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RADIATION EFFECTS IN SPACE [1]

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INTRODUCTION

The current radiation protection guidelines of the National Aeronautics and Space Administration (NASA) are based on recommendations made in 1970 by a committee of the National Academy of Sciences (NAS) /1/. In a preface to the proceedings of workshops held at the COSPAR meeting held in Ottawa, Canada in 1982, Casarett and Lett /2/ suggested that a re-evaluation of NASA's radiation protection guidelines was required. At that workshop, Sinclair /3/ pointed out that if the current estimates of the risk of radiation-induced leukemia had been available in 1970 the approach used by the NAS would have resulted in a career limit of 235 rem (2.35 Sv) instead of 400 rem (4.0 Sv). Lett, Casarett and Sinclair thought the time had come to re-evaluate the risks that radiation in space posed. NASA concurred.

Since 1970 information has accumulated about the risk of radiation-induced cancer in a number of organs in humans, and the approaches to protection standards has changed. Also, results are now becoming available from studies of the effects of heavy ions in particular, iron.

Perhaps, of equal importance there has been a change in the population for whom radiation protection guidelines are needed. In the early stages of the space program the astronauts were a small elite group of seasoned and experienced male pilots. Recently, women astronauts and specialists of both sexes in various disciplines have joined the ranks and the age distribution is changing to the younger groups. Future missions will

involve more persons spending more time in space than has been the case.

The Committee of the National Academy of Sciences Space Board in 1970 /1/ knew its recommendations would be temporary. The committee's concern about keeping radiation risks in perspective has proven sage because radiation exposures have been low and the very risks of space vehicles and travel themselves, sadly have proven formidable.

Reaction to the Challenger tragedy may alter the U.S. timetable for manned space activities but in the future there will be more people involved in space travel than in the past and exploratory missions will be undertaken. The history of man indicates it will be so. Already more missions of longer duration are being undertaken by USSR cosmonauts.

The aims of this workshop are two-fold. First, to have some of the members of, and consultants to, the committee of the National Council of Radiation Protection and Measurements (NCRP) in the U. S. that have been examining radiation protection in space report on the approaches taken and the progress made. Second, to have other experts discuss their work that is relevant to the understanding of both the radiation environments in space and the biological consequences of exposure to the environment.

The proposed space station was an impetus to the re-examination of radiation protection guidelines for space. Although the radiation environment that will be experienced by workers in the space station is considered relatively benign the difference from a terrestrial environment is considerable. At the proposed altitude of 450 km, an inclination of 28-1/2^{o}, and shielding of 0.15 gms Al/cm^{2}, an occupant of the space station would be exposed to about the same level of radiation in a day as in a year from the environment on earth. That is not a trivial increase and obviously planning

for greater shielding depends on the assessment of the risk such as environment would pose.

RADIATION ENVIRONMENT

The radiation exposure that astronauts and space workers may incur is determined by duration of the mission, the shielding, the inclination of the orbit and the altitude. Both radiation quality and dose rate vary with altitude. At certain inclinations the relatively small change from 300 to 500 km in altitude can increase the proton dose rate at the surface of the skin, perhaps 25 fold. In geosynchronous orbits (GEO) the prediction of precise radiation exposure levels are complicated by cycles that can result in changes by a factor of ten in the radiation level and the changes of the same order that occur with the intermittent magnetic storms.

As I indicated in 1984 /4/ the NCRP committee chose a number of mission scenarios to focus the questions that were important and pertinent to particular missions. Although some of the scenarios are pure speculation they have served their purpose and they will be redefined by Warren Sinclair.

The questions about the radiation environments that would be experienced in these missions and our request for answers from various experts, especially those at NASA centers, have stimulated a rethinking and an examination of some salient points about modeling of radiation environments. Those questions are the subject of the paper by S. B. Curtis.

