

ON THE USE OF QUALITY FACTORS AND FLUENCE TO DOSE
RATE CONVERSION IN HUMAN RADIATION EXPOSURES

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In principle, the distribution of absorbed energy in the tissues of a human exposed to ionizing radiation can either be measured more or less directly by *in situ* dosimetry, or it can be calculated from a knowledge of the energies and angular distributions of the particle fluences impinging on the individual or phantom. The first method can quickly and simply determine the quantity of interest: dose, without the intervening complications, approximations and uncertainties of the second method. In fact, one reason the quantity "dose" was invented was just the elimination of these intermediate steps. But direct measurement is not always possible, and it can seldom be used to obtain dose values at more than a few points within the tissues. The second, more indirect method is now developed to a degree of detail sufficient to produce a virtually complete description of the dose distribution resulting from any arbitrary combination of radiation fluence and energy. Conversion to dose by calculation, however, not only requires charged particle telescope or spectrometer data, but a computer and a program of some complexity as well, imposing even greater practical limitations than does the first method.

But a far more fundamental limitation applies in either case. The use of dosimetric data to assess the biological implications of a given exposure requires additional knowledge of the kinds and degree of effects which result, not simply from the given total amount of absorbed energy, but much more critically, from the way in which that quantity may be distributed both microscopically and macroscopically, in both space and time, from one case to another. The radiobiological uncertainties which occur at this stage are so marked and so incompletely defined that the ability to establish an exposure status still clearly lags behind the technical means of obtaining, by either of the above methods, the dose data on which to base it.

How then do we arrive at conclusions about the status of the human individual - which is, after all, what we are trying to assess - by any combination of these factors? The question is so broad and still so debatable that one can only attempt here to sum up briefly some areas in which much work has been done in the past, and to try to illustrate how imprecise are our attempts to evaluate whole body exposure, as distinct from the highly local doses so well discussed by Dr. Curtis. To paraphrase Dr. Drew, we are indeed trying here to make our technology of physical measurement serve the cause of human values - numerical ones, to be sure, but none the less human - and it is no easier here than it is elsewhere.

In Fig. 1 the familiar regulations referring to ordinary exposures are summarized; in regard to space radiation exposure they belong to an earlier and simpler age. Nevertheless, there are several assumptions implicit in these values which underlie their apparent simplicity. For example, quality factors are built in; they are not mentioned, but a QF is inherent in each rem unit used. How to decide what these QF's shall be is of course left up to the technician who must hold the personnel exposures within these levels.

More importantly perhaps, the approach used in setting these regulations is that of the critical organ or group of organs. The body is subdivided into regions or systems, and to a great extent they are treated separately. This is due not only to the kind of data available but also as much as anything else to the necessity of designing regulations which can handle both internal and external exposures. When radioisotopes are taken up by the body, of course many of them tend to concentrate in certain organs; but when an exposure is external the nonuniformity of dose distribution occurs for entirely different reasons.

In the case of space radiation exposure this nonuniformity can reach an extreme degree, not only with respect to dose distribution and LET but even to the extent of microscopically localized high doses of the kind Dr. Curtis has just discussed. In attempting to deal with such exposures we are used to a certain kind of thinking, and although we do not follow it explicitly in setting astronaut doses we still tend to think in terms of critical organs, which may not necessarily be the best approach in all cases. When we know that an effect is local, confined to the retina of the eye for example, we can certainly use this approach; but if we think that a number or set of numbers must be sought to describe the overall physiological status of an individual post-exposure, the critical organ approach can lead to contradictions.

Fig. 2 sets forth the other half of this somewhat simplistic approach, which has still been found to be practical enough for most cases. We simply make another set of rules: depending on the LET of the radiation involved, regardless of its type, we now multiply any dose by a number, the QF, and so arrive at its relative "effectiveness". This can presumably be done for any tissue location and volume in which this radiation is deposited, and doses to different regions of the body are thus multiplied by the appropriate QF's and treated almost independently.

