

Chapter 15

In Vivo Analysis and the Whole-body Radiation Counter

L. Burkinshaw

*M.R.C. External Scientific Staff, Department of Medical Physics, University of Leeds,
The General Infirmary, Leeds LS1 3EX, U.K.*

INTRODUCTION

The discovery of radium was announced in 1898, and almost immediately the new element began to be used in industry and in medicine. By the late 1920s, the serious toxic effects of internal contamination with radium were apparent, and in order to study this toxicity it became necessary to be able to measure the total quantity of radium in the living human body. Such measurements are feasible because members of the radium series emit penetrating gamma radiation. Some of the emitted radiation escapes from the body, where its intensity can be measured, and from the measured intensity, the total activity in the body can be estimated. The same technique can be applied to other γ -emitters, and in some cases to β -emitters, if the bremsstrahlung emission is sufficiently intense.

The development of whole-body counting techniques has been reviewed by Spiers¹. During the 1920s and early 1930s, measurements were made using ionization chambers to detect the γ -radiation, although the equipment was insensitive and difficult to calibrate. In 1937, Evans² described the alternative approach of quantum counting. He used a single Geiger-Müller counter placed at the centre of an arc of radius 1 m on which the subject lay. He considered the effects of absorption of radiation by the body, and showed that the response of his counter was relatively independent of the distribution of activity in the body.

With the increasingly widespread use of radioactive materials in post-war years, and with their dissemination as fallout from nuclear weapons testing, more sensitive methods for measuring total body radioactivity were sought. Ionization techniques were improved, using chambers containing gas at high pressure, until the γ -ray emission from the uncontaminated body (principally arising from the natural radioisotope of potassium, ^{40}K) could be estimated with a standard error of about 20% in a two hour measurement. With the development of the scintillation counter, however, much greater sensitivity could be achieved by quantum counting, and by 1962 a counter had been built, using a liquid scintillator, which could determine the γ -emission from the ^{40}K in an average man with a precision of $\pm 2\%$ in 100 s.⁴

The whole-body radiation counter continues to play an important role in monitoring the radioactivity of people liable to radioactive contamination, occupationally or otherwise, but it has also become a powerful tool in medical investigation. Not only can it be used to study the behaviour of administered radioactive tracers, but, as will be seen, it allows us to carry out a detailed elementary analysis of the living human body.

THE MODERN WHOLE-BODY RADIATION COUNTER

General design

The primary purpose of a whole-body radiation counter is to determine the total amounts of γ -emitting radionuclides in the body. In many applications, activities of the order of a few nanoCuries have to be measured. Therefore the designer's aim is usually to surround the subject with sensitive radiation detectors in a low-background environment. It is important to shield the detectors from background radiation, not only to improve signal-to-noise ratio, but also to reduce the disturbing effect of the body of the subject being measured; with no shielding, the body would reduce the observed counting-rate, by absorbing background radiation, much more than it would increase it by emitting the radiation being measured.¹

The designer tries to arrange the detectors in such a way that their overall response is independent of the distribution of activity within the body. If mixtures of isotopes are to be measured, he will choose detectors which as far as possible combine high sensitivity with good energy resolution.

Inspection of the I.A.E.A.'s Directory of Whole Body Monitors⁵ shows that when it was published in 1970, no single design was universally accepted. This is still true in 1977, but two general categories of counter can be distinguished — the 'steel room' counter and the 'shadow shield' counter.

In the former category, the person being measured, and the radiation detectors, are completely enclosed in a room with walls made of some heavy shielding material, usually steel. The subject may sit on a chair or lie on a couch, and he may be viewed by only one detector⁶ or by more than one; on one installation as many as 54 sodium iodide scintillation counters are used⁷. Background counting-rate is minimized by careful selection of materials, and stabilized by removing airborne contamination such as radon daughter products⁸. The individual detectors are scintillation counters, usually with phosphors of sodium iodide, although plastics⁹ or liquids¹⁰ may be used to give higher counting rates at the cost of poorer energy resolution. Ge(Li) detectors have far better energy resolution, but are too insensitive for use in a general purpose whole-body counter.

