.9	35	19.3	0.00	0.07
All Sites Combined	100.0			3.88	23.8					3.88	3.38

distinguishing mutations induced by background and medical sources of radiation from mutations induced by occupational radiation sources. Background and medical radiation exposures can be appreciable in the context of lifetime cumulative dose. Official estimates of national average background radiation exposure are about 100 rem/year (1 mSv/year). Medical exposures to diagnostic x-rays--which are likely to be highly variable from person to person--are said to average an effective dose equivalent of 39 mrem/year based on early 1980's technology.[57] Over a 50 year period, the mean from these two non-occupational sources would add up to about 7 rem--considerably greater than the mean career dose of a little more than 2 rem in recent retirees from selected DOE facilities.

Conclusions--The Trajectory of Future Technical Developments

The foregoing should be sufficient to indicate that, marvelous as the new technology is for understanding the molecular basis for some tumors, there is no near term prospect that, by itself, it will solve the problem of under compensation of radiation-induced tumors. Nevertheless, there is some hope that further basic research, with the cooperation of DOE and its former contractors/workers, could eventually lead to better results. A systematic program of sequencing the p53 genes and other cancer related genes (as techniques become available) in former workers with known relatively high accumulated lifetime exposures (say, over 5 rem), and concurrent controls with lower known exposures, could eventually yield the kind of spectacular enrichment of specific mutations at specific places by specific kinds of radiation that we saw in the radon example. (The radon example itself, of course, requires confirmation in further studies). With such observations, radiation cancer epidemiology could be enhanced; dose-time-response relationships could be better defined at low dose rates, and possibly some additional tumors could be more definitively linked to their causes.

4.3 The Prospect of Bayesian Modification of Individual Doubling Doses for Cancer Cases in the Light of Uncertainties in the Individual Estimation of Dosage

There is one other possible "technical fix" that may be useful in securing compensation for some workers without changing the current rules. This has been suggested informally by Robert Goble (a physicist in the Environmental Science and Policy Program at Clark University). The extent of its potential applicability is difficult to assess at this time.

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[57]National Council on Radiation Protection and Measurements (NCRP), "Ionizing Radiation Exposure of the Population of the United States," Report 93, Bethesda, Md. (1987) quoted by Mettler, F. A. and Upton, A. C. Medical Effects of Ionizing Radiation, Second Edition, W. B. Saunders Company, Philadelphia. 1995. p. 31.

Essentially the argument rests on a recognition that (1) there is uncertainty in the radiation dose estimates and (2) because of that uncertainty, the workers presenting with tumors of types that are sometimes caused by radiation may be more likely to have had higher doses than estimated directly from their personal radiation records.

For example, imagine that we are dealing with a type of leukemia that we believe has a 40 rem doubling dose given the time pattern of estimated radiation exposures in a large group of 1,000 workers. Now let us say that we have an estimate that the average worker in the group received 30 rem (30,000 total-person-rem), but that the group is actually a composite of two indistinguishable subgroups of workers--80% (800) of the workers actually received only 20 rem/person for a total of 16,000 person-rem, and the remaining 200 workers actually received the other 14,000 person-rem (average dose/person = 14,000/200 = 70 rem).[58] Now taking the lifetime background incidence of the relevant kind of leukemia to be about 1%, we expect the following results:

Subgroup	Number of Workers	Expected Number of Background Cancers	Expected Number of Radiation-Induced Cancers	Average Dose (Rem)/Worker With Cancer
Less Exposed	800	8	$4\ (=8*\frac{20}{40})$	20
More Exposed	200	2	$3.5\ (=2*\frac{70}{40})$	70
Total	1000	10	7.5	35.7 $(=\frac{12*20+5.5*70}{12+5.5})$

It can be seen from the calculation in the bottom right hand box that the average true radiation dosage per worker with cancer is about 36 rem in this example--larger than the 30 rem average for the group as a whole, but less than the 40 rem doubling dose required to meet the "more likely than not" standard.

If we make our hypothetical distribution of exposure more extreme (representing a case with still more uncertainty in individual dosimetry) we can pass the 50% probability of causation threshold. Let us suppose for this modified example that the 80% subgroup with less exposures got only 15 rem/person instead of 20 rem/person. Subtracting their total dose of 12,000 person-rem from the 30,000 person-rem of overall exposure, the average dose in the more highly exposed group would now be 18,000/200 workers = 90 rem/worker, and the calculation of average dose per worker with cancer would be give us:

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[58]This type of situation could be produced either by uncertainty in dosage or. in theory, uncertainty in individual effective dose caused by individual differences in susceptibility to radiation-induced cancers.