<i>Exposed Part of Body</i>	<i>Occupationally Exposed Persons</i>	<i>Public at Large</i>
Whole body, blood-forming organs and gonads	5 rems/yr 3 rems/quarter*, provided the cumulated dose to age N years is less than 5 (N-18)	0.5 rems/yr
Bone, thyroid, skin	30 rems/yr 15 rems/quarter	3 rems/yr†
Hands, forearms, feet and ankles	75 rems/yr 40 rems/quarter	7.5 rems/yr
All other organs	15 rems/yr 8 rems/quarter	1.5 rems/yr

* A planned special exposure for occupationally exposed workers of twice the yearly dose is permitted when alternative techniques are either unavailable or impractical. This is 10 rems/exposure to the whole body.

† 1.5 rems/yr to children up to 16.

FIGURE 1

LET _∞ (keV/μ IN WATER)	QF
X rays and electrons of any LET	1
3.5 or less	1
3.5-7	1-2
7-23	2-5
23-53	5-10
53-175	10-20

*From NCRP [1954].

FIGURE 2

In practice, most records that are kept today are not broken down into these categories. Generally one is fortunate when one has a single number to describe a person's exposure. In space, we are trying to refine things somewhat further because of the different radiations and higher doses with which we are concerned, and it is here that we encounter difficulties in attempting to apply sets of numbers. The characteristics of space radiation which are of chief importance in this regard are the range of energies which occur and the change of both energy and fluence rate with time. Dr. Lushbaugh has discussed the effects of time very thoroughly; some of the other properties will be mentioned here. The situation is indeed far more complex than are those for which the ordinary MPD concepts were developed.

Fig. 3 shows what is perhaps one of the most important characteristics of heavy particle interactions; the "transition curve" and the build-up of dose to a maximum due to production of secondary radiations (1). The phenomenon has been known for some time; its effect on dose distributions is much greater than that of the Bragg Peak doses at the ends of the paths of charged particles. The transition build-up results from the production of secondary particles from two main processes: intranuclear cascades and evaporation processes, each of which vary as a function of both incident particle energy and the mass number of the target material.

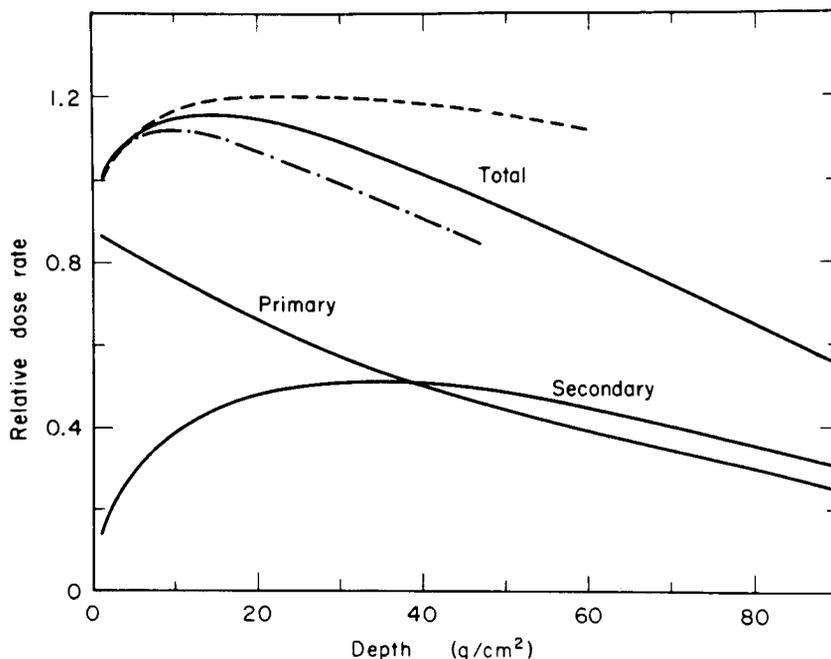


FIGURE 3

Fig. 4 illustrates one instance in which a program was designed to compute dose build-up due to these secondary processes (2). The experimental data fits the calculated values fairly well for a beam of the energy indicated (3). Fig. 5 is from another more recent program which converts flux to dose at given energies (4). These are both representative instances of the kinds of calculations that are possible. When one also folds in the energy spectrum of a solar flare, of trapped radiation, or of galactic cosmic ray charged particles, the sum of such a set of curves results in the familiar steep fall-off of dose with depth.

