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A REVISED ESTIMATE OF MAXIMUM PERMISSIBLE BURDEN FOR ^{90}Sr

ABSTRACT: *A maximum permissible burden (MPB) of 9.5 μCi of ^{90}Sr is proposed for adult radiation workers. It is based on the MPB of 0.1 μCi of ^{226}Ra and the ratio of average skeletal doses from ^{90}Sr and ^{226}Ra for equal incidences of osteosarcomas in mice.*

INTRODUCTION

The calculation of the maximum permissible burden (MPB) of ^{90}Sr in man needs revision because of more extensive data kindly made available by Dr. M. P. Finkel.[12] Comparison of the oncogenic effects produced by ^{90}Sr and ^{226}Ra is possible by means of data given in Ref. 12, *Fig. 3*, based on observations of osteosarcomas arising in several thousand mice.

By confining attention to an osteosarcoma expectancy of 0.2 down to 0.03 tumors per mouse, one observes that roughly similar expectancies†

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† This statement has been challenged from different quarters. It will suffice to state here that if the ^{226}Ra data from Dr. M. P. Finkel are connected by a line located *between* the experimental points and said line is transposed by factors of 200 and 400 to the right as in *Fig. 1*, one observes that 3 points of the ^{90}Sr data can be considered to fall to the left of the 200 × Ra curve (at 1.3, 1.5, and 44 μCi/kg) and the other 3 points (8.9, 88, and 200 μCi/kg) fall almost on or to the right of the 400 × Ra line. This argument is not conclusive since the number of tumors available at these levels is insufficient to allow a firm choice between a factor of 2: the control background dilutes the significance of the data still further. It seems reasonable, however, to proceed on the more conservative assumption while waiting for more data on the 10–200 μCi/kg ^{90}Sr and the 0.05–1.0 μCi/kg ^{226}Ra levels in mice and on later results from the Beagle.

are obtained when the activity of ^{90}Sr injected per unit weight is about 200 times that of radium expressed in the same units. Since for a given level of incidence the time sequence of osteosarcoma appearance is approximately the same for both radionuclides (Ref. 5, *Fig. 1*), the absorbed doses relevant to the injected $\mu Ci/kg$ should be calculated for a single average latent period. To be on the safe side, I have chosen 600 days because it is the life expectancy of the control mice. Calculations for 800 days (approximately the latest time at which osteosarcomas have appeared in these animals) (Ref. 5, *Fig. 5*) differ by only a few percent (vide infra). Extreme assumptions relating to shorter induction times will be considered later.

DOSES IN MICE

^{226}Ra

The dose to the skeleton of a female mouse injected at about 70 days of age has been calculated according to the equation (Ref. 4, confirmed in Ref. 3):

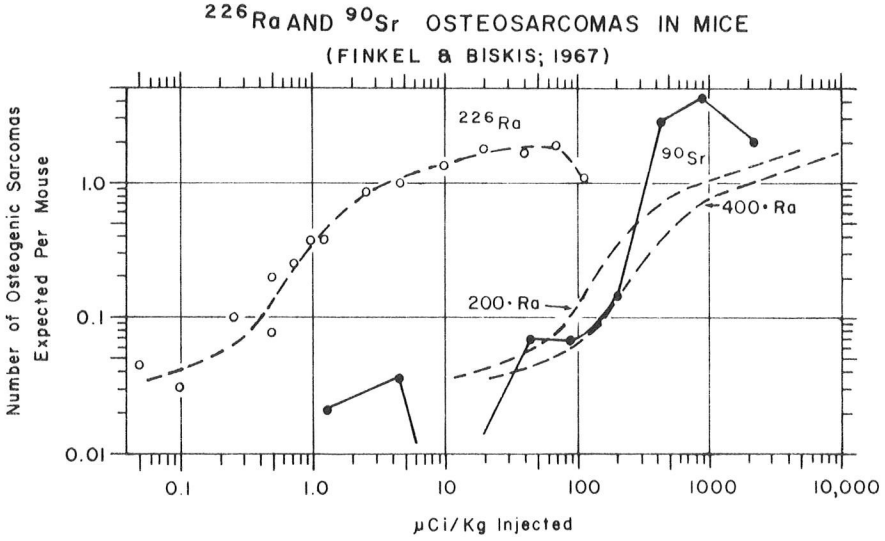

Figure 1. ^{226}Ra and ^{90}Sr osteosarcomas in mice. In the non-irradiated controls for the Ra and Sr groups, the tumor expectancy was about 0.02 osteosarcomas per mouse.

Dose (^{226}Ra) = I ($3.22t^{0.72} + 0.5t^{0.935}$) rads, where I = the number of μCi/kg injected and t is the number of days after injection.

For I = 1, t = 600 days $D^{Ra}_{600} = 520$ rads
t = 800 days $D^{Ra}_{800} = 655$ rads

^{90}Sr

The retention of ^{90}Sr in mice has been reported by many authors.[1,6,7] I have chosen Ref. 6, since it is the most relevant to the experiments in question.

