BODY WEIGHT DECREASES IN SOME PROTON EXPOSED PRIMATES*

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Abstract. Immature *Macaca mulatta* were exposed to varying doses of whole body irradiations utilizing 2 MeV X-rays; 55, 138 and 400 MeV protons; and 2.3 GeV protons. Over 200 primates remain in a life-long study of space type irradiation effects. Mean body weight decreases as a function of age, sex, dose and irradiation type have been found in the 55 MeV proton exposed group but not in the other groups. The cause of the decreased weights is unknown at present, as is the reason for the lack of this effect in the more penetrating irradiations.

1. Introduction

For many years the USAF School of Aerospace Medicine, Brooks AFB, Texas has been collaborating with the National Aeronautics and Space Administration on studies to determine with nonhuman primates what effects might be anticipated following irradiation in space. Some six years ago, a large group of primates (*Macaca mulatta*) were exposed to several radiations. These animals have been maintained since exposure in a life-long study of irradiation effects. It is the purpose of this paper to document a significant trend toward decreased mean body weight in the group of primates exposed to 55 MeV protons. Other groups to be considered are primates exposed to 2 MeV X-rays, 138 and 400 MeV protons, and 2.3 GeV protons.

2. Materials and Methods

From an original group of over 1000 *M. mulatta* exposed to protons at approximately two years of age, 204 irradiated primates remain. These animals were individually housed from age two through six years. From this point, they were housed in carefully selected pairs in a breeding colony arrangement. The colony is maintained in open air cages subject to seasonal climatic variations. They are fed commercial monkey biscuits containing isoniazid, and water is available at all times. Lettuce and apple supplements are fed weekly. Another group of 26 nonirradiated primates which were sham irradiated is maintained under identical conditions for comparison purposes.

Body wieghts have been obtained for the primates on a periodic basis for the past

* The animals involved in this study were maintained in accordance with the *Guide for Laboratory Animal Facilities and Care* as published by the National Academy of Sciences – National Research Council.

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seven years beginning prior to the irradiation exposure. The weights presented in the paper are taken from the month of March for each year.

The primates were irradiated with a single, whole-body exposure of protons. Proton energies of 55, 138, and 400 MeV and 2.3 GeV were utilized. For comparison, 2 MeV X-irradiations were also performed. Dose rates varied between 10 and 100 rad per minute. Primates in the exposure groups up to about 700 rad will be discussed. Higher dose groups primarily used for acute observations are no longer present (800–1200 rad). The 55 MeV protons had a calculated tissue penetration of approximately 2.5 cm (Traynor and Casey, 1971). The 2 MeV X-rays and the 138 and 400 MeV and 2.3 GeV protons have enough range in tissue to provide homogeneous depth dose distribution (Lindsay and Dalrymple, 1967). All the animals were rotated in Lucite chairs or mesh wire cylinders during exposure at 2 rpm. Specific exposure parameters are published elsewhere (Williams *et al.*, 1966).

3. Results

Due to insufficient remaining animals (<3), some of the dose groups will not be included in the report. In other cases, animals in similar dose groups will be combined to increase the numbers within a particular group. The mean weights for the control animals were found to be statistically different for the males and females after 3 yr of age (Kirk, 1971b); therefore, the body weights will be compared as a function of both sex and age. The mean weights with a single standard deviation for the exposed animals as a function of exposure type, dose, and sex are presented in Tables I-V. The mean weights for the irradiated primates are generally equal to or lower than the mean weights for the control animals with few exceptions.

The Student's t test was calculated for the purpose of determining statistically significant differences between the control and irradiated means. The $t=0.05$ level of confidence was utilized. Differences are noted in Tables I–V by asterisks. No area of difference was noted in the 2 MeV X-ray exposed animals. In the 55 MeV proton exposed group, the 400 rad males at five years and the 600 rad males at 3 yr were significantly smaller. These differences persisted through the eighth year. The females within the 55 MeV proton exposed group showed some variability in that the 25–50 rad group was significantly heavier in the 4th and 6th years, while the 600 rad group was significantly smaller in the 6th and 7th years. Within the 138 MeV proton irradiated group, the males and females at 210 rad and 360 rad in the second year were significantly larger than the controls. The females in the 100 rad group within the 400 MeV exposed primates were larger by a significant amount in years 6 and 8. The females within the 395 rad, 2.3 GeV proton exposed group also showed some variability and were found to be smaller during years 3, 4 and 8. The calculated t values for the points of significant difference are shown in Table VI.

