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*The status of the human body's major components (adipose mass, lean mass, body water, etc) and their change with time are of clinical importance. Deviation of these body components from a stable condition may be imposed by nutrition or disease, and a return to the normal body state may be brought about by appropriate medical care. Thus accurate quantitation of these components is an important goal. This field of study can be traced to the early 1800s, with a major thrust starting in the 1940s and continuing to the present. The last four decades have shown an accelerated development of advanced biophysical techniques and associated instrumentation for the noninvasive assay of the body's major fractions. A few methods have now been used in clinical practice, and others have provided basic data on the makeup of the normal and abnormal body as well as on the effectiveness of medical treatment in restoring normal component ratios. The adipose tissue mass is of special concern since it serves as the body's energy reservoir. Determination of the body's fat fraction is a difficult but avidly sought after quantity in body composition measurement. We describe the major principles and technology currently in use for body component measurement and the clinical applicability of these systems for the determination of the adipose fraction. (Henry Ford Hosp Med J 1988;36:92-102)*

Interest in and scientific study of the composition of the human body can be traced to about a century and a half ago. Much of the early work involved chemical analysis. Toward the end of the 1800s and the early 1900s, the concept of body "compartments" was developed. Metabolic balance measurements also became important during this period.

Not until the 1930s, when von Hevesy (1) used the heavy isotope of hydrogen (deuterium) to study the body's fluid compartment, did the modern era of measurement of the main body fractions begin. This period, which extends to the present, has brought important quantitative methods into use for the assay of body composition. Besides von Hevesy, Behnke (2), Keys (3), Brozek (4), Widdowson (5), and Sievert (6), among others, all were instrumental in establishing the foundation of much of the current body composition field. Other important investigators are now providing new technologies to help further the study of this medically important field. The current period is thus an exciting time in which a number of new methods are producing critical body component data on normal subjects as well as on those afflicted with disease. As new systems and instruments continue to evolve and are standardized, new tools are added to the armamentarium of the life science researcher and the practicing clinician, both in the service of basic knowledge and in practical medical care.

Because of the obvious relationship between body adiposity and dyscrasias, such as cancer, diabetes, hypertension, cardiovascular disease, anorexia nervosa, and others, the determination of the fat fraction, its disposition in the body, and particularly its change with treatment can be of practical concern to the attending clinician.

The direct in vivo measurement of the body's fat mass is a difficult problem. Few methods currently exist for this type of adipose assay. In many of the measurement systems described herein, the first step involves the direct assay of a body component other than the adipose fraction which is then determined, in a second or third step, by a difference method.

We provide an overview of the biophysical techniques by which body composition may be estimated and from which the adipose level may be derived. The following areas will be described: anthropometry, Archimedean methods, infrared absorption, confinement chamber techniques, imaging methods, isotopic tracers, neutron bombardment, electrical conductivity, X and gamma ray absorption, and combinations of these systems. As each method cannot be thoroughly discussed, a comprehensive review of each technique can be found in the literature.

In this brief overview of the body composition field, we provide an introduction to each method, a critique on each method's application (for routine or basic research), and an introduction to the archival references for each system. Although biochemical

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methods have been developed to assay change in a body fraction (eg, nitrogen loss), our survey does not deal with the field of chemical analysis.

We designed our review as an aid for the practicing clinician in evaluating the various body composition measurement methods. Our review provides a starting point from which further study may be undertaken and reasonable decisions made on the application of a given method of adipose compartment assay for a specific clinical use.

Some formulas for computing body composition are provided for use with specific methods of body component measurement. In some cases other expressions may be more appropriate for a given subject group (such as females versus males). In this case, the clinician planning such a use is encouraged to explore the literature.

As several terms recur in this review of body composition systems, some definition is necessary. The body generally can be divided into two compartments: the "body fat mass" and the "lean body mass." The body fat is the ether-extractable neutral fat which lies in body stores such as that found subcutaneously or intramuscularly. The lean body mass then is the body mass minus the body fat. The lean body mass is sometimes called the "fat-free mass," but the terms can be used synonymously (7). The "total body water" consists mainly of the intracellular and extracellular body fluids. The intracellular fluid is contained in cells, while the extracellular fluid consists of the blood plasma and interstitial fluid.

