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DOSIMETRY OF PARANASAL SINUS AND MASTOID EPITHEBIA IN RADIUM EXPOSED HUMANS, RADIOLOGICAL & ENVIRONMENTAL RESEARCH DIVISION ANNUAL REPORT - (USED AS A REFERENCE IN OU1, OU2 AND OU5 RI REPORTS)

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RADIOLOGICAL AND ENVIRONMENTAL RESEARCH DIVISION ANNUAL REPORT

Center for Human Radiobiology

July 1979–June 1980

R. E. Rowland, Division Director
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Center for Human Radiobiology

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DOSIMETRY OF PARANASAL SINUS AND MASTOID EPITHELIA IN RADIUM-EXPOSED HUMANS*

Robert A. Schlenker

Dose calculations for ^{228}Ra and ^{226}Ra are presented for the sinus and mastoid epithelia and lead to the conclusion that the isotopes are of comparable dosimetric significance for the production of carcinomas in patients exposed to comparable levels.

Introduction

Carcinomas arise in the sinus and mastoid epithelia of persons exposed to ^{226}Ra and ^{228}Ra. They have appeared sporadically over the last 40 years and have been discussed by various authors. Their importance lies in the fact that they have occurred in humans following internal exposure and, therefore, might be induced by other radioisotopes. It is hoped that by careful study of epithelial cell dosimetry, dose-response relationships developed for radium can be more widely applied.

To begin with, some background information should be considered. Table 1 gives the frequency of occurrence of the two types of cancer known to be induced by radium.[1] The data refer to 2164 persons whose body burdens have been measured by the Center for Human Radiobiology or its predecessors. As can be seen, the carcinomas far exceed the expected number and are about half as abundant as the bone sarcomas. There seems to be no doubt among scientists that the latter would be induced by other bone seekers at comparable exposure levels. The evidence from ^{224}Ra-exposed humans and from animal experiments seems overwhelming.

There is, however, no consensus about the risk of sinus and mastoid carcinomas. This is because of what might be called "the radon hypothesis." Both the ^{226}Ra and ^{228}Ra decay series include isotopes of the noble gas, radon. In

*Edited version of an invited paper with the same title presented June 3, 1980 at the 28th Annual Scientific Meeting of the Radiation Research Society, New Orleans.

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Table 1. Radium-induced cancer among 2164 measured cases.

Type	Observed	Expected
Sinus, mastoid carcinomas	28	∿0.8
Bone sarcomas	60	∿2

the case of ^{226}Ra, most of the radon produced is not retained in the body but is excreted through the lungs. In the late 1930's, shortly after the first sinus carcinoma appeared, Martland[2] proposed that such cancers might be caused by radon gas entering the sinuses from the exhaled breath. Evans[3] later proposed that radon could accumulate in poorly ventilated sinuses and in the mastoid air cells and act in concert with alpha particles from bone to produce these tumors. He observed that the tumor yield at high ^{228}Ra levels was low. Recently, Rowland, Stehney, and Lucas[4] made the same observation and assumed in their dose-effect analysis of the radium data, that ^{228}Ra plays no role at all.

From this history arises the familiar conclusion that ^{226}Ra in combination with radon gas is the sole cause of these tumors. According to this point of view, the risk of sinus and mastoid carcinomas from any other bone seeker would be quite small if the body burdens were comparable to those in the radium cases. Is this really true?

Incidence Data

It should be possible to gain clues from tumor incidence data. Table 2 presents some facts about a well-defined subpopulation of radium cases, radium dial painters first exposed before 1930. Some were exposed only to ^{226}Ra and some were exposed to ^{226}Ra and ^{228}Ra in combination. Of principal interest are the numbers of carcinomas and the numbers of subjects in the high risk group; this latter comprises persons whose ^{226}Ra exposure exceeded the least intake observed to produce a tumor. These data establish one fact with certainty: that

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Table 2. Carcinomas in various exposure categories for radium dial workers first exposed before 1930.

Exposure	At risk	High Risk	Observed	Expected
^{226}Ra	552	61	6	∿0.2
$^{226,228}Ra$	247	53	11	∿0.09
High ^{228}Ra [a]	62	10	0	∿0.02

[a] This group is a subset of the $^{226,228}Ra$ group.

^{226}Ra alone can produce tumors well in excess of expected numbers. In addition, they suggest that when ^{226}Ra and ^{228}Ra are in combination, people in the high risk group are more likely to get a tumor than when ^{226}Ra alone is present. Before accepting this, one would have to carry out a thorough dose-response analysis of the data. While this has not been done, we have found that the dose-effect data for the combined exposure group can be fit well with equations that assume the tumors to be produced by the action of ^{226}Ra alone or by the action of ^{228}Ra alone. In light of this, what seems confounding is that no carcinomas are observed among subjects whose intake of ^{228}Ra was high compared with their ^{226}Ra intake ($\geq 5:1$). Thus, the radium data establish the importance of ^{226}Ra in tumor production but present a picture for ^{228}Ra which is difficult to interpret, yet to conclude from these data that ^{228}Ra is unimportant would be unjustified.

The absence of sinus and mastoid carcinomas among persons injected with ^{224}Ra for therapeutic purposes[5] is sometimes offered as evidence in support of the radon hypothesis. However, this evidence is unconvincing because, as can be seen in Figure 1, the absence of tumors may simply be a reflection of the rather short period of followup compared with tumor appearance time among ^{226}Ra and ^{228}Ra cases.