Subgroup	Number of Workers	Expected Number of Background Cancers	Expected Number of Radiation-Induced Cancers	Average Dose (Rem)/Worker With Cancer
Less Exposed	800	8	$3\ (=8*\frac{15}{40})$	15
More Exposed	200	2	$4.5\ (=2*\frac{90}{40})$	90
Total	1000	10	7.5	42.8 $(=\frac{11*15+6.5*90}{11+6.5})$

Under these circumstances, we now do pass the 40 rem doubling dose, but we have had to work pretty hard to create an example with these properties. It is clear that this Bayesian-updating argument could have some influence on the outcome of workers' compensation cases that would otherwise be very close calls (i.e., assessed doses very near to the relevant doubling dose). However it seems unlikely that this will prove a major factor for the great bulk of occupational radiation-induced cancers which occur at much less than half of a doubling dose.

5. The Likely Effects of Alternative Settlement Policies Which Lower the Threshold for Recovery

With the highly skewed distribution of radiation exposures, and the substantial background of cancers from other agents, the "more likely than not" threshold leaves a substantial portion of radiation-induced cancers outside the realm of the workers' compensation system. To that extent, the goals of the system are unmet.

In this section I will therefore consider the likely effects of changes in the probability of causation threshold for recovery for the numbers and types of radiation-induced cancers (and "background" cancers) that would be eligible for compensation. Tables 29 and 30 show the changes in the proportion of various radiation-induced cancers that are expected to be compensable based on compensation standards of (a) 20% of a doubling dose, (b) 10% of a doubling dose, and (c) 7.5% of a doubling dose. In parallel with tables 19 and 20, Table 29 gives data for total cases, and Table 30 provides similar information for fatal cancers only. It can be seen that as

Table 29

Percentage of Total Radiogenic Cancer Cases Occurring in Different Time Periods That Would Be Eligible for Compensation

A. Requirement for 20% of the Doubling Dose--% Cases Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	2.83	1.315	1.176	0.000	5.32
Liver	0.45	0.332	0.297	0.298	1.37
Bladder	1.17	0.870	0.785	0.794	3.61
Ovary	0.06	0.046	0.045	0.048	0.20
Stomach	0.46	0.341	0.574	0.812	2.18
Kidney	0.04	0.028	0.025	0.025	0.12
Colon/Intestine	0.09	0.067	0.185	0.287	0.63
Esophagus	0.02	0.013	0.011	0.009	0.05
Breast	0.00	0.000	0.005	0.008	0.01
Remainder	0.00	0.000	0.000	0.000	0.00
Lung	0.00	0.000	0.000	0.000	0.00
Total	5.11	3.01	3.10	2.28	13.5

B. Requirement for 10% of the Doubling Dose--% Cases Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	3.21	1.487	1.344	0.000	6.04
Liver	0.57	0.427	0.382	0.382	1.76
Bladder	1.68	1.253	1.125	1.131	5.19
Ovary	0.12	0.089	0.082	0.084	0.37
Stomach	1.24	0.923	1.005	1.134	4.30
Kidney	0.14	0.105	0.094	0.094	0.44
Colon/Intestine	0.90	0.673	1.103	1.379	4.06
Esophagus	0.10	0.073	0.062	0.055	0.29
Breast	0.04	0.028	0.038	0.050	0.15
Remainder	0.80	0.598	0.521	0.511	2.43
Lung	0.12	0.092	0.036	0.000	0.25
Total	8.91	5.75	5.79	4.82	25.27

Table 29, Continued
Percentage of Total Radiogenic Cancer Cases Occurring in Different Time Periods That Would Be Eligible for Compensation

C. Requirement for 7.5% of the Doubling Dose--% Cases Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	3.41	1.54	1.40	0.00	6.35
Liver	0.59	0.45	0.41	0.41	1.86
Bladder	1.76	1.35	1.21	1.21	5.53
Ovary	0.13	0.10	0.09	0.09	0.42
Stomach	1.43	1.09	1.13	1.21	4.86
Kidney	0.20	0.15	0.13	0.13	0.61
Colon/Intestine	1.72	1.31	1.90	2.16	7.09
Esophagus	0.16	0.12	0.10	0.10	0.48
Breast	0.06	0.05	0.07	0.09	0.27
Remainder	1.32	1.01	0.85	0.86	4.05
Lung	0.31	0.24	0.13	0.05	0.73
Total	11.09	7.41	7.43	6.31	32.2

Table 30

Percentage of Total Radiogenic Cancer Deaths Occurring in Different Time Periods That Would Be Eligible for Compensation

A. Requirement for 20% of the Doubling Dose--% Deaths Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	3.99	1.885	1.686	0.000	7.56
Liver	0.60	0.457	0.409	0.409	1.87
Bladder	0.83	0.631	0.569	0.576	2.60
Ovary	0.06	0.048	0.047	0.050	0.21
Stomach	0.58	0.445	0.748	1.059	2.84
Kidney	0.03	0.027	0.024	0.024	0.11
Colon/Intestine	0.07	0.054	0.148	0.229	0.50
Esophagus	0.02	0.018	0.015	0.012	0.07
Breast	0.00	0.000	0.003	0.006	0.01
Remainder	0.00	0.000	0.000	0.000	0.00
Lung	0.00	0.000	0.000	0.000	0.00
Total	6.19	3.56	3.65	2.37	15.8

