15
25-17
LA-6717-MS

Informal Report

A 217
UC-48

Issued: February 1977

Delayed Radiation Injury of Gut-Exposed and Gut-Shielded Mice.

I. The Decrement in Resistance to Continuous Gamma-Ray Stress

by

J. F. Spalding
R. F. Archuleta
J. E. London
J. R. Prine

los alamos
scientific laboratory
of the University of California
LOS ALAMOS, NEW MEXICO 87545

An Affirmative Action/Equal Opportunity Employer

This work was supported by the US Energy Research and Development Administration, Division of Biomedical and Environmental Research.

**Printed in the United States of America. Available from
National Technical Information Service
U.S. Department of Commerce
5285 Port Royal Road
Springfield, VA 22161
Price: Printed Copy \$3.50 Microfiche \$3.00**

This report was prepared as an account of work sponsored by the United States Government. Neither the United States nor the United States Energy Research and Development Administration, nor any of their employees, nor any of their contractors, subcontractors, or their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights.

DELAYED RADIATION INJURY OF GUT-EXPOSED AND GUT-SHIELDED MICE.

1. THE DECREMENT IN RESISTANCE TO CONTINUOUS GAMMA-RAY STRESS

by

J. F. Spalding, R. F. Archuletta, J. E. London, and J. R. Prine

ABSTRACT

Two mouse strains (RF/J and C57Bl/6J) were exposed to x-ray doses totaling 400, 800, or 1200 rad. Total doses were given in 200-rad fractions at 7-day intervals to the whole body, gut only, or gut shielded. Animals treated as above (conditioned) were divided into 2 groups to form a two-part investigation. In Part II (to be reported later), conditioned mice were retained in a normal animal laboratory environment for observation on life span and histopathology at death. In Part I (reported here), x-ray-conditioned and control mice were subjected to a continuous gamma-ray stress (challenge exposure) 28 days after the last x-ray dose. Delayed injury was measured as a reduction in mean after-survival (MAS) time and was observed in whole-body, gut-conditioned, and gut-shielded groups. The cause of death was attributed to hemopoietic hypoplasia in all groups. MAS reduction in all conditioned groups in both strains was linear with dose within the dose range used. Delayed injury per volume dose (measured as a reduction in MAS) was independent of the tissue initially conditioned with an acute dose of x rays. Thus, delayed injury per unit weight of gut tissue exposed was equal to that of either whole-body or gut-shielded radiation injury. Comparative weight loss observations during the continuous gamma-ray challenge exposure revealed a decrement in metabolic processes associated with body weight maintenance. This decrement was seen in all x-ray-conditioned groups.

1. INTRODUCTION

That different tissues of the mammalian system exhibit radiosensitivity in different degrees was reported nearly 8 decades ago.¹ Experimental investigations on the comparative effects (particularly acute effects) of partial-body irradiation were done by a number of investigators dating to as early as 1920.²⁻⁶ Although some work has been done on late effects or delayed radiation injury of partial-body exposure,⁷⁻¹¹ life shortening and response to general stress of mammals with partial-body exposure in which all bone tissue was either exposed or shielded have not been reported.

A more thorough understanding of the general site origin, nature, and magnitude of delayed radiation injury is of interest in radiation therapy, civil defense, military, and manned space mission planning. Radiation exposures to be dealt with by all the above would be predominantly partial- rather

than whole-body. This report deals with the results of part I of a two-part investigation designed to obtain information on the parameters of late effects.

II. METHODS AND MATERIALS

Two hundred sixty-four strain C57Bl/6J and 276 strain RF/J virgin female mice 3-months-old were used. Mice of each strain were divided randomly into 11 groups of approximately 24 mice each. The various groups were exposed to x-ray conditioning doses of 400, 800, or 1200 rad to the whole body, gut only, or total body with gut shielded, as shown in Table 1. Conditioning doses were given while the mice were anesthetized (~0.125 mg Nembutal/g body weight) in plastic jigs (Fig. 1) in 200-rad fractions at 7-day intervals.