A fairly typical steel room counter is the one installed in the Department of Medical Physics, University of Leeds (Fig. 1). Eight sodium iodide scintillation detectors are used, with crystals 15 cm in diameter and 10 cm thick. They are placed four above and four below a horizontal couch on which the patient lies supine; if necessary,

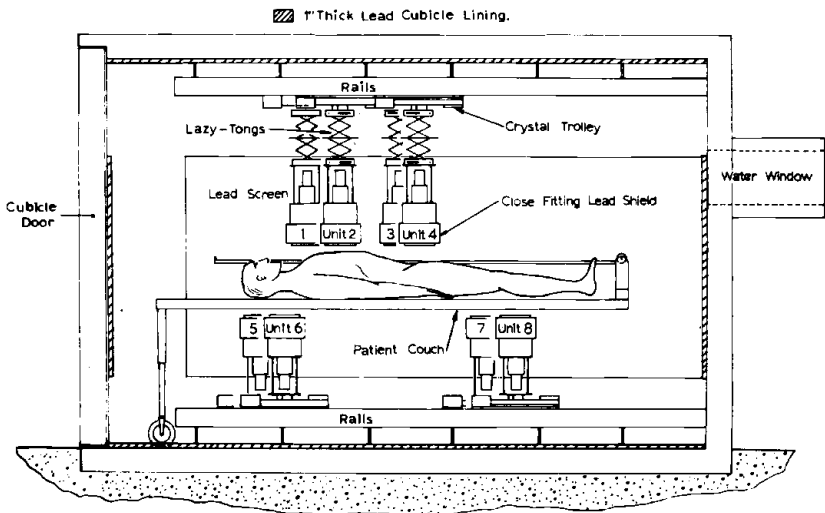


Fig. 1 Whole-body radiation counter with eight sodium iodide scintillation detectors.

the detectors may be driven along the couch at constant speed. The whole is enclosed in a room with steel walls, 5 in thick, partly lined with 1 in of selected low activity lead. The cubicle is ventilated by air passed through coarse filters and an electrostatic precipitator. Background counting-rate within the shield is approximately 1/50 of that outside. The overall sensitivity of the counter is such that the counting-rate from 140 g of potassium in the body can be determined with a standard error of 1% by measuring the subject for 30 min and background for 60 min.

The shadow shield counter was proposed independently by Palmer and Roesch¹¹ and by Boddy¹². In this design, the patient lies on a moving couch and is drawn at constant speed past one or more stationary detectors surrounded by local shielding. Less shielding material is used than in a steel room counter,¹³ so that the equipment is cheaper and lighter. Both Boddy¹³ and Palmer and Roesch¹¹ have built mobile counters on this pattern. Boddy *et al.*¹⁴ describe a counter using a single detector with a sodium iodide crystal 29 cm in diameter and 10 cm thick with which the counting rate from 140 g of potassium in the body can be determined with a standard error of 2.3% if patient and background are each measured for 40 min.

The counters described above have been designed for maximum sensitivity. Simpler counters using both static¹⁵ and shadow-shield¹⁶ arrangements have been described for use with microCurie levels of administered isotopes.

Associated equipment

For optimum performance, stable high voltage supplies and pulse amplifiers are required. Amplified pulses from sodium iodide counters are usually passed to a multi-channel pulse-height analyser, but with detectors of lower energy resolution, one or more single channel analysers with scalers may be adequate. If mixed spectra are to be analysed, the multi-channel analyser must either be on-line to a computer, or it must be able to store data on some medium such as punched paper tape for analysis by a remote computer. In the Leeds system, spectra from the eight detectors are collected simultaneously into different parts of the memory of a 4096-channel pulse-height analyser, and subsequently processed by a small on-line computer.

Detector geometries

When the total amount of radioactivity in the body is to be measured, without regard to its distribution, it is helpful to have an arrangement of detectors whose overall response is as far as possible independent of the distribution. No single arrangement is universally accepted. Figure 2 shows a static geometry

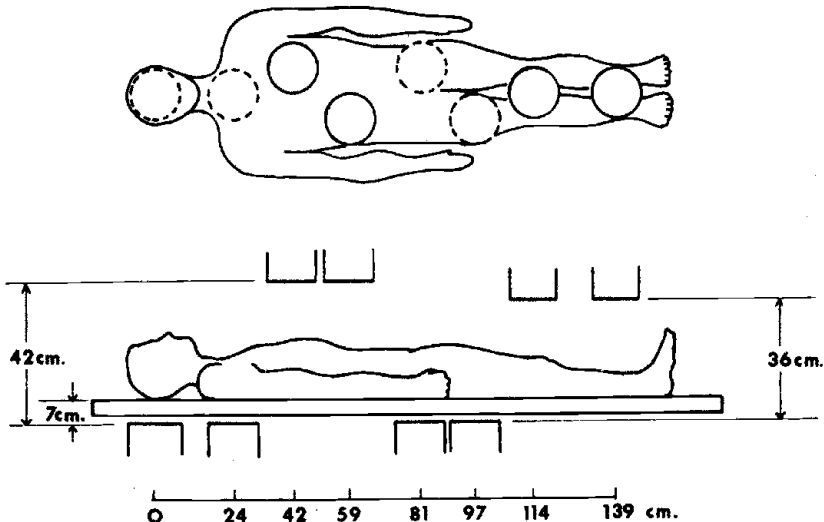


Fig. 2 Static arrangement of eight detectors for whole-body counting.