Quite some time ago, Dr. Schaefer very clearly pointed out that in addition to the distribution of dose on the macro scale, one should take into account the high LET at the ends of proton tracks which result either from neutron interactions or from primary proton cascades or other secondary processes. At the ends of their tracks, protons reach about a three-fold higher value of local LET than do the secondary electrons produced by electromagnetic radiation. All this is familiar ground; the problem lies in the distribution and concentration of such track ends under the conditions we are talking about.

Fig. 6, from Schaefer, illustrates the distribution of LET produced by a flux of charged particles passing through tissue (5). Three cases are shown; the first is for orthovoltage 250 KVP x-rays, showing the LET distribution of the secondary electrons produced by the gamma photons. The second is for a typical solar flare proton energy spectrum, which produces essentially the same distribution in LET as do the x-rays, and should therefore have very much the same RBE and QF, with the exception of the small portion of track enders. As Dr. Schaefer pointed out yesterday, this distribution varies between earth orbital and free space exposures. The LET distribution shown in the third case is that for the recoil protons produced by neutrons with the fission energy spectrum.

Fig. 7 shows how the use of the QF values which result from these differing LET distributions were first applied to the calculation of dose and dose equivalent for tissue for a variety of different energies. This figure, from Kinney and Zerby (6), shows first the dose and then the dose equivalent in rem for both normally incident and isotropically incident proton fluxes at five centimeters depth in tissue, as a function of proton energy. Many such curves have since been generated to estimate how rad and rem dose should vary with energy at given tissue depths under a variety of shielding conditions.