B. Requirement for 10% of the Doubling Dose--% Deaths Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	4.52	2.132	1.927	0.000	8.58
Liver	0.77	0.587	0.525	0.526	2.41
Bladder	1.19	0.909	0.816	0.820	3.74
Ovary	0.12	0.093	0.086	0.088	0.39
Stomach	1.58	1.203	1.310	1.479	5.57
Kidney	0.13	0.100	0.089	0.089	0.41
Colon/Intestine	0.70	0.536	0.879	1.099	3.22
Esophagus	0.13	0.100	0.084	0.076	0.39
Breast	0.03	0.021	0.028	0.037	0.11
Remainder	0.70	0.534	0.465	0.526	2.22
Lung	0.17	0.126	0.050	0.000	0.34
Total	10.03	6.34	6.26	4.74	27.4

Table 30, Continued
Percentage of Total Radiogenic Cancer Deaths Occurring in Different Time Periods That Would Be Eligible for Compensation

C. Requirement for 7.5% of the Doubling Dose--% Deaths Compensable

	Before 1991	1991-2000	2001-2010	2011-2035	Total. All Times
Leukemia	4.88	2.21	2.00	0.00	9.10
Liver	0.82	0.62	0.56	0.56	2.55
Bladder	1.28	0.98	0.88	0.88	4.01
Ovary	0.14	0.11	0.10	0.10	0.44
Stomach	1.86	1.42	1.47	1.58	6.34
Kidney	0.19	0.14	0.13	0.13	0.58
Colon/Intestine	1.37	1.05	1.52	1.72	5.65
Esophagus	0.22	0.16	0.14	0.13	0.66
Breast	0.05	0.03	0.05	0.07	0.20
Remainder	1.18	0.90	0.76	0.77	3.62
Lung	0.43	0.33	0.18	0.07	1.01
Total	12.41	7.96	7.78	6.00	34.1

the threshold for compensation is relaxed, to 10% or 7.5% of the doubling doses, approximately a quarter to a third of the radiogenic cancers (cases or deaths) could become eligible, respectively.

As the threshold for recovery is relaxed, one can expect an increasing fraction of compensated cases to be in people whose cancers were not in fact caused by their occupational radiation exposures. The ratio of total cases compensated to "true" radiation-induced cancers compensated (Table 31) is simply the inverse of the probability of causation as given in equation (1) (page 38).

One other distinction is crucial for calculating the "false positive" costs for any compensation threshold. The values shown in Table 31 for any compensation rule provide the maximum ratio of total cases to true radiation-induced cases for any specific compensation threshold. Thus, for the ordinary rule for 1 doubling dose, one can say that if the system is working correctly, there should be no more than two total cases for each true positive cases. But in practice there would be expected to be fewer false positives. The compensation threshold is a minimum threshold for compensability. Different compensated workers will necessarily have exposures that exceed the applicable minimum by various amounts. What we need for cost calculations is the average ratio of total cases to true radiation-induced cases for the entire exposure distribution above the minimum cutoff. The results of such calculations for the various cancer sites and compensation thresholds are shown in Tables 32A-32E for total cancer cases, and in Tables 33A-33E for cancer deaths. In each case, the series of tables covers thresholds for compensation ranging from 1 doubling dose (the current system) down to as little as 7.5% of the doubling dose. The first column in each table summarizes earlier data on the percentage of all tumors induced by 1944-1992 exposures that are expected to be compensable *in the period after 1990*. We have elected to exclude pre-1991 cancers from the calculated effects of our alternative policies because we are doubtful that cancers appearing more than 5 years in the past will be the subjects of many workers' compensation claims. The subsequent columns show the expected ratios of total cases compensated ("false positives" + "true positives") to the previously calculated numbers of true radiogenic cancer cases in each period.

The overall policy-relevant findings from these calculations are summarized in Table 34 and Figure 19. Basically, there is a tradeoff between the percentage of true radiogenic cancers compensated and the total expenditures made for both "true" cases and indistinguishable "false positive" cases. If a policy decision were made that it is desirable to compensate an equal number of cancer cases to those caused, this would be achieved by setting the threshold for compensability at about 10% of the doubling doses. At 7.5% of the doubling doses, the cases compensated would be about 60% greater than the cases caused. If the threshold is set at a higher level than 10% of the doubling doses, the percentage of true radiogenic cancers compensated declines rapidly. Using 20% of the doubling doses results in only one-third of the social costs being borne, while using

Table 31

Probability of Causation and Ratio of Total Cases/"True" Radiation-Induced Cases at Various Fractions of a Doubling Dose

