

**Table 2.** Precision and accuracy in measurements of a child-size bottle phantom containing a urea-salt solution.\*

Phantom Description	Measured Variable	Accuracy <sup>b</sup>		Precision (CV) <sup>c</sup>	
		Intra-assay	Inter-assay	Intra-assay	Inter-assay
33 kg bottle phantom containing:	Nitrogen	+0.1% ± 1.0%	+1.4% ± 1.4%	2.8%	2.3%
0.80 kg nitrogen					
60.0 g chlorine	Chlorine	+2.3% ± 4.3%	+3.9% ± 6.0%	7.9%	10.0%
3.7 kg hydrogen					

\* All measurements based on the subject measurement protocol; intra-assay statistics based on 47 measurements performed at a rate of 2 to 4 times per day for 13 days; inter-assay statistics based on 14 measurements performed once on each of 14 days.

<sup>b</sup> Measurement accuracy determined as: (measured mass less known mass)/ known mass; ± values represent 95% confidence interval.

<sup>c</sup> Coefficient of variation.

**Table 3.** Counting statistics from a 630 s (600 s live time) spectrum of a typical well-nourished child weighing 30 kg.\*

Region of Interest	Gross Counts	Background Counts		Net Counts	$\sigma_{\text{Net}}/\text{Net}^b$
Nitrogen	2080	791 (water)		1289	3.6%
Chlorine	4611	3540 (water)	408 (compton scattering)	663	10.9%
Hydrogen	1495994	269515 (air)		1226479	0.1%

\* Subject and phantom measurements performed according to the subject measurement protocol; calibration-phantom counts scaled to a 600 s live-time scan.

<sup>b</sup>  $\sigma_{\text{Net}}$  is calculated as  $\sigma_{\text{Net}} = \sqrt{\text{gross counts} + [(t_s^2/t_p^2) \times \text{background counts}]}$

where live times are  $t_s = 600$  s (subject scan) and  $t_p = 3600$  s (water phantom scan) or 2400 s (air phantom scan) (Watt and Ramsden<sup>33</sup>).

**Table 4.** Comparative data for measuring total body nitrogen and chlorine.\*

Facility	Target Population	Dose Equivalent <sup>b</sup>	Total Body Nitrogen		Total Body Chlorine	
			CV <sup>c</sup>	FM <sup>d</sup>	CV <sup>c</sup>	FM <sup>d</sup>
Melbourne (Present Study)	Children	0.25 mSv	2.3%	89	10.0%	20
Sydney (Baur <i>et al</i> ) <sup>3</sup>	Children	~ 0.14 mSv	4.3%	62		
Auckland (Mitra <i>et al</i> ) <sup>3</sup>	Adults	0.30 mSv	2.7%	68	4.9%	37

\* Statistics relate to measurement protocols at respective facilities.

<sup>b</sup> Q(neutrons) = 20 at Melbourne and 10 at Sydney and Auckland.

<sup>c</sup> CV: coefficient of variation.

<sup>d</sup> FM: figure of merit defined as:  $100/(CV \times \sqrt{\text{dose equivalent}})$ .

90 cm and containing a urea-salt solution (2.4% N, 0.18% Cl and 11.0% H by weight). This phantom was not used to calibrate the method. On each of fourteen days, the facility was calibrated according to the measurement protocol. Table 2 shows intra- and inter-assay coefficients of variation (CV). Table 2 also shows intra- and inter-assay accuracy expressed as a percentage difference between the measured and known content of nitrogen and chlorine. Table 3 presents counting statistics from spectra of a typical well-nourished child (30 kg) and calibration phantoms. The observed intra- and inter-assay precision (CV, Table 2) is consistent with the statistical fluctuations associated with nitrogen and chlorine counts ( $\sigma_{\text{Net}}/\text{Net}$ , Table 3). Furthermore, systematic errors for measuring nitrogen (+0.1%  $\pm$ 1.0%, intra-assay; +1.4%  $\pm$ 1.4%, inter-assay) and chlorine (+2.3%  $\pm$ 4.3%, intra-assay; +3.9%  $\pm$ 6.0% inter-assay) are less than or comparable to the natural variability of the method.