SPECIAL FEATURES OF RADIATION PROTECTION IN SPACE

From a radiobiological point of view missions below the magnetosphere pose few questions. From the point of view of radiation protection the not insignificant levels of radiation involved in prolonged sojourns in a space

station raise some interesting questions that have to be answered. We believe that for a considerable time missions to GEO, to the moon, and especially to Mars will involve an elite group of astronauts. NCRP SC 75 concurs with the views of the NAS panel /1/ that exploratory missions should be considered individually in the context of a risk-versus-gain philosophy.

Recommendations about radiation protection in space depend largely on terrestrial experience but must take into account the factors that make the radiation environments in space different from those on earth. The singular and striking difference between the radiation in space and on earth are HZE particles. But these heavy charged particles are of concern only in missions beyond the magnetosphere. At the altitudes and orbit planned for the space station the radiation environment will be dominated by protons of a wide range of energies.

EFFECTS OF PROTON IRRADIATION

Proton radiation is the major concern in LEO and from exposure to solar flares. There are few data for the effects of exposure to protons in either humans or experimental animals compared to other radiation qualities. NASA has selected a Q of 1.2 for the radiations that will be experienced in the space station. This figure is derived from knowledge of the energy for which LET values can be obtained, these in turn can be converted to Q using the values of relating LET to Q /5/.

In a recent study by Urano et al. /6/ the effects on various tissues of mice have been studied using the proton beams produced by the Harvard University 160 MeV synchrocylotron. Approximately 2% of the dose is from >100 keV/μm events and the study was designed to determine whether the high-LET component increased the RBE compared to ^{60}Co gamma rays. Three

tissues of special concern to the question of radiation protection guidelines in space were examined namely, skin, testes and the lens. The results are shown in Table 1.

Table 1

RBE values for 160 MeV proton spread out Bragg peak beam (Urano et al. 1984)

Tissue	Assay used for RBE determination	RBE
Skin	Peak acute reaction	1.14 ± 0.08
Testes	50% of control weight	1.23 ± 0.08
Lens	Complete cataract	1.09 ± 0.07

These RBE values have not been determined using low dose rates and therefore are not maximum values. However, the range of values obtained are consistent with the Q value of 1.2 for protons calculated by Hardy et al. at Johnson Space Center (personal communication).

The cataractogenic effect of 35-60 MeV protons was studied in mice and an RBE of 1 was reported /7/. Horn and Shifrine /8/ noted a threshold of 70-125 rad (0.7-1.25 Gy) for vision - impairing lens opacifications 6 months after exposure of Beagle dogs to 35 MeV protons.

Col. Wood will present the data for the induction of cancer in

monkeys by protons of different energies. While RBE values cannot be derived from the report the findings are consistent with those that might be predicted for a low-LET radiation /9/.

Burns et al. /10/ reported a RBE of 2.0-2.4 for the induction of skin tumors in rats 10 MeV protons compared to electrons. The data for cancer induction by protons are sparse but it appears reasonable to assume an RBE of close to 1.

HZE PARTICLES AND THEIR EFFECTS

The heavy ion component of galactic radiation was discovered in 1948 /11/. Today, it is intriguing to think that their discovery was a surprise considering the knowledge about cosmic rays at that time. Primary cosmic ray particles having a charge in excess of 2 have been described as heavy ions, heavy nuclei, heavy particles and high-Z particles.

It is not clear that there is a precise definition of the high-Z and -energy (HZE) particles. In the National Academy of Sciences' Monograph "HZE-Particle Effects in Manned Spaceflight" /12/ HZE particles were defined in clearly operational terms as those that have a $Z>2$ and sufficient energy to penetrate at least 1 mm of spacecraft or spacesuit shielding, which would require 10-35 MeV/nucleon initial energy.

The HZE particles in space that are of radiobiological concern are those with energies between 100 and 1000 MeV/nucleon. Galactic cosmic rays are the predominant sources of such heavy ions. There are two important questions concerning HZE particles. First, do they cause tissue lesions that have important differences from those induced by other radiations and second what are the RBE's for the effects they induce, especially cancer.