4. Discussion

Observations similar to these made in primates have been reported in at least two

TABLE I

2 MeV X-rays
(Body weights in kg)

Years of age	Control males (19)	538 rad males (4)	716 and 624 rad males (9)	Control females (7)	446 rad females (3)	538 rad females (6)	716 and 624 rad females (3)
2	3.40 ± 0.80[a]	–	–	3.24 ± 0.64	–	–	–
3	4.94 ± 0.86	5.19 ± 0.75	4.99 ± 0.91	4.40 ± 0.55	3.90 ± 1.35	3.94 ± 0.70	4.70 ± 0.24
4	6.83 ± 1.36	6.56 ± 0.66	6.19 ± 0.82	5.16 ± 1.28	4.81 ± 1.45	5.02 ± 0.57	5.19 ± 0.17
5	8.95 ± 1.22	8.37 ± 1.76	8.10 ± 0.89	6.03 ± 1.04	5.60 ± 1.50	5.19 ± 0.78	6.36 ± 0.78
6	9.70 ± 1.22	10.10 ± 2.89	9.04 ± 1.38	6.41 ± 0.60	7.26 ± 2.25	5.80 ± 0.99	5.99 ± 0.36
7	10.45 ± 1.56	10.31 ± 2.43	8.97 ± 2.11	7.80 ± 1.20	7.99 ± 1.57	6.57 ± 1.00	6.99 ± 0.54
8	11.49 ± 2.19	11.66 ± 3.71	9.91 ± 1.68	7.55 ± 0.89	9.43 ± 1.05	7.05 ± 0.39	6.73 ± 0.59
9	–	11.43 ± 4.64	10.92 ± 2.02	–	9.13 ± 1.72	6.72 ± 0.42	7.86 ± 0.30

[a] ± One standard deviation.

TABLE II

55 MeV protons
(Body weights in kg)

Years of age	Control males (19)	25 and 50 rad males (7)	200 rad males (7)	400 rad males (8)	600 rad males (4)	Control females (7)	25 and 50 rad females (6)	200 rad females (6)	400 rad females (3)	600 rad females (4)
2	3.40 ± 0.80	3.55 ± 0.30	3.22 ± 0.50	3.36 ± 0.33	2.84 ± 0.40	3.24 ± 0.64	3.47 ± 0.86	3.39 ± 0.91	2.65 ± 0.75	3.04 ± 0.55
3	4.94 ± 0.86	5.18 ± 0.58	5.08 ± 0.91	4.37 ± 0.44	3.66 ± 0.27[a]	4.40 ± 0.55	4.28 ± 0.68	4.50 ± 0.68	3.86 ± 0.69	3.70 ± 0.55
4	6.83 ± 1.36	6.75 ± 1.00	8.25 ± 1.15	6.12 ± 0.85	4.64 ± 0.77[a]	5.16 ± 1.28	6.39 ± 1.13[a]	5.60 ± 0.80	5.64 ± 1.50	4.68 ± 0.29
5	8.95 ± 1.22	8.21 ± 0.80	8.72 ± 1.36	7.54 ± 1.33[a]	5.62 ± 0.68[a]	6.03 ± 1.04	7.13 ± 1.37	5.14 ± 0.78	5.40 ± 1.88	4.79 ± 1.04
6	9.70 ± 1.22	8.40 ± 1.69	9.63 ± 1.73	7.90 ± 1.34[a]	6.56 ± 0.78[a]	6.41 ± 0.60	7.92 ± 1.25[a]	7.28 ± 1.02	6.10 ± 1.60	4.85 ± 1.14[a]
7	10.45 ± 1.56	9.76 ± 0.98	10.87 ± 1.81	8.64 ± 1.46[a]	7.48 ± 0.48[a]	7.80 ± 1.19	8.66 ± 1.61	7.42 ± 0.58	6.53 ± 1.50	6.07 ± 1.44[a]
8	11.49 ± 2.19	10.31 ± 1.35	10.78 ± 1.72	8.99 ± 1.54[a]	7.75 ± 1.39[a]	7.55 ± 0.89	7.76 ± 1.34	7.12 ± 1.54	6.70 ± 1.80	5.83 ± 1.64

[a] Points of difference.

