Review

In vivo neutron activation analysis; a new technique in nutritional research

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Introduction

In vivo neutron activation analysis (IVNAA) has ushered in a new era of clinical diagnosis, therapy evaluation, and modeling of body composition.[1-3] Direct determination of several key elements of the body has been made possible by delayed and prompt gamma IVNAA. Measurement of total body nitrogen (protein) by prompt gamma neutron activation (PGNAA) is of particular importance in nutrition studies. Measurement of total body calcium (TBCa) by delayed neutron activation (DGNAA) yields accurate information on the bone mineral mass, because 99% of the body calcium resides in skeletal tissue. Along with calcium, total body sodium, chlorine (TBCl), and phosphorus are activated and thus can be measured. Naturally occurring ^{40}K total body potassium (TBK) is automatically measured by whole body counting.

Elemental composition studies made with the use of IVNAA have shown the relationship between body elements and compartments. Body composition models have been considerably refined with the data obtained by in vivo nuclear techniques.[1-6] Determination of body composition has been used by a number of investigators to achieve nutritional assessment of individuals with a variety of disorders and dysfunctions.[4-9] The analyses rest both on a database derived from measurements made of normal subjects, reflecting the parameters of age and sex, and on serial measurements that reflect ongoing processes and the effects of therapeutic programs, such as nutritional regimens.

Current state of the art

Presently, worldwide there are 11 major centers that carry out studies on various aspects of body composition by IVNAA. In Great Britain, the Universities of Leeds, Birmingham, Edinburgh, Glasgow, and Swansea have such centers. These are located in physics research environments. In Canada, a neutron activation facility is located at the University of Toronto, attached to a hospital. The newest activation facilities, designed solely for the measurement of total body nitrogen, are in Auckland, New Zealand;[1] Sydney, Australia;[10] Melbourne, Australia[11] and Goteborg, Sweden.[12] In addition, there are a number of smaller centers in North America, Europe, and Asia.

In the United States, Brookhaven National Laboratory (BNL) is presently the major center for in vivo neutron activation research. It is located in a medical facility, although it began in conjunction with medical physics research. As these facilities represent the leading edge of IVNAA technology, they will be the focus of this review.

The elements in the body that can presently be measured absolutely and non-invasively by IVNAA, their abundance, and the technique employed for measurement are shown in *Table 1*. The relationship between these elements and the components of body composition are shown in *Table 2*.

Current developments in IVNAA are taking place in both instrumentation and application. System development focuses on improving accuracy and precision, increasing the number of elements susceptible to measurement, and reducing the dose required for the measurement. In the area of clinical applications, studies are being extended to new groups of patients.

Techniques

Delayed gamma neutron activation analysis

The BNL neutron activation facility for the measurement of TBCa and TBCl has been described.[13] The technique is based on DGNAA, in which the subjects receive a bilateral exposure to partially moderated fast neutrons from ^{238}Pu,Be sources. The induced activities are then measured in the BNL whole body counter, which was designed for the absolute measurement of the neutron-induced radioactivities and for measurement of naturally occurring total body potassium. The counter is unique in having a relatively invariant response with respect both to the size of the individual and to the internal location of the radionuclide.[13]

Prompt gamma neutron activation analysis

Total body nitrogen (TBN) is measured with the BNL prompt gamma neutron activation facility *(Figure 1)*.

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Received February 18, 1992; accepted March 23, 1992.

Table 1 Body elements measured at Brookhaven by in vivo nuclear techniques

Body element	Standard (g)[17]	Humans (%)*	Measurement technique used at Brookhaven	
Total body				
Hydrogen	7000	10	n,γ	prompt γ (2.2 MeV)
Nitrogen	1800	2.6	n,γ	prompt γ (10.8 MeV)
Calcium	1000	1.4	n,γ	delayed γ (3.10 MeV)
Phosphorus	780	1.1	n,α	delayed γ (1.78 MeV)
Potassium	140	0.2	^{40}K	natural (1.46 MeV)
Sodium	100	0.14	n,γ	delayed γ (2.75 MeV)
Chlorine	95	0.12	n,γ	delayed γ (2.2 MeV)
Partial body				
Iron (liver, heart)	4.2	0.006	NRS†	prompt γ (0.846 MeV)
Cadmium (kidney, liver)	Trace	Trace	n,γ	prompt γ (0.559 MeV)
Mercury (brain)	Trace	Trace	n,γ	prompt γ (0.368 MeV)
Silicon (lung)	Trace	Trace	n,n'γ	prompt γ (1.78 MeV)
Lead (bone)	Trace	Trace	XRF‡	prompt x-rays
Lithium (brain)	Trace	Trace	n,α	delayed (^{3}H counting)
Aluminium (bone)	Trace	Trace	n,γ	delayed γ (1.78 MeV)

