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Collected original data on distribution of ^{90}strontium in plasma, whole body, and excreta of monkeys[a,b]

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[b]These experiments were begun in 1973 under the auspices of the U.S. Atomic Energy Commission and were supported until 1980 by the USAEC and its successor agencies, the U.S. Energy Research and Development Administration and the U.S. Department of Energy. Support was provided from 1981 to 1987 by the U.S. Nuclear Regulatory Commission, and the project was reinstated by the USDOE in 1988.
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ABSTRACT

Two long-term studies of the biokinetics of ^{90}Sr in non-human primates were conducted at three sites: Lawrence Berkeley Laboratory (LBL, 37 monkeys injected; studies in progress 1954 to 1983) and the Atomic Energy Project at the University of Rochester (UR, 24 monkeys injected and 10 fed; studies in progress 1954 to 1964). The UR project was moved and continued at the Delta Primate Center (Delta) from 1964 to 1968, at which time eight live monkeys and all project records and materials were sent to LBL. The total study population of injected or fed monkeys comprises 71 male and female Macaques (*Macaca mulatta*), who ranged in age from 2 to 13.5 years at exposure; dosages for 61 injected monkeys ranged from 23 to 1858 kBq kg^{-1}, and for 10 fed monkeys from 2681 to 10278 kBq kg^{-1}. The kinetics of ^{90}Sr in monkeys was studied at LBL by radioanalysis of serial blood samples and continuously (later periodically) collected excreta, and after 1968 by external photon counting; at UR and Delta only external counting was used. Lengths of study periods ranged from 1 to 7168 d after ^{90}Sr intake for individual monkeys. Total skeletal retention of ^{90}Sr was determined at death by radioanalysis of all the bones (76 monkeys); estimates of skeletal ^{90}Sr are available from external counting data for 11 of the 13 monkeys whose skeletons were not radioanalyzed. This document, which is the companion to, "Collected original data on distribution of ^{90}strontium in bones of monkeys," LBL-28649, contains the tabulated original data for ^{90}Sr content of the blood and excreta samples and of the whole body as measured by external photon counting.

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INTRODUCTION

This is the companion document to LBL-28649 (Du93), "Collected original data on distribution of ^{90}strontium in bones of monkeys," and it completes the compilation of original numerical data from the Lawrence Berkeley Laboratory (LBL), University of Rochester (UR), and Delta Primate Center at Covington, LA (Delta), studies of Sr in monkeys. This document contains the kinetic (timed) data for Sr in plasma or whole blood, excreta, and whole body (by subtraction of summed excreta or external measurement of Bremsstrahlung emissions) of monkeys that were injected with or fed Sr or were born to Sr-burdened mothers.

These studies of Sr biokinetics in monkeys were conducted by three investigators at the three sites. The LBL studies were initiated by the late J.G. Hamilton and carried forward by P.W. Durbin, 37 monkeys injected, four Sr-burdened offspring (Du56, 58, 73); the UR studies were supervised by the late L.W. Tuttle, 24 monkeys injected, 10 fed, five Sr-burdened offspring (Tu60; Ca61,62; Gö62; Ho63); the UR study was moved to Delta in early 1964, and from 1967 to its termination in 1968 it was directed by M.W. Parrott, 10 Sr-burdened offspring born at Delta Tu67ab; Pa68).

I. LBL Series

Table 1 lists the monkeys injected at LBL (7M through 191M), the date of injection, days to death, times after injection when serial blood sampling and external whole-body counting were started, fraction of injected Sr (%ID) recovered in the body (mainly the skeleton) and in the summed excreta (corrected for non-sampled intervals), and the interval of continuous excreta collections. Blood was drawn periodically from 13 monkeys from injection to death; semiannual blood samples were drawn from five additional monkeys starting at later post-injection times. Periodic whole-body counting of four monkeys was started soon after injection and continued semi-annually until death; semiannual whole-body counts were started for six other monkeys several years after injection. Collections of excreta were continuous for 17 monkeys from injection to

death. Excreta collection was continuous for six monkeys for 365 d followed by four or five 2-week collections per year; excreta collections from 11 monkeys were continuous for the first 6 mo and periodic thereafter, as described above. Excreta collections from the four earliest injected monkeys (7M, 8F, 9M, 10F) were complete only for the first 7 to 8 d; no additional excreta were collected from 7M or 10F; periodic collections from 8F and 9M were started at about 2.5 y p.i.; thus, total Sr excretion and material recoveries from these four monkeys are estimates.

II. UR-Delta Series

Table 2 lists the monkeys in the main UR-Delta study (LBL numbers 301M to 374M), the colony number (or name) assigned at UR and/or Delta, the date of Sr injection or feeding (mid-point), days to death, the site(s) of death and radioanalysis, and the time after exposure when whole-body counting was started. Whole-body counting was the only method used at UR or Delta to follow the elimination and retention of Sr. Equipment for detection of Bremsstrahlung was not available in 1954 to 1960, when the first seven Sr-fed monkeys were initially under study; in only one case (314M, Bozo), a few such measurements were made starting about 9.5 y after feeding. Frequent whole-body measurements of Sr retention were made for four adolescent monkeys (310M, 311M, 312M, 313M) from injection to death and for three Sr-fed nursing females (309F, 335F, 347F) and their offspring (416M, 418M, 420M) starting soon after the initiation of Sr feeding. The first whole-body counts of the 18 adult monkeys injected June 17, 1963 were made at 26 to 40 d after injection, and measurements were irregular thereafter. Attempts were made to measure Sr in all the offspring of the Sr-injected females and the later offspring of the three fed females by external counting, but instrument backgrounds were high, the Sr content of the infants was small, and the results were of such low statistical significance that they were omitted from this compilation.

Table 1. 90Sr-injected monkeys in the LBL study group and availability of metabolic data (blood excreta and samples, whole-body counts) and material recovery of administered ^{90}Sr. Monkeys are listed in chronological order of entry into the study.