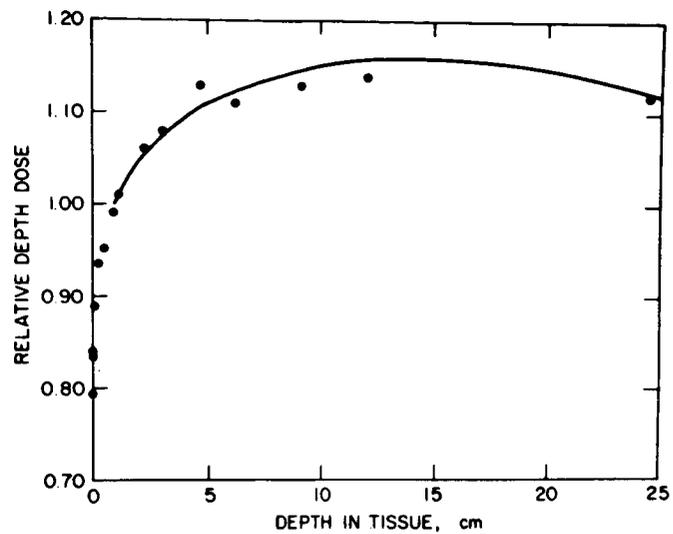


FIGURE 4

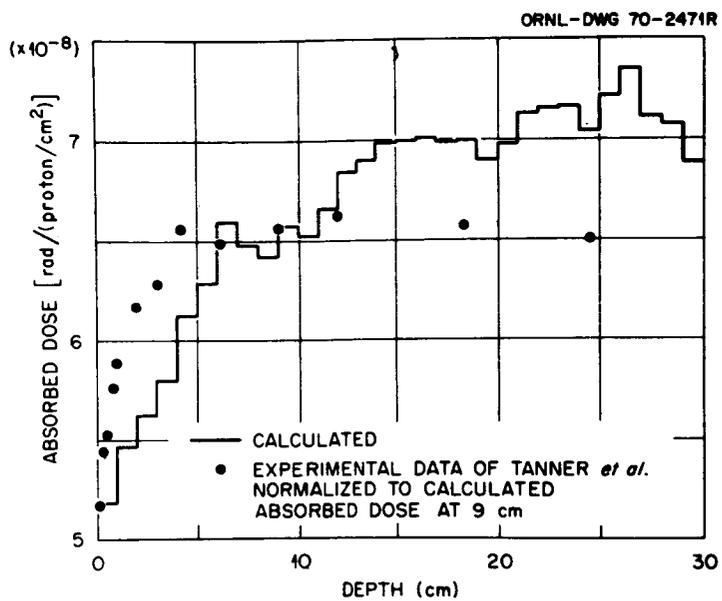


FIGURE 5

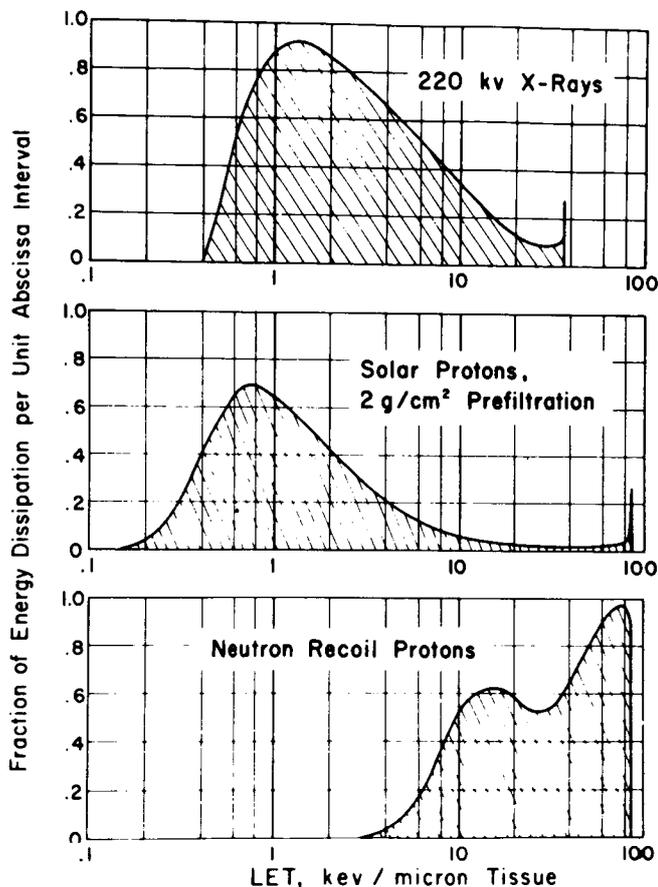


FIGURE 6

Another way to present the same data is to calculate separately the dose and dose equivalent for each type of secondary particle as a function of depth so that, for example, normally incident protons can be treated as producing ionization from both primary and secondary protons, secondary neutrons, heavy nuclei, pions, and so on. All of these sub-classes and their dose equivalents can then be added together to give a dose equivalent at any depth.

Fig. 8 shows another way in which such data have been treated (7). In this figure, the dose at the center of a water sphere whose radius varies from one centimeter to several tens of cm is calculated, and a quality factor is also calculated for its center as a function of the primary proton energy and hence, of the residual energy of protons which reach the sphere center. This quality factor is simply the number of rem per rad; again, each of the calculated values simply results in a number by which to multiply a dose which one may or may not be able to measure directly.

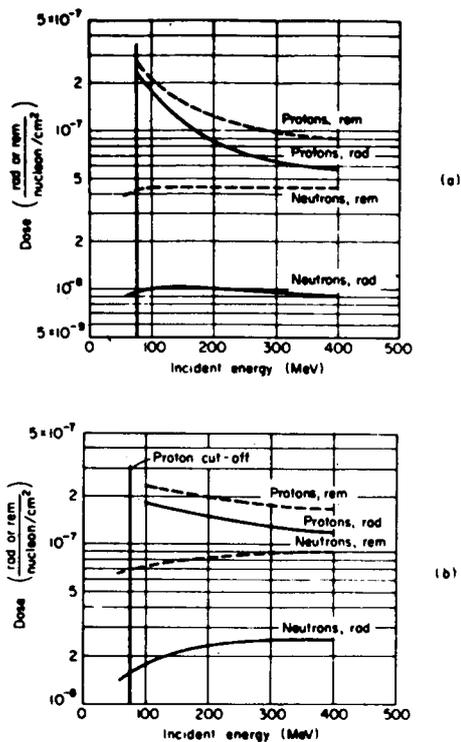


FIGURE 7

An important question is: how closely can any of these numbers be calculated, or applied, to the quite irregular geometry of the human? Some heroic efforts to deal with this question are currently being made. Dr. Kase will talk on this tomorrow and I will only mention it. Briefly, coordinate systems are assigned to an average human geometry, including those body elements which can be considered as separate systems which remain internally constant even though their configurations relative to each other change when seated, standing, and so on.