A typical exposure schedule for radiation therapy is 200 rad/day, 5 days/wk. We used 7 days between exposures to permit the accumulation of

TABLE 1

EXPOSURE INFORMATION FOR TWO STRAINS OF MICE USED TO DETERMINE
THE GENERAL SITE ORIGIN AND MAGNITUDE OF DELAYED RADIATION INJURY

Region Receiving X-Ray Conditioning	Total Dose Accumulated ^a (rad)	Number of Mice Used		Acute Mortality ^b		Body Weight Exposed ^c (g)
		C57	Pr	C57	Pr	
Control (no anesthesia)	0	24	24	0	0	0
Control (anesthetized)	0	24	24	0	0	0
Whole body	400	24	24	0	0	100
	800	24	28	8	4	100
	1200	24	32	79	4	100
Gut only	400	24	24	8	29	25-26
	800	24	24	12	0	25-26
	1200	24	24	17	0	25-26
Gut shielded	400	24	24	8	0	74-75
	800	24	24	8	0	74-75
	1200	24	24	8	4	74-75

^aRad dose accumulated in 200-rad fractions at 7-day intervals.

^bPercent lethality from acute doses prior to challenge exposure.

^cBoth strains are represented by these figures.

Fig. 1. Plastic restraint and positioning jigs used to expose or shield mouse gut tissue during x-ray conditioning doses. The shaded area indicates the region shielded with 6.35 mm of lead.

1200 rad in the whole-body exposed animals. This 7-day period is approximately 1 recovery half time for the RF strain.¹² The exposure schedule was such that each group received the last 200-rad fraction on the same day. Thus, 800-rad group exposures were started 2 wk after the 1200-rad groups and 400-rad groups 2 wk later. One control group and all

conditioned groups were anesthetized at the time each 200-rad fraction was given, whether or not the group was scheduled for exposure. Thus, regardless of the total conditioning dose received, each group was given the same number of anesthesia treatments all at the same time. A second control group which received no x-ray conditioning dose also received no treatment with anesthesia.

Exposure arrangements for the x-ray conditioning doses were as follows: dose rate, 208 rad/min; voltage, 250 kVp; filament current, 30 mA; filter, Thoreaus 11; HVL, 2.6 mm Cu; and target-to-specimen distance, 320 mm. Dose rates were measured with Victoreen high-energy 100-R chambers in the Lucite exposure jig (Fig. 1). Victoreen readings were corrected for barometric pressure and temperature and were converted to tissue dose by the factor 1 R = 0.96 rad. The scatter radiation beneath the 6.35-mm shielding, measured by lithium fluoride thermoluminescent dosimeters, was insignificant.

Twenty-four mice were quick-frozen while under anesthesia in the exposure jigs (Fig. 1), and the exposed and shielded areas were dissected at delineation of the 6.35-mm lead shield to determine critical organs and body weight exposed under the two shielding conditions. These observations are shown in Table 11.

TABLE 11
WEIGHT OF BODY, ORGAN, OR TISSUE EXPOSED
TO X-RAY CONDITIONING DOSES^a

Whole Body	Stomach	Gut	Bone	Kidneys		Liver	Spleen	Pelt
				Right	Left			
<u>Gut Shielded</u>								
74	4	2	100	100	77	53	15	66
<u>Gut Exposed</u>								
26	96	98	0	0	23	47	85	34

^aIn percent.

Twenty-eight days after the last 200-rad x-ray conditioning dose [approximately 4 times the recovery half time (RT_{50}) of strain RF mice],¹² all conditioned and control groups were placed in a ⁶⁰Co gamma-ray environment for invariant challenge exposures until death. The mice were positioned around the source at a mean radius of 2.3 m where they accumulated approximately 54 rad/each 24 h of exposure. The dose rate was such that animals in the center of the exposure cage accumulated 54 rad/each 24 h of exposure.

The mice were weighed prior to and after the conditioning exposure schedule, after the 28-day recovery period, and periodically during the invariant challenge exposure. Four mice (randomly selected at each bleeding) were bled prior to the challenge exposure and periodically during the gamma-ray challenge.

Mice were housed 6/cage on wood shavings in stainless steel box-type cages (125 by 200 by 300 mm) during conditioning exposures and recovery. They were housed 8-10/cage in plastic cages measuring 170 by 280 by 120 mm during the continuous gamma-ray challenge exposure. Rockland-Teklad Mouse and Rat Diet and water were provided *ad libitum*, and clean bottles and cages were provided twice weekly.

III. RESULTS AND DISCUSSION

Some acute lethality occurred during the conditioning exposures. The percent mortality during x-ray conditioning and the 28-day period following the last 200-rad conditioning fraction is shown in Table 1. Strain C57 mice were generally more sensitive to the acute conditioning exposures than were strain RF mice.

