

INVITED PAPER DELIVERED AT THE 25TH ANNUAL  
MEETING OF THE HEALTH PHYSICS SOCIETY

INCEPTION OF STANDARDS FOR INTERNAL  
EMITTERS, RADON AND RADIUM

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THERE are three basic radiation protection standards which have their roots in observations on man. The detailed guidance for various situations of radiation exposure is derived in several ways from these three basic standards, or bench marks. The three basic standards are: (1) for external X-rays and  $\gamma$ -rays, (2) for internal emitters, specifically radium, and (3) for inhaled radioactive aerosols, specifically radon and its short-lived decay products.

There is an excellent, brief history of the development of these three standards and their application to plutonium, by W. Langham and J. Healy in the giant tome *Uranium, Plutonium, Transplutonic Elements* (Edited by H. Hodge, N. Stannard and J. Hursh), Springer-Verlag, Berlin, 1973. There are also many valuable historical chapters on the early years of radiation protection in the 1980 book, edited by R. Kathren and P. Ziemer, called *Health Physics: A Backward Glance*, just published by Pergamon Press.

The emphasis requested of speakers in this session is a personal, anecdotal play-back of their interactions with persons and with ideas.

Forty-eight years ago, in 1932, I first became involved in radium metabolism just as I was finishing my doctoral thesis at Caltech under Prof. R. A. Millikan. That thesis had involved, among other things, the

development of highly sensitive and accurate methods for analyzing various materials for radium and radon, with mostly geophysical applications.

Recall that, as late as 1932, the only elementary particles known in physics were the Proton and the Electron. Persons studying radioactivity were a very small clan in 1932, about  $1 \pm 1$  person per institution at places like Caltech, Berkeley and MIT. Substantially all of our radiation measuring equipment was homemade from radio and telephone parts.

The precipitating event which put me on the path of exploring the biological effects of radiation was the heavily publicized death from "Radium Poisoning" of Mr. E. M. Byers, in April 1932. Mr. Byers was a prominent and wealthy Pittsburgh industrialist, banker and sportsman, and an attractive 51-year-old Mr. Byers in 1965, 33 yrs later as "Good Lady Friends" had consumed for years a then-popular commercial radium tonic water called Radithor. (When we exhumed Mr. Byers in 1965, 33 yrs later as part of the MIT radium program, our measurements showed that he had retained at death in 1932 more than  $6 \mu\text{Ci}$   $^{226}\text{Ra}$  and that his total intake of radium had been about  $500 \mu\text{Ci}$  ( $1/2 \text{ mCi}$ ) of  $^{226}\text{Ra}$  plus an equal activity of  $^{228}\text{Ra}$ .)

Mr. Byers' death, coupled with the experiences of the New Jersey radium watch-dial painters 8 yrs earlier, shocked the Los Angeles County Health Officers. They wan-

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ted no radium scandal in sunny California, and came to Caltech for help. County Health Officer Dr. F. Crandall's visit aroused my interest in the quantitative study of the uptake, metabolism and excretion rate of radium in living persons, and in the possibility of minimizing their symptoms, by accelerating the excretion of radium by some form of therapy.

After I moved from Caltech to Berkeley in the summer of 1932, I was persuaded to present an invited paper at the Annual Meeting of the American Public Health Association on "Radium Poisoning: A Review of Present Knowledge". For the details, this 1933 paper is reprinted in the 25th Anniversary Issue of *Health Physics*, June 1980.

In collaboration with Dr. E. Richmond Ware of Los Angeles, exhaled breath radon analyses, radium excretion rates and therapeutic trials were begun in 1933 on a patient of his who had been a radium-dial painter in Connecticut. The details are given in a chapter in R. Kathren and P. Ziemer's *Health Physics—A Backward Glance*.

(She died in 1966, 33 yrs after this treatment, at the age of 74, with a residual body burden of  $2 \mu\text{Ci}$   $^{226}\text{Ra}$  and only minimal symptoms. She had willed her body to me. The subsequent studies of her skeletal tissues showed the presence of mesothorium ( $^{228}\text{Ra}$ ) as well as  $^{226}\text{Ra}$ . Her initial intake of  $^{228}\text{Ra}$  and  $^{226}\text{Ra}$  had been about  $600 \mu\text{Ci}$  of each. Her lifetime skeletal average dose was over 15,000 rads.)

In 1934 I moved from Berkeley to join the physics faculty at the Massachusetts Institute of Technology. The two previous years had been a golden age in nuclear physics. The neutron had been discovered, the positron, deuterium, artificial radioactivity and the first man-made nuclear reactions had been produced by accelerated protons and deuterons. My students and I became engaged in a broad range of exciting problems in pure and applied radioactivity.

The radium poisoning studies continued, on a "back burner" basis, as new patients appeared and were studied. A direct and long-standing collaboration began in 1934 with Dr. J. Aub at the Huntington Memorial Hospital in Boston. The first phases involved efforts to

remove radium from the skeletal tissues of three radium patients. We used parathyroid hormone and a low calcium diet, alternated with periods of high calcium diet plus viostero (vitamin  $\text{D}_2$ ). Dramatic clinical improvement was seen in the first of these patients (who had a body burden of  $23 \mu\text{Ci}$  Ra), but was marginal in others. Although there was a significant elevation in radium excretion, the fraction of the body burden removed by the parathyroid therapy amounted to only a few percent of their body burden.

