Postprandial Changes in the Exhalation Rate of Radon Produced in vivo

Abstract. *The rate of exhalation of radon by persons with long-standing radium burdens increases about twofold shortly after a meal. The increase is short-lived and "normal" values are regained in 1.5 to 2 hours. The effect may account in part for the poor reproducibility in estimates of the freely emanating part of the radium content.*

We report here the observation of a major postprandial change in the rate of exhalation of radon by persons with long-standing burdens of radium. A short-lived decrease in the rate by about a factor of 2 has been observed in all subjects tested serially soon after breakfast or lunch. Consideration of all the evidence shows that the decrease was a return to "normal" following a rapid increase associated with the intake of food.

The late biological effects, especially carcinogenesis, of radium in man and the evaluation of the radiation dose to the critical tissues of the skeleton provide the basis for radiation protection standards for all alpha-particle-emitting radionuclides which deposit in bone. These include the important heavy radioelements in the nuclear fuel cycle. About 3500 persons with a history of exposure to radium have been located and are under study at the Center for Human Radiobiology. An important part of the program is the determination of the current radium content of each person and clarification of the metabolism, especially the retention pattern, of radium in the human body.

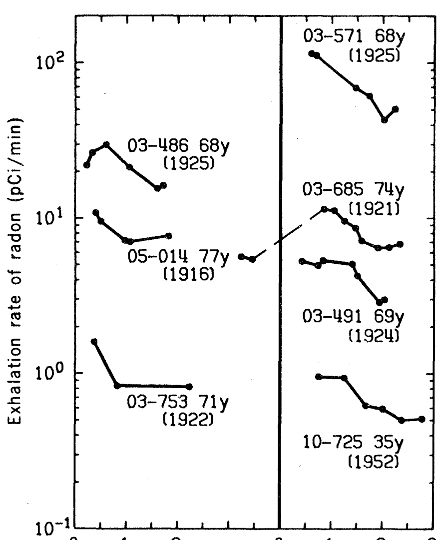

Fig. 1. Exhalation rates of radon for seven subjects as a function of time after a meal. The ages of the subjects at the time of the measurements are shown after the subject numbers, and the year of first exposure to radium is given in parentheses. The freely emanating content of ^{226}Ra in nanocuries is obtained by multiplying the equilibrium rate of exhalation of radon in picocuries per minute by 7.94.

For more than half a century investigators of the metabolism, radiation dosimetry, and toxicity of radium in man have taken into account the fact that more than half of the radon produced in the skeleton is exhaled in the breath (*1*). An estimate of the body's content of ^{226}Ra is thus made by summing the nonemanating part (^{214}Bi, or RaC, content), assayed by γ-ray spectrometry, and the emanating part, determined from the rate of exhalation of radon. Estimates of the RaC content show good reproducibility (*2, 3*), but much variability in determinations of the emanating content has long been recognized (*3, 4*). We have propagated with other known errors a standard error of ± 13 percent of our estimates of the exhalation rate of radon to allow for this variability. At the same time, we have been investigating the nature and magnitude of the variability.

Examination of results accumulated over several years showed that the fraction of radon exhaled was sometimes markedly higher for subjects who were examined in the early afternoon than for those who were examined in the forenoon. In one subject (03-426) where measurements were made in the early afternoon and again the next morning, the apparent fraction exhaled decreased overnight from 0.65 ± 0.05 to 0.55 ± 0.02. In 1974 we made a week-long study in which two subjects (03-529 and 03-685) were tested in both the morning and the early afternoon each day. The reproducibility of the estimates of the RaC content by γ-ray spectrometry was very good for each subject; in one case all observations agreed to within the statistical error of counting (standard deviation of ± 3 percent for a single observation), and in the other case there was an excess coefficient of variation of 2.5 percent. However, in seven out of eight pairs of observations the exhalation rate of radon was higher (by as much as a factor of 2) in the afternoon than in the morning (*5*). We suspected that the increase may have been related to the recent meal, and we have now demonstrated that this is indeed the case.

Figure 1 shows the exhalation rate of radon for seven subjects, determined serially after breakfast or lunch. All but one of the subjects were female and were former radium dial painters first exposed to radium in the years 1916 to 1925; they were aged 68 to 77 years at the time of the tests. Subject 10-725 was a 35-year-old male involved in a radium spill in 1952 (*6*). The rates of exhalation of radon, and therefore the radium contents of the seven subjects, ranged over two orders of magnitude. While the exhalation rates showed different patterns of behavior, they had one thing in common—the rate decreased with time and seemed to have stabilized by 1.5 to 2 hours after the meal. In only one of the subjects in Fig. 1 (03-685) were there observations before the meal, and the first observation after lunch showed a rate twice that before lunch. At about 2 hours after the meal the rate of exhalation of radon was consistent with, though still a little higher than, that before lunch. Similar results were obtained for subject 05-014 on a second occasion when the breath was sampled at intervals for more than 8 hours, starting just after breakfast. We have now observed a postprandial exhalation rate of radon that was higher than before the meal on nine occasions in three different subjects. In two subjects (03-486 in Fig. 1 and 03-607 in Fig. 2),

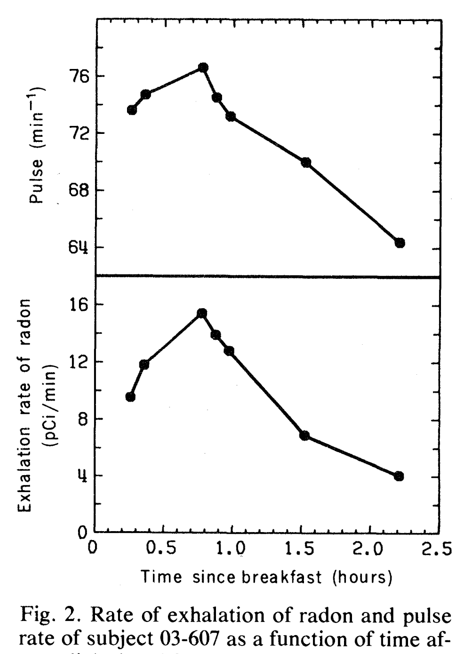

Fig. 2. Rate of exhalation of radon and pulse rate of subject 03-607 as a function of time after a light breakfast (about 360 calories). The subject was a 71-year old former radium dial painter first exposed to radium in 1922.