Fraction of Doubling Dose	Probability of Causation	Ratio of total cases/true positive cases
2	0.667	1.500
1.95	0.661	1.513
1.9	0.655	1.526
1.85	0.649	1.541
1.8	0.643	1.556
1.75	0.636	1.571
1.7	0.630	1.588
1.65	0.623	1.606
1.6	0.615	1.625
1.55	0.608	1.645
1.5	0.600	1.667
1.45	0.592	1.690
1.4	0.583	1.714
1.35	0.574	1.741
1.3	0.565	1.769
1.25	0.556	1.800
1.2	0.545	1.833
1.15	0.535	1.870
1.1	0.524	1.909
1.05	0.512	1.952
1	0.500	2.000
0.95	0.487	2.053
0.9	0.474	2.111
0.85	0.459	2.176
0.8	0.444	2.250
0.75	0.429	2.333
0.7	0.412	2.429
0.65	0.394	2.538
0.6	0.375	2.667
0.55	0.355	2.818
0.5	0.333	3.000
0.45	0.310	3.222
0.4	0.286	3.500
0.35	0.259	3.857
0.3	0.231	4.333
0.25	0.200	5.000
0.2	0.167	6.000
0.15	0.130	7.667
0.1	0.091	11.000
0.075	0.070	14.333
0.05	0.048	21.000

Table 32
Ratios of Total Compensated Cases/"True" Radiogenic Cancer Cases for Various Thresholds for Compensation

A. Requirement for One Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Cases			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	0.426	1.718	1.694		1.706
Liver	0.041	1.858	1.858	1.858	1.858
Bladder	0.043	1.914	1.909	1.903	1.909
Ovary	0.000				
Stomach	0.017			1.887	1.887
Kidney	0.000				
Colon/Intestine	0.000				
Esophagus	0.000				
Breast	0.000				
Remainder	0.000				
Lung	0.000				
Total	0.527	1.738	1.715	1.884	1.740

B. Requirement for 50% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Cases			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	1.325	2.279	2.221		2.247
Liver	0.345	2.426	2.426	2.426	2.426
Bladder	0.496	2.481	2.482	2.456	2.474
Ovary	0.015	2.681	2.654	2.616	2.657
Stomach	0.253	2.741	2.625	2.447	2.536
Kidney	0.000				
Colon/Intestine	0.000				
Esophagus	0.000				
Breast	0.000				
Remainder	0.000				
Lung	0.000				
Total	2.433	2.351	2.315	2.445	2.351

Table 32, Continued
Ratios of Total Compensated Cases/"True" Radiogenic Cancer Cases for Various Thresholds for Compensation

C. Requirement for 20% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Cases			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	2.491	2.977	2.931		2.96
Liver	0.927	3.584	3.584	3.584	3.58
Bladder	2.449	3.926	3.973	3.922	3.94
Ovary	0.139	4.375	4.327	4.239	4.31
Stomach	1.727	4.583	4.257	3.878	4.14
Kidney	0.078	4.781	4.781	4.781	4.78
Colon/Intestine	0.540	5.446	5.235	5.131	5.21
Esophagus	0.033	5.181	5.195	5.247	5.20
Breast	0.012		5.212	5.256	5.24
Remainder	0.000				
Lung	0.000				
Total	8.40	3.60	3.69	4.04	3.75

D. Requirement for 10% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Cases			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	2.831	3.825	3.624		3.73
Liver	1.192	4.635	4.635	4.635	4.64
Bladder	3.509	5.108	5.061	4.991	5.06
Ovary	0.254	6.012	5.862	5.794	5.89
Stomach	3.062	6.606	5.822	4.987	5.75
Kidney	0.294	7.528	7.528	7.528	7.53
Colon/Intestine	3.156	8.231	8.176	8.013	8.12
Esophagus	0.190	8.041	8.034	8.168	8.08
Breast	0.115	8.638	7.937	8.183	8.21
Remainder	1.630	8.754	8.869	8.863	8.82
Lung	0.128	9.467	9.561		9.49
Total	16.36	5.91	5.90	6.37	6.04

Table 32, Continued
Ratios of Total Compensated Cases/"True" Radiogenic Cancer Cases for Various Thresholds for Compensation

E. Requirement for 7.5% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Cases			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	2.94	4.31	4.07		4.19
Liver	1.26	4.89	4.89	4.89	4.89
Bladder	3.77	5.78	5.73	5.65	5.72
Ovary	0.29	6.85	6.47	6.42	6.59
Stomach	3.43	7.61	6.45	5.45	6.46
Kidney	0.42	8.86	8.86	8.86	8.86
Colon/Intestine	5.37	10.54	9.82	9.67	9.94
Esophagus	0.32	9.90	9.88	10.05	9.94
Breast	0.21	10.44	10.20	10.06	10.20
Remainder	2.73	10.32	10.33	10.30	10.32
Lung	0.42	11.26	11.94	12.31	11.59
Total	21.2	7.50	7.34	7.83	7.54

Table 33
Ratios of Total Compensated Cases/"True" Radiogenic Cancer Deaths for Various Thresholds for Compensation

