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# COMPARISON OF THE EFFECTS OF INHALED $^{239}PuO_2$ AND $\beta$-EMITTING RADIONUCLIDES ON THE INCIDENCE OF LUNG CARCINOMAS IN LABORATORY ANIMALS

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**ABSTRACT:** The health effects of inhaling radioactive particles when the lung is the primary organ irradiated were studied in rats and dogs. The animals were exposed to aerosols of $^{239}PuO_2$ or fission-product radionuclides in insoluble forms and observed for their life span. Lung carcinomas were the primary late-occuring effect. The incidence rate for lung carcinomas was modeled using a proportional hazard rate model. Linear functions predominated below 5 Gy to the lung. The life-time risk for lung carcinomas per $10^4$ Gy for beta emitters was 60 for rats and 65 for dogs, and for $^{239}PuO_2$ it was 1500 for rats and 2300 for dogs.

**INTRODUCTION:** Irradiation of the lung in sufficiently high doses is known to result in lung carcinomas. This result has been demonstrated in populations of patients with ankylosing spondylosis treated with thoracic irradiation, in survivors of atomic bomb explosions in Japan, and underground miners exposed to radon and radon daughter products. None of these situations, however, directly applies to chronic alpha or beta irradiation of the deep, or alveolar, portions of the lung. Such can occur if individuals inhale radioactive particles such as might be released in reactor accidents or waste transportion accidents. No human populations are available for study that have inhaled particles of alpha- or beta-emitting radionuclides which deposit deep in the lung. To address this situation, studies were initiated at the Inhalation Toxicology Research Institute to establish the dose-response relationships resulting from the inhalation of plutonium dioxide or beta-emitting radionuclides with different radioactive halflives. This paper briefly summarizes the dose-response for lung carcinomas induced by these types of lung irradiation.

**METHODS:** Details of the experimental design, animal exposure, dosimetry, and husbandry techniques have been reported. [1-3] Beagle dogs were exposed briefly, per nasum, to aerosols of $^{239}PuO_2$ of different monodisperse particle size or $^{90}Y$, $^{91}Y$, $^{144}Ce$ or $^{90}Sr$ in relatively insoluble forms. F344 rats were similarly exposed but only to $^{239}PuO_2$ or $^{144}CeO_2$. The animals were observed for their life spans for resulting biologic effects. At present, all animals have died, except for some of the dogs exposed to $^{239}PuO_2$. The incidence rate for lung carcinomas was modeled as the observed time course for the appearance of carcinomas using a proportional hazard rate model. The proportional hazards calculation of relative and absolute risks was made using the following relationships:

Proportional hazards: $\lambda(t)=\lambda_o(t)(1+\beta D(t))$.

In this relationship, $\lambda(t)$ is the age-specific lung tumor incidence rate at dose D(t), $\lambda_o(t)$ is the background lung tumor incidence rate, $\beta$ is the relative risk coefficient, and D(t) is the

time-dependent, cumulative absorbed dose to the lung. The relative and lifetime absolute risks are:

$$\text{Relative risk per Gy} = \beta$$

$$\text{Lifetime risk per Gy} = \frac{1}{D(t)} \int_0^t S(\tau)\,(\lambda(\tau) - \lambda_o(\tau)\,d\tau,$$

where $S(\tau)$ is the fractional survival at time $\tau$. This method is similar to the techniques used in the BEIR IV and BEIR V models of risk analysis.

**RESULTS:** The biological effects of these expsoures have been documented elsewhere. [3-6] Briefly, at the highest doses, animals died within months to 3 years with pulmonary injury. Those living longer (rats >1 yr, dogs >2 yr) developed a high incidence of lung tumors. Table 1 gives the total number of lung tumors seen, the relative distribution of tumor types for each species and the types of radiation.

**TABLE 1**

Distribution (%) of Lung Tumor Types in Animals that Inhaled Radionuclides and Were Observed for Life Span

| LUNG TUMOR TYPE | RATS | | DOGS | |
|---|---|---|---|---|
| | $\alpha$-emitters | $\beta$-emitters | $\alpha$-emitters | $\beta$-emitters |
| (# of Tumors) | (172) | (24) | (108) | (110) |
| Adenoma | 9 | 13 | 1 | 2 |
| Adenocarcinoma | 70 | 62 | 96 | 59 |
| Squamous Cell Carcinoma | 19 | 21 | 1 | 9 |
| Hemangiosarcoma | 1 | 4 | 0 | 25 |
| Other Sarcomas | 1 | 0 | 2 | 5 |

The predominant tumor types were adenocarcinomas and squamous cell carcinomas for rats and for dogs, adenocarcinomas and hemangiosarcomas. The hemangiosarcomas and other sarcomas are unusual tumors and occured at higher doses. The dose-response analyses are based on the carcinoma incidences.