The daily dose rate D_0 in an extended medium with a concentration of C μCi/g is given by:

$$D_0 = 51.2 \times \overline{E}_\beta \times C \text{ rads per day}$$

In our case, $\overline{E_\beta}$ (the average energy in MeV per disintegration of $^{90}Sr + {}^{90}Y = 0.20 + 0.93 = 1.13$) must be multiplied by the fraction $\varepsilon = 0.32$ of the energy absorbed by the average mouse skeleton.[2] Hence: $D_0(^{90}\text{Sr in mice}) = 51.2 \times 1.13 \times 0.32 = 18.55$ rads/day per μCi/g of mouse skeleton. Since ^{90}Sr is retained (Ref. 6) in mouse bone according to:

$$R = 0.75 \times t^{0.3} \text{ (t in days)}$$

and the weight of the mouse skeleton = 0.075 × the weight of the mouse,[2] or 75 g/kg the concentration C(t) of ^{90}Sr in the skeleton of the mouse, per *μCi/kg injected* will be:

$$C(t) = \frac{0.75}{75} t^{0.3} = 10^{-2} t^{-0.3} \; \mu Ci/g \text{ of mouse skeleton.}$$

It follows that the average absorbed dose D_t^{Sr} accumulated by the mouse skeleton will be:

$$\text{at: } t = 600 \text{ days}, D^{Sr}_{600} = 18.55 \times 10^{-2} \int_0^{600} t^{-0.3} dt = (0.186/0.7)(600)^{0.07}$$
$$= 23.3 \text{ rads per } \mu\text{Ci/kg injected;}$$

at: t = 800 days, $D^{Sr}_{800} = 28.5$ rads per μCi/kg injected.

Then the ratio of the average absorbed doses to the skeleton, D(Sr)/D(Ra) — producing equal incidence of osteosarcoma in mice (RBE)* comes to:

* The term, RBE, is used herein because it pertains exclusively to radiobiological experiments; it is recognized, however, that the ratio in question may depend not only on the difference in LET, but also on the marked differences in the spatial dose distribution in mice[13].

$$D(Sr)/D(Ra) = \frac{200 \times 23.3}{520} = 8.95 \quad (t = 600 \text{ d})$$

$$D(Sr)/D(Ra) = \frac{200 \times 28.5}{655} = 8.7 \quad (t = 800 \text{ d})$$

It should be realized, however, that although the exponent b in the retention equation ($R = At^{-b}$) is about the same for both Ra and Sr in mice, the ratio of the average dose-rates is not a constant in time, owing to the proportionately greater retention of radon with the passage of time; this fact does not change matters much, however, unless the absorbed dose responsible for oncogenesis is delivered in the first few T_0 days after injection. If this were the case, the RBE would be higher: thus in the extreme case of $T_0 = 1$ day

$$RBE = D(Sr)/D(Ra) = \frac{(200 \times 0.186)/0.7}{(3.22 + 0.50)} = \frac{53.1}{3.72} = 14.3$$

Hence, the value of RBE = 8.8, calculated by neglecting the osteosarcoma induction period, is on the conservative side.

CALCULATION OF THE MPB IN MAN

If one assumes that the main risk of ^{90}Sr contamination in the human skeleton is the production of osteosarcoma, and one assumes also that the magnitude of this risk in man, vis-a-vis the risk of ^{226}Ra, is the same as in the mouse, namely, equal to about 1/(8.8), then the MPB for ^{90}Sr in man follows from the product of the inverse ratios of the dose-rates by the RBE.

The dose-rates follow the average energy per disintegration: namely, 10.7 MeV for ^{226}Ra (+30% Ra[B + C]) (Ref. 8) and $1.13 \times 0.88 = 0.99$ MeV for ^{90}Sr. (The factor of 0.88 is the average utilization of ^{90}Sr + ^{90}Y β-ray energy in the human skeleton.)[2]

Hence, since MPB (^{226}Ra) = 0.1 μCi:

$$MPB\ (^{90}Sr) = 8.8 \times \frac{10.7}{0.99} \times MPB\ (^{226}Ra) = 95 \times 0.1\ \mu Ci$$
$$= 9.5\ \mu Ci$$

Note: If one considers the accumulation of Ra(D + E + F) found in Ra patients[11] the MPB (^{90}Sr) in man would be higher by about 10%.

DISCUSSION

The following data and/or comments are in order:

1. In dogs, preliminary estimates from Utah[9] indicate that the lowest skeletal doses producing osteosarcomas are 8100 rads from ^{90}Sr in a dog

dying 960 days after injection and 490 rads from ^{226}Ra in a dog dying 4108 days after injection. The ratio of 16.5 between these values should be regarded provisionally as a maximum since: (a) it is based on minimal doses producing osteosarcomas at *widely different times*, and (b) the accumulated dose required for oncogenesis seems to be *inversely* related to the average latent period[5, 14, 15].