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breath collection was started soon enough after breakfast, and with short enough sampling times, for an increase to a peak value to be observed.

The mean of the ratio of the highest exhalation rate of radon to the lowest after breakfast was 2.08 (range 1.42 to 3.81) for five subjects (two sets of observations for one of these); after lunch it was 2.04 (range 1.78 to 2.65) for five subjects. The mean times of the maximum and minimum were at about 0.5 hour and 1.8 hours, respectively, after either breakfast or lunch. The variability in the manner in which the exhalation rate of radon decreased, evident in Fig. 1, precluded more detailed comparison of the results.

We observed a strong correlation between the exhalation rate of radon and the pulse rate in the five subjects where this was measured simultaneously with the breath collection. The most striking data (subject 03-607) are shown in Fig. 2. The correlation coefficient was +0.93 ($N = 7$), which was highly significant ($P < .001$). The correlation coefficients for the data from the four other cases ranged from +0.86 to +0.97, and these were all highly significant ($P < .001$ to $P \leq .01$). These correlations suggest that the change in the rate of exhalation of radon observed postprandially is related in some way to the change in blood flow associated with the digestive process, since the blood carries the radon to the lung. A possible explanation is that the increased blood flow in the viscera flushes out a reservoir of radon dissolved in one or more organs (for example, the liver). Whatever the cause, it is clear that a representative value of the exhalation rate of radon cannot be determined from analysis of breath collected less than about 2 hours after a meal. The relatively short duration of the phenomenon, and the longer sampling times than used by us, may be the most likely reasons that such a pronounced effect has not been observed before.

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Muscle Crossbridge Stroke and Activity Revealed by Optical Diffraction

Abstract. *Optical diffraction measurements during rapid releases of active toad muscle show that the sarcomeres contract within 1 millisecond by an amount up to but not greater than 12 nanometers. This distance is identified with the effective working stroke of a crossbridge. The crossbridges immediately start cycling to produce the normal contraction velocity in unloaded muscle.*

Recent advances in our understanding of muscle contraction rest largely on experiments in which step functions of length or tension are applied to an active muscle (*1, 2*) and the mechanical response is measured with a time resolution in the order of 1 msec. These macroscopic measurements involve a whole muscle fiber or at least a substantial part of its length. We have now obtained direct evidence of the structural response at the sarcomere level, using a redesigned form of our dynamic optical diffraction equipment (*3*) to provide a time resolution of better than 0.5 msec and a spatial resolution (*4*) of the order of 2 nm. The results show that (i) the effective crossbridge stroke in a freely contracting muscle is approximately 12 nm, and (ii) crossbridges are cycling at their normal rates within 1 msec after a large rapid release (> 1 percent).

In essence, the experimental system measures the angular spacing of the first-order diffraction beams produced by directing a He-Ne laser beam normally on a muscle specimen (*3*). The two beams are sampled by a rotating slotted disk at a rate of 2.4 kHz and each beam passing through a slot falls on a photodiode. Measurements of the time interval between the outputs of the two photodiodes, together with a knowledge of the system geometry, give the desired angular separation, from which the sarcomere length can at once be deduced. The photodiode outputs are fed into a Hewlett-Packard 2100 S computer, which provides digital data at the sampling rate of 2.4 kHz and also removes systematic noise produced by flutter of the rotating disk. A quick-release device allows specimens to contract freely by amounts up to 2.5 percent of their lengths (that is, 30 nm per half-sarcomere) in a time between 0.1 and 0.2 msec. The experiments reported here were carried out on bundles of four or five semitendinosus fibers from the toad *Bufo marinus*, mounted in Ringer solution at 10°C. Figure 1 shows the data points from two experiments in which the specimen was released abruptly while in dynamic equilibrium during an isometric tetanus.

In Fig. 1a the specimen was allowed to contract freely by 1 percent; as the initial sarcomere length was 2.5 μm, this was equivalent to a contraction of 12.5 nm per half-sarcomere. In Fig. 1b the contraction was 2 percent, equivalent to 30 nm per half-sarcomere as the initial sarcomere length in this experiment was 3.0 μm.

It can be seen in Fig. 1a that the sarcomere contraction closely follows the applied displacement throughout the interval between successive sampling points; that is, in a time $\leq$ 0.4 msec. Within the scatter of approximately $\pm$ 2 nm about the mean level after the displacement, it is of course possible that there could be some exponential recovery or some undetected fluctuations.

To the accuracy of these experiments, however, the sliding filaments in a half-sarcomere undergo a relative displacement of 12.5 nm in a time $\leq$ 0.4 msec, so that their relative velocity is $\geq$ 30 μm/sec. The velocities of frog muscle fibers contracting under a very light load have been measured by Gordon *et al.* (*5*); their values, adjusted to a temperature of 10°C, indicate a maximum relative velocity (V_{max}) of 3.1 μm/sec. Thus the velocity in a half-sarcomere when the tension is released is at least ten times greater than the maximum that the muscle itself can generate.

Evidently this sarcomere contraction of 1 percent is not achieved by the crossbridge cycling action that drives normal muscle contraction. It could be produced entirely by the elastic recovery of stretched crossbridges, as in Harring-