*Proportion of total weight for 70 kg man
†Nuclear resonant scattering (NRS)
‡X-ray fluorescence (XRF)

Table 2 Relationship between elements and components of body composition

Total body element	Nuclear measurement technique	Body composition compartments
Hydrogen	PGNAA	Water, fat
Nitrogen	PGNAA	Protein
Calcium	TBNAA	Bone (mineral ash)
Potassium	WBC	Muscle
Sodium	TBNAA	
Chlorine	TBNAA	Extracellular fluid
Phosphorus	TBNAA	Bone, soft tissue

PGNAA, Prompt gamma neutron activation analysis.
TBNAA, Total body neutron activation analysis.
WBC, Whole body counting (^{40}K).

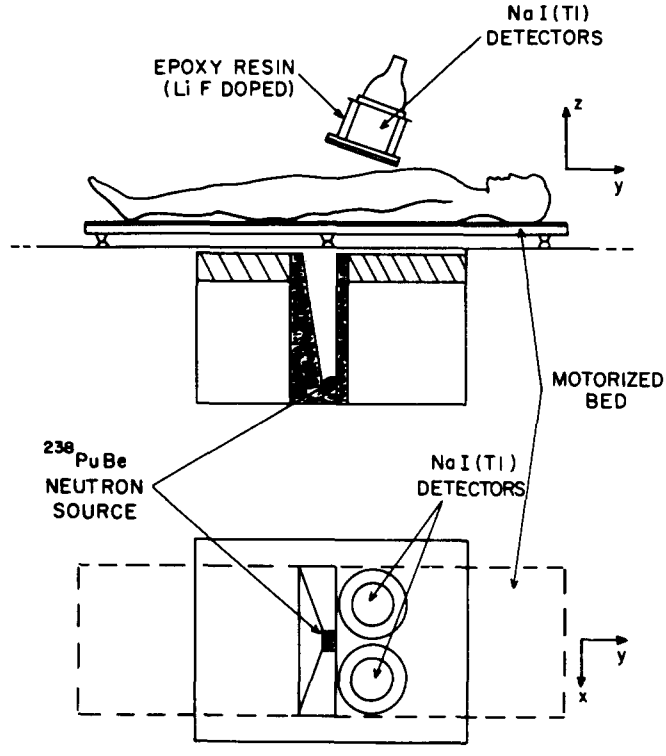

Figure 1 Brookhaven prompt gamma neutron activation facility for total body nitrogen. Patient is scanned over a collimated neutron beam from 50-Ci source of ^{238}Pu,Be.

A detailed description of the prompt gamma neutron activation technique for the measurement of whole body nitrogen has been presented.[14–16] Because the primary emphasis of this review is on TBN, its measurement in the BNL facility will be discussed in greater detail here.

PGNAA utilizes the $^{14}N(n,\gamma)^{15}N^*$ reaction. Some neutrons are slowed by body tissue and captured by body elements. The $^{15}N^*$ has a lifetime of the order of 10^{-15} sec before decaying to its ground state. About 15% of the de-excitations occur with the emission of 10.8 MeV γ rays. The γ rays are detected by two 15.25 cm × 15.25 cm NaI(Tl) detectors operated in a fractional charge collection mode.[14,15]

The reactions of interest, $^{14}N(n,\gamma)^{15}N$ and $^{1}H(n,\gamma)D$, occur predominantly with slow neutrons. As slow neutrons penetrate the body poorly, (diffusion length about 3 cm in soft tissue), it is necessary to employ fast neutrons. The BNL ^{238}Pu,Be source delivers neutrons with energies ranging from 0–≈11 MeV. The mean energy is about 4.5 MeV; the neutron yield is 2.3 × 10^5 n/sec.

