用體內氮的中子激活測定總體蛋白質的誤差

Errors in determination of total body protein by in vivo neutron activation of nitrogen due to non-uniform neutron fluence inside the patient

Jukka Tölli, Lars Larsson and Magne Alpsten

Department of Radiation Physics, University of Göteborg, Sahlgren Hospital, Göteborg, Sweden.

Total body protein can be estimated by *in vivo* neutron activation of nitrogen. The method is based on capture of thermal neutrons in a $^{14}N(n,\gamma)^{15}N$ reaction. Sources of error associated with this method, such as background subtraction, variations in detection efficiency, etc, are analysed. Different neutron reactions (absorption, elastic and inelastic scattering) cause the neutron fluence to decrease inside the body. The activation profile through the body is non-uniform which causes errors in the calculation of total body nitrogen. A reduction of nitrogen by 5% in a 3 cm thick volume near the body surface would result in an error in the determination of total body nitrogen of approximately 0.3%. The error induced by changes in thickness of the subcutaneous fat has also been estimated and the results show that a 5 mm change in subcutaneous fat thickness changes the count rate from nitrogen by 5%.

The experimental arrangement

A ^{252}CF source is used for in vivo neutron activation analysis (IVNAA). The source is contained in a polyethylene block which forms a collimator, surrounded by a 140 cm (diameter) x 80 cm (height) water tank. The patients are irradiated from below by a 15 cm x 50 cm neutron field. The distance between the neutron source and patient is 70 cm.

The 10.8 MeV photons emitted in the reaction are detected by two 15 cm x 15 cm NaI(Tl)-detectors. A boron/plastic shield reduces the neutron fluence inside the detectors. The reduction is 96%. The detectors are also shielded with lead for reduction of the background gamma radiation. The system is equipped with fast photomultiplier tubes and an active type of dynode chains[1]. In this way stability at high count rates has been obtained.

The pulses from each dynode chain is amplified by two separate double delay line [DDL]-amplifiers. These amplifiers are modified so that the 'delay lines' are removed and the they act like fast amplifiers. The resulting pulse length at the output of the dynode chain as well as from the fast amplifiers is less than 1μs. Each amplifier is connected to a fast ADC. The signals from both ADCs are analysed in a fast multichannel analyser, which is connected to a personal computer. The signal from each detector is handled and analysed separately. The electronic system has been described more in detail recently[2]. In this work hydrogen is not used as internal standard as recommended by Vartsky et al. (1979)[3] because of the high hydrogen background and the other reasons quoted below.

Irradiation geometry

In this work unilateral irradiation geometry has been used with irradiation of the patient from below. Bilateral irradiation is achieved by turning the patient through 180° half-way through the measurement.

In the beginning of this project the detectors were mounted side by side above the patient outside the primary neutron field. This would partly compensate the lack of non-uniformity in the neutron fluence inside the body. The detection efficiency of 10.8 MeV photons was determined for various depths using a 3 cm thick phantom containing nitrogen at different depths in a water phantom. The results from this experiment were compared to the results of a measurement of thermal neutron fluence with In foils. The results of these two measurements agree within 1SD. Our conclusion is therefore that the benefit of mounting the detectors above the patient is small.

In recent measurements the detectors have been positioned beside the patient and in a plane perpendicular to the neutron flux. It is much easier to shield the detectors in this position. There are a number of other advantages in having the detectors placed in this way. First, since the detectors can be shielded more effectively, the count rate and the dead time decreases. The fact that the count rate decreases gives a better signal-to-background ratio in the region of interest. Second, the probability of pile-up events decreases which gives a better energy resolution in all detected peaks in the pulse height distribution. Thirdly, the mean energy of the neutrons which reach the detector is lower, since they are scattered at least 90° thus reducing the probability of neutron activation of the detectors and surrounding materials.

Table 1 illustrates the improvements gained after changing

Correspondence address: Jukka Tölli, Department of Radiation Physics, University of Göteborg, Sahlgren Hospital, 5-413 45 Göteborg, Sweden.

the detector positions. In this experiment phantoms of two different sizes containing a 4.2% (by weight) solution of nitrogen, were irradiated. As can be seen the count rate is decreased for both phantoms.