Monkey no.	Inject date	Death (d.p.i.)	Start day: Blood	Start day: Body counts[a]	Recovery (%ID): Body	Recovery (%ID): Excreta	Recovery (%ID): Total	Excretion collections: Continuous (to t days)
7M	3/16/54	181	—[b]	—	24.2	(56.8)[c]	—	10 (remainder estimated)
8F	4/1/54	3506	—	—	3.0	(78.9)[c]	—	10 periodic after 603d
9M	4/16/54	2520	—	—	21.6	(42.3)[c]	—	8, periodic after 624d
10F	8/8/55	94	—	—	44.4	(37.1)[c]	—	10 (remainder estimated)
20F	1/15/57	707	—	—	14.2	80.4	94.6	133, periodic thereafter
21F	1/15/57	6449	2219	4286	4.6	80.7	85.3	133, periodic thereafter
23M	1/15/57	3175	—	—	7.5	70.2	77.8	133, periodic thereafter
33F	2/21/58	2278	1	—	6.5	66.0	72.5	140 periodic thereafter
34F	2/21/58	1921	1	—	15.4	74.3	89.7	147, periodic thereafter
35F	2/21/58	2040[d]	1	—	—	(79.8)[c]	—	140, periodic thereafter
27M	9/10/58	3159	0[e]	—	11.3	80.6	92.0	413, periodic thereafter
28F	9/10/58	2087	0[e]	—	16.1	78.9	95.0	413, periodic thereafter
29F	9/10/58	280	0[e]	—	38.9	59.5	98.4	death
31F	10/27/59	2663	1	—	5.6	80.8	86.4	364, periodic thereafter
32F	10/27/59	7168	1	3271	5.9	93.5	99.4	357, periodic thereafter
36F	2/15/60	4	—	—	58.6	43.0	101.6	death
37F	2/15/60	1	—	—	45.3	58.2	103.5	death
50F	11/13/61	1212	—	—	24.6	68.8	93.4	378, periodic thereafter
51F	11/13/61	441	—	—	28.5	69.3	97.8	death
52F	11/13/61	21	—	—	53.4	44.4	97.8	death
53F	11/13/61	66	—	—	73.9	27.2	101.1	death
61M	2/25/63	5372	497	2054	2.8	94.7	97.5	196, periodic thereafter
62M	2/25/63	5853	497	2054	1.2	96.1	97.3	196, periodic thereafter
83F	9/13/63	3411	287	1850	2.3	86.1	88.4	182, periodic thereafter
39F	9/13/63	5650	287	1850	0.9	101.	101.9	196, periodic there after
135F	9/13/63	147[d]	—	—	—	(89.7)[c]	—	death
63F	1/9/67	3287	0[e]	2	5.3	89.9	95.2	217d, periodic thereafter
40F	1/9/67	99	0[e]	2	6.4	90.0	96.4	death
64F	3/27/67	427	0[e]	2	16.4	82.6	99.0	death
65F	3/27/67	4427	0[e]	2	4.3	91.2	95.5	364, periodic thereafter
188M	9/9/69	2	—	—[a]	35.3	56.9	92.2	death
98F	10/28/69	35	—	—[a]	17.0	78.2	95.2	death
191M	6/8/70	16	0[e]	—[a]	51.4	44.6	96.0	death
152F	10/26/81	302	—	—[a]	6.6	86.9	93.5	death
153F	10/26/81	668	—	—[a]	9.5	83.2	92.7	death
154F	10/26/81	870	—	—[a]	2.7	88.7	91.4	death
160F	1/4/82	204	—	—[a]	9.8	89.1	98.9	death
161F	1/4/82	8	—	—[a]	15.4	83.4	98.5	death

[a]Periodic whole-body counts. Body content of ^{90}Sr was determined by external measurement only after death for monkeys 98F, 152F, 153F, 154F, 160F, 161F, 188M, and 191M.

[b]Dash (—) indicates no measurement.

[c]Total Sr excreted in continuous collections.

[d]Monkey 35F was reinjected accidentally at 2040 d. Cumulative Sr excretion to that time is shown. After the second injection (animal renumbered 135F) it was assumed that excretion of the first injection contributed insignificantly to the current total; the value shown for 135F is the total excretion after the second injection.

[e]First blood sample was taken within 4 h after the Sr injection.

Table 2. ^{90}Sr injected or fed monkeys in the UR-Delta study group and availability of whole-body counting data. Monkeys are listed in chronological order of entry into the studies; colony numbers used at UR and Delta are shown to identify monkeys cited in early reports.

Monkey number			Exposure data		Death data		
LBL	Delta	UR	date	mode	(d.p.e.)	place[a]	Whole-body counting history
302F	—	Susie[b]	6/17/54	fed	1059	UR/LBL	Used as frozen standard
314M	14	Bozo[b]	9/5/54	fed	4252	Delta	Periodic after 3530d
301M	—	Psycho[b]	10/5/54	fed	1462	UR/Davis	Wax phantom made from bones
303F	—	508[b]	11/13/56	fed	556	UR	None
304F	—	515[b]	11/13/56	fed	1346	UR/Delta	After death
307M	—	507[b]	11/13/56	fed	131	UR/—	None
308F	—	504[b]	11/13/56	fed	1104	UR/—	After death
335F	35	517[c]	12/15/60	fed	2737	Delta	Periodic from 7d after last feeding to death
347F	47	711[c]	12/15/60	fed	2736	Delta	Periodic from 7d after last feeding to death
309F	9	512[c]	12/27/60	fed	1275	Delta/LBL	Periodic from 7d after last feeding to 513d
310M	9	710[c]	1/23/61	i.v.	67	UR	Frequent from injection to death
311M	—	810[c]	1/23/61	i.v.	150	UR	Frequent from injection to death
305F	—	713[c]	1/26/61	i.v.	7	UR/—	Used as frozen standard
312M	—	901[c]	1/26/61	i.v.	103	UR	Frequent from injection to death
306F	—	903[c]	1/30/61	i.v.	14	UR/Delta	Used as frozen standard
313M	—	902[c]	1/30/61	i.v.	150	UR	Frequent from injection to death
327F[d]	27	706[c]	6/17/63	i.v.	3927	LBL	Periodic after 42d
329F[d]	29	707[c]	6/17/63	i.v.	2813	LBL	Periodic after 41d
331F	31	709	6/17/63	i.v.	1800	Delta	Periodic after 41d
333F	33	712	6/17/63	i.v.	1809	Delta	Periodic after 42d
337F	37	505	6/17/63	i.v.	1823	Delta	Periodic after 41d
339F	39	811	6/17/63	i.v.	1418	Delta	Periodic after 46d
341F	41	905	6/17/63	i.v.	1692	Delta	Periodic after 46d
343F[d]	43	705	6/17/63	i.v.	5846	LBL	Periodic after 46d
345F	45	704	6/17/63	i.v.	1824	Delta	Periodic after 46d
349F	—	702	6/17/63	i.v.	133	UR/Delta	Periodic after 42d
350M[d]	50	701	6/17/63	i.v.	5860	LBL	Periodic after 41d
360M[d]	60	513	6/17/63	i.v.	2040	LBL	Periodic after 46d
362M[d]	62	510	6/17/63	i.v.	4599	LBL	Periodic after 46d
364M[d]	64	503	6/17/63	i.v.	5232	LBL	Periodic after 41d
368M[d]	68	516	6/17/63	i.v.	2835	LBL/—	Periodic after 46d
370M	70	509	6/17/63	i.v.	740	Delta	Periodic after 42d
372M	72	501	6/17/63	i.v.	1803	Delta	Periodic after 42d
374M	74	703	6/17/63	i.v.	728	Delta/LBL	Periodic after 42d

[a]Site where monkey died and bones were radioanalyzed. When a single site is shown, radioanalysis of the bones was conducted at the site of death. When two sites are shown divided by a bar, for example, UR/LBL, the monkey died at the site to the left (UR) and bones were radioanalyzed at the second site to the right of the bar (LBL). When a dash (—) is inserted to the right of the bar, the body was lost, and no bones were radioanalyzed. Some monkeys that had died at UR were shipped to Delta as whole frozen carcasses or as loose bones cleaned of soft tissue and partly dried with ethylenediamine; Monkey 301M (Psycho) was shipped to UC Davis for radioanalysis in the form of one-half of a frozen carcass and one-half of a cleaned dry skeleton. The entire skeletons of two monkeys that died at UR (309F, 374M) were shipped to LBL as cleaned dried bones along with eight live animals.

[b]Pathological findings reported by Casarett et al. (Ca61,62).

[c]Monkeys included in Göksel's thesis (Gö62).

[d]Monkey shipped alive to LBL in June 1968.

