MEASUREMENT OF TOTAL-BODY CALCIUM, SODIUM CHLORINE, NITROGEN, AND PHOSPHORUS IN MAN BY IN VIVO NEUTRON ACTIVATION ANALYSIS

S. H. Cohn and C. S. Dombrowski

Medical Research Center, Brookhaven National Laboratory, Upton, New York

The measurement of total-body levels of calcium, sodium, chlorine, nitrogen, and phosphorus are of obvious importance in normal individuals as well as those with various disease states. However, until recently there were only two techniques available for making these measurements. Chemical analysis of the total body is possible, of course, but being a destructive type of analysis, it is of limited utility. Radioisotopic tracer techniques have also been useful in the measurement of elements such as Na and Cl since the tracer mixes rapidly and fairly completely with the exchangeable pools of the element. However, with elements such as Ca, P, and N, the appropriate tracers do not mix rapidly with the major pools of these elements, and hence total-body levels cannot be measured.

Significant progress in the determination of totalbody levels of Ca, Na, and Cl was achieved when current research demonstrated that measurements made by in vivo neutron activation are feasible (1-4). Further, activation analysis has been shown to be a precise technique for the in vivo measurement of whole-body calcium in man (5,6). Recently it has been shown that it is possible to obtain measurements that are not only reproducible, but also accurate in that absolute levels of calcium in man can be determined (7). The accuracy developed in this latter technique is dependent on the use of an advanced type of whole-body counter with an invariant counting response (8).

In the present study, activation analysis was used for the simultaneous measurement of absolute levels of total-body Ca, Na, and Cl in human subjects. These elements are activated by the n,γ reactions listed in Table 1. Use of partially moderated 14-MeV neutrons also results in the production of other activities as a result of interaction with the thermal and fast-neutron components (Table 1). For exam-

Received May 27, 1970; revision accepted Jan. 28, 1971. For reprints contact: S. H. Cohn, Medical Physics Div., Medical Research Center, Brookhaven National Laboratory, Upton, L.I., N.Y. 11973.

Reaction	T _{1/2}		Decay scheme*	Measured total activity (nCi)†	Yield‡
²¹ Na(n,γ) ²⁴ Na	15.0	h	1.389 β(100), 2.75 γ(100), 137 γ(100)	9.6	1.0
³⁷ Cl(n,γ) ³⁸ Cl	37.2	m	4.81 β(53), 2.77 β(16), 1.11 β(31), 1.60 γ(31), 2.17 γ(47)	23.4	1.55
⁴⁸ Ca(n,γ) ⁴⁹ Ca	8.7	m	1.95 β(88), 0.9 β(12), 3.1 γ(89), 4.05 γ(10), 4.68 γ(0.3)	19.3	0.99
³¹ P(n,α) ²⁸ Al	2.31	m	2.86 β(100), 1.79 γ(100)	1331.0	7.66
¹⁴ N(n,2n) ¹³ N	9.99	m	1.19 $\beta^{+}(100)$, (0.51 γ from β^{+})	107.0	25.90
³⁷ Cl(n,p) ³⁷ S	5.06	m	4.3 β(10), 1.6 β(90), 3.1 γ(90)	2.1	0.06
²⁴ Mg(n,p) ²⁴ Na	15.0	h	1.389 β(100), 2.75 γ(100), 1.37 γ(100)		
[™] Mg(n,γ) ^{₽7} Mg	9.5	m	1.75 β(58), 1.59 β(42), 0.18 γ(0.7), 0.84 γ(70), 1.01 γ(30)		
³¹ P(n,2n) ³⁰ P	2.56	m	3.24 $\beta^{+}(99.5)$, 1.01 $\beta^{+}(0.5, 2.16 \ \gamma(0.5)$, (0.51 γ from β^{+})		
³⁹ K(n,2n) ³⁸ K	7.7	m	2.68 $\beta^{+}(100)$, 2.17 $\gamma(100)$, (0.51 γ from β^{+})		
"K(n,γ)"K	12.5	h	3.56 β(82), 1.97 β(18), 1.52 γ(18)		
⁴¹ K(n,α) ³⁸ Cl	37.2	m	4.81 β(53), 2.77 β(16), 1.11 β(31), 1.60 γ(31), 2.17 γ(47)		

ple, the fast neutrons produce the following two reactions in human tissue: ${}^{14}N(n,2n){}^{13}N$ and ${}^{31}P(n,\alpha)$ ${}^{28}Al$. These two reactions have been used successfully as the basis for the determination of total-body P and N in mice (9) and, as will be demonstrated, can be used for the same measurements in man.

