Supplementary Figures For:

Revisiting the Historic Strontium-90 Ingestion Beagle Study Conducted at the University of California-Davis: Opportunity in Archival Materials

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Running Title: The UC-Davis Strontium-90 Ingestion Beagle Study

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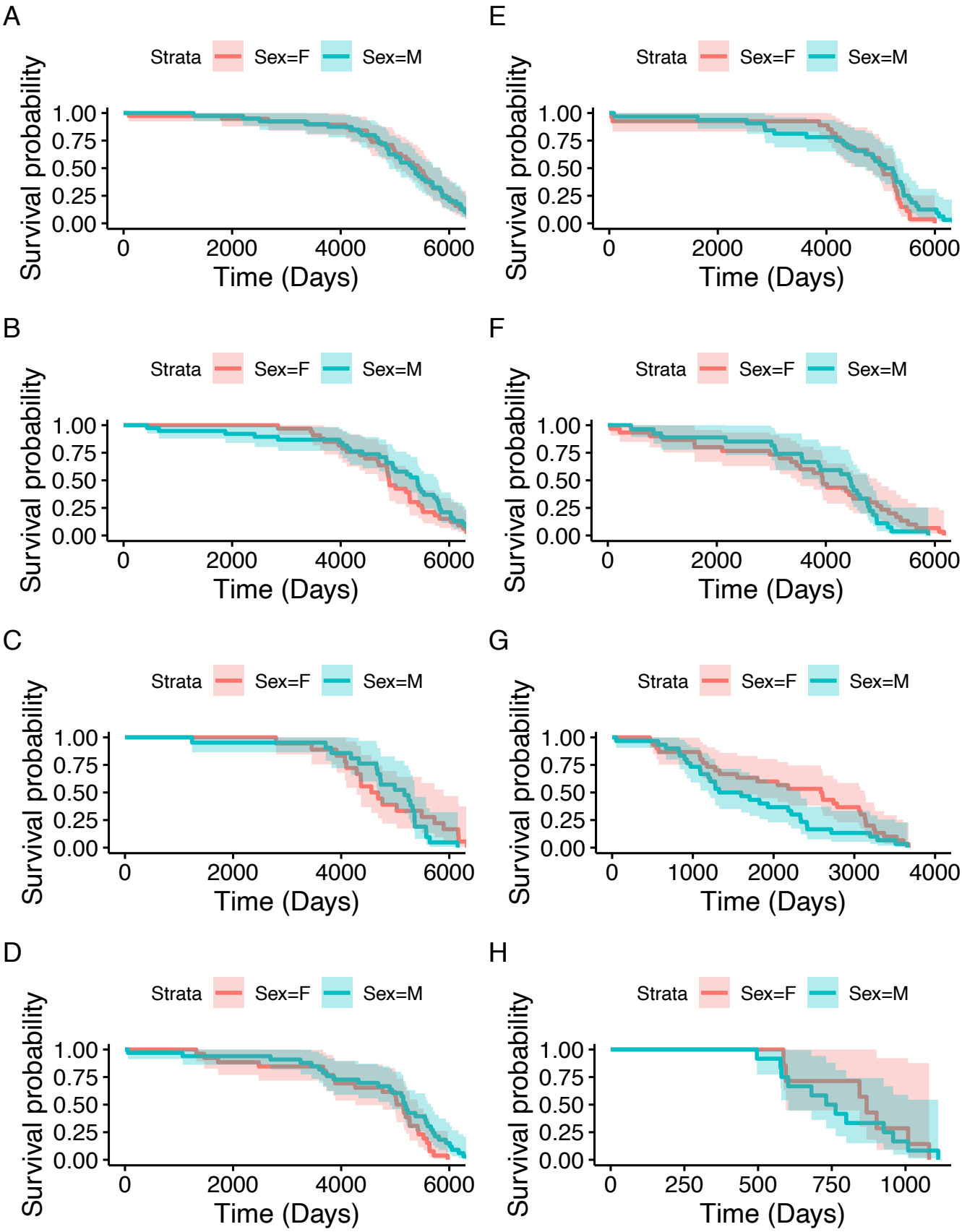
Pairwise Survival Difference Significance: Exact Values							
	D00	D05	D10	D20	D30	D40	D50
D05	1.0	-	-	-	-	-	-
D10	2.1×10^{-1}	1.0	-	-	-	-	-
D20	7.8×10^{-1}	1.0	1.0	-	-	-	-
D30	1.4×10^{-2}	9.5×10^{-1}	1.0	1.0	-	-	-
D40	2.4×10^{-8}	3.1×10^{-5}	6.2×10^{-2}	5.6×10^{-3}	4.5×10^{-2}	-	-
D50	Nearly Zero	Nearly Zero	Nearly Zero	Nearly Zero	Nearly Zero	1.1×10^{-13}	-
D60	Nearly Zero	Nearly Zero	Nearly Zero	Nearly Zero	Nearly Zero	4.9×10^{-15}	6.4×10^{-10}