Using the standard Air Force man, a machine computation can then produce distributions of tissue depth surrounding any point in the body, which will indicate what percent of the total solid angle subtended by that point is shielded by a given tissue thickness. In this way the build-up factors, the attenuation, the production of secondaries and all of the other physical phenomena which intervene between flux and dose can be treated separately and summed up for the point in question.

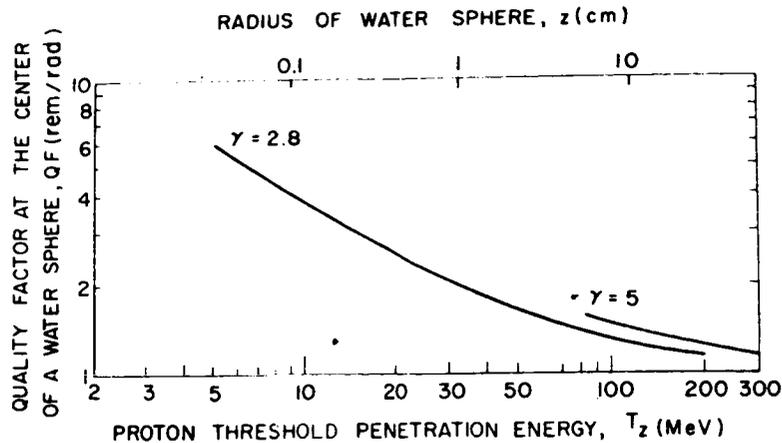


FIGURE 8

For example, in Fig. 9 the dose point is the heart; the curves compare various degrees of detail in such man models and show to what degree simplification influences the calculated tissue thickness distribution (8). In a previous study (9) a given proton spectrum, that measured on a Gemini mission, was used to determine a dose conversion factor for several points (e.g., the center of the gut in Fig. 10); that is, the number of rads per hour per 10^4 protons per square centimeter per second. One can say further that for this particular case, the greatest contribution to the dose at this particular point in this particular standard man is due to the particular calculated range of incident proton energies indicated.

What then does physical data of this kind imply in biological terms? We really do not have data which is precise enough on the biological side (particularly the human biological side, as Dr. Lushbaugh has pointed out) to match the degree of detail in the physical data; the kinds of biological data we do have are considerably more "overall" in character. For example, one can compare experimentally, as Jackson did almost a decade ago, two types of exposure in which the familiar depth dose pattern of solar flare protons is contrasted with an idealized uniform case.

But, in order to do this, he had to do something physically analogous to what the computational programs have usually limited themselves to; that is, he compressed his animals literally into cylinders, into regular shapes which could be irradiated with Co-60 gamma radiation through a wedge filter, producing the dose distribution by rotation. It was of course found that the LD-50 dose for a uniform exposure could be described by a single number, but that for the non-uniform case, one had to choose some other way of characterizing the dose distribution; for example, the ratio of midline to surface dose, or the dose at some reference depth, e.g., 5 cm.

In Fig. 11, from Dr. Bond and associates at Brookhaven, another method of comparing different dose distributions is illustrated (10). Bilateral and unilateral exposure data were obtained for the dog, and the LD-50 dose for 30-day mortality was expressed as a midline air dose, as a midline tissue dose, and as an entrance and an exit dose. Since the bilateral exposure produces a symmetrical pattern with a build-up in the center, the midline LD-50 dose is 280 rads, whereas the doses at entrance and exit are somewhat less; but it is still almost a flat dose pattern. These values do not mean a compressed dog, or a cylinder, or rotation, or anything of the sort; they are simply data that were already on hand. If one now considers the unilateral case, with a midline air dose of 384 rads, it takes 337 rads at the midline, with 530 rads at entry and 168 rads at exit, to produce the same LD-50 in 30 days.

