Sensitivity to Cancer Induction by Radiation
A parametric model for variation with exposure age and cancer latency

George W. Kneale, Birmingham

Introduction

This paper is concerned with fitting a single statistical model to three large epidemiological studies that are wholly, or in a large part, concerned with the relationship between exposure to ionizing radiation and the possible later development of malignant disease. These three studies, which coincidentally all started collecting data in the 1950's, and all involved radiation exposures as early as the 1940's, are: 1) the Oxford Survey of Childhood Cancers (OSCC) [22-27] which was started by Dr Alice Stewart and one of whose major findings was the risk of childhood malignancy as the result of being exposed as a foetus to obstetric radiography; 2) the study of the survivors (to 1950), of the A-bombs on Hiroshima and Nagasaki, by the Radiation Effects Research Foundation (RERF) [21] and whose numerically largest subgroups were exposed at ages between 10 and 54, since a large part of the initially exposed population outside that age range had died, of more or less immediate effects of the bombing, before the detailed epidemiological study started in 1950; 3) the study of US workers involved in the various industrial activities that produced nuclear weapons, initially by Dr Mancuso, and later taken 'in house' by the Department of Energy (DOE) [2, 3], and whose major finding, according to Mancuso, Stewart and Kneale [10-14, 17-19, 28], is, controversially, that the risk of malignancy from external exposure to penetrating radiation is much larger, for exposures after the age of 55, than for exposures before that age.

Early Conflicts between the OSCC and RERF

Initially, when the OSCC and the RERF started publishing their findings, and the radiation risk found for exposed foetuses, by the OSCC, proved to be much larger than that found, either directly for the small exactly comparable subpopulation in the RERF, or indirectly by extrapolation from large subpopulations at higher ages, it was generally assumed that the RERF was more likely to be correct, since the RERF inference seemed to be based on a simple natural experiment, whereas the OSCC inference was, from a retrospective survey, which at the time (late 1950's, early 1960's) was commonly supposed to have greater possibilities of bias than prospective surveys, or natural, or designed experiments. However, as the statistical properties of retrospective surveys came to be better understood, and the much greater detail in the OSCC, than in the RERF allowed the possible influences of a much wider range of confounding factors to be taken into account [6, 7], by steadily improving statistical techniques on steadily improving computers, it was gradually accepted that the OSCC was correct, at least for exposure as a foetus. Meanwhile, Dr Stewart had come to the conclusion that, if the RERF inference of a low risk were mistaken, it was probably because RERF analysts had not taken into account the possibility that those who were exposed as foetuses, or as very young children, and who were beginning to develop early symptoms of malignancy, would have exceptionally high chances of dying

before the detailed collection of data began in 1950. This conclusion seemed justified when Stewart and Kneale [25] showed that, in the first half of the century, when epidemics of fatal infections, in young children, were common, most epidemics were immediately followed by a fall in the childhood leukaemia rate, otherwise generally increasing. Similarly, in OSCC data itself, it was shown that, even in children developing leukaemia, but before the first symptom directly so attributable, there was a noticeable increase in infection incidence [5, 9]. Thus, there seemed a definite possibility that the starting population (in 1950) of the RERF data was a selected one compared with the actually exposed population (in 1945), and, in particular, selected in favour of resistance to infection, and possibly malignancy. Later Stewart and Kneale showed [29, 31] that, though the subgroup of RERF deaths, presumed to be most influenced by the immune system, showed no significant linear trend in risk with dose level, in agreement with RERF findings, yet this subgroup showed a significant quadratic trend, with the slope of the regression, of risk on dose, being negative at low dose levels, and positive at high dose levels. This could be easily explained, according to Dr Stewart, on the basis of her hypothesis, by selection being most important at low dose levels, and being counteracted at high dose levels by the known effect of radiation in damaging the immune system (marrow damage hypothesis), which, being a high dose effect, would probably have a threshold at medium dose levels, and thus the overall regression of risk, for deaths dependent on the immune system, on dose would be predicted to have the shape explained above.