Note: $p < 2 \times 10^{-16}$ = Nearly Zero

Supplementary Table 1. Exact Bonferroni-corrected p-values from pairwise log-rank comparisons of survival between dose groups. D00 n = 78, D05 n = 71, D10 n = 39, D20 n = 59, D30 n = 59, D40 n = 57, D50 n = 60 and D60 n = 19.


A
E
B
F
C
G
D
H
Strata
Sex=F
Sex=M
Survival probability
1.00
0.75
0.50
0.25
0.00
0
1000
2000
3000
4000
6000
250
500
750
1000
Time (Days)

Supplementary Figure 1. Kaplan-Meier survival curves show no significant difference in survival between sexes within dose groups. 95% confidence intervals are shown. Chi-square p-values were computed for the comparison between sexes for each dose group.

A. Survival curves for the D00 dose group; n = 38 females, 40 males; Chi-square = 0.1, degrees of freedom = 1 and p-value = 0.8.

B. Survival curves for the D05 dose group; n = 33 females, 38 males; Chi-square = 1.9, degrees of freedom = 1 and p-value = 0.2.

C. Survival curves for the D10 dose group; n = 18 females, 21 males; Chi-square = 0.5, degrees of freedom = 1 and p-value = 0.5.

D. Survival curves for the D20 dose group; n = 26 females, 33 males; Chi-square = 3.1, degrees of freedom = 1 and p-value = 0.08.

E. Survival curves for the D30 dose group; n = 27 females, 32 males; Chi-square = 2.1, degrees of freedom = 1 and p-value = 0.1.

F. Survival curves for the D40 dose group; n = 30 females, 27 males; Chi-square = 0.5, degrees of freedom = 1 and p-value = 0.5.

G. Survival curves for the D50 dose group; n = 30 females, 30 males; Chi-square = 2.9, degrees of freedom = 1 and p-value = 0.09.

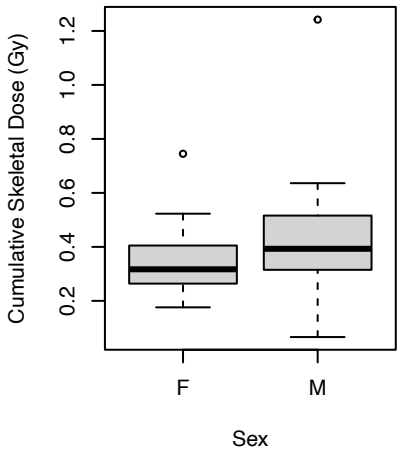
H. Survival curves for the D60 dose group; n = 7 females, 12 males; Chi-square = 0.2, degrees of freedom = 1 and p-value = 0.7.

Pairwise Dose Difference Significance: Exact Values							
	D00	D05	D10	D20	D30	D40	D50
D05	Nearly Zero	-	-	-	-	-	-
D10	Nearly Zero	1.6×10^{-15}	-	-	-	-	-
D20	Nearly Zero	Nearly Zero	2.5×10^{-15}	-	-	-	-
D30	Nearly Zero	Nearly Zero	4.2×10^{-15}	Nearly Zero	-	-	-
D40	Nearly Zero	Nearly Zero	7.0×10^{-15}	Nearly Zero	2.9×10^{-12}	-	-
D50	Nearly Zero	Nearly Zero	3.2×10^{-15}	Nearly Zero	2.4×10^{-15}	2.1×10^{-4}	-
D60	Nearly Zero	2.1×10^{-9}	5.0×10^{-8}	5.2×10^{-9}	6.3×10^{-9}	1.2×10^{-7}	4.3×10^{-1}

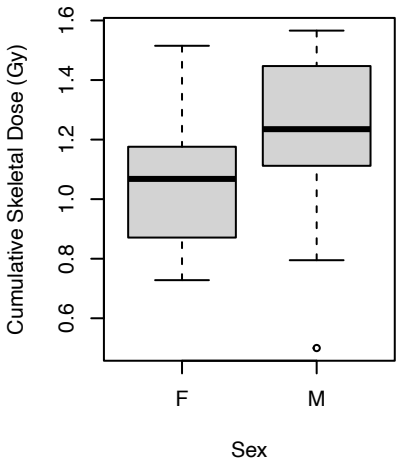
Note: $p < 2 \times 10^{-16}$ = Nearly Zero

Supplementary Table 2. Exact Bonferroni-corrected p-values from pairwise Wilcoxon rank sum comparisons of calculated total accumulated skeletal doses between dose groups. D00 n = 77, D05 n = 70, D10 n = 39, D20 n = 58, D30 n = 56, D40 n = 54, D50 n = 57 and D60 n = 18.

