Chapter 16

What is the Value of Whole-body Counting in Medicine?

Keith Boddy, Ph.D., D.Sc., F.Inst.P.

Scottish Universities Research & Reactor Centre, East Kilbride, Glasgow G75 0QU, Scotland.

Whole-body counters, the first constructed some years ago, were developed originally to measure radioactivity ingested or inhaled accidentally by radiation workers[1]. At a relatively early stage, it became conventional to house the detectors (and subject to be examined) in a complete room with walls, floor and ceiling of lead (some 10 cm thickness) or steel (usually about 15 cm thickness) in order to reduce the background counting rate.

The potential usefulness of these devices in medicine was quickly appreciated[2]. However, their widespread application to patients was probably retarded by the cost and weight of the equipment in relation to the hospital environment and by the remoteness of major nuclear centres, in which most counters were established initially, from centres of population. More recently, simpler and cheaper designs of whole-body counter have evolved for clinical use, as reviewed elsewhere[3]. Our own whole-body counters[4-6] have a high clinical utilization but this situation is not common to all groups of workers. The purpose of this paper is to reassess the value of whole-body counting in medicine, based on our experience. The factors considered are the uniqueness of the clinical data provided, the accuracy of the results, compared with alternative methods where these are available, the convenience to the patient and economic aspects.

MEASUREMENTS OF BODY COMPOSITION

The total body content of several important body elements can be measured directly and uniquely by whole-body counting.

Total body potassium (TBK) can be determined by detection of the 1.46 MeV gamma rays from the naturally occurring radionuclide ^{40}K, which is a constant fraction of TBK. The counter can be calibrated to take account of the variation of the counting-rate with body habitus either by administration of ^{42}K, which emits 1.52 MeV gamma rays of similar energy to those of ^{40}K and assumes a similar distribution in the body[7], or by using a range of anthropomorphic phantoms containing known amounts of potassium. It is then only necessary to make a single measurement on the patients. The accuracy of the TBK value is about 2-5% for a subject with 3500 mmol of potassium[8-12]. Potassium is an important body electrolyte influenced by a number of clinical disorders and by their treatment. Some of the facets we have studied are summarized in Table 1.

Although no other body elements are naturally radioactive the content of several others in man is sufficient and their nuclear characteristics such that radioactivity can be induced *in vivo* and measured subsequently by whole-body counting. Following the pioneering studies of Anderson and colleagues[13], several groups[14-21] now measure the body content of one or more elements by *in vivo* activation analysis. Two groups have reported the simultaneous determination of six body elements[15,21], calcium, phosphorus, sodium, chlorine and nitrogen as well as potassium and we have recently described also the measurement of total body oxygen in man[23] simultaneous with these

Table 1. Some clinical applications of whole-body counting in three areas.

Potassium	Iron	Vitamin B_{12}
Essential hypertension	Healthy controls (A and T)	Healthy controls (A and T)
Primary hyperaldosteronism	Influence of succinic acid (A)	Pernicious anaemia (A)
		Excretion of large doses (T)
Rheumatoid arthritis	Rheumatoid arthritis (A)	Renal disease (T)
Childhood coeliac disease	Pernicious anaemia (A)	Hepatic disease (T)
		Influence of analogue form (T)
Ureterosigmoid anastomoses	Blood in kidney coils (T)	Equilibration (T)
Chronic renal failure	Chronic renal failure – non-dialysed	Double tracer diagnosis (A)
Cardiac diseases	Blood loss and transplantation (T)	Dose levels of analogues (A)
Oedema	Dialysis (A and T)	Diet and other factors (A)
Cor pulmonale	Renal transplantation (A and T)	Serum and total body B_{12} (T)
Healthy controls	Ulcerative colitis (T)	Erythropoietic status (T)
'Ultra-fit' subjects	Parenteral therapy (T)	Therapeutic schedules (T)
XXY, XYY chromosome abnormalities		Partial gastrectomy (A)
Obesity		
Physiology		
Effects of various diuretics		
Effects of K supplements		
Effects of beta blockers		
Relation of TBK and cell content		
Relation of TBK and K_e etc.		
Pernicious anaemia		
Liquorice compounds		
Carbenoxoline sodium		

(A) = Oral absorption or retention
(T) = Long-term turnover

elements. Calcium and phosphorus are obviously important in bone diseases, sodium and chloride with potassium in electrolyte disorders, nitrogen in relation to protein and nutrition and oxygen with respect to total body water.