Of interest too is the relatively high imprecision for measuring TBCl (CV  $\approx$ 10%, table 2). In part, this value reflects the relatively small chlorine content in child-like masses and suggests the method is better suited to the measurement of groups of children rather than individual children. There is however scope for reducing this imprecision by doubling the scanning time and adding more NaI(Tl) detectors. Although this option doubles the health risk, the resulting dose (0.50 mSv) falls within the same ICRP category of health risk as the current dose (0.25 mSv) which is described as "minor to intermediate" (i.e. a health risk of about 1 in  $10^5$ ). Alternatively, bismuth germanate (BGO) detectors could be added to the existing NaI(Tl) detectors to measure chlorine  $\gamma$ -rays. In particular, BGO has been suggested as a more suitable alternative to NaI(Tl) because of its relatively high counting efficiency for chlorine  $\gamma$ -rays and a reduced sensitivity to neutron induced background.<sup>32</sup>

### Inter-Facility Comparisons

Table 4 compares the performance statistics for the facility at Melbourne with those from two other IVNAA facilities with comparable irradiation-detection geometries. In particular, the Sydney facility<sup>5</sup> is applied to the measurement of TBN in children and the Auckland facility<sup>6</sup> is calibrated for the measurement of TBN and TBCl in adults. Furthermore, the coefficients of variation relate to the measurement of tissue-equivalent solutions in a bottle phantom (33 kg, Melbourne), an anthropomorphic phantom (26 kg, Sydney), and a Bush phantom (60 kg, Auckland). Despite these phantom differences, the TBN measurement precision of the facility at Melbourne compares favourably with the TBN measurement precision of both the Sydney and Auckland facilities. Table 4 also shows the precision-

dose performance for each facility expressed as a figure of merit ( $\text{FM} = 100/(\text{CV} \sqrt{\text{dose equivalent}})$ ). Notably, FM for the measurement of TBN at Melbourne is comparable to the FM values from Sydney and Auckland. In contrast, the CV and FM values for the measurement of chlorine at Auckland are at present superior to the corresponding values at Melbourne. This most probably reflects the fact that, at Auckland, adult masses of chlorine are measured which are typically twice that found in children. This factor increases the precision of measuring chlorine, and hence improves the Auckland facility's precision-dose performance.

### Conclusions

We report the construction, calibration and evaluation of a clinical facility for the simultaneous in vivo measurement of nitrogen and chlorine with particular reference to use in children. Total body nitrogen and chlorine are determined from the respective prompt-reactions  $^{14}\text{N}(n,\gamma)^{15}\text{N}$ ,  $^{35}\text{Cl}(n,\gamma)^{36}\text{Cl}$ , and  $^1\text{H}(n,\gamma)\text{D}$ . Total body hydrogen is used as an internal standard and is derived independently from a four compartment model of body weight based on the measurement of total body water by  $\text{D}_2\text{O}$  dilution, total body protein from IVNAA, bone mineral content from dual energy x-ray absorptiometry and body fat estimated as body weight less the sum of total body water, protein and bone mineral. The effective dose for a 630 s, bilateral, shoulder-to-mid-thigh scan is 0.25 mSv ( $Q=20$ ) which, according to the ICRP (1991b), represents a "minor-to-intermediate" level of health risk and is justified if the exposure leads to a health benefit.

The measurement protocol applies primary corrections for body width and secondary corrections for body thickness to measurements of nitrogen and chlorine background. The protocol also accounts for the differential-attenuation rates of nitrogen, chlorine and hydrogen  $\gamma$ -rays in body tissue by applying a correction of approximately 0.9% per centimetre width and 0.2% per centimetre thickness to measurements of nitrogen-to-hydrogen and chlorine-to-hydrogen count ratios.

Repeated measurements of a child-size bottle phantom (33 kg) containing a physiological concentration of urea-salt solution demonstrate a measurement precision of less than 3% for TBN and about 10% for TBCl in child-like masses. Reproducibility measurements also suggest the systematic error of the method to be less than 2% for the measurement of nitrogen, and less than 4% for the measurement of chlorine. The performance characteristics of the Monash Medical Centre IVNAA facility compare favourably with other similarly constructed IVNAA facilities and characterise this

facility as a useful instrument for the study of nutritional health in children.