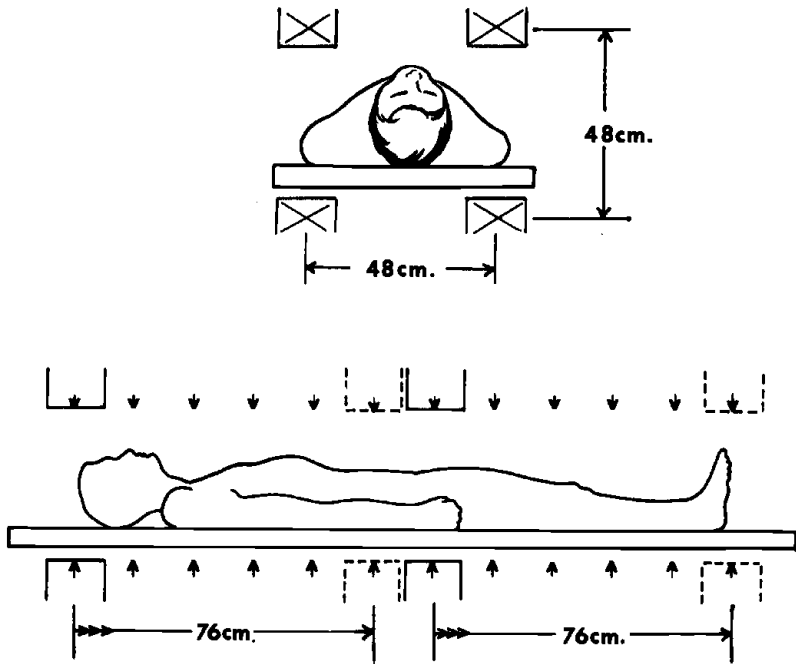


Fig. 3 Stepwise scanning of the body with eight detectors.

used with the eight-crystal counter at Leeds; in which the detectors are distributed as evenly as possible over the projected area of the body.

A scanning counter may have only one detector over the couch, in which case the effects of variable distribution of activity can be minimized by scanning the patient both prone and supine. Alternatively, two detectors may be used, one above and one underneath the couch, and the patient traversed only once. Palmer *et al.*¹⁷ recommend passing the patient horizontally through an array of four detectors situated at the corners of a vertical square. We have adapted this geometry for use with our eight-crystal counter, as shown in Fig. 3. The detectors are arranged at the corners of two vertical squares, one surrounding the subject's head and the other his abdomen. Counts are acquired for, say, 5 min, then the whole array is moved 15 cm towards the subject's feet and a further five minute count taken. The process is repeated until the whole body has been scanned in five steps. Of all arrangements we have tried, this 'stepping geometry' gives the most uniform response¹⁸.

Many other arrangements have been tried in the search for high efficiency and invariant response. For instance, in an early counter, 4π geometry was approached by placing the subject inside a tube whose walls contained liquid phosphor⁴; at the Brookhaven National Laboratory, the patient lies between two parallel arrays of 27 sodium iodide scintillation counters; a counter has been built in which 19 detectors describe a helical path around the patient as they scan along his body¹⁹.

When sodium iodide detectors are used, the degree of uniformity obtained depends to some extent on which part of the γ -ray spectrum is used in computing counting-rates. The photopeak is not the best choice, since it is the region most affected by absorption and scattering in the tissues of the body. We¹⁸ agree with Palmer *et al.*¹⁷ that the counting rate in the Compton region of the spectrum depends least on the distributions of activity and scattering material. However, this part of the spectrum cannot be used if multiple isotopes are being measured, and with low activities the reduction in sensitivity consequent upon using only part of the spectrum may be unacceptable.

Calibration

When the activity in an inanimate sample is measured by γ -ray counting, calibration is usually straightforward, for in most cases standard sources of the radioisotopes present can be made up in a geometry identical to that of the sample. If only a single isotope is present, then the measurement is simply a comparison of the counting rates of sample and standard. If several isotopes are present in the sample, then the spectrum of emitted γ -rays will have to be examined, and a more complicated analysis used, such as the method of least squares²⁰.