Measurement of the absorbed dose from fast neutrons and gammas is made with tissue-equivalent chambers and lithium fluoride thermal luminescent

dosimeters. For a prone-and-supine irradiation, the total dose is 2.5 mrad for neutrons and 1.2 mrad for the gammas. The dose to the skin is approximately 26 mrem, based on an RBE of 10 for fast neutrons. The dose to the body is smaller, due to the attenuation of the fast-neutron flux in the body.

Measurement of total body nitrogen by means of the $^{14}N(n,\gamma)^{15}N$ reaction was first carried out at Birmingham with the use of a cyclotron.[5] Subsequently, the measurements were made at Toronto and at Brookhaven with the use of isotopic neutron sources.

The problem of converting detected γ ray counts to an absolute mass of total body nitrogen was first solved by Vartsky et al.[14,15] The habitus corrections derive from the different attenuation coefficients for 10.8 and 2.22 MeV γ rays in human tissue. Because capture of slow neutrons by ^{14}N nuclei results in the prompt emission of 10.83 γ rays, while capture by hydrogen nuclei generates emission of 2.23 MeV gamma rays, body hydrogen can be used as an internal standard for the measurement of TBN. Vartsky et al.[15] found that the ratio of nitrogen to hydrogen counts was much less dependent on body habitus than nitrogen counts alone. Both the nitrogen and hydrogen signals developed depend on thermal neutron capture, with the capture cross-section of the two elements varying in the same manner with neutron velocity. As the range of values of percentage hydrogen composition in the major compartments is not large, (11.1% for water, 12% for fat, and 7% for protein), departures from the 1975 International Commission on Radiologic Protection "Reference Man"[17] body composition have a relatively small effect on the estimation of total body hydrogen.

With the use of PGNAA at BNL as described above, it is possible to estimate total body protein with a precision of ± 3%; total body water to ± 1.5%; and total body fat to ±5% for a typical subject under investigation. These figures assume that the total body mineral and glycogen compartments can be estimated with precisions of ±10% and ±20%, respectively. In practice, fewer random errors will be incurred by relating minerals and glycogen to skeletal size. The fat-free mass parameter, frequently used in body composition studies, can be estimated to within ±1.6%. Most of the error derives from the estimate of tritium dilution, because 70% of the fat-free mass is water.

Evaluation of the absolute accuracy of the prompt gamma technique can be made directly only by studies of human cadavers. However, the technique has been partially evaluated against two other systems in a series of studies of 41 normal volunteers.[16] Predictor equations derived empirically at Leeds[18] and Brookhaven[19] have been applied to the data from these volunteers. These predictor equations relate TBN in normal men and women to age, height, weight, and sex. The mean ratios of measured:predicted TBN are 1.002 ± 0.014 and 1.013 ± 0.017, respectively.

Dilmanian et al.[20] and Pierson et al.[21] describe recent improvements in the prompt gamma technique that considerably increase both its precision and accuracy. Improvements in the precision of the measurements of elements and refinements in the calculation of the compartment sizes considerably expand the utility of body composition measurements. In the past, the range of studies of body composition were confined to individuals within a restricted weight range. Both grossly obese subjects and severely cachectic individuals, such as acquired immune deficiency syndrome (AIDS) patients, can now be studied with the modifications made in the calibration of the BNL facility.

Physiological studies made with neutron activation analysis

Skeletal tissue

One of the major studies made with IVNAA is the measurement of total body calcium, designed with the goal of defining and predicting the onset of osteoporosis. Early studies concentrated on the relation of bone loss to age, sex, and body habitus within a group to quantify the extent and nature of the problem. Once these studies provided baseline data, the goal was more sharply defined. To treat individuals, it is necessary to predict who is at risk before the debilitating clinical symptoms appear. The very definition of osteoporosis is in the process of change.

When the studies began, osteoporosis was acknowledged to exist only when spontaneous fractures of the vertebrae occurred. With the increasing ability to determine baseline values from the extensive studies of normal individuals (predicted from sex, age, height, and body habitus), it is possible to quantify a calcium deficit and to identify as osteoporotic, individuals with a significant deficit.[22] This identification is of the utmost importance, as ameliorative measures must be initiated early to be effective. Little, if anything, can be done to aid the individual when calcium loss has advanced to the stage at which spontaneous fractures occur. An excellent presentation of the osteoporotic syndrome is that of Avioli and Lindsay.[23] Predisposing factors such as genetic, lifestyle, nutritional, medical, and drugs are discussed, along with the various regimens undertaken for prevention and therapy, including increased calcium intake, exercise, estrogen, fluoride, calcitonin, parathyroid hormone, vitamin D metabolites, and coherence therapy.[23]

A model has been developed for determining women at risk for developing osteoporosis.[22] With step-wise multiple logistic regression (MLR), probabilistic classification equations were developed to identify asymptomatic women who are at risk for developing fracture of the spine. The accuracy of the MLR model to discriminate "normal" women at risk with both high sensitivity and specificity was verified by receiver operating characteristic analysis.