This report discusses the calibration techniques for the in vivo measurement of total-body Ca, Na, and Cl as well as of P and N in human subjects. In addition, data obtained from the application of these techniques to the measurement of these elements in patients with various disease states are presented.

METHODS

Neutron exposure. A Texas-Nuclear generator supplying 14-MeV neutrons generated by the ${}^{3}H(d,n){}^{4}He$ reaction was used as the source of fast neutrons. To maximize the uniformity of the thermal neutron fluence through the body of the irradiated subject, a moderator and a bilateral exposure were used (7). The polyethylene moderator (3.8 cm thick) was placed up against the front and



FIG. 1. Patient is positioned in exposure chamber between two sheets of polyethylene moderator. Patient is standing on turntable which is turned to provide bilateral irradiation.

back of the body, as is illustrated with a patient in the exposure chamber (Fig. 1). The fast neutrons are further thermalized in their passage through the body to produce a variable range of energies from thermal to fast neutrons. The minimum usable thermal neutron flux for the experimental conditions described is 4.54×10^4 n/cm²/sec (7).

The incident fast neutron flux density from the neutron generator measured with ²⁷Al foils was found to be 0.925 of the peak thermal neutron flux density (7). During each patient exposure, the fast neutron flux is monitored by proton-recoil scintillation detectors connected to a rate meter and scaler. In addition, indium foils are placed on the abdomen and on the back of each patient and phantom before irradiation to monitor the incident thermal neutron flux. Indium foils with cadmium shields are exposed simultaneously to correct for the resonance. The total absorbed dose to the patient was 0.6 rem (RBE of 10) as measured by a Rossi tissue-equivalent chamber and a LiF dosimeter (7).

The uniformity of the thermal neutron flux distribution through a phantom was previously determined to be $\pm 5\%$ (7). At a distance of 1.5 meters the incident neutron flux at the head and foot of the patient is considerably lower (30%) than that to the midportion of the body. However, a series of measurements in a bilaterally irradiated Alderson phantom indicated that the values of thermal flux along the central axis of the phantom from head to foot varied from the average by $\pm 6\%$. Thus the decrease in incident flux received by the head and limbs due to the inverse-square-law drop-off was apparently to a large extent compensated for by the increased thermal neutron flux resulting from the decrease in the attenuation of the neutron flux density in the legs and head as compared with the thicker portions of the body-the trunk and the chest. Further, when there is an air gap between the moderator and the body, a secondary buildup in flux occurs at the surface of the body. This increased thermalization also tends to normalize the flux received by the head and the extremities.

The maximum variation in the fast neutron flux density through the phantom was estimated to be of the order of $\pm 20\%$ for a subject of average thickness.

EXPERIMENTAL PROCEDURE

The activations were performed by irradiating the subject or the Alderson phantom containing the target material at 1.5 meters from the target. The phantom and the patients were irradiated bilaterally, front and back, for 5 min and transported rapidly to the 54-detector whole-body counter to measure



FIG. 2. Gamma-ray spectrum of patient (WIL) at 6 min following exposure to flux of 9×10^4 n/cm²/sec of 14-MeV neutrons.

the induced activities. As previously described, the Brookhaven counter, particularly when used with an empirical correction program, has a relatively invariant counting response to body weight and the internal localization of the radionuclide (8).

Two 15-min counts were taken on each subject, beginning at 6 and 23 min postirradiation. The data were processed and analyzed with the on-line computer used in conjunction with the counting system. The spectral data of the induced activities of a typical subject in a 15-min count starting at 6 min postirradiation are shown in Fig. 2. A gamma spectral analysis is performed using a computer program to determine the photopeak areas of each induced radionuclide. The amounts of each element in grams are then determined by applying the following calibration technique.

