DESIGN AND CALIBRATION OF A "BROAD-BEAM" ^{238}Pu, Be NEUTRON SOURCE FOR TOTAL-BODY NEUTRON ACTIVATION ANALYSIS

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In 1964 Anderson, et al (*1*) demonstrated the feasibility of determining levels of elements in the body by measuring the induced gamma activities in humans following exposure to neutrons. Two basic problems emerged as absolute levels of body elements were determined by the neutron activation technique. The first problem is that of obtaining a uniform neutron flux density through the body. The second problem is that of measuring the gamma emissions of the induced radionuclides with equal counting efficiency.

Battye, et al (*2*) was able to achieve uniformity of the radiation by employing 14-MeV neutrons moderated by polyethylene and by the use of bilateral irradiation. Palmer, et al (*3*), Nelp, et al (*4*), and Chamberlain, et al (*5,6*), using lower-energy neutrons from a cyclotron, were able to achieve a fairly uniform incident neutron flux. Palmer, et al and Nelp, et al expressed the induced activity of ^{49}Ca in terms of a calcium standard simultaneously irradiated; Chamberlain, et al expressed the induced ^{49}Ca in terms of induced ^{24}Na. Thus both achieved a relative measurement. Cohn, et al (*7,8*), using partially moderated 14-MeV neutrons from a generator and a bilateral exposure along with an advanced whole-body counter-computer system (*9*), measured absolute levels of Ca, Na, and Cl along with relative levels of N and P.

All of the neutron sources used in the studies mentioned above were originally designed for studies in physics and were neither designed nor situated with a consideration for possible medical research studies. Now that total-body neutron activation analysis (TBNAA) is well established as a research technique in medicine, new systems such as the one described in this study will use neutron sources designed specifically for medical investigation and located near the clinical facilities.

Previous studies employing portable α,n neutron sources (*7*) have shown that such sources have a number of advantages for TBNAA over a cyclotron or neutron generator. The α,n sources allow a simultaneous bilateral exposure from a "broad-beam" source of neutrons to be made. The advantages are considerable: the irradiation geometry is substantially improved, significantly greater stability is achieved in the neutron output, and the absorbed dose to the patient can be reduced significantly. The reduced dose and the inherent simplicity of operation make α,n sources attractive for use in TBNAA.

The present report describes the design and construction of the first patient irradiation facility using radioactive α,n neutron sources for TBNAA. The system is composed of an array of fourteen 50-Ci encapsulated ^{238}Pu,Be neutron sources. The calibration of the system for the measurement of total-body levels of Ca, Na, Cl, and P is presented below. Clinical applications of the TBNAA technique are also discussed.

METHODS AND INSTRUMENTATION

Neutron sources. Fourteen sources, each containing 50 Ci of ^{238}PuO$_2$-Be (80% enriched ^{238}Pu) are used. The ^{238}Pu was obtained from the USAEC and encapsulated in stainless steel cylinders (1.5 in. in diam and 1.5 in. in height) by Monsanto Chemical Company.

Mechanical positioning of sources. When not in use, the sources are stored beneath the patient irradiation facility in 14 steel casings, 10 ft under ground level. Aluminum tubes serve to guide the sources from their storage position to the fixed exposure positions, seven above and seven below the supine patient. The exposure cell and aluminum guide tubes are shown in Fig. 1.

