Isotope techniques in the measurement of human body composition

By J. S. GARROW, *Clinical Research Centre, Watford Road, Harrow, Middlesex*

Most of the papers in this symposium are concerned with dynamic studies: isotopic tracers may provide information about the metabolism of labelled molecules within the living body which cannot be obtained by any other means. However, in the measurement of body composition, isotope techniques are in general less powerful. If you wish to know how much water, protein, fat or mineral a whole body or a particular tissue contains the most accurate way of obtaining the answer is to subject the body or tissue to the appropriate chemical analysis. With small animals this is a perfectly practicable procedure: for example one can determine the total energy content of a rat by direct bomb calorimetry (Miller & Stock, 1969). In the measurement of human body composition, however, such an approach is obviously not acceptable, so the total energy content of a living man must be determined by less direct, and consequently less accurate, methods.

Before going on to consider the place of isotope techniques in the estimation of human body composition, it is useful to review briefly the information which has been derived from the chemical analysis of a small number of human adult cadavers. Table 1 summarizes the results obtained by Mitchell, Hamilton, Steggerda & Bean (1945), Widdowson, McCance & Spray (1951), Forbes, Cooper & Mitchell (1953) and Forbes & Lewis (1956) from the analysis of six adult bodies. Table 2 shows the composition of some human tissues, determined by direct chemical analysis (Dickerson & Widdowson, 1960; Widdowson & Dickerson, 1960). The composition of the whole bodies shown in Table 1 is given in relation to fat-free weight, and on this basis there is quite good agreement between the analyses of bodies

Table 1. *Contribution of water and protein to the fat-free weight of six adult human bodies*

Age (years)	Water (g/kg)	Protein (g/kg)	Remainder (g/kg)	Potassium (mmol/kg)	K:N ratio
25	728	195	77	71·5	2·29
35	775	165	60	—	—
42	733	192	75	73·0	2·38
46	674	234	92	66·5	1·78
48	730	206	64	—	—
60	704	238	58	66·6	1·75
Mean	725	205	70	69·0	2·05

For sources of these values, see above.

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Table 2. *Composition of some organs in the human adult*

Organ	Water (g/kg)	Protein (g/kg)	Remainder (g/kg)	Potassium (mmol/kg)	K:N ratio
Skin	694	300	6	23·7	0·45
Heart	827	143	30	66·5	2·90
Liver	711	176	113	75·0	2·66
Kidneys	810	153	37	57·0	2·33
Brain	774	107	119	84·6	4·96
Muscle	792	192	16	92·2	2·99

For sources of these values, see p. 25.

ranging in age from 25 to 60 years. The fat in these bodies, as a percentage of total body-weight, varied from 4·3 to 27·9. Thus it appears that the human body may be thought of as a lean body mass, of fairly constant composition, with a variable amount of fat added. As a first approximation, for subjects of normal body composition, this is a useful concept. However, inspection of the values shown in Table 2 will demonstrate that, if the lean body mass is of constant composition, this is not because all its components have the same composition, but rather that a mixture of similar proportions of these components will have a constant composition. For example, skin has a relatively low content of water and potassium compared with the body as a whole, while brain and muscle are rich in K. Since any normal adult body will contain roughly the same proportions of skin, brain and muscle the K concentration of the lean body mass is fairly constant at about 69 mmol/kg.

It is very fortunate that K contains a constant fraction of the natural isotope ^{40}K, which has a radioactive half-life which is long compared with the human lifespan, and which emits a γ-ray with an energy of 1·46 MeV. The high energy of this radiation ensures that wherever an atom of K may lie within the human body, there is a high probability that the γ-ray will penetrate the tissues and emerge from the skin, so, provided that suitable arrangements are made to record the emergence of these γ-rays, the K content of the body can be calculated. Two types of detector are used to record the K radiation from human subjects: one consists of an annular tank of scintillation fluid in which the subject is placed, and the other is an array of crystal scintillation detectors so placed about the body that the sample of radiation captured by the crystals is as large as possible and as far as possible representative of the radiation from the whole body. In each instance the detector system (often called a whole-body counter or gamma spectrometer) must be surrounded by a massive screen of lead or steel to protect the extremely sensitive detector system from external sources of radiation. The amount of radiation which comes from the ^{40}K content of a normal adult is very small compared with background radiation, even within a well-constructed radiation shield, but development of better detectors and sophisticated data handling systems have improved the accuracy with which the K radiation can be differentiated from other types of radiation. The limitations to the accuracy of the technique lie in the statistical uncertainties of a random counting rate and in the problems of calibration. Since the emission of γ-rays from ^{40}K is a random event in time the statistical accuracy of the answer can be increased by

taking a larger sample of radiation; that is, by counting for a longer time. Counting times of 10–30 min are commonly used, and are limited by the tolerance of the subject and the work load on the apparatus. However, even with infinite counting times and infinitely stable electronics, it would not be possible to obtain infinitely accurate estimates of total body K, since each gamma spectrometer must be calibrated with a phantom containing a known amount of K which should, ideally, be distributed in an identical fashion to that in the subject. We do not know the distribution of K in the subject, so the ideal phantom cannot be constructed. An ingenious way round this difficulty is to give the subject a known dose of the short-lived isotope ^{42}K, which by another lucky chance has radiation characteristics similar to those of the naturally occurring ^{40}K. On the assumption that the distribution of the administered ^{42}K is the same as the subject's own ^{40}K, it is now possible, for this subject, to make an absolute calibration of the spectrometer. In practice the standard error of ^{40}K measurements of an adult in a good spectrometer is about 3% and recently this order of accuracy has been claimed for measurements on human infants also (Novak, 1973).