Absolute calibration of the counter for the measurement of Ca, Na, Cl, P, and N. The levels of ⁴⁹Ca, ²⁴Na, ³⁸Cl, ¹³N, and ²⁸Al(P) induced following exposure to partially moderated 14-MeV neutrons were determined by whole-body counting and compared with the induced activities produced by irradiating an Alderson phantom containing known concentrations of the various elements.

For the calculation of the mass of each element in the body, it is first necessary to determine the calibration factor (CF) which relates the amount of each target element to the average neutron flux density and to the corresponding induced activities as measured by the whole-body counter (7):

$$CF = \frac{m\phi_{th}}{A}$$

in which m is mass of target (gm), ϕ_{th} is thermal flux density (n/cm²/sec), and A is corrected counts/

15 min in photopeak of each radionuclide corrected back to t = 0.

Individual measured targets of Ca, Na, Cl, N, and P were homogeneously distributed in a water-filled Alderson phantom and irradiated. Three separate irradiations of the phantom were performed for each of the five elements, followed by two 15-min wholebody counts. Each time the phantom was irradiated for 5 min in the exact geometry as that used for human subjects. The induced activity (A), measured in each 15-min count under standardized conditions, and the ϕ_{th} , measured by averaging the activity induced in the standardized indium foils positioned on the front and back of the subject, were used to determine the mass of each element (7).

RESULTS

The yields of the principal nuclear reactions produced by the irradiation of a human subject under the experimental conditions outlined are presented along with the measured total induced activity for each radionuclide (Table 1). From the measured gamma counts (normalized to standard man) obtained by irradiating the subject for 5 min at the minimal usable thermal flux, the total induced activity was determined. The yield for each element, i.e., the measured count of the principal gamma energy expressed in terms of the sodium count, is also shown in Table 1.

The composite results of all the individual phantom calibration runs are given in Table 2. The values

			Amount (gm):								
Run	Count	N	P	CI	Να	Ca					
1	1	738	829	79	79	1,012					
	2	736		83	77						
		737		81	78						
2	1	675	807	76	77	975					
	2	692		80	79						
		684		78	78						
3	1	646	775	75	79	1,006					
	2	719		77	78						
		683		76	78						
×		701	804	78	78	998					
% s.c	l.	±4.40	±3.38	±3.20	±0.74	±1.98					
Absol	ute con-										
cen	tration	700	807	80	80	1,000					
% de pho	viation o antom	f									
me ab	an from solute cor	1-									
Can	tration	0.14	0.37	2.50	2.50	0.20					

listed are the average of the two 15-min counts. A comparison of the mean of three individual phantom runs for each element with the absolute concentration of the element distributed in the phantom indicates that the maximum percent deviation from the mean for Ca, N, and P was less than 0.5%, while that for Na and Cl was 2.5%. The standard deviation of the averages of the three runs, which reflects the precision of the technique, ranges from 0.74% for Na to 4.40% for N as indicated in Table 2.

The peak at 0.85 MeV seen in most irradiated subjects is assumed to be due largely to ⁵⁶Mn although the amount of target Mn reported for standard man has been stated to be 20 mg. Studies with an irradiated phantom into which were placed 0.1, 0.2, and 0.1 gm of Mn target (homogeneously distributed), indicated a well-defined peak of ⁵⁶Mn with the correct value for half-life ($T_{1/2} = 2.58$ hr). The amount of activity induced leads to a calculated whole-body content of Mn on the order of 200 mg. The counting statistics for induced ⁵⁶Mn at the level of 200 mg, however, are very poor. Further, the normally present 35 gm of Mg in the body also produces a peak at 0.85 MeV, for which correction must be made. The overall result is that it is difficult to achieve reliable statistical accuracy in Mn measurement at this time.

