GROWTH DYNAMICS OF
OSTEOSARCOMAS
IN BEAGLES

MASTER

RECEIVED BY DTIC MAR 24 1971

GARY BOYD THURMAN

Radiobiology Division
Anatomy Department
University of Utah-College of Medicine
Salt Lake City, Utah 84112
January 1971

SUPPORTED BY... NATIONAL INSTITUTES OF HEALTH FELLOWSHIP
(5-FOI-GM-38-740) and
RADIOBIOLOGY DIVISION... T.F. DOUGHERTY, Director
(CONTRACT No. AT (11-1)-119)

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

GROWTH DYNAMICS OF OSTEOSARCOMAS
IN BEAGLES

Radiobiology Division of the Department of Anatomy
University of Utah College of Medicine

Supported by

National Institutes of Health
National Institute of
General Medical Sciences
(5-F01-GM-38-740)

and Radiobiology Division
T. F. Dougherty, Director
Contract No. AT(11-1)-119

January 1971

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

Gary Boyd Thurman

DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED

phi

TABLE OF CONTENTS

	Page
ABSTRACT	iii
I. INTRODUCTION	1
II. LITERATURE REVIEW	3
A. Histocical Review of Radiation-induced Bone Sarcomas in Man and Dogs	3
B. Tumor Growth Models	8
1. Introduction	8
2. Exponential Growth Model	11
3. Linear Growth Model	13
4. Gompertzian Growth Model	14
5. Summary	18
III. MATERIALS AND METHODS	20
A. Introduction	20
B. Experimental Methodology	20
C. Tumor Measurement	22
D. Tumor Volume Calculation	25
E. Growth Rate Calculation	26
F. Tumor Starting Time Estimation	29
G. Oncogenic Skeletal Dose Calculation	29
IV. RESULTS	30
A. Growth Model	30
B. Relative Tumor Calcification	30
C. Tumor Growth Parameters	30
D. Starting Times and Skeletal Doses	31
E. Skeletal Distribution of Osteosarcomas	32
F. Parameter Relationships for ^{226}Ra , ^{239}Pu , ^{228}Ra , and ^{228}Th Tumors	32
V. DISCUSSION	72
A. Growth Model	72
B. Relative Tumor Calcification	73
C. Tumor Growth Parameters	73
D. Starting Times and Skeletal Doses	74
E. Skeletal Distribution of Osteosarcomas	76
F. Parameter Relationships for ^{226}Ra , ^{239}Pu , ^{228}Ra and ^{228}Th	77
VI. SUMMARY AND CONCLUSIONS	79
REFERENCES	80
APPENDIX	85
Legend	85
"A" Tumors	87
"B" Tumors	96
"C" Tumors	103

ABSTRACT

This study presents an analysis of the growth dynamics, oncogenic skeletal doses and skeletal locations of radiation-induced osteosarcomas in Beagles at the University of Utah, Division of Radiobiology as of March, 1970. Two hundred and fifty-six well-documented osteosarcomas have been induced in 201 Beagles, each receiving a single intravenous injection of ^{226}Ra (80 tumors), ^{239}Pu (64 tumors), ^{228}Ra (43 tumors), ^{228}Th (56 tumors), ^{90}Sr (8 tumors) or ^{224}Ra (5 tumors). Radiographs of each osteosarcoma were taken during the period of the tumor's growth. The growth dynamics of these osteosarcoma were estimated by measuring the tumor dimensions on as many radiographs as possible. It was clearly evident that the tumor volumes were increasing exponentially with time. Exponential growth constants were calculated for 249 tumors, the corresponding volume doubling times ranged from 4.7 to 60.3 days and averaged 12.4 days. Using individual exponential growth constants, a starting time for each tumor was estimated as the time when the extrapolated tumor's growth curve reached the volume of one cell 10μ ($\mu = 10^{-4}\text{cm}$) in diameter. The accumulated average skeletal dose during the time from injection to tumor starting time was calculated for each tumor and called the oncogenic skeletal dose. It was found that the larger the amount of radionuclide injected, the larger the oncogenic skeletal dose. High incidences of radiation-induced osteosarcomas in the

Beagles were noted in vertebrae, pelvic bones, humerii, femora and tibiae. Radiation-induced osteosarcomas of the vertebrae and pelvic bones had much higher incidences than the corresponding incidences of naturally-occurring osteosarcomas in dogs. (51 references).

I. INTRODUCTION

Soon after the discovery of ionizing radiation, its biological effects began to be observed and studied. It soon became obvious to some that radiation exposure constituted a serious health hazard. However, because of the painless nature of exposure to ionizing radiation, there was (and still is) a tendency to disregard its possible deleterious effects. Only unfortunate experiences could adequately convey the message of the perils involved with radiation exposure. Ingestion of long-lived radionuclides that deposit in the body proved to be especially dangerous because of incessant radiation to body parts.

In modern times, common use of radionuclides in medicine, research, industry and defense makes it imperative to know the biological effects these radionuclides could cause in man.

This paper presents a study of bone tumors (osteosarcomas) induced in Beagles by an intravenous (i.v.) injection of one of six radionuclides: ^{226}Ra (radium), ^{239}Pu (plutonium), ^{228}Ra (mesothorium), ^{228}Th (radiothorium), ^{90}Sr (strontium) or ^{224}Ra (quickradium).

Of main interest to this study are:

1. Determining the osteosarcomas' growth rates through measurements from serial radiographs.
2. Estimating the tumor starting times.
3. Determining the skeletal dose at the estimated tumor starting times.

4. Determining if the tumor growth rates are dependent on factors such as calcification, oncogenic dose, or sex.

5. Determining if some skeletal locations are inherently more susceptible to radiation-induced osteosarcomas.

II. LITERATURE REVIEW

A. Historical Review of Radiation-induced Bone Sarcomas in Man and Dogs

With the advent of the "Atomic Age," it has become important to determine the interaction of radiation in biological systems, especially in man. Furth and Lorenz (1) state that their study of the literature showed that most internal tumors in man exposed to either X-radiation or radioactive substances arose in bone. This has also been true for Beagles at the University of Utah where the vast majority of the radiation-induced tumors were osteosarcomas (2).

The development of a malignant tumor in a normal bone that had been exposed to heavy doses of X or γ radiation was first described by Beck in 1922 (3); and in 1945, Hatcher (4) could collect 24 such cases from the literature. In 18 of the cases, the irradiation was given for chronic joint infection. In three cases, the bone sarcoma followed irradiation given for treatment of other tumors. In 23 of the 24 cases a large amount of radiation was administered in fractional doses over a long period. The median interval between irradiation and recognition of sarcoma was 6 years; the shortest interval was 3 years; the longest, 11 years.

Auerbach et al. (5) reported in 1951, a case of an extra-skeletal osteosarcoma originating in soft tissues of the back. This tumor arose directly beneath the skin in an area that had

received a skin dose of 4000R of X-radiation delivered in 10 exposures over a period of 70 days. The latent period of the tumor was about 4 years.

The characteristic sequences of changes in bone following irradiation and preceding the carcinogenic transformation has been described by Ewing (6) who named this change "radiation osteitis." This is essentially a degenerative change with necrosis and atypical new bone formation. Koletsky, Bonte, and Friedell (7) reviewed radiation effects on bone in a work published in 1950.

An industrial hazard in the early 1900s has added to our knowledge of the effects of internal emitters on bone. Radium dial painters of this period "tipped" their brushes in the mouth and thereby ingested some of the radioactive paint containing radium and mesothorium. This material, ingested over a period of months to years, deposited in the bones, causing severe anemia and bone tumors. Death with bone tumors occurred for some dial painters within 6 years after ingestion started. The bone changes were first noticed by a dentist named Blum when he observed deterioration of the jaw (so-called "phossy jaw") in some of his patients. Martland (8,9,10) was one of the early investigators and reported the transition from radiation osteitis to malignant growth such as primary bone tumors. Martland's observations give impetus to the study of experimental induction of bone tumors by radionuclides and to practices that protect handlers and users of radionuclides.

The study of a group of radium dial painters has been

continued by Evans and his co-workers (11,12,13,14,15,16). Some of their conclusions are:

1. When the cumulative skeletal dose in rads decreases, the tumor appearance time for the sarcomas and carcinomas associated with skeletal deposits of radium or mesothorium appears to increase. This leads to the identification of a "practical threshold" of dosage, below which the required tumor appearance time may generally exceed the life span and hence radiation-induced tumors appear with negligible frequency.

2. The fraction of persons with malignant tumors arising from skeletal radium and mesothorium was roughly the same in their series for all dosage levels from 1200 to 50,000 rads skeletal average dose, and is about 30-40%.

3. No tumors have been seen so far in persons having a skeletal average dose at death under 1200 rads.

4. Approximately $2/3$ of the radiation-induced tumors are bone sarcomas.

5. "Everything is more complicated than most people think." (16)

Various others have also studied radium in man (17,18) and studies have been expanded to include the biological effect of numerous other radionuclides. References to recent publications reviewing this area are cited for general interest (19,20,21).

The study of osteosarcomas in dogs was of interest only to veterinarians until dogs came into use as experimental animals in radionuclide studies. Spontaneous osteosarcomas in dogs predominately appear in the giant breeds (22). Beagles, and probably

other small breeds of dogs as well, have a low natural frequency of osteosarcomas (23). In 1962, Dougherty (24) gave an interim report on the incidence of bone cancers in dogs injected with Radium-226, Plutonium-239, Radium-228 (MsTh), Thorium-228 or Strontium-90 at the University of Utah Radiobiology Lab. Of the dogs that had died at that time, approximately 70% of them had developed a radiation-induced osteosarcoma.

Mays (25) reported on the same project in 1967 and at that time 64% of the injected Beagles that had died had developed osteosarcomas. (This percentage will go lower with time because the high level dogs are dead and the lower level dogs are beginning to die of causes other than osteosarcoma.) Mays also calculated osteosarcoma RBE for the five radionuclides based on the average skeletal doses in rads one year before death. His results relative to $^{226}\text{Ra} = 1$ are: $^{239}\text{Pu} = 6$; ^{228}Ra (MsTh) = 2.5; and $^{90}\text{Sr} = 0.07$ to 0.24 ; at 8 years after radionuclide injection. Mays mentioned his preliminary study on osteosarcoma growth rates indicated a tendency for slower tumor enlargement in the lower level Beagles and expressed a desire to quantify the effect of radiation dose-rate during the growth period with the rate of tumor enlargement. As evidence for this possibility Mays cites Miriam Finkel and her co-workers (26) who injected mice with ^{90}Y , which quickly decayed out because of its short half-period. The induced bone tumors from pure ^{90}Y grew much more slowly than those in mice injected with ^{90}Sr , in which the dose-rates (primarily from the supported daughter ^{90}Y) continued throughout life.

Many of the radioactive by-products of nuclear explosions deposit in bone when ingested by man or animals. Therefore, the study of radiation-induced osteosarcomas is well justified; for if man is ever foolish enough to venture into an atomic war, the ecological distribution of bone-seeking radionuclides might make osteosarcomas one of the predominate types of malignancies in man and beast.

B. Tumor Growth Models

1. Introduction

The growth dynamics of tumors have been studied for many years and various different approaches have been used. Out of the studies three main models have emerged: exponential growth, linear growth and Gompertzian growth.

a. The exponential model assumes that the tumor volume enlarges exponentially with time, Eq.

(A), and that the rate of change of the volume with time, $\frac{dV}{dt}$, is proportional to the volume, Eq. (B).

$$V = V_0 e^{bt} \quad (A)$$

$$\frac{dV}{dt} = b V_0 e^{bt} = bV \quad (B)$$

V = tumor volume at time t

V_0 = initial tumor volume

b = exponential growth constant

t = time

Fig. 1. Exponential tumor growth model
Note that "Y" axis is a log scale.

- b. The linear model assumes that the tumor diameter increases linearly with time, Eq. (C), or that the cube root of the product of the three tumor diameters increase linearly with time, Eq. (D).¹

$$D = kt \quad (C)$$

$$\sqrt[3]{w \times l \times h} = D = kt \quad (D)$$

$$V = \frac{\pi}{6} D^3 = \frac{\pi}{6} k^3 t^3 \quad (E)$$

$$\frac{dV}{dt} = \left(\frac{\pi}{2}\right) k^3 t^2 = \frac{3V}{t} \quad (F)$$

D = mean tumor diameter

k = constant

t = time

w = width

l = length

h = height

V = tumor volume

Fig. 2. Linear tumor growth model.

¹For ascites tumors the cube root of the total number of tumor cells is the linear parameter.

The rate at which the tumor enlarges, $\frac{dV}{dt}$, is proportional to the volume but also is inversely proportional to the time, Eq. (F). The tumor does not have a limiting volume, but continues to enlarge until it causes death to the host.

- c. According to the Gompertzian model of growth, the tumor's volume increases according to the equations:

$$V = V_0 e^{\frac{A}{\alpha} (1 - e^{-\alpha t})} \quad (G)$$

$$\frac{dV}{dt} = AV e^{-\alpha t} \quad (H)$$

$$V_{max} = V_0 e^{\frac{A}{\alpha}} \quad (I)$$

V = tumor volume at time = t

V_0 = initial tumor volume at $t = 0$.

A = a constant related to the initial slope

α = retarding constant

t = time

V_{max} = theoretical maximum tumor volume

Fig. 3. Gompertzian tumor growth model.
"Y" axis is logarithmic.

The rate at which the volume increases is proportional to the product of the volume and a term exponentially decaying with time, Eq. (H).

The maximum volume the tumor can reach is a function of the initial tumor volume and the constants "A" and "α".

2. Exponential Growth Model

Willis defines cancer as a change in a cell which allows it to become independent of the homeostatic mechanisms of the body that control cellular proliferation (27). If this is the case, that transformed cell would proliferate at its own rate, giving rise to the geometrical progression of binary fission (28). A limitation on this model is that the host must be able to supply nutrients to all the tumor cells rapidly enough for the tumor to maintain its exponential growth.

Collins, Loeffler and Tivey (29) formulated this theory from experience with certain human tumors and point out that a specific exponential growth constant seems to be characteristic of an individual tumor. The exponential growth constant can easily be visualized by plotting tumor volume vs. time on semi-log paper, as in Fig. 4. The slope of that straight line is the exponential growth constant and leads to the calculation of a doubling time.

$$\text{Doubling Time} = \frac{\ln 2}{\text{Exponential Growth Constant}} \quad (J)$$

Fig. 4. Growth of pulmonary metastasis of case no. 20 from Fig. 4 of Collins, Loeffler and Tivey (29).

The volume doubling time represents the length of time needed for the tumor to double its volume, and the doubling time remains constant as long as the tumor is undergoing exponential growth. Collins and his associates give doubling times ranging from 11 days to 164 days for lung metastases in 24 types of tumors in humans.

Brues, Weinger and Andervont (31) assumed a constant doubling time in their study of the relation between latent period and growth rates in chemically-induced tumors in mice. They calculated the growth rates of their tumors with two methods: (a) by assuming the hourly increase in tumor volume is proportional to the number of cells in mitosis, and (b) by serially measuring the tumor's diameters with calipers, in vivo. Then they calculate by both methods the time required for a single cell 10^{-9} cm³ to reach a volume of 0.1 cm³. Although many questions were left

unanswered, they did find a high degree of correlation of the observed latent period and their calculated latent period using the exponential growth model.

3. Linear Growth Model

During his research on the effect of X-irradiation on the growth of the Jensen rat sarcoma, Mayneord (32) found that the major diameter of the untreated tumors (controls) increased linearly with time, Fig. 5.

Fig. 5. Linear growth of Jensen's rat sarcoma, from Fig. 1. of Mayneord (32).

Mayneord goes on to show how this can be mathematically explained if only a thin layer of cells near the surface of the tumor are in active division. This could indeed be the case with solid tumors whose centers were necrotic.

Schrek (33) used the cube root of the product of the three diameters of the subcutaneously transplanted Walker tumor and called this the mean diameter of the tumor, Eq. (D). He showed that the mean diameter gave as good a straight line as Mayneord's

measurement of the major diameter, but that the mean diameter was much better physically justified for use as a parameter of growth. Schrek also demonstrated the obvious correlation that the latent period increases as the amount of implanted tumor tissue decreases. He checked to see if the growth rate (mm/day of the mean diameter) was dependent upon the volume of the implant and found that it was not.

Klein and Révész (34) studied the growth of two ascites tumors and found that the cube root of the free tumor cell number increases linearly with the time after implant during the major part of the tumor's growth. During the terminal part of the tumor's growth, cell multiplication slowed down considerably, or stopped, when an optimum number of free tumor cells was attained. A problem with this work was that about 100 hours after implant, infiltration by the tumor cells into the intra-abdominal tissues of the host were demonstrable, and these cells were not included in the count of total tumor cells. With an ascites tumor in mice, Siegler and Koprowska (35) found that the tumor cells proliferated mainly in the mesentery and retroperitoneal organs and then exfoliated into the peritoneal fluid.

4. Gompertzian Growth Model

The Gompertz equation was not derived to fit tumor growth. It was first presented in 1825 when Benjamin Gompertz published a paper, "On the Nature of the Function Expressive of the Law of Human Mortality" (36). Wright (37), in 1926, appears to have first suggested the use of the Gompertz curve for representing

biological growth, and Casey (38) used the Gompertz equation to fit tumor growth in a paper published in 1934.

The major support of the theory of Gompertzian tumor growth was work done by Laird (39) in which she collected much of the data on tumor growth that had been reported in the literature up to 1964. To each of the sets of data she fit the equation:

$$V = V_0 e^{\frac{A}{\alpha} (1 - e^{-\alpha t})} \quad (G)$$

where:

V = tumor volume at time t

V_0 = initial tumor volume

A = constant related to initial slope of curve

α = retarding constant

t = time

Listed in her paper (39) are values for V_0 , A , α and the theoretical upper limit (V_{max}) for 19 examples of tumors in mice, rats and rabbits, representing 12 different types of tumors. Most of these 19 examples were work done with transplanted tumors and V_0 has meaning as the initial effective growth mass of the tumor. However, what meaning V_0 has for primary tumors, spontaneous or induced, is not elucidate in Laird's paper.

Of special interest in the Laird paper (39) is the work done on ^{90}Sr -induced osteosarcomas in mice from the data of Finkel, Bergstrand and Biskis (40). In analyzing the growth for these radiation-induced osteosarcomas, Laird obtained the following constants: $A = 1.02 \pm 0.115 \text{ weeks}^{-1}$, $\alpha = 0.159 \pm 0.026 \text{ weeks}^{-1}$, $V_0 = 0.01 \text{ cm}^3$, $V_{max} = 6.03 \text{ cm}^3$.

Fig. 6. Gompertzian growth of ^{90}Sr -induced osteosarcomas in mice. Plots of Laird's curve (39) — and the data of Finkel, Bergstrand and Biskis (40) ○ ○ ○.

Referring to the Finkel paper (40) shows that the fit of the curve to the data leaves something to be desired.² For example, 203 measurements were made on tumors having an av. initial volume of 0.0055 cm^3 , whereas the Laird analysis estimates the initial tumor size, (V_0) to be 0.01 cm^3 . Laird defends this by stating that V_0 is only a suggested value and not really important to the essential parameters, A and α . However, Finkel's osteosarcomas

²A check of Laird's (39) calculations of the theoretical upper limits (V_{max} , Eq. (I), pg. 10) for her 19 tumor examples showed disagreement from the values obtained using her listed values for A , α and initial tumor volume, weight or cell number.

were primary tumors and not transplanted tumors. If one sets $V_0 = 5.2 \times 10^{-10} \text{ cm}^3$, (one 10μ cell) then $A = 3.68 \text{ weeks}^{-1}$, not 1.02 weeks^{-1} , if α and V_{max} remain the same. This shows that A depends on what is defined as V_0 . Laird (39) says that the ratio $\frac{A}{\alpha}$ is remarkably similar in spite of the differences in the individual values for A and α . This may be an artifact of her calculations because of her varying V_0 for different tumors. The ratio $\frac{A}{\alpha}$ is not a constant for any Gompertz curve, but changes when V_0 is changed.

In a later work Laird (41) extrapolated her Gompertzian curves back to values for one cell. In this paper she alleged that any Gompertz curve can be considered to begin ($t = 0$) as a simple exponential process. Then she followed the Gompertz curves back from $t = 0$, $V = V_0$, to a negative time when $V = \text{one cell}$. A plot of one of these curves, Fig. 7, shows that the Gompertz is continually being retarded no matter where it is examined, or where the axes are placed. However, any small segment of the Gompertz resembles exponential growth.

Laird (41) also states that the Gompertzian retardation of growth is not a fortuitous result of the failure of the dying host to afford nutritional support to tumor growth, but is a characteristic property of the growth of tumors in the animal host.

Summers (42) reaches the opposite conclusion, that the tumor growth is limited by the total flux of metabolites across the vascular surface. However, the vascular flux model of Summer's has not explained the wide range of V_{max} for various tumor types

Fig. 7. Laird's Gompertz curve (39) for the mouse osteosarcoma data of Finkel, Bergstrand and Biskis (40) extrapolated backwards in time to the size of one cell. Note continual retardation.

shown in Laird's paper (39).

McCredie et al. (43) also discusses Gompertzian tumor growth in their paper, "The Rate of Tumor Growth in Animals." The title of the paper is very misleading and in my estimation should have been, "The Rate of Growth of Four Selected Transplantable Tumors in Mice and Rats." McCredie and his associates try to interpret their results as applicable to all tumors. No justification was given for applying results from subcutaneously transplanted tumors in mice and rats to primary tumors in any host, even humans.

5. Summary

Each tumor growth model has its proponents and supporting data. However, they are by no means exclusive of each other and there is probably no model that will fit the tumor growth dynamics of all tumors. The results of a tumor growth experiment on pri-

mary tumors may depend on many factors such as what parameters of the tumor are measured (physical or radiographic diameters, volume, cell number, weight, etc.), the tumor type, the amount of dedifferentiation of the tumor cell type, the anatomical site of growth, etc.

It is of most interest to do serial measurements on primary tumors in vivo. Studies on transplanted tumors are the most convenient and yield the best results but there is difficulty applying the results to the growth of primary tumors. This is because of the changes that take place in a primary tumor upon transplantation. It usually takes two or more transplant generations to stabilize the tumor in its growth patterns and to give reproducible results (44). It is unfortunate that most of the tumor growth experiments reported in the literature were done with transplanted tumors and not primary tumors.

