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Note

AN ABSORBED DOSE MAP OF BONE TISSUE TREATED WITH A RADIOPHARMACEUTICAL IN VIVO

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Fn1 *Abstract*—**A beagle humerus treated with ^{166}Ho-chelate radiopharmaceutical in vivo was examined by electron paramagnetic resonance (EPR) dosimetry. The bone was sectioned and the absorbed dose to each bone fragment was determined by additive re-irradiation of the bone tissue with calibrated doses of gamma radiation. The measured doses ranged from 4.3 Gy to 62 Gy. The highest doses were recorded in the predominately trabecular bone tissue and the lowest doses in the predominately cortical bone tissue. The mean absorbed dose for the entire bone was 17 Gy. The data from 50 bone fragments were combined to create an absorbed dose map of the interior bone surface.**

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Key words: dose, absorbed; electrons; radiopharmaceuticals; dosimetry

INTRODUCTION

THE USE of mineralized biological tissues in dosimetry was proposed nearly four decades ago (Brady et al. AQ: A 1968). Brady and coworkers proposed that the radiation-induced electron paramagnetic resonance (EPR) signal in hydroxyapatite be used to measure the tissue absorbed dose. However, the first quantitative application of this form of biodosimetry in human bone tissues was not realized until much later (Desrosiers 1991; Schauer et al. 1993). The utility of this technology to medical research was first demonstrated by Desrosiers et al. (1991). That work showed the feasibility of using EPR to measure the absorbed dose in bone tissue treated with bone-seeking radiopharmaceuticals. The first direct physical measurement of absorbed dose for radiopharmaceutical-treated mineralized tissue was reported by Desrosiers et al. (1993). In that study, a beagle humerus that was treated with a ^{166}Ho chelate was sectioned and examined by EPR dosimetry. The cortical bone tissue about the midpoint of the humerus recorded an average absorbed dose (9.9 Gy) that was about three times lower than the calculated average skeletal dose of 30 Gy for this animal (Desrosiers et al. 1993). A modeling study by Parks (1991) estimated two to five times lower distributions of bone-seeking radionuclides in cortical bone compared to trabecular bone. Parks' estimate is consistent with the higher surface area and tissue turnover rate for trabecular bone. Since only the cortical bone data was reported by Desrosiers et al. (1993), the absorbed dose discrepancy was never resolved in the literature. However, in 1994, a complete series of EPR measurements that included cortical and trabecular bone for the ^{166}Ho-treated humerus were performed. For no specific reason, this work was never published. This paper rectifies this omission by reporting the complete EPR dosimetry analysis of the ^{166}Ho-treated beagle humerus.

METHODS

A beagle humerus was treated with ^{166}Ho according to the procedure described previously (Desrosiers et al. 1993). The humerus measured 104 mm in total length. The bone was cut transversely across the length of the bone's shaft to produce five cylindrical sections using a diamond-blade saw; the bone sectioning scheme has been graphically displayed (Desrosiers et al. 1993). The lengths of the sections were (1) 12 mm (2) 24 mm; (3) 23 mm; (4) 10 mm; and (5) 10 mm. The sum of the individual sections is not equal to the total length because the cartilaginous ends of the humerus are not suitable for EPR dosimetry due to the diminished concentration of mineralized tissue. The extremities of the humerus that were judged (visually) to be unsuitable were discarded and not measured. Each cylindrical section of bone was then cut longitudinally to produce nine to fifteen bone fragments (the number varied with the diameter of the bone) that averaged 15 mm in length and 3 mm in diameter.

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Some bone material was lost in the cutting process and some fragments were not measured because they fractured during the cutting process; accurate records accounting for lost bone mass with respect to its position were not kept. The residual marrow and tissue were scraped off the fragments and the position of each fragment on the humerus was labeled. No efforts were made to separate cortical bone from trabecular bone (i.e., some fragments contained both bone types). All bone samples were air-dried in a fume hood for at least 24 h.