A. Requirement for One Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Deaths			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	0.610	1.718	1.694		1.706
Liver	0.057	1.858	1.858	1.858	1.858
Bladder	0.031	1.914	1.909	1.903	1.909
Ovary	0.000				
Stomach	0.023			1.887	1.887
Kidney	0.000				
Colon/Intestine	0.000				
Esophagus	0.000				
Breast	0.000				
Remainder	0.000				
Lung	0.000				
Total	0.721	1.733	1.709	1.880	1.732

B. Requirement for 50% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Deaths			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	1.90	2.28	2.22		2.25
Liver	0.47	2.43	2.43	2.43	2.43
Bladder	0.36	2.48	2.48	2.46	2.47
Ovary	0.02	2.68	2.65	2.62	2.66
Stomach	0.33	2.74	2.63	2.45	2.54
Kidney	0.00				
Colon/Intestine	0.00				
Esophagus	0.00				
Breast	0.00				
Remainder	0.00				
Lung	0.00				
Total	3.08	2.34	2.30	2.44	2.33

Table 33, Continued
Ratios of Total Compensated Deaths/"True" Radiogenic Cancer Deaths for Various Thresholds for Compensation

C. Requirement for 20% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Deaths			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	3.57	2.98	2.93		2.96
Liver	1.28	3.58	3.58	3.58	3.58
Bladder	1.78	3.93	3.97	3.92	3.94
Ovary	0.15	4.37	4.33	4.24	4.31
Stomach	2.25	4.58	4.26	3.88	4.14
Kidney	0.07	4.78	4.78	4.78	4.78
Colon/Intestine	0.43	5.45	5.24	5.13	5.21
Esophagus	0.05	5.18	5.20	5.25	5.20
Breast	0.01		5.21	5.26	5.24
Remainder	0.00				
Lung	0.00				
Total	9.58	3.50	3.57	3.99	3.65

D. Requirement for 10% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Deaths			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total. All Times
Leukemia	4.06	3.82	3.62		3.73
Liver	1.64	4.64	4.64	4.64	4.64
Bladder	2.55	5.11	5.06	4.99	5.06
Ovary	0.27	6.01	5.86	5.79	5.89
Stomach	3.99	6.61	5.82	4.99	5.75
Kidney	0.28	7.53	7.53	7.53	7.53
Colon/Intestine	2.51	8.23	8.18	8.01	8.12
Esophagus	0.26	8.04	8.03	8.17	8.08
Breast	0.09	8.64	7.94	8.18	8.21
Remainder	1.52	8.75	8.87	8.86	8.83
Lung	0.18	9.47	9.56		9.49
Total	17.34	5.68	5.60	6.22	5.80

Table 33, Continued
Ratios of Total Compensated Deaths/"True" Radiogenic Cancer Deaths for Various Thresholds for Compensation

E. Requirement for 7.5% of the Doubling Dose

		Ratio of Total Compensated/"True" Radiogenic Deaths			
	Total % Radiogenic Cancers Compensated 1991+ of all Caused by 1944-1992 Exposures	1991-2000	2001-2010	2011-2035	Total, All Times
Leukemia	4.21	4.31	4.07		4.19
Liver	1.74	4.89	4.89	4.89	4.89
Bladder	2.73	5.78	5.73	5.65	5.72
Ovary	0.30	6.85	6.47	6.42	6.59
Stomach	4.47	7.61	6.45	5.45	6.46
Kidney	0.39	8.86	8.86	8.86	8.86
Colon/Intestine	4.28	10.54	9.82	9.67	9.94
Esophagus	0.44	9.90	9.88	10.05	9.94
Breast	0.16	10.44	10.20	10.06	10.20
Remainder	2.44	10.32	10.33	10.30	10.32
Lung	0.58	11.26	11.94	12.31	11.59
Total	21.74	7.17	6.94	7.57	7.20

Table 34

Final Tradeoffs Between Compensating "True" Radiogenic Cancers and the Overall Ratio of Cases Compensated to Cases Caused