Body weight changes in control animals with no anesthesia were somewhat different than sham controls with anesthesia (Figs. 2 and 3). For this reason, all comparative data in this report are based on anesthetized sham control mice. Comparative weight changes during x-ray conditioning, recovery, and gamma-ray challenge periods are shown for whole-body conditioned strains RF and C57 mice in Figs. 4 and 5, respectively.

The conditioning exposures adversely affected weight gain in both mouse strains, and the effect was influenced by the number of 200-rad conditioning fractions given. Strain C57 showed a more uniform response (Fig. 5) in this effect than the RF strain (Fig. 4). Although body weights were depressed (according to conditioning dose) on the day following the last 200-rad conditioning fraction, all x-ray-conditioned groups reached or exceeded control body weight levels after the 28-day recovery period (Figs. 4 and 5). This comparative weight response was less distinct in gut-shielded conditioned and gut-conditioned mice. However, overrecovery (as measured by body weight) was observed in all groups receiving either partial- or whole-body conditioning exposures. Comparative body weights in all x-ray-conditioned groups in both strains indicated that any injury detrimental to metabolic processes involved in normal tissue proliferation and growth was of a transient nature and that the mice had completely recovered 28 days after the last 200-rad x-ray conditioning dose (Figs. 4 and 5). However, this was apparently not true as body weight in x-ray-conditioned groups subjected to the same gamma-ray challenge dose rate (approximately 50 rad/day) as nonconditioned controls dropped more sharply than in controls. With the exception of the 400-rad whole-body challenged group in RF mice (Fig. 4), the drop in body weight during the challenge exposure was directly related to the size of the x-ray conditioning dose. To a lesser degree, this was true in both bone- and gut-conditioned groups (Figs. 6, 7, 8, and 9). Although weight changes were less pronounced in both bone- and gut-conditioned groups during the conditioning period, both of these partial-body-exposed groups showed more overrecovery during the 28-day recovery period than whole-body-conditioned animals.

Fig. 2. Comparative weight changes of control mice with and without anesthesia during x-ray conditioning and recovery periods and during gamma-ray challenge exposure (strain RF/J mice).

Fig. 3. Comparative weight changes of control mice with and without anesthesia during x-ray conditioning and recovery periods and during gamma-ray challenge exposure (strain C57Bl/6J mice).

It is interesting that this physiological response from delayed radiation injury is observed in animals with bone tissue totally exposed and totally shielded. The dose-dependent decrement in metabolic processes associated with body weight maintenance during a general physiological stress observed here suggests a persistent radiation lesion of a rather nonspecific nature and is an end point not known to have been reported previously. Studies by Kuzina¹³

Fig. 4. Comparative weight changes of whole-body-conditioned strain RF/J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

Fig. 5. Comparative weight changes of whole-body-conditioned strain C57Bl/6J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

on the hydrolytic function of the intestines of mice for 30 days following 600 R to the whole body or with one shin shielded showed shin-shielded animals to have substantially less disturbance in enzyme activity and less weight loss than whole-body-exposed mice. Thus, nonirradiated hemopoietic tissue not directly associated with the intestines appears capable of a sparing effect on radiation-induced injury to the intestinal digestive process;

Fig. 6. Comparative weight changes of gut-conditioned strain RF/J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

Fig. 7. Comparative weight changes of bone-conditioned strain RF/J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

conversely, these observations suggest that irradiated hemopoietic tissue distant to the intestines can adversely affect the metabolic function of the unirradiated gut. The nature of this decrement is not apparent but may be due to an intercellular injury information transfer factor (IIITF) which affects the production and/or transport of digestive enzymes during the cephalic, gastric, or intestinal phase of gastric juice production. Whatever the nature of the decrement may be, it does appear to be quite persistent.