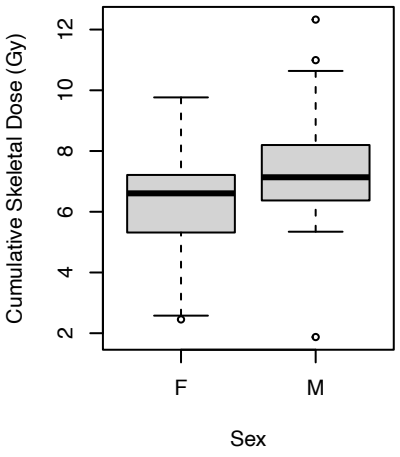
A


Cumulative Skeletal Dose (Gy)
0.2
0.4
0.6
0.8
1.0
1.2
F
M
Sex

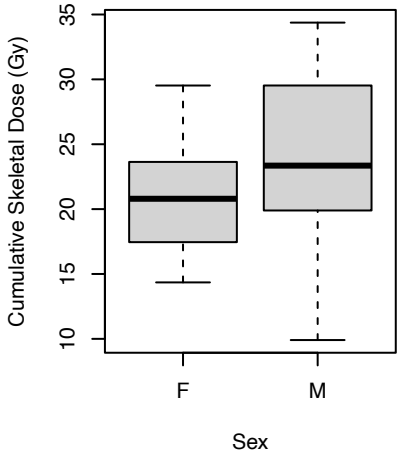
B


Cumulative Skeletal Dose (Gy)
0.6
0.8
1.0
1.2
1.4
1.6
F
M
Sex

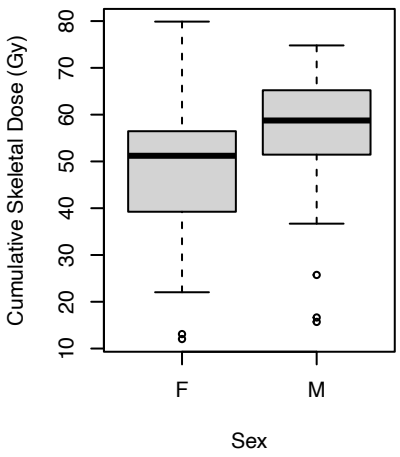
C


Cumulative Skeletal Dose (Gy)
2
4
6
8
10
12
F
M
Sex

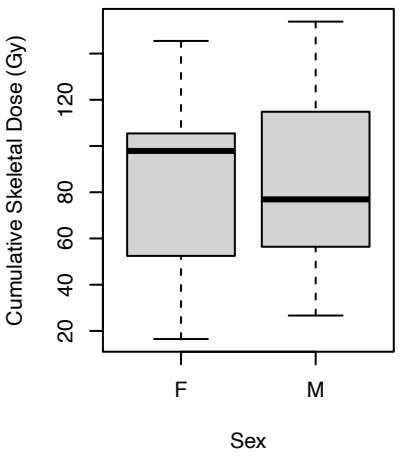
D


Cumulative Skeletal Dose (Gy)
10
15
20
25
30
35
F
M
Sex

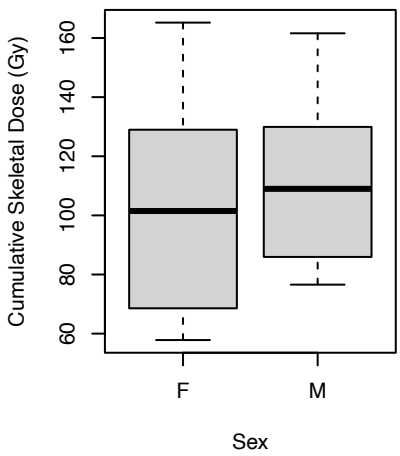
E


Cumulative Skeletal Dose (Gy)
10
20
30
40
50
60
70
80
F
M
Sex

F


Cumulative Skeletal Dose (Gy)
20
40
60
80
120
F
M
Sex

G


Cumulative Skeletal Dose (Gy)
60
80
100
120
140
160
F
M
Sex

Supplementary Figure 2. Boxplots comparing calculated cumulative skeletal doses between sexes for each dose group. Wilcoxon rank sum p-values were calculated for the comparison for each dose group.