In order to arrive at some way of characterizing numerically such a difference in uniformity (Fig. 12) one very roughly divides the body into three equal regions, each containing part of the total pool of stem cells which are located in the marrow and produce the formed elements of the blood. An estimate is then made of the fraction of the total stem cell pool which is in the volume nearest to the source, the fraction located medially, and the fraction which is in the distal region. If one then estimates the average dose to each of these three parts, one can now apply the known reproductive survival curves for stem cells, making the assumption, which seems to be justified, that they are applicable *in vivo*. If one then calculates the fraction of each of these three parts of the marrow cell population which would be expected to go on proliferating after its respective dose, and multiplies that part of the pool population by its calculated fractional survival, then one can estimate the total relative number of surviving stem cells; this is shown in the last column. If one does the same thing for

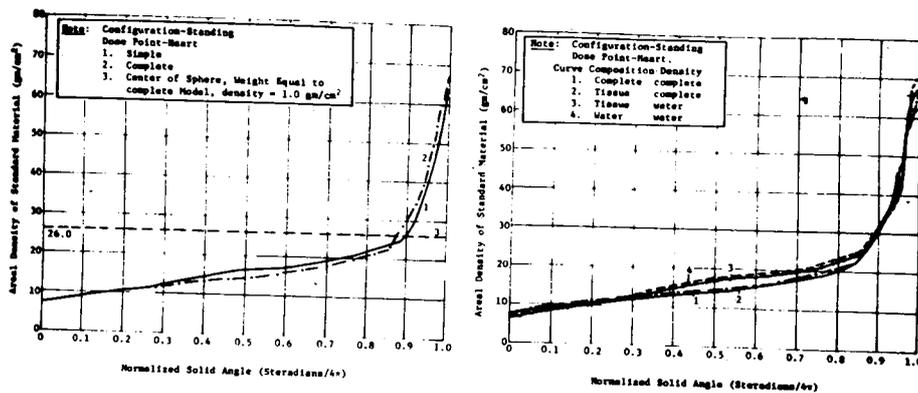


FIGURE 9

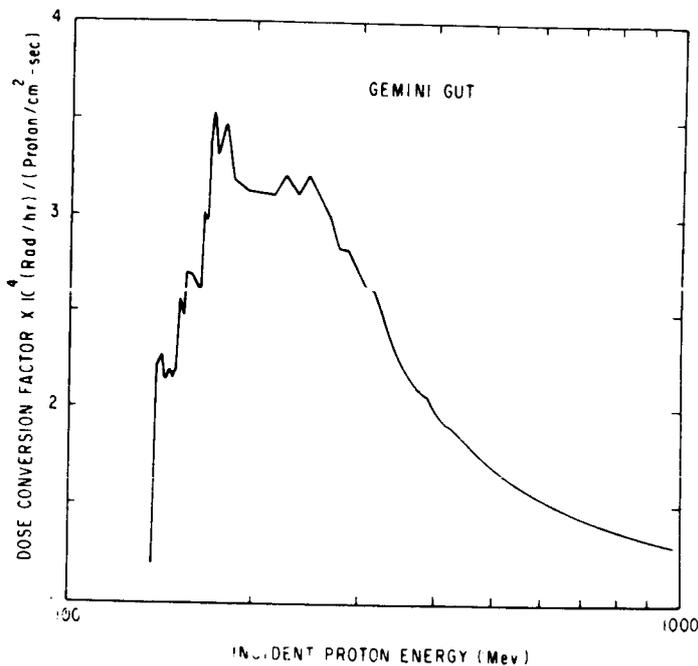


FIGURE 10

the bilateral case, which is much more uniform, one can work backwards from the dose (although as Dr. Lushbaugh says, "its in a way circular") and it can be seen that approximately the same fractional number of surviving, dividing cells results whether the exposure is uniform or not.

This analysis applies only to a regenerating tissue; in the case of a tissue which is not proliferating, of course, a different set of considerations apply. Dr. Curtis has pointed out how the Fractional Cell Lethality concept, a similar procedure applied to cells surviving high, localized particle track doses in an organ which is not proliferating, serves a somewhat

similar purpose.

Figs. 11 and 12 illustrate an attempt to normalize and compare whole animal doses, and to use something similar to an FCL for the whole exposed mass of proliferating tissue (here, of course, for radiation of QF 1). As a result of this analysis, an effectiveness factor can be estimated for the non-uniform distribution compared to the uniform one; the ratio turns out to be about 0.78 in this case. In this way, a non-uniform dose distribution can be weighted by a "Distribution Effectiveness Factor" analogous to a QF, but now not due to differences in micro dose distribution, but to dose pattern differences on the gross level.