In whole-body counting, the samples are living human bodies, and the shape and size of each one is unique. Furthermore, the distribution of activity within the body is never known in detail, and may vary with time. Nevertheless, often the only way to calibrate is to make up a full size anthropomorphic phantom containing a known quantity of the isotope being measured, and to compare the counter's responses to patient and phantom. Phantoms may range in complexity from a set of cylindrical polythene containers roughly mimicing the shape and size of the head, trunk, arms and legs, to elaborate phantoms containing a skeleton, and 'organs' which can be filled individually with radioactive solutions. Whichever type of phantom is used, it can never reproduce accurately all variations of human size and shape. Thus the calibration it gives will be more or less inaccurate, according to the extent to which the response of the whole-body counter depends upon the shape and size of the body and on the distribution of activity within it. The response of the counter can be corrected for self-absorption of radiation within the body by observing the degree to which it attenuates γ -radiation passing through it. Evans did this for his 'metre arc' geometry by recording counting rates from standard radium sources placed against the side of the patient further from the counter. Cohn et al. describe a somewhat similar arrangement in which they observe the attenuation of radiation from a uniform plane sheet of ^{137}Cs .

A whole-body counter can in principle be calibrated for any individual subject by observing the increase in counting rate which results when his body content of the isotope of interest is increased by a known amount. If the response of the counter depends on the distribution of activity in the body, then the method is useful only for isotopes which reach a steady state before an appreciable fraction has been excreted; it cannot be applied if the extra activity administered for calibration purposes delivers an excessive dose of radiation. This technique of internal standardization is commonly used in measuring the retention of administered tracers, (see p.116) and, in modified form, in the measurement of total body potassium (see p.117).

APPLICATIONS

Measurement of internal radioactive contamination

Whole-body radiation measurements were first made in the course of studies of harmful contamination with radioactive substances, and whole-body radiation counters continue to serve in such investigations. For example, by the end of 1975, the Argonne National Laboratory had acquired data on over 1800 people with radium burdens, and direct measurement of body burden by whole-body counting had been made on many of them²¹. The results are being accumulated as part of a long-term study of the effects of radium poisoning. Whole-body ^{137}Cs counters are also used to study the turnover of artificial radioisotopes, e.g. ^{137}Cs ²².

Routine whole-body monitoring of people working with radioactive substances is expensive and time consuming, and is not generally practised. The International Commission on Radiological Protection²³ recommends that, in general, individuals should be monitored only when there is good reason to believe that significant intake may have occurred, but that measurements should then be extended sufficiently to add to our knowledge of the metabolism of the contaminant. The Commission does, however, define a few types of work where they feel routine monitoring is advisable. Among these is work with plutonium. Plutonium contamination is likely to be acquired by inhalation, and special techniques have been developed for measuring plutonium in the lungs, using the L X-rays of uranium, which have energies in the region of 13 to 20 keV²⁴.

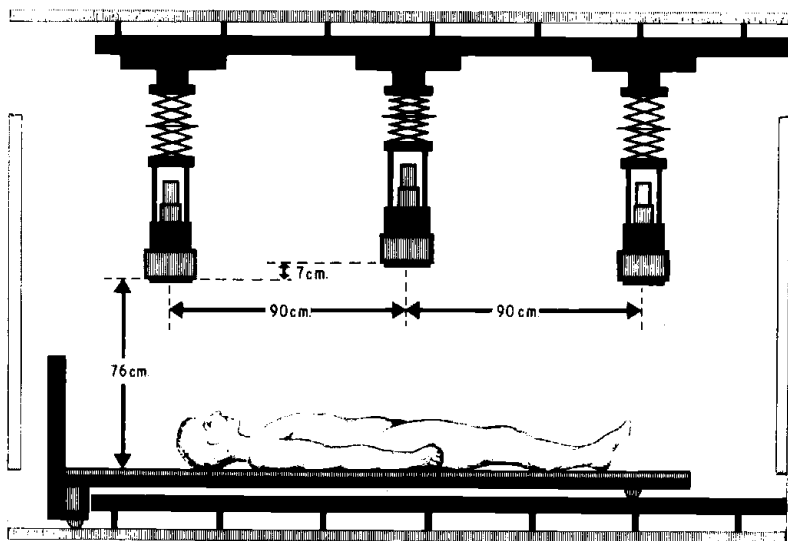


Fig. 4 Arrangement of three sodium iodide scintillation counters for measuring microCurie quantities of administered radioisotopes.

Clinical measurements with administered radioisotopes

Some investigations with administered radioactive tracers require an estimate of the fraction of the activity retained by the body at various times after administration. The obvious technique of collecting and measuring urine and faeces is unpleasant, and it is surprisingly difficult to ensure complete collections for more than a very few days; moreover activity lost by other routes, such as sweat, is not recorded. If the tracer emits suitable γ -radiation, a whole-body radiation counter can be used to measure retention directly, with little or no inconvenience to the patient or nursing staff.