It was suggested that because of the length of the track the density

of the ionizations in the particle track, and the penumbra of delta rays there were important differences in the radiobiology of HZE particles from other radiations /12/. So began the concept of the microlesion. Todd /13/ has illustrated the type of HZE track that would cause a microlesion. For example, a microlesion would be caused by a track that extends over a distance of 10 or so cell diameters, a core with a LET of 200 keV/μm, or greater, along the length of the entire track. In addition the cells in the prenumbra, that stretches about 20 μm in width, could receive 0.25 Gy upto several Gray. A microlesion is said to consist of a number of contiguous inactivated cells. A sufficiently high fluence of particle tracks that did in fact cause microlesions could pose an unusual risk to small but critical groups of cells, such as centers in the floor of the 4th ventricle and the fovea of the retina. The concern about these poorly understood lesions induced by HZE particles has remained over the years. While there have been some findings that keep the concern alive there have been none, especially on the eye or brain, that in my opinion substantiate the fear that vital functions will be lost in space because of inactivation of critical groups of cells or cause dramatically more severe late effects than other high LET-radiations. Unfortunately, assays of particle-induced loss of function is absent from the armamentarium of most radiobiologists. Assays of cell survival are inappropriate and the interpretation of cytological evidence is fraught with difficulties. Microlesions have been sought in rodent brains after exposure to heavy ions /14/. These workers have found evidence of lesions that result in some functional and behavioral change. But the "smoking gun" for HZE-particle effects has not been demonstrated. The evidence that more than one heavy ion particle track is required to inactivate cells <u>in vitro</u> suggests

the probability of microlesions is lower than thought a decade ago. Perhaps the most reassuring evidence is the lack, of any reports of clinically evident damage in astronauts or cosmonauts.

THE RBE's FOR HZE PARTICLE EVENTS

The relationship of RBE to LET for cell killing was established by Barendsen et al. /15/ and Todd /16/. Track segment experiments have revealed much about the relationship of cross section and track structure to cell killing and the induction of chromosome aberrations /17/. The measured inactivation cross section has been shown to saturate and at a level dependent on atomic number /18/. These determinations on cells confirmed the results of Katz and Sharma /19/ based on experiments studying particle tracks in emulsion.

In the last few years there have been extensive studies on the cellular /20/ and tissue /21/ responses to heavy ions (see also Radiation Research Supplement 8, 1985). Not surprisingly, the RBE:LET relationship noted in cell studies has been found to hold for nonstochastic effects and cellular responses in vivo. The RBE values for killing of cells assessed from in vivo survival curves or assays of tissue and whole animal damage for helium, carbon, neon, argon and iron range from 1 to about 5 depending on the ion and the energy. There is no evidence that fractionation increases the effects to a degree of concern for protection guidelines. Unfortunately, fewer studies have been carried out with iron than other ions. The Lawrence Berkeley Laboratory group have studied the effects of ^{56}Fe on hematopoietic stem cells and on testes and they have not found the RBEs to be high. The relative effects of heavy ions on cataractogenesis is of importance in the estimates of risk for this late effect in travelers beyond the magnetosphere.

The committee will not have a precise RBE value for cataract induction by the relevant ions although the studies are in progress and will be reported on in these proceedings by Lett /22/ and Worgul /23/. Except perhaps in the case of very long missions such as to Mars the contribution of HZE-particles to the total dose is relatively small. Thus, even if the RBE turns out to be greater than 20 the dose limit recommendations will not be compromised.

There are even less data for RBE values for stochastic effects. All the data available for life shortening is reported by Ainsworth in these proceedings /24/. There are no data for genetic effects.

Yang et al. /25/ have carried out a systematic study of the RBE as a function of LET for malignant cell transformation in C3H10T1/2 cells. The relationship follows the pattern found for cell killing and mutation /26/ peaking at an RBE of about 10 at 100 keV/ m cells in stationary phase. An interesting finding was that radiations with LET values greater than 140 keV/μ m, unlike low-LET radiations did not require cell division to fix the transformation lesion.

