Measuring body composition by fast neutron activation analysis

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ABSTRACT

The recent availability of a small compact sealed tube neutron generator, incorporating an associated-particle alpha detector, makes it feasible to measure the concentrations of C, N and O in the body with a very low dose of ionising radiation. We describe this new technique and the equipment needed to use it for measuring body composition. Calibration data from a prototype instrument relate the counts of gamma rays due to C, N & O from phantoms to the number of incident 14 MeV neutrons and phantom mass. Applying the technique to one 29 kg Romney wether hogget, we estimated it contained 0.69 kg N, 5.52 kg C and 16.5 kg O. These results indicate that the technique holds promise for monitoring the body composition of paediatric and malnourished patients and for measuring the body composition of young experimental animals such as goats, pigs or sheep.

Keywords: body composition; fast neutrons; activation analysis.

INTRODUCTION

Measuring proximate composition of the whole body without killing the animal has been the goal of countless research projects. Most have relied upon the dilution of a marker whose distribution is limited to specific anatomically or chemically defined compartments. More recently we have seen the use of ultrasound, X-rays and nuclear magnetic resonance as externally applied signals with sophisticated algorithms and circuitry for producing images of discrete tissues. Developments in ways of using neutron activation analysis have continued alongside these other procedures.

Our goal of measuring the proximate composition of the body *in vivo* is based upon the following premises: (1) the elements C, N, O and H comprise 95% of body mass, (2) fat, protein and water have relatively fixed stoichiometric proportions of these elements, and (3) each element produces gamma rays of characteristic energies when bombarded with 14 MeV neutrons. The present report describes the associated particle, time of flight technique, the way it is used to measure composition of the whole body in experimental animals, and calibration data from homogenous phantoms.

DESCRIPTION OF THE TECHNIQUE

Neutron Generator

The 14 MeV neutrons we use are produced by a nuclear reaction between deuterium ions and tritium atoms in a sealed tube neutron generator (STNG). The deuterons are accelerated through a potential of 100 kV on to a target containing tritium. The reaction produces an alpha particle (a helium nucleus) and a 14 MeV neutron whose trajectories are diametrically opposite one another. It is this intrinsic physical property of the reaction that makes possible the associated particle technique and the huge improvements in signal-to-noise ratio over other methods of neutron activation analysis.

The associated particle technique is implemented by having a zinc sulphide scintillator mounted within the chamber of the STNG and against a quartz window. A fast photomultiplier tube is attached to the window for recording the scintillations resulting from each alpha particle striking the detector. For each alpha particle detected, a 14 MeV neutron is emitted from the target in the opposite direction. Thus, if the alpha detector subtends a solid cone from the focus point of the target, it gives a direct measure of the 14 MeV neutron flux emitted into the complementary cone.

FIGURE 1: Schematic diagram of the Sealed Tube Neutron Generator, showing the solid cone of 14 MeV neutrons subtended by the alpha particle detector. The diagram shows the STNG-sample-detector geometry used for present studies.

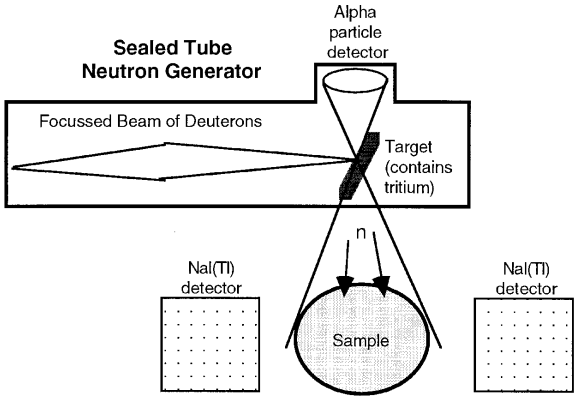


Figure 1 depicts this geometry and shows how the sample is positioned so that it encounters virtually all the neutrons within this cone. For the tube we have used, which has a 3.7 cm diameter alpha detector positioned 4.5 cm from the focus point of the target, just 4.3% of the total

neutrons produced by the tube have alpha particles that are seen by the alpha detector. The remaining neutrons are emitted in other directions and are not utilised. In conventional methods of neutron activation analysis, however, such neutrons are scattered from surrounding structures, enter the NaI detectors and are the main cause of background counts in the gamma ray spectrum. A key feature of the new technique is use of time resolution to almost eliminate this background.