The sources are raised from their storage vault by teleflex control cables, each operated by a separate motor. The source guide tubes were rendered ad-

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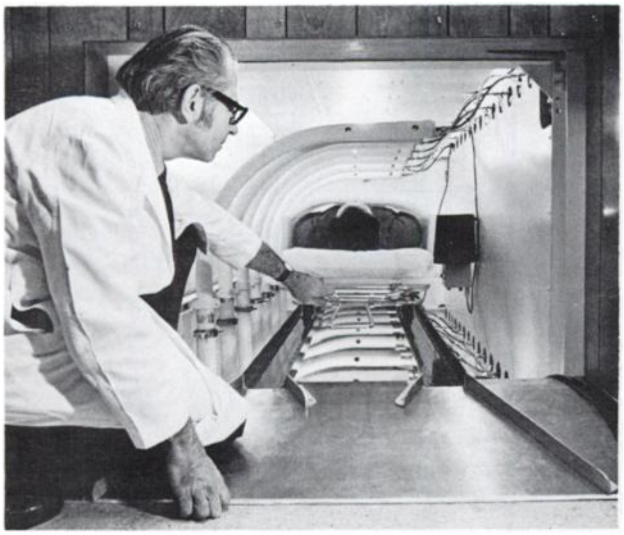

FIG. 1. ^{238}Pu,Be neutron irradiation facility. Patient is positioned as shown between upper and lower guide tubes which are used to position fourteen 50-Ci sources of ^{238}Pu,Be.

justable by inclusion of telescoping joints. Thus it is possible to position the individual sources over a considerable range both laterally and vertically. The sources in the present study were positioned 26–31 cm above and below the surface of the patient and were separated longitudinally by 28.6 cm. The end sources were positioned closer to the body to compensate for the end effect in the exposure geometry.

Shielding. The exposed sources and the patient are surrounded by 3 ft of concrete. Only the front or loading end of the exposure cell is left unshielded (see Fig. 1). The shielding was designed to reduce the total radiation dose at the outer surface of the shield to 1 mrem/hr when the sources are exposed. Inside the concrete exposure cell a 3-in. lining of bismuth provides a neutron reflector with a minimum of energy degradation. The shielding is further enhanced by ¼-in. Boral sheets which are placed between the concrete and the bismuth reflector.

Safety measures. Administrative control, two safety mechanisms, and an automatic warning system minimize the possibility of accidental exposure of hospital personnel to radiation. Administrative control is provided by key locks on both the operating controls and the room entry gate. An interlock between the room entry gate and the radiation sources prevent accidental entry into the exposure room and accidental exposure while the sources are exposed. The automatic warning system sounds when intentional unsafe entry takes place. The sources are automatically retracted if the entry gate is unlocked and opened during an exposure. Emergency access can always be gained by opening the gate with a pass key. A second automatic warning of unsafe radiation level in the cell is also provided by a radiation detection monitor which visually indicates cell radiation levels at all times and sounds an alarm when the cell entry gate is not locked.

Neutron exposure. The fourteen 50-Ci sources of ^{238}Pu,Be provide a fairly uniform broad beam of neutrons (average energy about 5 MeV) by the reaction $^{9}\mathrm{Be} + {}^{4}\mathrm{He} \rightarrow {}^{12}\mathrm{C} + \mathrm{n}$. The 3-in. bismuth reflector of the irradiation cell serves to enhance the uniformity of the neutron flux density in the cell.

The average neutron yield of the sources is 2.0×10^{6} n/sec/Ci of ^{238}Pu. The specific activity is 17.2 Ci/gm of ^{238}Pu. To monitor the output of fast neutrons, a BF$_3$ proportional counter surrounded by a polyethylene moderator is positioned inside the cell with a remote meter on the control panel.

Uniform neutron flux density in the patient. The problem of measuring reliably depth-flux density of thermal neutrons in man is complicated by the nonuniform human shape. The technique for measuring the thermal neutron flux densities generated in a tissue equivalent (TE) phantom has been previously described (*10*). A more realistic estimate of the neutron flux density in the patient was made with sodium foils placed throughout an anthropomorphic phantom.

The uniformity of the thermal neutron flux distribution was determined in a cubic TE 28 × 36 × 36-cm phantom placed in the patient's exposure geometry. The neutron flux distribution was measured with sodium foils placed on the surface and through the center of phantom. The maximum deviation from the mean dose over 28 cm was ±15%. From these measurements the optimum thickness of the buildup layer was determined to be equivalent to 2 cm of polyethylene.