The induction of tumors by heavy ions has been studied in 3 tissues. Skin /27,28/, mammary gland (Shellabarger, personal communication), and Harderian gland /29/. Only in the latter tissue has a number of heavy ions been studied, ranging in LET from 1 to at least 190 keV/μ m. It can be seen in Fig. 1 that RBE increases going from ^{60}Co radiation upto ^{40}Ar. The estimates of LET are not plotted because in all of the beams, except ^{56}Fe, a ridge filter, that causes some fragmentation, was used. It can be seen that the RBE for ^{56}Fe and ^{40}Ar are similar. These RBE values are comparable to the estimate of RBE for fission neutrons (fn) determined in somewhat different experiments /29/. It seems likely that RBE reaches a maximum at

about 100-200 keV/μm and the RBE for induction of cancer by heavy ions with an LET > 100 keV/μm is similar to the RBE for fn. If this is the case the selection of value of Q for setting protection guidelines becomes a simpler task. A value of 20 has been recommended for Q for neutrons /30/ and appears, at least now, appropriate for heavy ions.

RADIATION PROTECTION GUIDELINES

Stochastic Effects

It never seems to be the right time to make recommendations about radiation protection limits because new information is always just about to become available. Today is no exception. Reassessment of the doses incurred by the atomic bomb survivors is complete and the application to the cancer data will follow. Another 4 years of cancer data is also at hand. We have not had the advantage of these important pieces of information. Although there is no reason to believe that the new data will make it necessary to make changes in our recommendations they will be examined. The guidelines that we will recommend will, for the first time, take into account age-dependent changes in susceptibility. Furthermore, the recommended dose limits are different for women and men. The advantage of these approaches are discussed by Sinclair /31/.

The risk of damage, especially at critical periods, is so great that the radiation environments in space are no place for the embryo or fetus.

Non Stochastic Effects

Terrestrial protection standards are set to prevent non stochastic or threshold effects. The limits for whole body irradiation are governed by stochastic effects and at levels that do, in fact, prevent the threshold effects. Since irradiation may well be non uniform separate limits for sensitive organs are required.

In Table 2 are shown the dose equivalent limits that NCRP's scientific committee are considering. The proposed limits are compared to the current guidelines and those set by ICRP.

Table 2

Dose Equivalent*
rem

	Skin			Lens			Gonad		
Time Period	NAS 1970	ICRP 1977	NCRP 1986	NAS 1970	ICRP 1980	NCRP 1986	NAS 1970+	ICRP 1977	NCRP 1986
30 Day	75	-	150	37	-	100	13		25
Annual	225	50	300	112	15	200	38	20	50
Career	1200	(2500)**	600	600	(750)**	400	200	(600)++	150

*Divide by 100 for dose equivalent in Sv.
**Based on 50 year.
+Previous recommendation was for testes.
++Based on 30 years, e.g. starting at 20 years of age and until menopause, ~ 50 yrs of age.

These limits have been selected in order to protect against threshold effects, to be internally consistent and to offer a reasonable flexibility

for planning of missions. The most difficult limits to set are those for the gonads. The evidence indicates the testes can tolerate 1 rem (1m Sv) per day indefinitely without significant decrease in fertility /32/. The dose limits are important for persons in their early productive period when siring or bearing children. The limits become of less importance with increasing age. There is a case for adjusting the limits for the gonads based on the ages over which exposure occurs.

The reduction in career limits for the eye and skin should guarantee that cataracts do not occur and any damage to the dermal microvasculature is insignificant.

NASA follows the principle of ALARA (As Low As Reasonably Achievable) and therefore the recommended limits are unlikely to be reached, a fact that provides further protection.

Finally, it is important to note that the changes in the recommendations for dose limits are not made because the current protection practice of NASA can be faulted. On the contrary, they are being made to meet the changing needs and to incorporate the best understanding of risks.

REFERENCES

1. National Academy of Sciences, Radiobiological Space Sciences Board, Advisory Board. Radiation Protection Constraints Guides and Constraints for Space - Mission and Vehicle - Design Studies involving Nuclear Systems. 1970. National Academy of Sciences, Washington, DC.