It is lucky for students of human body composition that K has its own natural radioactive tracer, but by neutron activation many more elements can be brought within the grasp of a gamma spectrometer. A technique has recently been described (Boddy, Holloway & Elliott, 1973), by which the subject passes through a shadow shield neutron generator and then through an adjacent shadow shield detector system, so that in the course of 40 min the body content of calcium, phosphorus, sodium, chlorine and nitrogen can be determined. I have no personal experience of these techniques, which are expensive and involve a significant dose of radiation to the subject, but it is clear that neutron activation is likely to make a great contribution to the measurement of human body composition, as it has done in analysis of inanimate material.

Isotope tracer methods can be used to measure the amount of material in any well-mixed pool. For example, if a known amount of water, labelled with either deuterium or tritium, is given to a human subject, this will over the next few hours become mixed with the water in all the fluids in the body. When equilibrium conditions are reached, a sample of any of these fluids can be taken (usually blood or urine or both) and the concentration of tracer is determined. Allowance is made for the loss of tracer during the equilibration period, and from the concentration of tracer at equilibrium, and the dose remaining at that time, the total body water pool can easily be calculated. The accuracy of estimates of pool size by this dilution method depends on two factors: the extent to which the tracer is really uniformly distributed throughout the pool to be measured, and the accuracy with which the concentration of tracer at equilibrium can be measured. Theoretically the experimental conditions can be manipulated to achieve almost infinite accuracy in both respects, but in clinical work the tolerance of the subject determines practical limits. The longer the equilibration period the better equilibration must be, since any mixing of body fluids can only increase the uniformity with which the tracer is distributed, always provided that no unlabelled water is taken in the meantime. It is convenient to

measure total body water in patients by giving the tracer dose in the evening, and taking the blood sample in the morning before breakfast, since in this way the whole night is available for equilibration, and this is a time when insensible water losses are small and it is not unduly inconvenient for the subject to refrain from eating and drinking. The tracer used for water may be either tritiated or deuterated water. The former is more convenient to measure, since it is radioactive, but deuterium can be measured with very high accuracy by mass spectrometry. For measurements of high accuracy it is necessary to take a sample of body fluids before giving the tracer dose, since the natural abundance of deuterium in water varies from place to place.

The tracer dilution principle is applicable to any well-mixed pool, and it has been used to estimate total (or more accurately 'exchangeable') K and Na in human subjects. These measurements are not very satisfactory, since total K is better measured by the natural ^{40}K, as described above, than by dilution of administered ^{42}K, and the total body Na pool is by no means well-mixed. A dose of radioactive Na does not equilibrate with the Na in bone, so exchangeable Na is considerably less than total Na determined by direct analysis. In some circumstances, however, exchangeable Na may be of interest. Another application of the tracer dilution principle is in the measurement of total body fat from the absorption of fat-soluble gas. Hytten, Taylor & Taggart (1966) obtained very good results with radioactive krypton gas, and Lesser, Deutsch & Markofsky (1971) used cyclopropane. The disadvantage of the technique for clinical use is that it requires the subject to breathe in a leak-proof, closed-circuit apparatus until equilibrium is reached, and this is not acceptable to any but highly co-operative subjects.

The third general method by which isotopes may assist in the determination of human body composition is by photon absorption. Here the isotope, such as ^{241}americium, is used as a constant source of 60 keV photons, and the absorption of this radiation as it passes through tissue is determined by the thickness and composition of the tissue. The technique of scanning a limb with a collimated photon beam is used principally to estimate skeletal mass (West, 1973), but the difference in specific absorption of fat and lean tissue makes it possible to use a similar system to estimate the fat:lean ratio in a limb (Mazess, Cameron & Sorenson, 1970).

This symposium is concerned with techniques, not applications. However, it is relevant to consider whether available techniques are good enough, and this in turn raises the question: why did you want the information in the first place? For most purposes available methods for measuring human body composition are good enough. For example it is reasonable to relate many physiological measurements, and the dosage of certain drugs, to the lean body mass of the subject rather than his total body-weight or surface area. An estimate of lean body mass within a kilogram or two is quite adequate for such purposes. There is a need for a more precise definition of obesity than mere overweight, but here too available methods are good enough, although the accurate methods for measuring body fat are inconvenient for field use. The point at which our present methods for measuring human body composition

are seen to be quite inadequate is in the study of energy balance. At the beginning of this paper, I noted that one could determine the total energy content of a rat by bomb calorimetry, but that this approach was inapplicable to man. Unfortunately none of the techniques which have been reviewed above, or any combination of these techniques, can tell us the energy stores of a human subject with an accuracy better than about 10 MJ (2400 kcal). In the study of disorders of energy balance we are concerned with imbalances of the order of 200 kJ/d (48 kcal/d), but by measurement of body composition this would take 2 months to detect. A tenfold increase in the precision with which human energy stores can be measured would therefore be very welcome.

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