Enter the DOE Data

Meanwhile, Stewart and Kneale had been invited by Mancuso to become consultants to his Hanford study, at that time the most advanced in data preparation of the DOE studies, and showed [10-14, 17-19, 28] that there was a risk of malignancy for persons exposed to occupational levels of radiation, especially if the exposure occurred late in life, after age 55. Later Stewart and Kneale were enabled to gain access to the remainder of the DOE studies, as a result of being appointed consultants to the Three Mile Island Public Health Fund, and showed that several of these studies show a similar effect to Hanford. This was independently confirmed by Wing [33, 34] for the study of the facility known as X10 (actually the Oakridge National Laboratory) but rebutted by Gilbert [4], the differences between her findings and those of Stewart and Kneale later being shown [15] to be due to her neglect of possible effects of exposure age on risk. Thus, since the OSCC study differed from RERF at very low ages, and the Stewart and Kneale conclusions from the DOE study differed from the RERF at high ages, it became important to see, precisely what recorded factors in the RERF study had not yet been taken into account, and if they were, what effects they would have on the dependency of risk on exposure age. Dr Stewart's opinion, of which factor this was likely to be, was injuries received directly as a result of the bombing. The RERF, on being informed of this scientifically testable hypothesis, were kind enough to supply Stewart and Kneale with RERF data further classified by the early radiation injuries, which classification had only been explored by RERF itself to a very limited degree.

Principles of Statistical Analysis

As far as possible, for this paper, identical statistical hypotheses, concerning radiation risks, have been applied to the three studies: OSCC, RERF and DOE. The risk is allowed to depend on two factors: exposure age and interval between exposure and death. For the OSCC study the minimum interval between exposure and death has

been found to be less than two years [8], and for the DOE study about 15 years [15, 32]. Thus a plausible hypothesis about the way, the minimum interval to death varies with exposure age, is a linear regression on exposure age. Similarly, a plausible hypothesis about the way, excess relative risk varies, with exposure age, provided the minimum latency has been passed, is that it is a weighted sum of the dose at each exposure, the weights being dependent on exposure age. Suppose the dose at exposure age a to be X_a, and the weight (or risk per unit dose) at age a to be β_a, then the total relative risk is $1+\Sigma\beta_a X_a$. However, it is possible in some data sets for the β_a to be negative at some ages, and to avoid negative relative risks, the above formula is replaced by $\exp(\Sigma\beta_a X_a)$ if the weighted sum $\Sigma\beta_a X_a$ is negative. This formula for the relative risk due to exposure at ages before death at age d is to be combined with the minimum latency given by $d-a>\alpha+\delta_a$ where α is the latency for exposures near conception and δ is the increase per year of exposure age. These formulae are fitted to the various data sets by methods previously described [15, 16], being maximum likelihood where the maximisation algorithm used is the simplex method [20], and the resultant log likelihoods relative to hypotheses of no radiation effect being quoted as deviance chi squares (or minus twice the maximised log likelihood), which can be used to test homogeneity between subpopulations.

Grouped Ages: DOE and (Conventional) RERF

In order to get a general impression of the variation, of excess relative risk of malignancies per Gray, with exposure age, the β_a and δ are first estimated according to grouped ages. Table 1 shows such an analysis for subgroups of the DOE data according to facility, the total DOE data and (for convenience) the RERF data with just the conventional controlling factors. This shows the contrast between the DOE analysis taking account of exposure age and the conventional RERF analysis. It should be noted that though the residual DOE group (Y12, K25 and Fernald) shows no definite effect according to previous analyses [23], yet in this analysis the largest risk happens to be in the age group 55+, just as the other DOE subgroups which do show a definite effect. This is possibly of relevance to the analysis, of all nuclear workers internationally monitored, by Cardis [1], which includes European nuclear facilities as well as all the DOE facilities. Cardis has agreed (personal communication) that the DOE facilities do show an increased risk at ages over 55, but according to her the European facilities do not. However, the above mentioned result, for the residual DOE facilities, suggests that if the risks in individual age groups were estimated, as in the present analysis, for the European data, they too might show a (possibly non-significant) increase for exposure ages above 55.

Grouped Ages: RERF by Levels of Single Injuries

Tables 2 to 5 show the excess relative risk of malignancies per Gray according to exposure age group for each of three levels (Denied, Claimed and No Record) of each of four early radiation injuries considered separately. Table 6 shows the corresponding tests of homogeneity of effect according to injury level by deviance chi squares. The test of homogeneity is rejected decisively only by the oropharyngeal lesion classification, otherwise there appear to be no noteworthy differences. The very high estimates for certain age groups at certain levels are due to small numbers of individuals, especially in the zero dose level for those strata. In any case, the relatively high numbers of individuals who denied injuries, means that Stewart's original hypothesis,

that the RERF cohort as a whose was significantly at less risk than a normal population, because injured individuals had a greater risk of dying before 1950, fails on the grounds that too large a proportion of the population never claimed an injury.

