Radiation Effects on Bone Mineral Content

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Adverse effects on skeletal tissue due to routine radiotherapy treatment protocols can appear as such immediate effects as increases in spontaneous or abnormal fractures or as such delayed effects as radiation-induced sarcomas. An increase in the number of abnormal fractures during the post-irradiation period may be preceded by a local loss of bone mineral. Monitoring of the mineral content of bones which lie in a radiation treatment field thus could have clinical value.

Changes in bone mineral possible during routine radiotherapy treatment schedules were measured by the system developed by Cameron and Sorenson ⁽¹⁾. This direct photon absorption technique has been shown to be a precise method for determining small changes in bone mineral content ⁽²⁾.

We divided 8 New Zealand white rabbits approximately 10 weeks old into two groups, Blue and Gray. One rabbit from each group was a control and the remaining three rabbits in the group were experimental animals. The right tibia was selected as the experimental limb and the left tibia served as a secondary control.

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The right tibias from the knee to the ankle of all experimental animals were irradiated according to the fractionation schedule (Table I) in a field, 6 cm x 8 cm, at an SSD of 30 cm with a 2000 mCi ^{137}Cs teletherapy unit. The total doses and fractionations were deliberately chosen to represent typical radiotherapy treatment protocols.

Modification of the Cameron and Sorenson technique to determine mineral content in small animals has been described previously by Smith, et al. (3). We used an ^{125}I resin source (4) to obtain maximum differentiation between tissue and bone. Our source and detector apertures of 3 mm. and 2 mm. were similar to those used by Smith. The scanning mechanism used was a modified version of our new linear bone mineral scanner (5). Since the rabbit tibia is approximately 1/4 the size of a human tibia, the scanning speed was reduced to 1/4 the normal rate of 2.8 mm/sec so that the same number of data points would be collected per scan.

The midshaft of the rabbit tibias were scanned with the animals lying on their side in a lucite animal holder which had a shallow tray attached to support the animal's lower limb. The foot was clamped so that the axis of the tibia was perpendicular to the linear scan path. The constant tissue thickness required by the Cameron and Sorenson technique was obtained by wrapping the limb in Super Stuff (6) and covering it with a thin sheet of lucite, 1/16 in. thick, supported at a constant height

above the bottom of the tray.

The experimental and control animals were scanned on alternate days. All experimental animals were scanned at least 6 times during the two week study. At least one bone mineral measurement was made on or before the day the irradiations began, and the last bone mineral determinations were made 2 days after the irradiations ended. The control animals were scanned 4 times. Each time the animals were measured, 0.5 cm aluminum bar, which is approximately the same width as a rabbit tibia, was scanned to check day-to-day variations in the system.

The counts were recorded with a parallel digital line printer (Baird-Atomic Model 620-2) and the results were calculated by an Olivetti 101 calculator programmed for our bone mineral calculation⁽⁷⁾.

After the last in vivo scans the rabbits were sacrificed. The tibia and foot were removed intact. These tibia-foot combinations were clamped in the scanner with the foot clamp so that the now excised tibias were scanned in the same position as the in vivo scans.

Sections 1 cm long were removed from the excised tibias at each scan site with a slotting saw on a milling machine and were ashed at 600°C for 48 hours and weighed.

Another bone sample was cut from the proximal end of each tibia. Decalcified bone slides have been made from these samples, and they will be subsequently read by a clinical pathologist.

The results of this two week longitudinal study of ^{137}Cs radiation effects on mineral content of rabbit tibias appear to be inconclusive. The mineral content of the tibias of both the irradiated and the control animals continually increased during the two week period. The total increase in mineral content for the controls (Fig. 1) range from 10% to 20%. The increases in the mineral content of both tibias for the Blue group (Fig. 2) range from 10% to 35%; those for the Gray group (Fig. 3) range from 8% to 19%. The small aluminum bar which served as a phantom showed no change (<1%) during this same 2 week period.

Since the mineral content in both the control group and the experimental group increased by approximately the same amount and since the mineral content of the left tibias (control) and right tibias (irradiated) in the experimental group increased by approximately the same amount, the irradiation of the right tibias appears to have had no effect on bone mineral during the 2 week study. What apparently was observed was a change in mineral content due to animal growth. Moreover, since no other measurements were made to monitor animal growth (e.g. daily weight), one cannot separate changes in bone mineral due to irradiation effects from those due to normal growth.

The histological bone slides have not been analyzed. Consequently, the extent of cellular radiation damage which

occurred due to the radiation exposures is not known at present.

The precision of our measurements was determined by comparing the ash weights of the 1 cm long bone sections with the mineral content calculated from the Olivetti bone mineral program (Fig. 4). The mineral content in computer units is simply the sum of logarithms, $\sum \log(I_0^*/I)$, of the counting rates⁽⁸⁾.

From standard linear regression analysis, the relationship between the two measured quantities is:

$$\text{Ash Wt. (gm/cm)} = 12.7 \text{ Computer Units} + 0.57.$$

The correlation coefficient between the two quantities is greater than 0.94. The standard error of estimate of ash weight from the computer units is ± 0.04 gm/cm ($\sim 2\%$). The above equation can be used to convert the arbitrary units in Figures 1, 2, and 3 to gm/cm of ashed bone.

To conclude, we were able to demonstrate that it is feasible to apply the Cameron and Sorenson direct photon absorption technique to the measurement of bone mineral of small animals. The technique has been demonstrated to be accurate and reproducible ($\pm 5\%$). Furthermore; no immediate ($<2\text{wk}$) changes occurred in the mineral content of the bones in a radiation field receiving routine therapeutic doses of ^{137}Cs γ -rays.

Unfortunately, this study had to be terminated after 2 weeks. In future studies the post-irradiation measuring period

should be much longer, and the effects due to growth should be eliminated by measuring mature animals.

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Table I

Fractionation Schedule To Irradiate The Rabbits' Right Tibias

Animal Group		Fractionation	Total Exposure, R
Blue Control	Gray Control	R_a/d ; 5d/wk 0	0
1	1	300	3000
2	2	400	4000
3	3	500	5000

Fig. 1. Mineral content of control rabbits versus the date of the measurement. The mineral content in both animals continuously increased during the two week study.

Fig. 2. Mineral content of the Blue experimental group versus the date of the measurement. The mineral content for all three animals continuously increased during the two week study. The increases range from 10% to 20%.

Fig. 3. Mineral content of the Gray experimental group versus the date of the measurement. Again the mineral content for all three animals increased during the two week study. The increases range from 8% to 19%.