For dogs, the relative risk was estimated by summing a linear function of dose and a power function of dose. The power function applies to the higher doses and the linear function of dose predominates over the power function at doses below 5 Gy for beta irradiation and 0.5 Gy for alpha irradiation (Fig. 1).

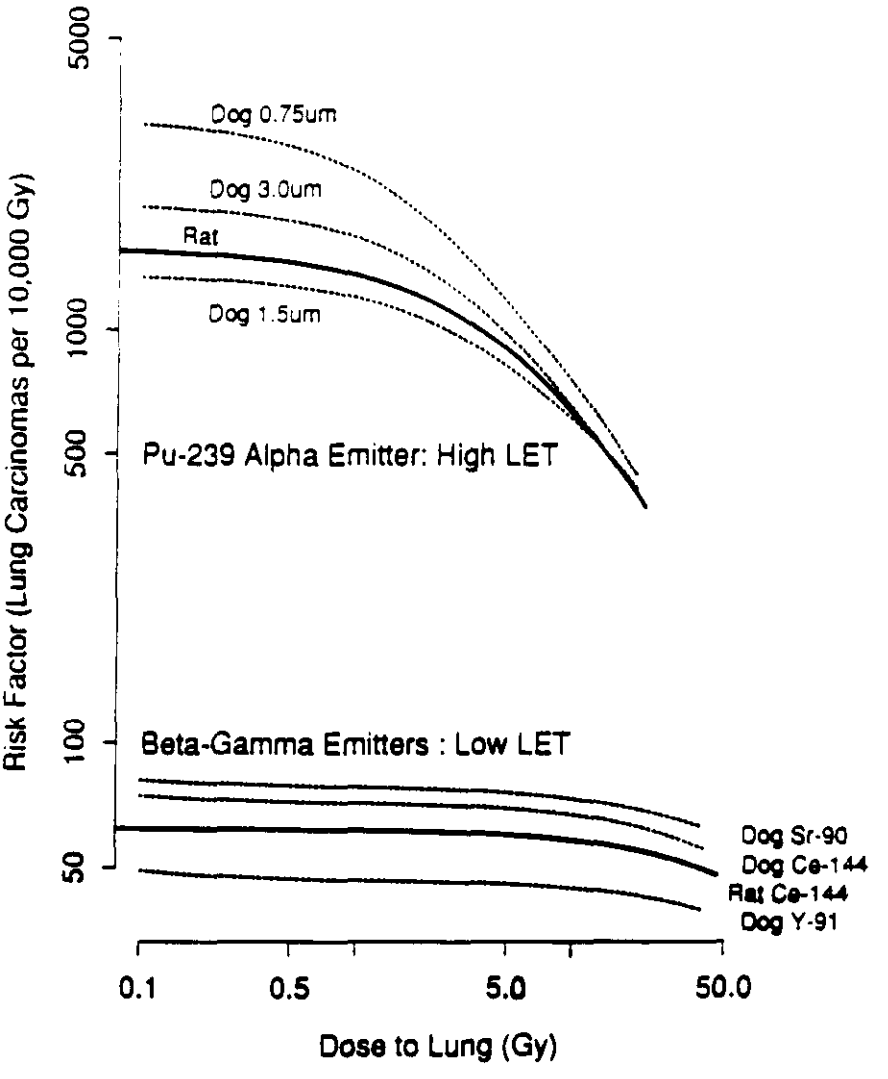


FIGURE 1 - Risk factors for lung carcinomas in dogs and rats that inhaled $^{239}PuO_2$ or beta-emitting radionuclides.

These analysis show a reasonable agreement between the life-time risks for lung carcinomas for rats and dogs for both alpha- and beta-emitting radionuclides.

Lifetime risks of lung carcinomas were calculated by integrating, over the life-time, the sum of the estimated lung carcinoma incidence rate at 1 Gy from the proportional hazard rate model and the mortality rate for competing causes of death in the control animals. The dose of 1 Gy was used because it did not cause an increase in competing causes of death. The lifetime risks of lung carcinomas per $10^4$ Gy for beta-emitting radionuclides were 60 for rats and 65 for dogs. For $^{239}PuO_2$ the lifetime risk was 1520 for rats and 2300 for dogs. The ratio of $^{239}PuO_2$ risk to beta-emitter risk is 25 for rats and 36 for dogs. Although those ratios are higher than the presently accepted quality factor of 20 for alpha and x-irradiation, the uncertainties in this analysis would not exclude a value of 20. On the other hand, the results may indicate that the quality factor of 20 is too low for comparing radiation-induced lung carcinoma incidence of alpha irradiation with that of beta irradiation.

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