III. MATERIALS AND METHODS

A. Introduction

This study is a small portion of a long-term project at the University of Utah to study the effects of selected radionuclides on biological systems. The objectives of the project and its materials and methods are reported in detail elsewhere (45) and will not be reiterated here. Only the details of the project pertinent to this study are reported below.

B. Experimental Methodology

Beagles were chosen as the experimental animal in this project for three main reasons: 1. advantageous size and disposition, 2. skeletal similarity to humans, and 3. low natural incidence of osteosarcomas (23). Because of the third reason it can be assumed that all or virtually all of the osteosarcomas observed in these Beagles injected with radionuclides are radiation-induced tumors (25).

Dogs are put into the toxicity study at graded injection levels. At each level, half the dogs are male and half female. Litter mates are used whenever possible. Each animal receives the designated dose of one radionuclide in a single i.v. injection. The animals are injected at approximately 17 months of age. At this age the skeleton is mature with all epiphyses fused except those of the ribs. Twelve such groups have been injected for each of the five radionuclides, ^{226}Ra , ^{239}Pu , ^{228}Th , ^{228}Ra , and ^{90}Sr .

The five injection levels designated by integers are those specified at the early meetings of the consultants, and those designated by nonintegers have been added by the laboratory staff. Since those injection levels were originally specified in "retained" activities, the actual injections are four times the desired "retained" levels of ^{226}Ra , ^{228}Ra (Mesothorium), and ^{90}Sr , and 1.11 times the desired "retained" levels of ^{239}Pu and ^{228}Th (Radiothorium). The desired "retained" activities are the same for all the radionuclides except ^{90}Sr , in which case they are greater by a factor of 10. Injection level 1 is the basis of the scheme, and is 10 times the maximum permissible concentration of ^{226}Ra in man. Level 1 = $\frac{0.1 \mu\text{Ci } ^{226}\text{Ra}}{70 \text{ kg man}} = 0.0143$ "retained" $\mu\text{Ci/kg}$. All other injection levels are simple multiples of level 1 as shown below.

Level 1.5 is 2 times level 1

Level 1.7 is 3 times level 1

Level 2 is 6 times level 1

Level 3 is 18 times level 1

Level 4 is 54 times level 1

Level 4.5 is 94 times level 1

Level 5 is 162 times level 1

The numbering system for the dogs has been built around the injection program and serves as a code to describe each dog's place in the experiment. The first letter tells the sex of toxicity animals (M = male, F = female). When the first letter is T, the dog is a test animal. M, F, or T is followed by a num-

ber which denotes chronological order of groups in the case of toxicity dogs and of individual test dogs.

Next comes a code letter for the radionuclide: R = ^{226}Ra
P = ^{239}Pu , M = ^{228}Ra , T = ^{228}Th , S = ^{90}Sr and Q = ^{224}Ra . The last number designates the injection level.

Example: M1R5 is a male animal in the first Radium-226 group at the highest injection level.

"A" following the regular dog number means that the dog is a replacement.³ "H" following the regular dog number means that the dog received its dose in more than one injection.

Although M1R5, M1R4, M1R3, M1R2, and M1R1 constitute a group and were injected at the same time, the tables are arranged according to injection level to facilitate comparison of all the R5 animals, all the R4 animals, etc. (2).

C. Tumor Measurement

Each beagle in the colony received standardized radiographic examinations at regular time intervals. Whenever a bone lesion was observed radiographically, the interval between radiographic examinations was shortened. If the lesion showed the typical radiographic appearance of an osteosarcoma, radiographic examinations were made at intervals varying from 5 to 40 days. Because of this procedure, sets of serial radiographs were available for almost all of the osteosarcomas that occurred in the colony. An

³Designation of individual tumors for multi-tumor dogs are in parentheses following the code name and are not to be confused with the replacement dogs. For example, M6S5A(A1) is a replacement dog that had more than one tumor. An "A" in parentheses just means that that tumor has been classified as an "A" tumor. See page 23.

example of such a set is shown in Fig. 8, page 24, which illustrates the radiographic appearance of osteosarcoma growth in dog F8R5.

Two-dimensional measurements of the tumor were made from the serial radiographs. Each set of two-dimensional measurements was treated as the major and minor axes of an ellipsoid of revolution and the calculated volume of the ellipsoid assigned as the tumor's volume. In some cases, a second radiographic view of the tumor was available and in these cases three diameters were measured and used in calculating the volume corresponding to the tumor.

At the time the radiographic dimensions were measured, the tumors were classified as either "A", "B", or "C". "A" tumors have three or more sets of well-defined measurements over a period greater than 15 days. "B" tumors have two sets of well-defined measurements and may have more sets of measurements that were considered poorly defined. "C" tumors have only one set of well-defined measurements, usually on the excised tumor at autopsy.

If the tumor was visible radiographically but not measurable, it was recorded as a "?". When the tumor did not appear on the x-ray film, it was recorded as "Not Visible" (N.V.). The only measurements used in calculating volumes were those measurements on tumors which had broken through the cortex of the bone.

An approximate measurement of the calcification of the tumor was made by judging the radio-opacity of the tumor in vivo. using a scale of 0.0 to 1.0. Zero represents the radio-opacity of soft tissue and 1.0 represents the radio-opacity of cortical bone.

Fig. 8. Photographic reproduction of serial radiographs of an osteosarcoma that developed on the distal right ulna of Beagle F8R5.

The tabulation of this data is found in Appendix I.

D. Tumor Volume Calculation

The tumors were assumed to approximate the shape of an ellipsoid of revolution that revolves about its major axis. From the measurements of the major and minor axes, the volume was calculated by Eq. (K).

$$V = \frac{\pi}{6} c^2 d \quad (K)$$

where:

V = volume

c = minor axis of ellipsoid

d = major axis of ellipsoid

The major axis was chosen to be that dimension of the tumor parallel to the bone or the bone group and in most cases was the largest tumor diameter. The minor axis was measured perpendicular to the major axis. The radiographic measurement of the tumor diameters was made to include the full dimensions of the tumor and was not made just over the calcified portion.

Tumors which yielded three-dimensional measurements allowed a check on the assumption that the third dimension of the tumor was more closely correlated to the minor axis than to the major axis. The assumption proved valid. When it was possible to measure all three dimensions of a tumor on all sets of measurements, then the tumor volumes were calculated using Eq. (L).

$$V = \frac{\pi}{6} c_1 c_2 d \quad (L)$$

where:

V = volume

c_1 and c_2 = two minor axes

d = major axis

For most tumors it was possible to measure all three dimensions of the excised tumor at autopsy and Eq. (L) was used to calculate this volume.

E. Growth Rate Calculation

1. "Fitted Slopes"

Plots of the volumes of the "A" tumors on semi-log paper, pages 33 to 40, made it apparent that the majority of the tumors showed exponential growth. Least-squares straight line fits were made to these points, and the regression coefficient (slope of the line) was calculated and called the "Exponential Growth Constant."

$$\text{Exponential Growth Constant} = \frac{\sum X_i Y_i - \frac{(\sum X_i)(\sum Y_i)}{n}}{\sum X_i^2 - \frac{(\sum X_i)^2}{n}} \quad (M)$$

where: X_i = days post injection

Y_i = natural log of tumor volume

This method of calculating exponential growth constants was used for the "A" and "B" tumors, and the exponential growth constants obtained this way were labeled "Fitted Slopes" in the tabulation of the parameters of growth, Tables 2 and 3.

The advantages of this method are that it uses the most data and that the determined volumes are fairly accurate. The disadvantages are that the measurements are only able to be made during a relatively short period of the tumor's existence and that this calculation could be made for only about one-third of the tumors.

2. "Constructed Slopes"

Referral to the raw data in Appendix I shows that when the tumor is radiographically visible but the diameters are not accurately measurable, it is indicated by a "?". When there is no radiographic evidence of the tumor's presence, it is indicated by a "N.V." meaning "Non-visible." By taking an average of the days post injection of the "N.V." reading and days post injection of the "?" reading closest to the "N.V." reading, an estimate was obtained of the days post injection when the tumor was at the limit of radiographic detection.

The smallest tumor diameter measured on the radiographs was 0.1 cm (M7R4 and F3R4A). From this fact it was assumed that the limit of radiographic detection for these tumors was a sphere 0.1 cm in diameter ($5.2 \times 10^{-4} \text{ cm}^3$ volume). Spratt (47) uses 0.3 cm as his "Limit of Roentgenographic Distinction (99%)" for lung metastases of human skeletal sarcomas. However, the Beagle radiographs were read backwards in time, starting with the autopsy radiographs. Thus, the tumor was followed from its largest dimensions down to its smallest dimensions. This procedure gives "hindsight" and it was known exactly where to look on the radiograph for indications of the tumor's presence. This was felt to justify a limit of radiographic detection smaller than that used by Spratt.

From reading the x-ray films it was known what day the tumor was first visible on the radiograph (tumor volume greater than $5.2 \times 10^{-4} \text{ cm}^3$) and what day the tumor was not visible on the

radiograph (tumor volume less than $5.2 \times 10^{-4} \text{ cm}^3$). The average of these two days was used to construct the point in time when the tumor's volume was approximately $5.2 \times 10^{-4} \text{ cm}^3$. In a few instances the tumor was very small but still visible on the radiograph. If the average tumor diameter was less than 0.2 cm, the date of that radiograph was used for the constructed point.

Using the constructed point and the terminal tumor volume at the autopsy date, an exponential growth line (semi-log plot) was constructed, Fig. 9. The exponential growth constant was obtained by calculating the slope of the constructed line. Exponential growth constants calculated in this manner are called "Constructed Slopes" in the tabulation of the parameters of growth. Tables 2, 3, and 4.

Fig. 9. Illustrative example of method used in determining "Constructed Slopes." "V." is the earliest date the tumor was radiographically visible, and "N.V." is the latest date the tumor was not visible on the radiographs. "R.D. Limit" is the limit of radiographic detection for this study and equals $5.2 \times 10^{-4} \text{ cm}^3$.

An advantage of this method is that it is possible to calculate constructed slopes for 248 out of 256 tumors. It also has the advantage of using the largest and most accurately known volume plus the widest span of time. The obvious disadvantage is that one of the points determining the line is not precisely known, but has to be estimated from two other points.

F. Tumor Starting Time Estimation

The volume of each individual tumor was extrapolated backwards in time until it was equivalent to a 10μ spherical cell (volume = $0.5 \times 10^{-9} \text{ cm}^3$). This was taken as an estimate of the tumor starting time.

For the "A" and "B" tumors, starting times were calculated using both the fitted slope and the constructed slope and the average of the two was used in the dosage calculations. These are tabulated in Table 6 as "Fitted T_0 ", "Constructed T_0 " and "Average T_0 ". "C" tumors only have a "Constructed T_0 ".

G. Oncogenic Skeletal Dose Calculation

Using the well documented methods developed by Lloyd et al. (48), of calculating the average skeletal dose from injected radionuclides, the skeletal dose to the estimated tumor starting time was calculated and listed in Table 6.

IV. RESULTS

A. Growth Model

For osteosarcomas induced in Beagles by bone-seeking radio-nuclides, the exponential model of tumor growth seems generally to fit the data best. Neither the Gompertzian model nor the linear model can account for the growth curves of the "A" tumors shown in Fig.10. The exponential growth model represents their measured growth very well. For this reason, all of the tumors were considered to be growing exponentially.

B. Relative Tumor Calcification

The calcification of individual tumors are listed in Tables 2, 3 and 4, and also in Appendix I. Table 1 lists the average calcification of the 3 tumor groups.

Table 1. Average Calcification of Tumor Groups

<u>Group</u>	<u>Ave. Calcification^a ± S.D.</u>
"A" tumors	0.5 ± 0.2
"B" tumors	0.4 ± 0.2
"C" tumors	0.3 ± 0.2

^a1.0 = cortical bone, 0.0 = soft tissue

The distribution of the calcification measurements for the 3 tumor groups is shown in Fig.11, in the form of histograms.

C. Tumor Growth Parameters

Tables 2, 3 and 4 list the growth parameters of each individual tumor. The distributions of the slopes in the "A", "B" and

"C" tumors are shown in Fig. 12, Fig. 13 and Fig. 14. The average exponential growth constants (slopes) for the 3 tumor groupings is shown in Table 5.

Table 5. Average Growth Parameters

Group	Ave. Fitted Slope ($\pm$ S.D.)	Ave. Constructed Slope ($\pm$ S.D.)
"A" tumors	0.0458 $\pm$ 0.0201 days ⁻¹ (T ₂ = 15.1 days)	0.0525 $\pm$ 0.0213 days ⁻¹ (T ₂ = 13.2 days)
"B" tumors	0.0590 $\pm$ 0.0330 days ⁻¹ (T ₂ = 11.7 days)	0.0635 $\pm$ 0.0317 days ⁻¹ (T ₂ = 10.9 days)
"C" tumors	Unavailable	0.0586 $\pm$ 0.0245 days ⁻¹ (T ₂ = 11.8 days)

D. Starting Times and Skeletal Doses

Table 6 groups the "A", "B" and "C" tumors together and lists them according to the injected radionuclide and the level of injection. Included in Table 6 are the estimated tumor starting times and the accumulated skeletal dose to that time.

Table 7 summarizes the average oncogenic skeletal dose at the various injection levels and compares it with similar information that Mays et al. (49) calculated using the skeletal dose one year before autopsy for the Utah Beagles.

The average tumor duration time (the time from estimated starting time to autopsy) for the tumors was 487 days or 1.33 years.

E. Skeletal Distribution of Osteosarcomas

Table 8 summarizes the skeletal locations of the tumors for each radionuclide, and Table 9 lists the average tumor growth rate of tumors occurring on each skeletal bone group, the tumor incidence of each bone group and the fraction of the total skeleton each bone group represents (wet weight). Table 10 gives the osteosarcoma incidences for the skeletal bone groups of Beagles (radiation-induced osteosarcomas), dogs (naturally occurring osteosarcomas) and humans (naturally occurring osteosarcomas).

F. Parameter Relationships for ^{226}Ra , ^{239}Pu , ^{228}Ra and ^{228}Th Tumors

For each radionuclide, parameters were paired and statistically checked for significant correlation. The exponential growth constants were not significantly related to the following;

1. Relative calcifications, Fig. 15
2. The amount or type of radionuclide injected
3. The Beagle's sex
4. Days post injection to autopsy, Fig. 16
5. Terminal tumor volumes
6. Skeletal location of tumors

The oncogenic skeletal doses were highly correlated to the activity of radionuclide injected, see Fig. 17, Fig. 18, Fig. 19 and Fig. 20. The average oncogenic dose at each injection level was highly related to the activity of radionuclide injected. Plots of these data on a log-log scale closely approximated straight lines with positive slopes, Figures 21, 22, 23 and 24.

Figure 10

"A" tumors have 3 or more sets of well-defined measurements over a period greater than 15 days
 T_2 = Volume doubling time

Figure 10 (Cont.)

Figure 10 (Cont.)

GROWTH OF BEAGLE OSTEOSARCOMAS
"A" TUMORS

Figure 10 (Cont.)

GROWTH OF BEAGLE OSTEOSARCOMAS
"A" TUMORS

Figure 10 (Cont.)

GROWTH OF BEAGLE OSTEOSARCOMAS
"A" TUMORS

Figure 10 (Cont.)

Figure 10 (Cont.)

GROWTH OF BEAGLE OSTEOSARCOMAS
"A" TUMORS

Figure 10 (Cont.)

Table 2
Growth Parameters of Beagle Osteosarcomas - "A" Tumors

Dog	Location	Calc. ^a	Fitted Slope ^b	Const. Slope ^b	Ave. Slope ^b	Ave. D.T. ^c
M2R3	Mid. L. Radius	0.2	.0140	.0127	.0134	51.7
F12R3	Mid. L. Tibia	0.8	.0688	.0511	.0600	11.6
F6R4 (A1)	Prox. R. Humerus	0.4	.0379	.0633	.0506	13.7
F6R4 (A2)	Dist. R. Tibia	0.6	.0444	.0725	.0584	11.9
M7R4 (A1)	Prox. R. Tibia	0.6	.0279	.0256	.0268	25.9
M7R4 (A2)	Prox. L. Humerus	0.3	.0286	.0357	.0322	21.5
M2R5 (A1)	Prox. L. Tibia	0.3	.0728	.0631	.0680	10.2
F8R5	Dist. R. Ulna	0.7	.0805	.0826	.0816	8.5
F9R5 (A1)	Dist. R. Tibia	0.6	.0491	.0449	.0470	14.7
F9R5 (A2)	Dist. L. Tibia	0.4	.1089	.0927	.1008	6.9
M8P1	R. Ilium	0.3	.0589	.0767	.0678	10.2
M3P2	Prox. L. Femur	0.4	.0390	.0313	.0352	19.7
F9P2	Dist. R. Femur	0.5	.0417	.0448	.0432	16.0
M4P3 (A1)	Prox. L. Humerus	0.8	.0115	.0181	.0148	46.8
M3P4	L. 10th Rib	0.2	.0417	.0750	.0584	11.9
F5P4	3rd Lumbar Vert.	0.8	.0309	.0512	.0410	16.9
F9P4	Prox. L. Radius	0.9	.0413	.0545	.0479	14.5
M1P5	Prox. L. Femur	0.5	.0781	.0919	.0850	8.2
M4P5	Mid. R. Ulna	0.4	.0470	.0330	.0400	17.3
F5M1.7 (A1)	Mid. R. Femur	0.8	.0422	.0355	.0388	17.9
F1M2	Dist. R. Femur	0.2	.0476	.0374	.0425	16.3
M4M2	Prox. R. Humerus	0.6	.0327	.0482	.0404	17.2
F11T1.5	Prox. R. Humerus	0.2	.0165	.0216	.0190	36.5
M7T2 (A1)	R. 10th Rib	0.2	.0152	.0325	.0238	29.1
M1T3 (A1)	Dist. L. Femur	0.5	.0519	.0674	.0596	11.6
F6T3 (A1)	Prox. R. Femur	0.6	.0548	.0504	.0526	13.2
M5S4.5	Prox. L. Tibia	0.4	.0556	.0445	.0500	13.9
F1S5	Dist. R. Femur	0.3	.0632	.0861	.0746	9.3
M6S5A	L. 8th Rib	0.5	.0591	.0660	.0626	11.1
T1R5	Prox. R. Tibia	0.8	.0538	.0584	.0561	12.4
T18R5H	Dist. R. Humerus	0.4	.0333	.0514	.0424	16.3
T19R5H	R. Tibial Tarsal	0.6	.0557	.0431	.0494	14.0
T26R4H (A1)	Prox. R. Tibia	0.7	.0260	.0466	.0363	19.1
T27R4H (A1)	Dist. R. Tibia	0.6	.0574	.0417	.0496	14.0
T34R3	Dist. R. Femur	0.6	.0469	.0488	.0478	14.5
T38R4	Prox. L. Humerus	0.6	.0586	.1016	.0801	8.7
T70R3 (A1)	Prox. R. Tibia	0.4	.0398	.0431	.0414	16.7
T51P5 (A1)	Dist. R. Humerus	0.2	.0228	***	***	30.4
T2Q4 (A1)	R. Ilium	0.9	.0310	.0525	.0418	16.6
Ave.		0.51	.0458	.0525	.0488	
s.d.		0.21	.0201	.0213	.0195	

^a Calc. = Calcification

^b Slope = Exponential growth constant (days⁻¹), the slope of the growth curve on a semi-log plot.

^c D.T. = Doubling time (days), the time necessary for the tumor to double its volume.