WHOLE-BODY COUNTING COMPARED WITH OTHER METHODS

Body composition

The methods just described provide direct measurements of some elements of body composition. Alternatively, isotope dilution is commonly used to measure body water and the exchangeable fractions of potassium, sodium, chloride, and, occasionally, calcium. However, the time required for and the extent of equilibration render the method questionable in some clinical circumstances. In some cases, notably chloride, the specificity or suitability of the marker can be problematical. Also, there is evidence that the fraction of body sodium that is exchangeable may vary in certain diseases[22,24]. Conventional balance studies can provide data on short-term changes in body composition but require immaculate techniques if substantial cumulative errors are to be avoided. The method is not practicable for long-term changes.

Oral absorption

The oral absorption of elements or labelled compounds of medical interest can be measured directly by whole-body counting[3]. The procedure is simple. A measurement of the patient's natural body radioactivity is made. A small dose (usually a few microCuries) of the appropriate radionuclide (such as ^{59}Fe, ^{47}Ca etc.) or labelled compound (e.g. ^{57}Co or ^{58}Co-vitamin B_{12}) is administered orally and the whole-body count repeated, giving the counting-rate corresponding to 100% retention. A final whole-body count is made 7 days or more later and, after correction for background, radioactive decay (usually by reference to a standard) etc., the counting-rate due to the radionuclide is expressed as a percentage of the initial counting-rate to give the absorption. The general procedure has wide applications in medicine and double tracers, such as ^{58}Co-vitamin B_{12} and ^{57}Co-vitamin B_{12} with intrinsic factor[25], may be used simultaneously, increasing the usefulness of the method.

The alternative technique for the direct estimation of oral absorption involves the administration of the radionuclide followed by collection and assay of excreta. An obvious and common pit-fall is the 'fatal-flush catastrophe', which results in an incomplete collection, the patient often being reluctant to admit the toiletry indiscretion(s). In some cases, an inert marker, such as ^{46}Sc or ^{51}Cr, can be administered at the same time as the test radionuclide, obviating the need for complete collection[26]. Indirect methods are available for assessing the absorption of, for instance, vitamin B_{12}, iron and calcium and are often clinically convenient. The results are usually more susceptible to interference from concurrent clinical conditions, such as renal failure with respect to the Schilling test.

Long-term retention and intermittent losses

The long-term retention of a radionuclide or labelled compound is an important indicator of turnover by the body and, in particular, of intermittent losses such as of iron in menstruation or haemorrhages. Sequential measurements by whole-body counting provide these data in a simple manner for which there is no really satisfactory alternative. As mentioned earlier, long-term conventional balance studies will rarely achieve adequate accuracy. The labelling of red cells with, say, ^{51}Cr can be a highly sensitive procedure for detecting blood losses provided that the loss is sufficiently predictable (and accommodating) to occur within the examination period. However, this is a rare example of a specific and suitable test,whereas whole-body counting can be applied clinically to any relevant radionuclide, having an appropriate decay scheme.

Range of clinical applications

The range of clinical applications of whole-body counters was summarized some years ago[27] and this has been updated in Table 2. However, each category contains a multiplying of investigations as illustrated by three examples in Table 1, which is derived entirely from our own experience and is, therefore, by no means exhaustive.

PATIENT CONVENIENCE AND ECONOMIC CONSIDERATIONS

As a general rule, the reliability of a test is inversely proportional to (its dependence on patient co-operation)$^{\underline{x}}$, where the coefficient, $\underline{x}$, > 1 and varies from patient to patient. Usually, patients prefer not to be hospitalized unless it is unavoidable, presumably because the environment is strange and entails separation from family and friends, disruption of domestic arrangements and, often, loss of income. In addition, there is abundant evidence of a lack of devoted co-operation from patients not only in painful cases but also those which are aesthetically distasteful or involve changing life-long established habits. Excreta collection would fall into the latter category being inconvenient not only for the patient but also for nursing and other staff. Personal involvement suggests that the failure to provide a complete collection is less surprising than, perhaps, 50% of patients actually achieving the goal. Especially over periods of a week or more and bearing in mind the vagaries of excretion, the momentary aberration in conventional use of the toilet seems understandable.