The method with the highest probability of identifying osteoporotics in all age categories was found to be one based on TBCa data. With these data and the use of MLR, discrimination of osteoporotic women (50–59 years) was made correctly for 86.2% of the total osteoporotic subjects.

There is little comparable data for comparison of total skeletal calcium loss.[24] The indirect measure of total body bone mass by dual photon absorptiometry provides a linear density measure of total body calcium that agrees well with TBCa data.[25] CT scanning also provides quantification of changes, particularly on the trabecular bone of the spine.[26]

Soft tissue

After the application of calcium measurement to bone studies, the next major advance in body composition occurred in soft tissue measurement. Quantification of TBN by neutron activation provided another technique for measuring lean body mass (LBM), and hence body fat, as well as measuring total body protein.

Non-fat tissue. Data from TBK and TBN measurements provide most of the new concepts in body composition covered in this review. For example, Burkinshaw[5] has developed a mathematical model for estimating both the mass and the protein content of the muscle and the non-muscle compartments. The differential tissue distribution of TBK and TBN provides the primary data for this model. The mathematical models used for compartmental analysis have been presented.[5] Burkinshaw extended this analysis to measure the distribution of protein, water, and electrolytes in the human body.[27,28] With these models, it is possible to determine age-related changes in the size and distribution of body protein in muscle, non-muscle, extracellular, and intracellular compartments.

Fat. One of the most difficult measurements to be made in body composition studies is that of the highly important constituent, fat. Quantification of body fat is needed not only for studies of obesity, but also for the study of diseases with nutritional factors. Such studies are necessary because changes in body composition (relative proportions of fat, lean tissue, and water) as a function of age, sex, and diet in abnormal individuals are not well understood.

Measurement of fat is extremely important in the evaluation of a variety of disorders and dysfunctions. Obesity is highly correlated with heightened risk in surgery, as well as with morbidity and mortality in general.[16] Illnesses associated with diminished fat, such as anorexia nervosa, are also correlated with increased morbidity, and are increasingly of interest. The association of dysmenorrhea with diminished fat is beginning to be investigated, as more attention is being directed to studies of women.

To date, there is no well-developed technique for the direct, in vivo measurement of body fat. The only direct method employs fat-soluble radioactive gases such as krypton, argon, and xenon, using the isotope dilution principle. This technique is difficult to apply because of the long equilibration time required for the gas to mix with the fat compartment.

A promising new technique for a relatively direct measurement of fat is based on total body carbon.[29–31] Body fat has a high concentration of carbon (77%), compared with fat-free tissue. Thus, total body fat can be derived from the known proportions of carbon in fat, protein, and bone mineral. As this method has yet to be validated completely, its accuracy is not well established. However, because it is based on absolute elemental measurement, it is more likely to be accurate than the indirect techniques, particularly for abnormal patients.

Indirect techniques infer the fat content from the difference between total body mass and lean body mass; they are imprecise to varying degrees, and depend on the validity of a number of assumptions. Some of these assumptions have been validated in animals, but many others have not, particularly for patients with various metabolic disorders.

Measurement of fat in the aging population presents particular problems because each measurement technique involves assumptions that, while they may be valid for normal, young individuals, do not necessarily hold for older individuals. For example, the assumption of constant hydration of lean tissue (the basis for quantifying LBM from the measurement of water), first developed by Pace and Rathburn[32] through studies of young, healthy animals, may not hold for older individuals, for whom the distribution of extracellular and intracellular water has changed as they aged. Also, this constant hydration may not hold for obese individuals, who may have an abnormal distribution or accumulation of water.

Other sources of error in the measurement of LBM also affect the inferred value of total body fat. The assumptions made for the measurement of LBM from the density obtained by underwater weighing may not hold for older individuals because they have lost bone mineral, and hence have a skeletal density markedly different from that of younger persons. Also, in cases of fluid retention seen in many disease conditions, the altered density yields a higher value of LBM and therefore a lower estimate of body fat.