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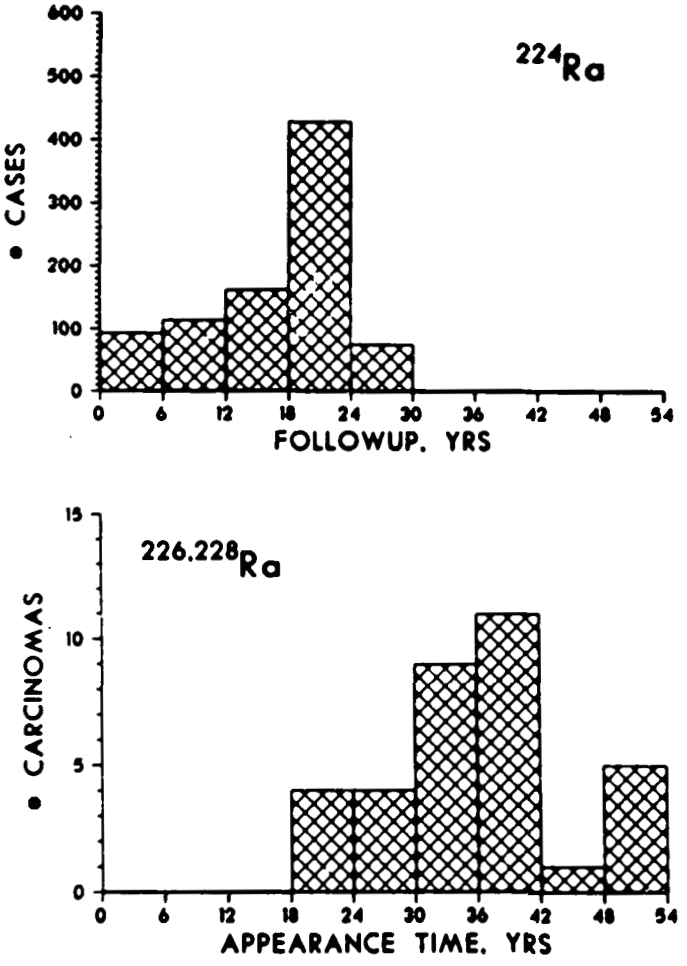

FIG. 1.--Distribution of follow-up times for ^{224}Ra cases compared with distribution of appearance times for sinus and mastoid carcinomas in ^{226,228}Ra cases.

There are no other human populations which offer relevant incidence data. Among studies of animals exposed to radionuclides, the beagle dog project at the University of Utah is the most relevant. Carcinomas have been observed in the frontal sinus and tympanic bulla,[6,7] an area comparable to the mastoid region in humans. Compared with bone cancer, the carcinoma yield has been small, but it is significantly higher than expected. Data are presented in Table 3. The control population at Utah and the combined control populations for the Utah and Davis projects are insufficiently large to establish the statistical significance of the observed carcinomas. The expected values are, therefore, based on epizootiological studies of tumor incidence among pet dogs.[8-12]

The data demonstrate that, in the beagle at least, isotopes other than ^{226}Ra are effective carcinogens. Since the incidence for ^{226}Ra is not greater than the incidence for other isotopes, it appears that radon gas in the air spaces was not

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Table 3. Carcinoma of the frontal sinus and the tympanic bulla among Utah beagles

Isotope	At risk	Observed	Expected
^{226}Ra	107	1	0.01
$^{224,228}Ra$	94	1	0.01
Actinides	558	3	0.04
All	789	5	0.06
Utah controls	145	0	0.02
Utah & Davis controls	343	0	--

a major additional carcinogenic factor.

It is clear that the incidence data support conflicting hypotheses about the importance of ^{226}Ra. It should be possible to resolve this situation by study of the target cell dose. The rest of the paper will be devoted to this with the primary objective of showing that at least one isotope besides ^{226}Ra, i.e., ^{228}Ra, is capable of producing doses in the carcinogenic range.

Dosimetry

A microradiograph of a section from the frontal sinus is shown in Figure 2; it contains a large central air cavity with cancellous bone surrounding it. The epithelial cells lie in the mucous membrane which, in life, would line the walls of this cavity and separate the airspace and bone. With ^{226}Ra present in the body, radon gas would flow into the airspace and bombard the mucous membrane from one side, while ^{226}Ra and its daughters deposited in bone would bombard it from the other side. Although the possibility is generally discounted, the same picture holds when ^{228}Ra is in the body, as will be shown. Only, in that case, the gaseous daughter product is ^{220}Rn rather than ^{222}Rn. This point is emphasized because it has been thought that significant amounts of ^{220}Rn could not accumulate in the sinuses and mastoid air cells because of the short radioactive half-life.