TABLE III

138 MeV protons
(Body weights in kg)

Years of age	Control males (19)	210 rad males (6)	360 rad males (7)	650 and 500 rad males (4)	Control females (7)	210 rad females (3)	360 rad females (5)
2	3.40 ± 0.80	4.01 ± 0.47[a]	4.61 ± 0.50[a]	4.32 ± 0.30	3.24 ± 0.64	4.32 ± 0.41[a]	4.39 ± 0.42[a]
3	4.94 ± 0.86	5.26 ± 0.67	5.78 ± 0.69	5.63 ± 0.67	4.40 ± 0.55	4.62 ± 0.17	5.02 ± 0.71
4	6.83 ± 1.36	6.73 ± 0.90	7.49 ± 0.91	7.42 ± 0.92	5.16 ± 1.28	6.42 ± 1.11	5.89 ± 1.16
5	8.95 ± 1.22	8.35 ± 0.56	9.14 ± 0.90	8.45 ± 0.92	6.03 ± 1.04	5.99 ± 1.00	7.22 ± 1.10
6	9.70 ± 1.22	9.04 ± 0.89	9.46 ± 0.90	9.03 ± 0.97	6.41 ± 0.60	7.78 ± 1.94	6.48 ± 0.75
7	10.45 ± 1.56	9.90 ± 1.51	10.16 ± 1.52	9.97 ± 1.47	7.80 ± 1.20	8.40 ± 0.69	7.08 ± 0.97
8	11.49 ± 2.19	10.48 ± 1.76	10.33 ± 1.81	10.30 ± 1.56	7.55 ± 0.89	8.96 ± 1.08	6.84 ± 1.42

[a] Points of difference.

TABLE IV

400 MeV protons
(Body weights in kg)

Years of age	Control males (19)	100 rad males (8)	200 rad males (3)	400 rad males (7)	600 rad males (3)	Control females (7)	100 rad females (4)	200 rad females (8)	400 rad females (7)
2	3.40 ± 0.80	3.51 ± 0.63	3.45 ± 1.15	4.20 ± 0.20	–	3.24 ± 0.64	3.21 ± 0.44	3.84 ± 0.58	–
3	4.94 ± 0.86	5.49 ± 0.96	5.00 ± 1.86	5.63 ± 0.99	5.34 ± 1.36	4.40 ± 0.55	4.74 ± 0.28	4.91 ± 0.42	4.55 ± 0.81
4	6.83 ± 1.36	7.34 ± 1.23	6.86 ± 1.16	7.13 ± 1.30	6.29 ± 0.25	5.16 ± 1.28	5.98 ± 1.30	5.78 ± 1.12	6.02 ± 2.01
5	8.95 ± 1.22	8.87 ± 1.50	8.36 ± 0.33	8.55 ± 1.04	8.20 ± 0.80	6.03 ± 1.04	7.39 ± 1.34	6.87 ± 1.46	6.69 ± 1.89
6	9.70 ± 1.22	9.64 ± 1.90	8.65 ± 0.70	10.01 ± 1.53	8.69 ± 0.91	6.41 ± 0.60	8.30 ± 0.36[a]	7.06 ± 1.43	7.42 ± 1.98
7	10.45 ± 1.56	10.37 ± 1.78	9.03 ± 0.15	10.18 ± 2.20	9.87 ± 1.46	7.80 ± 1.20	9.67 ± 1.22	8.23 ± 1.49	7.99 ± 2.21
8	11.49 ± 2.19	10.50 ± 1.30	9.30 ± 0.26	11.20 ± 2.09	9.93 ± 1.91	7.55 ± 0.89	8.23 ± 0.82[a]	7.45 ± 0.96	7.84 ± 2.27

[a] Points of difference.