The calibration data obtained with the phantom were then applied to the measurement of these elements in a number of patients with various diseases (Table 3). The first two patients (LIN and WIL) were undergoing chemotherapy for extensive metastatic bone neoplasms. Patient WIL was activated and counted three times over a period of 5 months, and the change in total-body Ca from the initial count following therapy roughly corresponded to her improved clinical condition. The next six subjects were

		w.	ы				Amou	nt (gm):					gm,	/100 gn	n K	
Sex	Age	(ib)	(in.)	Diagnosis	к	N	P	CI	Na	Ca	P/Ca	N	P	CI	Na	Ca
F	35	106	57.5	Metastatic	65.0	2,257 ±1.7*	416	58 ±2.5	68 ±2.9	751	0.55	3,472	640	89	105	1,15
F	44	135	63.7	cancer	79.9	2,007 ±0.57	402	64 +2.4	66 +2.9	688	0.58	2,540	509	81	84	87
F	44	135	63.7	of	79.9	2,096 ±0.45	476	67 +0	70 +2.1	736	0.57	2,653	603	85	89	93
F	44	135	63.7	breast	79.9	2,166 ±0.93	399	72 ±2.7	71 ±0.7	695	0.57	2,741	505	91	90	88
M	57	150	62.0	Osteo-	92.1	2,705 ±1.9	575	77 ±0	95 ±2.6	1,000	0.57	3,189	624	84	103	1,08
M	62	163	65.0	porosis	104.6	2,504 ±2.1	551	70 ±2.1	86 ±1.2	949	0.58	2,394	527	67	82	90
F	61	117	57.2		77.4	1,972 ±0	358	71 ±4.1	79 ±5.4	620	0.58	2,548	462	92	102	80
F	50	1 <i>5</i> 0	64.0		66.6	2,332 ±0.8	420	68 ±0.8	70 ±0.7	734	0.57	3,502	631	102	105	1,10
F	70	151	60.5		60.1	2,233 ±1.0	364	72 ±2.1	75 ±1.4	637	0.57	3,715	606	120	125	1,06
F	57	111	57.0		68.7	1,838 ±0	325	54 ±2.7	64 ±0.7	544	0.59	2,675	473	79	93	80
M	26	146	68.8	Azotemic	121.8	3,086 ±1.6	716	91 ±3.7	107 ±0	1,281	0.56	2,534	588	75	88	1,05
M	29	164	68.0	with	128.9	3,372 ±2.1	746	105 ±2.8	117 ±2.1	1,345	0.56	2,616	579	81	91	1,04
M	23	136	70.0	chronic	114.3	2,878 ±5.8	854	81 ±0	91 ±1.6	1,213	0.70	2,518	747	71	80	1,06
M	49	174	64.5	renal	130.5	2,797 ±1.3	586	82 ±5.7	88 ±6.8	965	0.61	2,143	449	63	67	73
F	56	103	59.0	failure on	66.6	1,624 ±0.9	336	57 ±0	63 ±0	568	0.59	2,438	505	86	95	85
F	38	130	62.5	hemodialysis	58.7	1,798 ±0.9	412	92 ±2.8	91 ±1.1	758	0.54	3,063	702	157	155	1,29
M	15	127	61.0	Cushing's	69.5	1,852	412	62	42	769	0.54	2,665	852	89	60	1,10

elderly osteoporotic patients measured before being placed on a therapeutic regime designed to diminish the loss of Ca from the skeleton. The following six are azotemic patients undergoing hemodialysis. The last patient, HOF, has Cushing's disease.

DISCUSSION

There are four requirements that must be fulfilled for absolute measurement of total-body concentrations by in vivo activation analysis. First, a uniform neutron distribution exposure of the target elements in the subject must be obtained. Second, the induced activities must be measured in a counter with uniform counting sensitivity. Third, correction must also be made for interfering reactions produced from different target elements in the body (see Table 1). Finally, correction must be made for errors inherent in the bilateral exposure and the induction of shortlived radionuclides.

Uniformity of neutron fluence. It has already been demonstrated that the use of 14-MeV neutrons moderated by polyethylene in a bilateral exposure results in a relatively high uniformity of the thermal flux density $(\pm 5\%)$ through a phantom (7).