A source of error in estimating LBM from TBK is the assumption of a fixed ratio of potassium to LBM. The assumption that the TBK:LBM ratio is constant with age and sex has been shown to be incorrect, although the constancy of the potassium:body cell mass ratio has substantially been established.[33] The lean body mass now can be considered to consist of body cell mass and extracellular water *(Figure 2)*. It is the extracellular water that increases with age, and that leads to a decrease in the ratio of potassium to LBM.

Models for estimating body fat

Currently, the best approximation of body fat is obtained by an indirect assessment based on determination of the fat-free mass or measurement of LBM by non-invasive techniques. Indirect techniques for measuring body fat cannot be completely validated, but they can be partially validated by determining LBM from two different models.[34]

Two models of body composition employing data

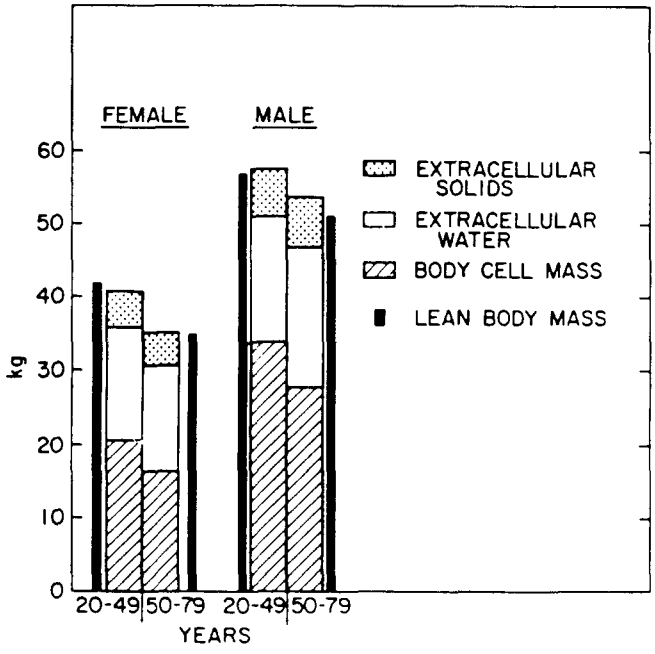

Figure 2 Relationship between lean body mass and body cell mass.

obtained by nuclear techniques are utilized. The new models were developed in response to the following conceptual difficulty with current compartment models. The LBM includes the non-muscle compartment, which has a slowly metabolizing component (essentially composed of noncellular structural elements, such as cartilage, fibrous tissue, and skeletal tissue) along with more actively metabolizing components (muscle and viscera). Thus, because of the heterogeneity of LBM, it is more useful to consider TBN (reflecting the protein), total body water (TBW) and bone mineral ash (BMA), respectively, (Equation 1).

$$LBM_1 = TBN + TBW + BMA. \quad (1)$$

In Equation 2, body cell mass (BCM), extracellular water (ECW), and extracellular solids (ECS) are utilized.

$$LBM_2 = BCM + ECW + ECS \quad (2)$$

It is BCM rather than LBM that most closely reflects the actively metabolizing tissue. TBK has been shown to reflect BCM better than the LBM. Thus, total body fat (TBF) can be estimated as the difference between body weight (BWT) and LBM_1 and LBM_2 as follows:

$$TBF_1 = BWT - (TBN + TBW + BMA) \quad (3)$$

$$TBF_2 = BWT - (BCM + ECW + ECS) \quad (4)$$

The equations presented above reflect the changes in patients with altered hydration states or osmolality. The closely correlated results ($r = 0.96$, $P < 0.001$) obtained with the two models based on different nuclear measurements support the conclusion that both techniques reliably determine total body fat.