In neutron activation techniques previously reported, either no moderator was used to thermalize the fast neutrons over the major portion of the body (*3,4*) or the moderation was achieved by placing the patient in a polypropylene chamber, 0.9 × 0.9 × 2 meters (*6*). In the former study, special procedures were employed to provide moderation over the head and extremities where the bones are very close to the surface (*4*).

A closely-fitted moderator of 1.9 cm polyethylene was used to maximize the uniformity of the thermal neutron fluence through the body of the irradiated subject. A solid plastic TE anthropomorphic phantom (Alderson) containing a human skeleton was used to establish empirically the optimal thickness and position of the moderator. The patient is positioned on top of a sheet of polyethylene and covered with a number of form-fitting sections of polyethylene which are selected to fit the individual patient (see Fig. 2). The choice of sections and position of the

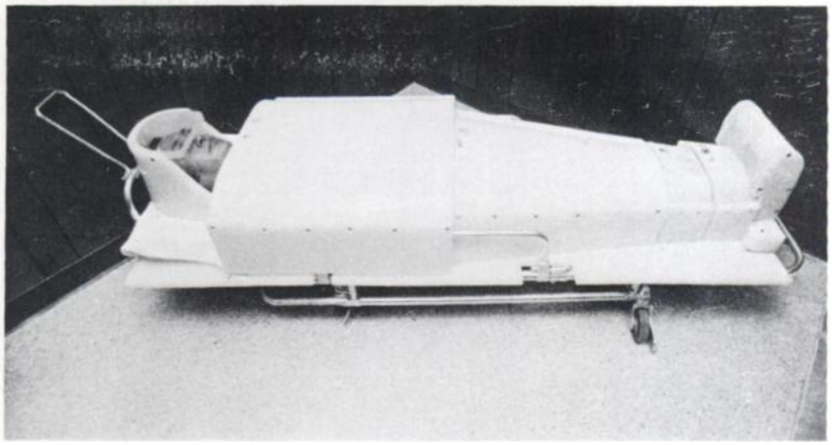

FIG. 2. Polyethylene moderator surrounding patient before irradiation exposure. Moderator is sectional and is fit to conform to shape of individual patient.

moderator is recorded, and both can be reproduced for subsequent activations. The close-fitting moderator also serves to fix the position of the patient in a standardized and reproducible exposure geometry.

A series of measurements were obtained with a water-filled Alderson phantom (Remcal) which closely simulates the shape of the human body. Both sodium and indium foils were positioned on the front and back surfaces and throughout the moderator-covered phantom. The details of the study of flux-density distribution in the phantom will be covered in a separate report. Assuming an average additional buildup layer of 1 cm of tissue, the overall variation in thermal flux density from front to back was ±8% (see Fig. 3). The higher flux density noted in the back of the phantom is presumably due to the greater neutron reflectance from the bottom of the cell. The variation in flux density along the midline axis from the center of the lower head to the feet was ±4%. The incident flux along the front surface of the phantom was ±10% excluding head. (It was not practical to provide adequate moderation for the head without causing discomfort to the patient.) Lowering the two end ^{238}Pu sources 5 cm improved the uniformity only slightly. The variation of the incident flux on the front surface was proportional to the size of the air space between the moderator and the body surface. The variation in the flux on the back surface was ±8%.

During the exposure of each patient, the average incident thermal neutron flux to the patient and the phantom is measured with indium foils placed on the abdomen and back of the subject. (Indium foils with cadmium shields are exposed simultaneously to provide data for the correction factor for the associated neutron-capture resonance cross section.) The coefficient of variation in incident neutron flux, determined from an average of the measurement of the front and back foils in repeated irradiations of the phantom, was ±1.0%. In a series of patient activations, the average incident neutron flux varied by ±1.1%. The variation did not appear to depend on the size or shape of the patient.