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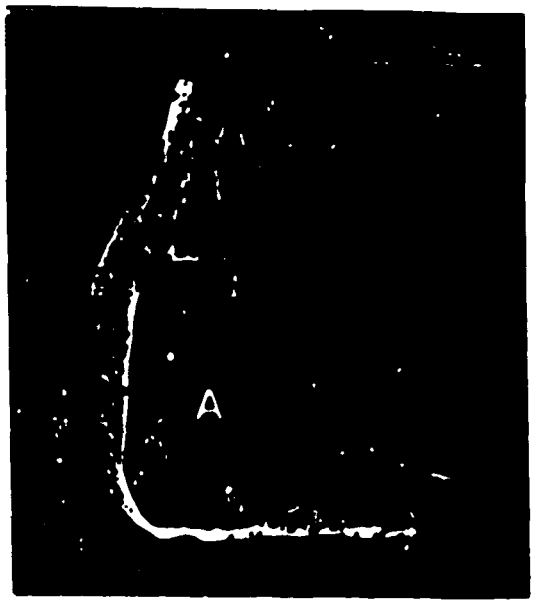

FIG. 2.--Cross-sectional view of frontal sinus showing large air-space (A) surrounded by a region of cancellous bone.
ANL Neg. 149-78-402

The airspace radon flows in from the surrounding bone, but it also may flow out before it can decay. The outflow is by two routes; the mucosal blood flow and by the ostium, the ventilatory duct which connects every sinus with the nasal cavity. Thus, the radon level in the airspace is a balance between the rate of inflow and the rate of outflow.

The actual target cell dose is determined by anatomical variables and by the levels of radioactivity in the bone and airspace.

Anatomical Variables

There are three such variables, two relating to the structure of the mucous membrane and one relating to the size of the airspace.

Lamina Propria. Figure 3 shows the mucous membrane, the bone and air-space. The target cells lie in the epithelial layer. In order for alpha particles to reach this layer, they must pass through the connective tissue portion of the mucosa, the so-called lamina propria. Since alpha particles have a range which is comparable to the thickness of the lamina propria, the latter serves as a shield which protects the epithelium from the alphas from bone.

Table 4 gives data on the thickness of the lamina propria. The values shown have not been corrected for tissue shrinkage nor for obliquity of the sectioning plane. It is thought that these two corrections approximately cancel one another. The data were collected from normal subjects. Keeping in mind that the maximum

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FIG. 3.--A typical region of sinus mucosa showing the epithelial layer (E) and the lamina propria (L) positioned between the bone (B) and airspace (A). (ANL Neg. 149-78-404)

Table 4. Lamina propria thickness.

Number of cases	Site	Range, μm	Fraction <75 μm
2	Maxillary	29 - 541	--
3	Frontal	14 - 207	<0.25
5	Ethmoid	45 - 350	<0.25
5	Sphenoid	55 - 410	<0.25
9	Mastoid	5 - 350	~0.75

alpha particle range is about 66 μm for the ^{226}Ra decay series and about 80 μm for the ^{228}Ra series, one can see that the lamina propria can be either thinner or thicker than the maximum alpha range. A better picture of the dimensions is provided by the right-most column of Table 4 which states the fraction of the lamina propria which is less than 75 μm thick. From this statistic, it is obvious that the sinuses, as a group, have a much thicker lamina propria than the mastoid. This means that, for equal specific activities, the dose from bone in the mastoids will exceed that in the sinuses.

Figure 4 presents the dose-rate from radium in bone as a function of lamina propria thickness, in the sinuses and mastoids. Two conclusions can be drawn

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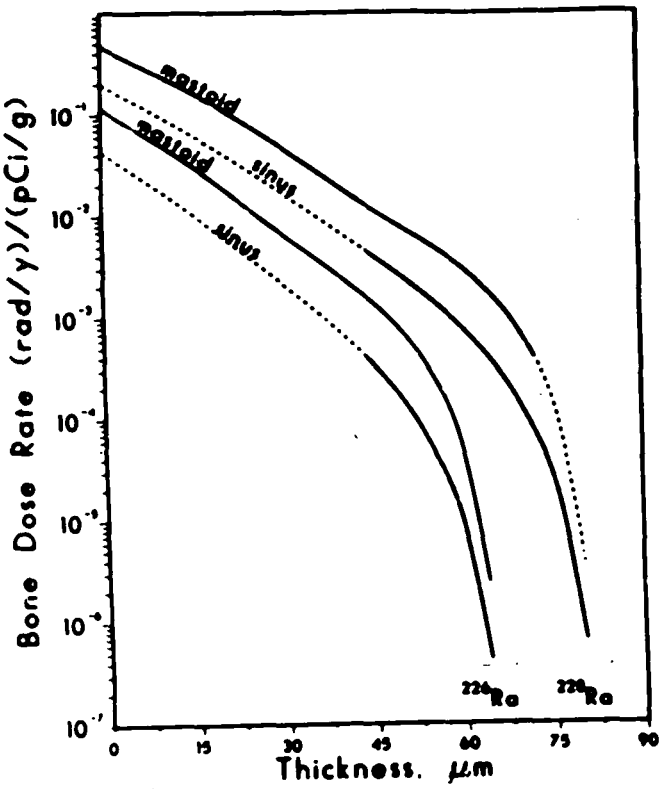

FIG. 4.--Dose rate to the sinus and mastoid epithelia per unit of ^{226}Ra and ^{228}Ra activity in bone. The solid portion of each curve shows the range within which the lamina propria thickness is most likely to fall.

immediately: (1) The dose rate in the mastoid exceeds that in the sinuses, quite likely by a large amount, and (2) the dose rate from ^{228}Ra exceeds that from ^{226}Ra per unit of specific activity. This is our first piece of evidence that, in the case of combined exposure, ^{228}Ra can be as important a source of dose as ^{226}Ra.

