INFLUENCE OF TIME AND DOSE RATE ON CANCER RISK FROM INTERNALLY DEPOSITED RADIONUCLIDES

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ABSTRACT

The effect of time and dose rate on cancer risk from protracted irradiation by internally deposited radionuclides forms a three-dimensional mathematical dose-rate/time/response relationship. Data were reviewed from lifetime studies with beagles exposed by injection, ingestion, or inhalation to either beta emitters or alpha emitters. The cumulative absorbed dose required to yield a specified level of cancer risk was found to be less at lower dose rates than at higher dose rates, but the time required for tumors to manifest tends to be much longer at lower dose rates and can exceed the natural life span, yielding a virtual threshold for fatal radiation-induced cancer. The RBE(α/β) was found to vary from about 1 at high dose rates to above 50 at low dose rates. These results can be scaled by life-span normalization to predict similar relationships in people.

INTRODUCTION

This report focuses on risks associated with radiation-induced cancer from internally deposited radionuclides with respect to the separate and independent risks of death associated with natural aging. Precise data obtained in lifetime studies utilizing beagles provide the basis for understanding the relationship of these risks.

The effect of time and dose rate on cancer risk from protracted irradiation by internally deposited radionuclides forms a three-dimensional mathematical dose-rate/time/response surface in which the coordinates for protracted exposure to the ionizing radiation are time-weighted average dose rate, elapsed time after intake, and risk given as the independent probability of death with radiation-induced cancer (1-2). Raabe et al. (3) used life-span normalization to scale response relationships from laboratory animal species to human risks.

METHODS

Selected data were reviewed from published reports of life-time studies of internally deposited radionuclides in young adult beagles at four laboratories: University of California, Davis (4), Lovelace Inhalation Toxicology Research Institute, ITRI (5), University of Utah (5), and Battelle Pacific Northwest Laboratory, PNL (6). Data were reviewed for skeletal burdens of Sr-90 via ingestion at Davis, via injection at Utah, and via inhalation at ITRI, for lung burdens of inhaled Ce-144, Y-91, and Sr-90 in fused aluminosilicate particles (FAP) at ITRI and of inhaled Pu-239 dioxide at PNL, skeletal burdens of inhaled

Pu-238 at ITRI and of injected Ra-226 at Davis and Utah, and skeletal burdens of injected Ra-228, Pu-239, and Am-241 at Utah. Throughout this report, doses refer to average absorbed doses from parent and decay products in their appropriate proportions, where all X-ray and gamma emissions are ignored, and beta emissions are ignored when in combination with alpha emitters.

Because of an observed pattern of linearity between the logarithm of time to radiation induced cancer deaths and logarithm of lifetime average dose rate, standard log-linear survival models and maximum likelihood regression methods were used to describe the response functions (7). In terms of the natural logarithms, the log-linear regression line is thus given by:

$$\ln t_m = \ln K_m - s \ln \bar{d} \qquad (1)$$

where $\bar{d}$ is the time-weighted average dose rate, t_m is the median value of survival time, s is the negative slope of the regression line for the specified effect, and K_m is the coefficient describing the median risk. This regression line is equivalent to the power function:

$$t_m = K_m \bar{d}^{-s} \qquad (2)$$

which describes the median survival time after intake.

RESULTS AND CONCLUSIONS

The results of these analyses are summarized in Fig. 1. The alpha emitting radionuclides all yielded cancer risk distributions with negative slopes of 1/3 and the beta emitting radionuclides all yielded cancer risk distributions with negative slopes of 2/3, showing that two beta particles are needed to cause the same cellular transformations produced by one alpha particle. Also, the underlying slope of 1/3 indicates that the distance between these events controls the response as a function of survival time as discussed by Raabe (2).

Because of the negative slopes of these distributions, the cumulative absorbed dose required to yield a specified level of cancer risk is less at lower dose rates than at higher dose rates, but the time required for tumors to manifest is much longer at lower dose rates and can exceed the natural life span, yielding a virtual threshold for fatal radiation-induced cancer.

This threshold occurs at about 0.08 Gy for Pu-238 and Pu-239 in bone, 0.2 Gy for Am-241 in bone, 0.5 Gy for Ra-228 in bone, 0.9 Gy for Pu-239 in lung, 1.4 Gy Ra-226 in bone, 28 Gy for Sr-90 in bone, 70 Gy for Y-91 in lung, 110 Gy for Ce-144 in lung, and 130 Gy for Sr-90 in lung.