Table 1. Improvements after change of detector positions.

Phantom Weight (kg)	Count rate (cps) [9.7–11.3] MeV	FWHM (keV) at 2.23 MeV	System dead time (%)
2.0 before	13 800	167	11
after	3900	133	7
14.6 before	9900	154	11
after	4500	134	9

We can also see that as the phantom size increases the count rate decreases before the change by 28%, but after the change the count rate increases by 15%. This result is due to the fact that before a large phantom shielded the detectors more effectively than small phantoms, which leads to a lower count rate. After the change the count rate increases as a result of the increased amount of neutron reactions in the irradiated object. The FWHM was measured at the hydrogen peak at 2.23 MeV. The most important result is that the signal-to-background ratio increased from 0.77 (old geometry) to 1.04 (new geometry).

Errors due to non-uniform neutron fluence

Fast neutrons incident on the irradiated body are slowed down by inelastic and elastic scattering reactions with the body tissue until thermal equilibrium is reached. Once thermalized, radiative capture causes the neutron fluence to decrease. A result of this is a non-uniform neutron fluence through the irradiated body and activation varying with depth inside the patient.

The fluence of thermal neutrons was determined by activation of thin In foils in a water phantom. In Figure 1, thermal neutron fluence is plotted versus depth in a water phantom for both unilateral and bilateral irradiation geometry.

From this figure it is obvious that if the patient gains protein near the body surface the result from IVNAA will overestimate the true change in body nitrogen. In a similar way, if protein is lost deeper in the body the IVNAA will underestimate the loss of nitrogen.

The fluence in Figure 1 was divided in 20 sections; the width of each section was 1 cm. The mean fluence through the body is calculated by summation of each section. The mean fluence is a measure of the probability of thermal neutron interactions in the phantom. The percentage difference between the mean fluence and the true fluence in each section was defined as the ratio:

$$\varepsilon_n = \frac{1/20 \sum_{k=1}^{20} (\text{fluence})_k - (\text{fluence})_n \cdot 100}{1/20 \sum_{k=1}^{20} (\text{fluence})_k}$$

The result from this calculation is shown in Figure 2.

The error resulting from the non-uniform neutron fluence has been estimated by neutron activation of a large phantom containing water, for background estimation. Thereafter the phantom was filled with a known amount of nitrogen (urea). The net signal from nitrogen reactions was used for calculation of a calibration factor. Into this phantom a second phantom, formed as a 3 cm thick slice, containing water, was introduced. Since the total amount of nitrogen is known and constant, it is possible to estimate the relative error caused by the second phantom at various depths. During irradiation the net number of counts from nitrogen was measured. The error is calculated as percentage difference between the measured nitrogen content and the true nitrogen content. The result from this experiment is shown in Figure 3. The solid line corresponds to the error in unilateral geometry and the dotted line corresponds to bilateral geometry. It should be noticed that this error represents a total loss of nitrogen in the actual