A patient's body burden of  $^{226}\text{Ra}$  could not in 1932 be determined from exhaled breath radon analyses alone. This is because only a fraction of the radon produced continuously by radium in the skeletal tissues escapes from the bone, reaches the circulating blood and the respiratory system and can be exhaled. The remaining fraction (roughly one-third) of the radon, decays within the bone and its short-lived daughter products emit the characteristic  $\gamma$ -ray spectrum of a sealed radium or radon source. It was therefore necessary to develop a quantitative method of whole-body counting, for determining the skeletal content of  $\gamma$ -ray emitting nuclides.

This was done at MIT in 1934 for measuring the radium patients. No phantom, spiked cadaver, or postmortem data are involved. The basic mathematical and physical principles are relatively simple and have many other uses in applied health physics, but must be omitted today because of time constraints. However, you can find them in R. Kathren and P. Ziemer's book *Health Physics—A Backward Glance*, p. 144. As in Fig. 1, the body is positioned in an arc with the detector at the center of curvature. There are four unknowns: (1) the strength of the internal  $\gamma$ -ray source; (2) the effective depth of burial of the source within the body; (3) the effective attenuation coefficient within the body for emerging  $\gamma$ -rays; and (4) the absolute calibration constant of the detector. From the general theory of equations, 4 proper and independent measurements will suffice to determine each of these 4 unknowns. The first measurement is shown in Fig. 1. The body is then rotated through  $180^\circ$ ,

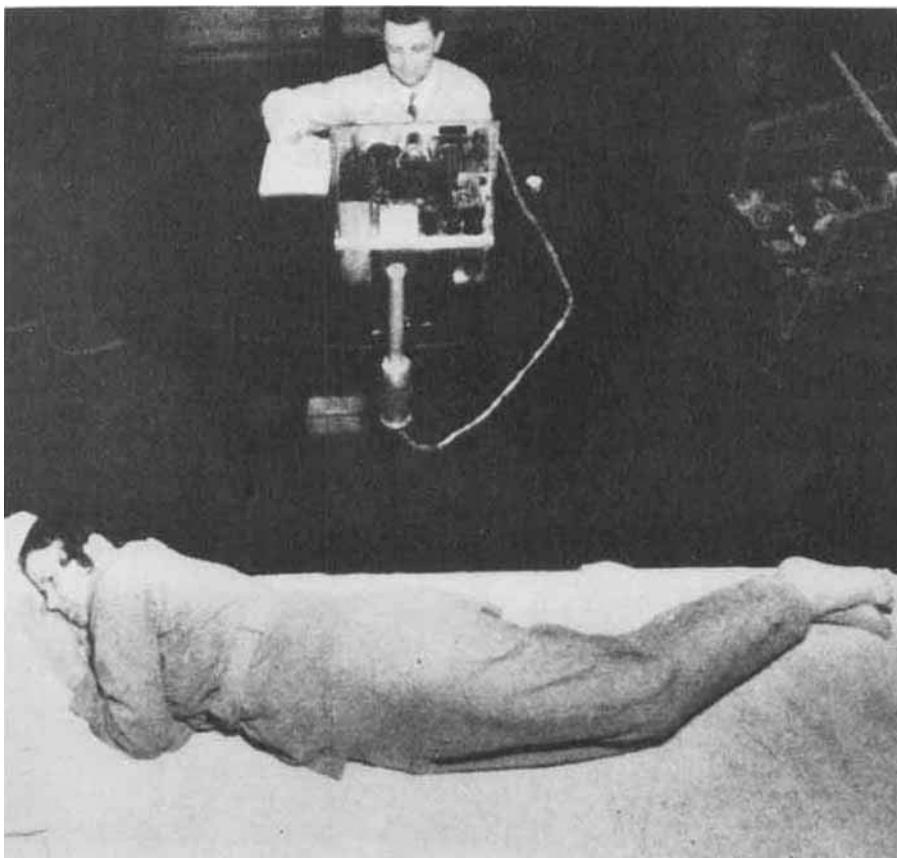


FIG. 1. A patient whose body burden is to be determined is positioned with the body curved so that with the  $\gamma$ -ray detector as an axis, an arc of about 1 m radius falls on the ventral aspect of the patient's body, touching at the forehead, shoulder, abdomen, knees and toes.

as in Fig. 2, for the second measurement. For the third measurement, standardized sources are added behind the body (at the head, shoulder, back and thighs). Finally, the fourth measurement is of the standard sources alone with the body removed. Proper combination of these 4 readings gives all 4 unknowns, especially the absolute value of the internal whole-body burden of the  $\gamma$ -ray emitter directly.

For these measurements we used, in 1934 and 1935, homemade copper-screen-cathode Geiger-Muller counters. The amplifier and output comprised the world's first counting

rate-meter, which we had developed to circumvent the resolving-time problems inherent in available electromechanical pulse counters.

Two patients, with residual body burdens of 23 and 18  $\mu\text{Ci}$ , were carefully studied by this so-called "meter-arc" method. Then the  $\gamma$ -radiation (Fig. 3) at various locations from the body, while seated in a light wooden chair, was measured in order to provide the so-called chair calibrations. This figure shows the results, where the numbers represent the absolute  $\gamma$ -ray intensity at the marked locations due to the daughter products of 1  $\mu\text{Ci}$