Patient absorbed dose. The radiation dose absorbed by a patient exposed in the whole-body neutron irradiator was determined to be 277 mrem for a 5-min exposure. The total dose consisted of 25.6 mrad from fast neutrons and 20.6 mrad from gamma rays. A quality factor (QF) of 10 was employed for the conversion of fast neutron rads to rems. The dose measurements were made with a W-type TE chamber (*11*). The concomitant gamma-ray dose was measured with LiF-TLD-100 dosimeters. The measurements were repeated five times; the probable error was less than 4%. A second independent measurement was made with a TE P-type ionization chamber. These measurements were within 10% agreement with the above measurements. The difference was attributed to the rather large ionization chamber used in the second method.

EXPERIMENTAL PROCEDURE

Subject irradiation. The activations are performed by irradiating the human or the Alderson phantom, each surrounded by the polyethylene moderator. The

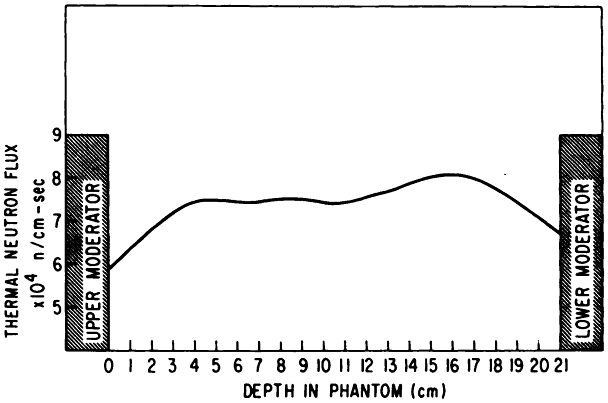

FIG. 3. Depth-flux distribution through anterior-posterior axis of Alderson phantom following irradiation in ^{238}Pu,Be neutron irradiation facility.

patient is placed on a portable cot which is wheeled into the radiation cell and fixed in a predetermined position (see Fig. 1). The operator then leaves the room, closes a safety gate, and initiates the exposure by activating a switch at the control panel located on the outside of the shielded room. The exposure time may be set from 3 to 5 min and is then controlled automatically by the built-in timer mechanism. At the termination of the radiation exposure, the sources are automatically retracted below ground. The patient is removed from the radiation cell and quickly transported down the hall to the whole-body counter in the hospital.

Measurement of induced activity by whole-body counting. The operation and characteristics of the Brookhaven whole-body counter and its associated computer facility have been previously described (*9*). The counter, when used in conjunction with an empirical correction program, has a relatively invariant response to body weight and to the internal localization of radionuclides.

A 15-min count is taken on each subject beginning 3 min postirradiation. The data are processed and analyzed with the on-line computer. From the spectral data of the induced activities of a typical subject in a 15-min count at 3 min postirradiation the amounts of each element in grams are determined by the computer program as in previous studies (*7,8*).

Absolute calibration. The levels of ^{49}Ca, ^{24}Na, ^{38}Cl, and ^{28}Al (from P) induced following exposure to the moderated ^{238}Pu,Be neutrons are determined by whole-body counting and compared with the induced activities produced by irradiating an Alderson phantom containing known concentrations of the individual elements.

For the calculation of the mass of each element in the body, a calibration factor (CF) was first determined to relate 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*):

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

where m is the mass of target (gm); ϕ_{th} the thermal flux density (n/cm^2/sec); and A the corrected counts/15 min in the photopeak corrected back to $t = 0$.

Individual measured targets of Ca, Na, Cl, and P were homogeneously distributed in a water-filled Alderson phantom and subsequently irradiated. Three separate irradiations of the phantom were performed for each of the four elements followed by a 15-min whole-body count. Each time the phantom was filled and irradiated for 5 min in the exact geometry as that used for the humans. The ϕ_{th} was determined from the average of the activity induced in standardized indium foils positioned on the front and back of the subject.

