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The Radiobiology of Radium and Thorotrast

Edited by W. Gössner, G. B. Gerber, U. Hagen, A. Luz

81 Figures and 99 Tables

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Bone Sarcoma Cumulative Tumor Rates in Patients Injected with ^{224}Ra*

C. W. Mays, H. Spiess, D. Chmelevsky, A. Kellerer

Introduction

This paper serves as an overview for the Symposium's other 5 papers on the biological effects of ^{224}Ra in German patients [1, 12, 17, 19, 22]. It will deal specifically with the follow-up, started by Spiess in 1952, of 899 children and adults who received weekly or twice-weekly intravenous injections of ^{224}Ra, mainly for the treatment of tuberculosis and ankylosing spondylitis. ^{224}Ra is an α-emitting isotope of radium with a half-life of 3.62 days. The dose from ^{224}Ra and its decay products has been calculated [6, 8, 14] but may require future revision when reliable values have been established for the *in-vivo* escape of the decay products from bone [6, 11]. The patients are contacted by mail questionnaire, and we verify their diseases with help from their physicians, hospitals, and health offices [8, 13].

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Status of the Spiess Patients

Table 1 summarizes the follow-up to June 1984. The follow-up times, from first injection to death or last known health status, ranged from 0 to 38 years and averaged 22 years. Half of these patients are known to have died. The injected dosage in μCi/kg averaged twice as high in the juveniles as in the adults, but because of the enhanced uptake of ^{224}Ra in growing bone, the calculated skeletal dose in rads for juveniles averaged 5 times that for the adults.

Table 2 lists diseases of increased incidence. The numbers of naturally-expected malignancies were calculated from the person·years post injection and the cancer incidence rates in the German Democratic Republic [20]. Bone sarcomas were reported in 53 patients compared to only 0.2 case naturally expected. Thus all, or virtually all, of these bone sarcomas can be regarded as radiation induced. The last bone sarcoma occurred in 1974, 25 years after ^{224}Ra injection, and no additional bone sarcomas

Table 1. Summary of the Spiess ^{224}Ra Patients (June 1984)

	Age at First Injection		
	1–20 yr	Adult	Total
Traced patients	218	681	899
Deaths	81	369	450
Av. inj. ^{224}Ra (μCi/kg)	28	15	18
Av. skel. dose (rad)	1062	206	416
Skeletal Diseases			
Bone sarcoma	35	18	53
Exostosis (benign)	28	0	28
Severe growth retardation	28	0	28
Tooth breakage	27	17	44
Soft-Tissue Diseases			
Cancer of soft-tissue	9	59	68
Leukemia	0	5	5
Kidney disease	8	56	64
Liver disease	2	23	25
Cataract	12	32	44

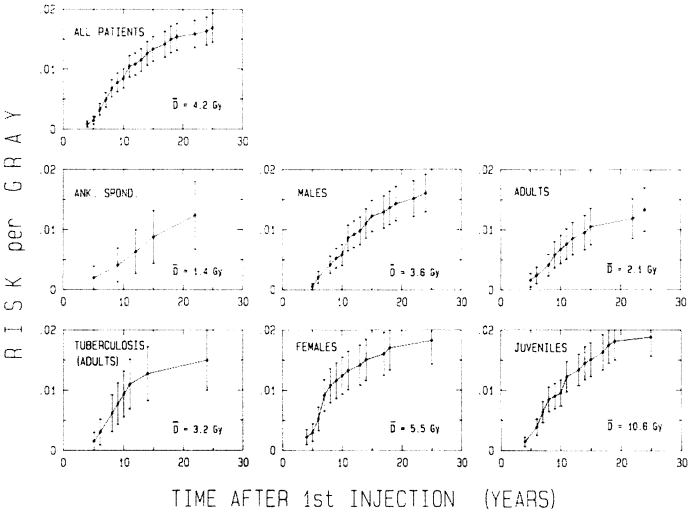

Fig. 1: Bone sarcoma cumulative tumor risks in the major classifications of the ^{224}Ra patients. The cumulative risk per gray (or 100 rad) progressively increased with time and was similar among the various classifications of patients. Thus, the susceptibility to bone sarcoma-induction was relatively independent of age at irradiation, sex, or whether the original disease during treatment was tuberculosis or ankylosing spondylitis.

confirmed – based on our dosimetric assumptions, the age at irradiation, sex, and original disease state had no significant influence on the susceptibility to ^{224}Ra-induced bone sarcoma. Reprints of the previous, more detailed analysis are available from C. W. Mays [8].

Summary

At 3 year intervals the health status is updated for 899 German patients who received repeated injection of ^{224}Ra, mostly for the treatment of tuberculosis and ankylosing spondylitis. The follow-up times, from first injection to death or last known health status, ranged from 0 to 38 years and averaged 22 years as of June 1984. The 0–3 excess cases of leukemia attributable to ^{224}Ra is small compared to the 53 patients developing bone sarcomas. Kidney cancers occurred in 4 patients vs. 1 case naturally expected, whereas nonmalignant kidney diseases (usually fatal) were reported for 64 patients vs. 3 cases naturally expected. Additional disease conditions of elevated frequency were: liver diseases, cataracts, tooth breakage, benign exostoses, and growth retardation. Based on our dosimetric assumptions and using the sum-limit method to correct for the effects of deaths and incomplete follow-up, no statistically-significant differences were found in the bone sarcoma risk per rad between (a) juveniles vs. adults, (b) males vs. females, and (c) TB patients vs. ankylosing spondylitis patients.

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