## Methods

### Anthropometry

*Skinfold method*—Anthropometry is perhaps the best understood body composition technique. The most common form of anthropometry is based on the hypothesis that the subcutaneous fat layer is linearly related to the body's total adiposity level. The method involves the use of a special caliper to produce a skinpinch value at various points on the body and the use of this skinfold value (in millimeters) in standardized expressions to obtain an estimate of the regional or total body fat fraction (8-10). Obviously, this method does not account for deep-lying adipose tissue. Although different studies have produced varying expressions, one formulation in use for determination of body density through skinfold measurements is:

$$D = 1.1765 - 0.0744 \log S \text{ (males)} \quad (1)$$

$$D = 1.1567 - 0.0717 \log S \text{ (females)} \quad (2)$$

where D is body density, and S is the sum of skinfold in millimeters taken at the biceps, triceps, subscapular, and suprailiac locations.

Once the body density is obtained from these equations, the total body fat fraction can be obtained by other formulations (11):

$$F = 4.570/D - 4.142 \quad (3)$$

where F is percentage of body fat, and D is body density. This expression is best applied to women.

A second method for calculating total body fat uses two skinfold measurements and a body circumference (12):

$$F = 0.37W + 0.13C + (0.10S - 21.1) \quad (4)$$

where F is total body fat, W is body weight, C is circumference at the buttocks, and S is the sum of subscapular and triceps skinfolds.

These methods benefit from lack of complexity, simple instrumentation, low cost, rapidity and ease of measurement, and no subject discomfort. However, as with other anthropomorphic methods, the caliper skinfold system lacks precision. The skinfold value depends heavily on the caliper operator and can vary substantially in certain disease states and with age. The texture and firmness of the skinfold can change, which will also introduce errors in the caliper reading. Therefore, routine clinical use should employ the same well-trained operator for serial measurements on a particular individual.

Despite these problems, this anthropomorphic method continues to be useful clinically and is in widespread use because of its well-developed, simple instrumentation. However, the values obtained for total body fat must be used with caution. The best application of this method is for healthy adults, not including the elderly population.

*Height and weight index*—In 1970, Mellits and Cheek (13) published expressions which used only body height and weight to determine total body water. The formulas are presented in the form of four expressions, which are divided between male and female and also for two height ranges. An example of their expressions is the following formula for females who are shorter than 110.8 cm (44.6 in):

$$L = 0.076 + 0.507\,W + 0.013\,H \quad (5)$$

where L is body water in liters, W is weight in kilograms, and H is height in centimeters.

The other three expressions, provided in the original papers (13,14), are closely related but have different constants. A full evaluation of the precision and accuracy of these expressions was given by Forbes (7) in 1987. Given the total body water value in liters from these expressions, the body's lean fraction can be computed, and from the lean fraction the total fat mass can be derived.

Like other anthropomorphic methods, the height and weight index is simple, causes no subject distress, has minimal cost, and requires no special technique. However, this method is indirect in its determination of the adiposity level and is thus subject to serious question since the entire range in stature is covered, from the infant to the adult and in age from birth to the elderly. This method does not account for changing adiposity effects in infants and adolescents or in the ill, aged, grossly obese, and emaciated and may have limited applicability for normal adults. Caution should be taken in applying fat mass values obtained by this method.

*Body mass index*—The body mass index (BMI), given as weight in kilograms divided by height in meters squared, is proposed as an anthropomorphic measure (15). BMI presumably is

not dependent on stature. The range of BMI for normal men and women is from 19 to 27 kg/m$^2$. Although the BMI is related to adiposity, the correlation between these two quantities is not good. However, BMI is more commonly used than the older ponderal index, which is body weight to the one-third power divided by height. Although useful as a rough index, the BMI cannot be used for the quantitative determination of the body's fat mass.

*Photogrammetric method*—This is a seldom used anthropomorphic method for the determination of body volume and, from volume and weight, thereby density. Photographic views of the naked subject from various angles (16) are used to reconstruct the three-dimensional image and the total body volume. Once the density is obtained using body weight, the body lean mass and, indirectly, fat mass may be derived using formulations described elsewhere [see Equation (3)]. The East German optical firm, JENA, has developed photographic devices and techniques for this purpose.

This method has not been used extensively because of poor patient cooperation, high cost, and requirements of professionally trained operators and a special facility.

*Circumference method*—Anthropometry takes many forms. Fuchs et al (17) proposed a simple test which was applied to normal males. These subjects had a wide range of adiposity, from the very thin to those with over one third of their total weight in adipose tissue. Only the height and the circumference of the flexed biceps were measured. No skinfolds were taken. Their expression for the lean body mass is:

$$LBM = 0.514H + 0.0178C^2 - 49.7 \quad (6)$$

where LBM is lean body mass, H is height in centimeters, and C is the circumference of the biceps in centimeters. The body fat mass is obtained indirectly in a second step by difference with total body weight.