2. G. W. Casarett and J. T. Lett, Factors involved in the evaluation of space radiation standards - a preface, Adv. Space Res. 3: 147-150, 1983.

3. W. K. Sinclair, Radiation safety standards, space hazards vs terrestrial hazards, Adv. Space Res. 3: 151-159, 1983.

4. R. J. M. Fry, Approaches to radiation guidelines for space travel, Adv. Space Res. 4: 121-130, 1984.

5. International Commission on Radiation Units and Measurements (ICRU),

Linear Energy Transfer, ICRU Report No. 17, Bethesda, MD, 1970.

6. M. Urano, L. J. Verhey, M. Goitein, J. E. Tepper, H. D. Suit, D. Phil, O. Mendiondo, E. S. Gragoudas, and A. Koehler, Relative biological effectiveness of modulated proton beams in various murine tissues, Int. J. Radiat. Oncol. Biol. Phys. 10: 509-514, 1984.

7. E. B. Darden, Jr., K. W. Christenberry, J. J. Beauchamp, R. S. Bender, M. C. Jernigan, J. W. Conklin, and A. C. Upton, Comparison of 60-MeV protons and 300-kVp X-rays for induction of lens opacities in RF mice, Radiat. Res. 43: 598-612, 1970.

8. P. L. Horn and M. Shifrine, Proton irradiation of Beagle eyes. 2. Clinical and histopathologic observations for 35 MeV protons, Radiat. Res. 53: 255-266, 1973.

9. D. H. Wood, M. G. Yochmowitz, K. [illegible] Hardy, and Y. L. Salmon, Animal studies of life shortening and cancer risk from space radiation, this issue.

10. F. J. Burns, P. Strickland, M. Vanderlaan, and R. E. Albert, Rat skin tumor incidence following single and fractionated exposures to proton radiation, Radiat. Res. 74: 152-158, 1978.

11. P. Freier, E. J. Lofgren, E. P. Ney, F. Oppenheimer, M. L. Bradt, and B. Peters, Evidence for heavy nuclei in the primary cosmic radiation, Phys. Rev. 74: 213-217, 1948.

12. National Academy of Sciences. Radiobiological Advisory Panel, Committee on Space Biology and Medicine. Space Science Board, National Research Council. HZE-Particle Effects in Manned Spaceflights. Ed. D. Grahn. National Academy of Sciences, Washington, DC, 1970.

13. P. W. Todd, Unique biological aspects of radiation hazards - an overview, Adv. Space Res. 3: 187-194, 1983.

14. D. E. Philpott, J. Sapp, J. Miquel, K. Kato, R. Corbett, J. Stevenson, S. Black, K. A. Lindseth, and E. V. Benton, The effect of high energy (HZE) particle radiation (^{40}Ar) on aging parameters of mouse hippocampus and retina, in: Scanning Electron Microscopy III, 1985, p. 1177.

15. G. W. Barendsen, H. M. D. Walter, J. P. Fowler, and D. D. Bewley, Effects of different ionizing radiations on human cells in tissue cultures, Radiat. Res. 18: 106-119, 1963.

16. P. W. Todd, Heavy ion irradiation of human and Chinese hamster cells in vitro, Radiat. Res. 61: 288-297, 1965.

17. H. Wulf, W. Kraft-Weyrather and H. G. Miltenburger, E. A. Blakely, C. A. Tobias, and G. Kraft, Heavy-ion effects on mammalian cells: Inactivation measurements with different cell lines, Radiat. Res. 104: S122-S134, 1985.

18. G. Kraft, E. A. Blakely, L. Hieber, W., W. Kraft-Weyrather, H. G. Miltenburger, W. Muller, M. Schuber, C. A. Tobias and H. Wulf, HZE effects on mammalian cells. Adv. Space Res. 4: 219-226, 1984.

19. R. Katz and S. C. Sharma, Response of cells to fast neutrons, slopped pions and heavy ion beams, Natl. Inst. Meth. 111: 93-116, 1973.