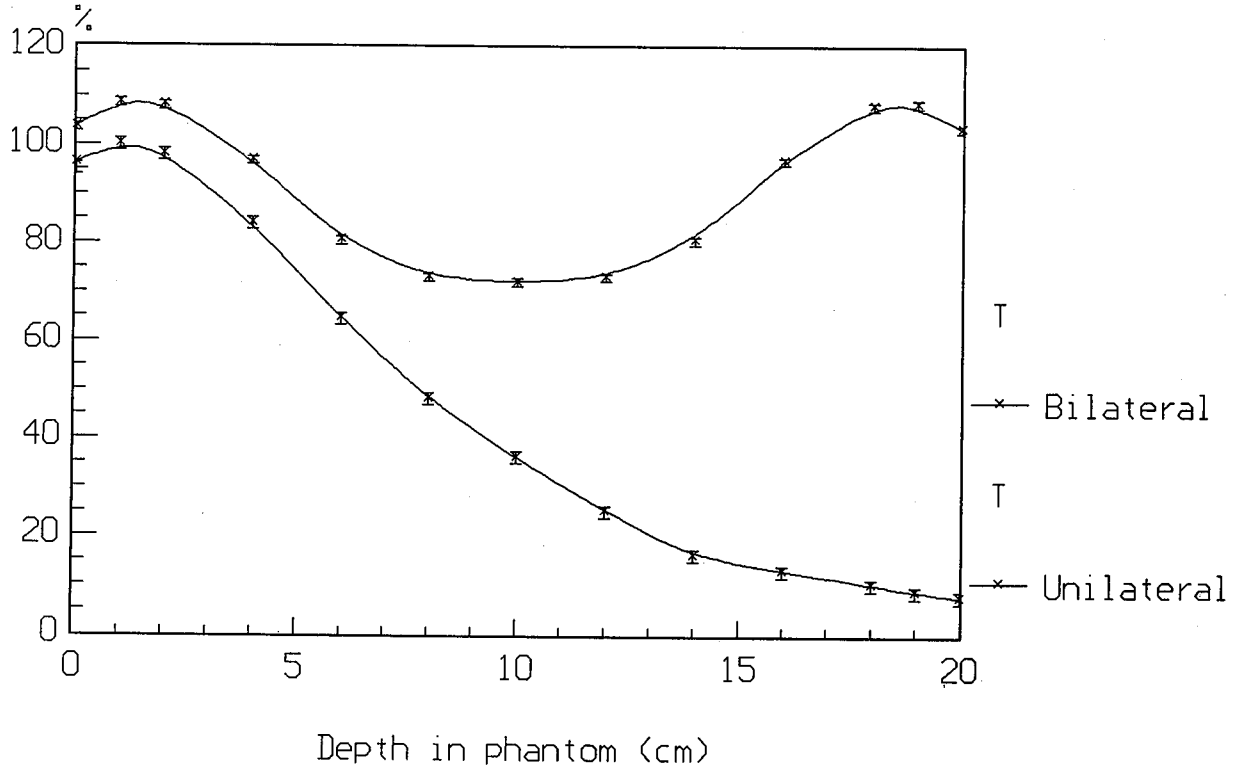

Figure 1. Thermal neutron fluence through patient.