With fast-neutron reactions this high degree of uniformity cannot be attained; it is of the order of $\pm 20\%$. To date, fast-neutron reactions have not been used in activation of human subjects because of this nonuniformity of fluence, the low crosssections of many target elements to fast neutrons, and the high threshold required. With the present source of 14-MeV neutrons the amount of both the ¹³N and the ²⁸Al produced from N and P in the body are in sufficient quantity for the determination of the levels of these elements in man. The fact that even with fast neutrons the fluence falls off significantly with greater body thickness makes it impossible to obtain an absolute measurement of N and P, as was the case for Ca, Na, and Cl. The present data indicate that the precision, or reproducibility, of the N and P measurement in any individual repeatedly counted is quite high, 4.4 and 3.4%, respectively. For subjects of the approximate dimensions of the phantom, and assuming a similar distribution of N in both cases, the approximation can be not only precise but also achieves a degree of accuracy.

Uniformity of counting response. The counting efficiency for each activated atom is required to be approximately the same. The induced activities measured with a whole-body counter having an invariant counting response to geometry and attenuation provides this required absolute measure of activity. The details of the counting technique have been discussed (8). It is this technique which enables the measurement of absolute levels of Na, Cl, and Ca

to be made. Unless correction can be made for the effects of spatial localization of the induced radionuclide and the variable attenuation of the body size, it is at most possible to make precise or reproducible measurements of radionuclides in individual subjects; under these conditions absolute measurements cannot be attained.

Interfering reactions. While the use of 14-MeV neutrons has many advantages in activation analysis, there are also minor disadvantages in the induction of other activities which interfere with the measurement of the elements under analysis (Table 1). For example, it has been pointed out that ²⁴Na produced by the ${}^{24}Mg(n,p){}^{24}Na$ reaction can interfere with the analysis of ²⁴Na produced by the ²⁸Na (n,γ) ²⁴Na reaction (2,5). However, when a phantom containing 35-gm Mg (stated amount in standard man) was irradiated under the experimental condition described, no significant amount of ²⁴Na (2.76 MeV) was produced to interfere with the analysis of Na. As previously mentioned, the 0.85-MeV peak of ²⁷Mg does interfere with the similar peak resulting from induced ⁵⁶Mn.

For the measurement of Ca, the ${}^{37}Cl(n,p){}^{37}S$ reaction is the principal interfering reaction. Sulfur-37 has the same energy as ${}^{49}Ca$ (3.1 MeV), and its half-life is close to that of ${}^{49}Ca$. This is corrected for by determining the relationship between net Cl and ${}^{37}S$ produced under the experimental conditions. The derived correction is applied to the induced ${}^{49}Ca$ count by the computer. For the two counts the correction is equal to 3.9 and 0.37% of the net ${}^{38}Cl$ (2.2 MeV) count, respectively. Thus approximately 6 and 1.4% of the ${}^{49}Ca$ counts at 6 and 23 min after irradiation, respectively, are contributed by the induced ${}^{37}S$.

The only positron emitter that might be confused with ¹³N is ³⁰P formed from P in the body. The contribution from ³⁰P can be eliminated by counting after 20 min, which insures the complete decay of ³⁰P ($T_{1/2} = 2.55$ min). The potential interference to ¹³N from ^{38m}K formed in the body was also investigated by irradiation of the phantom containing 140 gm of K. No significant interference from the products of irradiated K was observed.

Indirect evidence that the appropriate corrections for interference have been made is provided by the fact that the counts obtained in each of the two 15-min counts, when corrected for interferences and for radioactive decay to T_0 , are approximately equal. For example, the difference between the first and second counts of ¹⁸N in any patient averages $\pm 1.6\%$ for 28 patients studied. The average difference in the two counts of ²⁴Na and ³⁸Cl in the same 28 patients was $\pm 1.8\%$ and $\pm 2.1\%$, respectively. Because of the short radioactive $T_{1/2}$ of ⁴⁹Ca and ²⁸Al, it is not possible to obtain two successive counts with sufficient statistical accuracy. However, in most patients counted the P/Ca ratio varies between 0.56 and 0.59. This compares with the ratio of 0.56 determined by chemical analysis of the human body (10).