The EPR spectra for each bone fragment were measured with a Bruker ESP300e X-band electron paramagnetic resonance spectrometer[‡] equipped with a transverse magnetization resonator. The following parameters were used: modulation frequency, 100 kHz; microwave frequency, 9.84 GHz; microwave amplitude, 0.2 mT; microwave power, 80 mW; time constant, 655 ms; conversion time, 81.92 ms; and a 5.0 mT sweep width about the center field value of 351.0 mT. The peak-to-peak amplitude of the $g_{\perp} = 2.002$ resonance attributed to the mineralized tissue was used as a measure of the absorbed dose response (Desrosiers 1991).

[‡] The mention of commercial products throughout this paper does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that products identified are necessarilythe best available

The absorbed dose for each bone fragment was determined by the additive re-irradiation method (Desrosiers et al. 1993). After an initial measurement session, added doses (1.8% expanded uncertainty at the 95% confidence level, $k = 2.13$) were administered using a ^{60}Co vertical beam source (0.6 Gy min^{-1}) or a ^{60}Co pool source (30 Gy min^{-1}). EPR spectra were measured at each dose increment. After the administration of approximately five additional doses, the EPR signal amplitudes at each dose were subjected to a linear regression that was extrapolated to the negative dose axis to estimate the initial absorbed dose. Representative graphs of this determination have been published (Desrosiers et al. 1993).

RESULTS AND DISCUSSION

A two-dimensional bar chart of the absorbed dose distribution in the beagle humerus is shown in Fig. 1a. The transverse-section axis represents the five cylindrical sections that comprised the entire calcified tissue of the humerus. The plot represents the dose for the mineralized tissue only and not the entire volume of the bone that includes the cartilaginous ends (joints). It does, however, represent two types of bone material, predominately trabecular towards the ends (sections 1, 4, 5 of Fig. 1a) and predominately cortical in the center