METHODS

I. Sr in Plasma Volume

The methods used for radioanalysis of ^{90}Sr in blood or plasma samples were described by Durbin et al. (Du93). the measured Sr concentrations (%ID mL^{-1}) in whole blood or plasma can be calculated from the entries in the Tables of Data from the weight and Sr content of individual samples. Results are also expressed as Sr (%ID) in the total plasma volume. For those calculations, the densities of plasma and whole blood of monkeys were assumed to be the same as for Reference Man (ICRP74): plasma 1.027 g mL^{-1} and whole blood 1.058 g mL^{-1}. Total Sr in the plasma volume was calculated using the measurements of Gregerson et al. (Gr59) of red blood cell and plasma volumes of monkeys of both sexes weighing 3 to 7 kg: plasma (mL) = 36.4 mL kg^{-1}, blood volume (mL) = 54.1 mL kg^{-1}, whole body hematocrit = 0.66. For plasma samples,

$$\text{Plasma Sr (\%ID)} = 36.4 \times \text{BW} \times \text{\%ID(sample)} \times 1.027 \times \text{w(sample)}^{-1} \quad , \qquad (1)$$

and for samples of whole blood,

$$\text{Plasma Sr (\%ID)} = 36.4 \times \text{BW} \times \text{\%ID(sample)} \times 1.058 \times \text{w(sample)}^{-1} \times 0.66^{-1} \quad . \qquad (2)$$

Body weight (BW) is kg, sample weights are g, Sr is %ID.

All monkeys in the LBL colony were tested for TB semiannually, at which time they were tranquilized and weighed and a blood sample was drawn. Monkeys were also weighed at the time of their semiannual body count. In those cases when an animal was not weighed at the time a blood sample was drawn, BW was interpolated from the two measured weights bracketing the blood sampling time.

II. Sr in Excreta

The methods used to collect excreta samples, process them, and measure their ^{90}Sr content are described in Durbin et al. (Du93). For the first year after injection Sr was measured in 1% aliquots of acid solutions of excreta, ash (representing collections

made over 1 to 4 d) neutralized and evaporated on glass plates (≤200 mg of dry ash, mainly $Ca_3(PO_4)_2$), per plate). Near the end of the first year the Sr content of a 1% aliquot of a 3- or 4-d sample of mixed excreta had declined so much that statistically significant counting rates, in excess of counter background plus ^{40}K, could be achieved only with counting times greater than 1 h. At that point, the sample preparation method was changed to accomplish separation of the ^{40}K and concentration of the Sr. Larger aliquots, 1% of 1-week excreta samples, were processed by precipitation of Ca oxalate, which was collected in steel dishes (≤200 mg of dried Ca oxalate per dish). The Sr in these samples was detected using the coincidence-shielded low background system. By about the fourth year after injection, depending on the Sr excretion rates of the individual monkeys, accurate detection of Sr in the Ca oxalate preparations required counting times of several hours, and a more sensitive method was needed. Large aliquots of excreta samples (10% of a 1-week collection that had been ashed and dissolved in acid were sent to a commercial analytical laboratory along with an aliquot of the dose standard for each monkey for ^{90}Sr determination by the ^{90}Y-milking procedure.

As each procedural change was made, the Sr in four to six excreta samples was measured by the method being abandoned and the one being adopted to provide a period of overlap. In general, the Ca oxalate procedure yielded sample Sr %ID 10 to 15% less than either evaporation on glass plates or ^{90}Y-milking. The poorer results of the Ca oxalate method appeared to have been caused by two incompletely controllable factors. First, we were unable to prepare Sr counting standards that precisely matched the somewhat variable geometry of the dried Ca oxalate spread on the bottom of a steel dish, because a small and variable fraction of the contents of each dish crept up the inner wall. Second, and probably more importantly, the endpoint of the pH titration involved in the quantitative scavenging of Sr by Ca oxalate depends on the judgment of the analyst: Retrospective analysis of all the data for Ca oxalate samples prepared by four analysts demonstrated systematic operator-related losses of Sr presumably due to

underestimation of the final pH of the reaction solution. The Sr content of excreta samples for each monkey radioanalyzed by the Ca oxalate method was adjusted upward using the average ratio of Sr %ID in its set of overlap samples.

a. Accounting for missing excreta samples: Starting 6 mo to 1 y after injection, excreta collections were made for two consecutive weeks four or five times each year. The following method was adopted to estimate Sr excretion during the unsampled intervals. In the Tables of data these calculated values are shown enclosed in (parentheses). For the sampled interval, $(t_1–t_2)$,

$$Sr(t_1–t_2)(\%ID) = 0.5\ \ 14^{-1}\ (t_2 - t_1)[\%ID(t_1 - 14)\ \ - t_1) + \%ID(t_2 - (t_2 + 14)]\ \ , \qquad (3)$$

where t_1 and t_2 are the start and end dates of the missed interval $(t_1–t_2)$, $Sr(t_1–t_2)$ (%ID) is the Sr excreted in the missed interval, $(t_2–t_1)$ is the number of days not sampled, and $(\%ID(t_1 - 14) - t_1)$ and %ID $(t_2 - (t_2 + 14))$ are the Sr contents of the sampled two-week periods immediately before and after the unsampled interval, respectively.

b. Recovery of injected Sr: Excreta were not radioanalyzed for Sr at UR, so the following discussion pertains only to those monkeys injected at LBL (Table 1). Excretion data are incomplete for the first four injected monkeys (7M, 8F, 9M, 10F) and monkey 35F, who was accidentally reinjected, and Sr recoveries cannot be calculated for those animals. Average Sr recovery was 89.1 ± 8.8 %ID for the 10 monkeys injected between January 1957 and February 1960 (time to death ranged from 280 to 7168 d). Preliminary examination of the Sr excretion data accumulated to 1958 suggested there might be technical problems in collecting excreta (Du58). At that time we were still inexperienced in Sr radioanalysis and our techniques and detection equipment were not yet sufficiently reliable to give us enough confidence in the radioanalytical results to question seriously the adequacy of the excreta collection procedures. Two personnel changes were made in 1960 (new animal caretaker, new supervising technician for the monkey colony) that provided the opportunity to introduce more rigorous collection

procedures and improve Sr recoveries. The new procedures included more thorough cleaning of urine pans (soaking and scraping up adhered solids in addition to simple rinsing), radioanalysis of cage washes collected during the continuous excreta collection interval each time a monkey's cage was changed for steam cleaning, and frequent cleaning of urine pans with dilute acid for the first few days after a Sr injection (when the largest fraction of injected Sr is excreted). Improved Sr recoveries were achieved by these procedural changes as is shown by the increased average Sr recovery to 96.6 ± 3.7 %ID for the 22 monkeys injected after February 1960 (time to death ranged from 1 to 5853 d). The Sr recoveries of the 22 monkeys injected during and after 1960 are significantly greater than those for the 10 monkeys injected in the early years ($p \leq 0.01$, t-test) (Fi54).

Recovery of Sr was independent of days to death for the 22 monkeys injected after 1960, even though periodic excreta collections for seven of them extended from 2 to 14 y and involved three technical staff members and three animal caretakers. However, Sr retention in the body predicted from summed excreta frequently exceeded that measured by whole-body counting. During most of those years of periodic collections, Sr was radioanalyzed by the reliable ^{90}Y-milking procedure, so Sr detection errors were not likely to have been a major factor. We concluded that the periodic excreta collections were probably incomplete.