A. Cumulative skeletal dose boxplots by sex for the D05 dose group; n = 33 females, 37 males; p-value = 0.009.

B. Cumulative skeletal dose boxplots by sex for the D10 dose group; n = 18 females, 21 males; p-value = 0.015.

C. Cumulative skeletal dose boxplots by sex for the D20 dose group; n = 26 females, 32 males; p-value = 0.015.

D. Cumulative skeletal dose boxplots by sex for the D30 dose group; n = 25 females, 31 males; p-value = 0.081.

E. Cumulative skeletal dose boxplots by sex for the D40 dose group; n = 28 females, 26 males; p-value = 0.040.

F. Cumulative skeletal dose boxplots by sex for the D50 dose group; n = 29 females, 28 males; p-value = 0.843.

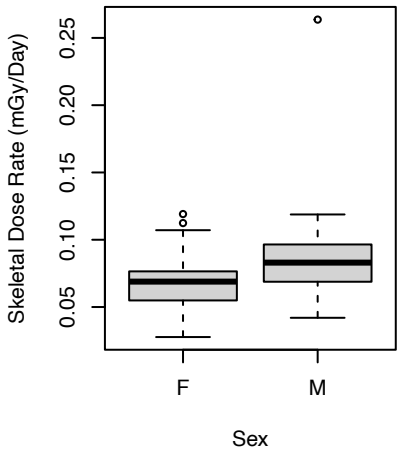
G. Cumulative skeletal dose boxplots by sex for the D60 dose group; n = 7 females, 11 males; p-value = 0.536.

Pairwise Dose Rate Difference Significance: Exact Values							
	D00	D05	D10	D20	D30	D40	D50
D05	Nearly Zero	-	-	-	-	-	-
D10	Nearly Zero	7.4×10^{-16}	-	-	-	-	-
D20	Nearly Zero	Nearly Zero	2.5×10^{-15}	-	-	-	-
D30	Nearly Zero	Nearly Zero	4.2×10^{-15}	Nearly Zero	-	-	-
D40	Nearly Zero	Nearly Zero	7.0×10^{-15}	Nearly Zero	Nearly Zero	-	-
D50	Nearly Zero	Nearly Zero	3.2×10^{-15}	Nearly Zero	Nearly Zero	Nearly Zero	-
D60	Nearly Zero	2.1×10^{-9}	5.0×10^{-8}	5.2×10^{-9}	6.3×10^{-9}	7.6×10^{-9}	5.7×10^{-9}

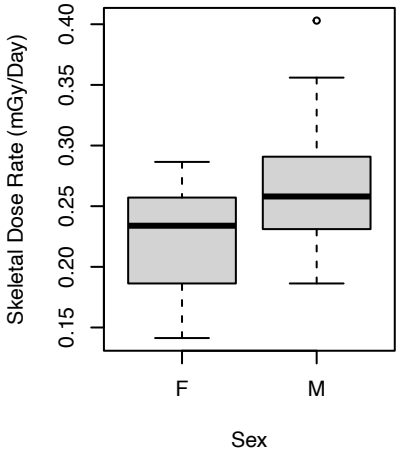
Note: $p < 2 \times 10^{-16}$ = Nearly Zero

Supplementary Table 3. Exact Bonferroni-corrected p-values from pairwise Wilcoxon rank sum comparisons of calculated average daily accumulation of skeletal dose between dose groups. D00 n = 77, D05 n = 70, D10 n = 39, D20 n = 58, D30 n = 56, D40 n = 54, D50 n = 57 and D60 n = 18.