Epithelial Cytoplasm. The second variable related to the mucous membrane structure is illustrated by the contrast between Figures 5 and 6. In Figure 5, a section is shown of mucous membrane typical of the mastoid air cells: Substantial lamina propria covered by a thin epithelial layer, usually only one cell thick. Contrasted with this is the sinus mucosa seen in Figure 6, which again has a substantial lamina propria, but a much thicker epithelial layer. Notice the structure of this layer: Cell nuclei concentrated toward the bottom with the cytoplasm from elongated cells extending to the surface of the epithelium. The cytoplasm shields the cell nuclei, which we believe to be the true targets for malignant transformation, from alpha particles entering from the airspace.

Thickness data, presented in Table 5, show that (1) the sinus epithelium

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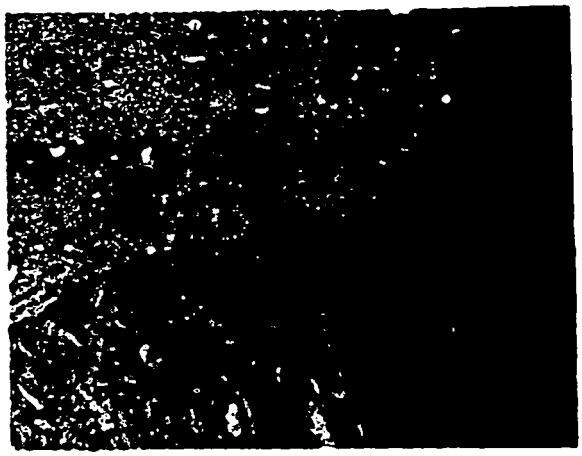

FIG. 5.--Section of mucous membrane typical of the mastoid showing an epithelial membrane one cell thick.

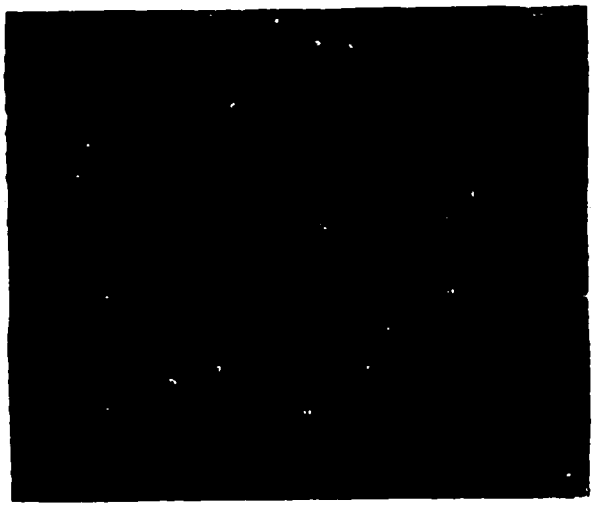

FIG. 6.--Section of mucous membrane typical of sinuses showing epithelial layer in which cell nuclei cluster toward the bottom with a substantial layer of cytoplasm extending above them. A, airspace; E, epithelial layer; L, lamina propria; B, bone. (ANL Neg. 149-78-406)

Table 5. Epithelial thickness in micrometers.

	Sinus	Mastoid
Total		
Range	11 - 136	3 - 40
Typical	40 - 90	5 - 10
Over nuclei		
Range	12 - 84	0 - ∿5
Typical	35	<2

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is generally thicker than the mastoid epithelium, (2) the sinus nuclei lie below a thickness of cytoplasm which can exceed the range of the most energetic alpha particles in either the ^{226}Ra or the ^{228}Ra decay series, and (3) the layer of cytoplasm in the sinus far exceeds the thickness of the layer in the mastoid. Since the layer in the mastoid is so thin, it will be neglected.

The impact on the dosimetry is shown in Figure 7, which applies to the sinuses only. The upper solid and dashed lines refer to ^{220}Rn and the lower ones refer to ^{222}Rn. The solid lines indicate a constant target layer thickness, and the dashed lines indicate it was varied with the thickness of the cytoplasm layer. We see that the layer of cytoplasm has a major impact on the dosimetry. At the typical thickness of 55 μm, the dose rate is reduced by a factor of about 5 for ^{220}Rn and about 10 for ^{222}Rn. Thus, a unit concentration of radon in a sinus airspace may be an order of magnitude less effective than in the mastoid air cells. Furthermore, per unit concentration, ^{220}Rn delivers more dose than ^{222}Rn. This is the second clue we have that the ^{228}Ra decay series may be an important source of epithelial dose.

Airspace Size. The third of the anatomical variables is airspace size. The most dramatic differences in size occur between the sinuses and mastoid air cells, and within the air cell system itself. To illustrate, the distance across the airspace in the frontal sinus of Figure 2 is 1 to 1.5 cm, but the distance across the typical air cell in this mastoid section of Figure 8 is 0.2 cm, although the sizes range from less than 0.1 cm to more than 1 cm. The effect of size on dose rate per unit of ^{222}Rn concentration is seen in Figure 9. First notice that two types of behavior occur, an increase in dose rate with size for the mastoid and ethmoid and a relative constancy for the other sinuses. Note that the mastoid receives a much higher dose rate than any of the sinuses. Among the sinuses, the typical ethmoid receives the highest dose rate, but this is strongly size-dependent. The typical frontal and sphenoid sinuses receive the same dose rate, which is a little higher than that received by the typical maxillary.