It is reasonable to conclude that almost all if not all loss of Sr was the result of incomplete collection of urine, which is the pathway for about two-thirds of the excreted Sr. In the early years some Sr was lost soon after injection, because the inner surfaces of the cages were not cleaned and not all solid material was scrupulously removed from the collection pans. Throughout the studies there was uncontrollable loss from spraying or dribbling of urine outside of the cages (mainly a problem with the larger males) and from unreported or incompletely cleaned-up spills (spillage was a problem caused by the need to manipulate full, heavy, large area pans during transfer of their contents to

the 2 L beakers lined up on the colony room floor). Special care was taken in collecting excreta from the last group of monkeys studied in 1981 to 1984, and all collections were made by technical staff. It was found that a variable but sometimes significant fraction of urinary Sr coprecipitated with calcium urate and other sparingly soluble calcium salts that formed as urine evaporated while standing for 3 to 4 d in the large-area, open pans. That precipitate, which lightly coated the inner surface, could be completely removed only by vigorous scraping with a metal spatula and rinsing with dilute acid. Urine evaporation was a problem mainly with the smaller females whose urine output was small. During most of the years of the Sr studies periodic excreta collections were made by the animal caretakers, who were not made aware of that potential avenue of Sr loss.

c. Correcting for material loss: We expect eventually to be able to use the Sr biokinetic data to construct and verify biokinetic models for Sr. For that purpose, it is desirable that the material recovery for each animal be normalized such that at any time after injection,

$$\%ID(\text{skeleton}) + \%ID\ (\text{cumulated excretion}) = 100\ \%ID \quad . \tag{4}$$

In order to obtain the most realistic normalization of the data for each monkey, the following assumptions are made:

- The amount of Sr injected into each monkey is accurately represented by its individual dose standard, an aliquot of which was counted along with bone, tissue, and excreta samples to correct internally for variations in detector efficiency and radioactive decay.
- The preparation and radioanalysis techniques used to measure the Sr content of the bones were accurate and provide a reliable measurement of the fraction of the injected Sr present in the whole skeleton at death.

- The methods used to prepare excreta samples for radioanalysis and three of the radioanalytical techniques applied to excreta samples (evaporation, neutralization on glass plates, and ^{90}Y-milking) are accurate.
- The whole-body Sr content of each monkey, determined by external Bremsstrahlung counting, is accurate when standardized by the Sr content of its radioanalyzed skeleton at death.
- All losses of Sr can be attributed to (i) our inability to collect excreta quantitatively in the early years of the experiment, and (ii) our failure, after more rigorous collection methods were developed and applied to collection of excreta during the first few months after a Sr injection, to apply those rigorous techniques consistently to periodic collections made later on.

Based on the reasonable assumption that all of the deviation of Sr recovery from 100 %ID was caused by incomplete collection of excreta, two methods were adopted to adjust the excretion data so that the material balance required by eqn (4) is met:

(i) For 22 of the monkeys for whom there are excretion data, no whole-body measurements were made before death. For 18 of those animals, Sr recovery was less than 100 %ID, and Sr losses were assumed to be systematic and proportional to the measured amount in each excreta sample. All the excreta values for each monkey (including the estimates of Sr excretion between periodic collections) were adjusted upward by a common factor for that animal, f_{ex},

$$f_{ex} = \text{measured cumulative excretion (\%ID)}\,[100\ \%\text{ID} - \text{skeleton \%ID}]^{-1} \quad . \qquad (5)$$

The Sr recovery of four animals slightly exceeded 100 %ID, f_{ex} was less than 1.0, and the measured excretion values were adjusted downward.

(ii) For 10 monkeys, several independent measurements of Sr retention were obtained by whole-body counting. Their Sr retention was anchored to the first whole-body count, and f_{ex}, calculated to the time of that count, was applied to all preceding

excreta samples. Excretion data for the intervals between whole-body counts were adjusted by the f_{ex} appropriate for that interval, so that at the time of each whole-body count, Sr retention calculated from adjusted cumulative excretion matched the external measurement.

Adjustment of excretion data to match the Sr retention measured in the body at death or in life by photon counting generally does not change the shapes of the excretion-retention curve or the slopes of their components. However, the adjusted values of the excretion data points, hence the daily excretion rates, are for the most part greater than the measured values. In 27 cases the adjusted excretion values are only a few percent greater than the measured values, but for three cases (21F, 31F, 38F) they are 10 to 20% greater, and in two outlying cases (23M, 31F) they are 30 to 40% greater.

The excretion data presented in the Tables have been adjusted to 100 %ID Sr recovery. If desired, the measured values can be reconstructed by use of the recovery data given in Table 1.

III. Whole-Body Bremsstrahlung Counting at LBL

Beginning in mid-1968, *in vivo* measurements of Sr retention (whole-body counts) were made semi-annually for all Sr-injected monkeys in the LBL colony. Four monkeys (40F, 63F, 64F, 65F) were injected in early 1967 with a mixture of ^{85}Sr and ^{90}Sr–^{90}Y; frequent external measurements of ^{85}Sr were made during the first year; whole-body counting of ^{90}Sr was begun in June 1968. The excretion rates (%ID d^{-1}) and cumulative excretion of both Sr isotopes, determined by radioanalysis of excreta, were identical, and whole-body retention of both Sr isotopes was assumed also to be the same. The curve of the later ^{90}Sr whole-body counts was a continuation of the early portion of the Sr retention curve defined by the ^{85}Sr counting data.

In preparation for whole-body counting, monkeys were tranquilized with Sernylan later Ketamine, and weighed. Each animal was placed in a carrying box on its left side in a curled position with its spine against the rear wall of the box; movement was

somewhat curtailed by packing empty spaces around the animal with wedges of plastic foam. The boxes used for transport and whole-body counts of the females and smaller males were commercial cat carriers made of heavy cardboard with several 2.5 cm air holes at each end and hinged tops with latches (bottom dimensions 25.4 × 45.7 cm). The boxes used for the five largest males were custom made of wood and plastic with air holes and carrying handles at the ends and a hinged top with latches (bottom dimensions 38 × 52 cm). The tranquilized monkeys were transported in their individual boxes by truck from the animal colony to human whole-body counter at the Donner Laboratory. Counting sessions usually involved four monkeys; measurements of the monkeys and ^{90}Sr standards and travel time required 3 to 4 h, so booster shots of the tranquilizer were needed occasionally.

a. The Donner Laboratory human whole-body counter: This walk-in whole body counting facility (Sa62) is contained in a low-background iron-shielded below grade basement room. It consists of a large sodium iodide crystal (24 cm diameter, 10 cm thick) suspended by an extendible arm from a ceiling track that permits precise three-dimensional positioning at any point in the room. Light pulses were processed and recorded using a multichannel analyzer. During the 16 y occupied by these studies, power supplies, multichannel analyzers, and data recording equipment were continuously upgraded. The consistency and reproducibility of our measurements of Sr retention in monkeys benefited greatly from the careful upkeep of the equipment, which was in continual use for detection of gamma-ray emitting radionuclides in experiments with patients and radiation safety monitoring of employees.

The best ratio of net signal-to-noise for ^{90}Sr was obtained using the ^{241}Am peak channels. The counting equipment was calibrated before each use such that the peak of the 60 keV gamma rays emitted by ^{241}Am was consistently located in the same channel and the peak was seven channels wide. Room background was measured for 30 min before and after each monkey counting session; background with the empty

monkey carrying box in place ranged from 75 to 100 counts per minute (cpm) over the entire course of these studies (1968 to 1984).

The crystal was positioned for whole-body counts of monkeys at a specific location near the room door, and the vertical distance between the crystal face and the floor was adjusted to 1 m. Standards were counted with their geometric mid-point located immediately beneath the midpoint of the crystal. Animals in carrying boxes were placed for counting such that the marked central point of the box lid was immediately below the midpoint of the crystal face.

b. Whole-body Sr counting standards: There were two counting standards for the ^{90}Sr measurements: (i) a 1 L plastic bottle filled with a calibrated ^{90}Sr solution (bottle), (ii) a wax cylinder containing half of the dried bones of monkey 301M (Psycho, wax cylinder). The ^{90}Sr content of those bones, inferred from radioanalysis of the other half of the skeleton, was calibrated against known ^{90}Sr standards (radioanalysis of the bones of 301M, preparation of the wax phantom, and its calibration were performed by Dr. Marvin Goldman of the Radiobiological Laboratory at the University of California, Davis). Surveys of various placements of the ^{90}Sr standards and monkeys of a range of sizes inside the animal carrying boxes showed that, for a 1 m distance from crystal to floor, photons emitted in the upward direction from standards and monkeys were recorded at the same overall efficiency. The average distance from the crystal face to the animal midline was about 95 cm for the smaller animals in the cat carriers and about 96 cm for the large males in the large boxes.