LD₅₀₍₃₀₎ VALUES FOR DOGS AND SWINE EXPOSED BILATERALLY VERSUS UNILATERALLY TO MEGAVOLTAGE X-RADIATION

Species, exposure type	LD ₅₀₍₃₀₎			
	Midline, air	Entrance, tissue	Midline, tissue	Exit, tissue
Dog, bilateral	319 ^a	266 ^b	280 ^b	266 ^b
Dog, unilateral	384 ^a	530 ^b	337 ^b	168 ^b
Swine, bilateral	375 ^a (350-400)	272 ^a (253-290)	234 ^a (218-250)	272 ^a (253-290)
Swine, unilateral	500 ^a	584 ^a	312 ^a	131 ^a

^a Exposure in roentgens.

^b Absorbed dose in rads.

FIGURE 11

CALCULATION OF THE SURVIVING FRACTION OF STEM CELLS IN THE DOG EXPOSED UNILATERALLY TO 1000-KVP X-RADIATION

Body region	Dose (rads)	Relative number of stem cells	Surviving (%) (from Fig. 1)	Relative number of surviving stem cells
Proximal third	530	43	0.5	0.0
Middle third	337	31	4	1.2
Distal third	168	26	23	6.0
Total		100		7.2

FIGURE 12

In Dr. Lushbaugh's discussion it was shown that if one attempts to do something similar with man, one cannot extrapolate from all the animal data, and one cannot of course do the same kind of studies on man. But at least, for ordinary gamma radiations such as from Co-60 and Cs-137, determining a distribution of the same kind and making some assumptions based on the known percentages of the total marrow which lie at different depths, one can in principle arrive at a similar distribution effectiveness factor and compare this for cases in which, accidentally or otherwise, such non-uniform exposures have been received. There has been a fair degree of success in doing this so far. It is clearly a totally different process than just multiplying a dose distribution by a QF value, although it ideally should result in at least an equal degree of prediction confidence.

As Dr. Curtis has already shown, if one considers radiations of higher LET's, the kinds of survival curves which can be used to predict the survival of stem cell populations change in their shape as well as in their slope. It is the ratio of dose from a curve for x- or gamma radiation to that for a higher LET radiation for a given level of effect which defines the relative biological effectiveness on which all the QF's are based. There is a "multievent" shoulder on the low LET curve; as first shown by Elkind, if one divides the dose into fractions separated by a time interval long enough for recovery, by the next time a dose is given the same shoulder has reappeared. The increase in dose necessary to give the same degree of effect when a low LET dose is protracted can be explained on this basis. In the case of the straight exponential survival curve seen for high LET radiation, there is little or no recovery. The time factor is thus applicable to low LET, but not significantly to high LET exposure, just as the oxygen enhancement ratio that Dr. Curtis has mentioned also differs for high and low LET.

Another consequence of the fact that the low LET curve has a shoulder and the high LET one does not is that the ratio "RBE" is a function of the degree of effect. One therefore has a range of RBE values for any two radiations, depending upon how far down the pair of survival curves one is comparing doses. For low dose rate levels or for many small doses one is therefore comparing effectiveness at a different ratio. This generally leads to higher RBE values at low doses than have usually been obtained experimentally, where it is much easier to do an experiment by irradiating with higher doses. Caution in the use of QF's is thus necessary because of this time factor as well.

Reliable collections of animal data now exist for reasonably monoenergetic primary neutron exposures. The production of recoil protons in the tissues of rather small animals results in a fairly predictable mean LET for each of a series of energies. Experiments at these energies by several different groups of investigators using a number of endpoints have produced RBE values which follow a reasonably definite relation to LET. This "whole animal RBE" is the combined result of a number of things happening together, and it does not agree very closely with the RBE from cell survival curves, although a whole body RBE is clearly the end result of the processes that a single cell survival curve depicts for each cell type. For these small animals, one gets RBE's in the range of 5 or 6; if the animal is larger and the distribution of secondaries is different, different neutron RBE values may result.

Dr. Lushbaugh has derived a total body RBE for the human in a mixed field of gamma and neutron radiation by using Hiroshima and Nagasaki data and comparing the 60-day survival curves (11). As shown in Fig. 13, they can be superimposed as a function of horizontal range for light steel buildings, for which the most recent (T-65) dose estimates of gamma and neutron radiation yield approximately equal gamma and neutron doses in Hiroshima, but neutron to gamma ratios of about 1 to 12 in Nagasaki. Under these shielding conditions, he could then try different RBE factors for the neutron component to make the 50% survival doses match one another; in this way a human total body RBE of 2 was estimated. This should be compared with the value which he discussed earlier today, which may be about twice as high when estimated differently and with better data.