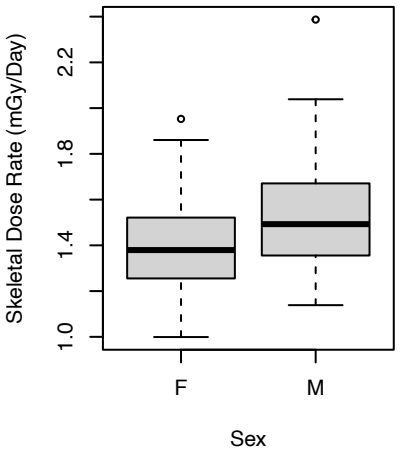
A


Skeletal Dose Rate (mGy/Day)
0.05
0.10
0.15
0.20
0.25
F
M
Sex

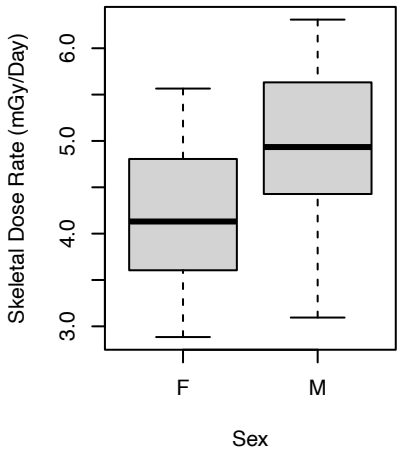
B


Skeletal Dose Rate (mGy/Day)
0.15
0.20
0.25
0.30
0.35
0.40
F
M
Sex

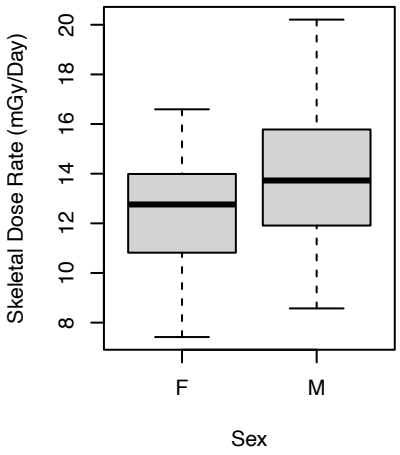
C


Skeletal Dose Rate (mGy/Day)
1.0
1.4
1.8
2.2
F
M
Sex

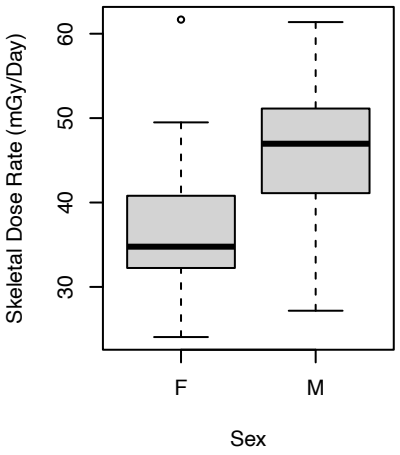
D


Skeletal Dose Rate (mGy/Day)
3.0
4.0
5.0
6.0
F
M
Sex

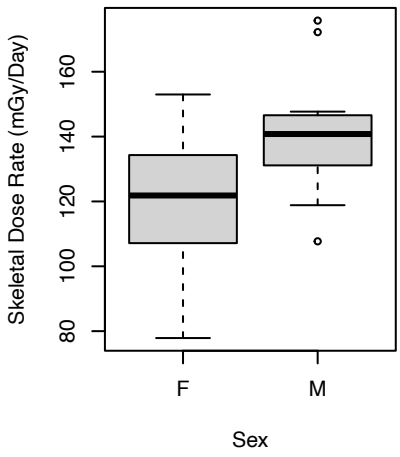
E


Skeletal Dose Rate (mGy/Day)
8
10
12
14
16
18
20
F
M
Sex

F


Skeletal Dose Rate (mGy/Day)
30
40
50
60
F
M
Sex

G


Skeletal Dose Rate (mGy/Day)
80
100
120
140
160
F
M
Sex

Supplementary Figure 3. Boxplots comparing calculated average daily accumulation of skeletal dose between sexes for each dose group. Wilcoxon rank sum p-values were calculated for the comparison for each dose group.

A. Average daily accumulation of skeletal dose boxplots by sex for the D05 dose group; n = 33 females, 37 males; p-value = 0.006.

B. Average daily accumulation of skeletal dose boxplots by sex for the D10 dose group; n = 18 females, 21 males; p-value = 0.040.

C. Average daily accumulation of skeletal dose boxplots by sex for the D20 dose group; n = 26 females, 32 males; p-value = 0.096.

D. Average daily accumulation of skeletal dose boxplots by sex for the D30 dose group; n = 25 females, 31 males; p-value = 0.001.

E. Average daily accumulation of skeletal dose boxplots by sex for the D40 dose group; n = 28 females, 26 males; p-value = 0.073.

F. Average daily accumulation of skeletal dose boxplots by sex for the D50 dose group; n = 29 females, 28 males; p-value < 0.001.