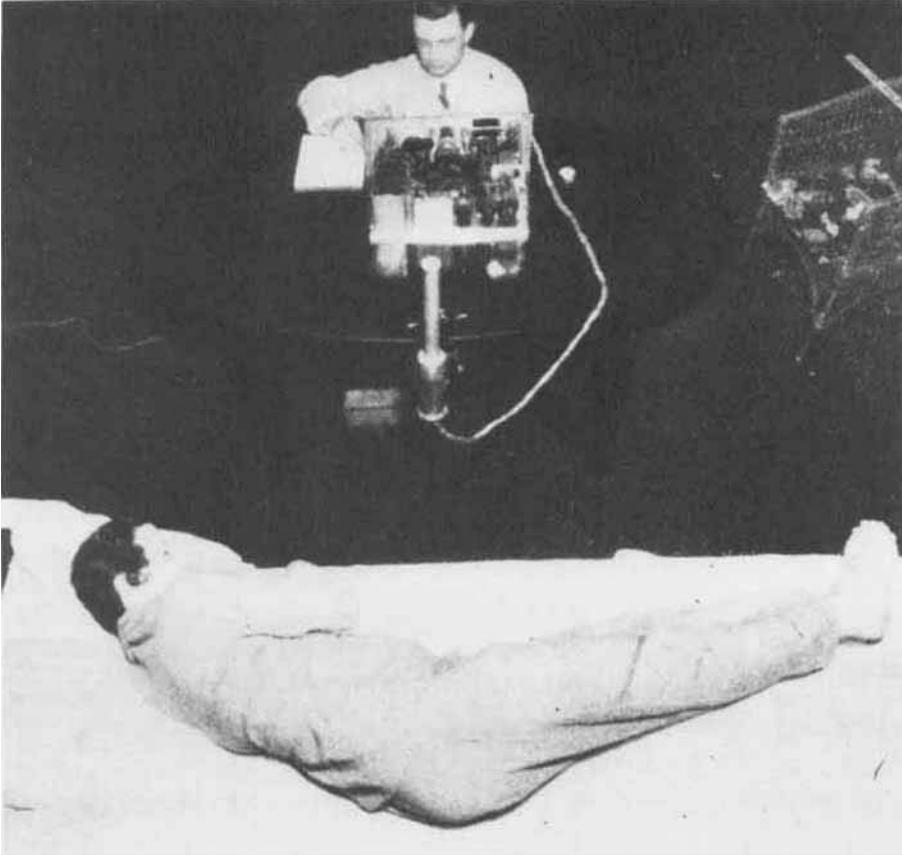


FIG. 2. The counterpart of Fig. 1, with the patient's body reversed so that the arc about the axis of the  $\gamma$ -ray counter now falls on the dorsal aspect of the body, touching at the head, shoulders buttocks and heels.

of retained radon in skeletal tissues, in units of the  $\gamma$ -ray intensity at 1 m from a  $1 \mu\text{Ci}$  sealed radium source.

Several persons who were measured during life were later exhumed for detailed microscopic and autoradiographic studies of their skeletons, and for measurement of the nonuniform distribution of skeletal radium. It is comforting to a bench scientist that in all cases these detailed postmortem analyses gave total radium body burdens which were in excellent agreement with the *in vivo* whole-body  $\gamma$ -ray measurements.

In 1954, 20 yrs later, L. Marinelli and J. Rose at the Argonne National Laboratory,

built the first low-background or "iron room" and tilting stainless steel chair with a NaI scintillation detector. Figure 4 compares the original wooden chair configuration of patient and detector with that of the tilting chair. Figure 5, in which the photograph of the tilting chair is rotated, shows the compatibility with the old 1934 arrangement.

In 1936 the U.S. Food and Drug Administration was having problems with the continuing sale of consumer products which were spiked with multimicrocurie amounts of radium. These products included face creams, contraceptive jelly, etc. Dr. H. O. Calvery of the FDA came to MIT for help in



FIG. 3. Patients previously measured by the "meter-arc" method of Figs. 1 and 2 are placed in a seated position to provide the "chair calibrations". The absolute  $\gamma$ -ray intensity due to  $1 \mu\text{Ci}$  of RaB and RaC distributed throughout the skeletal tissues is shown at various locations in units of the  $\gamma$ -ray intensity at 1 m from a  $1 \mu\text{Ci}$  sealed radium source.

establishing some quantitative basis for permissible amounts of radium in consumer products.

In 1936 a sufficient number of human cases had not yet been studied quantitatively to be a firm basis for a suggested permissible body burden of radium. Accordingly, we conducted a 4-yr series of studies of radium toxicity in Wistar rats, in collaboration with Profs. J. Bunker and R. Harris of the MIT Biology Department. We found that the production of a good yield of osteogenic sarcomas in Wistar rats required a skeletal concentration of radium which was several hundred times that which we already knew produced bone

cancers in humans. Thus, our conclusion was that *absolute values* of permissible doses of radiation for man could not be properly determined from animal studies alone. More briefly, that *the proper subject for the study of man is man*.

In collaboration with Dr. H. Martland of New Jersey, Dr. Aub and I continued to study radium patients who were referred to us by a number of physicians throughout the United States. At MIT we built and supplied Dr. Martland with  $\gamma$ -ray instrumentation and standard radium sources which were litter-mates of the MIT apparatus. Hence his  $\gamma$ -ray measurements on New Jersey radium-dial painters after about 1938 are on the same microcurie basis as the MIT measurements. The exhaled breath radon analyses on Martland's patients were all done at MIT. Hence his patient series could be added to that of Aub and Evans.

Towards the end of 1940, the U.S. military establishment was cranking up for World War II. Radium-dial instruments were being produced in profusion. U.S. Navy Medical-Corps Captain Dr. C. Stephenson took the lead in insisting that standards of radiation safety be set for the radium-dial industry. Captain Stephenson came by my laboratory at MIT and told me that I must soon provide him with safety standards or else he would have me inducted into the Navy and force me to do it.