It would follow that whole-body counting, which can be conducted on an out-patient basis and obviates the need for excreta collection, causes minimal inconvenience to the patient. The results are direct and reliable. There is also an economic benefit that is often overlooked since the cost of hospitalization (at least £150 per week) is avoided. Using our mobile whole-body counter[5], more than 1000 measurements on patients have been made in a year and this value could easily

Table 2. Summary of clinical applications of whole-body counters

Element or Compound	Absorption	Metabolic or Kinetic Studies	Comments
<u>Electrolytes</u>			
^{42}K, ^{24}Na, ^{22}Na	✓	✓	Administered
^{82}Br, ^{28}Mg	✓	✓	Radionuclides
^{40}K		✓	Direct counting
Na, Cl		✓	*In vivo* activation analysis
<u>Bone</u>			
^{47}Ca, ^{85}Sr	✓	✓	Short- and long-term kinetic studies
Ca, P		✓	*In vivo* activation analysis
<u>Haematology</u>			
^{59}Fe	✓	✓	Iron metabolism
^{51}Cr		✓	Measurement of blood loss
^{57}Co and ^{58}Co vitamin B_{12}	✓	✓	Vitamin B_{12} metabolism
<u>Thyroid</u>			
^{131}I		✓	Detection of thyroid metastases
Thyroxine ^{131}I		✓	Thyroid function and kinetic studies
<u>Protein</u>			
Protein ^{131}I		✓	Degradation of globulins and albumins
N	✓	✓	*In vivo* activation analysis
<u>Enzyme</u>			
^{65}Zn and $^{69}Zn^{m}$		✓	Enzyme relationships

have been exceeded if absorption measurements only had been made; these taking less counter time than ^{40}K determinations. It is possible, therefore, to measure absorption in more than 500 patients annually and, if each examination avoided hospitalization for a week, the saving to be set against the costs of whole-body counting would be about (500 x £150 =) £75 000 per annum. This approach to costing is based on only one facet of the counter's utilization. In another aspect, it would scarcely be feasible to hospitalize a patient for a year or more in order to determine the changes in body composition by conventional balance but, in any case, the cost would be prohibitive at about £7500 per patient. Only two outpatient visits would be required for *in vivo* activation analysis and the data on the seven body elements would be more accurate.

For comparison, the costs of whole-body counting can be evaluated as the capital cost of equipment amortized over, say, five years and the salaries etc. associated with one or two assistants. The amortization period is highly conservative since our counters[4-6] have operated for more than a decade (and others even longer). Indeed, the lead bricks of the shields and the detectors have actually appreciated by more than 100% over this period, representing an investment! The equipment costs can vary from, perhaps, £2000 or less for a single counter[4,28] with sufficient sensitivity to measure gastrointestinal absorption, of the order of £10 000 for a highly sensitive shadow-shield counter[5,6,29] to about £100 000 or so for an elaborate shielded room counter. These figures suggest that whole-body counters can have economic, as well as practical, advantages; the annual amortization, ranging from about £400 to £20 000, being substantially less than the £75 000 per annum estimated earlier for hospitalization.

CLINICAL UTILIZATION OF WHOLE-BODY COUNTERS

Some groups, having established a whole-body counter in the clinical environment, have experienced a recalcitrance or lack of interest in using the equipment on the part of their medical colleagues. In some instances, the counter may be grossly underutilized and, in view of its clinical potential, this is disappointing and wasteful. A number of factors may contribute to this situation and, if it is to be remedied, the causes need to be identified as far as possible. Some speculative reasons may be: the 'scientific toy' syndrome; the 'blinding with science' approach; the 'medicine is for medics' philosophy; the 'new-fangled methods' or 'I did it my way' attitude.

There is a discernible and, to some degree, understandable approach by the scientist when presented (or having constructed) a 'new toy' to want to play with it for a protracted period. It is laudable to seek the ultimate in scientific accuracy and precision even with 'samples' as complex as the human body. However, the measurement of absorption or total body content to better than a few per cent is not only very difficult to achieve but is also rarely justifiable in practice because of the biological variability both within a patient and among patients. For example, in a healthy consultant physician the absorption of oral iron on consecutive occasions ranged from 1.2 to 21.4%. These results had good accuracy and the difference may have been due to such unestablished factors as a surfeit of steaks some days before the first measurement and compensatory dieting before the second! Certainly, a programme of familiarization and optimization may be necessary but the law of diminishing returns should be critically applied, ideally before initial clinical curiosity and interest in the instrument wanes.

When the counter itself is established, it may sometimes be necessary to nurture the interest of clinical colleagues in its utilization. In enthusing over the new tool, it is easy to blind the uninitiated with science, however unintentionally, and to create the illusion that the results must, therefore, be equally complex and incomprehensible. It is important to realize that a potential barrier of language exists and the scientist promoting the whole-body counter should be aware not only of the clinical applications of the technique but of its advantages (and drawbacks) for patient care or research compared with other methods in current use. The philosophy that 'medicine is for the medics' can lead to a sterile impasse whereas an intelligent, though necessarily incomplete, understanding of the clinical problems can yield fruitful common ground. There are, presumably, physicians and surgeons intuitively opposed to 'new-fangled methods' who will be impervious to any other technique than that learnt at their father's knee. However, it seems unlikely that we have simply been fortunate in not encountering any.