TABLE V

2.3 GeV protons
(Body weights in kg)

Years of age	Control males (19)	113 rad males (8)	225 rad males (5)	395 rad males (5)	Control females (7)	225 rad females (10)	395 rad females (5)
2	3.40 ± 0.80	2.68 ± 0.32	3.18 ± 0.13	3.22 ± 0.13	3.24 ± 0.64	2.86 ± 0.12	2.39 ± 0.19
3	4.94 ± 0.86	3.86 ± 0.53	4.00 ± 0.58	3.88 ± 0.38	4.40 ± 0.55	3.89 ± 0.64	3.18 ± 0.35[a]
4	6.83 ± 1.36	5.47 ± 1.11	6.56 ± 1.13	5.68 ± 0.93	5.16 ± 1.28	5.32 ± 1.48	4.04 ± 0.59[a]
5	8.95 ± 1.22	7.98 ± 1.18	8.47 ± 0.49	7.67 ± 0.92	6.03 ± 1.04	7.05 ± 1.56	4.94 ± 0.80
6	9.70 ± 1.22	9.09 ± 1.48	9.44 ± 1.23	9.50 ± 0.63	6.41 ± 0.60	7.80 ± 1.79	5.39 ± 0.91
7	10.45 ± 1.56	9.78 ± 1.66	10.50 ± 0.66	11.02 ± 1.47	7.80 ± 1.20	8.87 ± 1.58	6.78 ± 1.23
8	11.49 ± 2.19	10.59 ± 3.06	11.76 ± 1.74	11.76 ± 1.07	7.55 ± 0.89	8.42 ± 2.23	5.88 ± 1.22[a]

[a] Points of difference.

TABLE VI

Significantly different mean body weights
(Student's $t = 0.05$)

Males			Females		
2 MeV X-rays – None			None		
55 MeV Protons – 400 rad			25–50 rad		
5 yr	$t = 2.84$	df = 26	4 yr	$t = 2.26$	df = 11
6 yr	$t = 3.62$	df = 26	6 yr	$t = 2.26$	df = 10
7 yr	$t = 3.58$	df = 26			
8 yr	$t = 2.91$	df = 25			
600 rad			600 rad		
3 yr	$t = 2.85$	df = 20	6 yr	$t = 2.39$	df = 9
4 yr	$t = 3.01$	df = 21	7 yr	$t = 2.23$	df = 10
5 yr	$t = 5.22$	df = 21			
6 yr	$t = 5.60$	df = 21			
7 yr	$t = 4.19$	df = 21			
8 yr	$t = 3.11$	df = 21			
138 MeV Protons					
360 rad			210 rad		
2 yr	$t = 3.441$	df = 24	2 yr	$t = 2.622$	df = 8
			360 rad		
			2 yr	$t = 3.585$	df = 10
400 MeV Protons – None			100 rad		
			6 yr	$t = 4.882$	df = 7
			8 yr	$t = 3.34$	df = 9
2.3 GeV Protons – None			395 rad		
			3 yr	$t = 4.32$	df = 10
			4 yr	$t = 2.606$	df = 10
			8 yr	$t = 3.036$	df = 10

cases for human populations where long term studies are being made following radiation exposure. During the 13th, 14th and 15th years after exposure, slight retardation in growth and development has been noted in the boys on Rongelap who were exposed at ages less than 12 yr. A relationship to hypothyroidism is being investigated in these small boys (Conrad *et al.*, 1970). In the people of Hiroshima, a slight but statistically significant decrease in mean body weight ($P \leqslant 0.05$) has been noted during the period 1958–1968 in males exposed to greater than 100 rad at ages 0–19 yr (Belsky *et al.*, 1971).

Exposure to 55 MeV protons in doses of 400 and 600 rad to the whole body surface of immature primates has previously been shown to reduce mean body weights (Kirk, 1971a). This is particularly true for the male primates where a steady growth pattern is present for the normal animals. No certain statement can be made as to the irradiation effect on the female primates for they normally exhibit considerable variation in their growth patterns, presumably due to menstruation and pregnancies.

The reason why mean body weights are reduced in the 55 MeV proton group and not in the X-ray or more penetrating proton groups is not readily apparent. All the animals were rotated during exposure to negate the Bragg peak effect and produce a uniform exposure (Mitchell *et al.*, 1966 and Hardy *et al.*, 1969). If anything, the 55

MeV proton exposure would be expected to reduce the amount of damage produced since the inner core of the primates was not directly exposed. The protons of greater energy than 138 MeV would penetrate the complete primate, thereby exposing all the tissues.

Although not directly germane to body weights, it has been our finding that the 55 MeV proton exposures have also caused more pathology (i.e. stenosis of the gut, liver disease, cataracts, neoplasms) than any of the other exposure types in our colony (Kirk *et al.*, 1971). Perhaps an end-of-range phenomenon for the 55 MeV protons within the primates is responsible, as this would be absent with the higher energy proton and the X-rays.

The exact nature of the decrease in mean body size is also unknown at this time. It does, however, appear to be a real finding and another example of the chronic or latent effects of irradiation. Further studies such as anthropometric measurements and thyroid function tests are being considered to discover the cause of this growth dysfunction.

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