The bottle standard was placed for counting on its side in a watertight plastic box. The wax cylinder was marked with a straight inked line along the long dimension surface, which was labeled "top." It was counted in three positions (top up, top down, top facing away from operator) inside an animal carrying box, and the average net count was collected, to take account of the non-uniform distribution of the bones within.

c. Standardization of measurement conditions: The net counts of the standards for 60 whole-body counting sessions beginning June 4, 1968, D(O), and ending September 27, 1984, D(5818) were tabulated by calendar date and elapsed time, D(t), and a radioactive decay correction was calculated for each D(t) (^{90}Sr half-life 28.6 y, Ko81). Based on the count rates of the standards on D(O), each count thereafter was corrected for radioactive decay to obtain the expected count rate. A counting equipment sensitivity correction, sens(t), was calculated for each D(t) in the form of the ratio of the measured to the expected count. Counting sensitivities ranged from 0.805 to 1.09. The grand mean sens(t) of the wax cylinder was 0.957 ± 0.046 (60 counting sessions, average of three counts per session). The net count for a monkey on D(t) was adjusted for sens(t),

$$\text{Adjusted net count (cpm)} = \text{Measured net count}\,[\text{sens(t)}]^{-1} \quad . \qquad (6)$$

d. Calibration of whole-body counts of individual monkeys: The date of injection of each monkey was designated as its D(O). The quantity of Sr injected, ID(kBq), based on as many as three independent calibrations of each monkey dosage standard, Table 1, Durbin et al. (Du93), was corrected for radioactive decay at each D(t) on which that animal was whole-body counted.

For each monkey that died or was killed after 1967, the Sr content (live animal or intact carcass after death) was determined by external measurement just before or after death, respectively. Retention of Sr in the body (almost entirely in the skeleton) was determined by radioanalysis of the dissected bones and soft tissue (Table 1, Du93) and reported as both %ID and kBq at date of death. The measured Sr retention was then used to standardize the photon detection efficiency for that monkey, eff(monkey)(cpm kBq^{-1}),

$$\text{eff(monkey)(cpm kBq}^{-1}) = [\text{net count monkey(D)}][\text{sens(D)}]^{-1} \qquad (7)$$

where D is the date of the terminal whole-body count. In those few cases where a significant time elapsed between the last external measurement and the radioanalysis of the bones, Sr excretion in the interval between the last measurement and death was taken into account, and a decay correction was applied to obtain the Sr body content, kBq, on the date of the last external measurement.

e. Calculation of Sr retention: Each in-life external measurement [net count monkey(t)] was adjusted for sens(t), converted by its specific photon detection efficiency factor, eff(monkey) to Sr retained (kBq), and finally converted in turn to Sr retained, %ID(t), through division by its injected Sr dosage, ID(t)(kBq), corrected for radioactive decay. Collecting all the steps, the overall equation for converting the whole-body counting data to Sr retention, %ID(t), is as follows:

$$\text{Sr retention } [\%ID(t)] =$$

$$100\,[\text{net count monkey}(t)][\text{sens}(t)]^{-1}\,[\text{eff(monkey)}]^{-1}\,[ID(t)e^{-\lambda t}]^{-1}\quad , \qquad (8)$$

where sens(t) is dimensionless, [net count monkey(t)] is cpm, eff(monkey) is cpm kBq^{-1}, ID(t) is kBq, and λ is 28.6 y (Ko81).

IV. Whole-Body Bremsstrahlung Counting at UR and Delta

The first two groups of monkeys fed Sr at UR (first seven entries in Table 2) were established several years before the UR whole-animal external counting system was installed. The body of one of those monkeys (307M) was lost and not radioanalyzed. One (303F) was dissected and radioanalyzed before the whole-body counter was constructed. Retention of Sr in the body at death was eventually measured by whole-body counting of four stored frozen carcasses; among that group, the body of one (308F) was later lost and not radioanalyzed; one (301M Psycho) was skeletonized, half of the skeleton was radioanalyzed, and the other half was incorporated as dried bones into the wax cylinder phantom; the remaining two (304F, 302F Susie) served for several years as frozen counting standards, and their bodies were eventually radioanalyzed.

One monkey in the group (314M Bozo) was whole-body counted several times before death starting at 3530 d, and the body was later radioanalyzed. Estimates of skeletal Sr at death or at the time of reporting were published by Casarett et al. (Ca62).

After the UR whole-animal counter was fabricated, three nursing female monkeys (309F, 335F, 347F) were fed Sr daily for 30 d, and whole-body measurements of Sr retention were made several times during the ensuing year starting at 7 d after the last feeding; retention measurements continued periodically until death, except for the long lapse caused by the move to Delta. Retention of Sr in their infants (416M, 418M, 420M) was measured by whole-body counting frequently during their first year starting at 7 d after the mother's last feeding; whole-body counting continued sporadically until the death at Delta of one (416M) at 1753 d of age and donation of the other two alive at about 2720 d of age to the Delta colony, when the UR-Delta project was terminated in 1968.

Six monkeys were injected with Sr by Göksel (Gö62). Two (305F, 306F) were killed at 7 and 14 d, respectively, to serve as frozen counting standards; the body of 305F was later lost and not radioanalyzed; the body of 306F was eventually radioanalyzed at Delta. Four of those monkeys (310M, 311M, 312M, 313M) were whole-body counted several times, beginning a few hours after injection, until they were killed at 67 to 150 d after injection and radioanalyzed. The original analysis of the whole-body counting data from the three nursing mothers and their infants and the six injected monkeys was reported by Göksel (Gö62).

Whole-body counting of the 18 adult monkeys in the main UR Sr injection group started at 42 to 46 d after injection and continued periodically until death; eight of those monkeys were shipped alive to LBL in 1968, where regular whole-body measurements were continued.

a. The UR whole-body counting system: The facility for *in vivo* detection of ^{90}Sr in monkeys at UR was designed by L.W. Tuttle, and the details of its construction and

operation were reported by Göksel (Gö62). A summary is provided here for completeness. The radiation detector was a sodium iodide crystal 10 cm in diameter and 5.1 cm thick coupled to a 7.6 cm diameter Dumont 6363 photomultiplier tube. Pulses were fed into an RIDL Model 200 scaler and a 100 channel analyzer. The device was set to detect pulses with energies in the range 40 to 200 keV, which were registered in channels 0 to 50 and summed. The crystal-phototube assembly and the animal holder were enclosed in a large box with shielded top and sides (2.5 cm of old steel on the sides and top plus 5.1 cm of lead bricks on the sides and 7.6 cm of lead bricks on the top) and fitted with a hinged door on one side at the end where the monkeys were inserted. The inside dimensions of the shield were 107 cm length, 66 cm width, and 35.5 cm height.

Monkeys were placed in rigid polyethylene cylinders that were positioned with the long dimension facing the crystal by a lucite supporting frame. The internal dimensions of the monkey holders were 51 cm length and 20 cm diameter. They were permanently closed at one end and the other end could be closed and secured by screwing on a lucite plate that also served as one member of the support frame. The moveable cover contained a 1.3 cm diameter hole through which oxygen could be supplied through an inserted tube. A row of 0.6 cm diameter holes perforated the length of the upper surface to provide additional ventilation. The monkey holder and frame were placed in a low secondary metal container to prevent contamination of the interior of the chamber by passed urine. Once a monkey was introduced into a holder, it assumed a crouching position, and movement was restricted by the cylinder wall and ends.