Grouped Ages: RERF by Number of Injuries

For this purpose the three levels of each of four injuries were combined into three combined levels: 1) all injuries denied, 2) multiple injuries (or a least two injuries claimed) and 3) the residue group with at most one injury. Table 7 shows the excess relative risk of malignancy per Gray by grouped exposure ages and the above levels of number of injuries. This shows the striking finding that for multiple injuries the excess risk is notably great in those age groups (0-9 and 55+) where the OSCC and DOE data differ most from the conventional RERF analysis. This suggests that Dr Stewart's hypothesis be revised in the following way. Whereas the original selection hypothesis had predicted that the multiply injured, being most selected, would have less risk (after 1950) than those who denied all injuries, or, otherwise, that in the post-1950 RERF population the risk of late radiation effects (malignancy) be negatively correlated with experience of early effects (the injuries), what is actually found, is that such a correlation exists, but is in fact positive.

Such a positive correlation suggests the following considerations. It has long been known, from in vitro tests of the cell killing dose for cultured cells of a biopsy, that most natural populations are heterogeneous in what is supposed to be the basic biological mechanism of early radiation damage. In some cases the cause of this heterogeneity has been identified and proves to be heterozygosity (or less often homozygosity) for genes responsible for such things as repairing DNA damage due to radiation. The classic example of such a gene is ataxia telangiectasia but this was only discovered by examining biochemically the characteristic syndrome of homozygotes, and so there probably exists other genes that are also responsible for repairing, at the biochemical level, other forms of radiation damage. But such other genes may as yet have escaped detection, because they do not have such a characteristic syndrome in homozygotes, but in spite of this, may contribute to heterogeneity at a population level in resistance to early effects of radiation, and such late effects of radiation, as malignancy, that are also mediated by presumed damage to DNA. Thus, to simplify, one may suppose that a natural population is composed of two parts; a part naturally sensitive to all effects of radiation, both early and late, and a part naturally resistant to such effects. In RERF data the sensitive part would be decimated by its response to early effects before 1950, just as in the original version of Stewart's hypothesis, and thus the surviving part would be more resistant to late effects such as malignancy. It appears to be a fortunate coincidence, that due to the late start of the RERF study, both positive and negative correlations, between early and late effects of radiation, predict that the RERF would be biased in favour of low apparent effects of the delayed radiation kind.

Table 8 gives the deviance chi squares for testing various hypotheses concerning the exposure age variation in risk for malignancies in RERF data. First, the null hypothesis of no radiation effect is tested assuming a constant exposure age effect. Then the increase in deviance is tested for a hypothesis in which the two extreme age groups 0-9 and 55+ are allowed to differ from the rest, and finally all age groups are allowed to differ. This shows the most important variation is that in which the extreme age groups are allowed to differ from the rest.

A General Model for all Data Sets

It is clear from the above considerations, that if the argument from subgroups of natural populations being naturally sensitive or resistant to all effects of radiation, both early and late, is to reconcile the, at first sight, disparate analyses of the OSCC, the RERF and DOE data sets, then the OSCC and DOE variations of risk with exposure age must lie between the results of the presumably most sensitive part of the RERF population (multiply injured) and the presumably most resistant part (all injuries denied), with these RERF results being extrapolated, if necessary, by fitting to some general formula. This general formula actually chosen was the sum of two parts: one for exposures near conception, and one for exposures late in life. The formula, for the excess risk per Gray, b(a) , at an age a (in years since conception) early in life, was chosen as an inverse power law gradually changing to a negative exponential, $b(a) = \beta_1 \exp(-\gamma_1 \ln(\exp(a/\alpha)-1))$ and, for ages late in life, a positive exponential $b(a) = \beta_2 \exp(\gamma_2(a-25))$. These formulae are to be understood as combining with the formula for the linear regression of minimum latency on exposure age explained earlier. A dose at exposure age a only influences the risk at death age d if $d-a>\alpha+\delta.a$, where for convenience the parameter α, corresponding to latency for exposures near conception, has been chosen as the same as the α corresponding to the age at which, the excess risk per Gray early in life, changes from an inverse power law to a negative exponential. Table 9 gives the estimated parameter values for α, β_1, γ_1, β_2, γ_2, and δ according to the multiply injured part of the RERF, the all injuries denied part of RERF; and separately, for the parameters corresponding to the early part of life α, β_1 and γ_1 and the OSCC; and the parameters for late in life β_2 and γ_2 and δ, and the DOE. Finally, Figure 1 plots the curves corresponding to these formulae, from which it can be seen that, at all ages at which they differ significantly (i.e. under 5 or over 55), the curve, corresponding to the extrapolated OSCC data and the DOE data, lies between the curves, for multiply injured RERF data, and all injuries denied RERF data, as is required if the results of the three surveys are to be reconciled.