There was soon established by the National Bureau of Standards an advisory committee charged with preparing an NBS Handbook on *Safe Handling of Radioactive Luminous Compound*. This 9-man committee included the 4 people who had actually done quantitative work in the field of radium toxicity at that early date (Martland, Flinn, Failla and Evans), plus representatives of industry and government.

We discussed the MIT Wistar rat experiments and quickly concluded that judgmental decisions had to be made on the basis of observations on man.

By February 1941 we had a total of some 27 persons with accurately measured body burdens, all of whom had been measured at MIT or in New Jersey with MIT apparatus.

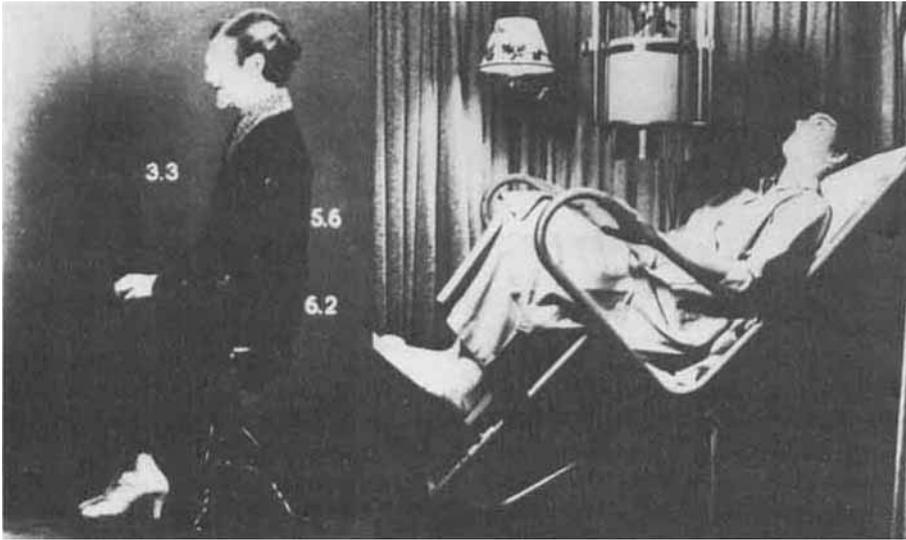


FIG. 4. The chair position of the late 1930s on the left is compared with the now widely used tilting-chair on the right introduced about 1954 by Marinelli and Rose.

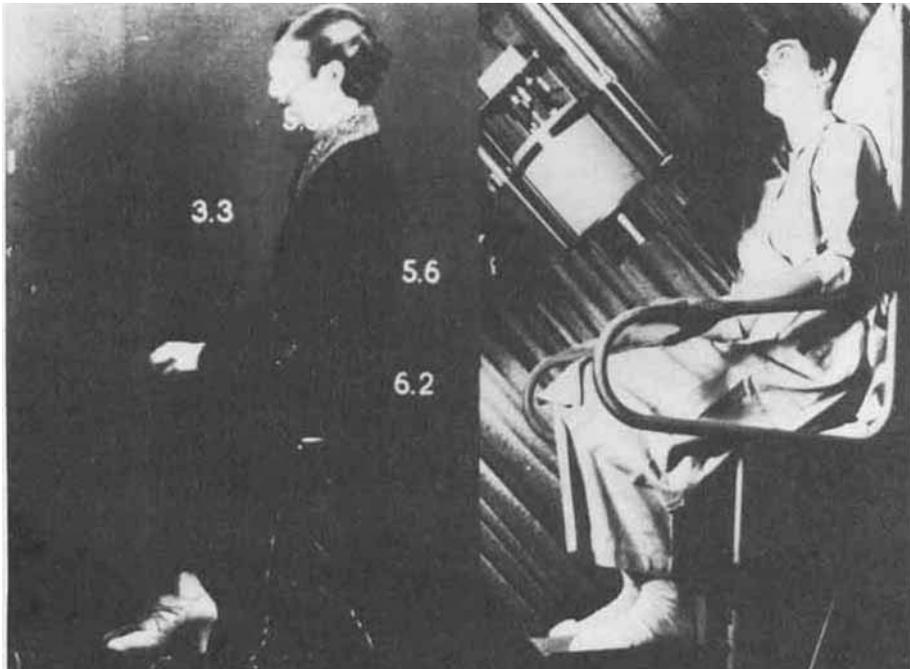


FIG. 5. The tilting chair of Fig. 4 is rotated (note angle of the actually-vertical draperies) by about  $40^\circ$ . Comparison with the original chair position on the left indicates the compatibility of the geometrical relationships between the  $\gamma$ -ray detector and the patient.

We had observed 7 persons with residual body burdens below  $0.5 \mu\text{Ci}$  and no injuries, whereas some 20 persons with residual burdens of  $1.2\text{--}23 \mu\text{Ci}$  showed various degrees of injury.

After reviewing these 27 cases, and noting that we were obliged to make an "informed judgment" decision, I suggested that we should set the "tolerance level" for residual radium burden in radium-dial painters at such a level that we would feel perfectly comfortable if our own wife or daughter were the subject. I then asked each of the other 8 committee-men individually in turn if he would be content with  $0.1 \mu\text{Ci}$ . Unanimously, we all were.

Thus  $0.1 \mu\text{Ci}$  of  $^{226}\text{Ra}$  residual body burden was adopted in NBS Handbook 27 which was issued 2 May 1941, some 7 months before Pearl Harbor, 2 months after the then-secret discovery of plutonium, and 18 months prior to the first demonstration of a nuclear reactor.