Monkeys weighing 5 to 8 kg were counted in these holders. Smaller monkeys and the three infants were first put into a smaller diameter ventilated cylinder, which was secured with supports inside the regular monkey holder to maintain a constant distance of 25.5 cm from the vertical midline of the monkey to the crystal face. That geometric configuration was used for all measurements. The records available to us are silent on

the subject of sedation of the monkeys for whole-body counting, so we assume that the animals reported by Göksel (Gö62) were awake.

The first three whole-body measurements made for the group of 18 adult monkeys injected with ^{90}Sr June 13, 1963, and the measurements made of monkeys remaining from the earlier studies of Göksel (Gö62) and Casarett et al (Ca62) were made under tranquilization with Sernylan. A larger holder was constructed for the adult males that were counted *in vivo* after June 1963; the animal midline to crystal distance would have been somewhat less than 25.5 cm for those measurements.

b. The UR whole-body counting system at Delta: The UR whole-body counter was dismantled and moved to the Delta Center along with the Sr-burdened monkeys. The detector-analyzer system was modified and upgraded. The new detector was a larger sodium Iodide crystal 17.8 cm in diameter and 10 cm thick coupled to three photomultiplier tubes. Pulses were collected and analyzed with an RIDL Model 34-12B 400-channel analyzer. A narrower window was used, since the Bremsstrahlung peak was located in channels 7 and 8; counts were recorded for channels 0 to 29 and 0 to 39 (Pa68).

The shield and framework were reassembled at the new site. The shield was enlarged by steps so that by 1965 its inner dimensions were 213 cm length, 122 cm width, and 76 cm height. The shielding was uniform above and around the structure—5.1 cm of old steel, 5.1 cm of lead bricks, and an inner liner of 20-ga copper. The enlarged interior space permitted whole-body counting of monkeys at midline to crystal distances up to 1 m. The precise schedule of shield modification is not clear, but the written records suggest a sequence of events, as follows: whole-body measurements taken soon after the move to Delta were made against a large background count (2600 to 3000 cpm in channels 0 to 29), much greater than could be explained by the increased crystal volume alone. The initial effort in April 1964 to obtain a greater distance between the animal and crystal seems to have involved opening one end of the

shield and extending the overall length of the apparatus by shifting part of the electronic gear (amplifier, preamplifier, phototubes) to a less well shielded space outside the main enclosure. Over time, the primary shield was enlarged to accommodate all of the electronic gear within shielded space (background in channels 0 to 29 was reduced to about 1400 cpm). Apparently, the shielding thickness was also increased, so that by October 1964 the background in those channels had been reduced to 800 to 1000 cpm. Additional unspecified improvements later stabilized the background in the channels of interest to 650 to 750 cpm. Whole-body counts made at Delta were at animal to crystal distances of 0.5 or 1 m.

c. Reduction of whole-body counting data from UR and Delta: The approach to reduction of the raw monkey whole-body counting data obtained at UR and Delta, that is, conversion of [net count monkey(t)] at a specific geometry (animal to crystal distance) on a specific calendar day, was essentially the same as that described above for the whole-body counting results obtained at LBL (eqn. 6, 7, 8). First we sought to develop, through the Sr standards, internally consistent date-specific equipment-geometry sensitivity correction factors, sens(t), that could be applied to the entire chronologic sequence of whole-body measurements made at UR and Delta. Next, we sought to develop a photon detection efficiency factor for each monkey, eff(monkey), based on radioanalysis of its skeleton and the specific whole-body counting geometry used for the last external Sr measurement.

Whereas, at LBL two Sr standards were measured at each animal whole-body counting session and the counting geometry was rigidly maintained throughout the 16 y of measurements, the whole-body counting history at UR and Delta can only be described as chaotic. No one counting standard was measured at each counting session throughout the 7 y of measurements; at some counting sessions no standard was measured; there were at least two major changes in the detector-analyzer equipment, and several changes were made in the quality of the shielding and the

configuration of the counting enclosure; monkeys were counted at three distances from the crystal—about 26 cm at UR, initially at 0.5 m at Delta, and later at Delta at 1.0 m. The net result of the equipment changes, site moves, variable geometry, and inconsistent standardization is the introduction of much uncertainty in the measurements of %ID(t) at both UR and Delta. There is much less uncertainty in the whole-body measurements of the monkeys reported by Göksel (Gö62), because all measurements were made with one set of equipment at a fixed geometry and two standards were routinely measured: Those data were recalculated here for consistency, and agreement with the original report is good. The uncertainty is also somewhat less for the eight monkeys that were eventually sent to LBL, because the earlier measurements at UR and Delta could be anchored to those made at LBL.

It was necessary to introduce some assumptions and approximations into the reduction of the original UR and Delta whole-body counting in order to use as much as possible of those data sets. The major points where estimates were needed in that data reduction process occurred when equipment counting geometry or standards were changed and when standards were not measured at whole-body counting sessions.

d. Whole-body Sr counting standards at UR and Delta: ^{90}Sr sourses used to standardize whole-body counting at UR and Delta, and from which values for sens(t) must be derived, were of three kinds:

(i) Phantoms—The first Sr standards used at UR were the so-called "monkey phantoms." These were a set of plastic cylinders with a size range such that the final preparations weighed from 1 to 8 kg. A known amount of ^{90}Sr was intimately mixed with dried beef bone powder (10% by weight of final preparation), the labeled powder was suspended uniformly in a 3% agar gel (90% by weight), and the suspension was poured into the cylinders (Gö62). The 8 kg phantom was used from 1/6/61 to 3/31/61.

(ii) Frozen monkey carcasses—The first two of these monkeys were injected with ^{90}Sr and killed a few days later and frozen—305F (UR713), 5.5 kg weight, killed at 7 d

and 306F (UR903, originally erroneously identified as male), 2.8 kg weight, killed at 14 d (Gö62). Frequent reference is made to the "known" ^{90}Sr content of these frozen monkeys. Their Sr content was in fact estimated by secondary standardization, as follows: Frozen 305F and 306F were counted on the same day that two other injected monkeys of comparable body weight were counted and then killed—310M (UR710), 6.7 kg weight and 312M (UR901), 3.4 kg weight. The latter two monkey's skeletons were radioanalyzed, and eff(monkey) was calculated for each from their last whole-body count. Those values of eff(monkey) for the larger monkey 310M and for the smaller monkey 312M were then applied directly as estimates of the eff(monkey) of the frozen carcass of comparable size. Göksel (Gö62) reported that carcass 305F contained 2220 kBq and that of 306F, 1332 kBq.

The larger frozen monkey 305F was counted a total of 58 times between 2/3/61 and 2/17/65, at which time she was shipped to UC Davis, and her ^{90}Sr body content was measured (it is unclear whether by radioanalysis of the bones or external measurement in a well-calibrated whole-body counting system, or both). Correcting for radioactive decay, her body Sr content at death was 2220 kBq, in exact agreement with the value reported by Göksel (Gö62). The smaller frozen monkey 306F was counted less often, 23 times between 2/23/61 and 1/20/65. The body was stored frozen at Delta until 1968, when it was thawed and radioanalyzed. Correcting for radioactive decay, her body Sr content at death was 1454 kBq, about 9% more than the reported value.