Obviously, the RBE may also depend on how one chooses the endpoint, and how confident one is that other factors are not involved, such as blast and burn damage in the case of the Japanese. One clearly cannot be as exact or as confident with the human data as is possible with cells, or even with small animal data. This is one reason the total body, approximate but presumably over-cautious QF values were invented, to be distinguished from RBE's. It also should illustrate the logical inconsistency of multiplying the dose at each point in a distribution by such QF values, a practice which has unfortunately become rather widespread.

Air-Dose Estimates for 50% Survival from Atomic Bomb Irradiation Under Various Shielding Conditions

Situation ^a	50% survival distance (km)	50% survival		REM RBE _n	REM RBE _n = 2.0	
		γ Rads	η Rads			
<i>Hiroshima</i>						
OU	1.18	102	78	180	258	± 39 ^b
LSF	0.73	1000	1000	2000	3000	
SRC-L	0.13	9000	10,000	19,000	39,000	
<i>Nagasaki</i>						
OU	1.35	250	5	255	265	± 27 ^b
LSF	0.76	2900	250	3150	3400	
SRC-L	0.54	6500	600	7100	8300	

^a OU = outside, unshielded; LSF = inside light steel frame buildings; SRC-L = inside seismic reinforced concrete buildings on the lower floor.

^b Possible error in dose estimate (Auxier, 1968).

FIGURE 13

Fig. 14 summarizes the situation that obtains if one varies yet another parameter, the area of field in a skin exposure (12). This is a collection of data from radiotherapy which shows skin tolerance in roentgens as a function not only of the number of fractions into which a given dose is divided, but also how big an area of skin is irradiated. It can be seen that there is an area factor as well as a time factor. The 2000 rad figure for a single dose that is listed, for example, in the NAS-NRC Space Radiation Study Panel Report (13) is also seen here; but fractionating the dose raises it, increasing the area lowers it, and so forth.

In summary, it can be seen that we are able by various combinations of numbers and factors to arrive at estimates of dose and dose effectiveness from values of fluence; but as yet it has not been possible to use the biological data with the same degree of precision with which one can obtain or estimate the physical data. Certainly, a QF, even properly used, is by no means the only modifying factor that one must apply to a flux-to-dose conversion; the distribution factor and the time factor are there to contend with, and the area factor as well. But above all, one must at least consider the possibility of treating a total exposure not simply on the basis of a collection of separate organs wired together, each with its own sensitivity, but by applying a separate organ approach only very judiciously as a part of the characterization of a total body exposure. It would seem that the most reasonable way one can use the human data that exists is to apply it as far as possible to the human animal as a whole(14). To conclude: the particular dosimetric problems of the space environment have been a stimulus to such efforts - but the results can clearly be useful in terrestrial human affairs.

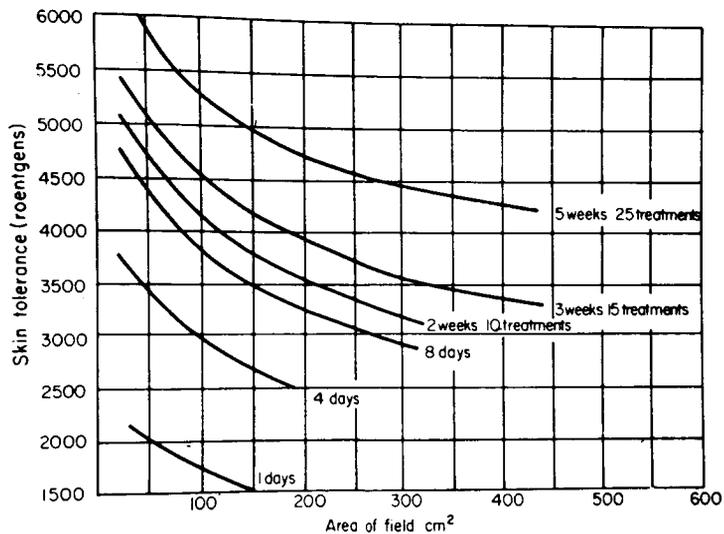


FIGURE 14

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