In summary, the mastoid receives a greater dose from bone and a greater dose from the airspace than do the sinuses; the bone dose from the ^{228}Ra decay series exceeds that from the ^{226}Ra series in both the sinuses and mastoids; the

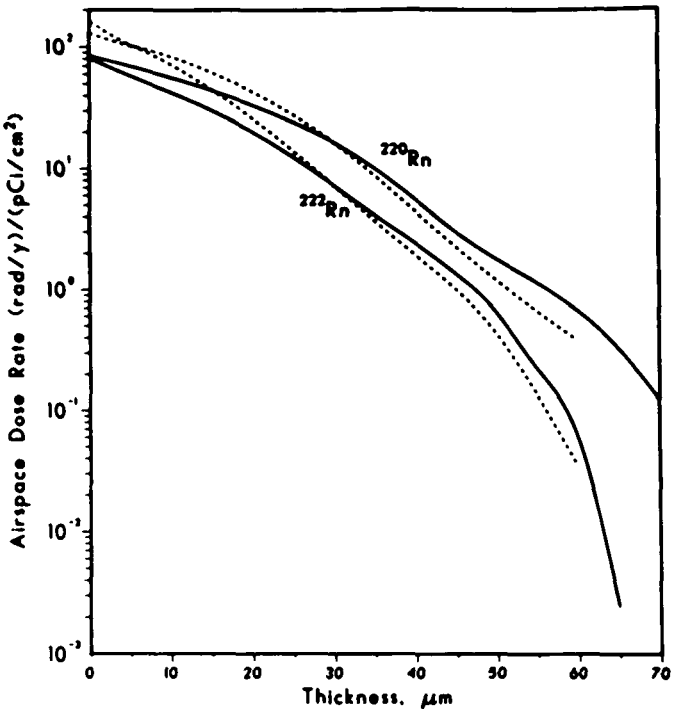

FIG. 7.--Dose rate to the epithelium per unit of radon concentration as a function of the thickness of cytoplasm layer. The upper solid and dashed lines represent ^{220}Rn, and the lower ones refer to ^{222}Rn.

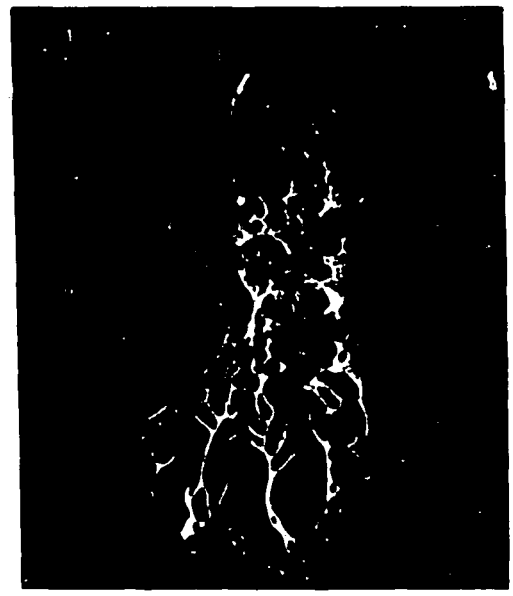

FIG. 8.--Cross section of mastoid showing an extensive set of interconnecting air cells typified by the areas labeled "a" and bordered by a narrow region of cancellous bone. (ANL Neg. 149-7ℓ-403)

dose from ^{220}Rn exceeds that from ^{222}Rn in the sinuses but is the same in the mastoids.

Radioactivity

The next factor that must be considered is the levels of radioactivity which produce the dose.

Airspace Radon. As I mentioned earlier, the radon level in the airspace is a balance between the influx from bone and the efflux through the ventilatory duct and the circulatory system. Studies of sinus and mastoid function by introduction of ^{133}Xe into the airspaces have revealed that clearance follows a single exponential curve, the half-time of which is determined by the status of ventilation or circulation. In general, clearance through the ventilatory duct is much more rapid than clearance by the circulation. Thus, the half-time is relatively short if the duct is open and quite a bit longer if it is obstructed as is

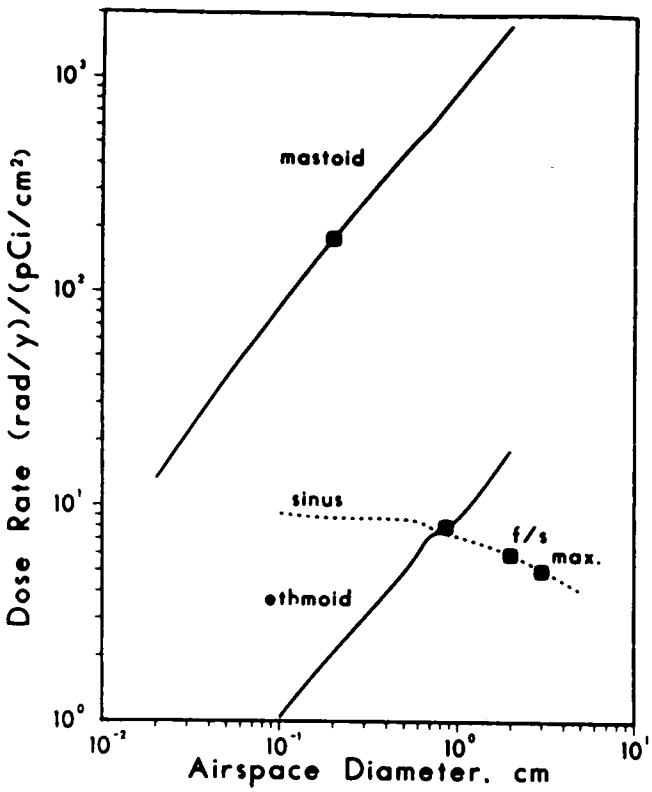

FIG. 9.--Dose rate per unit of ^{222}Rn concentration for the mastoid, the ethmoid and the other sinuses. The typical diameters of the various airspaces are indicated as solid points; f/s designates the frontal and sphenoid which have the same typical sizes.