Peripheral blood values of control and conditioned groups 28 days after x-ray conditioning are tabulated in Table III. White blood cell (WBC) counts in RF/J conditioned animals remained

Fig. 8. Comparative weight changes of gut-conditioned strain C57B1/6J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

Fig. 9. Comparative weight changes of bone-conditioned strain C57B1/6J mice during x-ray conditioning, recovery, and gamma-ray challenge exposure.

depressed below control values and were generally dose-related in whole-body and bone-exposed groups. In strain C57 mice, the gut-exposed groups showed essentially no depression in WBC count, while their strain RF counterparts showed substantial WBC count depressions (Table III). Packed cell volume (PCV) in most of the conditioned mice of both strains was slightly depressed 28 days after the last 200-rad conditioning exposure. However, only the whole-body-conditioned groups of the C57 strain showed

TABLE III
PACKED CELL VOLUME AND WHITE BLOOD CELL COUNTS
OF AREA X-RAY-CONDITIONED MICE 28 DAYS AFTER CONDITIONING

Region Receiving X-Ray Conditioning	Dose (rad)	White Blood Cell Count		Packed Cell Volume	
		Mean	% Control	Mean	% Control
<u>Strain C57Bl/6J</u>					
Sham control	0	9414	0	54.6	0
Whole body	400	5078	46.2 ^a	50.4	7.6 ^a
	800	4425	53.0 ^a	48.5	11.2 ^a
	1200	4274	45.0 ^a	44.8	17.9 ^a
Gut only	400	8802	6.5 ^a	52.8	3.3 ^a
	800	9796	4.1	54.6	0
	1200	9379	0	54.0	1.1 ^a
Gut shielded	400	7635	18.9 ^a	54.1	1.0 ^a
	800	6140	34.8 ^a	54.0	1.1 ^a
	1200	5223	55.5 ^a	52.8	3.3 ^a
<u>Strain RF/J</u>					
Sham control	0	11 999	0	58.1	0
Whole body	400	6149	48.8 ^a	56.9	2.1 ^a
	800	5633	53.1 ^a	55.8	4.0 ^a
	1200	5259	56.2 ^a	55.9	3.8 ^a
Gut only	400	6725	44.0 ^a	59.8	2.9
	800	9082	24.3 ^a	56.0	3.6 ^a
	1200	6797	43.4 ^a	56.0	3.6 ^a
Gut shielded	400	7965	33.6 ^a	54.6	6.0 ^a
	800	4036	66.3 ^a	55.1	5.2 ^a
	1200	3655	69.5 ^a	55.5	4.5 ^a

^aLess than control.

more than minor changes, and in these groups the depression in PCV was dose-dependent.

The end point utilized to meet the primary objective in part I of this investigation was the comparative response of conditioned and control mice to a continuous whole-body physiological challenge of an ~50-rad/day gamma-ray environment. Persistent injury in the whole-body-, gut-, and bone-conditioned mice was determined by comparative survival times in the gamma-ray field. Mean after-survival (MAS) and reduction in MAS, uncorrected and corrected for body weight exposed (integral dose or per volume dose), are listed for strain C57Bl/6J in Table IV and for strain RF/J in Table V.

Strain C57 mice were more sensitive to the acute conditioning regime than were strain RF mice (Table I). However, this strain difference in radioresistance was reversed with the invariant challenge exposure (Tables IV and V). Strain C57

controls survived approximately 25 days longer than strain RF controls and, with the exception of the 1200-rad whole-body-exposed groups, only 20% of the mice in this group survived the conditioning exposures (Table I). All doses and area-conditioned strain C57 mice were more tolerant of the challenge exposure than strain RF mice. Mean life spans of the C57Bl/6J and RF/J mouse strains are reported to be 693 and 452 days, respectively.¹⁴ Although the degree of response to the gamma-ray challenge was different in the two strains, the nature of the response was quite similar. Survival curves for conditioned and control mice during continuous gamma-ray exposure at 50 rad/day are shown for strain RF/J mice in Fig. 10 and for strain C57Bl/6J mice in Fig. 11.

Mean after-survival (MAS) times of whole-body- and bone-conditioned animals were clearly dependent on conditioning dose, with similar survival curve

TABLE IV
MEAN AFTER-SURVIVAL (MAS) TIME OF X-RAY-CONDITIONED
C57/6J STRAIN MICE DURING INVARIANT GAMMA-RAY STRESS

Conditioning Treatment	Dose (rad)	MAS (days)	Reduction in MAS		
			Per 100 rad of Exposure	Corrected to Whole-Body Exposure ^a	Mean
Sham control	0	100.4	0	0	0
Whole body	400	66.0	4.30	0	5.55
	800	51.2	6.15	0	
	1200	26.1	6.19	0	
Gut only	400	99.1	0.32	1.30	4.60
	800	86.4	1.75	7.00	
	1200	83.8	1.38	5.52	
Bone shielded	400	87.2	3.30	4.40	4.30
	800	77.0	2.92	3.90	
	1200	59.0	3.45	4.60	

^aGut exposed x 4.00 and bone exposed x 1.33.