CONCLUSIONS

The value of whole-body counting lies in the wide range of its clinical applications, the accuracy of the results it provides and the minimum of inconvenience caused to the patient. However, there appears to be also an economic justification for whole-body counters in the clinical environment. Nevertheless, the true potential and value of whole-body counting is unlikely to be realized without excellent co-operation between medical and scientific staff; a goal now being achieved by many centres.

REFERENCES

1. F.W. Spiers, Whole-Body Counting, IAEA, Vienna, 1962, p.3.
2. P.R.J. Burch and F.W. Spiers, Nature (London), 172, 519 (1953).
3. K. Boddy, Radioactive Tracer Techniques for the Study of Gastrointestinal Absorption, IAEA-188, Vienna, 1973, p.6.
4. K. Boddy, Phys. Med. Biol., 12, 43, (1967).
5. K. Boddy, Br.J. Radiol., 40, 631, (1967).
6. K. Boddy, A. Elliot, I. Robertson et al, Phys. Med. Biol., 20, 295 (1975).
7. A.R. Wilson, Ph.D. Thesis, University of Leeds, 1964.
8. L. Burkingshaw, Phys. Med. Biol., 12, 447 (1967).
9. K. Boddy, P.C. King, P. Tothill et al, Phys. Med. Biol., 16, 275 (1971).
10. C.F. Barnaby and B.M. Jasani, Phys. Med. Biol., 13, 561 (1968).
11. P.A. Delwaide, Int. J. Appl. Radiat. Isot., 20, 623 (1969).
12. G. Joyet and A. Baudray, Experientia, 24, 865 (1968).
13. J. Anderson, S.B. Osborn, R.W.S. Tomlinson et al, Lancet ii, 1201 (1964).
14. M.J. Chamberlain, J.H. Fremlin, D.K. Peters et al, Br. Med. J., ii, 581 (1968).
15. S.H. Cohn and C.S Dombrowski, J. Nucl. Med., 12, 499 (1971).
16. W.B. Nelp, H.E. Palmer, R. Murano et al, J. Lab. Clin. Med., 76, 151 (1970).
17. J.E. Harrison, K.G. McNeill, H. Meema et al, J. Nucl. Med., 15, 929 (1974).
18. K. Boddy, I. Holloway and A. Elliot, Nuclear Activation Techniques in the Life Sciences, IAEA, Vienna, 1972, p.589.
19. A. Guey, In Vivo Neutron Activation Analyses, IAEA, Vienna, 1973, p.151.
20. T.J. Spinks, in Proceedings of the Second East Kilbride Conference on Progress and Problems of In Vivo Activation Analysis (K. Boddy, Ed), S.U.R.R.C. 57/76 (1976).
21. C.B. Oxby, I. McCarthy and L. Burkinshaw, Br. J. Radiol., 50, 455 (1977).
22. K. Boddy, J.J. Brown, D.L. Davies et al, Clin. Sci. Mol. Med. (in press).
23. E.D. Williams and K. Boddy. Submitted for publication.
24. D.H.P. Streeten, A. Rapoport and J.W. Conn, J. Clin. Endocrinol. Metab., 23, 928 (1963
25. K. Boddy, G. Will and B.M. Holmes, Phys. Med. Biol., 14, 455 (1969).
26. R.D. Ganatra, K. Sundaram, K.B. Desai et al, J. Nucl. Med., 6, 459 (1965).
27. Clinical Uses of Whole-Body Counting, IAEA, Vienna, 1966, p.274.
28. R.K. Hukkoo and D.S. Katoch, Bhabba Atomic Research Centre Report BARC-548 (1971).
29. T. Hawkins and A.W. Goode, Phys. Med. Biol., 21, 293 (1976).

DISCUSSION

V. MARKS: Why do you want to measure total body oxygen?

K. BODDY: Total body oxygen measurements have three applications, at least. To correct the nitrogen determinations we need to know the amount of oxygen to take account of the $^{16}O(p,\alpha)^{13}N$ interference. The measurement also provides an indirect estimate of total body water. Alternatively, if we measure total body water separately, the difference between the measurements could provide an estimate of tissue oxygen, which might be of clinical interest.

A.R. WARE: What type of recors of radiation dose do you keep for the patients undergoing in vivo activation analysis? In view of the 1 rem per irradiation, what is the likely frequency of irradiations for a typical patient?

K. BODDY: We must first obtain approval from several bodies for each type of examination. The record forms, countersigned by a consultant, bear the radiation dose and, in our case, must be available for examination by the Nuclear Installations Inspectorate. The frequency of patient examination is also approved but is directly related both to patient care and his clinical condition as I illustrated during the presentation.