Table 3

Growth Parameters of Beagle Osteosarcomas - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Fitted Slope</u>	<u>Const. Slope</u>	<u>Ave. Slope</u>	<u>Ave. D.T.</u>
M2R2	Dist. L. Femur	0.1	.0387	.0422	.0404	17.2
M5R3 (B1)	L. 4th Phalanx ^a	0.4	.0113	.0518	.0316	21.9
F3R4A (B1)	3rd Thor. Vert.	0.5	.0421	.0542	.0482	14.3
F3R4A (B2)	R. 3rd Metacarpal	0.2	.0859	.0417	.0638	10.9
M5R4	L. Zygomatic Arch	0.1	.0992	.0371	.0682	10.2
F6R4 (B1)	R. Ischium	0.6	.0576	.0510	.0543	12.8
F9R4 (B1)	R. Ischium	0.8	.0346	.0529	.0438	15.8
M2R5 (B1)	Dist. L. Femur	0.2	.0998	.0960	.0979	7.1
M5R5	Prox. L. Femur	0.2	.0457	.0468	.0462	15.0
F9R5 (B1)	Dist. L. Femur	0.2	.0350	.0361	.0356	19.5
F2P1.7	R. Ischium	0.3	.1045	.0449	.0747	9.3
F6P1.7	L. Ischium	0.8	.0321	.0475	.0398	17.4
M1P2	Prox. L. Humerus	0.8	.0413	.0359	.0386	18.0
F7P3	Prox. L. Femur	0.9	.0297	.0681	.0489	14.2
F1OP3	R. & L. Ischium	0.8	.0109	.0603	.0356	19.5
M1P4 (B1)	Prox. R. Humerus	0.4	.0385	.0548	.0466	14.9
F2P4 (B1)	Sacrum	0.9	.0440	.0508	.0474	14.6
M4P4	Prox. R. Femur	0.3	.0993	.1359	.1176	5.9
F6P5	R. Ischium	0.4	.0628	.0751	.0690	10.0
F7P5	Mid. L. Humerus	0.5	.0418	.0608	.0513	13.5
M6M1.7	Dist. R. Femur	0.2	.0864	.0625	.0744	9.3
F5M2	Prox. L. Ulna	0.2	.0444	.0473	.0458	15.1
M1OM2	L. 7th Rib	0.3	.0709	.0288	.0498	13.9
M4M3	L. Ilium	0.8	.0491	.0559	.0525	13.2
M12M3 (B1)	Mid. R. Humerus	0.4	.0384	.0247	.0316	21.9
F1M4	R. Olecranon	0.1	.1657	.0748	.1202	5.8
M2T1.5	Prox. R. Femur	0.4	.0628	.1019	.0824	8.4
M4T2A (B1)	Prox. R. Humerus	0.8	.0320	.0340	.0330	21.0
M5T2	L. 6th Rib	0.4	.0472	.0568	.0520	13.3
F12T2 (B1)	L. Mandible	0.7	.0219	.0370	.0294	23.6
F6T3 (B1)	Dist. R. Tibia	0.8	.0567	.0880	.0724	9.6
F9T3 (B1)	R. Mandible	0.2	.0314	.0566	.0440	15.8
M3S5	Prox. R. Tibia	0.2	.1183	.1200	.1192	5.8
F8S5	R. Ilium	0.5	.0446	.0783	.0614	11.3
T2OR5H	Dist. R. Humerus	0.4	.0387	.1131	.0759	9.1
T26R4H (B1)	Prox. L. Tibia	0.2	.0500	.0390	.0445	15.6
T32R3	Dist. L. Humerus	0.3	.0317	.0443	.0380	18.2
T33R3	R. Occipital Bone	0.7	.0917	.0806	.0862	8.0
T36R4	R. 6th Rib	0.3	.0839	.0414	.0626	11.1
T37R4	L. Parietal Bone	0.3	.1159	.1799	.1479	4.7
T8T3	R. Ilium	<u>0.4</u>	<u>.0833</u>	<u>.0952</u>	<u>.0892</u>	<u>7.8</u>
Ave.		0.44	.0590	.0635	.0613	
s.d.		0.25	.0330	.0317	.0278	

^aFront

Table 4

Growth Parameters of Beagle Osteosarcomas - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Const. Slope</u>	<u>D.T.</u>
M5R1.7	Cribiform Plate	0.2	.0490	14.1
M5R2	L. Maxilla	0.8	.0362	19.2
M7R2	L. Ischium	0.7	.0278	25.0
M10R2	Dist. R. Femur	0.2	.0385	18.0
F11R2	Prox. L. Femur	0.2	.0341	20.3
M1R3	Prox. R. Radius	0.2	.0480	14.4
F3R3	L. Frontal Bone	0.6	.0595	11.6
M4R3	Mid. R. Femur	0.3	.0382	18.1
M5R3 (C1)	Prox. L. Femur	0.3	.0813	8.5
F6R3 (C1)	Dist. L. Humerus	0.8	.0158	43.8
F6R3 (C2)	Prox. L. Tibia	0.2	.0511	13.6
M7R3	2nd Cerv. Vertebra	0.2	.0491	14.1
F8R3	Prox. L. Humerus	0.2	.0695	10.0
F9R3	Prox. R. Mandible	0.4	.0333	20.8
M10R3	7th Cerv. Vertebra	0.1	.0661	10.5
M1R4	Prox. L. Tibia	0.6	.0663	10.4
M2R4 (C1)	3rd Thor. Vertebra	0.6	.0235	29.5
M2R4 (C2)	R. 5th Metatarsal	0.2	.0474	14.6
F3R4A (C1)	Prox. L. Tibia	0.4	.0435	16.0
M4R4	Dist. L. Femur	0.4	.0370	18.7
F6R4 (C1)	L. Ilium	0.2	.0562	12.3
F6R4 (C2)	Sacrum	0.1	.0565	12.3
F8R4	L. Acetabulum	0.6	.0787	8.8
F9R4 (C1)	3rd Cerv. Vertebra	0.2	.0429	16.2
M10R4	2nd Thor. Vertebra	0.2	.0898	7.7
F11R4	R. Mandible	0.5	.0641	10.8
F12R4	2nd Cerv. Vertebra	0.5	.0506	13.7
M1R5	6th Lumb. Vertebra	0.1	.0416	16.7
M4R5	7th Lumb. Vertebra	0.7	.0961	7.2
F6R5	Dist. R. Humerus	0.2	.0570	12.2
M7R5	Dist. R. Tibia	0.4	.0205	33.8
M10R5	Prox. L. Tibia	0.1	.0360	19.3
M1P1	L. 4th Rib	0.3	.0321	21.6
M3P1	Sacrum	0.2	.0634	10.9
F9P1	6th Thor. Vertebra	0.2	.1278	5.4
M1P1.7	2nd Cerv. Vertebra	0.1	.0415	16.7
M4P1.7	Prox. R. Scapula	0.4	.0553	12.5
F5P1.7	L. 2nd Rib	0.2	.0647	10.7
F7P1.7	Prox. L. Humerus	0.4	.0738	9.4
M8P1.7	L. Ilium	0.2	.1141	6.1
F9P1.7	3rd Lumb. Vertebra	0.4	.0782	8.9
F10P1.7A	L. 3rd Tarsal Bone	0.2	.0544	12.7
M1P2	12th Thor. Vertebra	0.3	.1015	6.8
F2P2	Mid. L. Femur	0.4	.0640	10.8
M4P2	2nd Lumb. Vertebra	0.1	.0478	14.5
F5P2	3rd Lumb. Vertebra	0.4	.0624	11.1
F6P2	L. Frontal Bone	0.3	.1160	6.0
F10P2	8th Thor. Vertebra	0.2	.0934	7.4

Table 4 (Cont.)

Growth Parameters of Beagle Osteosarcomas - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Const. Slope</u>	<u>D.T.</u>
M12P2	L. Scapula	0.5	.0482	14.4
M1P3 (C1)	4th Lumb. Vertebra	0.4	.0666	10.4
M1P3 (C2)	5th Cerv. Vertebra	0.1	.0588	11.8
F2P3	R. Ilium	0.3	.0706	9.8
M3P3	Prox. R. Femur	0.4	.0436	15.9
M4P3 (C1)	4th Cerv. Vertebra	0.1	.0353	19.6
F5P3	2nd Lumb. Vertebra	0.1	.0470	14.7
F6P3	1st Thor. Vertebra	0.4	.0742	9.3
M8P3	3rd Cerv. Vertebra	0.1	.0276	25.2
F9P3	4th Lumb. Vertebra	0.4	.0458	15.1
M11P3	Prox. R. Femur	0.2	.0717	9.7
M12P3	6th Thor. Vertebra	0.3	.0682	10.2
M1P4 (C1)	Prox. L. Femur	0.4	.1106	6.3
F2P4 (C1)	6th Cerv. Vertebra	0.5	.0526	13.2
F6P4	Prox. R. Tibia	0.2	.0346	20.0
F7P4	L. Ilium	0.3	.0666	10.4
M8P4	9th Thor. Vertebra	0.3	.0521	13.3
F10P4	7th Lumb. Vertebra	0.1	***	***
M11P4	4th Lumb. Vertebra	0.6	***	***
M12P4 (C1)	Mid. R. Ulna	0.5	.0860	8.1
M12P4 (C2)	Prox. L. Humerus	0.2	.0607	11.4
M12P4 (C3)	L. 10th Rib	0.3	.0421	16.5
F2P5	L. Mandible	0.1	.0531	13.1
F5P5	Dist. L. Mandible	0.5	.0268	25.9
F9P5	Prox. R. Tibia	0.2	.0614	11.3
F2M1	R. Maxilla	0.4	***	***
M3M1	7th Lumb. Vertebra	0.4	.0378	18.4
F2M1.7	R. Mandible	0.1	.0362	19.2
M3M1.7	L. Ilium	0.8	.0455	15.2
F5M1.7 (C1)	Mid. L. Femur	0.6	.0544	12.7
F7M1.7	L. Ischium	0.3	.0460	15.1
F8M1.7	R. Mandible	0.1	.0779	8.9
M9M1.7 (C1)	Mid. L. Ulna	0.7	.0716	9.7
M9M1.7 (C2)	4th Lumb. Vertebra	0.1	.0480	14.4
M6M2 (C1)	L. 8th Rib	0.0	.0205	33.8
M6M2 (C2)	5th Thor. Vertebra	0.2	.0539	12.9
F8M2	Prox. R. Humerus	0.2	.0558	12.4
M9M2	5th Lumb. Vertebra	0.5	.0376	18.4
M12M2	R. Scapula	0.1	.0361	19.2
F1M3	3rd Lumb. Vertebra	0.3	.1074	6.5
F2M3 (C1)	Sacrum	0.2	.0509	13.6
F2M3 (C2)	Prox. R. Humerus	0.2	.0433	16.0
M3M3	3rd Cerv. Vertebra	0.1	.0501	13.8
F5M3	Prox. R. Femur	0.4	.1160	6.0
M6M3	L. 7th Rib	0.8	.1013	6.8
F7M3	2nd Cerv. Vertebra	0.2	.0388	17.8
F8M3	Prox. R. Radius	0.3	.0314	22.1
M9M3	L. 6th Rib	0.2	.0469	14.8

Table 4 (Cont.)

Growth Parameters of Beagle Osteosarcomas - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Const. Slope</u>	<u>D.T.</u>
M10M3 (C1)	L. Ilium	0.3	.0692	10.0
M10M3 (C2)	5th Sternebra	0.5	.0437	15.9
F11M3	L. Mandible	0.5	.0787	8.8
M12M3 (C1)	Prox. L. Humerus	0.3	.0647	10.7
F2M4	13th Thor. Vertebra	0.1	.0397	17.5
M3M4A	Mid. L. Humerus	0.1	.0514	13.5
F5M4	Prox. L. Humerus	0.1	.0449	15.4
M6M4 (C1)	3rd Lumb. Vertebra	0.3	.0811	8.6
M6M4 (C2)	6th Thor. Vertebra	0.1	.0641	10.8
F7M4	Dist. L. Femur	0.1	.0929	7.5
M6M5	Prox. R. Tibia	0.1	.0439	15.8
M1T1	8th Thor. Vertebra	0.9	.0785	8.8
M4T1	Prox. L. Humerus	0.4	.0495	14.0
M1T1.5 (C1)	Mid. R. Radius	0.5	.0185	37.4
M1T1.5 (C2)	L. Pubis	0.2	.0477	14.5
M4T1.5	Sacrum	0.2	.0707	9.8
M5T1.5	L. Ilium	0.2	.0688	10.1
F6T1.5	9th Thor. Vertebra	1.0	.0654	10.6
M8T1.5 (C1)	Prox. L. Humerus	0.3	.0323	21.4
M8T1.5 (C2)	8th Sternebra	0.0	.0894	7.8
F9T1.5	Sphenoid Bone	0.2	.0257	26.9
F10T1.5	Prox. L. Femur	0.4	.0261	26.5
F12T1.5	11th Thor. Vertebra	0.3	.0511	13.6
M1T2	R. Ilium	0.2	.0301	23.0
M2T2	6th Thor. Vertebra	0.2	.1188	5.8
F3T2 (C1)	R. Ischium	0.7	.1057	6.6
F3T2 (C2)	Prox. R. Humerus	0.5	.1071	6.5
M4T2A (C1)	4th Thor. Vertebra	0.3	***	***
F6T2	1st Cerv. Vertebra	0.5	.0686	10.1
M7T2 (C1)	Prox. L. Humerus	0.6	.0353	19.6
M8T2	2nd Lumb. Vertebra	0.2	.0843	8.2
F9T2	Sacrum	0.1	.0624	11.1
F10T2 (C1)	3rd Cerv. Vertebra	0.1	.0480	14.4
F10T2 (C2)	5th Cerv. Vertebra	0.4	.0428	16.2
F11T2	5th Cerv. Vertebra	0.3	.0389	17.8
F12T2 (C1)	Prox. R. Tibia	0.2	.0347	20.0
F12T2 (C2)	Prox. R. Femur	0.2	.0290	23.9
F12T2 (C3)	Dist. R. Femur	0.2	.0261	26.5
M1T3 (C1)	L. 11th Rib	0.1	.0791	8.8
M2T3	5th Cerv. Vertebra	0.1	***	***
F3T3	13th Thor. Vertebra	0.2	.0733	9.5
M4T3	3rd Cerv. Vertebra	0.3	.0345	20.1
M5T3 (C1)	Prox. L. Humerus	0.4	.0458	15.1
M5T3 (C2)	R. Pubis	0.3	.0871	8.0
F6T3 (C1)	R. 10th Rib	0.2	.0256	27.1
F6T3 (C2)	L. Ischium	0.5	.0631	11.0
M7T3 (C1)	Prox. R. Femur	0.2	.0331	20.9
M7T3 (C2)	L. Frontal Bone	0.8	***	***

Table 4 (Cont.)

Growth Parameters of Beagle Osteosarcomas - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Const. Slope</u>	<u>D.T.</u>
M8T3	Prox. L. Humerus	0.5	.1016	6.8
F9T3 (C1)	Dist. L. Tibia	0.2	.0480	14.4
F10T3	R. Maxilla	0.5	.0523	13.3
F11T3 (C1)	Dist. R. Radius	0.1	.0772	9.0
F11T3 (C2)	5th Cerv. Vertebra	0.1	.1134	6.1
F11T3 (C3)	7th Lumb. Vertebra	0.1	.0828	8.4
M1T4	Mid L. Radius	0.1	.0633	11.0
M2T4	Mid R. Tibia	0.2	.0545	12.7
F9S4.5	R. Ilium	0.2	.0822	8.4
M2S5A	Sacrum	0.4	.0766	9.0
F4S5	L. Parietal Bone	0.6	.0503	13.8
T2R5	6th Cerv. Vertebra	0.5	.0928	7.5
T15R4 (C1)	L. Mandible	0.4	.0306	22.7
T15R4 (C2)	Sacrum	0.3	.0781	8.9
T17R5H	6th Cerv. Vertebra	0.7	.0777	8.9
T23R4H	R. Frontal Bone	0.1	.0523	13.3
T24R4H (C1)	R. Ilium	0.5	.0442	15.7
T24R4H (C2)	Prox. R. Femur	0.5	.0748	9.3
T25R4H (C1)	R. Ischium	0.3	.0609	11.4
T25R4H (C2)	L. Ischium	0.5	.0591	11.7
T26R4H (C1)	Dist. L. Humerus	0.5	.0365	19.0
T27R4H (C1)	1st Cerv. Vertebra	0.1	.0423	16.4
T27R4H (C2)	7th Lumb. Vertebra	0.3	.0314	22.1
T68R3	L. Ilium	0.3	.0972	7.1
T70R3 (C1)	Dist. R. Femur	0.2	.0303	22.9
T19P5	Dist. R. Tibia	0.2	.0335	20.7
T48P5	Mid. R. Humerus	0.2	***	***
T51P5 (C1)	Prox. R. Humerus	0.4	.0994	7.0
T2Q4 (C1)	5th Lumb. Vertebra	0.1	.0304	22.8
T4Q5	R. Scapula	0.1	.1291	5.4
T5Q5	Mid. L. Humerus	0.2	.0647	10.7
T7Q5	R. Mandible	<u>0.2</u>	<u>.0608</u>	11.4
		Ave. 0.31	.0586	
		s.d. 0.20	.0245	

Fig. 11
Distribution of the relative calcification measurements
for the Beagle osteosarcomas. Radio-opacity of soft
tissue = .0; radio-opacity of cortical bone = 1.0.

Fig. 12
Distribution of exponential growth constants
(slopes) for "A" tumors.

Fig. 13
Distribution of exponential growth constants
(slopes) for "B" tumors

Fig. 14
Distribution of exponential growth constants (slopes)
for "C" tumors and all tumors in this study.

Table 6

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>$\mu\text{Ci/kg}$</u>	<u>Days to Death</u>	<u>Slope^a</u>	<u>Fitted T_0^b</u>	<u>Const. T_0^b</u>	<u>Ave. T_0^b</u>	<u>Dose Rads</u>
<u>Radium-226</u>							
M5R1.7	0.151	4108	.0490	*	3665	*	452
M2R2	0.387	3775	.0404	3121	3175	3148	552
M5R2	0.267	4703	.0362	*	4011	*	896
M7R2	0.413	3424	.0278	*	2473	*	735
M10R2	0.345	3569	.0385	*	2880	*	1052
F11R2	0.31	3297	.0341	*	2532	*	684
M1R3	1.2	2850	.0480	*	2321	*	2074
M2R3	1.21	2226	.0134	406	236	321	407
F3R3	1.11	2497	.0595	*	2078	*	2042
M4R3	1.16	1917	.0382	*	1199	*	1690
M5R3 (B1)	0.846	2955	.0316	950	2519	1734	1593
M5R3 (C1)	0.846	2955	.0813	*	2615	*	2129
F6R3 (C1)	1.14	1932	.0158	*	455	*	773
F6R3 (C2)	1.14	1932	.0511	*	1443	*	1826
M7R3	1.29	2099	.0491	*	1612	*	2513
F8R3	1.03	2612	.0695	*	2228	*	1714
F9R3	0.987	2487	.0333	*	1754	*	1438
M10R3	1.06	1737	.0661	*	1402	*	2007
F12R3	0.883	1897	.0600	1523	1392	1458	1360
M1R4	3.51	1606	.0663	*	1262	*	5536
M2R4 (C1)	3.55	1884	.0235	*	971	*	3827
M2R4 (C2)	3.55	1884	.0474	*	1444	*	5093
F3R4A (B1)	3.1	1614	.0482	1111	1226	1168	3944
F3R4A (B2)	3.1	1614	.0638	1319	1020	1170	3948
F3R4A (C1)	3.1	1614	.0435	*	1073	*	3707
M4R4	3.47	1518	.0370	*	833	*	3924
M5R4	2.42	1659	.0682	1405	979	1192	3558
F6R4 (A1)	3.44	1939	.0506	1253	1527	1390	5636
F6R4 (A2)	3.44	1939	.0584	1364	1585	1474	5874
F6R4 (B1)	3.44	1939	.0543	1550	1505	1528	6028
F6R4 (C1)	3.44	1939	.0562	*	1530	*	6032
F6R4 (C2)	3.44	1939	.0565	*	1501	*	5953
M7R4 (A1)	3.88	1647	.0268	748	671	694	3112
M7R4 (A2)	3.88	1647	.0322	712	888	800	3464
F8R4	3.14	1324	.0787	*	1014	*	3808
F9R4 (B1)	3.02	1471	.0438	774	1006	890	2850
F9R4 (C1)	3.02	1471	.0429	*	946	*	2979
M10R4	3.28	1553	.0898	*	1301	*	6684
F11R4	2.84	1469	.0641	*	1072	*	4207
F12R4	2.81	1435	.0506	*	1036	*	3068

^aFor "A" and "B" tumors the slope is the average of the fitted slope and the constructed slope. For the "C" tumors it is the constructed slope.

^b T_0 =Tumor starting time.

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>μCi/kg</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T₀</u>	<u>Const. T₀</u>	<u>Ave. T₀</u>	<u>Dose Rads</u>
M1R5	10.5	908	.0416	*	354	*	6841
M2R5 (A1)	10.8	1380	.0680	1002	969	986	13823
M2R5 (B1)	10.8	1380	.0979	1148	1135	1142	15548
M4R5	10.6	1091	.0961	*	819	*	13021
M5R5	10.1	1220	.0462	632	654	643	9182
F6R5	10.2	1015	.0570	*	533	*	9098
M7R5	11.9	1288	.0205	*	100	*	1855
F8R5	9.68	968	.0816	646	651	648	8337
F9R5 (A1)	9.48	1288	.0470	784	738	761	10466
F9R5 (A2)	9.48	1288	.1008	1047	1008	1028	13352
F9R5 (B1)	9.48	1288	.0356	649	663	656	9262
M10R5	10.2	825	.0360	*	165	*	2815
T1R5	10.3	1074	.0561	559	599	579	5719
T2R5	4.39	1368	.0928	*	1127	*	4052
T15R4 (C1)	3.11	2127	.0306	*	1323	*	4735
T15R4 (C2)	3.11	2127	.0781	*	1824	*	6063
T17R5H	9.87	1147	.0777	*	841	*	10142
T18R5H	10.8	1226	.0424	509	740	624	6559
T19R5H	10.7	1219	.0494	762	623	692	6743
T20R5H	10.6	1330	.0759	656	1098	877	9526
T23R4H	4.05	1471	.0523	*	981	*	3112
T24R4H (C1)	3.24	1505	.0442	*	929	*	3698
T24R4H (C2)	3.24	1505	.0748	*	1152	*	4479
T25R4H (C1)	3.42	1309	.0609	*	915	*	3448
T25R4H (C2)	3.42	1309	.0591	*	908	*	3423
T26R4H (A1)	3.48	1780	.0363	827	1233	1030	3041
T26R4H (B1)	3.48	1780	.0445	1245	1084	1164	3366
T26R4H (C1)	3.48	1780	.0365	*	1152	*	3341
T27R4H (A1)	3.34	1414	.0496	982	820	901	2538
T27R4H (C1)	3.34	1414	.0423	*	824	*	2346
T27R4H (C2)	3.34	1414	.0314	*	711	*	2052
T32R3	1.13	2294	.0380	1402	1646	1524	1415
T33R3	1.15	1822	.0862	1556	1526	1541	1705
T34R3	1.12	1737	.0478	1061	1084	1072	1140
T36R4	2.99	1154	.0626	831	499	665	2426
T37R4	3.0	1627	.1479	1399	1478	1438	2962
T38R4	3.02	1503	.0801	1080	1249	1164	3046
T68R3	0.917	1667	.0972	*	1392	*	909
T70R3 (A1)	0.922	1996	.0414	1316	1366	1341	1594
T70R3 (C1)	0.922	1996	.0303	*	1232	*	1500

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>μCi/kg</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T₀</u>	<u>Const. T₀</u>	<u>Ave. T₀</u>	<u>Dose Rads</u>
<u>Plutonium-239</u>							
M1P1	0.015	4572	.0321	*	3747	*	81
M3P1	0.0165	4292	.0634	*	3889	*	93
M8P1	0.0172	3367	.0678	2904	3010	2957	74
F9P1	0.0168	2257	.1278	*	2045	*	51
M1P1.7	0.0475	3025	.0415	*	2506	*	175
F2P1.7	0.0431	3430	.0747	3176	2841	3008	189
M4P1.7	0.0484	3312	.0553	*	2816	*	199
F5P1.7	0.0493	2659	.0647	*	2246	*	163
F6P1.7	0.0459	2221	.0398	1433	1689	1561	107
F7P1.7	0.0481	3353	.0738	*	2985	*	210
M8P1.7	0.0479	3282	.1141	*	3050	*	213
F9P1.7	0.0485	2500	.0782	*	2164	*	155
F10P1.7A	0.0457	4214	.0544	*	3726	*	246
M1P2	0.0853	2985	.1015	*	2756	*	344
F2P2	0.112	2780	.0640	*	2361	*	390
M3P2	0.094	3185	.0352	2488	2328	2408	333
M4P2	0.0862	2948	.0478	*	2481	*	314
F5P2	0.0846	2423	.0624	*	2069	*	259
F6P2	0.0902	2947	.1160	*	2746	*	363
F9P2	0.101	2014	.0432	1352	1394	1373	209
F10P2	0.0968	2912	.0934	*	2693	*	382
M11P2	0.0961	1617	.0386	1009	894	952	140
M12P2	0.1	2284	.0482	*	1745	*	260
M1P3 (C1)	0.261	1476	.0666	*	1135	*	449
M1P3 (C2)	0.261	1476	.0588	*	1107	*	439
F2P3	0.312	1947	.0706	*	1579	*	738
M3P3	0.291	1604	.0436	*	1064	*	471
M4P3 (A1)	0.292	1950	.0148	0 ^b	632	316	147
M4P3 (C1)	0.292	1950	.0353	*	1325	*	583
F5P3	0.288	1504	.0470	*	1036	*	454
F6P3	0.282	1617	.0742	*	1318	*	561
F7P3	0.314	1627	.0489	760	1242	1001	479
M8P3	0.3	1771	.0276	*	1015	*	464
F9P3	0.3	1894	.0458	*	1396	*	630
F10P3	0.298	1547	.0356	0 ^b	1138	569	264
M11P3	0.309	1198	.0717	*	816	*	387
M12P3	0.308	1659	.0682	*	1337	*	621
M1P4 (B1)	0.823	1724	.0466	1100	1282	1191	1484
M1P4 (C1)	0.823	1724	.1106	*	1493	*	1844
F2P4 (B1)	1.03	1556	.0474	1007	1070	1038	1627
F2P4 (C1)	1.03	1556	.0526	*	1096	*	1715

^bEstimated tumor starting times that are before the time of radio-nuclide injection are set equal to zero.