After World War II, NBS Handbook 27 was designated as *NCRP Report 5*, and also the ICRP adopted the  $0.1 \mu\text{Ci}$  permissible burden. Now, 39 yrs later, and with more than 2000 radium patients studied at MIT, New Jersey, the Argonne Cancer Research Hospital and the ANL Center for Human Radiobiology, no exception has been found to the  $0.1 \mu\text{Ci}$  residual radium standard as an innocuous body burden.

The  $0.1 \mu\text{Ci}$  Ra bench mark was based on the *residual* body burden of patients, long after they had acquired a much larger initial burden, commonly the order of 100 times larger. When used as a radiation protection guide the  $0.1\text{-}\mu\text{Ci}$  bench mark represents not a *residual* burden but the *maximum* body burden reached during intake. Thus there is a substantial additional safety factor of between 1 and 2 orders of magnitude built into the conventional use of the  $0.1 \mu\text{Ci}$  Ra standard as a *maximum* body burden rather than as a *residual* body burden evaluated many years after exposure.

Permissible levels for some other bone-seeking radionuclides are based on observations of the *ratio* of their toxicity, relative to radium as a base line, as seen in experi-

mental animals. The relative toxicity of injected  $^{239}\text{Pu}$  to that of  $^{226}\text{Ra}$  in mice, rats and rabbits, combined with the  $0.1 \mu\text{Ci}$   $^{226}\text{Ra}$  base line in humans, is the basis for the  $0.04\text{-}\mu\text{Ci}$  permissible body burden of  $^{239}\text{Pu}$ , as set forth most clearly by Dr. A. Brues in 1950.

Occasionally a significant species difference between man and experimental animals is found. One is the effect of radium on the eye. Glenn Taylor and colleagues at the University of Utah noted some 10 yrs ago that  $^{226}\text{Ra}$  and especially  $^{228}\text{Ra}$  (mesothorium) could produce severe loss of pigmentation, and intraocular melanomas, in the beagle eye at whole-body burdens below the lowest at which osteogenic sarcomas appeared. The beagle eye has a tapetum lucidum. The human eye does not. Figure 6 shows on the left the iris of a control beagle eye and on the right an example of marked depigmentation. However in the human eye, there are no such effects. Figure 7 shows the normal-appearing iris of one of our long-lived, high-level human cases, a patient then in her 93rd year, with a skeletal-average dose of about 10,000 rad. She had willed her body to me. Following her death, microdissection of the eyes by Dr. M. Rodrigues in Philadelphia showed no abnormalities. Analysis of 8 dissected portions by Dr. R. Holtzman at ANL showed significant  $^{226}\text{Ra}$  only in the pigmented elements. Other cases have been studied in less detail, but with entirely similar findings. This marked species difference may possibly be related to the absence of a tapetum lucidum in the eyes of mankind. But if a radium protection standard for man had been based just on animal experiments, it would have been seriously wrong. This only emphasizes that the pivotal radium standard for man has to be based on the study of man.

After World War II and during the era of atmospheric weapon tests, interest intensified in predictions of the effects of low-level radiation. With support from the Office of Naval Research and the AEC the radium studies were expanded into epidemiological studies. Groups of similarly exposed persons were vigorously searched for, such as all veteran radium watch-dial painters from a given plant. The problem was, and still is, to

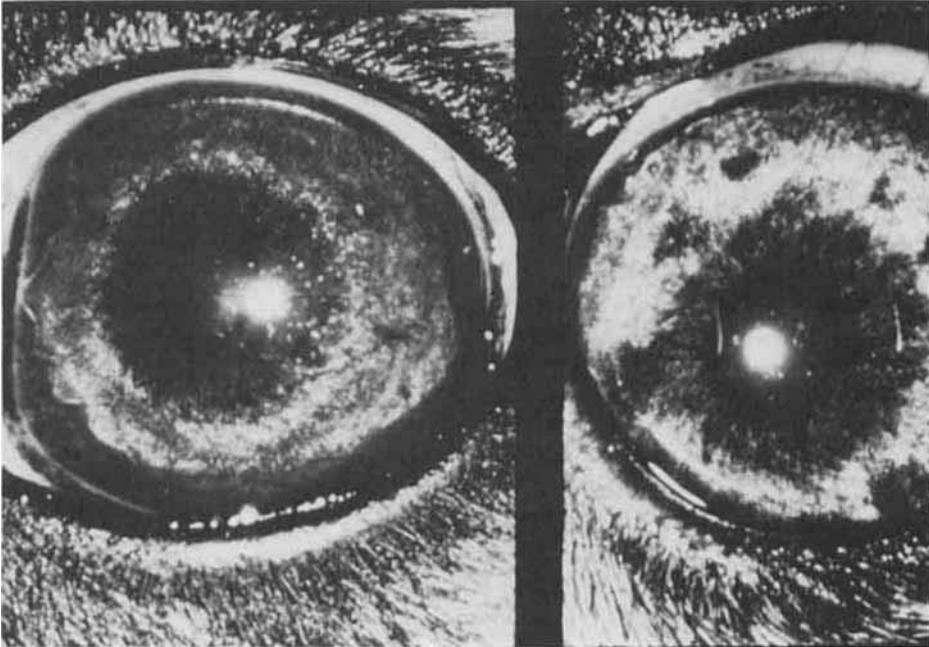


FIG. 6. Shown on the left is the iris of a normal control beagle. On the right is an example of marked depigmentation in the eye of a beagle 905 days post-injection of  $10.7 \mu\text{Ci } ^{226}\text{Ra/kg}$ . (Photos courtesy of Dr. G. Taylor.)