Errors associated with bilateral exposure and radioactive decay. With bilateral exposure there is a time lapse in turning the subject, and a decay correction must be made in the case of radionuclides of short half-lives. For the 5-min exposure the anterior-posterior irradiation time was 163 sec and the posterior-anterior irradiation time was 133 sec to compensate for the decay of the short-lived ⁴⁹Ca (8.8 min). The 180-deg turn required 4 sec, giving rise to a slight error in the overall dose. Since the exposure is based on Ca, appropriate corrections must be made for the unequal bilateral exposure in the estimation of the other radionuclides.

Application of the technique to the measurement in man. The values of the various elements measured in the subjects listed in Table 3 can be compared to the following stated values for standard man (ICRP). Parenthetical values in the table are explained in Table 4.

The values in Table 4, as stated by the ICRP, are based on relatively few chemical analyses of the human body. An ICRP task group is reconsidering the data on which these values were based and have, to date, changed only the value of Mn from 20 mg to 200 mg. The task group suggested that because of the paucity of data, effort should be made to obtain more accurate data for the chemical composition of the body.

While the value of 1,050 gm of calcium in a standard man has been often quoted, the body content of calcium in adult European and American skeleta has been reported to range from 796 to 1,510 gm (10-11). Although the ICRP values listed for Na and Cl are 105 gm, from this study and those of others (1,6), it appears that the total-body levels of Na and Cl are approximately 80 gm in a standard man (70 kg). The ⁵⁶Mn peak detected in most sub-

	VALUES	IN TABLE	3	
Element	gm/70-kg	body wt	gm/100	-gm k
N	2,100		1,500	
Ca	1,050		720	
Na	105	(80)	75	(57)
CI	105	(80)	75	(57)
P	700		500	
Mn	20	(200)	.14	(143)

jects appears to be of the order of 200 mg. However, with the poor counting statistics and the interference of ${}^{27}Mg$, the error is quite large and the measure is of questionable statistical validity.

The values obtained in elderly subjects (with osteoporosis) are in the lower range of the above quoted normal values. However, it is difficult at present to define the so-called "normal" values and values for osteoporotics as a group. The levels of each element in the women are considerably lower than in man, as expected. The patients STR and TUT with the most severe osteoporosis had the lowest total-body calcium. Many of the azotemic patients have total-body levels of Ca, P, N, Na, and Cl which could be considered in the "normal" range also. These values can be compared with the values obtained by chemical analysis of the body of a uremic patient weighing 71.8 kg. The values obtained by chemical analysis were Ca = 1,300 gm, Na = 129gm, and P = 855 gm (10). Obviously more data must be accumulated to define the ranges of body calcium in various disease states.

Because of the variability in percent fat, it is more meaningful to express whole-body levels of these elements in terms of lean-body mass. When the values obtained for each element are normalized to each patient's body K, which reflects lean-body mass, the range in the values in any group of patients is greatly reduced. For example, the levels of the various elements per 100 gm K in the female osteoporotics are not very different from the corresponding values in the male osteoporotics. Further, the spread in the levels of each element in the osteoporotic patients overlaps that observed in the azotemic patients. In conditions where the amount of lean-body mass (40 K) is known to be altered, this method of normalizing the data is, of course, less useful.

The significance of these total-body values and their interrelationship, particularly in terms of the disease state and therapy, will be considered in subsequent reports.

SUMMARY

In vivo activation with 14-MeV fast neutrons moderated with polyethylene has been shown capable of inducing the following activities in human subjects: ⁴⁹Ca, ²⁴Na, ³⁸Cl, ²⁸Al(P), ¹³N, and ⁵⁶Mn. The Ca, Na, and Cl activities produced by thermal neutrons with a uniform flux density throughout a phantom can be converted to absolute grams with an accuracy of $\pm 4\%$. It is, of course, possible that measurements might be less accurate in patients that differ grossly in shape or size from the phantom. However, the precision (that is, reproducibility) of the measurements in the same patient is better than $\pm 4\%$. Because of the nonuniformity of the fast-neutron fluence with depth, the levels of N and P produced by the fast neutrons cannot be determined with the same accuracy as Na, Cl, and Ca. Nevertheless, totalbody levels of N have been determined with high precision (average of $\pm 1.6\%$) in successive measurements on the same patient. The levels of ⁵⁶Mn produced are measurable, but because of its low level and the interference of ²⁷Mg, the statistical accuracy is not sufficiently satisfactory at present.