RESULTS

The composite results of all the individual phantom calibration runs are given in Table 1. The values listed are the average of two 15-min counts. A comparison of the means of the individual phantom runs for each element with the absolute concentration distributed in the phantom indicates that the percent s.d. of the mean for Ca, Na, Cl, and P was 0.99, 1.83, 2.1, and 3.9, respectively.

The gamma-ray spectrum of a male patient at 3 min following irradiation with ^{238}Pu,Be neutrons is given in Fig. 4. The spectrum of the same patient at 6 min following irradiation with 14-MeV neutrons is also given for comparison. Both sets of data were normalized to an absorbed radiation dose of 0.75 rem. It is readily noted that the Pu,Be neutrons produce considerably more ^{49}Ca, ^{24}Na, and ^{38}Cl than do the 14-MeV neutrons per unit absorbed dose to the patient. At the same time, however, there is considerably less production of ^{28}Al(P), and relatively no ^{13}N.

DISCUSSION

Absolute measurements of total-body levels of Ca, Na, and Cl based on whole-body neutron activation, require a relatively uniform neutron flux density throughout the body. The "broad-beam" structure of the radiation field developed by the spacing of the 14 separate sources and the considerable reflection of neutrons by the bismuth lining of the irradia-

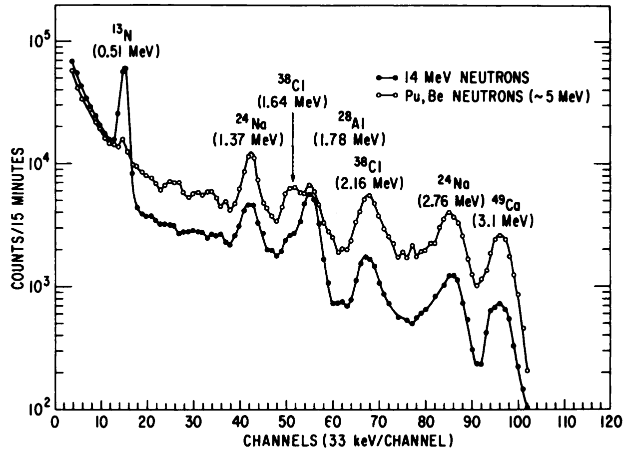

FIG. 4. Gamma-ray spectra of patient following irradiation with ^{288}Pu,Be neutrons (E ~ 5 MeV) and irradiation with 14-MeV neutrons from neutron generator. Data are normalized to same absorbed dose to patient (0.75 rem).

TABLE 1. PHANTOM CALIBRATION OF IN VIVO ACTIVATION ANALYSIS TECHNIQUE

Run	ϕ_{th}	P (gm)	ϕ_{th}	Cl (gm)	ϕ_{th}	Na (gm)	ϕ_{th}	Ca (gm)
1	6.31	611	6.25	81.9	6.40	81.2	6.29	1,005
2	6.22	565	6.16	79.5	6.36	80.4	6.22	990
3	6.34	588	6.19	78.7	6.25	78.3	5.98	1,006
4							6.19	989
5							6.31	1,010
Absolute Concentration		588		80		80		1,000
	% s.d.	±3.9		± 2.1		±1.83		±0.99

ϕ_{th} is the average incident thermal flux ($\times$ 10^4 n/cm^2/sec).

tion cell both contribute to the production of a very uniform incident neutron flux. However, the lower energy (about 5-Mev) neutrons from the Pu,Be sources yield a flux density through the body which varies by ±8% compared with the ±5% variation associated with the flux density from the 14-Mev neutrons from the neutron generator.