## Acknowledgments

This work was undertaken following a suggestion from Dr Julie Bines of the Royal Children's Hospital, Melbourne, that we undertake measurements in children with cystic fibrosis. The TLD monitors for the dose measurements were supplied and read by Dr G Morris's group at the Australian Radiation Laboratory. We acknowledge the enthusiastic support of Prof Alun Beddoe, formerly of the Royal Adelaide Hospital, South Australia. The IVNAA facility described in this paper incorporates all of the major features of the original MMC IVNAA facility designed by Prof Kenneth McNeill of the University of Toronto, Canada. The first author was funded by a Monash University Departmental Scholarship.

## References

1. Baur L.A., Waters D.L., Allen B.J., Blagojevic N. and Gaskin K.J., *Nitrogen deposition in malnourished children with cystic fibrosis*, Am. J. Clin. Nutr. 53: 503-11, 1991.
2. Baur L.A., Knight J.F., Crawford B.A., Reed E., Roy L.P., Allen B.J. and Gaskin K.J., *Total body nitrogen in children with chronic renal failure and short bowel syndrome*, Euro. J. Clin. Nutr. 48: 433-41, 1994.
3. Latham M.C., *Protein-energy malnutrition*, in Present knowledge in nutrition (International Life Sciences Institute-Nutrition Foundation: Washington): 39-46, 1990.
4. Rayner H.C., Stroud D.B., Salamon K.M., Strauss B.J.G., Thompson N.M., Atkins R.C. and Wahlqvist M.L., *Anthropometry underestimates body protein depletion in haemodialysis patients*, Nephron 59: 33-40, 1991.
5. Baur L.A., Allen B.J., Rose A., Blagojevic N. and Gaskin K.J., *A total body nitrogen facility for paediatric use*, Phys. Med. Biol. 36: 1363-75, 1991.
6. Mitra S., Plank L.D., Knight G.S. and Hill G.L., *In vivo measurement of total body chlorine using 8.57 MeV prompt de-excitation following thermal neutron capture*, Phys. Med. Biol. 38: 161-72, 1993.
7. ICRP, *Report of the task group on reference man*, ICRP Report 23 (Pergamon Press, New York), 1975.
8. Edelman I.S. and Leibman J., *Anatomy of body water and electrolytes*, Am. J. Med. 27: 256-77, 1959.
9. Lentner C., *Geigy Scientific Tables*, (Basle, Ciba-Geigy) 3: 78, 1984.
10. Stroud D.B., Borovnicar D.J., Lambert J.R., McNeill K.G., Marks S.J., Rasool R.P., Rayner H.C., Strauss B.J.G., Tai E.H., Thompson M.N., Wahlqvist M.L., Watson B.A. and Wright C.M., *Clinical studies of total body nitrogen in an Australian hospital*, in In vivo body composition studies: recent advances, eds Yasumura S., Harrison J.E., McNeill K.G., Woodhead A.D. and Dilmanian F.A., (New York: Plenum Press): 177-82, 1990.
11. Borovnicar D.J., Rasool R.P., Stroud D.B., Thompson M.N., *Spatial sensitivity measurements of a prompt gamma facility*, Australas. Phys. Eng. Sci. Med. 14, No.1: 1, 1991.
12. Vartsky D., Prestwich W.V., Thomas B.J., Dabek J.T., Chettle D.R., Fremlin J.H. and Stammers K., *The use of body hydrogen as an internal standard in the measurement of nitrogen in vivo by prompt neutron capture gamma-ray analysis*, J. Radioanal. Chem. 48: 243-52, 1979.
13. Stamatelatos I.E.M., Chettle D.R., Green S. and Scott M.C., *Design studies related to an in vivo neutron activation analysis facility for measuring total body nitrogen*, Phys. Med. Biol. 37: 1657-74, 1992.
14. Stamatelatos I.E.M., Chettle D.R. and Scott M.C., *Studies relating to the choice of  $\gamma$ -ray detectors for in vivo nitrogen measurement by prompt-capture neutron activation analysis*, Phys. Med. Biol. 38: 411-22, 1993.
15. McNeill K.G., Borovnicar D.J., Krishnan S.S., Wang H., Waana C. and Harrison J.E., *Investigation of factors which lead to the background in the measurement of nitrogen by IVNAA*, Phys. Med. Biol. 34: 53-9, 1989.
16. ICRP, *Radiological protection in biomedical research*, ICRP Publication 62 (Pergamon Press, Oxford) 22 No. 3: 1991.
17. Lone M.A., Leavitt R.A. and Harrison D.A., *Prompt gamma rays from thermal-neutron capture*, Atomic Data and Nuclear Tables 26: 511-59, 1981.