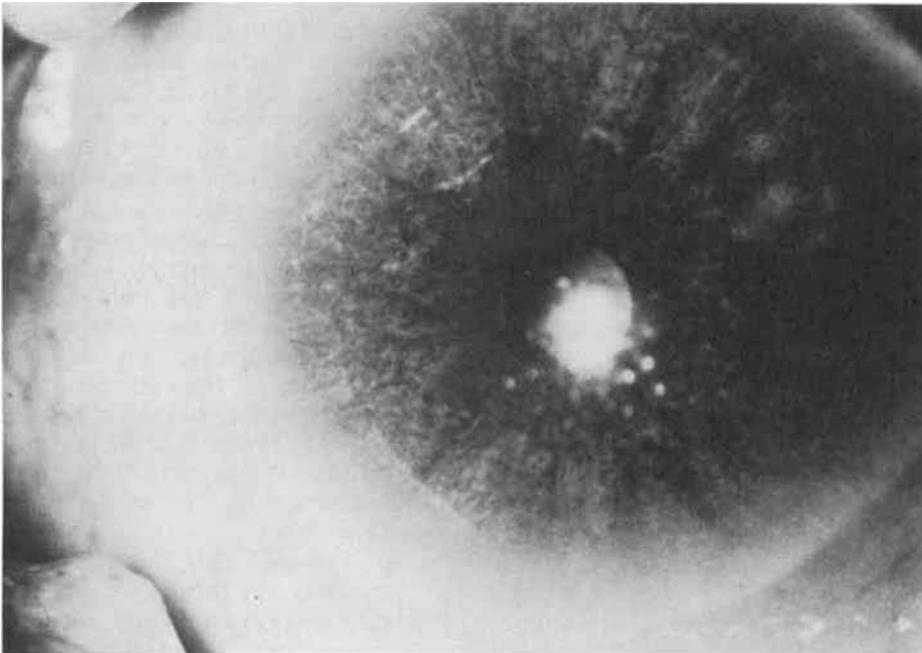


FIG. 7. Normal-appearing iris of a 92 yr old MIT patient 50 yr after ingesting a total of about  $700 \mu\text{Ci}$  of  $^{226}\text{Ra}$  plus  $700 \mu\text{Ci}$  of  $^{228}\text{Ra}$ . (Photo courtesy of Dr. P. Laibson.)

find a sound basis for extrapolation of risk estimates from the high-dose domain where injury was observed to the low-dose domain where no injuries have yet been seen.

Dose-response relationships for  $^{226}\text{Ra}$  and  $^{228}\text{Ra}$  in man were first proposed in 1967 based on the first 500 patients studied at MIT. Figure 8 is the familiar flat-topped dose-response relationship of 1970 for radiogenic bone sarcomas and head carcinomas in the *unselected* and *epidemiologically suitable* patients among over 600 MIT radium cases. Note the complete absence of radiogenic malignancies below cumulative skeletal-average doses of 1000 rad, and the approximately constant occurrence at about 28% for doses above 1000 rad. A linear nonthreshold model would have predicted in this group some 15 radiogenic tumors between 0 and 1000 rad. The probability of observing none, if a linear nonthreshold model were correct, is 1 in 5 million. Clearly

the conservative linear nonthreshold model used in much "prudent" radiation protection work is strongly rejected by the actual data in the case of  $^{226}\text{Ra}$  and  $^{228}\text{Ra}$  in man. Even a dose-square model between 0 and 1000 rad clearly overestimates the observed effects.

Figure 9 is from the sophisticated 2-hit model by John Marshall and Peter Groer (*Radiat. Res.* July 1977). The experimental data for unselected plus self-selected cases are shown as data points. They are in comforting agreement with the 2-hit model shown by the solid line. The dosage scale here is computed initial intake. Roughly  $2\ \mu\text{Ci}/\text{kg}$  body weight corresponds to a skeletal average dose of more than 1000 rad in 50 yrs. An interesting point is that below this level, where radiogenic tumors are not seen, this model predicts an occurrence slightly less than proportional to the square of dose.

