THE CANCER-LEUKEMIA RISK FROM FRC GUIDELINE RADIATION BASED UPON ICRP PUBLICATIONS

(Complete Consistency with Gofman-Tamplin Estimates)

by

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INTRODUCTION

Our original estimate of 16,000 additional cancer plus leukemia deaths annually in the U.S.A. from F.R.C. Guideline exposure (0.17 Rads per year) was based upon the conservative estimate of a 1% increase in cancer plus leukemia risks per rad, or a 100 rad doubling dose (1)(2). The doubling dose is defined as that amount of radiation productive of an excess occurrence of a malignancy equal to its spontaneous occurrence (1). More recently, analysis in detail of many data has indeed indicated the conservative nature of the early value of 1% increase in occurrence rate per rad, since the later analyses suggest 2% per rad, or a 50 rad doubling doubling dose (3). Even this may still be conservative, and thus underestimate the true risk of cancer and leukemia induction. The use of 50 rads as doubling dose leads to a revised estimate of 32,000 extra cancer + leukemia deaths annually from population exposure to FRC Guideline radiation.

Some critics of our estimates, the AEC-DBM staff noteworthy among them, quickly took refuge in a desperate hope that somehow, somewhere they could find disagreement with our estimates in some reputable source. Strangely enough, and for reasons we cannot understand, the refuge chosen by many is the work of the International Commission on Radiological Protection. We hold the ICRP in the highest regard, and realized that this body, above all, could be relied upon to treat the problem appropriately, once all the data were available.

Apparently our critics misconstrued one particular position expressed by a task force in ICRP Publication 14 (4). In that publication the ICRP Task Force suggested that it did not choose to consider the doubling dose concept as an appropriate approach to the treatment of radiation carcinogenesis and leukemogenesis. This is fine. Various investigators, at a particular point in time, interpret observations differently. However, the unsophisticated reader of documents such as the AEC-DBM Staff Comments (5) might be left with the utterly erroneous impression that the ICRP Task Force would, as a result of eschewing the doubling dose concept, arrive at a risk estimate drastically lower than ours. This erroneous impression can readily be corrected by

realization that our estimates are based upon observations; the doubling dose concept is hardly a requisite for estimating expected cancers and leukemias provided sufficient observational data are at hand.

It is our purpose here to estimate the extra cancers plus leukemias from FRC Guideline exposure using only data presented in one or another ICRP publication. No use whatever will be made of our doubling dose approach. As will be noted the ICRP data lead to estimates quite consistent with our own. We have previously pointed out the close similarity of ICRP-14 to our own position (6).

ICRP Publication 14-Revised estimates of cancers versus leukemia in irradiated persons.

In the ICRP Publication 14 the updated results of Court-Brown and Doll (7) on the ankylosing spondylitics are considered in detail. Court-Brown and Doll and the authors of ICRP 14 point out that with the passage of followup time, the number of cancers at "heavily irradiated sites" has grown steeply and progressively in comparison with the number of leukemias. In the last report the cancers at such sites dominate the picture over leukemia by far. In Table 2, p 22 of ICRP 14 are presented an important set of data, reproduced here without change, which demonstrate the progressive dominance of cancers at heavily irradiated sites versus leukemias.

TABLE 2 of ICRP 14 (p22)(Ref.4)

Change in rate of induced malignant disease with duration of time since exposure in irradiated ankylosing spondylitics (from data in Table VI of Court-Brown and Doll, 1965)(Ref.7)

Years after irradiation	Cases per 10,000 man-years at risk	
	Leukemia + aplastic anemia	Cancers at heavily irradiated sites
0-2	2.5	3.0
3-5	6.0	0.7
6-8	5.2	3.6
9-11	3.6	13.0
12-14	4.0	17.0
15-27	0.4	20.0
Total of expected cases in 10,000 persons in 27 years calculated from the rates given	67	369

Now, separately ICRP 14 quotes Dolphin and Eve's (8) estimate that the stomach received a mean dose of approximately 7% of the mean dose received by the spinal marrow, and further the ICRP 14 states, (p61)(Ref.4)

> (Quote) "Under the same conditions of spinal irradiation the dose to colon, pancreas, bronchi or pharynx is likely to be similar to the dose to the stomach and, judging by the observed excess of tumors, these organs may also seem to have a similar sensitivity to each other and to bone marrow and stomach."