18. Chettle D.R., Fremlin J.H., *Techniques of in vivo neutron activation analysis*, Phys. Med. Biol. 29: 1011-1043, 1984.
19. Yankuba S., Oldroyd B., Metcalfe S.C., Godfrey J.E. and Oxby C.B., *Examination of errors caused by random summing in in vivo prompt gamma ray analysis*, Phys. Med. Biol. 34: 1089-1102, 1989.
20. Humphries I.R.J., Allen B.J., Blagojevic N. and Gaskin K.J., *Hydrogen background in total body nitrogen estimations*, Phys. Med. Biol. 40: 201-207, 1995.
21. Wang H. and Waana C.M., *IVNAA investigation of factors affecting the background in the measurement of nitrogen*, J. Radio. Nucl. Chem. 151: 293-9, 1991.
22. Beddoe A.H., Zuidmeer H. and Hill G.L., *A prompt gamma in vivo neutron activation analysis facility for measurement of total body nitrogen in the critically ill*, Phys. Med. Biol. 29: 371-83, 1984.
23. Mackie A., Cowen S. and Hannan J., *Calibration of a prompt neutron activation analysis facility for the measurement of total body nitrogen*, Phys. Med. Biol. 35: 613-24, 1990.
24. McNeill K.G., Mernagh J.R., Jeejeebhoy K.N., Wolman S.L. and Harrison J.E., *In vivo measurements of body protein based on the determination of nitrogen by prompt analysis*, Am. J. Clin. Nutr. 32: 1955-61, 1979.
25. Beddoe A.H., Streat S.J. and Hill G.L., *Measurement of total body chlorine by prompt gamma in vivo neutron activation analysis*, Phys. Med. Biol. 32: 191-201, 1987.
26. Fomon S.J., Haschke F., Ziegler E.E. and Nelson S.E., *Body composition of reference children from birth to age 10 years*, Am. J. Clin. Nutr. 35: 1169-75, 1982.
27. Lentner C., *Geigy Scientific Tables* (Basle, Ciba-Geigy) 1: 219, 1981.
28. Brozek J., Grande F., Anderson J.T., Keys A., *Densitometric analysis of body composition: revision of some quantitative assumptions*, Ann. N.Y. Acad. Sci. 110: 113-140, 1963.
29. Lohman T.G., Roche A.F., Martorell R. (eds), *Anthropometric standardisation reference manual*, Human Kinetics Books (Illinois), 1988.
30. Morris N., *Personal radiation monitoring and assessment of doses received by radiation workers*, Australian Radiation Laboratory ARL/TR107, 1991.
31. ICRP, *Recommendations of the International Commission on Radiological Protection*, ICRP Publication 60 (Pergamon Press, Oxford), 21 No. 1-3: 1991.
32. Blagojevic N., Allen B.J. and Rose A., *Development of a total body chlorine analyser using a bismuth germanate detector system and a  $^{252}\text{Cf}$  neutron source*, in *In vivo body composition studies: recent advances*, eds Yasumura S., Harrison J.E., McNeill K.G., Woodhead A.D. and Dilmanian F.A., (New York: Plenum Press): 401-408, 1990.
33. Watt D.E. and Ramsden D., *High sensitivity counting techniques*, Pergamon Press (Oxford), 1-9, 1964.