Clinical investigations

The clinical usefulness of IVNAA has been demonstrated by numerous studies involving measurement of TBCa, TBN, and TBK. Quantification of changes in body composition in aging individuals and in patients with such varied disorders as obesity, cancer, and renal failure has been useful for nutritional assessment. An extensive review of various systems for partial and total body neutron activation and their many clinical applications is available in the accounts of the proceedings of two international symposia on in vivo body composition studies, one held in 1986 at Brookhaven National Laboratory,[35] and the other in 1989 at the University of Toronto.[36]

Aging

The quantitative assessment of the elemental composition of the human body as a function of age is of basic physiological interest as well as of clinical importance in the diagnosis of metabolic disorders. IVNAA has allowed for the measurement of elemental composition of an aging population of the United States.[3]

The change in the relationship between LBM and BCM for young (20–49 yr) and old (50–70 yr) males and females is shown in *Figure 2*. The marked loss in the LBM with age is caused primarily by the loss in the BCM compartment. Little change is seen in the ECW and ECS compartments.[37]

Significant age-related changes in the various body compartments were observed in the study. TBCa, TBK, and TBN decrease with increasing age for both males and females. TBNa and TBCl do not decrease with advancing age; they appear relatively constant throughout the adult lifespan. Changes in the levels of major body components (muscle, non-muscle, fat, and bone mineral) in normal males as a function of age are shown in *Figure 3*. The lean body compartment (especially muscle) shows slight-to-moderate decreases with advancing age, whereas TBF clearly increases.[37]

The selective loss of muscle mass and protein content compared with the relatively slow loss of the non-muscle mass indicates that muscle is especially vulnerable to the aging process. This loss may possibly result from the decrease in physical activity of the majority of older people. Further studies of selected groups of older individuals can clarify this hypothesis. There is also a need for further studies (particularly with the quantification of body composition made possible with IVNAA) on the role of nutrition in the general aging process.

Diet

The effects of caloric restriction on body composition have been measured.[38] The efficacy of two different isocaloric diets, with and without carbohydrate supplementation, on the preservation of LBM during weight reduction was evaluated with the use of TBN, TBK, and TBW measurements. Body composition studies

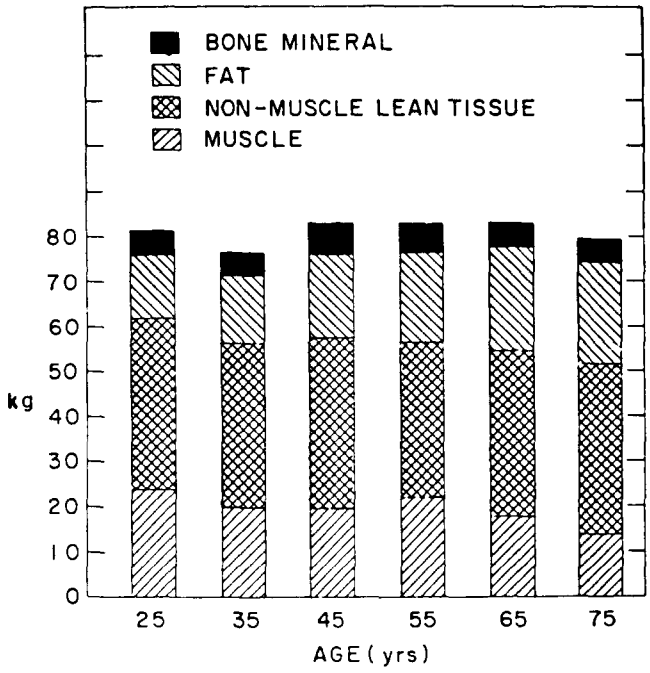

Figure 3 Changes in levels of major body components in normal males as a function of age.

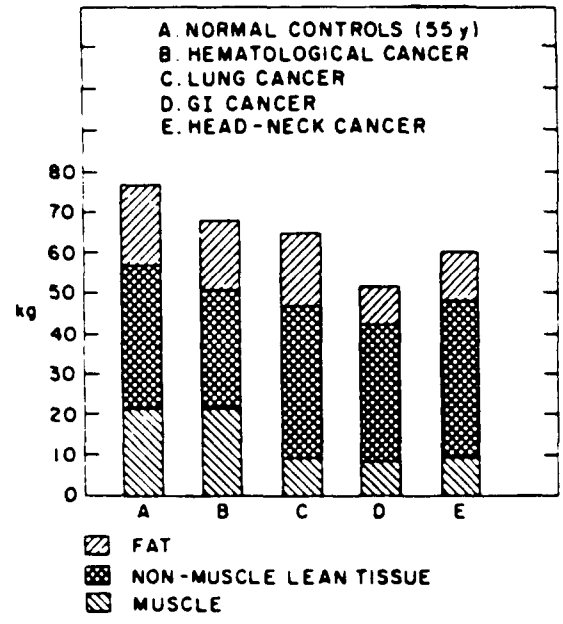

Figure 4 Body composition in male cancer patients.