Absolute calibration is usually unnecessary. The counting rate from the patient is measured soon after administration of the tracer, before any activity has been excreted, and subsequent counting rates are expressed as a percentage of the initial value. For this procedure to be valid, however, the counter's response must be independent of the distribution of the activity, for many ^{47}Ca tracers change their distribution drastically during the study. For example, ^{47}Ca given intravenously exchanges rapidly with the calcium of the extracellular fluid, but seven days later it is largely mixed with the calcium in bone, presenting a very different distribution to the counter. This particular isotope poses a further problem. Its half-life is 4.5 days, and some studies require measurements over a period of two to three weeks. Therefore, a relatively large amount (20-30 μCi) must be injected. The resulting count rate in a sensitive whole-body counter may cause errors due to random summing of pulses²⁵. Our own technique with ^{47}Ca has been to place three detectors 76 cm from a horizontal couch (Fig. 4) and to measure the patient prone and supine. Placing the detectors so far from the patient improves uniformity of response and reduces the counting rate; as the activity decays and its distribution stabilizes, measurements can be continued using a more sensitive geometry, after cross-calibration. An arrangement of four detectors, similar in principle to that shown in Fig. 4, has been used at the Oak Ridge National Laboratory¹⁵. A shadow-shield counter with two sodium iodide crystals 10 cm in diameter and 9 cm thick set 91 cm apart¹⁶ has proved valuable in work with administered isotopes.

In routine clinical work, whole-body counters are useful in measuring the intestinal absorption of ^{59}Fe , ^{26}Fe , and of vitamin B_{12} labelled with ^{57}Co or ^{58}Co . The technique is simply to give an oral dose of the substance, with a suitable carrier, and to measure the counting rate from the patient in the whole-body counter immediately after administration, and one to two weeks later when all unabsorbed

material has been excreted. Since both iron and vitamin B₁₂, once absorbed, are excreted very slowly, the ratio of the two counting rates gives the fractional absorption. A high absorption generally indicates a deficiency of the material. In the case of iron, this could result from chronic bleeding into the gut, and the amount of such bleeding can be estimated by measuring the rate of loss of the absorbed ⁵⁹Fe, and comparing it with the activity in the blood.

The disadvantage of using a whole-body counter to measure absorption is the length of time needed. This is particularly evident in the case of vitamin B₁₂, where the 'Schilling test'²⁸ provides an alternative, requiring only the collection and measurement of a 24 h urine sample. The Schilling test does, however, require the injection of a large dose of unlabelled vitamin B₁₂, which may interfere with other diagnostic procedures.

Whole-body counting has been used with other administered radioisotopes in less routine investigations. For example, with ⁴⁷Ca in studies of bone metabolism²⁹, with ²⁴Na in studies of the permeability of the bladder wall³⁰ and with ³²P, by measuring bremsstrahlung, in work on the dosimetry of that isotope³¹.

Analysis of the living human body

Prior to the development of whole-body radiation counters, the total quantity of any element in the living body could be estimated only by dilution. In this technique, a tracer for the element being measured, usually a radioactive isotope of the element, is administered to the subject either orally or intravenously, and its specific activity in the plasma or urine measured after it has mixed thoroughly with the stable element in the body. The activity administered, minus the amount excreted prior to the blood or urine measurement, divided by the specific activity, gives the 'exchangeable' mass of the element, i.e. the mass with which the tracer has mixed. The technique is well established for potassium and sodium. The 24 h exchangeable potassium is equal to about 95% of total potassium³²; the exchangeable sodium is only about 80% of total³³. Apart from this uncertainty in the interpretation of the results, the dilution technique suffers from the disadvantage that it takes a minimum of 24 h to carry out and requires a 24 h urine collection. It is clearly unsuitable for situations where body composition is changing rapidly.

Using a whole-body radiation counter, the potassium content of the body can be determined with an accuracy of a few percent in a single half-hour measurement, without irradiating the patient; if the body is given a small dose of neutrons, several other elements can also be estimated.

Determination of total body potassium. Potassium is an essential body constituent. A healthy adult man contains some 3500 mmol, of which about 98% is inside the cells. Some diseases, and some forms of treatment, may cause loss of potassium from the cells, and if the loss is big enough, muscle weakness may occur; this is especially serious when heart muscle is affected. The concentration of potassium in the plasma is not a reliable guide to the potassium status of the cells, and therefore it is useful to be able to measure the total amount of potassium in the body.