Representative value for Ca, Na, Cl, P, and N for a number of patients with various disease states are presented in application of the above techniques. When these values are normalized to lean-body mass, i.e., expressed in terms of measured ⁴⁰K, the variation between the different disease states and the sexes is greatly diminished.

It is clear that in vivo activation of Ca and P is an invaluable technique in kinetic studies of calcium metabolism in aging and in any condition involving changes in the total-body levels of Ca and P, such as immobilization and weightlessness. Disorders of calcium metabolism associated with chronic renal dialysis can be studied by this technique. The measurement of body Na and Cl are useful in electrolyte imbalance disease states. Nitrogen reflects protein metabolism, and it is of considerable usefulness in the evaluation of a number of disease states. Thus it is obvious that in vivo neutron activation analysis has considerable potential for use in medical research and diagnosis in living man.

ACKNOWLEDGMENT

The authors gratefully acknowledge the assistance of Jere Austin who operated the neutron generator and Michael Stravino for his assistance in the whole-body counting.

The data on azotemic patients on hemodialysis are derived from a study being conducted by J. Letteri and T. Cinque. The data on the patients with breast cancer are from a study being conducted by J. L. Bateman. The patient with Cushing's disease is part of a study being conducted by M. Roginsky and J. Aloia. The data on osteoporotic patients are derived from a study being conducted by S. H. Cohn, H. L. Atkins, W. Hauser, and J. F. Klopper.

This research was supported by the U.S. Atomic Energy Commission.

REFERENCES

I. ANDERSON J, OSBORN SB, TOMLINSON RWS, et al: Neutron activation analysis in man in vivo. A new technique in medical investigation. *Lancet* 1: 1201–1205, 1964

2. BATTYE CK, TOMLINSON RWS, ANDERSON J, et al: Experiments relating to whole-body activation analysis in man in vivo using 15-MeV incident neutrons. In Symposium on Nuclear Activation Techniques in Life Sciences, Amsterdam, May 1967

3. ANDERSON J, TOMLINSON RWS, BATTYE CK, et al: Total-body sodium, calcium and chlorine by whole-body neutron activation. In *Compartments, Pools, and Spaces in Medical Physiology*. USAEC Conf. 661010, 1967, p 111

4. NEWTON D, ANDERSON J, BATTYE CK, et al: Activation analysis in vivo using 5-MeV incident neutrons. Int J Appl Radiat 20: 61-68, 1969

5. PALMER HE, NELP WG, MURANO R, et al: The feasibility of in vivo neutron activation analysis of total body calcium and other elements of body composition. *Phys Med Biol* 13: 269–279, 1968

6. CHAMBERLAIN MJ, FREMLIN JH, PETERS DK, et al: Total-body calcium by whole-body neutron activation: New technique for study of bone disease. *Brit Med J* 2: 581– 585, 1968

7. COHN SH, DOMBROWSKI CS, FAIRCHILD RG: In vivo activation analysis of calcium in man. Int J Appl Radiat 21: 127-137, 1970

8. COHN SH, DOMBROWSKI CS, PATE HR, et al: A wholebody counter with an invariant response to radionuclide distribution and body size. *Phys Med Biol* 14: 645-658, 1969

9. NAGAI T, FUJII IH, MUTO H, et al: Total-body nitrogen and protein determined by in vivo fast-neutron activation analysis. J Nucl Med 10: 192-196, 1969

10. WIDDOWSON EM, MCCANCE RA, SPRAY CM: The chemical composition of the human body. *Clin Sci* 10: 113-125, 1951

11. NICOLAYSEN R, et al: Physiology of calcium metabolism. Physiol Rev 33: 424-444, 1953