References

1. Cardis E, Gilbert ES, Carpenter L, Howe G, Kato I, Armstrong BK, et al. Effects of low doses and low dose rates of external ionizing radiation: Cancer mortality among nuclear industry workers in three countries. Radiation Effects. IARC 1995;142:117-132.
2. Gilbert ES, Marks S. An analysis of the mortality of workers in a nucearl facility. Radiatin Research 1979;79:122-148.
3. Gilbert ES, Petersen GR, Buchanan A. Mortality of workers at the Hanford site: 1945-1981. Health Physics 1989;56:11-25.
4. Gilbert ES, Fry S, Wiggs L, Voelz GL, Cragle DL, Petesen GR. Analyses of combined mortality data on workers at the Hanford site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Wepons Plant. Radiation Research 1989;120:1-17.
5. Kneale GW. Excess sensitivity of pre-leukaemics to pneumonia. A model situation for studying the interaction of an infectious disease with cancer. Br J Prev Soc Med 1971;25:152-159.
6. Kneale GW, Stewart AM. Mantel-Haenszel analysis of the Oxford data I: Independent effects of several birth factors including fetal irradiation. J Natl Cancer Inst 1976;56:879-883.
7. Kneale GW, Stewart AM. Mantel-Haenszel analysis of the Oxford data II: Independent effects of fetal irradiation subfactors. J Natl Cancer Inst 1976;57:1009-1014.
8. Kneale GW, Stewart AM. Age variation in the cancer risks from foettal irradiation. Br J Cancer1977;35:501-510.
9. Kneale GW, Stewart AM. Pre-cancers and liability to other diseases. Br J Cancer 1978;37:448-457.
10. Kneale GW, Stewart AM, Mancuso TF.