Because the slopes of the response curves for alpha emitters differ from those for the low LET beta emitters, the

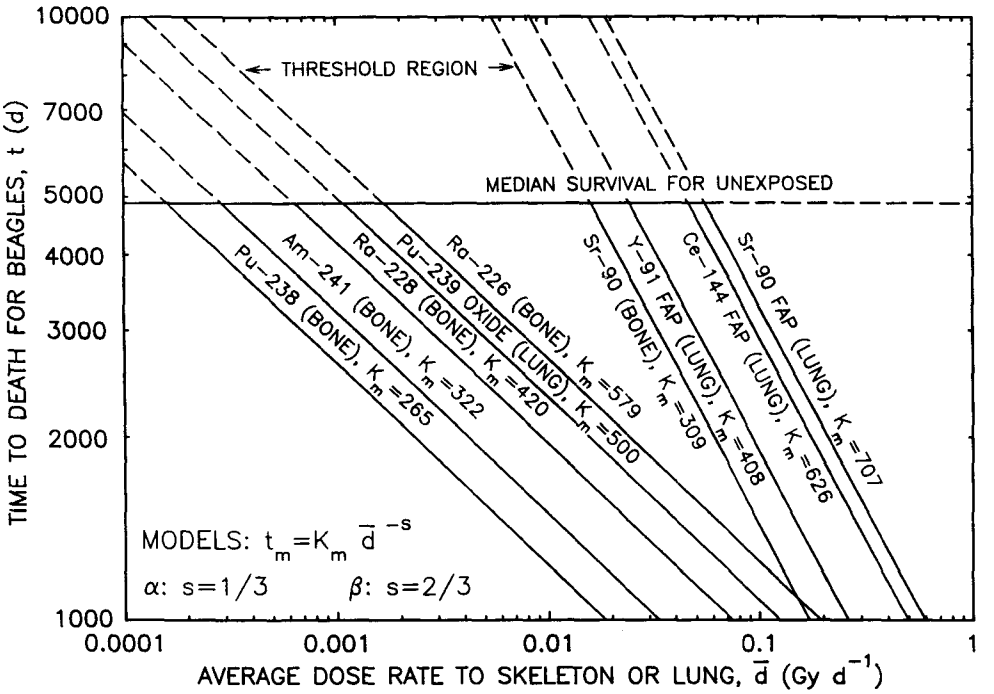

Figure 1: Median bone and lung cancer risks for beagles.

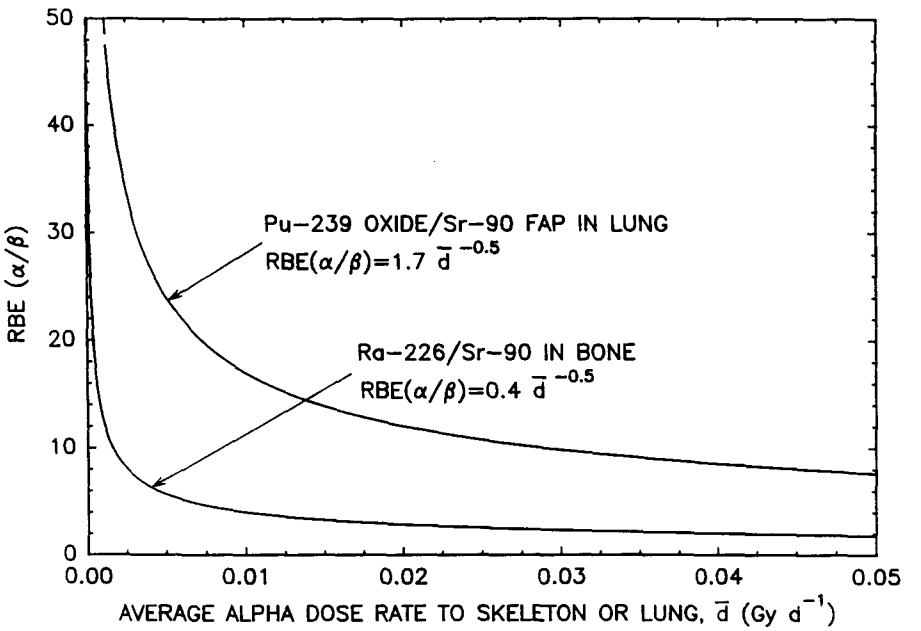

Figure 2: Apparent relative biological effectiveness, RBE(α/β), for beagle deaths with radiation-induced cancer.

observed relative biological effectiveness, RBE(α/β), varies as a function of dose rate, and rises as dose rate decreases. The RBE(α/β) contrasting Pu-239 dioxide with Sr-90 FAP at the median risk for fatal radiation-induced lung cancer in beagles and for Ra-226 versus Sr-90 bone cancer in beagles are shown in Fig. 2.

At high dose rates this radiation-induced cancer RBE(α/β) is small and rises to large values at low dose rates. As dose rate goes down the fatal radiation-induced cancer RBE(α/β) rises without limit; actually the beta effectiveness for producing radiation-induced cancer approaches zero. For example, for Pu-239 dioxide in lung at 0.1 Gy/day the RBE(α/β)=5, while at 1 mGy/day RBE(α/β)=50. The bone cancer RBE(α/β)=30 at 1 mGy/day for Ra-226/Sr-90 in bone. Since Pu-238 and Pu-239 are about 10 times more effective than Ra-226 in producing bone cancer, the apparent RBE(α/β)=300 for plutonium in bone at 1 mGy/day.

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