Figure 10 is the dose-square times an exponential decrement as presented in 1970

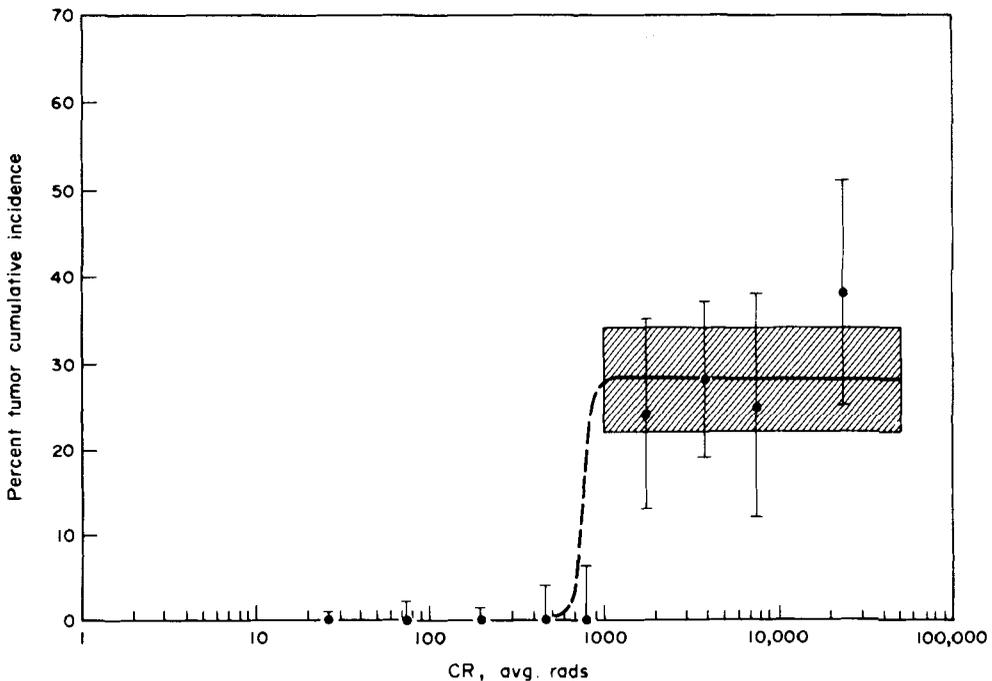


FIG. 8. Dose vs response relationship in 9 dosage cohorts of over 600 unselected and epidemiologically suitable MIT cases of radium in man. See text. (From Evans, *Health Physics* 1974.)

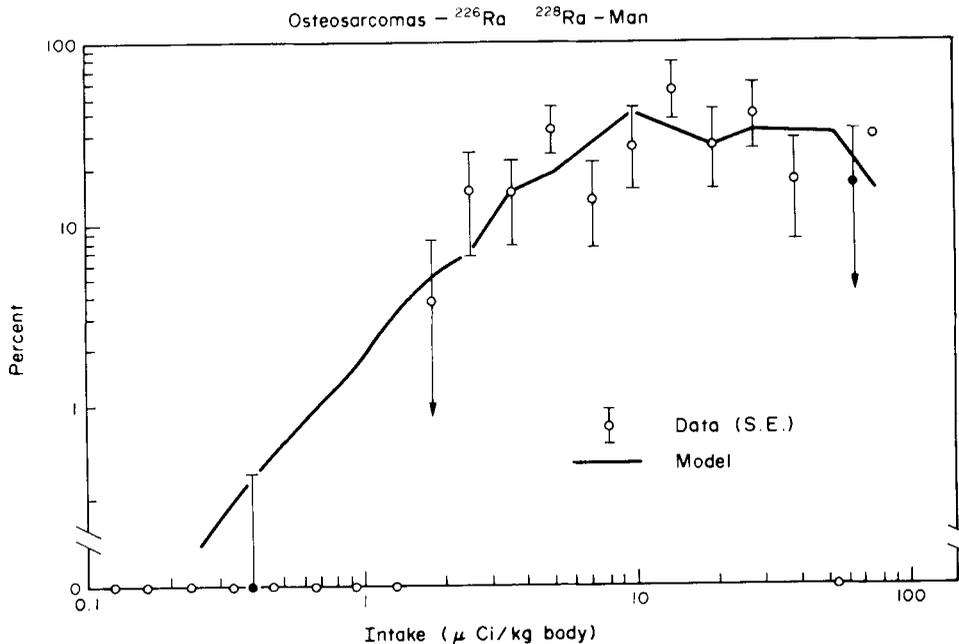


FIG. 9. Theoretical dose vs response curve (solid line) for bone sarcomas, according to the 2-hit model of Marshall and Groer, and data points for combined unselected and self-selected human subjects. In the domain below about 1000 rad ( $2 \mu\text{Ci/kg}$ ) where no tumors are observed, the model predicts a response slightly less than proportional to dose-square. (From Marshall and Groer, *Radiat. Res.* 1977.)

at Evian, France, by R. Rowland *et al.*, as being an acceptable empirical fit to the data from MIT plus ANL/ACRH on some 780 combined unselected and self-selected cases, at the start of operations at the ANL Center for Human Radiobiology. A more recent CHR analysis of 759 pre-1930 dial painters follows the same general pattern of an assumed dose-square occurrence in the low and intermediate dose domain, where no radiogenic tumors are actually observed.

All the available data are being restudied using newer epidemiological and statistical methodologies. Several points are clear.

First, the occurrence of radiogenic malignancies in radium-burdened persons does not follow an ICRP-type linear nonthreshold model. The lifetime risk at low doses is extremely small and may lie somewhere between a dose-square relationship and zero.

Second, the retention function for inter-

nally deposited radium cannot be represented by a single-compartment exponential function. The multicompartiment power-function retention model of W. Norris *et al.* (1955) gives a satisfactory representation out to at least 25 yrs. Beyond about 25 yrs, John Marshall's 1972 model, as given in *ICRP Report 20*, on Alkamine Earth Metabolism gives a smaller and more accurate fractional retention.

Third, as reconfirmed recently by A. Stehney *et al.*, when the radium-related malignancies (i.e. bone sarcomas, and carcinomas of the paranasal sinuses and the mastoid air cells) are excluded, there appears to be no nonspecific life-span shortening in the subgroup of heavily exposed pre-1930 radium-dial workers.