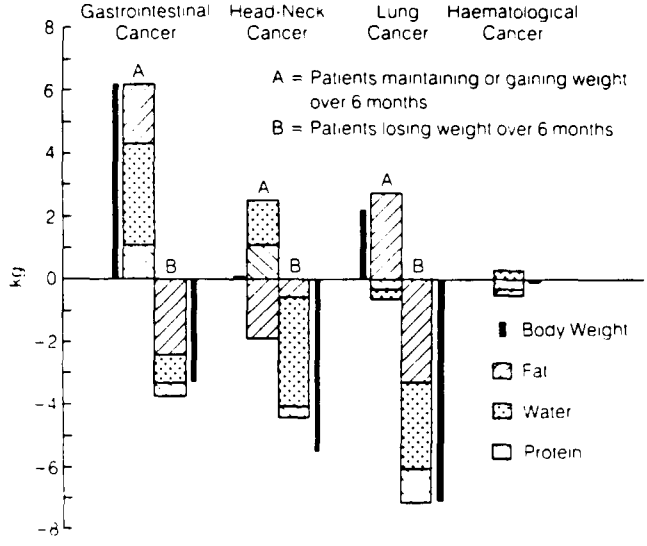

Figure 5 Changes in body composition of cancer patients over six months of chemotherapy.

were performed at the time of the first admission and after week 12 of dieting. Body weight, TBF, TBW, and TBK were shown to decrease significantly when compared with the baseline values. The loss of body elements, however, did not differ significantly in the subjects on the two diets. The addition of carbohydrate to the diet in the amount given did not significantly affect its protein-sparing quality.

Cancer and nutrition

The measurement of body composition in chronic wasting diseases is of clinical interest both in evaluating the patient's status and in selecting the appropriate management regimen.[4,8,16,39,40,41] IVNAA studies of male patients with hematological neoplasms and lung, gastro-intestinal, and head-neck cancers illustrate this clinical application *(Figure 4)*. The quantitative measurements of muscle, nonmuscle, and fat provide a specific analysis of the total weight change following hyperalimentation, and thus provide a more definite assessment of nutritional status than do other techniques.[40]

Changes in body composition in cancer patients can also be analyzed in terms of the original model proposed by Keys and Brozek, in which the body is considered to consist of carbohydrates, fat, and protein.[42] Because carbohydrate is present in only small amounts, it is dismissed as a significant component. Only with the development of IVNAA has it been possible to measure TBN, and hence, protein. The changes in body composition in cancer patients following 6 months of chemotherapy are shown in *Figure 5*. The model has also been applied most effectively in the study of surgical patients.[1,4,16]

In general, those patients who lost body weight had caloric and protein intakes markedly below normal levels. There also appeared to be a direct relationship between the protein intake and the TBK:TBW ratio in the cancer patients.[39] Nutritional support using hyperalimentation was indicated to combat the weight loss in these patients.

In another study, the effects of combined nutritional support (parenteral, enteral, and oral) for cancer patients over a 6-week period were evaluated on the

basis of new compartmental models.[40] Patients receiving total parenteral nutrition (TPN) showed a mean increase in body weight equally distributed between increases in total body water and total body fat, *(Figure 6)*.

The efficacy of the nutritional regimens has also been examined in terms of the TBN:TBK ratio.[39] This value decreased and returned toward a normal level for the patients on TPN, indicating an anabolic effect of the supplemental feeding. For patients experiencing weight loss, this ratio actually increased, indicating continued catabolism.

Information on the nature of the tissue gained was obtained by comparison of body composition data with the ratio of TBN:TBW:TBK for normal tissues.[39] Thus, use of the neutron activation techniques made possible the assessment of regimens of hyperalimentation for cancer patients losing or gaining weight.

Renal dysfunction

Evidence for protein-caloric malnutrition (PCM) was found in renal patients receiving both conservative and hemodialysis treatment.[43] PCM should be reflected in the long-term nitrogen balance and body mass for these patients. With the use of IVNAA techniques, both of these parameters were measured in a group of renal patients.[43] Their TBK and TBN values were slightly, but not significantly, lower when compared with age-matched controls. The TBCa values were also slightly lower than the controls. The TBCl values, on the other hand, were higher, indicating a significant increase in the extracellular water compartment in renal patients.