The 14 MeV neutrons which enter the sample primarily undergo inelastic reactions with the nucleii of light elements such as carbon, nitrogen and oxygen. As the nucleii return to their ground state within femto seconds, high energy gamma rays that are characteristic of the nucleus are emitted. A fraction of these gamma rays are captured by the sodium iodide detectors mounted on each side of the sample.

The key to obtaining a high ratio of signal to noise in the gamma ray spectrum is the use of events from the alpha detector to control output of the NaI detectors. As 14 MeV neutrons travel at 5 cm per nanosecond they enter the sample soon after an alpha particle is seen at the alpha detector. In practice the output of the NaI detectors is observed for just 25 nanoseconds following an alpha event. We thus capture the gamma rays of interest when they are most likely to occur and ignore all the other events which would otherwise contribute to background. Excluded events are those arising from neutrons outside of the defined beam that enter the detector and neutrons scattered by extraneous materials. The way nuclear instrumentation modules are configured to achieve this result was described by Mitra *et al.,* (1995).

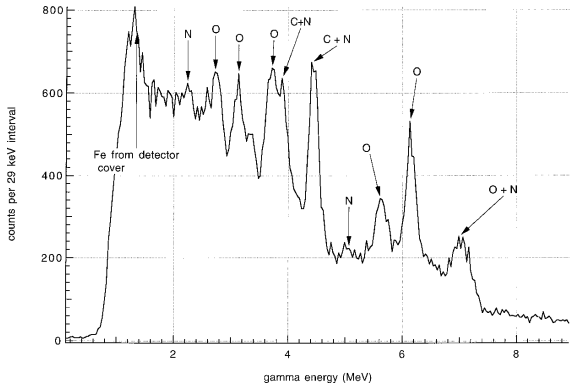
Gamma Ray Detection

While there are many different scintillation materials available for capturing gamma rays and converting the energy into photons, sodium iodide (with thallium doping) generally provides the best compromise of cost, efficiency, energy discrimination, and speed of response. Nevertheless, to make the technique feasible in terms of measurement precision several very large (15 cm x 15 cm x 45 cm) crystals are required and at their current cost of $50,000 (NZ) each, four such detectors would comprise nearly half the cost of an instrument.

Data on elemental composition of the sample are extracted from the gamma ray energy spectra. Best information is obtained when the gamma ray spectra of the elements present are distinctive from one another and counts in the regions of interest are high relative to the background.

Figure 2 shows the gamma ray spectrum obtained from a physiological solution of elements as found in a normal human body (ICRP, 1975). For many of the major peaks there are contributions from more than one of the three elements. Despite these common entities, the observed spectra for C, N and O are each unique and the contribution of each element in a mixture can be resolved using the traditional methods of gamma ray spectroscopy (DeSoete *et al.,* 1972). A series of simultaneous equations

FIGURE 2: Gamma ray spectrum observed from the 15 cm x 15 cm x 45 cm NaI detector using a 25 nanosecond time window and showing the elemental origin of major peaks. The sample contained a physiological solution of the elements as recommended by ICRP (1975) for reference man.



have been developed and used successfully to extract data that is specific for C, N and O (Mitra *et al.,* 1995).