A. Conclusions Based on Total Cancer Cases

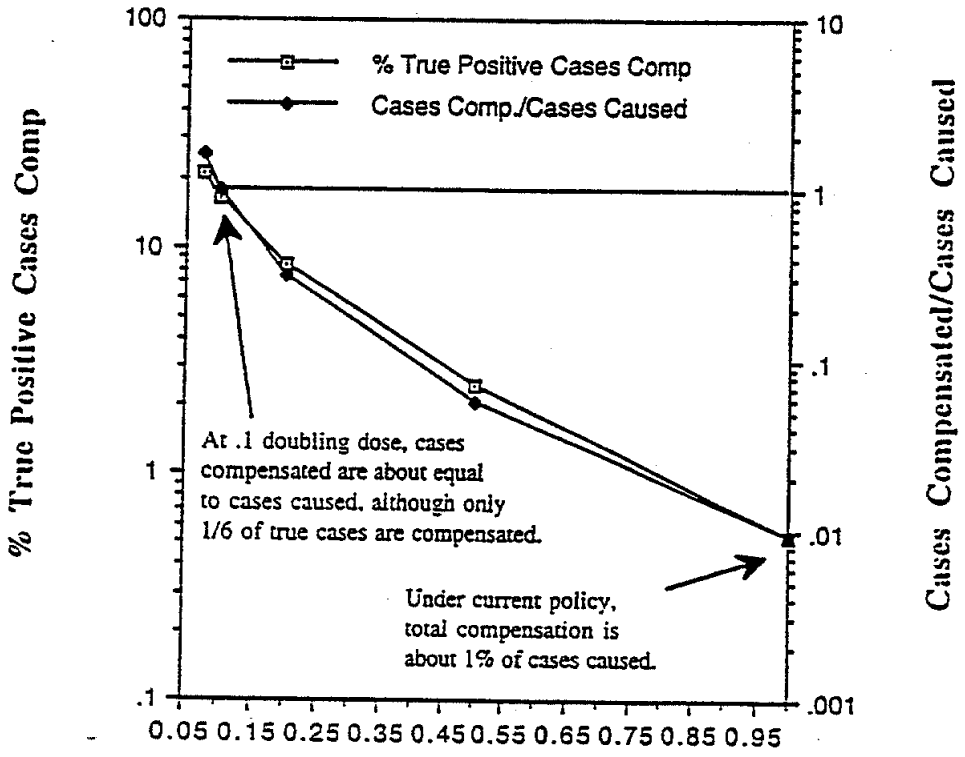
Threshold for Compensation (Fraction of a Doubling Dose)	% True Radiogenic Cancers Compensated, 1991+	Ratio of Total Cases to True Positive Cases	Ratio, Cases Compensated/Cases Caused
1	0.527	1.74	0.0092
0.5	2.43	2.35	0.057
0.2	8.40	3.75	0.32
0.1	16.4	6.04	0.99
0.075	21.2	7.54	1.60

B. Conclusions Based on Total Cancer Deaths

Threshold for Compensation (Fraction of a Doubling Dose)	% True Radiogenic Cancers Compensated, 1991+	Ratio of Total Cases to True Positive Cases	Ratio, Cases Compensated/Cases Caused
1	0.721	1.73	0.0125
0.5	3.08	2.33	0.072
0.2	9.58	3.65	0.35
0.1	17.3	5.80	1.01
0.075	21.7	7.20	1.57

Figure 19

Tradeoff Between Compensating True Radiogenic Cancers and Equalizing the Cases Compensated to Cases Caused



50% of the doubling doses compensates far less than 10%. The present system, of course, compensates about 1%

Finally, Table 35 shows projections of the absolute numbers of cases we expect to be eligible for compensation under our different scenarios for the three time periods when new policies might be effective (that is, 1991 and after).

Table 35

Central Projections of Absolute Numbers of Cases and Deaths That Would Be Eligible for Compensation Under Different Scenarios

A. Conclusions Based on Total Cancer Cases

Threshold for Compensation (Fraction of a Doubling Dose)	1991-2000	2001-2010	2011-2035	Total 1991+*
1	2.8 (1-5-4.2)	2.8 (1-5-4.2)	0.6 (0.3-0.9)	6 (3-9)
0.5	15 (8-22)	17 (9-25)	7 (4-10)	39 (21-57)
0.2	74 (39-109)	78 (41-114)	63 (33-92)	210 (113-320)
0.1	230 (122-340)	230 123-340)	210 (111-310)	670 (360-990)
0.075	380 (200-560)	370 (200-540)	340 (178-490)	1080 (570-1600)

B. Conclusions Based on Total Cancer Deaths

Threshold for Compensation (Fraction of a Doubling Dose)	1991-2000	2001-2010	2011-2035	Total 1991+*
1	2.2 (1.4-2.9)	2.2 (1.4-2.9)	0.4 (0.2-0.5)	5 (3-6)
0.5	11 (7-14)	12 (8-16)	4 (3-6)	27 (18-36)
0.2	47 (31-62)	49 (33-65)	35 (24-47)	131 (87-175)
0.1	135 (90-180)	131 (88-175)	111 (74-147)	380 (250-500)
0.075	210 (143-280)	200 (135-270)	170 (114-230)	590 (390-780)

* Totals may not add due to rounding.

Attachment A

Use of BEIR V Risk Coefficients to Calculate Doubling Doses

As a supplement to the presentation in Section 3.4 above, This section shows cancer potency values and the results of calculations of doubling doses based on the more aggregated cancer sites analyzed in the BEIR V report, and some other data for radon. Tables A1-A3 show risk coefficients for different kinds of ionizing radiation exposures, as a function of age at exposure, time after exposure, gender, and (in the case of radon progeny) smoking status.[59] The third column in Tables A1-A2 is a measure of the uncertainty--the Geometric Standard Deviation[60]--of the estimated risk coefficients (based on 10 rem exposures) in the fourth column.