With the closely-fitted moderator, thermalization of the incident fast neutrons occurs primarily in the moderator, thus optimizing the flux density of the neutrons entering the body (see Fig. 3). It is essential that the moderator be placed close to the body. Should this not be the case, divergence of the neutron beam occurs, and there is a consequent secondary buildup in the body tissue. Determination of the optimal thickness for the moderator was made with the solid plastic phantom in which a human skeleton had been embedded. While the neutron depth flux is not perfectly uniform, it is nevertheless sufficiently uniform to provide a sound basis for the activation measurements.

Absolute measurement of those elements which can be activated by TBNAA necessitates also that the counting of the induced activity be independent of both absorption by the body and the counting geometry. The Brookhaven whole-body counter has an invariant counting response with respect to size of the patient and location of the activated material, and hence is uniquely suited for this purpose. Thus it can be used for measurement of Ca which is localized in the skeletal tissue, as well as for Na and Cl which are distributed fairly homogeneously throughout the intracellular space.

Comparison was made of the dose absorbed by the patient as determined by the experimental procedure and by theoretical calculation. The ratio of the thermal-to-fast neutron flux had been previously determined for various α,n sources (7). Several factors were considered in determining the reduction of the absorbed dose achieved by replacing 14-MeV neutrons from the neutron generator with 5-MeV neutrons from the portable sources. Chief among these were: (A) ratio of dose to number of incident neutrons; (B) ratio of thermal neutrons generated per incident neutron; (C) effect of simultaneous bilateral irradiation on flux produced; (D) effect of "broad-beam" source on ϕ_{th}/ϕ_f ratio; and (E) reduction of time lag, irradiation to counting (i.e., transit time required to move patient between facilities).

The factors combined to provide an overall dose reduction factor of 4.7 (7). On the basis that the values of radiation parameters remain unchanged for the 14- and 5-MeV neutrons (minimum usable flux, 4.54 $\times$ 10^4 n/cm^2/sec), the dose absorbed by the patient exposed to the Pu,Be sources was calculated to constitute an exposure of 0.126 rem. With a 3-min transit time for the patient, the minimum measured value of absorbed dose is 0.175 rem. The original calculation was based on the assumption that the transit time would be 2 min. The good agreement between the theoretical and experimental values for the absorbed dose supports the assumptions required for the calculation.

It was originally calculated that a uniform simultaneous bilateral exposure for a 6-ft subject would require 672 Ci (7). In the study 700 Ci were used. This level may be slightly in excess of the amount actually required.

There are several advantages that are obtained by replacing the 14-MeV neutrons from the neutron generator with 5-MeV neutrons from the ^{238}Pu,Be sources in addition to the considerable reduction in the dose absorbed by the patient. The 14-MeV neutrons produce an interfering reaction ^{37}Cl(n,p)^{37}S which is troublesome inasmuch as ^{37}S has the same energy as ^{49}Ca. As this reaction has a threshold of 10 MeV, it is eliminated when the 5-MeV neutrons from Pu,Be sources are used. The Pu,Be sources allow for more exact control and hence provide a higher degree of precision (reproducibility is ±1%) in the measurements of the phantom or patients. The use of the portable sources allows the patient to assume a supine position on a bed; the neutron generator requires that the patient be standing. Thus it is possible to work with patients who have various types and degrees of disabilities.

Another advantage with the fixed Pu,Be sources is that it is not necessary to have the services of a highly trained technician to operate the facility and to maintain it as is the case with the neutron generator and the cyclotron. Finally, the design of this facility for medical applications permitted its location to be made in a convenient place in the hospital and thus permitted transit time (irradiation cell to counter) to be reduced. Patients are in a much more comfortable situation throughout the entire process.

There are some drawbacks associated with the use of the 5-MeV neutron sources. One is that it is no longer possible to measure relative levels of nitrogen as it was in the studies based on 14-MeV neutrons (*7,8*) because the threshold for the ^{14}N(n,2n)^{13}N is greater than 10 MeV. On balance, the portable 5-MeV sources offer more advantages in TBNAA particularly in clinical research programs.