INSTRUMENT CALIBRATION

Materials and Methods

Solutions containing either paraffin oil (Ondina Oil 68, Shell NZ Ltd, Mangere) or a mixture of the elements as found in a normal human body (ICRP, 1975) were contained in flexible polyethylene tubes (5 cm diameter x 80 cm) having a wall thickness of 0.15 mm and heat sealed. Five 80 cm long cylindrical phantoms ranging in mass from 10 to 36 kg were constructed from many such tubes, bundled together and wrapped with polyethylene film. Each phantom was weighed and held in an adjustable polyvinyl chloride sling that was connected to a movable carriage and mounted in the instrument to achieve the STNG-sample-detector geometry shown in Figure 1. Each phantom was bombarded with 14 MeV neutrons for ten one-hour periods while the emitted gamma rays were measured with two 12.5 cm diameter x 10 cm, and one 15 cm x 15 cm x 45 cm NaI(Tl) detectors coupled to the data acquisition system described by Mitra *et al.* (1995). Net counts in three regions of interest (ROI) (Mitra *et al.,* 1995) were extracted from the gamma ray spectra by deriving background counts from the paraffin oil phantoms for the two ROI covering N and O, while net counts from the ROI for C was obtained by peak stripping (DeSoete *et al.,* 1972). Neutron flux for each phantom was normalised to 28.3 x 10^6 neutrons as measured by the alpha counter and corresponded to a neutron output (into 4 þ) from the aging STNG of 2 x 10^5 neutrons.s^{-1}, well below the manufacturer's expected output for a new unit. The data were statistically analysed by linear regression.

Following the calibration procedure, we applied the technique to one Romney wether hogget which had a body mass of 26 kg (excluding a predicted weight of head and feet which were not scanned). The animal was suspended in a sling similar to the one used for the phantoms except that holes were cut for the legs to dangle and small darts

were cut in the material to shape the sling so that it fitted the animal's brisket and groin. It was positioned in the instrument to obtain a STNG-sample-detector geometry that was similar to that used for the phantoms and scanned for 6 one hour periods. Counts due to C, N and O were obtained as described above.

RESULTS AND DISCUSSION

The following equations show the relationship of calibration factors CF_C, CF_N and CF_O (counts per kg of element) for C, N and O, respectively, to the mass of each phantom (X in kg) and normalised to 28.3 x 10^6 neutrons:

$CF_C = 2075 (\pm 26) - 26.65 (\pm 1.08)\ X \qquad R^2 = 0.995,\ s_{y.x} = 22.1$

$CF_N = 7905 (\pm 342) - 183.2 (\pm 14.1)\ X \qquad R^2 = 0.982,\ s_{y.x} = 288$

$CF_O = 4393 (\pm 136) - 71.5 (\pm 5.6)\ X \qquad R^2 = 0.982,\ s_{y.x} = 114$

While these equations provide an adequate description of the data for phantoms ranging in mass from 10.5 to 36.4 kg, the higher error terms for N show the desirability of extracting more counts for N from gamma rays that have not been included in the ROI used hitherto. This is the topic of our continuing research effort.

For the wether hogget, observed counts for C, N and O were 2,131, 7,585 and 41,337 respectively, again normalised to a total neutron flux of 28.3 x 10^6 neutrons as measured by the alpha counter. Applying the above regression equations, we estimated that the animal's body and pelage contained 5.52 kg of C, 0.69 kg of N and 16.5 kg of O. Such values are to be compared against data obtained from chemically determined composition in future studies.

GENERAL DISCUSSION

By comparison with other techniques used for measuring body composition, such as the prompt gamma technique (Beddoe *et al.*, 1984), the fast neutron activation analysis technique has several important advantages and some limitations. The advantages stem from use of 14 MeV neutrons which have high cross sections for inelastic reactions with C and O, and the use of time resolution to almost eliminate the effects of neutron scattering from all materials extraneous to the sample being activated. Indeed it is the use of time resolution which provides the improvement of several orders of magnitude in the signal-to-noise ratio. For example, a prompt gamma instrument uses one or two radioactive neutron sources producing 10^9 neutrons.s^{-1} and can obtain a precision of ± 3.1% for measuring N in the whole body during a 30 minute scan. By comparison, the fast neutron technique needs a neutron output of just 5 x 10^6 neutrons.s^{-1} to achieve the same precision using the same detector configuration and scan time (Mitra *et al.*, 1995). In addition, much better precisions are attainable for C and O which cannot be observed using the prompt gamma technique because the background counts are high and these elements have weak interactions with the lower energy neutrons that are typically derived from radioactive sources.