Use of the geometric standard deviation to express uncertainties implies a lognormal distribution for the uncertainties. Lognormal distributions are asymmetrical--they are skewed with a hump at relatively low risk levels, and a long tail of probabilities that extends to higher risk values. Figure A1 shows a lognormal distribution, plotted arithmetically--indicating the typical skewed shape. Because of this skewness, the mean of a lognormal distribution exceeds the median (or 50th percentile) value. The fifth and sixth columns of the tables show calculations of doubling doses based on the median and mean risk values respectively. It can be seen that there is generally not a great deal of difference between these two interpretations of the risk data. I believe the lower values for the doubling doses, based on the mean risks, better reflect the appropriate values to be used in probability-of-causation calculations.

It is not completely straightforward to translate these data into doubling doses that are applicable to the case of a continuous working lifetime exposure to individual workers. Among the complications is that cancer incidence for most sites increases rapidly with age--generally in proportion to the fifth power of age or more--just as the estimated "excess" risks relative risks per

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[59]Data for Tables A1-A2 were taken from Table 4F-1 in Committee on the Biological Effects of Ionizing Radiations, National Research Council, Health Effects of Exposure to Low Levels of Ionizing Radiation, BEIR V. National Academy Press. Washington. D.C., 1990. pp. 225-226. Data for Table A3. on radon lung cancer risks. were taken from page 103 of Lubin. J. H., Boice, J.D. Jr., Edling, C., Hornung, R. W., Howe, G., Kunz. E., Kusiak. R. A., Morrison. H. I. Radford. E. P., Samet. J. M., Tirmarche, M., Woodward, A., Xiang. Y. S., and Pierce, D. A. Radon and Lung Cancer Risk: A Joint Analysis of 11 Underground Miners Studies, U.S. Department of Health and Human Services, National Institutes of Health, NIH Publication No. 94-3644, January, 1994.

[60]A geometric standard deviation is similar to a usual arithmetic standard deviation, but it is based on calculations done after transforming a variable into log form. In contrast to a usual arithmetic standard deviation, a geometric standard deviation is used multiplicatively to define a range of uncertainties. For example approximately 95% of a normal Gaussian distribution is expected to be between the mean $\pm$ 2 usual arithmetic standard deviations. Similarly approximately 95% of a lognormal population (a population in which the logarithms of the parameter values have a normal Gaussian distribution) would be expected to fall in the range from geometric mean/GSD^2 and geometric mean*GSD^2.

Table A1

Doubling Doses for Breast Cancer Mortality and Total Breast Cancer Incidence in Women

Age at Exposure	Time After Exposure (Years)	GSD	Excess Relative Risk Per 10 Rem	Implied Doubling Dose (Rem) Without Lognormal Correction	Implied Doubling Dose (Rem) With Lognormal Correction
Beast Cancer Mortality					
5	15	1.9	0.418	24	19
	25	1.6	0.427	23	21
	35	1.57	0.23	43	39
	45	1.89	0.105	95	78
15	15	1.9	0.418	24	19
	25	1.6	0.427	23	21
	35	1.57	0.23	43	39
	45	1.89	0.105	95	78
25	15	1.77	0.056	179	152
	25	1.54	0.057	175	160
	35	1.6	0.031	323	289
	45	1.99	0.04	250	197
35	15	1.9	0.03	333	271
	25	1.76	0.03	333	284
	35	1.85	0.016	625	517
45	15	2.31	0.016	625	440
	25	2.25	0.016	625	450
55	15	2.99	0.008	1250	686
Breast Cancer Incidence					
<20	15	1.45	0.52	19	18
	25	1.24	0.27	37	36
	35	1.3	0.18	56	54
	45	1.44	0.13	77	72
20-39	15	1.35	0.12	83	80
	25	1.26	0.06	167	162
	35	1.4	0.04	250	236
	45	1.57	0.03	333	301
≥40	15	2.9	0.05	200	113
	25	2.88	0.02	500	286
	35	2.99	0.02	500	274

Table A2

Doubling Doses for Cancer Mortality for Sites Other Than the Breast

Age at Exposure	Time After Exposure (Years)	GSD	Excess Relative Risk for 10 rem Dose	Implied Doubling Dose (Rem) Without Lognormal Correction	Implied Doubling Dose (Rem) With Lognormal Correction
Respiratory Cancer Mortality--Males					
All Ages	15	1.59	0.096	104	94
	25	2.03	0.046	217	169
	35	2.63	0.028	357	224
	45	3.23	0.02	500	251
Respiratory Cancer Mortality--Females					
All Ages	15	1.47	0.196	51	47
	25	1.76	0.094	106	91
	35	2.27	0.058	172	123
	45	2.8	0.04	250	147
Digestive Cancer Mortality					
Males, All Ages	All times > 10 Yr	1.5	0.081	123	114
Females, All Ages	All times > 10 Yr	1.33	0.141	71	68
Leukemia Mortality (Males and Females)					
≤20	<15	2.8	3.637	2.7	1.6
	16 to 25	2.53	0.291	34	22
	≥26	3.32	0.027	370	180
≥21	≤25	1.83	0.287	35	29
	26 to 30	2.52	0.139	72	47
	≥31	3.32	0.027	370	180
Other Cancer Mortality					
5	All times > 10 Yr	1.53	0.123	81	74
15		1.4	0.097	103	97
25		1.31	0.061	164	158
35		1.45	0.038	263	246
45		1.75	0.024	417	356
55		2.17	0.015	667	494
65		2.71	0.009	1111	676