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>μCi/kg</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T₀</u>	<u>Const. T₀</u>	<u>Ave. T₀</u>	<u>Dose Rads</u>
M3P4	0.929	1198	.0584	509	819	664	956
M4P4	0.974	1066	.1176	796	865	830	1242
F5P4	0.872	1245	.0410	448	756	602	817
F6P4	0.811	1357	.0346	*	615	*	775
F7P4	0.963	1198	.0666	*	822	*	1216
M8P4	0.887	1157	.0521	*	715	*	980
F9P4	0.96	1343	.0479	730	877	804	1188
F10P4	0.868	1241	*	*	*	*	***
M11P4	0.927	1288	*	*	*	*	***
M12P4(C1)	0.838	1463	.0860	*	1178	*	1495
M12P4(C2)	0.838	1463	.0607	*	1103	*	1404
M12P4(C3)	0.838	1463	.0421	*	922	*	1182
M1P5	2.67	1324	.0850	976	1032	1004	4088
F2P5	3.3	1576	.0531	*	1145	*	5729
M4P5	3.17	1562	.0400	1044	811	928	4498
F5P5	2.77	2059	.0268	*	1258	*	5266
F6P5	2.57	1194	.0690	783	850	816	3223
F7P5	2.99	1491	.0513	912	1094	1003	4572
F9P5	2.73	1145	.0614	*	764	*	3216
T19P5	2.91	1400	.0335	*	737	*	3312
T48P5	2.61	1327	*	*	*	*	***
T51P5(A1)	2.73	1055	.0228	0 ^b	*	*	***
T51P5(C1)	2.73	1055	.0994	*	804	*	3377

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>$\mu\text{Ci/kg}$</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T_0</u>	<u>Const. T_0</u>	<u>Ave. T_0</u>	<u>Dose Rads</u>
<u>Radium-228 (MsTh)</u>							
F2M1	0.0324	5267	*	*	*	*	***
M3M1	0.0589	3157	.0378	*	2556	*	264
F2M1.7	0.183	2383	.0362	*	1688	*	541
M3M1.7	0.18	2709	.0455	*	2151	*	604
F5M1.7 (A1)	0.141	3234	.0388	2610	2492	2551	528
F5M1.7 (C1)	0.141	3234	.0544	*	2799	*	567
M6M1.7	0.144	3424	.0744	3113	2990	3052	367
F7M1.7	0.146	2646	.0460	*	2068	*	489
F8M1.7	0.148	2486	.0779	*	2159	*	343
M9M1.7 (C1)	0.149	2799	.0716	*	2455	*	617
M9M1.7 (C2)	0.149	2799	.0480	*	2259	*	576
F1M2	0.276	1780	.0425	1249	1094	1172	621
M4M2	0.282	2282	.0404	1462	1723	1592	734
F5M2	0.295	2688	.0458	2111	2155	2133	769
M6M2 (C1)	0.306	2674	.0205	*	1473	*	797
M6M2 (C2)	0.306	2674	.0539	*	2281	*	1217
F8M2	0.3	2386	.0558	*	1908	*	762
M9M2	0.302	1254	.0376	*	658	*	242
M10M2	0.311	2373	.0498	2010	1477	1744	1094
M12M2	0.306	2471	.0361	*	1737	*	961
F1M3	0.858	918	.1074	*	664	*	1314
F2M3 (C1)	0.612	1856	.0509	*	1349	*	1507
F2M3 (C2)	0.612	1856	.0433	*	1301	*	1449
M3M3	0.965	1185	.0501	*	746	*	1400
M4M3	0.916	1176	.0525	667	725	696	812
F5M3	0.94	1869	.1160	*	1638	*	1885
M6M3	0.953	1421	.1013	*	1162	*	1514
F7M3	0.907	1463	.0388	*	883	*	1713
F8M3	0.95	1447	.0314	*	612	*	727
M9M3	0.918	1570	.0469	*	1027	*	1398
M10M3 (C1)	1.0	1575	.0692	*	1209	*	1728
M10M3 (C2)	1.0	1575	.0437	*	1026	*	1418
F11M3	1.19	1395	.0787	*	1080	*	1831
M12M3 (B1)	0.987	1638	.0316	981	605	793	996
M12M3 (C1)	0.987	1638	.0647	*	1250	*	1760
F1M4	2.6	841	.1202	706	541	624	4080
F2M4	1.86	778	.0397	*	195	*	350
M3M4A	2.64	1063	.0514	*	644	*	2893
F5M4	2.67	1064	.0449	*	478	*	1471
M6M4 (C1)	2.66	1121	.0811	*	842	*	3334
M6M4 (C2)	2.66	1121	.0641	*	796	*	3094

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>μCi/kg</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T₀</u>	<u>Const. T₀</u>	<u>Ave. T₀</u>	<u>Dose Rads</u>
F7M4	2.67	1253	.0929	*	967	*	3387
M6M5	8.67	792	.0439	*	283	*	1549
<u>Thorium-228</u>							
M1T1	0.0146	3172	.0785	*	2897	*	130
M4T1	0.0146	3217	.0495	*	2720	*	129
M1T1.5 (C1)	0.0289	2894	.0185	*	1599	*	224
M1T1.5 (C2)	0.0289	2894	.0477	*	2361	*	250
M2T1.5	0.0293	2576	.0824	2194	2330	2262	251
M4T1.5	0.0299	2309	.0707	*	2024	*	249
M5T1.5	0.0286	1624	.0688	*	1215	*	198
F6T1.5	0.0292	2373	.0654	*	2030	*	244
M8T1.5 (C1)	0.0324	2665	.0323	*	1886	*	265
M8T1.5 (C2)	0.0324	2665	.0894	*	2362	*	280
F9T1.5	0.0306	2983	.0257	*	2002	*	254
F10T1.5	0.0296	1859	.0261	*	859	*	171
F11T1.5	0.0305	2408	.0190	804	1152	978	189
F12T1.5	0.0329	2120	.0511	*	1693	*	260
M1T2	0.0976	1282	.0301	*	381	*	317
M2T2	0.0875	1234	.1188	*	1019	*	555
F3T2 (C1)	0.0908	1541	.1057	*	1312	*	651
F3T2 (C2)	0.0908	1541	.1071	*	1314	*	652
M4T2A (B1)	0.0899	1222	.0330	419	448	434	323
M4T2A (C1)	0.0899	1222	*	*	*	*	***
M5T2	0.0848	1085	.0520	503	612	558	368
F6T2	0.0879	1108	.0686	*	771	*	474
M7T2 (A1)	0.0881	1015	.0238	0 ^b	248	124	107
M7T2 (C1)	0.0881	1015	.0353	*	282	*	223
M8T2	0.0981	1078	.0843	*	793	*	539
F9T2	0.0979	1209	.0624	*	807	*	544
F10T2 (C1)	0.0919	1022	.0480	*	562	*	401
F10T2 (C2)	0.0919	1022	.0428	*	436	*	332
F11T2	0.0904	1038	.0389	*	454	*	337
F12T2 (B1)	0.1	1449	.0294	325	790	558	434
F12T2 (C1)	0.1	1449	.0347	*	765	*	537
F12T2 (C2)	0.1	1449	.0290	*	687	*	501
F12T2 (C3)	0.1	1449	.0261	*	634	*	475
M1T3 (A1)	0.301	988	.0596	492	602	547	1288
M1T3 (C1)	0.301	988	.0791	*	632	*	1426
M2T3	0.301	860	*	*	*	*	***

Table 6 (Cont.)

Skeletal Dose at Estimated Tumor Starting Time

<u>Dog</u>	<u>μCi/kg</u>	<u>Days to Death</u>	<u>Slope</u>	<u>Fitted T₀</u>	<u>Const. T₀</u>	<u>Ave. T₀</u>	<u>Dose Rads</u>
F3T3	0.272	547	.0733	*	177	*	458
M4T3	0.285	801	.0345	*	140	*	387
M5T3 (C1)	0.269	890	.0458	*	303	*	724
M5T3 (C2)	0.269	890	.0871	*	608	*	1241
F6T3 (A1)	0.282	1156	.0526	664	615	640	1347
F6T3 (B1)	0.282	1156	.0724	727	881	804	1562
F6T3 (C1)	0.282	1156	.0256	*	151	*	411
F6T3 (C2)	0.282	1156	.0631	*	768	*	1519
M7T3 (C1)	0.266	861	.0331	*	67	*	180
M7T3 (C2)	0.266	861	*	*	*	*	***
M8T3	0.313	685	.1016	*	419	*	1096
F9T3 (B1)	0.298	1062	.0440	261	612	436	1076
F9T3 (C1)	0.298	1062	.0480	*	569	*	1312
F10T3	0.28	971	.0523	*	495	*	1114
F11T3 (C1)	0.29	826	.0772	*	556	*	1256
F11T3 (C2)	0.29	791	.1134	*	633	*	1375
F11T3 (C3)	0.29	791	.0828	*	568	*	1275
M1T4	0.882	645	.0633	*	322	*	2497
M2T4	0.916	833	.0545	*	423	*	3231
T8T3	0.293	1043	.0892	736	773	754	1560

Strontium-90

M5S4.5	61.3	993	.0500	491	362	426	2999
F9S4.5	64.0	1028	.0822	*	708	*	4033
F1S5	103.0	960	.0746	534	633	584	5974
M2S5A	96.6	1740	.0766	*	1398	*	10728
M3S5	102.0	2256	.1192	2028	2032	2030	15539
F4S5	105.0	1448	.0503	*	991	*	7439
M6S5A (A1)	94.2	1021	.0626	544	593	568	7756
F8S5	90.5	1469	.0614	855	1125	990	8619

Radium-224

T2Q4 (A1)	2.91	2317	.0418	1497	1822	1660	100 ^c
T2Q4 (C1)	2.91	2317	.0304	*	1449	*	100 ^c
T4Q5	9.71	1462	.1291	*	1259	*	400 ^c
T5Q5	9.59	1638	.0647	*	1218	*	400 ^c
T7Q5	8.56	2053	.0608	*	1633	*	400 ^c

^cOnly the dose from ²²⁴Ra is given: all of these dogs had significant additional dose from ²²⁸Th & ²¹⁰Pb contamination in their injection solution.

Table 7
Average Oncogenic Dose at Various
Injection Levels for Six Radionuclides

Injection Level	Tumor Dogs	# of Tumors	Ave. $\mu\text{Ci/kg.}$	Ave. Oncogenic Dose	Mays et al. (49) Ave. Dose ^a
<u>Radium - 226</u>					
R1.7	1	1	0.151	452	458
R2	5	5	0.344	784	837
R3	16	19	1.06	1570	1940
R4	21	37	3.30	3981	4530
R5	15	18	10.0	8686	10900
<u>Plutonium - 239</u>					
P1	4	4	0.0164	75	78
P1.7	9	9	0.0472	184	191
P2	10	10	0.0946	299	313
P3	12	14	0.293	478	602
P4	12	16	0.901	1280	1310
P5	10	11	2.83	4142	4930
<u>Radium - 228 (MsTh) ^b</u>					
M1.7	5	7	0.145	498	485
M2	7	8	0.301	822	953
M3	9	11	0.977	1435	1650
M4	4	5	2.66	2836	2948
M5	1	1	8.67	1549	2830
<u>Thorium - 228</u>					
T1	2	2	0.0146	130	130
T1.5	10	12	0.0303	236	249
T2	12	19	0.0929	409	516
T3	12	21	0.286	1085	1150
T4	2	2	0.899	2864	2870
<u>Strontium - 90</u>					
S4.5	2	2	62.6	3516	3920
S5	6	6	98.6	9342	9100
<u>Radium - 224</u>					
Q4	1	2	2.91	100 ^c	---
Q5	3	3	9.29	400 ^c	---

^aAve. skeletal dose one year before death.

^bExcludes dogs injected with over 1% ²²⁸Th contamination.

^cSee page 57.

Table 8
Skeletal Distribution of Radiation-induced Osteosarcomas

Bone Group	^{226}Ra	^{239}Pu	^{228}Ra	^{228}Th	^{90}Sr	^{224}Ra	Total
Skull	7	1	1	3	1	-	13
Mandible	3	2	3	2	-	1	11
Vertebrae { Cerv.	7	5	2	7	-	-	21
Thor.	3	6	3	6	-	-	18
Lumb.	3	9	5	2	-	1	20
Sacrum	2	2	1	2	1	-	8
Sternebrae	-	-	1	1	-	-	2
Pelvis { Ilium	3	4	3	3	2	1	16
Ischium	5	4	1	2	-	-	12
Pubis	-	-	-	2	-	-	2
Acetab.	1	-	-	-	-	-	1
Ribs	1	4	4	4	1	-	14
Humerii { Prox.	4	6	5	8	-	-	23
Mid.	-	2	2	-	-	1	5
Dist.	6	1	-	-	-	-	7
Radii { Prox.	1	1	1	-	-	-	3
Mid.	1	-	-	2	-	-	3
Dist.	-	-	-	1	-	-	1
Ulnae { Prox.	-	-	2	-	-	-	2
Mid.	-	2	1	-	-	-	3
Dist.	1	-	-	-	-	-	1
Femora { Prox.	4	7	1	5	-	-	17
Mid.	1	1	2	-	-	-	4
Dist.	7	1	3	2	1	-	14
Tibiae { Prox.	10	2	1	1	2	-	16
Mid.	1	-	-	1	-	-	2
Dist.	5	1	-	2	-	-	8
Footbones	4	1	-	-	-	-	5
Scapulae	-	2	1	-	-	1	4
Totals	80	64	43	56	8	5	256

Table 9
Average Growth Rate of Osteosarcomas
Occurring in Various Bone Groups

Bone Group	No. of Tumors	Ave. Growth Rate	S.D.	% of Total Tumors	% of Total Skel. Wt ^a	Ratio
Skull	13	.0676	.0361	5.1	16.4	.31
Mandibles	11	.0486	.0194	4.3	7.0	.61
Cerv. Vertebrae	21	.0536	.0211	8.2	6.6	1.24
Thor. Vertebrae	18	.0720	.0276	7.0	6.7	1.04
Lumb. Vertebrae	20	.0593	.0237	7.8	6.0	1.30
Caudal Vertebrae	0	--	--	0	2.2	0
Sacrum	8	.0632	.0114	3.1	2.6	1.19
Sternbrae	2	.0666	.0323	0.8	1.0	.80
Pelvis (whole)	31	.0629	.0214	12.1	4.9	2.47
{ Ilium	(16)	.0661	.0219			
{ Ischium	(12)	.0566	.0209			
{ Pubis	(2)	.0674	.0279			
{ Acetabulum	(1)	.0787	--			
Ribs	14	.0515	.0225	5.5	10.2	.54
Humerii	35	.0508	.0232	13.7	5.8	2.36
Radii	7	.0428	.0232	2.7	2.2	1.23
Ulnae	6	.0742	.0293	2.3	2.5	.92
Femora	35	.0578	.0267	13.7	6.2	2.21
Tibiae	26	.0522	.0214	10.2	5.7	1.79
Footbones	5	.0493	.0118	2.0	9.8	.20
Scapulae	4	.0672	.0420	1.6	3.9	.41
Total =	256					

^aFrom Atherton, Stover and Bruenger (50), Table 3, wet weights.

Table 10

Distribution of Radiation-induced Osteosarcomas in Beagles,
and Naturally Occurring Osteosarcomas in Dogs and Humans

Bone Group	Beagles		Dogs ^a		Humans ^b		
	# of tumors	Distri- bution	# of tumors	Distri- bution	# of tumors	Distri- bution	
Skull	13	5.1%	18	9.3%	42	6.5%	
Mandibles	11	4.3%	6	3.1%	21	3.2%	
Vert.-	Cerv.	21	8.2%	1	0.5%	3	0.5%
	Thor.	18	7.0%	1	0.5%	2	0.3%
	Lumb.	20	7.8%	1	0.5%	5	0.8%
	Caudal	0	--	0	--		
Sacrum	8	3.1%	1	0.5%	4	0.6%	
Sternbrae	2	0.8%	2	1.0%	3	0.5%	
Pelvis-	Ilium	16	6.2%	1	0.5%	—	—
	Ischium	12	4.7%	1	0.5%		
	Pubis	2	0.8%	0	--	55	8.5%
	Acetab.	1	0.4%	0	--	—	—
Ribs	14	5.5%	8	4.1%	12	1.9%	
Humerii-	Prox.	23	9.0%	28	14.4%	55	8.5%
	Mid.	5	2.0%	0	--	4	0.6%
	Dist.	7	2.7%	2	1.0%	5	0.8%
Radii -	Prox.	3	1.2%	1	0.5%	1	0.2%
	Mid.	3	1.2%	1	0.5%	0	--
	Dist.	1	0.4%	53	27.3%	4	0.6%
Ulnae -	Prox.	2	0.8%	4	2.1%	1	0.2%
	Mid.	3	1.2%	3	1.5%	0	--
	Dist.	1	0.4%	5	2.6%	2	0.3%
Femora-	Prox.	17	6.6%	7	3.6%	31	4.8%
	Mid.	4	1.6%	1	0.5%	29	4.5%
	Dist.	14	5.5%	12	6.2%	214	33.1%
Tibae ^c -	Prox.	16	6.2%	11	5.7%	108	16.7%
	Mid.	2	0.8%	1	0.5%	14	2.2%
	Dist.	8	3.1%	20	10.3%	13	2.0%
Footbones	5	2.0%	3	1.5%	8	1.2%	
Scapula	4	1.6%	2	1.0%	11	1.7%	
Total	256		194		647		

^aFrom Fig. 3 of Brodey and Risen (22).

^bFrom Fig. 17-1 of Dahlin (51).

^cIncludes fibula.

CALCIFICATION VS. EXPONENTIAL GROWTH CONSTANT

Fig. 15. Exponential growth constants compared to relative calcification of tumor. The growth constants are not significantly correlated with tumor calcification ($p > 0.10$).

DAYS P.I. TO DEATH VS. EXPONENTIAL GROWTH CONSTANT

Fig. 16. Exponential growth constants compared with days post injection to death. The growth constants are not significantly correlated with days to death ($p > 0.10$).

Fig. 17. Oncogenic skeletal dose correlated to the amount of ^{226}Ra injected.

PU-239 BEAGLES - INJ. ACTIVITY VS. ONCOGENIC DOSE

Fig. 18. Oncogenic skeletal dose correlated to the amount of ^{239}Pu injected.

RA-228 BEAGLES - INJ. ACTIVITY VS. ONCOGENIC DOSE

Fig. 19. Oncogenic skeletal dose correlated to the amount of ^{228}Ra (MsTh) injected.

TH-228 BEAGLES - INJ. ACTIVITY VS. ONCOGENIC DOSE

Fig. 20. Oncogenic skeletal dose correlated to the amount of ^{228}Th injected.

Fig. 21. Average oncogenic dose to the skeleton at various injection levels for ^{226}Ra . The line is extrapolated to lower injection levels (shown by arrows) to estimate the doses necessary for osteosarcoma induction in the low-level Beagles.

Fig. 22. Average oncogenic dose to the skeleton at various injection levels for ^{239}Pu . The line is extrapolated to lower injection levels (shown by arrows) to estimate the doses necessary for osteosarcoma induction in the low-level Beagles.

Fig.23. Average oncogenic dose to the skeleton at various injection levels for $^{228}\text{Ra}(\text{MsTh})$. The line is extrapolated to lower injection levels (shown by arrows) to estimate the doses necessary for osteosarcoma induction in the low-level Beagles.

Fig. 24. Average oncogenic dose to the skeleton at various injection levels for ^{228}Th . The line is extrapolated to lower injection levels (shown by arrows) to estimate the doses necessary for osteosarcoma induction in the low-level Beagles.

V. DISCUSSION

A. Growth Model

Plots of the volumes for the "A" tumors, Fig. 10, show how well the exponential growth model fits the data. However, some of the plots could be interpreted as Gompertzian growth. If these primary osteosarcomas had grown according to the Gompertzian model, the tumors followed over the longest periods of time or over the greatest increases in volume should have shown the most evidence of the Gompertzian retardation.