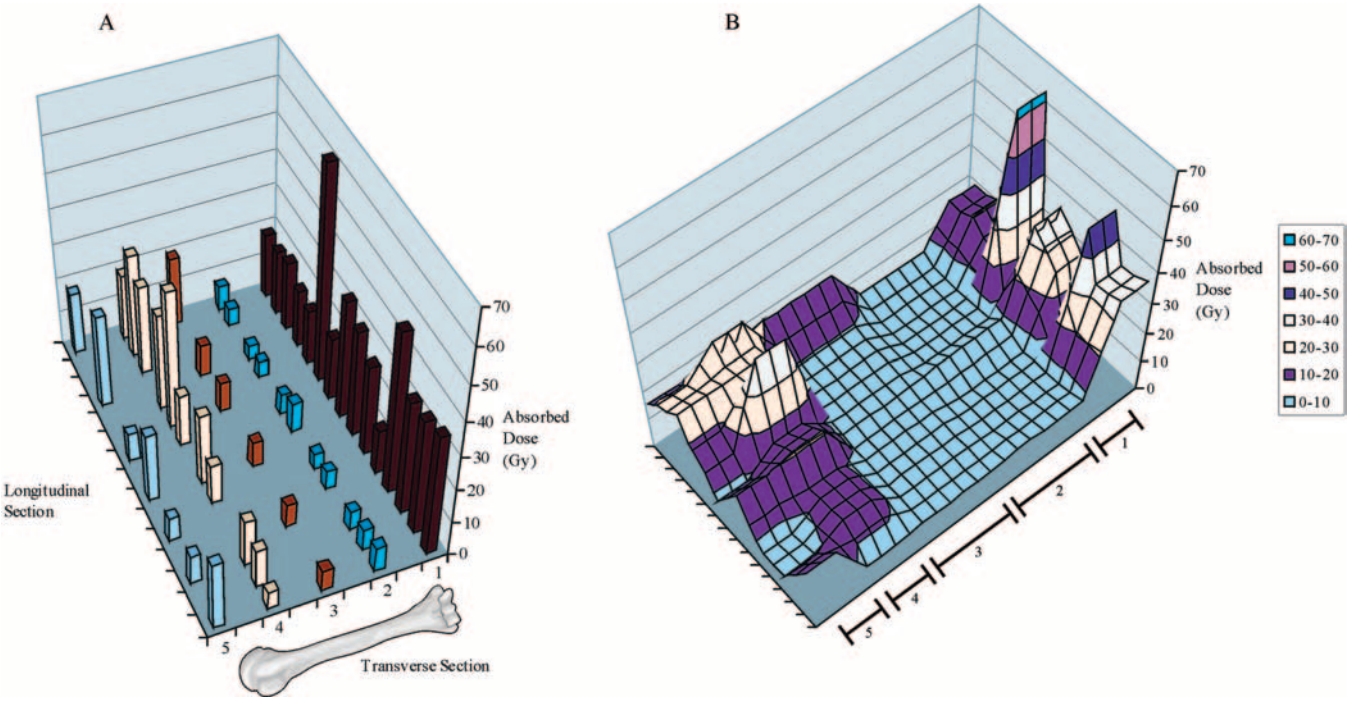

Fig. 1. The bar chart (a) registers the absorbed dose (Gy) for 50 bone fragments as a function of its original position in the radiopharmaceutical-treated beagle humerus. The surface chart (b) represents the same 50 absorbed dose measurements with additional interpolated points to form a continuous dose map that is representative of the internal surface dose distribution for the radiopharmaceutical-treated beagle humerus.

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(sections 2, 3 of Fig. 1a). The longitudinal-section axis represents the multiple sections cut lengthwise from each cylindrical transverse section. The number of longitudinal sections varied between the different transverse sections. Some longitudinal sections were not measured, either because they fragmented (trabecular bone is very porous) or were sacrificed in preliminary tests.

The maximum absorbed dose in each section (section number in parentheses) was 62 Gy (1); 8.7 Gy (2); 20 Gy (3); 40 Gy (4); and 27 Gy (5). The minimum absorbed dose in each section was 13 Gy (1); 4.3 Gy (2); 6.5 Gy (3); 5.1 Gy (4); and 6.9 Gy (5). The uncertainty associated with the dose interpolation is estimated from the x-axis intercepts of the confidence intervals of the linear regression. On average, the uncertainties (1 σ) ranged from approximately 100% for the lowest doses to approximately 10% for the highest doses measured. In terms of absorbed dose, this uncertainty is equivalent to $\approx$ 4 Gy. The mean absorbed dose of all measured bone sections was 17 Gy.

A two-dimensional area map (Fig. 1b) of the absorbed dose distribution in the beagle humerus was constructed from the bar chart data in Fig. 1a. This plot is presented as a visual aid for discerning spatial trends in the absorbed dose deposition; it is not intended to be to scale. A series of identical data points for each longitudinal section is used to artificially create an illusion of transverse section length. Three identical data points represent the transverse sections 1, 4, and 5, while six identical data points represent the transverse sections 2 and 3. A transitional data point is computed from the mean of the doses of adjacent transverse sections. Data points missing between longitudinal sections and between transverse sections were interpolated from the adjacent points to create a continuous dose map.

The highest doses were measured in the predominately trabecular bone tissue (sections 1, 4 of Fig. 1a and b). This is consistent with the radionuclide distributions measured by Parks (1991). Within the predominately trabecular bone tissue there were large variations in dose; for example, the range of doses in section 1 was 13 Gy to 62 Gy. Large dose variations are also observed in the opposite end of the humerus (sections 4, 5). The central (predominately cortical) shaft of the bone had the most uniform dose distribution; however, it was significantly lower than the doses measured at either end of the bone.

CONCLUSION

These data represent the first absorbed dose map of a bone irradiated in vivo by an internally-administered radiopharmaceutical. As such, it offers a unique view into the pattern of dose deposition within bone tissue. The average dose for these measurements was about 50% less than the computed average skeletal dose of 30 Gy (Desrosiers et al. 1993); however, the target tissue of these computations was the tissue that lined the surface of the mineralized bone that served as the dosimeter in this study. The EPR dosimetry measurements represent an absorbed dose averaged over the entire mass of the bone fragment. The dose distribution of the dense cortical bone fragments may be heterogeneous. Heterogeneity in the dose distribution could skew the bone-fragment dose measured by EPR (as an average over the entire mass of the bone fragment). In contrast, the high-surface-area "honeycomb" structure of the trabecular bone would effectively be a thinner detector and may be more representative of the absorbed dose at the surface of the bone. In fact, the average dose of the measurements for the fragments of sections 1 and 5 is 24 Gy, a value much closer to the average skeletal dose of 30 Gy.

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