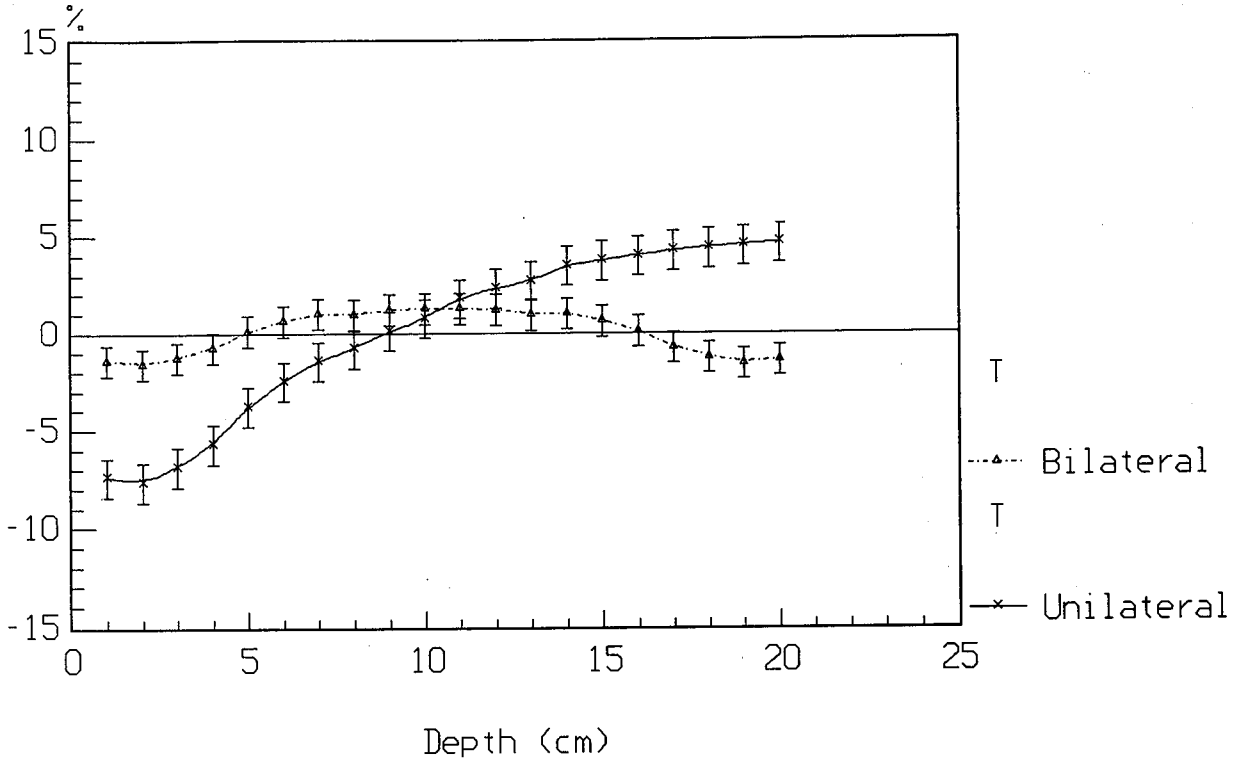

Figure. 2. Percentage difference between mean and true neutron fluence.

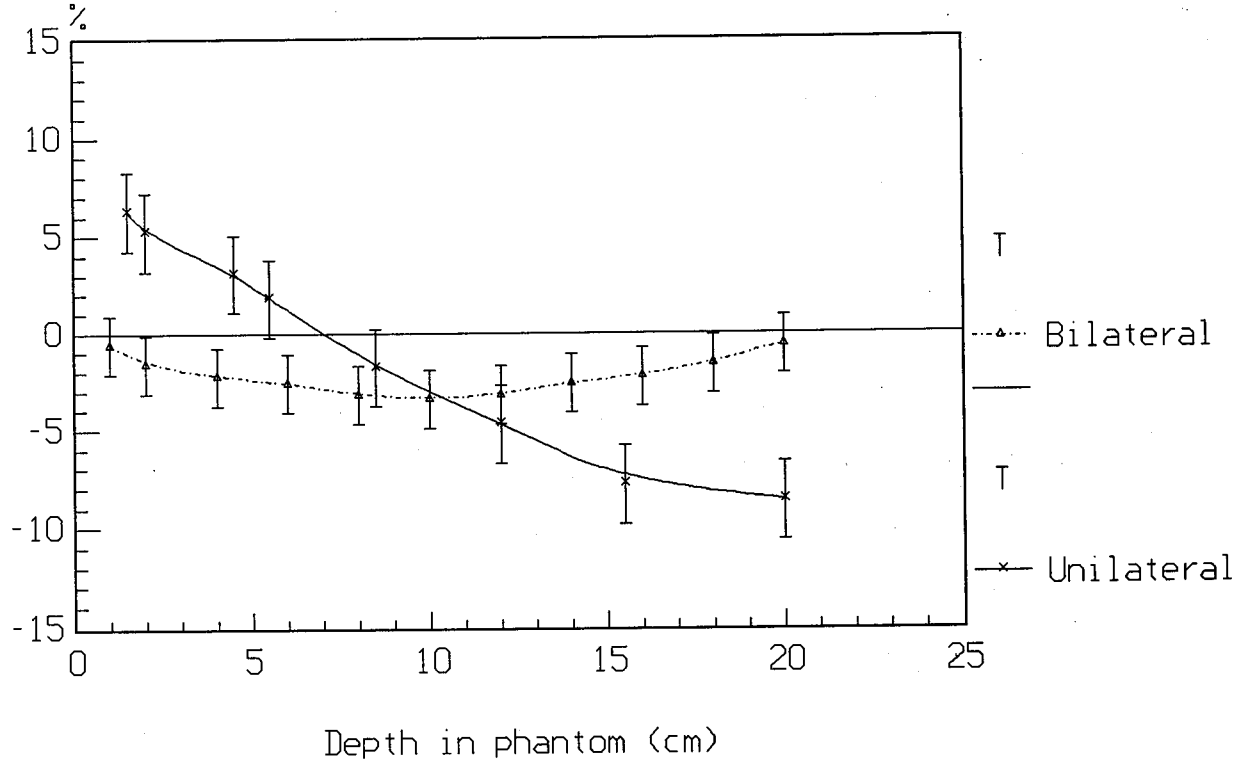

Figure 3. Error due to non-uniform neutron fluence.

slice. As an example, if a patient loses nitrogen in a region between 2 and 5 cm from body surface, a 100% loss in that region would result in an error of 5.2%, while a 5% decrease of nitrogen in that volume results in an error in the determination of TBN of approximately 0.3% if unilateral irradiation geometry is assumed.