The three tumors (M2R3, M7T2(A1) and F11T1.5) measured for more than 200 days, showed no indication of Gompertzian growth. The five tumors (M2R5(A1), M3P2, M5S4.5, M6S5A(A1) and T19R5H) which increased more than 150 fold ($\frac{\text{final measured volume}}{\text{initial measured volume}}$) also gave no indication of retardation of the exponential growth constant.

The sets of measurements on the eight tumors mentioned above are probably the best of all the 256 tumors studied in this work. The exponential growth model represented these tumors' growths very well and it was assumed that all radiation-induced osteosarcomas in Beagles grow exponentially.

It must be pointed out that:

1. Most of the Beagles were euthanized when death appeared imminent or when life could no longer be humanely prolonged. It is not possible to estimate how large the tumors would have been at full term. If all the dogs had been allowed to live until

the tumor caused their death, some retardation of the exponential growth constants may have been seen during the terminal growth of the tumor.

2. The calculated tumor volumes include everything within the radiographic boundaries of the tumor. These are gross measurements and may include necrotic areas, supportive tissue, and sometimes even bone encased within the tumor.

3. Tumors on the bones of the appendicular skeleton are easier to see and measure on radiographs than are tumors of the axial skeleton. The "A" and "B" tumors have the best measurements and are mostly tumors of the appendicular skeleton.

B. Relative Tumor Calcification

The more calcified the tumor, the easier it is to see and measure on x-ray film. This explains why the average calcification for the "A" tumors is higher than for "B" tumors, and why "B" tumors are higher than "C" tumors (Table 1). The relative calcification is not obtained from ashing a section of the tumor but from comparing radio-opacities on x-ray films.

C. Tumor Growth Parameters

The mean of the tumor volume doubling times for all the osteosarcomas was 12.4 days and the range was 4.7 days to 60.3 days. Both range limits for osteosarcomas in Beagles are about a factor of three lower than the range limits of the doubling times Collins, Loeffler and Tiver (29) found for pulmonary metastases

of different tumor types in humans (11 days-164 days).

D. Starting Times and Skeletal Doses

The estimated starting times obtained using the fitted slopes were unrealistic (before the time of injection) in four cases (M4P3(A1), F10P3, T51P5(A1) and M7T2(A1).) The constructed slopes gave no unrealistic starting times. Only one tumor out of the 80 "A" and "B" tumors did not have a constructed slope (T51P5(A1).) The fitted slope of this tumor gave an unrealistic starting time and a dose calculation could not be made. This means that only one, out of 249 measurable tumors, estimated an impossible starting time. Seven other tumors were not measurable or had insufficient radiographs and could not have a dose calculated for them from their own growth measurements.

The calculated oncogenic doses are definitely related to the injected $\mu\text{Ci/kg}$ over the injection range studied, as shown in Figures 17, 18, 19 and 20. Plots on log-log paper of the average oncogenic dose as a function of the injected $\mu\text{Ci/kg}$ gives straight line relationships, see Figures 21, 22, 23 and 24. One can then speculate as to the average oncogenic skeletal dose necessary at the lower injection levels where no osteosarcomas have yet occurred. This is done by extrapolating the line down to the lower injection levels and determining the dose necessary at that level. Then the time required to obtain that dose is calculated using the method of Lloyd et al. (48). These numbers are listed in Table 11. Most of the necessary burden times are longer than the median

life span for the Beagle (12.7 years). This predicts that few, if any, osteosarcomas should occur in these low level Beagles.

Table 11
Estimation of Burden Years for Osteosarcoma Induction
in Low Level Toxicity Beagles

Radio-nuclide Level	Average $\mu\text{Ci/kg}$	Estimated Oncogenic Dose	Burden Time Necessary
<u>^{226}Ra</u>			
R0.2	0.00742	49 rads	>22 yrs.
R0.5	0.0217	108 rads	>22 yrs.
R1	0.0625	230 rads	18.2 yrs.
<u>^{239}Pu</u>			
P0.1	0.00063	7 rads	21.7 yrs.
P0.2	0.00178	15 rads	16.2 yrs.
P0.5	0.00515	32 rads	11.8 yrs.
P0.7	0.0101	52 rads	9.7 yrs.
<u>^{228}Ra (MsTh) ^a</u>			
M0.5	0.0177	150 rads	>22 yrs.
M1	0.0494	270 rads	17.2 yrs.
<u>^{228}Th</u>			
T0.2	0.00171	27 rads ^b	>22 yrs.
T0.5	0.00518	58 rads ^c	>22 yrs.

^a uncontaminated (<1% ^{228}Th)

^b 0.00171 $\mu\text{Ci/kg}$ ^{228}Th would give only 16 rads in 22 years.

^c 0.00518 $\mu\text{Ci/kg}$ ^{228}Th would give only 48 rads in 22 years.

Only the future will show if this extrapolation is valid or not.

The average tumor duration of 1.33 years is quite close to the estimate of Mays (25) in 1969 when he used one year before death to estimate oncogenic doses. Thus, his estimates of average oncogenic dose for each injection level are quite similar to the values calculated in this work, as can be seen in Table 7.

There was not a sufficient number of ^{90}Sr and ^{224}Ra osteosarcomas to permit detailed analysis. The oncogenic doses calculated for the five ^{224}Ra tumors are only approximations because of con-

tamination of the injection solution with ^{210}Pb and ^{228}Th .

Some of the ^{228}Ra (MsTh) dogs received ^{228}Th contamination in their injection solution. Three tumor bearing dogs had received a 15% contamination (FlM2, FlM3, and FlM4) which means that about 50% of their oncogenic dose recorded in Table 6 is due to ^{228}Th . Because of the contamination, Table 7 excludes all Mesothorium dogs that received more than 1% of ^{228}Th .

E. Skeletal Distribution of Osteosarcomas

The ratio column in Table 9 (% tumor incidence divided by % of total skeleton) gives a rough indication of the susceptibility of various bone groups to radiation-induced osteosarcomas: the larger the ratio, the greater the susceptibility. The bone groups at the highest risk are the humerii, femora and pelvic bones. Those at very low risk are the caudal vertebrae and the footbones.

From Table 10, the major differences found by comparing the osteosarcoma-incidences of Beagles (radiation-induced), dogs (naturally occurring) and humans (naturally occurring) were:

1. The very large incidence of osteosarcomas in the vertebrae of Beagles (Beagles = 23.0%, dogs = 1.5% and humans = 1.6%).
2. The lower incidence of pelvic osteosarcomas in dogs (Beagles = 12.1%, dogs = 1.0% and humans = 8.5%).
3. The very large incidence of osteosarcomas in the distal radii of dogs (Beagles = 0.4%, dogs = 27.3% and humans = 0.6%).
4. The very large incidence of osteosarcomas in the distal femora

of humans (Beagles = 5.5%, dogs = 6.2% and humans = 33.1%.)

5. The large incidence of osteosarcomas in the proximal tibiae of humans (Beagles = 6.2%, dogs = 5.7% and humans = 16.7%.)

F. Parameter Relationships for ^{226}Ra , ^{239}Pu , ^{228}Ra and ^{228}Th Tumors

The exponential growth constants showed no obvious relation to any of the other parameters. It was expected that the highly calcified tumors would grow slower than the lowly calcified tumors. However, this turned out not to be the case and the growth rates varied widely, irrespective of the calcification of the tumor (see Fig. 15.)

It was of special interest to check whether or not the injection level (amount of radionuclide) influenced the tumors' growth rate. For ^{226}Ra , ^{228}Ra and ^{228}Th (intracomparisons), there was a tendency for the tumors of the higher injection level dogs to grow faster than the tumors of the lower injection level dogs. However, the variance was so large that statistics do not warrant any definite conclusion.

The days post injection to death is a relative measurement of the dogs age because all the Beagles were injected at approximately the same age (17 months.) The tumor growth rates were found not to be demonstrably dependent on the days post injection to death. This is interpreted to mean that radiation-induced osteosarcomas do not generally grow faster or slower in older dogs than in younger adult dogs (see Fig. 16.)

The rates of growth are also independent of the terminal

tumor volumes. If these tumors were experiencing Gompertzian growth, it would be expected that the larger tumors would be growing slower than the smaller tumors. This is not the case, in fact the larger tumors are larger because they are growing faster. Both the fast growing tumors and the slow growing tumors show a close approximation to exponential growth.

The skeletal location of the tumors did not effect the growth rates demonstrably (Table 9.) All of the average growth rates for the various bone groups are within one standard deviation of the average growth rate of all the tumors.

VI. SUMMARY AND CONCLUSIONS

1. Thus far the most significant long-term effect of the i.v. injection of ^{226}Ra , ^{239}Pu , ^{228}Ra (MsTh), ^{228}Th , ^{90}Sr or ^{224}Ra into Beagles has been the induction of osteosarcomas.
2. Of the three models tested, the exponential growth model best fits the growth measurements of the Beagle osteosarcomas.
3. The tumors' rates of growth were not statistically related to any of the other parameters measured, such as: sex, tumor calcification, days from injection to death, amount of radionuclide injected, or type of radionuclide injected.
4. Tumor volume doubling times ranged from 4.7 days to 60.3 days, and averaged 12.4 days.
5. The average time from the estimated start of tumor growth until death was 1.33 years.
6. The oncogenic skeletal dose varies with the radionuclide used and the injection level. For ^{226}Ra , ^{239}Pu , ^{228}Ra (MsTh) or ^{228}Th , average oncogenic skeletal doses decreased as the injected $\mu\text{Ci/kg}$ decreased.
7. In these irradiated Beagles, 12.1% of the osteosarcomas occurred in the pelvic bones and 23% in the vertebrae; whereas in non-irradiated dogs, only 1% of the osteosarcomas were in the pelvic bones and 1.5% in the vertebrae.
8. In Beagles, the bones having the highest risk (per unit weight) of osteosarcoma induction by internal irradiation are the pelvic bones, humerii, femora and tibiae.

REFERENCES

1. Furth, J. and Lorenz, E.: Carcinogenesis by ionizing radiations, In Radiation Biology (Nat. Res. Council) I. part 2, Hollaender, A. editor, McGraw-Hill Book Co. Inc., New York, 1954, chapter 18, pages 1145-1201.
2. Injection Tables: Research in Radiobiology, U. of Utah Report COO-119-242, March 31, 1970, pages 7-93.
3. Beck, A.: Zur Frage des Röntgensarkoms, zugleich ein Beitrag zur Pathogenese des Sarkoms, Münchener Med. Wchnschr. 69: 623, 1922.
4. Hatcher, C.H.: The development of sarcoma in bone subjected to roentgen or radium irradiation, J. Bone and Joint Surg. 27: 179-195, 1945.
5. Auerbach, O., Friedman, M., Weiss, L. and Amory, H.I.: Extraskkeletal osteogenic sarcoma arising in irradiated tissue, Cancer 4: 1095-1106, 1951.
6. Ewing, J.: Radiation osteitis, Acta Radiol. 6: 399-412, 1926.
7. Koletsky, S., Bonte, F.J. and Friedell, H.L.: Production of malignant tumors in rats with radioactive phosphorus, Cancer Research 10: 129-138, 1950.
8. Martland, H.S., Conlon, P. and Knef, J.P.: Some unrecognized dangers in the use and handling of radioactive substances: with a special reference to the storage of insoluble products of radium and mesothorium in the reticulo-endothelial system, J. Am. Med. Assoc. 85: 1769-1776, 1925.
9. Martland, H.S. and Humpheries, R.E.: Osteogenic sarcoma in dial painters using luminous paint, Arch. Pathol. 7: 406-417, 1929.
10. Martland, H.S.: The occurrence of malignancy in radioactive persons. A general review of data gathered in the study of radium dial painters, with special reference to the occurrence of osteogenic sarcoma and the interrelationship of certain blood diseases, Am. J. Cancer 15: 2435-2516, 1931.

11. Evans, R.D., Harris, R.S., and Bunker, J.W.M.: Radium metabolism in rats, and the production of osteogenic sarcoma by experimental radium poisoning, Am. J. Roentgenol. Radium Therapy 52:353-373, 1944.
12. Aub, J.C., Evans, R.D., Hempelmann, L.H. and Martland, H.S., The late effects of internally-deposited radioactive materials in man, Medicine 31:221-329, 1952.
13. Evans, R.D.: Quantitative aspects of radiation carcinogenesis in humans, Acta Unio Intern. contra Cancrum 6:1229-1237, 1950.
14. Evans, R.D.: The effect of skeletally deposited alpha-ray emitters in man, Brit. J. Radiol. 39:881-895, 1952.
15. Evans, R.D.: The radium standard for bone seekers-evaluation of the data on radium patients and dial painters, Health Phys. 13:267-278, 1967.
16. Evans, R.D., Keane, A.T., Kolenkow, R.J., Neal, W.R., Shanahan, M.M.: Radiogenic tumors in the radium and mesothorium cases studied at M.I.T. In Delayed Effects of Bone-seeking Radionuclides, Mays, C.W., editor-in-chief, U. of Utah Press, Salt Lake City, 1969, pages 157-194.
17. Finkel, A.J., Miller, C.E. and Hasterlik, R.J.: Radium-induced malignant tumors in man, In Delayed Effects of Bone-seeking Radionuclides, Mays, C.W., editor-in-chief: U. of Utah Press, Salt Lake City, 1969, pages 195-225.
18. Hems, G.: The risk of bone cancer in man from internally deposited radium, Brit. J. Radiol. 40:506-511, 1967. For critique of this paper see Evans, R.D., Finkel, A.J., Hasterlik, R.J., Keane, A.T., Kolenkow, R.J., Neal, W.R. and Shanahan, M.M.: Brit. J. Radiol. 41:391-393, 1968.
19. Dougherty, T.F., Jee, W.S.S., Mays, C.W., and Stover, B.J., editors: Some Aspects of Internal Irradiation, Pergamon Press, New York, 1962.
20. Mays, C.W. editor-in-chief: Delayed Effects of Bone Seeking Radionuclides, U. of Utah Press, Salt Lake City, 1969.
21. Moskalev, Yu.I.: Distribution and Biological Effects of Radioactive Isotopes, Atomizdat, Moscow, 1966. Translation #AEC-tr-6944 (Rev.), Clearing house for Federal Scientific and Technical Information, National Bureau of Standards, U.S. Dept. of Commerce, Springfield, Virginia 22151, Oct., 1968.

22. Brodey, R.S. and Riser, W.H.: Canine osteosarcoma: a clinicopathologic study of 194 cases, *Clinical Orthopaedics and Related Research* 62:54-64, January-February, 1969.
23. Mays, C.W. and Taylor, G.N.: Low natural incidence of osteosarcomas in Beagles, *Research in Radiobiology*, U. of Utah Report COO-119-231, pages 70-75, September, 1964.
24. Dougherty, T.F.: Incidence of bone cancer in internally irradiated dogs, *In* Some Aspects of Internal Irradiation Dougherty, T.F., Jee, W.S.S., Mays, C.W., and Stover, B.J. editors, Pergamon Press, New York, 1962, pages 47-61.
25. Mays, C.W., Dougherty, T.F., Taylor, G.N., Lloyd, R.D., Stover, B.J., Jee, W.S.S., Christensen, W.R., Dougherty, J.H., and Atherton, D.R.: Radiation-induced bone cancer in Beagles, *In* Delayed Effects of Bone-seeking Radionuclides, Mays, C.W., editor-in-chief, U. of Utah Press, Salt Lake City, 1969, pages 387-408.
26. Finkel, M.P., Jenkins, P.B. and Biskis, B.O.: Parameters of radiation dosage that influence production of osteogenic sarcoma in mice, *In* Control of Cell Division and Cancer Induction, National Cancer Institute monograph No. 14, 1964, pages 243-270.
27. Willis, R.A.: Pathology of Tumors, Appleton-Century-Crofts, Meredith Publishing Co., New York, 1967, pg. 2.
28. Harris, T.E.: A mathematical model for multiplication by binary fission, *In* The Kinetics of Cellular Proliferation, Stohlman, F. Jr., Grune and Stratton, New York, 1959.
29. Collins, V.P., Loeffler, R.K. and Tivey, H.: Observations on growth rates of human tumors, *The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* 76:988-1000, 1956.
30. Collins, V.P.: Time of occurrence of pulmonary metastasis from carcinoma of colon and rectum, *Cancer* 15:387-395, 1962.
31. Brues, A.M., Weinger, A.E. and Andervont, H.B.: Relation between latent period and growth rate in chemically induced tumors, *Proc. Soc. Exper. Biol. & Med.* 43:374-377, 1939.
32. Mayneord, W.V.: On a law of growth of Jensen's rat sarcoma, *Amer. J. Cancer* 16:841-846, 1932.
33. Schrek, Robert: A quantitative study of the growth of the Walker rat tumor and the Flexner-Jobling rat carcinoma, *Amer. J. Cancer* 24:807-822, 1935.

34. Klein, G. and Révész L.: Quantitative studies on multiplication of neoplastic cells in vivo. I. Growth curves of the Ehrlich and MClM ascites tumors, J. Natl. Cancer Inst. 14: 229-272, 1953.
35. Siegler, R. and Koprowska, I.: Mechanism of an ascites tumor formation, Cancer Res. 22:1273-1277, 1962.
36. Gompertz, B.: On the nature of the function expressive of the law of human mortality, and on a new method of determining the value of life contingencies, Phil Trans. Roy. Soc., pages 513-585, 1825.
37. Wright, S.: Book review, J. Amer. Stat. Assoc. 21:494, 1926.
38. Casey, A.E.: The experimental alteration of malignancy with homologous mammalian tumor material. I. Results with intratesticular inoculation, Amer. J. Cancer 21:760-775, 1934.
39. Laird, A.K.: Dynamics of tumor growth, Brit. J. Cancer 18:490-502, 1964.
40. Finkel, M.P., Bergstrand, P.J., and Biskis, B.O.: The latent period, incidence, and growth of Sr^{90} -induced osteosarcomas in CFl and CBA mice, Radiology 77:269-281, 1961.
41. Laird, A.K.: Dynamics of tumor growth: comparison of growth rates and extrapolation of growth curve to one cell, Brit. J. Cancer 19:278-291, 1965.
42. Summers, W.C.: Dynamics of tumor growth: a mathematical model, Growth 30:333-338, 1966.
43. McCredie, J.A., Inch, W.R., Kruuv, J. and Watson, T.A.: The rate of tumor growth in animals, Growth 29:331-347, 1965.
44. Wexler, H., Orme, S.K. and Ketcham, A.S.: Biological behavior through successive transplant generations of transplantable tumors derived originally from primary chemically induced and spontaneous sources in mice, J. Nat. Cancer Inst. 40:513-523, 1968.
45. Dougherty, T.F., Stover, B.J., Dougherty J.H., Jee, W.S.S., Mays, C.W., Rehfeld, C.E., Christensen, W.R., and Goldthorpe, H.C.: Studies of the biological effects of Ra^{226} , Pu^{239} , Ra^{228} ($MsTh_1$), Th^{228} ($RdTh$), and Sr^{90} in adult Beagles, Rad. Res. 17:625-681, 1962.
46. Andersen, A.C., editor: The Beagle as an Experimental Dog, The Iowa State University Press, Ames, 1970.

47. Spratt, J.S. Jr.: The rates of growth of skeletal sarcomas, Cancer 18:14-24, 1965.
48. Lloyd, R.D., Mays, C.W., Atherton, D.R. and Van Dilla, M.A.: Radium and mesothorium retention and skeletal dosimetry in Beagles, In Retention and Dosimetry of Some Injected Radionuclides in Beagles, R.D. Lloyd, editor, U. of Utah Report COO-119-241, March, 1970, pages 25-59.
49. Mays, C.W., Dougherty, T.F., Taylor, G.N., Stover, B.J., Jee, W.S.S., Christensen, W.R., Dougherty, J.H., Stevens, W. Jr., and Nabors, C.J. Jr.: In Hearings on environmental effects of producing electric power, Joint Congressional Committee On Atomic Energy, Vol. II, part 2 pages 2192-2210, Jan. 27-30 and Feb. 24-26, 1970; and also In Research in Radiobiology, U. of Utah Report COO-119-242, March 31, 1970, pages 385-401.
50. Atherton, D.R., Stover, B.J., and Bruenger, F.W.: Fractional weight of the Beagle skeleton, In Research in Radiobiology, U. of Utah Report COO-119-240, March 31, 1969, pages 162-171.
51. Dahlin, D.C.: Osteogenic sarcoma, In Bone Tumors, Charles C. Thomas, Springfield, 1967, chapter 17, pages 156-175.

APPENDIX

Legend - Beagle Osteosarcoma Data

EXAMPLE: Data read from radiographic series of dog F6R4.

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F6R4</u>	Prox. R.	0.4	1939 [†]	113.8	4.6 x 10.5 x 4.5
(A1)	Humerus		1939	107.4	4.8 x 8.9
			1914	35.8	3.7 x 5.0
			1886	14.1	2.5 x 4.3
			1856	4.4	1.6 x 3.3
			1822		(?)
			1791		(?)
			1760*		(?)
			1730*		N.V.

LEGEND:

F6R4

Code name for dog as explained on page

(A1)

Listing method for individual tumors in dogs that had more than one osteosarcoma. For example, this dog F6R4 had 5 tumors, 2 "A" tumors, 1 "B" tumor, and 2 "C" tumors. The tumors are listed as (A1), (A2), (B1), (C1), and (C2).

Prox. R. Humerus

Skeletal location of tumor.

Calc. = 0.4

Relative calcification of tumor.
0.0 = radio-opacity of soft tissue
1.0 = radio-opacity of cortical bone.

Days P. I.

Days post-injection. The number of days since the dog was injected with the radionuclide.

1939[†]

Autopsy radiographic series of defleshed skeleton. Measurement on excised tumor.

1760*

1730*

Days used in calculating constructed slope. When two days are marked (*) the average of the two is used as the estimated date when the tumor has an average diameter of 0.1 cm. When only one day is marked (*), that date is used.

113.8

Volume in cm^3 calculated from tumor dimensions assuming the tumor is an ellipsoid of revolution.

4.6 x 10.5 x 4.5

Radiographic dimensions of osteosarcoma in cm. Parentheses around the measurement, example: (4.5 x 6.7), mean that the tumor has not yet broken the cortex of the bone.