Potassium content is estimated by measuring the intensity of the 1.46 MeV γ -rays emitted by ⁴⁰K, the long-lived radioisotope of potassium, which forms a constant proportion (about 0.01%) of all natural potassium. The whole-body counter can be calibrated using anthropomorphic phantoms containing known amounts of potassium in solution, but a more accurate method is to use ⁴²K as an internal standard^{3,34}. This isotope emits γ -rays whose energy, 1.53 MeV, is very similar to that of the natural potassium. Its γ -rays are then attenuated by the body to the same extent as those of the natural ⁴⁰K. Thus, if the dose of ⁴²K is calibrated prior to administration, by comparing its γ -emission with that of a known mass of ⁴²potassium made up in a similar geometry, the increment in counting rate due to ⁴²K gives the counting rate per unit mass of potassium in the body.

The procedure can be carried out with an oral dose of about 1 μ Ci ⁴²K, so that the radiation dose to the patient, (about 1 mrem) is negligible, but the method is too time consuming for routine use. Therefore it is common practice to calibrate a new counter by giving ⁴²K to a sample of people spanning the range of body builds likely to be encountered in clinical work, and to use the results to estimate

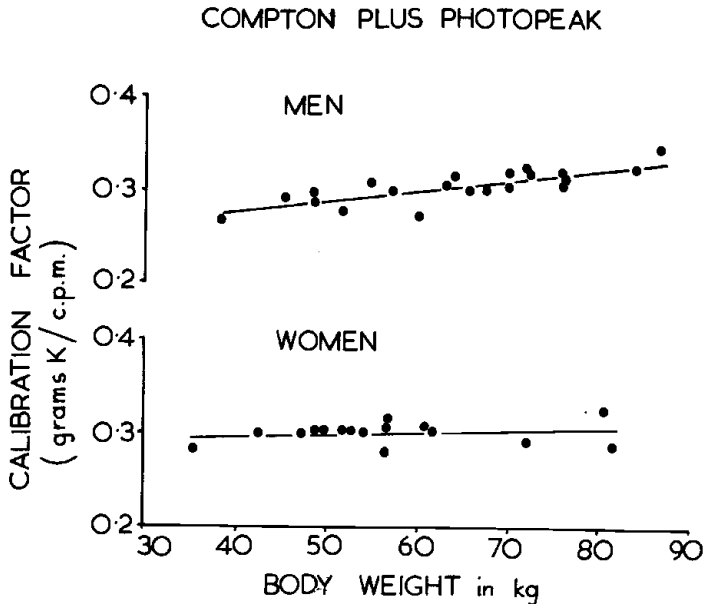


Fig. 5 Calibration of eight-detector 'stepping geometry' for the measurement of total body potassium. Variation of calibration factor, \bar{F} (g K/counts/min⁻¹) with body weight, \bar{W} (kg).

calibration factors for people measured subsequently, without giving them ⁴²K. Calibration factor is commonly found to be correlated with body weight, and the regression equation of calibration factor on weight may then be used to estimate the factor for anyone whose weight is known. Figure 5 shows the results of calibrating the 'stepping geometry' of the eight crystal counter at Leeds, using counting rates in the combined Compton and photopeak regions of the γ -ray spectrum. In this case, the men's values of the calibration factor are calibrated with body weight, whereas the women's are not; the reason for this difference is not known. Using the regression equation of calibration factor on body weight appropriate to the sex of the patient, the potassium content can be estimated with a standard error of between 3 and 4% from a 30 min measurement of the patient and a 60 min measurement of background.

It is probably true to say that it is easier to measure a patient's potassium content than to interpret the result. Practically all the potassium is within cells, and about 70% of it is in muscle; fat contains very little potassium. Therefore, because healthy people contain variable proportions of fat and muscle, potassium content varies considerably, even in people of the same weight. The coefficient of variation for men of a given weight is about 10%. Therefore a man may have a total body potassium 20% below the mean for his weight and be quite healthy, or he could have lost 40% of his potassium, having been 20% above the mean when well. By taking into account height, age and skinfold thickness, as well as weight, the coefficient of variation for normal subjects can be reduced to about 7%, but this is still comparable with the changes being studied. Normal values can be useful for assessing the potassium status of groups of patients, provided their body composition is not abnormal, e.g. because of oedema, but when individuals are being studied, the experiment must be designed to demonstrate a change in response to disease or therapy.

Measurements of total body potassium have been made in many clinical investigations. At Leeds we have studied, *inter alia*, the potassium status of patients undergoing haemodialysis³⁵ and of patients with heart disease, particularly with regard to the effects of diuretic drugs³⁶. Many other examples can be found in the literature.

In normal subjects, total body potassium can be regarded as a measure of cell mass, and therefore of musculature. This has led to its use in the field of exercise

Table 1. The principle reactions used for in vivo neutron activation analysis by the measurement of induced activity.