Table A3

Doubling Doses for Lung Cancer Mortality From Exposure to Radon Progeny

	Excess Relative Risk/WLM	Implied Doubling Dose (WLM)
Overall Risk from Radon Progeny Observed in 11 Studies	0.0049	204
Never-Smokers	.00103	97
Smokers	.0034	294

Figure A1

The Skewed Shape of a Simulated Lognormal Distribution With An Arithmetic Mean of 1, an Arithmetic Standard Deviation of 1, and a Geometric Standard Deviation of 2.3

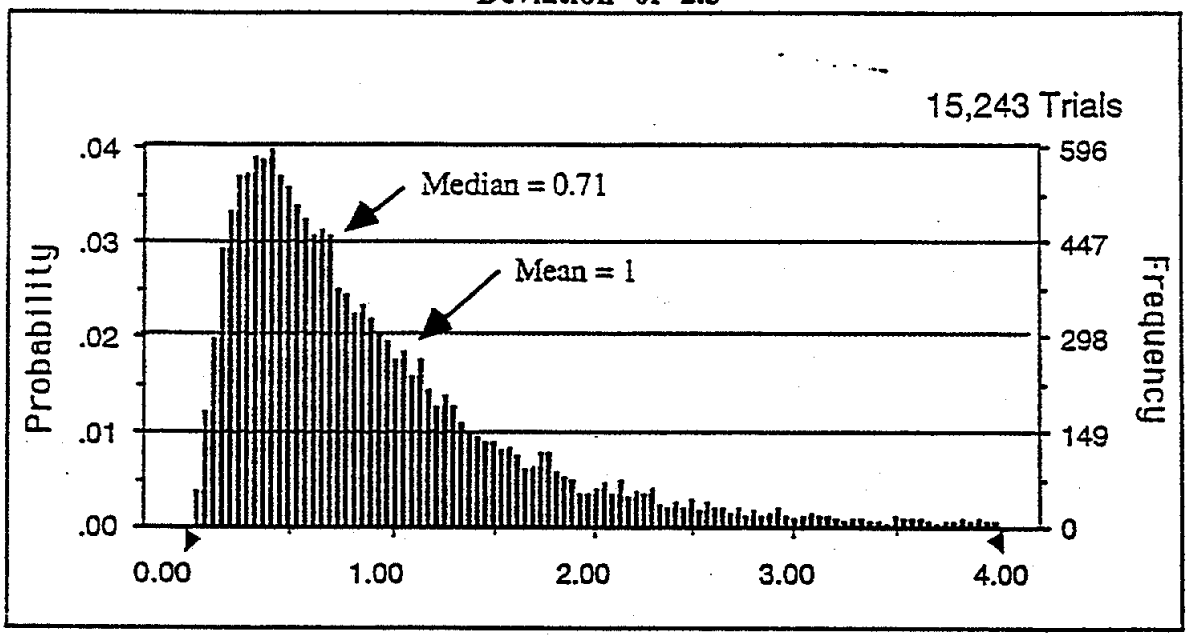

Table A4
Overall Estimated Average Working Lifetime Doubling Doses for Mortality By Cancer Site and Gender

Cancer Site and Gender	Approximate % Total Tumors Induced in Each Gender	Approximate Average Doubling Dose
Female breast cancers	14	184
Female respiratory cancer	21	178
Female digestive cancer	47	71
Female leukemia	8	69
Female--other tumors	10	463
Total	100	
Male respiratory cancer	23	361
Male digestive cancer	44	123
Male leukemia	13	69
Male--other tumors	20	463
Total	100	

rem of radiation exposure decline with age (See Tables A1-A2). The third column of Table A4 provides some crude overall estimates of doubling doses for cancers occurring by age 70, based on a uniform assumption that mortality rates for all the cancers increase with the fifth power of age, and an assumption that radiation exposure occurs relatively evenly between ages 25 and 55. The second column of this same table gives an approximate percentage distribution for ionizing radiation induced cancer mortality by site, based on the relative risk data in Tables A1-A2 and the 1995 estimated relative frequencies of mortality from cancers at various sites.[61]

These estimates would of course require adaptation to the specific exposure patterns experienced by individual workers. However, the generic estimates in Table 4 indicate that in most cases, for the more sensitive cancer sites, workers will need to show about 70-120 rem of accumulated working lifetime exposure in order to satisfy a "more likely than not" test of cancer causation. For the cancer sites that are less sensitive to radiation than average, the requirement will be for doses in the low hundreds of rem.

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[61] American Cancer Society, "Cancer Facts & Figures--1995" American Cancer Society, Inc., Atlanta, GA, 1995, p. 6.