?

Tumor radiographically observable but dimensions not measurable. Tumor may or may not have erupted through the cortex of the bone of origin. Parentheses, example: (?), mean that the tumor has not broken the cortex of the bone.

N.V.

Tumor not visible radiographically.

Radiographs were insufficient to determine when the tumor was or was not visible.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M2R3</u>	Mid. L. Radius	0.2	2226 [†]	49.4	3.5 x 7.7
			2226	60.2	3.7 x 8.4
			2198	48.4	3.4 x 8.0
			2167	40.2	3.2 x 7.5
			2136	29.2	3.0 x 6.2
			2104	10.4	2.1 x 4.5
			2073	6.0	2.1 x 2.6
			1976	2.3	1.3 x 2.6
			1886		(1.1 x 2.6)
			1793		(0.4 x 1.1)
			1596		?
			1415*		?
			1232*		N.V.
<u>F12R3</u>	Mid. L. Tibia	0.8	1897 [†]	83.1	4.6 x 7.5
			1897	75.0	4.4 x 7.4
			1878	24.6	2.8 x 6.0
			1849	2.8	1.0 x 5.4
			1763*		(0.5 x 4.1)
			1562*		N.V.
<u>F6R4</u> (A1)	Prox. R. Humerus	0.4	1939 [†]	113.8	4.6 x 10.5 x 4.5
			1939	107.4	4.8 x 8.9
			1914	35.8	3.7 x 5.0
			1886	14.1	2.5 x 4.3
			1856	4.4	1.6 x 3.3
			1822		(?)
			1791		(?)
			1760*		(?)
			1730*		N.V.
<u>F6R4</u> (A2)	Dist. R. Tibia	0.6	1939 [†]	73.7	4.5 x 6.8 x 4.6
			1939	49.4	4.0 x 5.9
			1914	25.2	3.2 x 4.7
			1886	8.8	2.5 x 2.7
			1856	1.2	1.1 x 1.9
			1822		(?)
			1791*		(?)
			1760*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M7R4</u> (A1)	Prox. R. Tibia	0.6	1647 [†]	37.4	3.2 x 6.2 x 3.6
			1647	39.1	3.5 x 6.1
			1623	20.6	2.7 x 5.4
			1598	11.6	2.3 x 4.2
			1570	4.4	1.6 x 3.3
			1539		(0.8 x 2.0)
			1505		(0.7 x 1.2)
			1435		(0.3 x 0.5)
			1340		(?)
			1211*		(0.1 x 0.2)
			1031		N.V.
<u>M7R4</u> (A2)	Prox. L. Humerus	0.3	1647 [†]	305.8	7.8 x 9.6
			1647	281.3	7.6 x 9.3
			1637	183.6	6.5 x 8.3
			1623	94.0	5.1 x 6.9
			1598	37.7	4.0 x 4.5
			1570	19.3	3.0 x 4.1
			1539	9.8	2.5 x 3.0
			1505	4.5	1.9 x 2.4
			1435		(1.7 x 2.7)
			1340*		(1.4 x 2.2)
			1211*		N.V.
<u>M2R5</u> (A1)	Prox. L. Tibia	0.3	1380 [†]	95.9	6.3 x 5.7 x 5.1
			1380	651.4	10.8 x 12.0 x 9.6
			1353	52.6	4.2 x 6.3 x 3.8
			1333	8.9	2.0 x 3.4 x 2.5
			1318	4.9	1.6 x 3.1 x 1.9
			1297	1.6	1.3 x 1.9 x 1.2
			1261		?
			1213*		(?)
			1163*		N.V.
<u>F8R5</u>	Dist. R. Ulna	0.7	968 [†]	120.3	5.7 x 7.2 x 5.6
			967	92.5	5.7 x 6.2 x 5.0
			953	27.2	3.3 x 4.5 x 3.5
			932	4.1	1.4 x 3.7 x 1.5
			920	2.3	1.0 x 3.2 x 1.4
			909		?
			896*		?
			741*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9R5</u> (A1)	Dist. R.	0.6	1288 [†]	27.3	3.1 x 5.6 x 3.0
	Tibia		1288	27.2	3.1 x 5.4
			1282	25.4	3.0 x 5.4
			1278	21.7	3.0 x 4.6
			1274	12.2	2.3 x 4.4
			1262	8.6	2.0 x 4.1
			1204		(?)
			1110*		(?)
			982*		N.V.
<u>F9R5</u> (A2)	Dist. L.	0.4	1288 [†]	98.0	4.6 x 7.4 x 5.5
	Tibia		1288	132.7	5.7 x 7.8
			1282	71.0	4.4 x 7.0
			1278	55.4	4.2 x 6.0
			1274	20.3	3.0 x 4.3
			1262	8.5	2.1 x 3.7
			1204*		?
			1110*		N.V.
<u>M8P1</u>	R. Ilium	0.3	3367 [†]	393.3	8.8 x 9.7
			3367	307.2	7.9 x 9.4
			3354	222.6	7.2 x 8.2
			3324	27.1	3.6 x 4.0
			3279*		(2.3 x 2.7)
			3102*		N.V.
<u>M3P2</u>	Prox. L.	0.4	3185 [†]	236.1	8.7 x 7.3 x 7.1
	Femur		3185	302.1	8.6 x 7.8
			3164	217.8	8.0 x 6.5
			3132	48.7	4.6 x 4.4
			3102	8.0	2.0 x 3.8
			3069	4.3	1.6 x 3.2
			3039	1.3	1.0 x 2.5
			2853*		(?)
			2685*		N.V.
<u>F9P2</u>	Dist. R.	0.5	2014 [†]	607.6	8.9 x 12.3 x 10.6
	Femur		2009	335.7	7.6 x 11.1
			1981	134.6	7.1 x 5.1
			1950	30.8	4.1 x 3.5
			1917	9.5	2.5 x 2.9
			1887		(1.4 x 2.4)
			1873		(1.3 x 2.0)
			1841		(1.2 x 1.7)
			1805*		(1.0 x 1.5)
			1600*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M4P3</u> (A1)	Prox. L. Humerus	0.8	1950 [†]	11.9	2.4 x 4.3 x 2.2
			1947	18.9	2.8 x 4.6
			1881	11.2	2.4 x 3.7
			1847	8.8	2.5 x 2.7
			1762	2.2	1.5 x 1.9
			1673		(?)
			1488*		(?)
			1304*		N.V.
<u>M3P4</u>	L. 10th Rib	0.2	1198 [†]	1166.7	13.8 x 11.7
			1198	1414.3	14.7 x 12.5
			1187	1220.6	14.3 x 11.4
			1171	472.8	10.9 x 7.6
			1086		?
			1036*		?
			970*		N.V.
<u>F5P4</u>	3rd Lum- bar Vert- ebra	0.8	1245 [†]	39.5	3.9 x 4.4 x 4.4
			1245	22.4	3.6 x 3.3
			1212	11.6	3.1 x 2.3
			1195	5.5	2.3 x 2.0
			1169	2.2	1.8 x 1.3
			1157		?
			1141		?
			1132		?
			1099		?
			1052*		?
			999*		N.V.
<u>F9P4</u>	Prox. L. Radius	0.9	1343 [†]	55.6	4.0 x 5.9 x 4.5
			1343	47.5	4.1 x 5.4
			1307	16.0	2.8 x 3.9
			1271	1.6	1.2 x 2.1
			1242*	1.0	1.0 x 1.9
			1019*		N.V.
<u>M1P5</u>	Prox. L. Femur	0.5	1324 [†]	243.3	6.5 x 11.0
			1324	176.6	6.3 x 8.5
			1309	124.7	6.1 x 6.4
			1302	97.7	5.2 x 6.9
			1289	32.5	3.8 x 4.3
			1264	1.5	1.0 x 2.9
			1213*	(0.1)	(0.4 x 0.7)
			1151*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M4P5</u>	Mid. R. Ulna	0.4	1562 [†]	30.6	2.9 x 7.2 x 2.8
			1562	27.9	2.8 x 6.8
			1545	5.1	1.6 x 3.8
			1507	1.7	1.1 x 2.7
			1316*		(?)
			1143*		N.V.
<u>F5M1.7</u> (A1)	Mid. R. Femur	0.8	3234 [†]	145.5	5.7 x 7.5 x 6.5
			3200	37.2	3.5 x 5.8
			3170	8.2	2.0 x 3.9
			3137	2.6	1.2 x 3.5
			2969*		?
			2792*		N.V.
<u>F1M2</u>	Dist. R. Femur	0.2	1780 [†]	72.4	4.8 x 6.7 x 4.3
			1780	45.4	4.6 x 4.1
			1771	34.9	4.3 x 3.6
			1738	6.5	2.0 x 3.1
			1652		(1.4 x 2.0)
			1554*		(0.9 x 1.4)
			1373*		N.V.
<u>M4M2</u>	Prox. R. Humerus	0.6	2282 [†]	262.7	7.3 x 8.7 x 7.9
			2282	234.9	7.1 x 8.0 x 7.9
			2250	84.1	5.1 x 6.7 x 4.7
			2222	33.0	4.2 x 5.0 x 3.0
			2191		?
			2158		?
			2106*		?
			1913*		N.V.
<u>F11T1.5</u>	Prox. R. Humerus	0.2	2408 [†]	314.3	7.5 x 11.6 x 6.9
			2408	211.3	6.2 x 10.5
			2389	98.9	4.8 x 8.2
			2327	45.2	3.7 x 6.3
			2297	19.3	2.5 x 5.9
			2239	11.9	2.2 x 4.7
			2204	5.8	1.8 x 3.4
			2173		(1.3 x 3.4)
			2145		(1.3 x 3.6)
			2114		(1.0 x 3.2)
			2086		(1.2 x 3.0)
			2053		(0.8 x 2.7)
			1890*		(0.6 x 1.7)
			1693*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M7T2</u> (A1)	R. 10th Rib	0.2	1015 [†]	34.9	3.0 x 7.4
			1015	31.7	2.9 x 7.2
			995	22.7	2.6 x 6.4
			965	12.5	1.9 x 6.6
			932	8.9	1.7 x 5.9
			764*	0.7	0.7 x 2.6
			582*		N.V.
<u>M1T3</u> (A1)	Dist. L. Femur	0.5	988 [†]	103.2	6.3 x 6.8 x 4.6
			988	81.7	5.1 x 6.0
			959	17.2	2.8 x 4.2
			945	8.9	2.2 x 3.5
			840*		?
			774*		N.V.
<u>F6T3</u> (A1)	Prox. R. Femur	0.6	1156 [†]	367.9	8.3 x 8.3 x 10.2
			1156	245.3	8.3 x 6.8
			1126	60.3	4.9 x 4.8
			1088	6.0	2.1 x 2.6
			987*		?
			791*		N.V.
<u>M5S4.5</u>	Prox. L. Tibia	0.4	993 [†]	824.0	11.5 x 11.9
			952	57.3	4.2 x 6.2
			919	8.6	2.2 x 3.4
			888	2.6	1.4 x 2.5
			778*		(?)
			566*		N.V.
<u>F1S5</u>	Dist R. Femur	0.3	960 [†]	915.2	10.8 x 11.9 x 13.6
			960	246.8	6.9 x 9.9
			923	29.2	3.6 x 4.3
			904	6.8	1.9 x 3.6
			892		(1.7 x 3.3)
			882		(1.7 x 3.2)
			871*		(1.3 x 2.5)
			715*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M6S5A</u>	L. 8th Rib	0.5	1021 [†]	969.4	11.5 x 14.0
			1021	1040.5	12.0 x 13.8
			1008	591.1	11.2 x 9.0
			986	116.6	5.9 x 6.4
			972	34.8	3.8 x 4.6
			947	6.2	2.1 x 2.7
			896*	0.9	1.0 x 1.7
			709*		N.V.
<u>T1R5</u>	Prox. R. Tibia	0.8	1074 [†]	597.3	10.5 x 11.2 x 9.7
			1071	397.4	8.8 x 9.8
			1059	321.6	8.5 x 8.5
			1032	53.6	4.2 x 5.8
			976*		(?)
			694*		N.V.
<u>T18R5H</u>	Dist R. Humerus	0.4	1226 [†]	37.7	3.9 x 4.5 x 4.1
			1219	8.5	2.5 x 2.6
			1184	3.8	1.9 x 2.0
			1151	0.9	1.1 x 1.4
			1119	0.3	0.8 x 1.0
			1086		(0.7 x 0.7)
			1056		(0.6 x 0.6)
			1024*		(?)
			993*		N.V.
<u>T19R5H</u>	R. Tibial Tarsal	0.6	1219 [†]	76.4	4.6 x 6.9 x 4.6
			1219	66.9	4.4 x 6.6
			1189	11.4	2.3 x 4.1
			1158	1.5	1.3 x 1.7
			1127	0.4	0.8 x 1.3
			1093		(0.6 x 1.3)
			1063		(0.6 x 1.1)
			1032		(0.5 x 0.8)
			1002*		(0.4 x 0.7)
<u>T26R4H</u> (A1)	Prox. R. Tibia	0.7	884*		N.V.
			1780 [†]	60.7	4.0 x 6.9 x 4.2
			1780	30.2	3.1 x 6.0
			1753	14.4	2.2 x 5.7
			1722	6.7	1.6 x 5.0
			1639		(?)
			1575*		(?)
			1485*		N.V.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T27R4H</u> (A1)	Dist. R. Tibia	0.6	1414 [†]	30.0	3.7 x 4.7 x 3.3
			1414	29.2	3.6 x 4.3
			1401	16.0	3.3 x 2.8
			1367	2.0	1.3 x 2.3
			1336		(?)
			1246*		(?)
			1056*		N.V.
<u>T34R3¹</u>	Dist. R. Femur	0.6	1618	106.8	5.4 x 6.4 x 5.9
			1613	87.5	5.1 x 6.3 x 5.2
			1606	72.4	4.9 x 6.0 x 4.7
			1597	52.5	4.3 x 5.3 x 4.4
			1577	15.4	3.4 x 4.8 x 1.8
			1459*		(?)
			1276*		N.V.
<u>T38R4</u>	Prox. L. Humerus	0.6	1503 [†]	84.2	4.8 x 6.7 x 5.0
			1503	31.4	3.5 x 4.9
			1489	13.1	2.6 x 3.7
			1468*	4.0	1.6 x 3.0
			1302*		N.V.
<u>T70R3</u> (A1)	Prox. R. Tibia	0.4	1996 [†]	321.6	7.5 x 11.7 x 7.0
			1996	305.5	7.6 x 10.1
			1993	268.7	7.2 x 9.9
			1961	68.2	4.7 x 5.9
			1930	22.0	2.9 x 5.0
			1898	6.1	1.8 x 3.6
			1786*		?
			1588*		N.V.
<u>T51P5</u> (A1)	Dist. R. Humerus	0.2	1055 [†]	64.9	5.2 x 5.3 x 4.5
			1055	60.3	4.9 x 4.8
			1041	45.6	4.5 x 4.3
			1002	25.1	3.7 x 3.5
			971	8.1	2.6 x 2.3
			943		?
			930		(?)
			881		(?)
			***		***

¹ Tumor Dimensions before Sr⁸⁹ therapy. For further information on this tumor see "Sr⁸⁹ Therapy of a Canine Osteosarcoma," R. D. Lloyd, et al., Research in Radiobiology, University of Utah Report COO-119-229, Mar. 31, 1964, pp. 152-169.

Beagle Osteosarcoma Data - "A" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T2Q4</u>	R. Ilium	0.9	2317 [†]	99.5	4.4 x 7.2 x 6.0
(A1)			2317	59.8	4.4 x 5.9
			2312	50.2	4.1 x 5.7
			2281	16.8	2.8 x 4.1
			2245	6.3	2.0 x 3.0
			2179	0.8	0.9 x 1.9
			2151		?
			2120*		?
			2051*		N.V.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M2R2</u>	Dist. L. Femur	0.1	3775 [†]	50.9	4.7 x 4.4
			3714	4.8	2.4 x 1.6
			3693		(1.5 x 1.3)
			3663		(1.1 x 1.5)
			3629		(1.1 x 1.3)
			3600*		(0.6 x 0.8)
			3406*		N.V.
<u>M5R3</u> (B1)	Prox. L. 4th Phalanx	0.4	2955 [†]	3.4	1.8 x 2.0
			2918	2.7	1.7 x 1.8
			2884	1.5	1.3 x 1.7
			2831*		?
			2740*		N.V.
<u>F3R4A</u> (B1)	3rd. Thor. Vertebra	0.5	1614 [†]	0.7	0.8 x 2.0
			1606	0.6	0.8 x 1.8
			1572	0.1	0.5 x 1.1
			1550		?
			1482*		(0.1 x 0.2)
			1298		N.V.
<u>F3R4A</u> (B2)	R. 3rd Metacar- pal	0.2	1614 [†]	29.5	3.2 x 5.5
			1606	25.9	3.0 x 5.5
			1572	1.4	0.9 x 3.3
			1550		?
			1482		?
			1405*		?
			1298*		N.V.
<u>M5R4</u> (B1)	L. Zygo- matic Arch	0.1	1659	46.6	3.7 x 6.5
			1652	23.6	3.1 x 4.7
			1649		?
			1644		?
			1626	1.8	1.3 x 2.0
			1448*		(0.9 x 2.1)
			1255*		N.V.
<u>F6R4</u> (B1)	R. Isch- ium	0.6	1939 [†]	2.2	2.0 x 1.6 x 1.3
			1939	2.9	1.7 x 1.9
			1914	0.7	1.0 x 1.3
			1886		(0.9 x 0.9)
			1856		(0.8 x 0.9)
			1822		(0.7 x 0.7)
			1791*		(0.5 x 0.4)
			1760*		N.V.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9R4</u> (B1)	R. Isch- ium	0.8	1471 [†]	24.8	3.4 x 4.1
			1471	19.4	3.3 x 3.4
			1451	5.8	2.1 x 2.5
			1379*	0.7	0.9 x 1.6
			1156*		N.V.
<u>M2R5</u> (B1)	Dist L. Femur	0.2	1380 [†]	8.5 ¹	2.0 x 2.9 x 2.8
			1353	0.4	0.7 x 1.6
			1333		(?)
			1318		(?)
			1297*		(?)
			1261*		N.V.
<u>M2R5</u>	Prox. L. Femur	0.2	1220 [†]	165.4	7.5 x 7.8 x 5.4
			1220	186.4	7.4 x 6.5
			1189	103.9	5.8 x 5.9
			1157	10.1	2.5 x 3.1
			1036*		(?)
			863*		N.V.
<u>F9R5</u> (B1)	Dist. L. Femur	0.2	1288 [†]	3.3	1.3 x 3.0 x 1.6
			1288	2.7	1.3 x 3.0
			1262	1.1	0.9 x 2.5
			1222		(?)
			1204		(?)
			1110*		(?)
			982*		N.V.
<u>F2P1.7</u>	R. Isch- ium	0.3	3430 [†]	163.0	6.2 x 8.1
			3430	166.3	6.3 x 8.0
			3424	114.9	5.6 x 7.0
			3410	21.7	3.3 x 3.8
			3242*		(1.6 x 1.5)
			3055*		N.V.
<u>F6P1.7</u>	L. Isch- ium	0.8	2221 [†]	49.7	4.4 x 4.9
			2221	50.9	4.5 x 4.8
			2178	12.7	2.8 x 3.1
			2074*		?
			1885*		N.V.
<u>M11P2</u>	Prox. L. Humerus	0.8	1617 [†]	98.1	5.1 x 7.2
			1617	42.1	3.6 x 6.2
			1570	6.0	1.9 x 3.2
			1361*		(0.7 x 1.5)
			1197*		N.V.

¹A volume of 6.1 cm³ (an ellipsoid 2.0 x 2.9) was used in calculating the fitted slope.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F7P3</u>	Prox. L. Femur	0.9	1627 [†]	131.1	5.4 x 7.6 x 6.1
			1626	76.5	5.2 x 5.4
			1596	31.4	4.2 x 3.4
			1549*		(1.5 x 1.5)
			1340*		N.V.
<u>F10P3</u>	R. & L. Ischium	0.8	1547	27.2	3.1 x 5.4
			1520	20.3	2.9 x 4.6
			1367*		N.V.
<u>M1P4</u> (B1)	Prox. R. Humerus	0.4	1724 [†]	17.4	3.3 x 3.6 x 2.8
			1723	13.7	2.7 x 3.6
			1703	8.3	2.3 x 3.0
			1618*		(0.7 x 1.7)
			1450*		N.V.
<u>F2P4</u> (B1)	Sacrum	0.9	1556 [†]	27.2	3.9 x 3.7 x 3.6
			1556	17.1	3.3 x 3.0
			1544	8.1	2.4 x 2.7
			1538	8.2	2.5 x 2.5
			1359*		?
			1326*		N.V.
<u>M4P4</u>	Prox R. Femur	0.3	1066 [†]	363.2	8.2 x 9.4 x 9.0
			1065	201.0	6.8 x 8.3
			1037	13.7	2.7 x 3.6
			1009		?
			966*		N.V.
<u>F6P5</u>	R. Isch- ium	0.4	1193	79.8	5.0 x 6.1
			1132	1.7	1.4 x 1.7
			1034*		N.V.
<u>F7P5</u>	Mid. L. Humerus	0.5	1491 [†]	16.0	2.7 x 4.2 x 2.7
			1491	19.8	2.9 x 4.5
			1479	8.1	2.1 x 3.5
			1443	2.4	1.3 x 2.7
			1404		(?)
			1367		(?)
			1337*		(?)
			1305*		N.V.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
M6M1.7	Dist. R. Femur	0.2	3424 [†]	313.4 ²	7.0 x 11.4 x 7.5
			3383	4.4	1.6 x 3.3
			3352	0.6	0.6 x 3.3
			3256*		(?)
			3166*		N.V.
F5M2	Prox. L. Ulna	0.2	2688 [†]	46.0	4.1 x 5.5 x 3.9
			2688	68.8	4.8 x 5.7
			2631	5.5	1.6 x 4.1
			2599		(1.0 x 2.5)
			2564		(1.6 x 3.7)
			2533		(1.5 x 3.8)
			2498		(0.7 x 3.7)
			2465*		(0.6 x 3.2)
M10M2	L. 7th Rib	0.3	2373 [†]	114.0	5.7 x 6.7
			2373	157.1	6.5 x 7.1
			2362	72.0	4.6 x 6.5
			2242		?
			2036*		?
			1857*		N.V.
M4M3	L. Ilium	0.8	1176 [†]	46.5	3.8 x 5.7 x 4.1
			1172	31.2	3.1 x 6.2
			1140	6.5	2.0 x 3.1
			972*		N.V.
M12M3 (B1)	Mid. R. Humerus	0.4	1638 [†]	63.3	4.5 x 6.4 x 4.2
			1638	47.1	4.2 x 5.1
			1631	36.0	4.0 x 4.3
			1603		?
			1574		?
			1543		?
			1511		?
			1479		?
			1448		?
			1263*		?
F1M4	R. Olec- ranon	0.1	1065*		N.V.
			841 [†]	2.9	1.6 x 2.2
			841	2.8	1.5 x 2.4
			834	0.9	0.9 x 2.1
			766		(0.5 x 0.8)
			737*		(?)
			714*		N.V.