common in sinus inflammation. Table 6 contains data on the clearance half-times. The circulation half-times are all based on ^{133}Xe clearance experiments,[13-16] and have been corrected for differences between the tissue solubilities of Xe and Rn. The ventilation half-times are based on Xe clearance,[13,14] O_2 exchange,[17,18] and on the frequency of eustachian tube opening.[19] The numbers in parentheses show the number of patients in which the values shown were based. For the frontal and maxillary sinuses, the half-times vary considerably among subjects, but as a rule, clearance is about 10 times more rapid when the ventilatory duct is open than when it is closed. In contrast, ventilation of the healthy mastoid is very slow because the eustachian tube is closed except when swallowing. Thus, a ventilation half-time is only about 1% of the circulatory half-time. For comparison, the radioactive half-times of ^{220}Rn and ^{222}Rn are shown. It is immediately clear that ^{220}Rn which flows into an airspace will, for the most part, decay there before it can be cleared either by the ventilation or circulation. On the other hand, ^{222}Rn will, for the most part, be cleared either by the circulation or the ventilation before it can decay.

Table 6. Half-times for radom removal in minutes.

Site	Circulation[a]	Ventilation[a]
Frontal sinus	>54 (5)	0.9-6.8 (10)
Maxillary sinus	24-117 (5)	∿6 (O_2 model)
Mastoid air cells	24-105 (9)	∿8000 (est.)

^{220}Rn: $T_{\frac{1}{2}}$ = 0.9 min

^{222}Rn: $T_{\frac{1}{2}}$ = 5500 min

[a] ( ) Number of patients.

This fact is expressed quantitatively in Figure 10 where the ratio of Rn activity in the airspace to the radium activity supporting it is plotted as a function of total clearance half-time. This shows that ^{220}Rn buildup is rather independent of the clearance half-time, whereas ^{222}Rn buildup is quite sensitive to it. In the region of the curve marked "ventilation," clearance is by both ventilation and circulation, but ventilation is dominant; in the region marked "circulation" the ventilatory route is blocked, and clearance is by circulation only. The uppermost curve for ^{220}Rn is based on the assumption the 100% of the unretained radon produced escapes into the airspace. Because of the isotope's short half-life, this is unlikely, so a second curve, based on breath ^{220}Rn measurements in humans, is shown in which it is assumed that 0.3% escapes. Now compare the ^{220}Rn and ^{222}Rn curves in the solid regions of the curves. First, consider the ventilation region. We see that the ^{220}Rn activity exceeds the ^{222}Rn activity, no matter which of the ^{220}Rn curves is considered. In the circulatory region, the upper ^{220}Rn curve exceeds the ^{222}Rn curve, and the lower ^{220}Rn curve is less. Apparently the ^{220}Rn level is comparable to, or will exceed, the ^{222}Rn level. These curves show that, despite the short radioactive half-life of ^{220}Rn, its level in the sinuses or mastoids can exceed the ^{222}Rn level in cases of combined ^{228}Ra and ^{226}Ra exposure. This is another indication of the importance of ^{228}Ra.

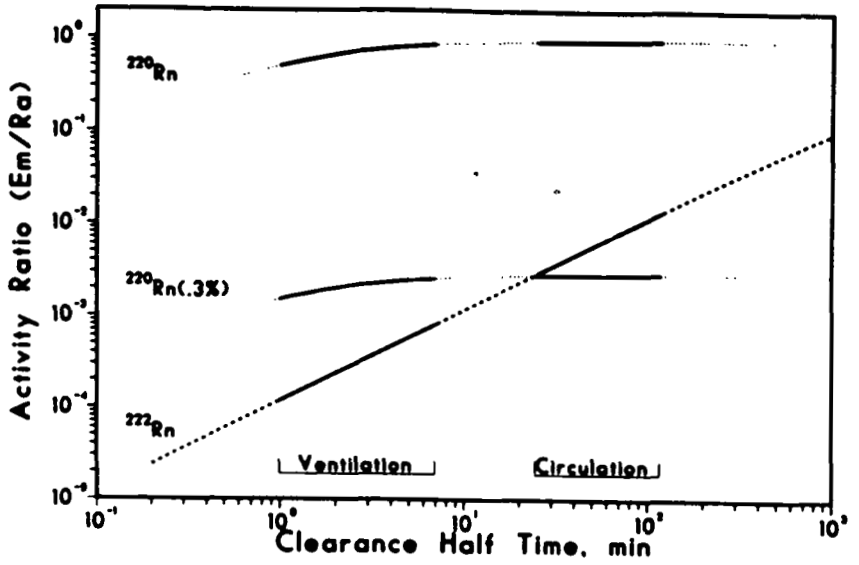

FIG. 10.--The effect of radon clearance from airspaces on radon activity. The solid portions of the curves correspond to the ranges of observed clearance half-times (see Table 6).