Errors due changes in subcutaneous fat

A common effect in several diseases is a change in total body fat (TBF). In a case where the thickness of body fat increases near the body surface the estimated nitrogen content will be underestimated. As an example, a common effect in patients treated with human growth hormone is that TBN increases and TBF decreases[4]. In these patients the measured change in TBN may partly be due to changes in body fat.

We have measured the effect of changes in the thickness of subcutaneous fat by irradiation of a phantom containing a constant amount of nitrogen. Layers of fat from a pig were placed between the neutron source and nitrogen phantom. After subtraction of the background the net numbers of

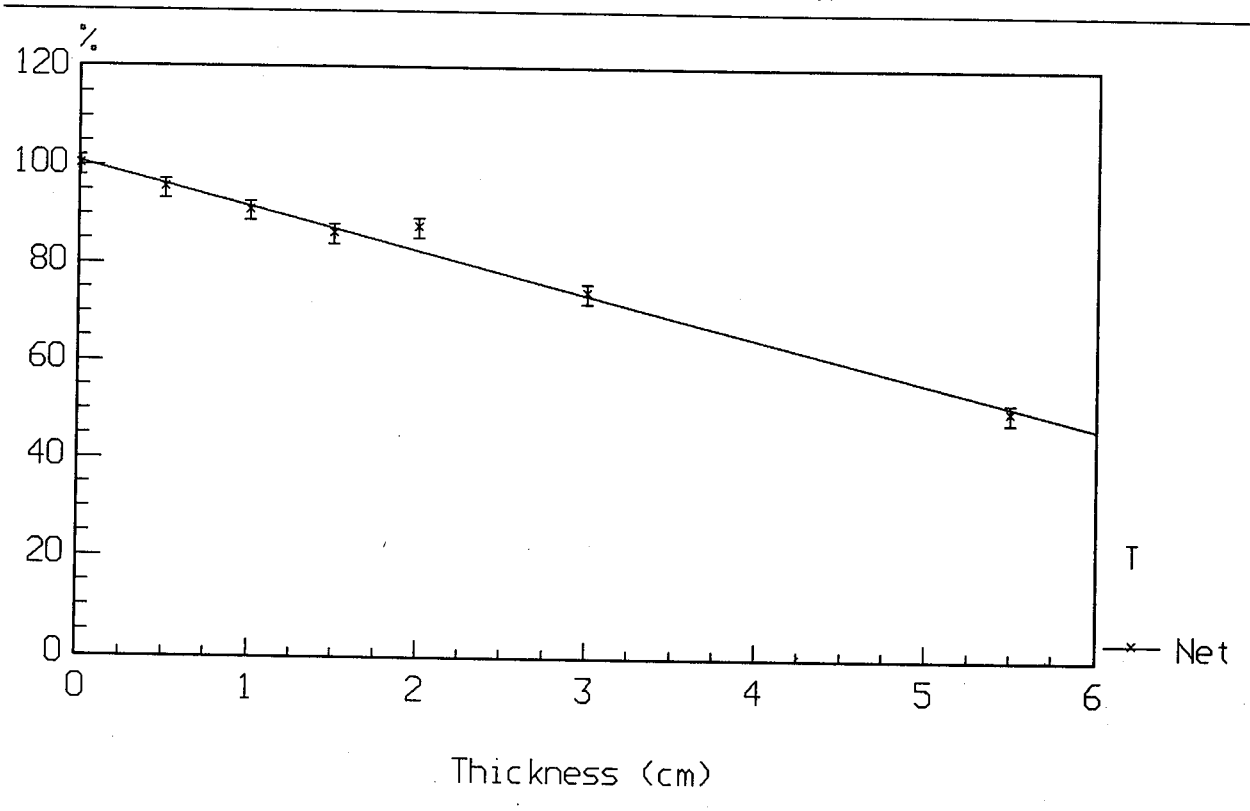

Figure 4. Relative changes in nitrogen counts due to changes in fat thickness.

counts from nitrogen were registered for different depths of fat. In Figure 4 the change of nitrogen signal is plotted versus fat thickness.