²A volume of 292.5 cm³ (an ellipsoid 7.0 x 11.4) was used in calculating the fitted slope.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M2T1.5</u>	Prox. R. Femur	0.4	2576 [†]	40.6	4.0 x 5.7 x 3.4
			2576	14.9	2.6 x 4.2
			2564	8.1	2.2 x 3.2
			2547	2.3	1.2 x 3.1
			2528*		(?)
			2403*		N.V.
<u>M4T2A</u> (Bl)	Prox. R. Humerus	0.8	1222 [†]	140.2	6.0 x 7.2 x 6.2
			1222	75.2	4.7 x 6.5
			1197	33.9	3.6 x 5.0
			1167		?
			1127		(?)
			934*		(?)
			774*		N.V.
<u>M5T2</u>	L. 6th Rib	0.4	1085 [†]	247.4	6.5 x 9.2 x 7.9
			1085	451.8	8.7 x 11.4
			1060	137.8	5.7 x 8.1
			953*		?
			757*		N.V.
<u>F12T2</u> (Bl)	L. Mand- ible	0.7	1449 [†]	20.7	2.9 x 4.7 x 2.9
			1449	25.7	3.5 x 4.0
			1428	16.0	2.8 x 3.9
			1262*		?
			1064*		N.V.
<u>F6T3</u> (Bl)	Dist. R. Tibia	0.8	1156 [†]	17.6	3.0 x 4.0 x 2.8
			1156	19.3	3.2 x 3.6
			1126	3.5	1.5 x 3.0
			1088*		(?)
			987*		N.V.
<u>F9T3</u> (Bl)	R. Mand- ible	0.2	1062 [†]	59.1	4.7 x 5.0 x 4.8
			1062	43.6	4.3 x 4.5
			1048	28.0	3.8 x 3.7
			951*		(?)
			762*		N.V.
<u>M3S5</u>	Prox R. Tibia	0.2	2256 [†]	252.4 ³	7.3 x 9.3 x 7.1
			2233	17.2	2.7 x 4.5
			2199		(0.7 x 2.0)
			2163*		(0.6 x 2.1)
			2131*		N.V.

³A volume of 259.5 cm³ (an ellipsoid 7.3 x 9.3) was used in calculating the fitted slope.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F8S5</u>	R. Ilium	0.5	1469 [†]	269.4	8.0 x 9.6 x 6.7
			1469	403.2	9.1 x 9.3
			1456	225.3	7.2 x 8.3
			1301*		N.V.
<u>T20R5H</u>	Dist R. Humerus	0.4	1330 [†]	132.3	6.0 x 7.8 x 5.4
			1330	107.4	5.3 x 7.3
			1296	30.8	3.5 x 4.8
			1266	9.0	2.4 x 3.0
			1234*		?
			1206*		N.V.
<u>T26R4H</u> (Bl)	Prox. L. Tibia	0.2	1780 [†]	307.2	7.7 x 12.7 x 6.0
			1780	287.7	7.2 x 10.6
			1753	29.7	2.6 x 8.4
			1722	15.2	2.3 x 5.5
			1639		(1.4 x 3.7)
			1575		(0.9 x 2.8)
			1485*		(?)
			1393*		N.V.
<u>T32R3</u>	Dist. L. Humerus	0.3	2249 [†]	209.9	6.2 x 10.6 x 6.1
			2249	229.4	7.4 x 8.0
			2218	96.7	5.1 x 7.1
			2204	53.6	4.2 x 5.8
			2191		?
			2051*		?
			1865*		N.V.
<u>T33R3</u>	R. Occip- ital Bone	0.7	1822 [†]	12.4	2.2 x 4.9
			1822	20.1	2.8 x 4.9
			1816	11.6	2.3 x 4.2
			1791*		?
			1603*		N.V.
<u>T36R4</u>	R. 6th Rib	0.3	1154 [†]	317.5	8.6 x 8.2
			1154	305.9	8.6 x 7.9
			1131	44.4	4.0 x 5.3
			937*		?
			728*		N.V.
<u>T37R4</u>	L. Pari- etal Bone	0.3	1627 [†]	242.1 ⁴	7.7 x 7.7 x 7.8
			1615	59.8	4.6 x 5.4
			1602	3.6	1.8 x 2.1
			1572*	0.3	0.6 x 1.7
			1539*		N.V.

⁴A volume of 239.0 cm³ (an ellipsoid 7.7 x 7.7) was used in calculating the fitted slope.