Other techniques for assessing body composition include dual photon X-ray absorption (DPX) and X-ray computerised tomography. Both of these techniques, however, rely on the differential absorption of X-rays by soft tissues to generate quantitative information. Absorption is only indirectly related to chemical composition and may account for the recently reported difficulties in obtaining repeatable results for the mass of soft tissues with separate but identical DPX instruments (Paton *et al.*, 1995).

Distinct advantages of fast neutron activation analysis are:

1. The associated particle time-of-flight technique can be used to measure the C, N, and O content of a bulk sample directly and simultaneously. Given the relatively fixed stoichiometry of fat, protein and water, and the fact that these entities make up 95% of body weight, we predict that body composition can be directly calculated in terms of fat, crude protein and water from the gamma ray energy spectrum, the alpha particle count and body mass. Content of minerals (or ash) in the body will be assumed to be a fixed proportion of fat-free mass.
2. With four large NaI detectors and a STNG producing 10^6 neutrons.s^{-1}, we predict that precise data for the proximate composition of the whole animal can be obtained within a 15 minute scan. Based on the data of Mitra *et al.*, (1995) precision is expected to be ± 4.4% for crude protein, ± 5% for fat and ± 2.1% for water (all standard deviations expressed as a percentage of the mean).
3. There is no large radioactive source to shield. The radiation hazard in proximity to the instrument is very low while it is producing neutrons and non-existent when the STNG is switched off. The radiation dose for using the associated particle time-of-flight technique is 5-10 times lower for a given precision than with any rival neutron activation analysis technique. We have calculated that the radiation dose to a subject during the measurement of body composition is comparable to the dose received from cosmic radiation during travel in a commercial airline for 16 hours at an altitude of 12,000 m.

Currently there are also some disadvantages:

1. At its present stage of development, the capital cost of an instrument comprising STNG, High Voltage Power Supply and Control System, four large NaI detectors and nucleonics is at least $500,000. Much of this is due to the one-off nature of the large NaI detectors, the STNG and its high voltage control system – these items comprise two-thirds of the total cost.
2. Care is needed for a high voltage power supply and cables to the STNG carrying 100 kV. The instrument thus cannot be expected to perform in either a wet or a very humid environment.
3. The gamma ray detectors contain a single large crystal of NaI. They are useless if the crystal is fractured so the instrument must be protected from gravitational shock. This will make it unsuitable for measuring animals that are not well restrained.
4. During the past three years operating characteristics of the STNGs made by Nuclear Diagnostic Systems

Inc have been too unpredictable for a commercially viable instrument. Development of this technology has continued since our STNG was purchased in 1993 and based on information received from MF Physics (Colorado Springs, CO, U.S.A.) and Multipixel Systems Inc (Lorton, VA, U.S.A.), the successor company to Nuclear Diagnostic Systems), we expect that the next generation of STNG should be capable of delivering a sustained neutron output of at least 10^6 neutrons.s^{-1} for at least 2000 hours of operational use.

5. Due to absence of large discrete peaks for N in the gamma ray spectrum, it will likely be difficult to measure N when it comprises less than 2% of body weight. This situation should only pertain in cases of extreme obesity.
6. As the body diameter increases there is likely to be more uncertainty over the corrections needed to compensate for non-homogeneity of body tissues. We aim to address this problem during the next one to two years of our research programme. We shall be making observations on animals with widely diverging body composition then comparing these results with chemical analyses of the same animals.

Despite these problems we predict an important role for fast neutron activation analysis in the future. It will likely be most valuable for measuring the proximate composition of paediatric or malnourished patients and young experimental animals where we expect that relatively small corrections will be needed to adjust for the non-homogeneity of body tissues. For larger animals or obese patients, it is likely that use of an ultrasonic probe to measure depth of subcutaneous fat may be required as an adjunct measurement.

ACKNOWLEDGMENTS

We gratefully acknowledge the support received from AgResearch, Ruakura and the Departments of Physics and Surgery at the University of Auckland during the early phases of the programme. Mr H Zuidmeer was responsible for design and fabrication of the prototype instrument. The research programme was supported by the New Zealand Foundation for Research, Science and Technology.

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