Although not originally intended to be a Sr counting standard, the external Sr measurements of frozen monkey 302F (UR Susie, fed ^{90}Sr in 1954, died in 1957) spanned the entire period of the UR-Delta study of 18 Sr-injected adult monkeys. Between 1/7/64 at UR and 1/9/68 at Delta external Sr counts were made 45 times. Frozen 302F was sent to LBL in June 1968, where external measurements continued until 1973. At that time the body was thawed and radioanalyzed. Body Sr content had also been measured in 1965 in the well-calibrated UC Davis whole-body counting

system. Transfers and prolonged frozen storage caused the loss of 2 kg of water from the body; body weight at death was 4.8 kg, and at radioanalysis it was 2.8 kg. How much effect that water loss would have had on the photon counting efficiency cannot be assessed, so no attempt was made to take account of the change in thickness of the soft tissue overlying the bones. Because so many measurements of Sr were made over such an extended period, and measurements were made at all three Laboratories under all of the geometric configurations used to measure live monkeys, frozen monkey 302F was selected as the primary standard for the purpose of reduction of the UR and Delta whole-body counting data.

Two other Sr-burdened monkeys that died at UR were stored frozen, and whole-body Sr measurements were made several times at UR and later at Delta; eventually the bodies were thawed at Delta and radioanalyzed. Frozen monkey 304F (UR515) was counted seven times between 1/7/64 at UR and 2/17/65 at Delta. Frozen monkey 349F (UR702) was counted eight times between 1/17/64 (at UR) and 7/25/66 (at Delta).

(iii) Wax cylinder—Monkey 301M (UR Psycho) was fed ^{90}Sr in late 1954 at UR and died 4 years later in 1958; the body was frozen (see also Section III.b.). Sometime later, but by late 1960, the 9 kg body had been divided lengthwise roughly into halves, which were wrapped separately and stored. Presumably, the reason for dividing the body had been to provide a frozen standard for Sr whole-body counting of the smaller monkeys being studied at UR at that time (Gö62). The Sr content of one of the "Psycho halves" was measured externally eight times between 1/6/61 at UR and 1/20/65 at Delta. In early 1965 the frozen parts of 301M were shipped to UC Davis, where a known fraction (about one-half) of all the bones was radioanalyzed. The rest of the bones were dried and embedded (distributed throughout the body of the wax as evenly as possible) in a right circular paraffin cylinder 30 cm long and 12 cm in diameter. The cylinder was covered by two layers of masking tape. The diameter is not a perfect circle, but is slightly flattened in one place lengthwise to provide a flat 4-cm wide base.

Along the upper surface opposite the center of the flattened base a lengthwise line was scribed and labeled "top" to provide a point of reference for Sr measurements of the wax cylinder in various positions with respect to the crystal face. The wax cylinder was calibrated at UC Davis, and the measurements agreed within a few percent with the value predicted from the radioanalyzed portion of the skeleton. It was returned to Delta, where it served as the primary Sr counting standard from 5/30/67 to 1/9/68. The wax cylinder was sent to LBL in June 1968, where it was the primary Sr whole-body counting standard until the Sr studies were ended in 1984.

e. Standardization of measurement conditions: No one Sr standard was counted on every day that live animals were measured at either UR or Delta, and on a number of occasions no Sr standard was measured along with the live monkeys. Therefore, it was necessary to normalize all the measurements of the seven Sr standards to one primary standard.

A complete chronology of the measurements of each Sr standard and experimental monkey was prepared from the original record books. Each individual chronology contained for each date of measurement; gross counting rate, background counting rate, net counting rate, and for measurements at Delta, the source to crystal distance (0.5 or 1.0 m). The ^{90}Sr content of each standard was known as of a specific date, as follows: the 8 kg phantom was prepared from a known amount of Sr; the skeletons of frozen monkey standards 302F, 304F, 306F, and 349F were radioanalyzed; the Sr content of the whole body of frozen monkey 305F and the wax cylinder were determined by calibration with known sources in the UC Davis whole-body counting system. Taking radioactive decay into account, the Sr content, kBq(t), of each Sr standard was calculated for each calendar date on which it was measured. The measured net count on that day, net count (standard i)(t)(cpm), was converted to a daily counting efficiency, eff(standard i)(t)[cpm(t) kBq^{-1}],

$$\text{eff(standard i)(t)[cpm(t) kBq}^{-1}] = [\text{net count(standard i)(t)}][\text{Sr(standard i)(t)}]^{-1} \quad . \qquad (9)$$

A master table was then prepared of the chronologic sequence of all dates on which any measurements were made of Sr standards and/or live (or recently dead) monkeys. The master table displayed by calendar date the identity and eff(standard i)(t) of all the Sr standards, and for measurements at Delta, the counting geometry. The master table of Sr standards identified the dates on which more than one Sr standard had been measured and those dates on which live animals but no Sr standard had been measured.

f. Normalization to primary Sr standard: Frozen monkey standard 302F (UR Susie) was selected as the primary Sr standard, because her measurements spanned nearly the entire time period of the UR-Delta studies, and because she was measured at least once in all configurations at all three laboratories. However, standard 302F was not measured during the early phase of the UR study and was measured infrequently during several intervals at Delta. To fill those gaps, the eff(standard i)(t) of the six other Sr standards (four frozen monkeys and two phantoms) were normalized to the counting efficiency of 302F to estimate the counting efficiency of 302F on the days she was not measured.

A relative efficiency ratio relating eff(302F)(t) to eff(standard i)(t) was calculated for each calendar date when 302F was measured along with one or more of the other Sr standards,

$$\text{Relative eff(standard i)} = [\text{eff(302)(t)}][\text{eff(standard i)(t)}]^{-1} \quad . \qquad (10)$$

For pairs of measurements made at the same geometry on the same day, relative eff(standard i) was nearly independent of the conditions of the measurements as is shown by the small standard deviations of the means of the individual relative eff(standard i). The mean relative efficiencies of 302F to the other Sr standards and the numbers of measurements are, as follows: 305F, 1.15 ± 0.11, nine; 306F, 1.19 ± 0.11, five; 349F, 1.21 ± 0.20, seven; 304F, 1.25 ± 0.13, five; wax cylinder, 0.94 ± 0.05, 24

measurements. Frozen monkey 302F and the 8 kg phantom were not measured at any time on the same day, and a relative efficiency of 302F to the 8 kg phantom was obtained indirectly: the relative efficiency of 305F to the 8 kg phantom was 1.36 ± 0.06, three measurements; the relative efficiency of 302F to 305F is 1.15 ± 0.11; the calculated relative efficiency of 302F to the 8 kg phantom is the product of the two relative efficiencies, 1.56 ± 0.17.

Daily values for estimated eff(302F)(t) were obtained from the measured daily efficiencies of the six other Sr standards and their individual mean relative efficiencies listed above,

$$\text{Estimated eff(302F)(t)[cpm(t) kBq}^{-1}] = \text{[eff(standard i)(t)][mean relative eff(standard i)]} \quad . \tag{11}$$

When more than one Sr standard was measured on a given day, all values for estimated eff(302F)(t) calculated from eq. (11) and any measured value of eff(302F)(t) were combined as a mean.

A distance correction was required to normalize all the measurements of 302F and the wax cylinder to the 0.5 m distance which was the counting configuration of the selected reference value for eff(302F)(t). During the first 2 years at Delta nearly all whole-body measurements were made at 0.5 m, but after mid-1966 nearly all such measurements were made at 1.0 m. Between April 1964 and June 1967, 302F was measured at both distances on six occasions. The mean ratio of the counting rates at the two distances (count at 0.5 m)(count at 1 m)$^{-1}$, was 3.32 ± 0.10.

g. Pooling data for the Sr standards: At this point, a chronology of whole-body Sr counting standards was in hand, based on eff(302F)(t), consisting of the following: (i) direct measurements of eff(302F)(t) at UR and at the 0.5 m distance at Delta; (ii) measurements of eff(302F)(t) made at the 1.0 m distance at Delta multiplied by the

distance correction, 3.32, to estimate eff(302F)(t) at 0.5 m; (iii) estimated eff(302F)(t) calculated from the measurements of the other six Sr standards using eqn. (10,11).