Beagle Osteosarcoma Data - "B" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T8T3</u>	R. Ilium	0.4	1043 [†]	77.7	4.6 x 6.2 x 5.2
			1043	67.9	4.1 x 6.2 x 5.1
			1025	15.2	2.6 x 4.0 x 2.8
			965		?
			933*		?
			903*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M5R1.7</u>	Cribiform Plate	0.2	4107 [†] 4115 3954*	1.4	1.1 x 2.2 ? N.V.
<u>M5R2</u>	L. Maxilla	0.8	4703 [†] 4703 4537 4418* 4367*	39.3	3.4 x 6.5 ? ? ? N.V.
<u>M7R2</u>	L. Ischium	0.7	3424 [†] 3424 3398 3321 3216 3026* 2914*	157.1	6.5 x 7.1 ? ? ? ? ? N.V.
<u>M1OR2</u>	Dist. R. Femur	0.2	3569 [†] 3569 3555 3549 3464 3369 3278* 3199*	174.1	5.6 x 10.6 ? ? ? ? ? ? N.V.
<u>F11R2</u>	Prox. L. Femur	0.2	3297 [†] 3297 3270 3269 3213 3117 3026* 2849*	110.3	4.8 x 5.7 x 7.7 ? ? ? ? ? ? N.V.
<u>M1R3</u>	Prox. R. Radius	0.2	2850 [†] 2850 2838 2770 2710* 2507*	56.3	4.1 x 6.4 ? ? ? (?) N.V.
<u>F3R3</u>	L. Frontal Bone	0.6	2497 [†] 2491 2410* 2210*	35.9	3.5 x 5.6 ? ? N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M4R3</u>	Mid. R. Femur	0.3	1917 [†]	429.9	9.2 x 9.7
			1916	553.2	9.8 x 11.0
			1820		?
			1660*		?
			1461*		N.V.
<u>M5R3</u> (C1)	Prox. L. Femur	0.3	2955 [†]	509.6	9.2 x 11.5
			2955		?
			2918		?
			2831*		?
			2740*		N.V.
<u>F6R3</u> (C1)	Dist. L. Humerus	0.8	1932 [†]	7.1	2.0 x 3.4
			1932	6.9	2.0 x 3.3
			1920	6.1	2.0 x 2.9
			1883	5.4	1.8 x 3.2
			1851		?
			1820		?
			1781		(1.6 x 3.4)
			1646		(0.8 x 2.4)
			1424*		(0.5 x 2.6)
			1238*		N.V.
<u>F6R3</u> (C2)	Prox. L. Tibia	0.2	1932 [†]	37.0	3.8 x 4.9
			1932		?
			1920		?
			1883		(?)
			1851		(?)
			1820		(?)
			1781*		(?)
			1646*		N.V.
<u>M7R3</u>	2nd Cerv. Vertebra	0.2	2099 [†]	12.6	1.8 x 3.6 x 3.7
			2089		?
			1975*		(?)
			1812*		N.V.
<u>F8R3</u>	Prox. L. Humerus	0.2	2612 [†]	208.1	6.8 x 7.9 x 7.4
			2612		?
			2596		?
			2564		?
			2534		?
			2502		(?)
			2473		(?)
			2442*		(?)
			2411*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9R3</u>	Prox. R. Mandible	0.4	2487 [†]	21.0	3.6 x 3.1
			2481		?
			2398*		?
			1940*		N.V.
<u>M10R3</u>	7th Cerv. Vertebra	0.1	1737 [†]	2.2	1.5 x 1.9
			1734		?
			1695*		?
			1526*		N.V.
<u>M1R4</u>	Prox. L. Tibia	0.6	1606 [†]	4.2	1.3 x 4.4 x 1.4
			1606	3.8	1.3 x 4.3 x 1.3
			1593	3.2	1.3 x 3.9 x 1.2
			1514*		(?)
			1427*		N.V.
<u>M2R4</u> (C1)	3rd Thor. Vertebra	0.6	1884 [†]	1.1	1.1 x 1.7
			1883	1.8	1.4 x 1.8
			1849	1.0	1.1 x 1.6
			1820	1.0	1.1 x 1.6
			1653*		?
			1463*		N.V.
<u>M2R4</u> (C2)	R. 5th Metatar- sal	0.2	1884 [†]	0.6	0.8 x 1.7
			1883	0.6	0.8 x 1.7
			1849	0.1	0.5 x 1.1
			1820*		(0.4 x 0.7)
			1653*		N.V.
<u>F3R4A</u> (C1)	Prox. L. Tibia	0.4	1614 [†]	8.8	2.5 x 2.7
			1606	1.6	1.3 x 1.8
			1572		(1.1 x 1.8)
			1550		(?)
			1482*		(?)
			1298*		N.V.
<u>M4R4</u>	Dist. L. Femur	0.4	1518 [†]	52.3	4.6 x 6.2 x 3.5
			1513	14.2	2.4 x 4.7
			1468		(1.6 x 3.0)
			1433		(0.9 x 3.0)
			1380		(0.8 x 1.8)
			1303*		(?)
			1111*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F6R4</u> (C1)	L. Ilium	0.2	1939 [†]	5.1	2.8 x 2.9 x 1.2
			1939		?
			1914		?
			1886		(?)
			1856		(?)
			1822		(?)
			1791*		(?)
			1760*		N.V.
<u>F6R4</u> (C2)	Sacrum	0.1	1939 [†]	30.1	3.5 x 4.7
			1939	10.6	2.9 x 2.4
			1914		(?)
			1886		(?)
			1856		(?)
			1822		(?)
			1791		(?)
			1760*		(?)
			1730*		N.V.
<u>F8R4</u>	L. Ace- tabulum	0.6	1324 [†]	20.0	3.0 x 4.1 x 3.1
			1324	15.6	2.7 x 4.1
			1282		?
			1190*		N.V.
<u>F9R4</u> (C1)	3rd Cerv. Vertebra	0.2	1471 [†]	3.2	1.8 x 1.9
			1471	3.6	1.9 x 1.9
			1451		?
			1379*		?
			1156*		N.V.
<u>M10R4</u>	2nd Thor. Vertebra	0.2	1553 [†]	3.5	1.6 x 2.6
			1547		?
			1455*		N.V.
<u>F11R4</u>	R. Mandi- ble	0.5	1469 [†]	58.6	3.7 x 5.4 x 5.6
			1469	29.1	3.3 x 5.1
			1450	9.2	2.1 x 4.0
			1382*		?
			1193*		N.V.
<u>F12R4</u>	2nd Cerv. Vertebra	0.5	1435 [†]	0.3	0.7 x 1.2
			1434	0.6	0.9 x 1.4
			1309*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M1R5</u>	6th Lumb. Vertebra	0.1	908 [†]	5.4	1.8 x 2.3 x 2.5
			891	2.4	1.4 x 2.3
			686*		N.V.
<u>M4R5</u>	7th Lumb. Vertebra	0.7	1091 [†]	120.9	5.2 x 7.4 x 6.0
			1085	76.9	4.3 x 6.1 x 5.6
			971*		?
			954*		N.V.
<u>F6R5</u>	Dist. R. Humerus	0.2	1015 [†]		?
			1014	415.6	9.0 x 9.8
			828*		(?)
			723*		N.V.
<u>M7R5</u>	Dist. R. Tibia	0.4	1288 [†]	19.8	2.6 x 5.6
			1287	15.0	2.2 x 5.9
			1283	14.4	2.2 x 5.7
			1262		(1.9 x 5.4)
			1231		(1.1 x 5.2)
			1179		(1.1 x 5.5)
			958		(0.9 x 4.1)
			797		(0.9 x 2.3)
			783*		(0.5 x 1.4)
			766*		N.V.
<u>M1OR5</u>	Prox. L. Tibia	0.1	825 [†]	10.8	(3.0 x 2.3 x 3.0)
			825		(2.6 x 2.3)
			635*		(?)
			463*		N.V.
<u>M1P1</u>	L. 4th Rib	0.3	4572 [†]	165.9	6.0 x 8.8
			4572		?
			4571		?
			4419		?
			4238*		?
			4117*		N.V.
<u>M3P1</u>	Sacrum	0.2	4292 [†]	64.8	4.7 x 5.6
			4292		?
			4272		?
			4270		?
			4202*		?
			4012*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9Pl</u>	6th Thor. Vertebra	0.2	2257 [†]	310.4	7.0 x 12.1
			2255	222.4	5.9 x 12.2
			2233		?
			2229		?
			2205		?
			2153*		N.V.
<u>M1Pl.7</u>	2nd Cerv. Vertebra	0.1	3025 [†]	1.2	0.9 x 2.9
			3025	1.8	1.1 x 2.9
			3023		?
			3009		?
			2838*		N.V.
<u>M4Pl.7</u>	Prox. R. Scapula	0.4	3312 [†]	425.3	8.8 x 13.0 x 7.1
			3312		?
			3277		?
			3172*		?
			2960*		N.V.
<u>F5Pl.7</u>	L. 2nd Rib	0.2	2659 [†]	206.4	7.4 x 7.2
			2659		?
			2642		?
			2460*		N.V.
<u>F7Pl.7</u>	Prox. L. Humerus	0.4	3353 [†]	331.3	7.8 x 10.4
			3353		?
			3325		?
			3311		?
			3172*		N.V.
<u>M8Pl.7</u>	L. Ilium	0.2	3282 [†]	165.0	6.2 x 8.2
			3282		?
			3271		?
			3171*		N.V.
<u>F9Pl.7</u>	3rd Lumb. Vertebra	0.4	2500 [†]	131.5	5.5 x 8.3
			2500		?
			2479		?
			2437*		?
			2245*		N.V.
<u>F10Pl.7A</u>	L. 3rd Tarsal Bone	0.2	4214 [†]	180.2	6.6 x 7.9
			4214	217.6	7.3 x 7.8
			4181*		?
			3778*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days-P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M1P2</u>	12th Thor. Vertebra	0.3	2985 [†]	6.6	1.9 x 3.0 x 2.2
			2985		?
			2982		?
			2976		?
			2965		?
			2963		?
			2892*		N.V.
<u>F2P2</u>	Mid. L. Femur	0.4	2780 [†]	228.5	7.9 x 8.5 x 6.5
			2774	232.8	7.7 x 7.5
			2577*		N.V.
<u>M4P2</u>	2nd Lumb. Vertebra	0.1	2948 [†]	2.6	2.7 x 2.6 x 0.7
			2948		?
			2941		?
			2925		?
			2924		?
			2770*		N.V.
<u>F5P2</u>	3rd Lumb. Vertebra	0.4	2423 [†]	2.0	1.1 x 1.8 x 1.9
			2423		?
			2410		?
			2291*		N.V.
<u>F6P2</u>	L. Fron- tal Bone	0.3	2947 [†]	7.1	2.2 x 2.8
			2947		?
			2933		?
			2918		?
			2865*		N.V.
<u>F10P2</u>	8th Thor. Vertebra	0.2	2912 [†]	0.4	0.8 x 1.3
			2912		(?)
			2900		(?)
			2856*		(?)
			2824*		N.V.
<u>M12P2</u>	L. Scap- ula	0.5	2284 [†]	102.7	5.4 x 7.9 x 4.6
			2284		?
			2248		?
			2213		?
			2169		(?)
			2078*		(?)
			1984*		N.V.
<u>M1P3</u> (CI)	4th Lumb. Vertebra	0.4	1476 [†]	3.9	1.8 x 2.2 x 1.9
			1474		(?)
			1461		(?)
			1435*		(?)
			1249*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M1P3</u> (C2)	5th Cerv. Vertebra	0.1	1476 [†]	1.4	2.2 x 1.2 x 1.0
			1474		?
			1461		?
			1435*		?
			1249*		N.V.
<u>F2P3</u>	R. Ilium	0.3	1947 [†]	101.9	5.9 x 7.5 x 4.4
			1946		?
			1857	9.8	2.5 x 3.0
			1785*		(?)
			1764*		N.V.
<u>M3P3</u>	Prox. R. Femur	0.4	1604 [†]	8.7	2.4 x 2.9 x 2.4
			1596		?
			1570		?
			1381*		N.V.
<u>M4P3</u> (C1)	4th Cerv. Vertebra	0.1	1951 [†]	2.0	1.3 x 1.7 x 1.7
			1947		?
			1912		?
			1881		?
			1847		?
			1762*		?
			1673*		N.V.
<u>F5P3</u>	2nd Lumb. Vertebra	0.1	1504 [†]	1.9	1.7 x 1.5 x 1.4
			1504		(1.6 x 1.6)
			1491		(1.4 x 1.2)
			1477*		(1.4 x 1.1)
			1183*		N.V.
<u>F6P3</u>	1st Thor. Vertebra	0.4	1617 [†]	2.3	2.1 x 1.3 x 1.6
			1617		?
			1608		?
			1504*		N.V.
<u>M8P3</u>	3rd Cerv. Vertebra	0.1	1771 [†]	0.6	1.1 x 1.0
			1771		1.0 x 1.0
			1766		?
			1606*		?
			1421*		N.V.
<u>F9P3</u>	4th Lumb. Vertebra	0.4	1894 [†]	4.2	1.8 x 2.5
			1886		?
			1802*		?
			1593*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M11P3</u>	Prox. R. Femur	0.2	1198 [†]	402.5	11.2 x 10.4 x 6.6
			1196		?
			1161		?
			1009*		N.V.
<u>M12P3</u>	6th Thor. Vertebra	0.3	1659 [†]	1.8	1.2 x 2.8 x 1.0
			1659		?
			1653		?
			1652		?
			1647		?
			1540*		N.V.
<u>M1P4</u> (Cl)	Prox. L. Femur	0.4	1724 [†]	64.9	6.3 x 4.8 x 4.1
			1723	80.2	5.9 x 4.4
			1710		?
			1703		?
			1618*		N.V.
<u>F2P4</u> (Cl)	6th Cerv. Vertebra	0.5	1556 [†]	16.7	3.5 x 2.6
			1556		?
			1544		?
			1538		?
			1359*		N.V.
<u>F6P4</u>	Prox. R. Tibia	0.2	1357 [†]	74.7	4.6 x 6.2 x 5.0
			1356	128.6	6.1 x 6.6
			1322		(?)
			1286		(?)
			1105*		(?)
			923*		N.V.
<u>F7P4</u>	L. Ilium	0.3	1194	30.0	3.2 x 5.6
			1162		(2.4 x 4.7)
			1120*		(1.0 x 2.9)
			939*		N.V.
<u>M8P4</u>	9th Thor. Vertebra	0.3	1157 [†]	5.3	2.6 x 1.4 x 2.8
			1157	4.9	2.5 x 1.4 x 2.7
			1150		?
			980*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F10P4</u>	7th Lumb. Vertebra	0.1	1241 [†]	1.2	1.1 x 1.9
			1241		?
			1233		?
			1214		?
			1186		N.V. ?
			***		***
<u>M11P4</u>	4th Lumb. Vertebra	0.6	1288 [†]	1.6	1.5 x 1.4
			1287		?
			1284		?
			1280		?
			1275		?
			1273		?
			***		***
<u>M12P4</u> (C1)	Mid. R. Ulna	0.5	1463 [†]	22.4	2.7 x 6.1 x 2.6
			1458	14.2	2.2 x 5.6
			1347*		(0.7 x 2.3)
			1331*		N.V.
<u>M12P4</u> (C2)	Prox. L. Humerus	0.2	1463 [†]	1.6	0.9 x 2.8 x 1.2
			1331*		N.V.
<u>M12P4</u> (C3)	L. 10th Rib	0.3	1463 [†]	4.1	1.8 x 2.4
			1458		?
			1331*		?
			1169*		N.V.
<u>F2P5</u>	L. Mandi- ble	0.1	1576 ⁺	4.6	2.0 x 2.2
			1576		?
			1444*		?
			1366*		N.V.
<u>F5P5</u>	Dist. L. Mandible	0.5	2059 [†]	1.1	1.0 x 1.6 x 1.3
			2002		?
			1820*		?
			1727*		N.V.
<u>F9P5</u>	Prox. R. Tibia	0.2	1145 [†]	7.4	2.1 x 3.2
			1133		?
			1041*		?
			938*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F2M1</u>	R. Maxi- lla	0.4	5267 [†] 5267 5260 4267 ***	44.1	3.4 x 8.0 x 3.1 ? ? N.V. ***
<u>M3M1</u>	7th Lumb. Vertebra	0.4	3157 [†] 3157 3156 3136 3114 3102* 2740*	3.9	1.5 x 1.9 x 2.6 ? ? ? ? ? ? N.V.
<u>F2M1.7</u>	R. Mand- ible	0.1	2383 [†] 2383 2375 2368 2170* 1968*	45.0	3.1 x 6.3 x 4.4 ? ? ? (?) N.V.
<u>M3M1.7</u>	L. Ilium	0.8	2709 [†] 2709 2691 2548* 2362*	54.6	5.4 x 4.6 x 4.2 ? ? (?) N.V.
<u>F5M1.7</u> (C1)	Mid L. Femur	0.6	3234 [†] 3234 3137* 2969*	9.8 2.6	1.9 x 4.3 x 2.3 1.1 x 4.1 (0.4 x 3.4) N.V.
<u>F7M1.7</u>	L. Ischium	0.3	2646 [†] 2646 2619 2460* 2277*	184.0	6.1 x 8.6 x 6.7 ? ? (?) N.V.
<u>F8M1.7</u>	R. Mand- ible	0.1	2486 [†] 2486 2431* 2242*	59.7	4.8 x 6.6 x 3.6 ? ? N.V.
<u>M9M1.7</u> (C1)	Mid. L. Ulna	0.7	2799 [†] 2791 2648*	25.9 16.7	3.0 x 5.9 x 2.8 2.5 x 5.1 N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M9M1.7</u> (C2)	4th Lumb. Vertebra	0.1	2799 [†] 2791 2648* 2445*	96.1	4.6 x 7.0 x 5.7 ? (?) N.V.
<u>M6M2</u> (C1)	L. 8th Rib	0.0	2674 [†] 2674 2654 2621 2453 2242* 2053*	26.9	3.0 x 5.7 ? ? ? ? ? ? N.V.
<u>M6M2</u> (C2)	5th Thor. Vertebra	0.2	2674 [†] 2674 2654 2621* 2453*	0.9	1.5 x 0.8 ? ? ? ? N.V.
<u>F8M2</u>	Prox. R. Humerus	0.2	2386 2337 2239* 2071*	206.3	7.2 x 7.6 (2.2 x 2.4) (?) N.V.
<u>M9M2</u>	5th Lumb. Vertebra	0.5	1254 [†] 1254 1224 1192 1162 1133 1100 1069 1041* 1010*	2.8	(1.9 x 1.9 x 1.5) (2.0 x 1.9 x 1.5) (1.8 x 1.8 x 1.5) (1.4 x 1.6 x 1.3) (1.4 x 1.3 x 1.0) (1.3 x 1.2 x 0.9) (1.2 x 1.2 x 0.9) (1.1 x 1.1 x 0.8) (0.7 x 0.9 x 0.6) N.V.
<u>M12M2</u>	R. Sca- pula	0.1	2471 [†] 2471 2451 2188* 2051*	167.0	5.9 x 11.5 x 4.7 ? ? ? N.V.
<u>F1M3</u>	3rd Lumb. Vertebra	0.3	918* 918 906 890 867 829 821* 765*	353.4 324.8	8.0 x 14.8 x 5.7 7.4 x 12.7 x 6.6 ? ? ? ? ? ? N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F2M3</u> (C1)	Sacrum	0.2	1856 [†]	85.5	4.0 x 6.8 x 6.0
			1841		?
			1809		?
			1778		?
			1746		?
			1712*		?
			1528*		N.V.
<u>F2M3</u> (C2)	Prox. R. Humerus	0.2	1856 [†]	14.4	2.7 x 3.4 x 3.0
			1841		?
			1809		(?)
			1778		(?)
			1712*		(?)
			1528*		N.V.
<u>M3M3</u>	3rd Cerv. Vertebra	0.1	1185 [†]	1.9	1.4 x 1.9
			1185		(1.4 x 1.7)
			1182		(1.3 x 1.6)
			1156		(0.9 x 1.6)
			1070*		(?)
			972*		N.V.
<u>F5M3</u>	Prox. R. Femur	0.4	1869 [†]	216.1	7.9 x 9.5 x 5.5
			1869	94.1	5.3 x 6.4
			1834		?
			1806*		(?)
			1709*		N.V.
<u>M6M3</u>	L. 7th Rib	0.8	1421 [†]	135.6	5.8 x 7.7
			1414	89.2	5.2 x 6.3
			1298*		N.V.
<u>F7M3</u>	2nd Cerv. Vertebra	0.2	1463 [†]	3.1	(1.6 x 2.3)
			1463		(1.3 x 2.5)
			1442		(1.2 x 2.3)
			1410		(0.6 x 2.1)
			1379		(0.6 x 2.1)
			1351		(?)
			1317		(?)
			1287		(?)
			1255*		(?)
			1224*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F8M3</u>	Prox. R. Radius	0.3	* 1447 [†]	126.0	5.8 x 6.8 x 6.1
			1447	172.0	6.9 x 6.9
			1416		?
			1344		?
			1146*		(?)
			958*		N.V.
<u>M9M3</u>	L. 6th Rib	0.2	1570 [†]	59.4	4.1 x 7.9 x 3.5
			1570	162.1	6.0 x 8.6
			1567		?
			1546		?
			1322*		N.V.
<u>M10M3</u> (C1)	L. Ilium	0.3	1575 [†]	102.5	5.3 x 7.1 x 5.2
			1575		?
			1562		?
			1399*		N.V.
<u>M10M3</u> (C2)	5th Stern- ebra	0.5	1575 [†]	21.7	3.6 x 3.2
			1575		?
			1562		?
			1387*		(?)
			1276*		N.V.
<u>F11M3</u>	L. Mand- ible	0.5	1395 [†]	29.5	3.8 x 3.9 x 3.8
			1395		?
			1372		?
			1256*		N.V.
<u>M12M3</u> (C1)	Prox. L. Humerus	0.3	1638 [†]	41.6	3.8 x 5.1 x 4.1
			1638		?
			1631		?
			1479*		?
			1488*		N.V.
<u>F2M4</u>	13th Thor. Vertebra	0.1	778 [†]	5.9	1.8 x 2.5 x 2.5
			778		?
			765		?
			733		?
			543*		N.V.
<u>M3M4A</u>	Mid L. Humerus	0.1	1063 [†]	1.2	1.0 x 2.3
			1063		?
			979*		(0.9 x 1.5)
			846*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F5M4</u>	Prox. L. Humerus	0.1	1064 [†]	142.1	5.4 x 7.5 x 6.7
			1063		?
			1018		?
			927		?
			834*		?
			737*		N.V.
<u>M6M4</u> (C1)	3rd Lumb. Vertebra	0.3	1121 [†]	3.6	1.7 x 2.4
			1119	3.9	1.8 x 2.3
			1058*		?
			966*		N.V.
<u>M6M4</u> (C2)	6th Thor. Vertebra	0.1	1121 [†]	0.6	1.2 x 1.0 x 0.9
			1119	0.5	1.0 x 1.0
			1058*		(?)
			966*		N.V.
<u>F7M4</u>	Dist. L. Femur	0.1	1253 [†]	176.2	7.5 x 6.6 x 6.8
			1239		?
			1116*		N.V.
<u>M6M5</u>	Prox. R. Tibia	0.1	792 [†]	2.7	2.0 x 1.5 x 1.7
			792	1.8	1.5 x 1.5
			766	1.3	1.3 x 1.5
			632*	0.6	1.1 x 0.9
			563*		N.V.
<u>M1T1</u>	8th Thor. Vertebra	0.9	3172 [†]	1.2	(1.3 x 1.3 x 1.3)
			3172		(1.2 x 1.0)
			3141*		(?)
			3007*		N.V.
<u>M4T1</u>	Prox. L. Humerus	0.4	3217 [†]	25.0	3.9 x 3.5 x 3.5
			3217		?
			3211	13.1	3.1 x 2.6
			3190		?
			3178*		?
			2821*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>MT1.5</u> (C1)	Mid. R. Radius	0.5	2894 [†]	13.2	(2.0 x 7.0 x 1.8)
			2894		(1.5 x 7.0)
			2882		(1.8 x 7.2)
			2848		(1.3 x 6.6)
			2817		(1.1 x 6.3)
			2651		(0.9 x 4.9)
			2447*		(0.8 x 3.0)
			2247*		N.V.
<u>MT1.5</u> (C2)	L. Pubis	0.2	2894 [†]	56.4	3.7 x 5.6 x 5.2
			2894		?
			2888		?
			2651*		N.V.
<u>M4T1.5</u>	Sacrum	0.2	2309 [†]	0.3	0.6 x 1.5
			2309		?
			2297		?
			2220*		N.V.
<u>M5T1.5</u>	L. Ilium	0.2	1624	854.6	10.1 x 16.0
			1583		?
			1506*		?
			1326*		N.V.
<u>F6T1.5</u>	9th Thor. Vertebra	1.0	2373 [†]	2.8	1.6 x 1.5 x 2.2
			2373		?
			2359	1.6	1.4 x 1.6
			2242*		N.V.
<u>M8T1.5</u> (C1)	Prox. L. Humerus	0.3	2665 [†]	44.3	4.0 x 4.5 x 4.7
			2665		?
			2648		?
			2613		?
			2581		?
			2560		?
			2529		?
			2499		?
			2472*		?
			2156*		N.V.
<u>M8T1.5</u> (C2)	8th Stern- ebra	0.0	2665 [†]	317.4	8.2 x 8.8 x 8.4
			2665		?
			2581		?
			2560*		?
			2472*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9T1.5</u>	Sphenoid Bone	0.2	2983 [†]	46.1	3.6 x 6.8
			2983		?
			2959		?
			2827		?
			2637*		?
			2444*		N.V.
<u>F10T1.5</u>	Prox. L. Femur	0.4	1859 [†]	114.2	6.1 x 6.5 x 5.5
			1859		?
			1817		(?)
			1659		(?)
			1476*		(?)
			1301*		N.V.
<u>F12T1.5</u>	11th Thor. Vertebra	0.3	2120 [†]	1.6	1.7 x 1.5 x 1.2
			2120		?
			2106		?
			2073		?
			2043		?
			2040*		?
			1886*		N.V.
<u>M1T2</u>	R. Ilium	0.2	1282 [†]	313.5 356.2	6.6 x 11.2 x 8.1
			1282		7.9 x 10.9
			1267		?
			1210		?
			1163		?
			949*		(?)
			732*		N.V.
<u>M2T2</u>	6th Thor. Vertebra	0.2	1234 [†]	66.9	3.8 x 5.6 x 6.0
			1233		?
			1232		?
			1221		?
			1172*		?
			1098*		N.V.
<u>F3T2</u> (C1)	R. Ischium	0.7	1541	16.5	3.0 x 3.5
			1507		?
			1443*		N.V.
<u>F3T2</u> (C2)	Prox. R. Humerus	0.5	1541 [†]	19.0 9.3	3.0 x 3.9 x 3.1
			1541		2.4 x 3.1
			1507		(?)
			1443*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M4T2A</u> (C1)	4th Thor. Vertebra	0.3	1222 [†] 1222 ***	1.5	1.5 x 1.3 ? ***
<u>F6T2</u>	1st Cerv. Vertebra	0.5	1108 [†] 1108 972*	5.9	2.7 x 2.0 x 2.1 ? N.V.
<u>M7T2</u> (C1)	Prox. L. Humerus	0.6	1015 [†] 1015 995 965 932 764* 582*	92.0	5.3 x 6.5 x 5.1 ? ? ? ? ? ? N.V.
<u>M8T2</u>	2nd Lumb. Vertebra	0.2	1078 [†] 1078 1069 957*	14.0	3.1 x 3.6 x 2.4 ? ? N.V.
<u>F9T2</u>	Sacrum	0.1	1209 [†] 1209 1203 1173 1142 1111* 946*	40.8	4.7 x 4.6 x 3.6 ? ? ? ? ? ? N.V.
<u>F10T2</u> (C1)	3rd Cerv. Vertebra	0.1	1022 [†] 1022 1006 942* 759*	2.0	1.8 x 1.5 x 1.4 ? ? ? ? N.V.
<u>F10T2</u> (C2)	5th Cerv. Vertebra	0.4	1022 [†] 1022 1006 759*	40.1	3.8 x 6.1 x 3.3 ? ? N.V.
<u>F11T2</u>	5th Cerv. Vertebra	0.3	1038 [†] 1038 1035 904* 715*	3.8	(1.8 x 1.9 x 2.1) (1.8 x 1.9) (?) (?) N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F12T2</u> (C1)	Prox. R. Tibia	0.2	1449 [†]	10.6	2.9 x 2.4
			1449		?
			1428		?
			1262*		?
			1064*		N.V.
<u>F12T2</u> (C2)	Prox. R. Femur	0.2	1449 [†]	2.1	1.4 x 2.6 x 1.1
			1449	2.4	1.3 x 2.7
			1428		?
			1262*		?
			1064*		N.V.
<u>F12T2</u> (C3)	Dist. R. Femur	0.2	1449 [†]	0.9	1.0 x 1.6 x 1.1
			1449		?
			1428		?
			1262*		?
			1064*		N.V.
<u>M1T3</u> (C1)	L. 11th Rib	0.1	988 [†]	867.3	10.0 x 16.4 x 10.1
			988		?
			982	648.9	9.0 x 15.3
			974		?
			966		?
			959		?
			945		?
			840*		?
			774*		N.V.
<u>M2T3</u>	5th Cerv. Vertebra	0.1	859 [†] ***	1.5	1.5 x 1.5 x 1.3 ***
<u>F3T3</u>	13th Thor. Vertebra	0.2	547 [†]	312.6	6.7 x 9.9 x 9.0
			547		?
			534		?
			527		?
			518		?
			515		?
			513		?
			511		?
			469*		?
			262*		N.V.
<u>M4T3</u>	3rd Cerv. Vertebra	0.3	801 [†]	4.2	2.3 x 2.2 x 1.6
			801	4.6	2.0 x 2.2
			794		?
			626*		(?)
			454*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>M5T3</u> (C1)	Prox. L. Humerus	0.4	890 [†]	250.3	6.8 x 8.9 x 7.9
			890		?
			862		?
			828		(?)
			798		(?)
			736		(?)
			643*		(?)
			566*		N.V.
<u>M5T3</u> (C2)	R. Pubis	0.3	890 [†]	23.6	3.0 x 5.0 x 3.0
			890	12.8	2.5 x 3.9
			862		?
			828		?
			798*		?
			736*		N.V.
<u>F6T3</u> (C1)	R. 10th Rib	0.2	1156 [†]	78.3	5.7 x 4.6
			1156		?
			1126		?
			987		?
			791*		?
			591*		N.V.
<u>F6T3</u> (C2)	L. Isch- ium	0.5	1156 [†]	22.4	3.6 x 3.6 x 3.3
			1156		?
			1126		?
			1088		(?)
			987*		(.1 x .4)
			791		N.V.
<u>M7T3</u> (C1)	Prox. R. Femur	0.2	861 [†]	136.8	5.4 x 8.2 x 5.9
			861		?
			832		?
			800		?
			769		(?)
			584*		(?)
			385*		N.V.
<u>M7T3</u> (C2)	L. Fron- tal Bone	0.8	861 [†]	6.3	2.2 x 2.2 x 2.5
			861		?
			832		?
			***		***
<u>M8T3</u>	Prox. L. Humerus	0.5	685 [†]	285.1	7.5 x 11.0 x 6.6
			685		?
			645		?
			555*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9T3</u> (C1)	Dist. L. Tibia	0.2	1062 [†] 1062 951* 762*	10.1	2.2 x 3.5 x 2.5 3.1 x 3.3 (?) N.V.
<u>F10T3</u>	R. Maxilla	0.5	971 [†] 971 963 942 759*	34.2 12.1 12.7	3.3 x 6.0 2.5 x 3.7 2.6 x 3.6 ? N.V.
<u>F11T3</u> (C1)	Dist. R. Radius	0.1	826 [†] 826 818 787 755* 715*	0.6	(0.8 x 2.0 x 0.7) (0.5 x 2.3) (0.6 x 1.8) (0.5 x 1.7) (?) N.V.
<u>F11T3</u> (C2)	5th Cerv. Vertebra	0.1	826 [†] 826 818 787 755*	1.6	(1.6 x 1.4 x 1.4) (1.5 x 1.5) (1.0 x 1.5) (?) N.V.
<u>F11T3</u> (C3)	7th Lumb. Vertebra	0.1	826 [†] 826 818 787 755* 715*	1.0	(1.2 x 1.3) (1.1 x 1.3) (1.0 x 1.1) (0.5 x 0.9) (?) N.V.
<u>M1T4</u>	Mid L. Radius	0.1	645 [†] 592* 490*	0.4	0.6 x 2.0 ? N.V.
<u>M2T4</u>	Mid R. Tibia	0.2	833 [†] 833 825 794 769 759 752 716 692* 660*	2.6 1.1 1.3	1.5 x 3.3 x 1.0 0.9 x 2.9 x 0.8 0.9 x 3.0 x 0.9 (0.8 x 2.5 x 0.6) (0.8 x 2.2) (0.8 x 2.1 x 0.5) (?) (?) (?) N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Day</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>F9S4.5</u>	R. Ilium	0.2	1028 [†]	134.3	5.5 x 8.8 x 5.3
			1028	94.3	4.9 x 7.5
			1023		?
			1007		?
			971*		(?)
			782*		N.V.
<u>M2S5A</u>	Sacrum	0.4	1740 [†]	123.7	5.6 x 7.4 x 5.7
			1739	31.1	?
			1735		3.2 x 5.8
			1703		?
			1679*		?
			1478*		N.V.
<u>F4S5</u>	L. Pari- etal Bone	0.6	1448 [†]	5.0	2.0 x 1.9 x 2.5
			1448		?
			1266*		N.V.
<u>T2R5</u>	6th Cerv. Vertebra	0.5	1368 [†]	2.8	1.5 x 1.7 x 2.1
			1364		?
			1340		?
			1334		?
			1326*		?
			1225*		N.V.
<u>T15R4</u> (C1)	L. Mand- ible	0.4	2127 [†]	25.6	3.6 x 4.0 x 3.4
			2127		?
			2092		?
			2056		?
			2023		?
			1979		?
			1840*		?
			1708*		N.V.
<u>T15R4</u> (C2)	Sacrum	0.3	2127 [†]	9.9	2.8 x 2.7 x 2.5
			2127		?
			2092		?
			2056		?
			2023*		?
			1979*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T17R5H</u>	6th Cerv. Vertebra	0.7	1147 [†]	11.4	2.2 x 3.0 x 3.3
			1147	6.1	2.3 x 2.2
			1127		?
			1095		?
			1066		?
			1035*		?
			1002*		N.V.
<u>T23R4H</u>	R. Front- al Bone	0.1	1471 [†]	71.3	4.8 x 6.3 x 4.5
			1471	79.3	5.2 x 5.6
			1462		?
			1431		?
			1245*		N.V.
<u>T24R4H</u> (C1)	R. Ilium	0.5	1505 [†]	59.1	(4.0 x 6.0 x 4.7)
			1505		?
			1492		?
			1462		(?)
			1431		(?)
			1242*		(0.2 x 0.2)
			1037		N.V.
<u>T24R4H</u> (C2)	Prox. R. Femur	0.5	1505 [†]	154.9	6.0 x 8.5 x 5.8
			1505		?
			1492		?
			1462		?
			1431*		(?)
			1242*		N.V.
<u>T25R4H</u> (C1)	R. Isch- ium	0.3	1309 [†]	13.6	2.9 x 3.2 x 2.8
			1309		?
			1296		?
			1245*		?
			1039*		N.V.
<u>T25R4H</u> (C2)	L. Isch- ium	0.5	1309 [†]	10.1	3.1 x 2.4 x 2.6
			1309		?
			1296		?
			1245*		?
			1039*		N.V.
<u>T26R4H</u> (C1)	Dist. L. Humerus	0.5	1780 [†]	4.8	1.5 x 3.6 x 1.7
			1780	4.8	1.6 x 3.6
			1753		?
			1722		(1.0 x 3.2)
			1639		(?)
			1575*		(?)
			1485*		N.V.

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T27R4H</u> (C1)	1st Cerv. Vertebra	0.1	1414 [†]	35.5	3.8 x 4.7
			1414		?
			1401		?
			1367		?
			1336		?
			1246*		?
			1056*		N.V.
<u>T27R4H</u> (C2)	7th Lumb. Vertebra	0.3	1414 [†]	2.0	1.5 x 1.7
			1414		?
			1401		?
			1367		?
			1336		?
			1246*		?
			1056*		N.V.
<u>T68R3</u>	L. Ilium	0.3	1667 [†]	214.7	6.2 x 10.5 x 6.3
			1667		?
			1633		3.3 x 4.1
			1601		?
			1580		?
			1549*		?
			1519*		N.V.
<u>T70R3</u> (C1)	Dist. R. Femur	0.2	1996 [†]	6.0	1.5 x 4.5 x 1.7
			1996		?
			1993		?
			1961		?
			1930		?
			1898		?
			1786*		?
			1588*		N.V.
<u>T19P5</u>	Dist R. Tibia	0.2	1400 [†]	2.3	1.5 x 2.7 x 1.1
			1400	2.5	1.6 x 2.5 x 1.2
			1149*		N.V.
<u>T48P5</u>	Mid. R. Humerus	0.2	1327 [†]	209.1	6.4 x 10.4 x 6.0
			1327		?
			1301		?
			1287		?
			1200		?
			***		***

Beagle Osteosarcoma Data - "C" Tumors

<u>Dog</u>	<u>Location</u>	<u>Calc.</u>	<u>Days P. I.</u>	<u>Volume</u>	<u>Dimensions</u>
<u>T51P5</u> (CI)	Prox. R. Humerus	0.4	1055 [†]	35.8	4.2 x 4.4 x 3.7
			1055		?
			1041		?
			1002		?
			943*		N.V.
<u>T2Q4</u> (CI)	5th Lumb. Vertebra	0.1	2317 [†]	151.3	6.4 x 7.4 x 6.1
			2317	105.5	5.7 x 6.2
			2212	2.8	1.5 x 2.4
			1919*		?
			1888*		N.V.
<u>T4Q5</u>	R. Scap- ula	0.1	1462 [†]	119.1	6.5 x 7.0 x 5.0
			1462		?
			1461		?
			1398*		?
			1335*		N.V.
<u>T5Q5</u>	Mid. L. Humerus	0.2	1638 [†]	331.5	9.8 x 9.5 x 6.8
			1638		?
			1623		?
			1609		?
			1573		?
			1533		?
			1476		?
			1465*		?
			1398*		N.V.
<u>T7Q5</u>	R. Mand- ible	0.2	2053 [†]	65.7	4.9 x 6.1 x 4.2
			2053		?
			2045		?
			1954*		?
			1766*		N.V.