Element	Reaction	Half-life of product	γ -ray Energies/MeV
N	$^{14}_N (n, 2n) ^{13}_N$	10 min	0.51 (annihilation)
Ca	$^{48}_{Ca} (n, \gamma) ^{49}_{Ca}$	9 min	3.1
P	$^{31}_P (n, \alpha) ^{28}_{Al}$	2.3 min	1.8
Na	$^{23}_{Na} (n, \gamma) ^{24}_{Na}$	15 h	1.38, 2.75
Cl	$^{37}_{Cl} (n, \gamma) ^{38}_{Cl}$	38 min	1.6, 2.15

physiology. For example, potassium content has been shown to be strongly correlated with physical work capacity³⁷, and reflects the muscular development of trained athletes³⁸. At Leeds, we found that young men undergoing weight training gained more weight if they also took an anabolic steroid drug; the added tissue was rich in³⁹ potassium, but whether it was muscle, or only intracellular fluid, was not clear.

In vivo neutron activation analysis. The products of many reactions between neutrons and atomic nuclei are radioactive, often emitting γ -rays as they decay. This forms the basis of a well established analytical technique. The sample to be analysed is irradiated with neutrons and the γ -ray spectrum of the radiation products is measured with a γ -ray spectrometer. The qualitative and quantitative composition of the sample can be deduced from the energies and intensities of the various quanta in the spectrum.

In 1964, Anderson *et al.*⁴⁰ showed that the technique could be applied to the living human body, using an acceptably small dose of neutrons. They gave a dose of 1 rem of partially moderated 14 MeV neutrons to each of two volunteers and examined the resulting γ -ray spectrum in a whole-body counter with NaI (Tl) crystals. They recognized reaction products from nitrogen, sodium, chlorine and calcium, and made estimates of the body contents of the last three of these.

The important reactions for this type of in vivo neutron analysis are given in Table 1. The half-lives of all the product isotopes except $^{24}_{Na}$ are short, but provided the patient can be taken to a whole-body counter within a few minutes of irradiation, it is possible to determine these five elements (and potassium by measuring the $^{40}_{K}$ radiation), in a single irradiation and measurement.

Although the reactions with sodium, chlorine and calcium are slow neutron reactions, the body must be irradiated with fast neutrons to ensure adequate irradiation of the deeper tissues. The body may act as its own moderator, or external moderating material may be used.

The neutrons in beams from reactors are not sufficiently energetic for total body activation analysis, but neutrons of adequate energy may be obtained either from radioactive sources, or from particle accelerators. Radioactive sources use the reaction $^{9}_{Be} (\alpha, n) ^{12}_{C}$, to generate neutrons with a mean energy of about 5 MeV; $^{238}_{Pu}$ is a suitable α -emitter for this type of work. Cyclotrons may be used to generate neutrons by a variety of reactions. For instance, the reaction $^7Li(p, n) ^9Be$, gives neutrons with a mean energy of about 3.5 MeV. A cheaper alternative is a sealed neutron generator tube, in which a tritium target is bombarded by deuterons accelerated through about 150 keV; the reaction $^3H(d, n) ^4He$ releases monoenergetic 14 MeV neutrons. Neutrons of this energy must be used if nitrogen is to be determined by the reaction given in Table 1, since its threshold is 11 MeV.

The problems of non-uniformity of counter response are compounded in this type of analysis by non-uniformity of irradiation.⁴¹ Various irradiation and counting geometries have been used. McNeill *et al.*,⁴¹ estimating calcium, use an array of twelve Pu-Be sources surrounding the trunk to deliver a dose of 400 mrem, then count the patient with a set of four counters also surrounding the trunk. Chamberlain *et al.*,⁴² also estimating calcium, place the patient 2 m from the target of a cyclotron and irradiate his anterior and posterior before transferring him to a whole-body counter. Boddy *et al.*⁴³ move the patient through the neutron field of two opposing neutron generator tubes, then measure the reaction products by passing him at the same speed between two NaI counters in a shadow-shield arrangement. At Leeds, we irradiate bilaterally with a single beam of 14 MeV neutrons, then transfer the patient to our eight-crystal counter. The system is described in detail in another paper in this book (see p.129)⁴⁴.

The γ -ray spectrum of the body after irradiation is complex, and must be analysed into its components. The method of weighted least squares may be applied using a library of standard spectra obtained by irradiating each element separately, distributed in an anthropomorphic phantom. A few minor reactions produce isotopes which emit radiation of energy either identical to, or close to, that emitted by one of the isotopes of interest, and corrections must be made for these interferences. This problem also is discussed elsewhere in these Proceedings⁴⁴.