A reference eff(302F) was selected based on the mean efficiencies of the first set of measurements of the five frozen whole monkeys and the frozen half of 301M made at Delta at the 0.5 m distance. The selected reference eff(302F) was 11.4 ± 1.2 cpm kBq^{-1}.

All values of eff(302F)(t), both measured and estimated, were recast as efficiency ratios, that is, the ratio of eff(302F)(t) to the reference efficiency of 11.2 cpm kBq^{-1},

$$\text{Efficiency ratio}(t) = \text{sens}(t) = 11.7^{-1}\ \text{eff}(302F)(t) \quad . \tag{12}$$

These efficiency ratios were used in the same way as sens(t) [see eqn. (6)] to regularize the whole-body counting data for the live UR-Delta monkeys and take account of major changes that took place in the detectors, shielding, and counting geometry and day-to-day fluctuations in the sensitivity of the detection systems.

h. Estimating missing sens(t) values: Whole-body counting sessions usually spanned several days to weeks. When standards were measured on most of the days of a counting session, missing measurements were estimated from adjacent measurements. When standards were measured intermittently and only a few times during a counting session, all available measurements were averaged to provide an overall sens(t) for the whole session. During a one-year period at Delta (mid-March 1965 to mid-March 1966) more than 75 whole-body counts were made of live monkeys, but no standards were measured. A gross estimate, the average of all standard measurements made in the two months before and after the skipped interval, was applied to all the live counts made during that time. The suitability of the estimates of missing sens(t) is shown by the general smoothness of the Sr retention curves prepared from the UR-Delta whole-body counting data.

i. Calculation of Sr retention: The procedure used to calculate Sr retention, %ID(t), for each whole-body measurements at UR and Delta was the same as that described for similar measurements made at LBL. The net count monkey(t) was adjusted for sens(t) using eqn. (6). The Sr content of each monkey at death, determined from radioanalysis of the skeleton, was used along with the final whole-body count and eqn. (7) to calculate eff(monkey). The individual Sr dosage (kBq fed or injected) was corrected for radioactive decay to the time of each whole-body count. The above calculations were combined in eqn. (8) to obtain Sr retention, %ID(t), for each whole-body count. For each of the eight monkeys sent alive to LBL, the whole-body counting data taken at LBL were plotted; a fitted log-linear regression line drawn through the points was extrapolated back to the time of its last whole-body count at Delta to estimate its Sr retention, kBq, at that time; the estimated Sr content and its last whole-body measurement at Delta were used to calculate its eff(monkey) in the Delta counting system.

All of the original whole-body counting record books have been preserved, so that a different analysis of these data can be conducted in the future, if needed.

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REFERENCES

Ca61 Casarett, G.W., Tuttle, L.W., and Baxter, R.C. Pathological effects of ingested strontium-90 in rats and monkeys. Univ. Rochester Atomic Energy Project report UR-597 (1961).

Ca62 Casarett, G.W., Tuttle, L.W., and Baxter, R.C. Pathology of imbibed Sr^{90} in rats and monkeys. In: *Some aspects of internal irradiation.* Dougherty, T.F. et al. editors. Pergamon Press, Oxford. pp. 329-339 (1962).

Du56 Durbin, P.W., Parrott, M.W., Williams, M.H., Johnston, M.E., Asling, C.W., and Hamilton, J.G. Metabolic studies with strontium-90 in the rhesus monkey. In: *The shorter-term biological hazards of a fallout field.* U.S. Atomic Energy Commission, Washington, D.C. pp. 173–183 (1956).

Du58 Durbin, P. and Jones, H. Estimation of the turnover equation of strontium-90 for human bones. *Second United Nations Geneva Conference on Peaceful Uses of Atomic Energy*, v. *23*, 140-141 (1958).

Du73 Durbin, P.W., Jeung, N., Williams, M.H., and Parrott, M.W., Long-term metabolism of ^{90}Sr in rhesus monkeys (*Macaca mulatta*). *Third Int. Congr. Intl. Rad. Prot. Assn. Proceedings.* Report CONF-730907, pp. 1412–1417 (1973).

Du93 Durbin, P.W., Jeung, N., Williams, M.H., Parrott, M.W., Kullgren, B., and Tuttle, L.W. *Collected original data on distribution of ^{90}strontium in bones of monkeys.* Lawrence Berkeley Laboratory report LBL-28649 (March 1993).

Fi54 Fisher, R.A. *Statistical methods for research workers.* Hafner Publishing Co., New York (1954).

Gö62 Göksel, S.A. *The toxicity of strontium-90 in the monkey skeleton.* Considerations of relationship of total radiation dose, dose-rate, dose-time product and biological injury. Thesis. University of Rochester (1967).

Gr59 Gregersen, M.I., Sear, H., Rawson, R.A., Chien, S., and Saiger, G.L. Cell volume, plasma volume, total blood volume and F_{cells} factor in the rhesus monkey, *Am. J. Physiol. 196*, 184–187 (1959).

Ho63 Hopkins, B.J., Göksel, S.A., and Tuttle, L.W. *The transfer of strontium-90 through milk to suckling monkeys and rats*, Univ. Rochester AEP report UR-635 (1963).

ICRP74 International Commission on Radiological Protection. Report of the task group on reference man. ICRP pub. 23. Pergamon Press, Oxford (1974).

Ko81 Kocher, D.C. *Radioactive decay data tables*, U.S. Department of Energy report DOE/TIC-11026. Technical Information Center, U.s. Dept. of Energy, Washington, D.C. (1981).

Pa68 Parrott, M.W. and Felsenfeld, O. *The late effects of Sr-90 in the monkey.* Progress Report No. 4 Contract AT-(40-1)-3297. Report ORO-3297-4 (1968).

Sa62 Sargent, T., Metabolic studies with Fe^{59}, Ca^{47} and C^{11} in various diseases, In: Whole-body counting. IAEA, Vienna (1962).

Tu60 Tuttle, L.W., Baxter, R.C., and Casarett, G.W. The chronic toxicity of strontium-90 inthe monkey. *Radiat. Res. 12*, 480 (1960). Abstract.

Tu67a Tuttle, L.W., and Parrott, M.W. The late effects of Sr-90 in the monkey. Progress Report No. 3 Contract AT(40-1)-3297. Report ORO-3297-3 (Oct. 1964 to June 1967).

Tu67b Tuttle, L.W., Parrott, M.W., and Nice, Jr., C.M. Roentgenographic skeletal changes in *Macaca mulatta* chronically irradiated with strontium-90. *Radiat. Res. 31*, 538–9 (1967).

TABLES of DATA

Notes to Tables of kinetic data: The pertinent Tables of kinetic data, as many as three (blood, excreta, whole-body counting) for each monkey, are collected together and then arranged in order of ascending monkey identification number.

In the excretion Tables, ^{90}Sr content of excreta samples and excretion rate (%ID, $\%(ID t^{-1})$ enclosed in (parentheses) are estimates, calculated as described in Methods, section II.a., inserted to account for unsampled intervals.

Whole-body Sr retention is expressed as percent of administered dosage (injected or fed), and in the case of the four animals (400 series), that acquired Sr through nursing Sr-fed mothers, Sr retention is expressed as percent of the mother's dosage.