Renal osteodystrophy has been studied in a number of renal patients. The metastatic calcification that occurs in these patients can be studied by neutron activation analysis.[43]

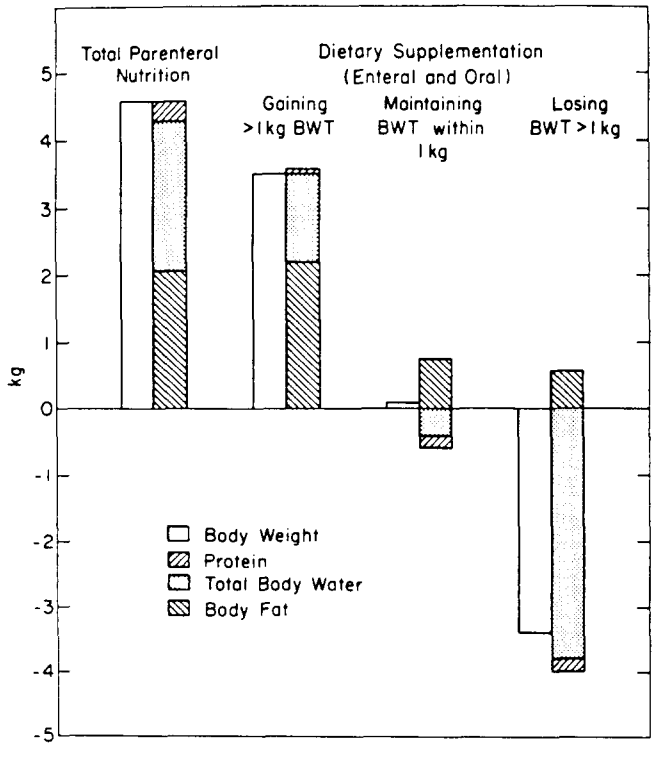

Figure 6 Changes in body composition of cancer patients over 6 wk of hyperalimentation.

AIDS

The newest on-going study involves the measurement of changes in body composition of AIDS patients.[44] The goal is to determine the pathogenesis of malnutrition in AIDS patients to design appropriate therapeutic nutritional regimens. The specific aims are to define the metabolic mechanisms that underly the alterations in body composition that occur as a result of AIDS. Measurements of body composition will permit precise determination of both depletion and repletion. Studies of nutritional support to these patients have indicated body mass repletion and a consequent increased quality of life. The ability to investigate the nutritional consequences of chronic infection in an AIDS patient may be important in reducing the morbidity of such complications.

Conclusion

Body composition studies made with the use of IVNAA have shown the relationship between key elements of the body and body compartments. The compartmental view of the human body is capable of yielding new data on the range of values for various elements, particularly TBN, in abnormal individuals. It also provides data and new insights on the quantitative and qualitative nature of variation corresponding to sex, age, body habitus, various diseases, and metabolic disorders. The efficacy of nutritional and therapeutic regimens can be investigated more fully because of the considerable advantage offered by in vivo nuclear techniques and refined compartmental models.

Studies relating TBN to dietary intake and nutritional support for normal aging subjects and patients with a variety of metabolic disorders have been performed. These findings are rapidly becoming the "gold standard" for other body composition studies. Thus, the outlook is for greater application of the neutron activation technique, particularly for the measurement of TBN.

Future studies are likely to be done at large medical centers that will focus on the more direct techniques. Proliferation of the equipment used for indirect techniques will, of course, continue. While these systems are considerably less expensive and generally simpler to operate, it should be noted that they depend on validation and calibration with established direct measurement techniques. Re-evaluation is required to incorporate the latest findings developed in basic research.

The Brookhaven facility is a prototype for a regional center, with respect to IVNAA, as it develops and uses state-of-the-art instrumentation. Suitably scaled-down versions, particularly for the measurement of

TBN, would be very useful in large medical centers where they can be used for assessing patients requiring nutritional intervention (such as obese, anorexic, cancer, and renal patients). It would also be useful to study patients for whom information is needed for diagnosis or evaluation of therapeutic regimens.

Whole body measurements provide information on the average body composition, even though only one organ system may be affected. Thus, other techniques are still required to study specific organ systems and compartments. No single technique, however, is able to provide all the answers for body composition questions. The challenge, then, is to determine the most effective way in which to combine various modalities; that is, to learn how these multifaceted instruments may be employed to best generate the information needed for diagnosis and therapy.

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