TABLE V
MEAN AFTER-SURVIVAL (MAS) TIME OF X-RAY-CONDITIONED
RF/J STRAIN MICE DURING INVARIANT GAMMA-RAY STRESS

Conditioning Treatment	Dose (rad)	MAS (days)	Reduction in MAS		
			Per 100 rad of Exposure	Corrected to Whole-Body Exposure ^a	Mean
Sham control	0	74.33	0	0	0
Whole body	400	61.79	3.14	0	3.63
	800	41.00	4.17	0	
	1200	31.33	3.58	0	
Gut only	400	71.79	0.64	2.56	3.20
	800	66.58	0.97	3.88	
	1200	64.80	0.79	3.16	
Bone shielded	400	59.29	3.76	5.01	3.84
	800	55.04	2.41	3.21	
	1200	44.63	2.48	3.31	

^aGut exposed x 4.00 and bone exposed x 1.33.

slopes in both strains (Figs. 10a,b and 11a,b). Although the tabulated MAS values for gut-conditioned animals of both strains showed a conditioning dose-related residual injury (Tables IV and V), survival curves for the 3 conditioning doses (Figs. 10c and 11c) were less distinct than either whole-body- or bone-conditioned mice.

Comparative survival curves of whole-body-, bone-, or gut-conditioned mice showed residual injury for all tissues conditioned with 400, 800, and 1200 rad in strain C57B1/6J (Figs. 11d,e,f). This residual injury was also distinct for 1200- and 800-

rad conditioning doses in strain RF/J mice, but at the 400-rad level, gut-conditioned mice were similar to controls and the bone- and whole-body-conditioned mice were different from controls but similar to each other (Figs. 10d,e,f).

Gut-conditioned animals included exposure to 25-26% of the body tissue by weight, and bone exposures included 74-75% (Table II). When reduction in MAS in gut- and bone-conditioned mice was corrected to whole-body exposure (effect/unit weight of tissue exposed), the residual radiation-induced injury of gut-exposed mice was similar in amount to

Fig. 10. Comparative survival curves of control and x-ray-conditioned strain RF/J mice during a continuous 50 rad/day gamma-ray challenge exposure: (a) control and whole-body conditioning doses of 400, 800, and 1200 rad; (b) control and bone conditioning doses of 400, 800, and 1200 rad; (c) control and gut conditioning doses of 400, 800, and 1200 rad; (d) control and 1200-rad conditioning dose to the whole body, bone, and gut; (e) control and 800-rad conditioning dose to the whole body, bone, and gut; and (f) control and 400-rad conditioning dose to the whole body, bone, and gut.

that incurred in bone-conditioned mice. Further, the combined reduction in MAS of gut- and bone-conditioned animals approached that of whole-body-conditioned strain C57P1/6J mice (Table IV) and approximated the whole-body-conditioned mice in strain RF/J (Table V).

Area shielding studies in which all bone tissue is exposed to ionizing radiation (conditioned)

or shielded have not been done previously. However, intuitively one might expect bone conditioning to provoke greater persistent injury/unit exposed than gut-conditioned animals. Mice¹⁵ and rats¹¹ with x-ray conditioning to the lower half of the body exhibited about twice as much life shortening as animals with x-ray conditioning to the upper half of the body. Life shortening/volume dose in the

Fig. 11. Comparative survival curves of control and x-ray-conditioned strain C57Bl/6J mice during a continuous 50 rad/day gamma-ray challenge exposure: (a) control and whole-body conditioning doses of 400, 800, and 1200 rad; (b) control and bone conditioning doses of 400, 800, and 1200 rad; (c) control and gut conditioning doses of 400, 800, and 1200 rad; (d) control and 1200-rad conditioning dose to the whole body, bone, and gut; (e) control and 800-rad conditioning dose to the whole body, bone, and gut; and (f) control and 400-rad conditioning dose to the whole body, bone, and gut.

whole body, head, trunk, and lower body (pelvis, legs, and tail) of mice exposed to a single x-ray dose of 400 R was reported by Sato *et al.*¹⁶ to be greatest in head-exposed mice and least (not significantly less than controls) for mice exposed to the lower body. The test end point in this and other partial-body irradiation studies was life shortening in a normal laboratory environment. Thus, results on the origin, magnitude, and nature of the effects may not be pertinent to observations in this study which utilized a reduction in MAS during a continuous physiological stress provided by a 50-rad/day gamma-ray environment. The physiological mechanisms involved in or measured by the two end points may be quite different.