2. Although MPB (^{90}Sr) = 9.5 μCi is conservative in some respects, it does not take into account the possible leukemogenic effect of ^{90}Sr + ^{90}Y β-rays on the human blood-forming organs.

3. The MPB (^{90}Sr) calculated above is almost identical to that proposed by Spiers[10] on the basis of ICRP limits to bone marrow.

4. The RBE (^{226}Ra/^{90}Sr = 8.8) in mice does not seem to change very much, if the dose to endosteal cells instead of average dose to the skeleton were considered. (See J. H. Marshall, ANL-6104, p. 56 [*Fig. 22*] and p. 61 [*Fig. 30*] for ^{90}Sr endosteal dose to femur and ^{226}Ra endosteal dose to lumbar spine.)

5. In view of (2) and (3) above, consideration might be given to acceptance of a new level of MPB for ^{90}Sr in man between 4 and 5 μCi. This value results from the assumption that following ^{90}Sr intake, osteosarcoma and leukemia incidence in man are equally probable; this assumption is debatable, of course, but it has the merit of leading to the lower value.

6. The possibility of the ratio of injected activities being of the order of 400 instead of 200, and the simplicity and logic of Spiers' proposal[10] have tempted many observers to favor the latter without further question. It must be realized, however, that the greater risk for leukemia induction which is therein assumed — and is implied in the lower MPB for the blood-forming organs — is supported by evidence in man irradiated only at higher dose-rates and/or over large parts of the body. No evidence exists that this greater susceptibility also exists in normal man when essentially only his skeleton is irradiated. Current observations on experimental animals indicate that ^{90}Sr irradiation of bone and marrow may produce either or both leukemia and osteosarcoma and that their relative incidence depends on injected activities, age of the animal, species, subdivision of the dose, etc.

Since no definite conclusions can be drawn at this moment as to whether leukemia or osteosarcoma is the greater risk under conditions relevant to MPB's, the most conservative assumptions should prevail.

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DIALOGUE

F. W. SPIERS: I was, of course, extremely interested in this paper. The proposed body burden of 9 μCi ^{90}Sr based on osteosarcoma risk is the same as I had calculated[10] on the basis of the permissible dose-rate to bone marrow of 5 rems per year. Although my original value of 9 μCi ^{90}Sr might have to be reduced a bit on the basis of my new calculations [see the paper by Spiers earlier in this symposium] the two quite different methods both lead to much the same result.

One day we may be able to determine fairly accurately the average dose from ^{90}Sr to bone marrow for both humans and mice so that we might be able to make an even better comparison in going from mouse to man.

CHARLES W. MAYS: Marinelli's calculation was made specifically for radiation protection from ^{90}Sr. He assumed a factor of 200 between the number of injected microcuries of ^{90}Sr vs. ^{226}Ra for equal osteosarcoma expectancy in mice. For protection purposes this seems adequately conservative.

However, for a deeper understanding of the radiobiology involved, the best estimate of this factor is of greater importance than a conservative estimate. From Miriam's original data[12] (replotted and fit with a new curve in Marinelli's Fig. 1) a factor of 400 seems more appropriate for data in the region of interest. Using this factor, the computed risk from osteosarcoma in man for a constant burden of 0.1 μCi ^{226}Ra equals that from 18 μCi ^{90}Sr. This is twice the conservative value of 9 μCi ^{90}Sr proposed by Marinelli for protection purposes.

JOHN H. MARSHALL: Perhaps the factor of 200 is on the conservative side, but we must keep in mind that this comparison is based on Dr.

Finkel's new ^{226}Ra curve and her old ^{90}Sr curve. In her original ^{226}Ra experiment, she found that injected doses for the same biological effect were larger by factors of 5 to 10, than the values found in this new experiment. Why were these two ^{226}Ra curves different?

There seem to be plenty of animals at the pertinent incidence points for ^{90}Sr, so I am not worried about the statistics of the old ^{90}Sr curve. I don't believe there was any unusual disease in the old ^{90}Sr experiment, but there was considerable extraneous disease in the original ^{226}Ra animals. Perhaps Miriam should say more about this. Although there are reasons to question the original ^{226}Ra curve, I am not sure whether disease can explain so large a difference.

MIRIAM P. FINKEL: The original radium experiment was done many years ago, and the animals were good animals for those days; however, we wouldn't consider using mice with their array of diseases today.

Marinelli's comparison involves two experiments, both done with healthy animals. The ^{90}Sr experiment contained about 920 mice, the ^{226}Ra over 3000. If we were to repeat the ^{90}Sr experiment now, we would have many more animals at the lower levels.

Now, let us turn to Chuck Mays' interpretation of my data. He suggested a factor of 400 for the ratio of injected ^{90}Sr to ^{226}Ra activity for equal effectiveness in mice, rather than the factor of 200 which Marinelli used. I feel the factor is closer to 500 at the lower levels.

ROBERT E. ROWLAND: The net result then is that Leo's assumption of 200 is very conservative, and therefore his calculation of the maximum permissible level for ^{90}Sr based on this arithmetic should be considered to be very much on the safe side.