While Figure 10 describes the dependence of radon accumulation on clearance half-time, it does not tell how much radon actually accumulates in the airspace. An accumulation model is quite difficult to formulate with certainty because the controlling variables are not all known. The broad features of such a model are, however, clear. First, the radon which accumulates must come from a thin layer of surrounding bone. The section of mastoid in Figure 8 will help to make this clear. The thin bony septa separating the air cells contain no internal blood supply and depend totally on the blood flowing through the surface mucosa for nourishment. Likewise, clearance of the unretained radon produced in these septa can only be via the ventilation or via the mucosal circulation. Thus, the radon from these bony septa will partition between the airspace, bone, and mucosal lining, probably in proportion to the solubility in each of these regions. In order to reach the airspace, radon from the cancellous bone must cross the marrow spaces, which are well vascularized. During its passage, there is a good chance that a radon atom would be entrapped by the circulation and carried off. Thus, bone which is separated from the airspace by a vascularized region will be a less important source of radon than bone which is adjacent to the airspace. The positions of the vascular spaces lead to the conclusion that bone within a

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few hundred micrometers of the airspace surface is the most important source of airspace radon. Exactly how much bone, however, is unknown.

The second major variable is radon solubility. There are no data for bone, so one can only speculate. Solubility within the bone crystals is unimportant since the diffusion times for radon through the mineral are orders of magnitude greater than the radon half-life. However, the bone crystals are very small and provide an enormous surface area which might absorb radon the same way that activated charcoal does. Thus, the solubility of radon in bone could be much higher than in tissue. On the other hand, if this were not an important mechanism for radon retention, then dissolution of radon in the fluids of bone could be the principal determinant of radon solubility and the total solubility in bone could be less than in soft tissue. A third important variable, for ^{220}Rn, is diffusion time from the site of production to the airspace. This is, however, not an important factor for ^{222}Rn. In this case, the simplest model is one which assumes rapid mixing between the bone and airspace. The predictions of such a model are shown in Figure 11 as a function of the ratio of bone solubility to tissue solubility. For comparison, we have just one in vivo measurement of the sinus radon concentration which was made in the frontal sinus. It compared well with the model predictions for a ventilated sinus.

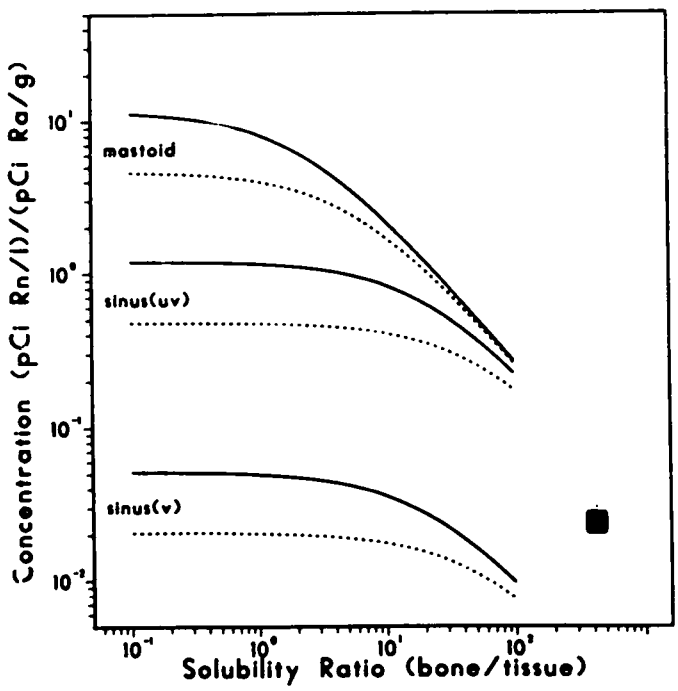

FIG. 11.--Concentration of ^{222}Rn per unit of ^{226}Ra specific activity in bone surrounding the mastoid, the unventilated sinus (uv) and the ventilated sinus (v). Bone layers of 0.05 cm thickness (solid lines) and 0.02 cm thickness (dashed lines) are envisioned as the source of ^{222}Rn gas. The solid point in the lower right shows the one measured value of radon concentration made in vivo. The solubility corresponding to this data point is unknown, and its placement on the right-hand side of the graph is for convenience only.

^{220}Rn results are not shown on this plot, principally because a different model is used to predict the ^{220}Rn concentration. This is necessary because, as mentioned earlier, the diffusion time is such an important factor in ^{220}Rn accumulation. It is likely that diffusion times are slow enough compared with the ^{220}Rn half-life, that the assumption of rapid mixing, on which the model shown is based, would be quite unjustified. To avoid the difficulties presented by this, the assumption is made, in the ^{220}Rn model, that 0.3% of the unretained fraction escapes from the bone which supplies ^{220}Rn to the airspace. This gives mastoid concentrations similar to those for ^{222}Rn and sinus concentrations in both the ventilated and unventilated cases, which are comparable to the unventilated levels for ^{222}Rn.

In summary, ^{220}Rn decays before it can escape from the airspace, whereas ^{222}Rn escapes before it can decay. This simple difference accounts for the fact that ^{220}Rn, despite its short half-life, can contribute substantially to the dose from the airspace in mixed exposures of ^{226}Ra and ^{228}Ra. The radon concentration in the mastoid exceeds, by a large amount, that in the sinuses, and this may help explain the tendency of these cancers to appear in the mastoid.