Let us accept the ICRP 14 suggestion (based upon Dolphin and Eve) that "the heavily irradiated sites" received approximately 7% of the mean dose to the spinal marrow. This puts us immediately in position to calculate the expectation for true whole body radiation, namely, where all organs receive identical rad doses. One additional parameter is useful, namely, the estimate quoted from ICRP Publication 8 that approximately 40% of the active red marrow was irradiated in the ankylosing spondylitics (ICRP 14, p 61)(Ref.4).

ESTIMATION OF EXPECTED CANCERS + LEUKEMIAS FROM ICRP PUBLICATIONS

From the spondylitis data, where 40% of the active marrow was irradiated, we have the ratio $\frac{\text{cancers at heavily irradiated sites}}{\text{leukemias}} = \frac{369}{67}$

But, from the data above the heavily irradiated sites received only ~ 7% of the mean spinal marrow dose. To correct this to true total body radiation, we must multiply the above ratio by 100/7, or 14.3

Therefore $\frac{\text{Cancer at heavily irradiated sites}}{\text{Leukemias}} = \frac{369}{67} \times 14.3$, or $\underline{\underline{78.7}}$

Thus, if we can now get absolute numbers of leukemias per rad, we shall by use of the ratio above be able to get the absolute number of cancers per rad. And then lastly we must account for leukemias arising in the remaining 60% of the active marrow, which was not irradiated in the ankylosing spondylitis studies.

Two sources of data, abundantly described in ICRP publications, are available to estimate leukemia incidence per 10^6 persons per rad:

(a) the spondylitis data themselves

(b) the Japanese data

The spondylitis data

Dolphin and Eve (8) quote an estimate of an average dose to the spinal marrow of 880 rads (with 40% of the marrow irradiated). This same value would be arrived at directly from Table 16 in the original Court-Brown and Doll publication (9).

For 880 rads, irradiating 40% of active marrow we had in Table 2 (from ICRP 14) above a total of 67 leukemias over a 27 year period in 10,000 persons.

Therefore, for 10^6 persons, the leukemia expectation per rad in 27 years

$$= 67 \times \frac{10^6}{10^4} \times \frac{1}{880}$$, or 7.6 leukemias per 10^6 persons per rad in 27 years (40% of marrow irradiated)

The Japanese (Hiroshima-Nagasaki) data

The leukemia produced by radiation in Hiroshima-Nagasaki survivors is cited (ICRP 14 p.64) as 20 cases per 10^6 persons per rad in 14 years subsequent to exposure. It is further suggested there that since leukemia, especially acute leukemia, was still occurring after 14 years, the final total number of leukemias was going to be appreciably increased above this figure. However, by comparing the Japanese data with the spondylitis data, ICRP 14 authors suggest the final total leukemia incidence, say by 27 years post irradiation, would not be likely to exceed 2 x 20, or 40 cases per 10^6 persons per rad. For conservatism, so as not to overestimate risk, let us use a value $\frac{1}{2}$ way between the observed number of cases and the upper limit suggested in ICRP 14 - this would be 30 leukemias per 10^6 persons per rad in 27 years. Now, the Hiroshima-Nagasaki data have been treated assuming true total body irradiation. Therefore, to compare these estimates with those for the spondylitics, we must calculate the expected leukemias if 40% of

the active marrow were irradiated.

$\therefore$ 40% of 30 = 12 leukemias per 10^6 persons per rad in 27 years (for 40% of active marrow irradiated).

Cancers at Heavily Irradiated Sites

We have 2 estimates for leukemia incidence (with 40% of active marrow irradiated).

(Spondylitis data) 7.6 cases per 10^6 persons per rad in 27 years

(Japanese data) 12.0 cases per 10^6 persons per rad in 27 years

Since we have little reason to choose between these values, the range will be preserved to estimate cancers at heavily irradiated sites. In the discussion above, it was shown, if the heavily irradiated sites received equivalent radiation to that received by the spinal marrow, there would be 78.7 times as many cancers as leukemias.