Fourth, actuarial analysis of the radium cases already being followed indicates that more than 100 will survive beyond the year

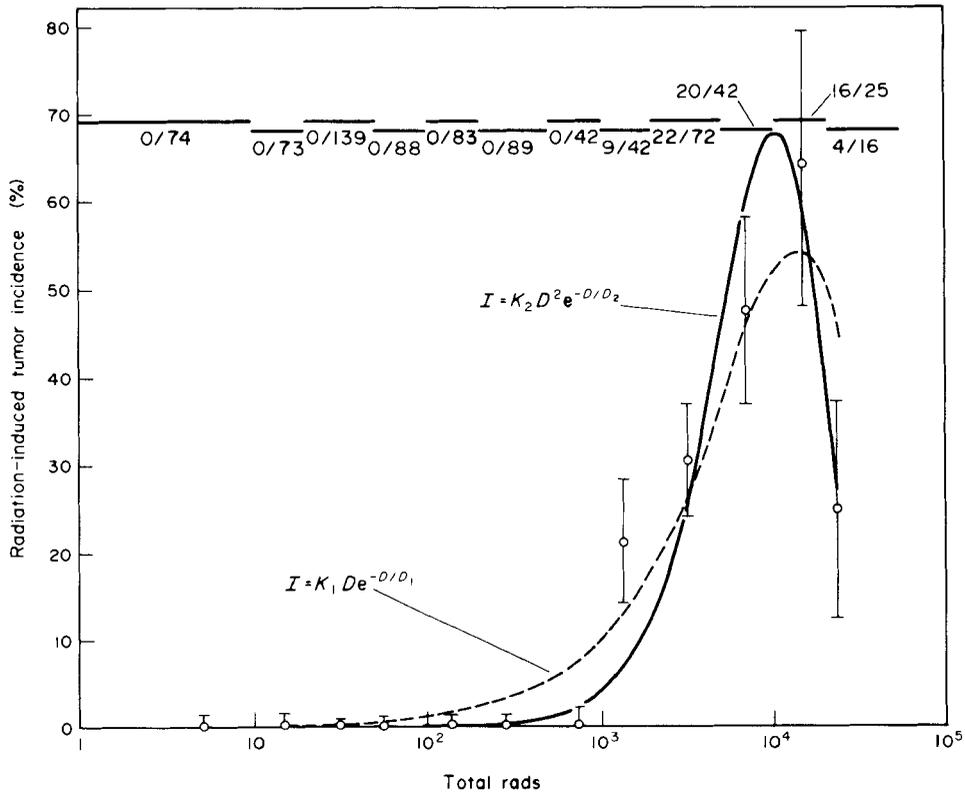


FIG. 10. Dose vs response for 777 unselected plus self-selected persons in combined studies by two research groups, compared with a dose-square times exponential decrement model (solid curve). The peak near 10,000 rad is mainly due to the inclusion of self-selected cases measured only at autopsy or after exhumation. Note the absence of cases below 1000 rad. (From Rowland *et al.*, ANL-7760-Part II, 1970.)

2001. The appearance time, or latency, of radiogenic tumors tends to lengthen with decreasing dose and dose rate. All surviving patients must continue under study until the end of their lives if the full lifetime risks of bone-seeking radionuclides are to be unequivocally quantified.

Finally, we look at the earliest permissible levels for inhaled radioactive aerosols, namely thoron and radon and their daughter products. In late 1937 questions arose in the minds of an insurance carrier concerning radiation safety in a very large thorium gas mantle manufacturing company which they insured. The principal radiation hazard was quickly identified as airborne thoron, Clark Goodman and I designed, constructed and

calibrated a field device for collecting the second daughter product, the ThB (<sup>212</sup>Pb), of airborne thoron on planchets, and airmailing these to MIT for  $\alpha$ -ray counting. Values as high as 4000 pCi Tn/l. were found in various parts of the plant. In a 1938 paper we judged these to be potentially hazardous.

We exposed mice continuously to high levels of radon, but could not produce any lung cancers. We studied the radon levels in contemporary radium-dial painting plants.

Further work by Evans and Goodman on lung cancer hazards in industry was published in 1940. Here we used a simple whole-lung dosimetric model. We calculated lung tissue dose in ergs/g, and compared this with bone dose rates in the radium patients. We

invoked also the lung cancer occurrence among miners of the Schneeberg and Jachymov regions in the Erz mountains of Saxony and Bohemia, compared with Dr. Behounek's measurements of the radon concentrations in these mines. (We had previously exchanged analyzed rock samples with Dr. Behounek, director of the Czechoslovak State Radium Institute in Prague, so we had confidence in the accuracy of his radon measurements.) From these considerations we recommended 10 pCi of radon per liter of air as a safe working concentration "in plants, laboratories and offices".

Bill Bale pointed out 11 yrs later, in 1951, the overriding importance of the short-lived daughter products of radon. This and many other changes involving units of measurement (working level months, etc.), free-ion attachment coefficients (Chamberlin and Dyson), etc. have still not greatly changed this 1940 recommendation.

The 10 pCi/l. value for permissible radon concentration in plants, laboratories and offices was incorporated in the *NBC Handbook 27* in 1941, which became *NCRP Report*

5, and was adopted by the ICRP in their Committee II report of 1959 for the case of continuous (168 hr/week) occupational exposure, with 30 pCi Rn/l. for a 40-hr week.

For those interested in the details, the 25th Anniversary Issue of *Health Physics* June 1980 reprints both the 1940 paper of Evans and Goodman and the widely respected, but seldom seen, unpublished memorandum of 24 March 1951 by Bill Bale.

In summary, there was in the 1930s only the radiation protection standard for external X-rays or  $\gamma$ -rays, as needed primarily for hospital and medical protection. By mid-1941 the remaining two basic standards, one for internal radium burden, and one for inhaled radon and thoron, were in place as the U.S. entered World War II and the Manhattan District's Plutonium Project subsequently got underway.

There are hundreds of physicists, physicians, pathologists, chemists, epidemiologists, support personnel, contracting officers and patients, whose cooperative efforts have made all these studies of men and women possible.