Hanford IIA: Reanalysis of data relating to the Hanford study of the cancer risks of radiation workers. In Late Biological Effects of Ionising Radiation IEAE Vienna, 1978;1:387-410.
11. Kneale GW, Mancuso TF, Stewart AM. Hanford radiation study III: A cohort study of the cancer risks from radiation to workers at Hanford (1944-77 deaths) by the method of regression models in life tables. Br J Indust Med 1981; 38:156-166.
12. Kneale GW, Mancuso TF, Stewart AM. Job-related mortality risks of Hanford workers and their relation to cancer effects of measured doses of external radiation. In Biological Effects of Low Level Radiation. IAEA Vienna, 1983:363-372.
13. Kneale GW, Mancuso TF, Stewart AM. Identification of occupational mortality risks of Hanford workers. Br J Indust Med 1984;41:6-8.
14. Kneale GW, Mancuso TF, Stewart AM. Job related mortality risks of Hanford workers and their relation to cancer effects of measured doses of external radiation. Br J Indust Med 1984; 41:9-14.
15. Kneale GW, Stewart AM. Factors affecting recognition of cancer risks of nuclear workers. Occup & Environ Med 1995;52:515-523.
16. Kneale GW, Stewart AM. Acute Injuries of A-Bomb Survivors:Their Epidemiological Importance. Under review.
17. Mancuso TF, Stewart AM, Kneale GW. Radiation exposures of Hanford workers dying from various causes. 10th Midyear Topical Symposium of the Health Physics Society. Proceedings of papers presented at Saratoga Springs, Rensselaer Polytechnic Inst Troy NY 12181, October 1976:204-230.
18. Mancuso TF, Stewart AM, Kneale GW. Hanford I: Radiation exposures of Hanford workers dying from cancer and other causes. Health Physics 1977;33:369-384.
19. Mancuso TF, Stewart AM, Kneale GW. Analysis of Hanford data: Delayed effects of small doses of radiation delivered at slow -dose rates. Banbury Report 9 - Quantification of Occupational Cancer. Eds. Richard Peto and Marvin Schneiderman 1981:129-150.
20. Nelder JA, Mead R. A simplex method for function minimization. Computer Journal 1965; 7:308-313.
21. Schull WJ. Effects of Atomic Radiation: A half-century of studies from Hiroshima and Nagasaki. Wiley Liss, Inc., New York 1995
22. Stewart AM, Webb J, Hewitt D. A survey of childhood malignancies. BMJ 1958; I:1495-1508.
23. Stewart AM, Hewitt D. Leukaemia incidence in children in relation to radiation exposure in early life. In Current Topics in Radiation Research. M Ebert and Alma Howard. North Holland and Publ Co, Amsterdam 1965;1;ch VI:223-253.
24. Stewart AM, Kneale GW. Changes in the cancer risk associated with obstetric radiography. The Lancet 1968;I:104-107.
25. Stewart AM, Kneale GW. Role of local infections in the recognition of haemopoietic neoplasms. Nature 1969;223;(5207):741-742.
26. Stewart AM, Kneale GW. Radiation dose effects in relation to obstetric x-rays and childhood cancers. The Lancet 1970;I:1185-1188.
27. Stewart AM, Kneale GW. Age distribution of cancers caused by obstetric x-rays and their relevance to cancer latent periods. The Lancet 1970;ii:4-8.
28. Stewart AM, Kneale GW, Mancuso TF. Hanford IIB: The Hanford data: A reply to recent criticisms. AMBIO 1980;ix:66-73.
29. Stewart AM, Kneale GW. Non-cancer effects of exposure to A-bomb radiation. J Epidemiology & Comm Hlth 1984;38;(2):108-112.
30. Stewart AM, Kneale GW. Late effects of A-bomb radiation: Risk problems unrelated to the new dosimetry. Health Physics 1988; 54; (5): 567-569.
31. Stewart AM, Kneale GW. A-bomb radiation and evidence of late effects other than cancer. Health Physics 1990;58;(6):729-735.
32. Stewart AM, Kneale GW. Relations between age at occupational exposure to ionizing radiation and cancer risk. Occup & Environ Med 1996;53:225-230.
33. Wing S, Shy CM, Wood JL, Wolf S, Cragle DL, Tankersley W, et al. Job factors, radiation and cancer mortality at Oak Ridge National Laboratory: Follow up through 1984. Am J Inudst Med 1993;23:265-279.
34. Wing S, Shy CM, Wood JL, Wolf S, Cragle DL, Frome EL. Mortality among workers at Oak Ridge National Laboratory: Evidence of radiation effects in follow up through 1984. JAMA 1991;265:1397-1402.

Table 1
Excess relative risk of malignancy per Gray by exposure age for DOE nuclear workers and total RERF data

Population	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Hanford	-	-	-1.67	1.71	-4.46	21.9	0.33
X10 (ORNL)	-	-	-7.98	2.62	16.7	19.7	0.34
Y12, K25 Fernald	-	-	-2.21	-10.0	1.76	221.2	0.38
Total DOE	-	-	-4.03	1.99	-1.55	21.6	0.33
Total RERF	2.93	0.78	0.31	0.33	-0.13	0.42	0.25

See text for interpretation of negative values and explanation of Latency Factor δ

Table 2
Excess relative risk of malignancy per Gray by exposure age and burn injury status for RERF data

Burn Status	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Denied	3.34	1.06	0.30	0.37	-0.14	0.47	0.25
Claimed	0.70	-0.02	0.35	0.25	-0.18	0.42	0.16
No Record	$4.0_{10}4$	3.03	$1.0_{10}2$	-3.59	-9.09	$-5.7_{10}2$	0.12

See text for interpretation of negative values, large values expressed in exponential form and Latency Factor δ

Table 3
Excess relative risk of malignancy per Gray by exposure age and epilation injury status for RERF data

Epilation Status	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Denied	2.95	0.73	0.38	0.31	-0.13	0.38	0.25
Claimed	$4.2_{10}3$	$5.6_{10}4$	0.04	1.32	-0.13	$9.2_{10}3$	0.14
No Record	-0.38	0.74	-0.29	-0.15	-16.5	21.9	0.47

See text for interpretation of negative values, large values expressed in exponential form and Latency Factor δ

Table 4
Excess relative risk of malignancy per Gray by exposure age and oropharyngeal lesion status for RERF data