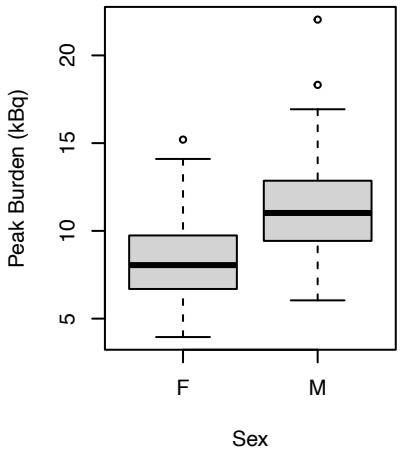
G. Average daily accumulation of skeletal dose boxplots by sex for the D60 dose group; n = 7 females, 11 males; p-value = 0.151.

Pairwise Peak Burden Difference Significance: Exact Values							
	D00	D05	D10	D20	D30	D40	D50
D05	Nearly Zero	-	-	-	-	-	-
D10	Nearly Zero	2.2×10^{-16}	-	-	-	-	-
D20	Nearly Zero	Nearly Zero	2.5×10^{-15}	-	-	-	-
D30	Nearly Zero	Nearly Zero	4.2×10^{-15}	Nearly Zero	-	-	-
D40	Nearly Zero	Nearly Zero	7.0×10^{-15}	Nearly Zero	Nearly Zero	-	-
D50	Nearly Zero	Nearly Zero	3.2×10^{-15}	Nearly Zero	Nearly Zero	Nearly Zero	-
D60	Nearly Zero	2.1×10^{-9}	1.8×10^{-13}	5.2×10^{-9}	1.8×10^{-6}	4.0×10^{-1}	1.0

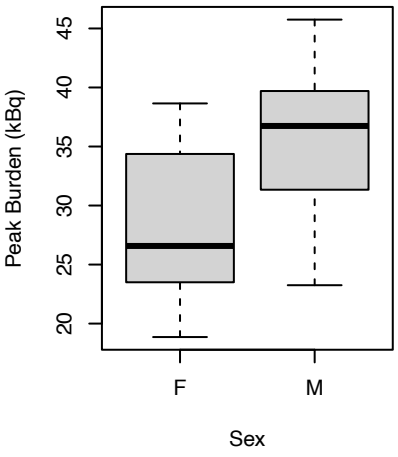
Note: $p < 2 \times 10^{-16}$ = Nearly Zero

Supplementary Table 4. Exact Bonferroni-corrected p-values from pairwise Wilcoxon rank sum comparisons of maximum measured burden of Sr-90 between dose groups. D00 n = 77, D05 n = 70, D10 n = 39, D20 n = 58, D30 n = 56, D40 n = 54, D50 n = 57 and D60 n = 18.