Therefore,

(Spondylitis data) 78.7 x 7.6, or 598.1 cancers per 10^6 person per rad in 27 years

(Japanese data) 78.7 x 12.0, or 944.4 cancers per 10^6 persons per rad in 27 years

ESTIMATED CANCERS FOR FRC GUIDELINE EXPOSURE OF U.S. POPULATION

At 0.17 Rads per year (FRC Guideline), the accumulated dose by age 30 years is $30 \times 0.17 \cong 5$ Rads.

There are $\sim 10^8$ persons over 30 years of age in the U.S.A.

There are 3 components to the total cancer + leukemia cases

(a) Leukemias calculated above for 40% of active marrow irradiated

(b) Cancers at heavily irradiated sites

(c) Leukemias to be added if remaining 60% of active marrow were irradiated (as of course it would be in true total body irradiation)

These can now be summed, both for the spondylitis estimates and for the Japanese data estimates, correcting to 10^8 persons and 5 rads from 10^6 persons and 1 rad. These are the following:

Cases per 10^8 persons for 5 rads in 27 years	From spondylitis data	From Japanese data
Leukemias (40% of marrow irradiated)	$7.6 \times \frac{10^8}{10^6} \times 5 = 3800$ cases	$12 \times \frac{10^8}{10^6} \times 5 = 6{,}000$ cases
Cancers at heavily irradiated sites	$598.1 \times \frac{10^8}{10^6} \times 5 = 299{,}050$ cases	$944.4 \times \frac{10^8}{10^6} \times 5 = 472{,}200$ cases
Leukemias (remaining 60% of active marrow)	$\frac{3}{2} \times 7.6 \times \frac{10^8}{10^6} \times 5 = 5700$ cases	$\frac{3}{2} \times 12 \times \frac{10^8}{10^6} \times 5 = 9{,}000$ cases
Total cancers + leukemias	308,550 cases	487,200 cases
But since these are estimates for 27 years, the value per year would be	$\frac{308{,}500}{27}$, or 11,425 cases/year	$\frac{487{,}200}{27}$, or 18,040 cases/year

For persons over 30 years of age, the Gofman-Tamplin estimates were:

14,000 cases per year - if doubling dose = 100 rads
28,000 cases per year - if doubling dose = 50 rads
(Gofman-Tamplin suggest the higher value probably closer to the true value)

The range estimated from ICRP publication data, namely 11,425 - 18,040 cases must be a minimum estimate for several important reasons:

(a) The ICRP data used here credit no cancers or leukemias beyond 27 years, although the ICRP indicated that the Court-Brown and Doll data used suggested that additional cases are to be expected, and possibly at a higher rate per year than that for the average of the 0-27 year period calculated.

(b) For the heavily irradiated sites, some of the cancers not proven statistically significantly elevated in the spondylitis cases might become so - if allowance for longer latency is made. (Suggested in ICRP 14).

(c) With true total body irradiation, all the "lightly irradiated sites"would become "heavily irradiated sites" and there should therefore accrue an appreciable increment in total number of cancers. But since we are here enjoining ourselves from all but direct observation, no credit at all will be given to this likely appreciable increment.

The estimates derived from ICRP publications we shall therefore leave as 11,425+ to 18,040+ cases per year from FRC Guideline exposure, where the + may be quite appreciable for the reasons cited above.

Conclusion

The estimate of additional cancers plus leukemias from FRC Guideline radiation exposure derived from observational material treated in ICRP publications is clearly consistent with the estimate derived by Gofman and Tamplin using the doubling-dose concept. If consideration is given to a number of factors that would necessarily operate to increase the estimates from ICRP reported data, it is entirely possible that these estimates, already similar to those of Gofman-Tamplin, may even exceed those arrived at by the doubling-dose approach.

Since the estimates derived from ICRP publications are based strictly upon observational material, one wonders how critics of Gofman and Tamplin make such incredible statements as "the Gofman-Tamplin estimates are based upon "questionable assumptions" or upon "the scientifically invalid doubling dose concept", etc., etc. Certainly such critics can find no support for their untenable position in ICRP publications, since as shown here estimates derived therefrom are similar to those of Gofman and Tamplin. The Main (ICRP) Commission has not yet published estimates since ICRP 14 has become available. We are confident they will arrive at the same general conclusions presented here.

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