An alternative method of analysis is to measure the prompt γ -rays emitted during nuclear reactions. Harvey *et al.*⁴⁵ have developed a technique for measuring total body nitrogen on these lines. The body is irradiated with fast neutrons in pulses 10 μ s long at a rate of 6 kHz. Between pulses, the fast neutrons are moderated by the tissues of the body and undergo the reaction $^{14}\text{N}(n, \gamma)^{15}\text{N}$ with the body's nitrogen, generating 10.8 MeV γ -rays. These are recorded by adjacent NaI (Tl) counters which are switched on only between neutron pulses. The prompt γ -ray technique has also been used to measure body hydrogen using the 2.2 MeV γ -rays generated in the reaction $^1\text{H}(n, \gamma)^2\text{H}$.⁴⁶ Similar equipment would serve to measure oxygen using the reaction $^{16}\text{O}(n, p)^{16}\text{N}$; ^{16}N emits γ -rays with an energy of 6.1 MeV, but its half-life is only 7 s, so it must be measured immediately after irradiation stops, before the patient is moved.

The dose of neutrons required depends on which elements are to be estimated, on neutron energy and on the precision required. Nitrogen can be determined with a precision of 2-3%, using either induced activity or prompt γ -rays, with a dose of 50-100 mrem. Sodium and calcium require a rather bigger dose; precisions of 1-3.7% have been obtained using doses ranging from about 0.3 to about 2 rem, depending on the equipment used.

Absolute accuracy is difficult to assess, since body elements cannot generally be measured in any other way. The measurement of calcium has perhaps been most thoroughly examined, and Nelp and Palmer⁴⁸ have shown, by irradiating and chemically analysing cadavers, that they can estimate calcium with a standard error of $\pm 5\%$. No similar comparisons have been published for other elements.

In vivo neutron activation analysis has to date generally been used to replace balance techniques, not only for its improved accuracy, but to permit observations to be carried on for months or years, which would be quite impossible using conventional balance techniques. It has been most widely applied to the study of calcium changes in bone disease. In normal subjects, calcium changes very slowly with age, probably by less than 1% per year, so that calcium work potentially makes formidable demands on long-term precision. However, more rapid changes are seen in⁴⁹ disease, and the technique has⁵⁰ been successfully applied to studies of osteomalacia, osteoporosis and renal disease.

Measurements of total-body nitrogen can also be expected to increase in importance, since the results give a direct measure of changes in body protein. We at Leeds are actively engaged in studying the nature of the weight loss which occurs after surgery, and many other applications can be foreseen in nutritional studies.

FUTURE DEVELOPMENTS

No major improvements can be expected in the sensitivity and energy resolution of the whole-body radiation counter, with present technology. Developments over the next few years are likely to be in applications, most immediately in the field of neutron

activation analysis. A great deal of detailed work remains to be done to establish the accuracy of absolute measurement of the elements currently being studied, and to extend the technique to other body elements.

In clinical work, measurements have to be made on very sick people, and it is often advantageous to be able to take the equipment to the patient. It is hard to imagine a general purpose whole-body radiation counter made small enough to take to a hospital ward, but it seems conceivable that a small pulsed neutron generator tube and a sodium iodide detector could be combined in a portable apparatus which would give a reproducible measure of body nitrogen by the prompt γ -ray technique.

A rather neglected aspect of whole-body counting is the study of the distribution of activity in the body. Any scanning or multi-detector counter will show the distribution of counting rate, but, because of the limited spatial resolution of detectors, and absorption of radiation in the body, this is always a distorted picture of the distribution of activity. Miller⁵¹ and Parr et al.⁵² have devised techniques for estimating activity in defined segments of the body, and at Leeds we are currently pursuing an extension of their ideas. Each volume element of the body can be regarded as a distinct source of activity, and the pulse-height spectrum it generates in external detectors is unique, since it depends on the position of the element relative to the detectors and the amount of intervening tissue. Therefore, given a library of spectra of unit activity in each element of the body, the actual activity in each body element of a patient can in principle be calculated from his complete pulse-height spectrum, by the method of least squares. Our results so far, using phantoms, are promising.

The most useful development in the technology of detectors for whole-body counters (and indeed, for many other applications) would be one which made possible a whole-body radiation counter with the energy resolution of a Ge(Li) detector, but with the efficiency of a present day whole-body counter, and at comparable cost. This would greatly facilitate the analysis of the complex γ -ray spectra acquired in neutron activation analysis, and might enable us to determine other elements whose reaction products are hidden in the pulse height spectrum of a sodium iodide counter.

CONCLUSIONS

The whole-body radiation counter provides the only means at present available of attempting a detailed analysis of the intact, living human body. It is potentially capable of estimating the quantity and distribution of most of the major body elements. With the help of administered radioactive tracers it can then go on to demonstrate the dynamic behaviour of these and other substances in the body. These techniques already have an established place in medical research and diagnosis. With further development, they will make increasingly valuable contributions in the future.

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