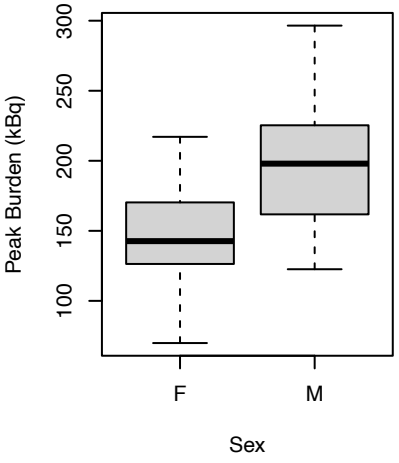
A


Peak Burden (kBq)
5
10
15
20
F
M
Sex

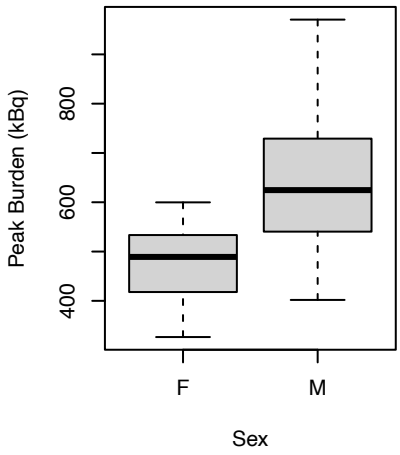
B


Peak Burden (kBq)
20
25
30
35
40
45
F
M
Sex

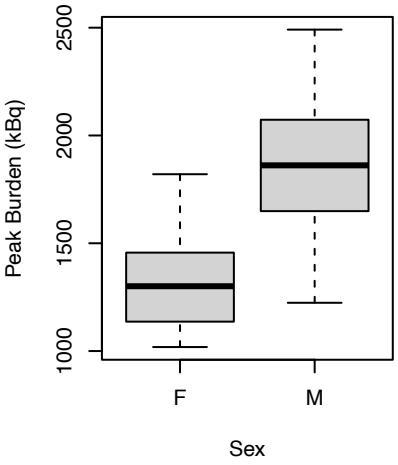
C


Peak Burden (kBq)
100
150
200
250
300
F
M
Sex

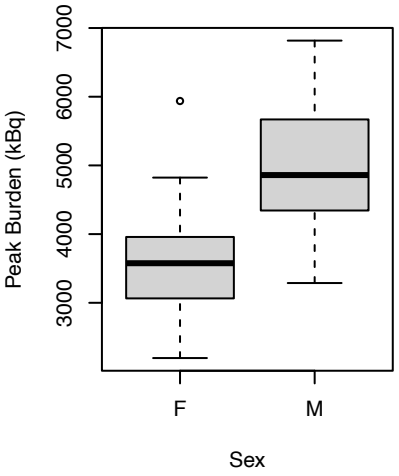
D


Peak Burden (kBq)
400
600
800
F
M
Sex

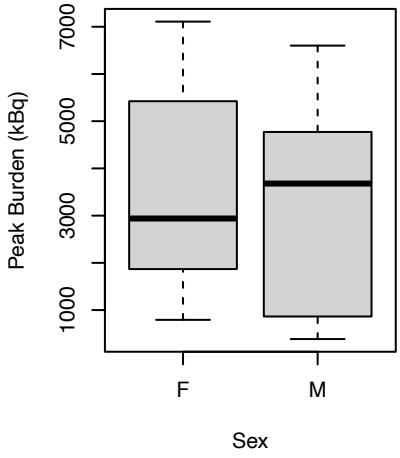
E


Peak Burden (kBq)
1000
1500
2000
2500
F
M
Sex

F


Peak Burden (kBq)
3000
4000
5000
6000
7000
F
M
Sex

G


Peak Burden (kBq)
1000
3000
5000
7000
F
M
Sex

Supplementary Figure 4. Boxplots comparing maximum measured burden of Sr-90 between sexes for each dose group. Wilcoxon rank sum p-values were calculated for the comparison for each dose group.

A. Maximum burden of Sr-90 boxplots by sex for the D05 dose group; n = 33 females, 37 males; p-value < 0.001.

B. Maximum burden of Sr-90 boxplots by sex for the D10 dose group; n = 18 females, 21 males; p-value < 0.001.

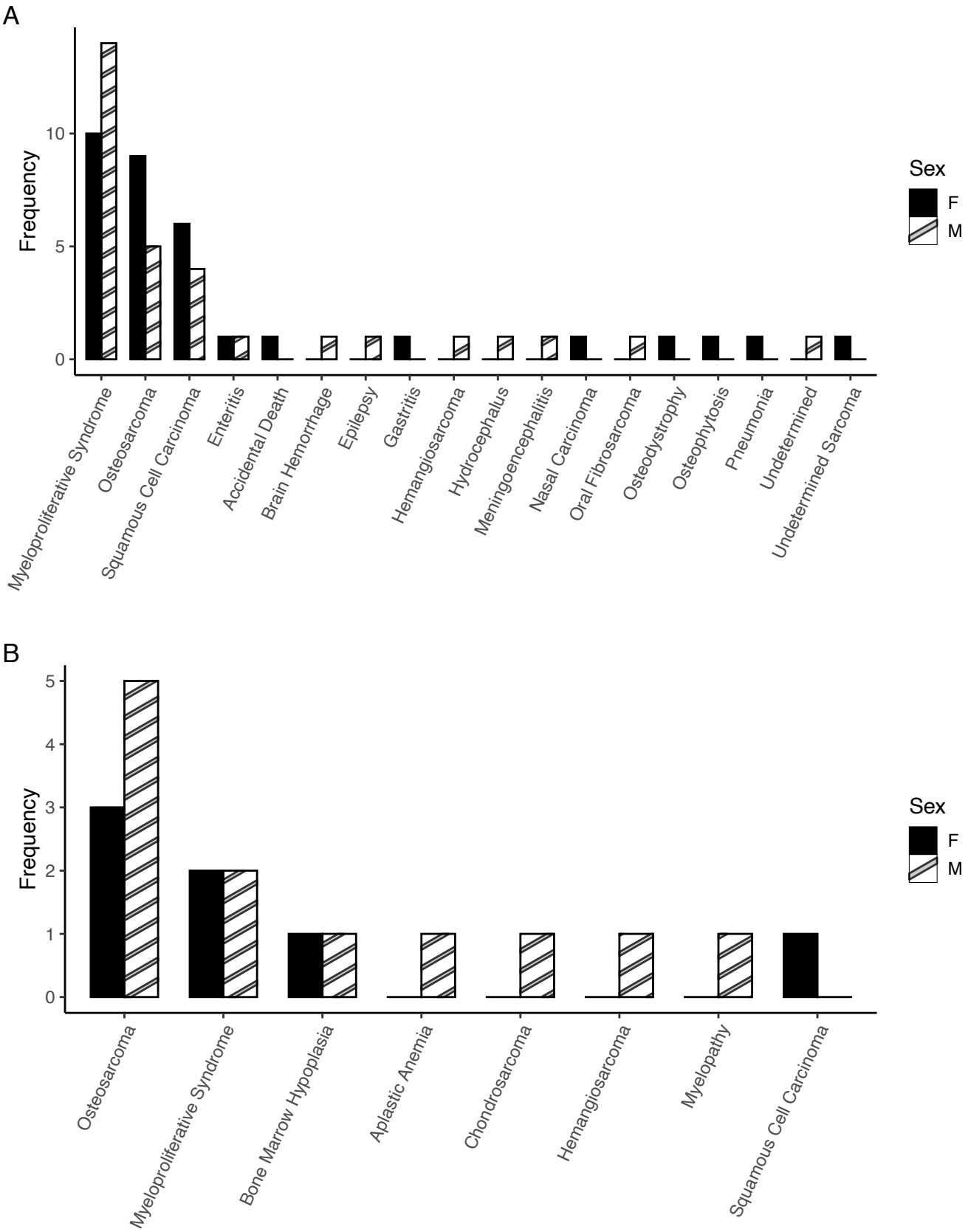
C. Maximum burden of Sr-90 boxplots by sex for the D20 dose group; n = 26 females, 32 males; p-value < 0.001.