The results of part I of this investigation may appear to conflict with earlier residual injury studies on partially shielded mice and/or rats. However, the shielding and x-ray conditioning techniques and residual injury measurement end point combination used here are different from other studies and make data comparison difficult. Part II of this investigation, in which life shortening in a normal laboratory environment is being used to study radiation effects from exposures described in Table I, has been designed to explore the comparative nature of the effects observed by these two end points.

ACKNOWLEDGMENTS

The cooperation of R. H. Wood in performing gross post-mortem and histopathology preparations and O. S. Johnson for x-, gamma-, and lithium fluoride thermoluminescent dosimetry is gratefully appreciated.

REFERENCES

1. D. Walsh, "Deep Tissue Traumatism from Roentgen Ray Exposure," *Brit. Med. J.* 2, 272 (1897).
2. W. Denis, C. L. Martin, and M. Aldrich, "A Study of the Relative Toxic Effects Produced by Regional Radiation," *Am. J. Med. Sci.* 160, 555-559 (1920).
3. V. P. Bond, M. N. Swift, A. C. Allen, and M. C. Fishler, "Sensitivity of Abdomen of Rat to X-Irradiation," *Am. J. Roentgenol.* 161, 322-330 (1950).
4. J. C. Crook, E. V. Hulse, C. H. Mulvey, and G. J. Neary, "The Acute Effects of Partial Body Beta Irradiation of Mice," *Brit. J. Radiol.* 31, 477-485 (1958).
5. H. A. Blair, "Acute Lethality of Partial Body in Relation to Whole Body Irradiation," University of Rochester Atomic Energy Project report UR-462 (1956).
6. C. L. Hansen, S. M. Michaelson, and J. W. Howland, "The Biological Effects of Upper Body X-Irradiation of Beagles," University of Rochester Atomic Energy Project report UR-580 (1960).
7. R. F. Kallman and H. I. Kohn, "Life-Shortening by Whole and Partial Body X-Irradiation in Mice," *Science* 128, 301-302 (1958).
8. G. E. Cosgrove and A. C. Upton, "Some Delayed Effects to Partial Body Irradiation in Mice of the RF Strain," *Int. J. Radiat. Biol.* 4, 97-103 (1961).
9. A. Dunjic, J. Maisin, P. Maldague, and M. Maisin, "Incidence of Mortality and Dose-Response Relationship following Partial-Body X-Irradiation of the Rat," *Radiat. Res.* 12, 155-166 (1960).
10. W. J. Quinlan, K. Scheer, R. W. Neidlinger, S. M. Michaelson, and J. W. Howland, "Late Manifestations of Whole and Partial Body Ionizing Radiation in the Dog: A Two Year Summary," University of Rochester Atomic Energy Project report UR-609 (1962).
11. A. L. Carsten and J. R. M. Innes, "The Effects of Partial Body Irradiation on Delayed Responses," *Ann. N. Y. Acad. Sci.* 114, 316-327 (1964).
12. J. F. Spalding, T. T. Trujillo, and W. L. LeSturgeon, "Dependence of Rate of Recovery from Acute Gamma-Ray Exposure on Size of the Conditioning Dose," *Radiat. Res.* 15, 378-389 (1961).
13. V. A. Kuzina, "Influence of Partial Shielding of the Bone Marrow and the Functional Size of the Intestinal Epithelium in Mice after Irradiation," *Radiobiologia (Moscow)* 12(4), 42-48 (1972), English translation.
14. J. M. Yuhas, "Genetic Control of Aging and Radiation-Induced Life-Shortening in Mice," The Jackson Laboratory report NYO-3314-15 (August 1969).
15. I. U. Boone, G. Trafton, L. Conklin, and R. C. White, "Effect of Partial and Whole Body X-Irradiation on Life Span and Tumor Incidence of CF₁ Mice," Los Alamos Scientific Laboratory report LA-2445-MS (1960), pp. 274-284.
16. F. Sato, S. Tsuchihashi, and N. Kawashima, "Life-Shortening of Mice by Whole or Partial Body X-Irradiation," *J. Radiat. Res.* 14, 115-119 (1973).