Radium in Bone. Our early autoradiographic studies, all of which were qualitative, revealed a common pattern of uptake in the mastoid air cells. A typical example is shown in Figure 12. Notice that the intensity is low within the air cell region compared with areas of bone cortex distant from the air cells. This is probably the result of the fact that the mastoid air cells are fully formed by age 15 and only a very few of our patients were exposed younger than this. This observation led to the supposition that the specific activity adjacent to the air cell surfaces was lower than the average skeletal specific activity and, therefore, quite possibly lower than the specific activity adjacent to the sinus surfaces. This would affect the comparative dosimetry of the mastoids and sinuses.

We have begun to collect quantitative autoradiographic information. We sample, as randomly as possible, areas adjacent to and distant from the airspace surfaces. Results on five patients are shown in Table 7. The specific activity of the bone adjacent to the air cell generally lies between the diffuse and hotspot

FIG. 19.--Autoradiographs of bone sections showing less radioactivity immediately adjacent to the air cells than in bone somewhat removed from the air cell boundaries. (ANL Neg. 149-78-345)

Table 7. ^{226}Ra specific activity in mastoid bone, picocuries/gram.

Case	Diffuse	Air cells	Average hotspot	Air cells / Uniform
00-006	390	610	900	0.92
01-014	46	140	550	0.30
01-046	120	180	390	1.0
01-145	200	180	5200	0.14
03-240	190	250	2100	0.21

levels observed in the more distant bone. In addition, the air cell specific activity is generally less than the average skeletal specific activity or uniform specific activity. In any case, it does not exceed it. What is interesting is that it can be several times less than the uniform specific activity and this may signal a major difference between the dosimetry of sinuses and mastoids.

From the radon accumulation model and the specific activities, the mastoid dose rates can be computed for these 5 patients. In computing the dose rate from airspace radon, I have used the conservative assumption that bone solubility is ten times higher than tissue solubility. This produces lower dose rates

than a smaller solubility ratio would. Table 8 shows that the airspace radon is the more important source of dose, a conclusion which is relatively independent of the model assumptions. The time-integrated dose from ^{226}Ra under these assumptions would be several thousand rads for these cases.

Dose Rates

At the beginning, I said that ^{228}Ra has been assumed to be unimportant to the dosimetry of sinus and mastoid carcinomas, and I have pointed out reasons why this may not be so. From all of the data presented so far, it is now possible to predict, with some certainty, the dose rate which would be produced by 1 μCi of ^{226}Ra or ^{228}Ra in the skeleton so that the two can be compared. The comparisons are presented in Table 9 for the sinuses and for the mastoids. Notice first that the bone dose rate from ^{228}Ra exceeds the bone dose rate from ^{226}Ra in all cases. Secondly, the dose rate from ^{228}Ra in the ventilated sinuses exceeds that from ^{226}Ra. Finally, observe that the airspace dose rate from ^{228}Ra is comparable to the airspace dose rate from ^{226}Ra in the unventilated sinuses and in the mastoid air cells. Now these are dose rates for a 1 μCi body burden. In many cases of mixed ^{226}Ra and ^{228}Ra exposure, the intakes were comparable or the ^{228}Ra intake was greater. Therefore, the values in this table

Table 8. Dose rate to mastoid epithelium at time of death, rad/year.

Case	Body burden, μCi ^{226}Ra	Bone	Airspace	Total
00-006	2.61	1.5	6.2	7.7
01-014	2.24	0.34	1.4	1.7
01-046	0.55	0.44	1.8	2.2
01-145	6.33	0.44	1.8	2.2
03-240	4.32	0.61	2.6	3.2

Dose rate ratio (bone/airspace) = 0.24

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Table 9. Dose rates to sinus and mastoid epithelia assuming a one microcurie body burden of ^{226}Ra or ^{228}Ra, rad/year.

Cavity	Isotope	Bone	Airspace, ventilated	Airspace. unventilated
Maxillary	226	0.0046	0.0092	0.21
	228	0.075	0.12	0.15
Ethmoid	226	0.0046	0.011	0.26
	228	0.075	0.12	0.28
Frontal, sphenoid	226	0.0046	0.0095	0.22
	228	0.075	0.16	0.24
Mastoid	226	0.58	--	3.0
	228	4.4	--	2.0

lead to the conclusion that ^{228}Ra is as important a source of dose as ^{226}Ra in such cases of mixed exposure. Furthermore, the absence of tumors, when the ^{228}Ra input was much greater than the ^{226}Ra input, was not due to the fact that ^{228}Ra is dosimetrically insignificant. Indeed, in those cases, ^{228}Ra would have delivered a dose in the carcinogenic range, and we are left to puzzle over the absence of tumors among this group.

Conclusions

Would radioisotopes other than ^{226}Ra produce such tumors at comparable exposure levels? The dose calculations indicate that pure ^{228}Ra would, since errors in the assumptions would affect the ^{226}Ra and ^{228}Ra dose values to about the same extent, and the conclusions about the relative dosimetric importance of the two isotopes would remain unchanged. It is also likely that ^{224}Ra would be carcinogenic at the levels used with humans; the actinides with higher alpha particle energies may well produce a non-negligible risk in the mastoid region where the lamina propria is thin enough for particles to reach the epithelium. Because of the present results, one cannot ignore carcinomas of the sinuses and mastoids as a potential risk from alpha emitting bone seekers.

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