D. Maximum burden of Sr-90 boxplots by sex for the D30 dose group; n = 25 females, 31 males; p-value < 0.001.

E. Maximum burden of Sr-90 boxplots by sex for the D40 dose group; n = 28 females, 26 males; p-value < 0.001.

F. Maximum burden of Sr-90 boxplots by sex for the D50 dose group; n = 29 females, 28 males; p-value < 0.001.

G. Maximum burden of Sr-90 boxplots by sex for the D60 dose group; n = 7 females, 11 males; p-value = 0.791.


A
Frequency
10
5
0
Myeloproliferative Syndrome
Osteosarcoma
Squamous Cell Carcinoma
Enteritis
Accidental Death
Brain Hemorrhage
Epilepsy
Gastritis
Hemangiosarcoma
Hydrocephalus
Meningoencephalitis
Nasal Carcinoma
Oral Fibrosarcoma
Osteodystrophy
Osteophytosis
Pneumonia
Undetermined
Undetermined Sarcoma
Sex
F
M
B
Frequency
5
4
3
2
1
0
Osteosarcoma
Myeloproliferative Syndrome
Bone Marrow Hypoplasia
Aplastic Anemia
Chondrosarcoma
Hemangiosarcoma
Myelopathy
Squamous Cell Carcinoma
Sex
F
M

Supplementary Figure 5. All causes of death for the D50 and D60 dose groups shown by sex.

A. All causes of death shown by sex for the D50 dose group; n = 30 females, 30 males. 64 cause of death diagnoses were made; three females and one male had two causes of death.

B. All causes of death shown by sex for the D60 dose group; n = 7 females and 12 males. 19 cause of death diagnoses were made; no animals had more than one cause of death.

Congestive Heart Failure: Binomal Proportion 95% Confidence Intervals			
	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	Dose Groups with Overlapping 95% Confidence Intervals
D00	0.051	0.133	D05, D10, D20, D30
D05	0.018	0.145	D00, D10, D20, D30
D10	0.020	0.220	D00, D05, D20, D30
D20	0.032	0.194	D00, D05, D10, D30
D30	0.022	0.173	D00, D05, D10, D20
D40	NA[a]	NA[a]	NA[a]
D50	NA[a]	NA[a]	NA[a]
D60	NA[a]	NA[a]	NA[a]

[a] Confidence intervals not calculated for dose groups with zero cases of congestive heart failure

Supplementary Table 5. Binomial proportion 95% confidence intervals for the frequencies of congestive heart failure as a cause of death across dose groups. Confidence intervals were not calculated for D40, D50 and D60, where no cases of congestive heart failure as a cause of death were observed.