Considerable potential for in vivo activation analysis in medical research and diagnosis has already been demonstrated (*12–14*). Determination of body composition in a variety of research studies is already underway.

SUMMARY

A neutron irradiation facility designed for performing total-body neutron activation analysis (TBNAA) for clinical research is described. Fourteen 50-Ci encapsulated sources of ^{238}Pu,Be that may be positioned above and below the midline of the subject provide a fairly uniform broad-beam source of neutrons. Absolute levels of total-body Ca, Na, and Cl, and relative levels of P are determined in subjects exposed bilaterally to the neutron flux (average energy, about 5 MeV), for 5 min. The induced ^{49}Ca, ^{24}Na, ^{38}Cl, and ^{28}Al (from P) are measured with a whole-body counter designed with a response invariant with respect to counting geometry and attenuation. This in vivo activation technique provides an accuracy and precision of ±1%, as determined by studies with a phantom.

The ^{238}Pu,Be neutron source offers a number of advantages in TBNAA over the previously used 14-MeV neutrons obtained from a neutron generator. The maximum total dose received by a patient is 277 mrem, or 45% of the minimum dose previously required for activation. The reduction in absorbed dose results primarily from reduced tissue dose per incident neutron and increased efficiency for generating thermal neutrons. The reduced dose together with an inherent simplicity in obtaining a uniform neutron flux from the Pu,Be sources, makes the new technique very desirable for TBNAA analysis in medical diagnosis and research.

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REFERENCES

1. Anderson J, Osborn SB, Tomlinson RWS, et al: Neutron activation analysis in man in vivo: A new technique in medical investigation. *Lancet* 2: 1201–1205, 1964

2. Battye CK, Tomlinson RWS, Anderson J, et al: Experiments relating to whole-body activation analysis in man using 14-Mev incident neutrons. In *Symposium on Nuclear Activation Techniques in Life Sciences,* Vienna, IAEA, 1967, p 573

3. Palmer HE, Nelp WB, 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

4. Nelp WB, Palmer HE, Murano R, et al: Measurement of total-body calcium (bone mass) in vivo with the use of total-body neutron activation analysis. *J Lab Clin Med* 76: 151–162, 1970

5. 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: 581–592, 1968

6. Chamberlain MJ, Fremlin JH, Holloway I, et al: Use of the cyclotron for whole body neutron activation analysis: Theoretical and practical considerations. *Int J Appl Radiat* 21: 725–734, 1971

7. Cohn SH, Dombrowski CS, Fairchild RG: In vivo neutron activation analysis of calcium in man. *Int J Appl Radiat* 31: 127–137, 1970

8. Cohn SH, Dombrowski CS: Measurement of total-body calcium, sodium, chlorine, nitrogen and phosphorus in man by in vivo neutron activation analysis. *J Nucl Med* 12: 499–504, 1971

9. Cohn SH, Dombrowski CS, Pate HR, et al: A whole-body counter with an invariant response to radionuclide distribution and body size. *Phys Med Biol* 14: 645–658, 1969

10. Fairchild RG: Development and dosimetry for an 'epithermal' neutron beam for possible use in neutron capture therapy. II. Absorbed dose measurements in a phantom man. *Phys Med Biol* 11: 15–30, 1966

11. Rossi HH, Failla G: Tissue equivalent ionization chamber. *Nucleonics* 14: No 2, 32–37, 1956

12. Cohn SH, Dombrowski C, Hauser W, et al: Effects of porcine calcitonin on calcium metabolism in otseoporosis. *J Clin Endoc* 33: 719, 1971

13. Cohn SH, Cinque TJ, Dombrowski CS et al: Body composition of patients with chronic renal failure undergoing hemodialysis therapy. *J Lab Clin Med*: to be published

14. Aloia JF, Roginsky MS, Jowsey J, et al: Skeletal metabolism and body composition in acromegaly. *J Clin Invest*: submitted for publication