The results show that if the fat thickness decreases by 5 mm the change in the nitrogen content will be overestimated by approximately 5% if no correction is made.

Discussion

The problem with non-uniform activation/detection profiles through the body is reduced in several other IVNAA facilities by using the number of hydrogen counts as an internal standard[5,6]. Hydrogen counts are used to reduce the corrections which are required for differences in activation and detection efficiency arising from differences in the body habitus. In this work the hydrogen counts are not used in the calculation of TBN. The main reason for this is that the polyethylene collimator contributes to the hydrogen signal so much that the main part of the counts in the hydrogen signal is from the collimator and not from the irradiated object. Another reason is that if the hydrogen signal is used as an internal standard the hydrogen and nitrogen must be distributed in a similar manner throughout the body. In several diseases the patients may gain or loose extracellular water which changes the relations between nitrogen and hydrogen.

The corrections required for differences in activation and detection efficiency are minimized if the phantoms used for background and calibration factors have the same size and shape as the patients. It has been found that if the count rate is different in patient measurements and the determination of calibration factors, the errors due to gain or loss of pulse caused by random summing of gamma rays are not negligible[7]. It is therefore important that the size of the phantom, used for calibration factors, have approximately the same size and shape as the patient, so that the measured overall count rates are equal in the phantom and patient studies.

It should be noticed here that the errors do not cause any problem if the patient gains or loses nitrogen uniformly. The problem arises when the changes in the nitrogen content are non-uniform.

The resulting changes in the count rate from nitrogen due to changes in body fat can be corrected if the thickness of body fat is measured.

References

1 Kerns, 1977.
2 Larsson, 1992.
3 Vartsky D, Prestwich WV, Thomas BJ, Dabek JT, Chettle DR, Fremlin JH, Stammers K. The use of body hydrogen as an internal standard in the measurement of nitrogen by prompt neutron capture gamma rays. J Radioanal Chem 1979;48:243.
4 Bengtsson B Å, Edén S, Lönn L, Kvist H, Stockland A, Lindstedt G, Bosaeus I, Tölli J, Sjöström L, Isaksson OGP. Treatment of adults with growth hormone (GH) deficiency with recombinant human GH. J Clin Endocrin Metabol 1993; 76:309.
5 Vartsky D, Ellis KJ, Cohn SH. In vivo measurement of body nitrogen by analysis of prompt gamma rays from neutron capture. J Nucl Med 1979; 20:1158.
6 Sutcliffe JF. A correction for total body hydrogen used as an internal standard in the measurement of total body protein by prompt gamma in vivo neutron activation analysis. Phys Med Biol 1989; 36:1681.
7 Yankuba S, Oldroyd B, Metcalfe SC, Godfrey JE, Oxby CB. Examination of errors caused by random summing in in vivo prompt gamma analysis. Phys Med Biol 1989;34:1089.
8 Cohn SH, Dombrowski CS. Measurement of total body calcium, sodium, chlorine and phosphorus in man by in vivo neutron activation analysis. J Nucl Med 1971;12:499.
9 Harvey TC, Dykes PW, Chen NS, Ettinger KV, Jain S, James H, Chettle DR, Fremlin JH, Thomas BJ. Measurement of whole body nitrogen by neutron activation analysis. Lancet 1973:395.
10 Leach MO, Thomas BJ, Vartsky D. Total body nitrogen measured by the $^{14}N(n,2n)^{13}N$ method: a study of the interfering reactions and the variation of spatial sensitivity with depth. Int J Appl Rad Isot 1977; 28:263.
11 McNeill KG, Borovnicar DJ, Krishman SS, Wang H, Waana C, Harrison JE. Investigation of the factors which lead to background in the measurement of nitrogen by IVNAA. Phys Med Biol 1989; 34:53.