Lesion Status	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Denied	2.96	0.86	0.37	0.30	-0.09	0.39	0.27
Claimed	-1.26	-0.02	0.10	0.62	-0.22	4.64	0.22
No Record	$1.1_{10}4$	10.9	29.7	-10.8	$-1.5_{10}2$	$-2.7_{10}3$	0.57

See text for interpretation of negative values, large values expressed in exponential form and Latency Factor δ

Table 5
Excess relative risk of malignancy per Gray by exposure age and subcutaneous bleeding status for RERF data

Bleeding Status	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Denied	2.83	0.79	0.34	0.33	-0.02	0.49	0.30
Claimed	2.46	0.48	0.22	0.46	-0.23	11.3	0.25
No Record	$9.6_{10}2$	$1.4_{10}4$	0.24	-2.79	-0.56	-3.55	0.20

See text for interpretation of negative values, large values expressed in exponential form and Latency Factor δ

Table 6
Deviance chi squares (and degrees of freedom) for testing hypotheses about age variation in radiation risk of malignancy by single injury status for RERF data

Injury Status	Injury Burn	Epilation	Oropharyngeal Lesion	Subcutaneous Bleeding
Denied	76.58(7)*	66.40(7)*	72.41(7)*	63.44(7)*
Claimed	$11.90(7)^{ns}$	24.57(7)*	20.84(7)*	20.32(7)*
No Record	$9.32(7)^{ns}$	$9.07(7)^{ns}$	25.79(7)*	$13.89(7)^{ns}$
Σ	97.80(21)*	100.04(21)*	119.04(21)*	97.65(21)*
Total Population	79.08(7)*	79.08(7)*	79.08(7)*	79.08(7)*
Heterogeneity Difference	$18.72(14)^{ns}$	$20.96(14)^{ns}$	41.96(14)*	$18.57(14)^{ns}$

Starred values are statistically significant at 5% level or better. Values marked ns are not significant

Table 7
Excess relative risk of malignancies per Gray by exposure age and number of injuries for RERF data

Injury Status	Age Group 0-9	10-19	20-34	35-44	45-54	55+	Latency Factor δ
Multiple Injuries	5.27	-0.06	0.26	0.60	-0.23	4.37	0.21
At Most One Injury	0.54	1.01	-0.02	0.16	-0.16	0.11	0.26
All Injuries Denied	3.40	0.94	0.61	0.36	0.04	0.38	0.23
Total Population	2.83	0.78	0.31	0.33	-0.13	0.42	0.25

See text for interpretation of negative values and explanation of Latency Factor δ

Table 8
Deviance chi-squares (and degrees of freedom) for testing hypotheses about the exposure age variation in radiation risk of malignancy for RERF data

Injury Status	Chi Squares: Constant Age Effect and Latency	Increase for Extremes of Age Range	Further Increase for Intermediate Ages	Number of Deaths	Estimated Radiogenic Deaths
Multiple Injuries	7.68(2)*	14.28(2)*	$1.00(3)^{ns}$	337	55.6
At Most One Injury	$1.64(2)^{ns}$	$0.71(2)^{ns}$	7.97(3)*	747	17.8
All Injuries Denied	35.80(2)*	33.59(2)*	$5.00(3)^{ns}$	4608	135.8
Σ	45.12(6)*	48.58(6)*	$13.97(6)^{ns}$	-	-
Total Population	37.89(2)*	24.99(2)*	13.64(3)*	5962	243.8
Heterogeneity Difference	$7.23(4)^{ns}$	23.59(4)*	$0.33(3)^{ns}$	-	-

Starred values are statistically significant at 5% level or better. Values marked ns are not significant

Table 9
Fitted parameter values for general model of malignancy risk from radiation applied to several data sources

Data Set	Parameter					
	α	β_1	γ_1	β_2	γ_2	δ
RERF All Injuries Denied	4.23	4.26	0.401	0.181	2.27_{10}-6	0.20
RERF Multiple Injuries	6.54	18.3	3.74	3.14_{10}-2	0.200	0.23
OSCC	1.59	24.3	0.614	-	-	-
DOE All Facilities	-	-	-	1.74_{10}-7	0.467	0.46

See text for interpretation of parameters (Greek letters). Some values are expressed in exponential form since they are very small

Figure 1
Relative Risk Per Gray of Malignancy by Exposure Age for three different studies