20. E. A. Blakely, F. Q. H. Ngo, S. B. Curtis, and C. A. Tobias, Heavy-ion radiobiology: Cellular studies, Adv. Radiat. Biol. 11: 295-389. 1984.

21. J. T. Leith, E. J. Ainsworth and E. L. Alpen, Heavy-ion radiobiology: Normal tissue studies, Adv. Radiat. Biol. 10: 191-236, 1983.

22. J. T. Lett, A. B. Cox, and A. C. Lee, Cataractogenic potential of ionizing radiations. in: Animal Models that simulate man, this issue.

23. B. V. Worgul, Cataract analysis and the assessment of radiation protection in space, this issue.

24. E. J. Ainsworth, Early and late mammalian responses to heavy charged particles: status and future requirements, this issue.

25. T. C. Yang, L. M. Craise, M. T. Mei and C. A. Tobias, Neoplastic cell transformation by heavy charged particles, Radiat. Res. 104: S177-S187, 1985.

26. R. Cox, J. Thacker, D. T. Goodhead, and R. J. Munson, Mutation and inactivation of mammalian cells by various ionizing radiation, Nature 267: 425-428, 1977.

27. J. T. Leith, G. P. Welch, W. A. Schilling, and C. A. Tobias, Life-span measurements and skin tumorigenesis in mice following total-body helium + ion irradiation of the skin to different maximum penetration depths, in: Radionuclide Carcinogenesis, AEC Symposium Series 129 Conf. 720505, 1973, pp 90-105.

28. F. J. Burns and R. E. Albert. In Biological and Medical Research with accelerated heavy ions at the BEVALAC 1977-78 (M. C. Pirucello and C. A. Tobias, eds.) pp 233-235, Report LBL-11220, Lawrence Berkeley Laboratory, 1981.

29. R. J. M. Fry, P. Powers-Risius, E. L. Alpen, and E. J. Ainsworth, High-LET radiation carcinogenesis, Radiat. Res. 104: S188-S195, 1985.

30. International Commission on Radiation Protection, Statement in Brit. J. Radiol. 58: 910, 1985.

31. W. K. Sinclair, Radiation protection standards in space, this issue.

32. United Nations, Ionizing Radiation: Levels and Effects, United Scientific Committee on the Effects of Atomic Radiation Report to the General Assembly with Annexes, United Nations, New York, 1982.

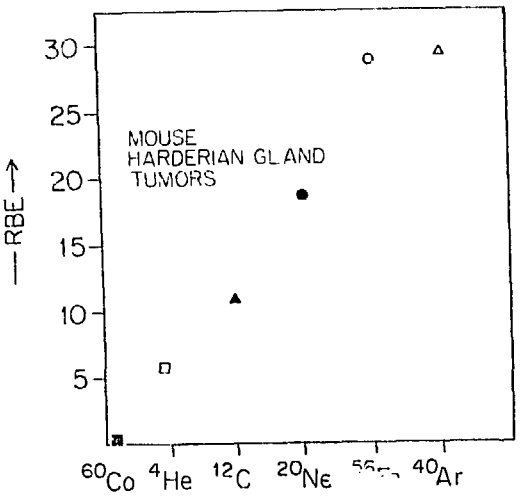

Fig. 1. RBE for the induction of Harderian gland tumors of female B6CF[1] mice with pituitary isografts exposed to Cobalt-60 gamma rays, and the spread out Bragg peaks of helium-4, carbon-12, neon-20 and argon-40 beams. The plateau of an iron-56 beam was used. The RBE was determined from the ratio of the initial slopes obtained by linear regression for the ion in question and for Cobalt-60 gamma rays, which was the reference radiation. The LET of the plateau portion of the iron-56 beam was 190 keV/μm. The dose averaged LETs of the other beams range from 1-2 keV/μm for helium-4 to 650 keV/μm for argon-40. But because of the fragmentation of the beams the LET values are tentative estimates.