Fuchs et al's results are subject to the same degree of error seen in other anthropomorphic systems, such as in the use of the skinfold technique where deep-lying adipose tissue is not measured. However, their research is of interest because it deals with a test cohort of special concern to the clinician, ie, the grossly obese. Others have also developed circumference formulas (18).

## Infrared interactance

Infrared (IR) spectroscopy is a well-established, analytical tool for the laboratory determination of chemical composition and can be applied to the assay of water, protein, and lipid. These components are also of interest in body composition and have, at various IR energies, strong absorption bands starting above 800 nm. At various points in the near-IR spectrum, these bands influence the diffuse reflectivity (interactance) of the components under analysis. The absorption by lipid in the IR is used in this system.

Several body sites are scanned, using an IR beam of known wavelengths, by automated spectrophotometry for interactance levels which are averaged (19,20). Since the IR penetration is modest, the system deals with the same subcutaneous fat layer measured by the skinfold technique.

In generalized form, the expression for percentage of body fat by IR interactance is:

$$F = C_1 + C_2R \quad (7)$$

where F is percentage body fat, $C_1$ and $C_2$ are constants, and R is the ratio of the second derivatives of the interactance at 867 and 914.5 nm obtained by IR spectroscopy. Further detail is provided in the literature (19,20).

IR interactance is a new approach involving custom instrumentation and holds promise as a rapid, simple method without subject discomfort. Its analysis does not reach deep-lying lipids (beyond 1 cm), but the test itself is not fully established. Despite its simplicity, this method will require a period of standardization and evaluation before being proved. IR interactance may be shown to have the same lack of precision as the skinfold method since it measures a smaller layer of subcutaneous body fat than the caliper method.

## Archimedes principle

*Underwater weighing*—Use of the Archimedes principle is an established method (2) for determining body composition fractions through body density values obtained by underwater weighing. In this procedure the subject is weighed in air and also when fully submerged (a highly accurate balance is required). Density is obtained from the simple expression:

$$D_b = W_a/(W_a - W_w) \quad (8)$$

where $D_b$ is body density, $W_a$ is weight in air, and $W_w$ is the underwater weight.

This formula requires corrections (21,22) for water temperature and air in the lungs and gastrointestinal tract, resulting in the following expression:

$$D_b = W_a/[(W_a - W_w)/D_w] - R - 100\,mL \quad (9)$$

where $D_w$ is water density, R is air volume in lungs (estimated), and 100 mL is the assumed air volume in the gastrointestinal tract.

Body composition by underwater weighing is currently in widespread use. From the value for $D_b$, the fat fraction can be obtained (7):

$$F = 457/D_b - 414.2 \quad (10)$$

where F is total body fat expressed in percent, and $D_b$ is body density. Other formulas exist, such as that of Siri (23), but the differences among them are slight.

Underwater weighing has been used as a standard against which other methods for body composition are tested. A large number of studies and varied cohorts have been done by this method which has a large and useful literature. Instrumentation for this method is well developed, commercially available, relatively large, and can be quite costly. The method cannot be used where submergence of a subject is impractical, such as with the very young or old or the ill. The question of residual air volume

in the lungs and gastrointestinal tract is an ubiquitous problem and continues to stimulate controversy regarding the accuracy of the system. In addition, Eq (10) and others like it, though widely used, may be most accurate for young adult men (24).

The underwater weighing method is fully developed and can be utilized without further research or new instrument fabrication.

*Water displacement*—The displacement method is closely related to the underwater weighing technique for the determination of body density. Water displacement can be combined with the underwater weighing method since the apparatus is similar.

With the subject fully submerged, the displaced volume of water is measured and the subject's weight is taken in air. Knowing volume and weight, the body density is then obtained. From density, the lean body mass and adipose mass may be derived using expressions described elsewhere [Eq (3)]. This, then, is an indirect method for the determination of the lean and adipose components.

As with underwater weighing, the displacement method involves bulky equipment at more than moderate cost and some trauma or discomfort to the subject may occur. Compliance is difficult with some subjects, but a system without head submergence is available. The methods used have been well documented in the literature (25-28). The displacement method is subject to the same sources of error as in underwater weighing, such as in the difficulty in correcting for air trapped in the lungs and the gastrointestinal tract. Forbes (7) has a complete treatment of the range in the coefficient of variation which may be expected for various combinations of lean and adipose tissue ratios.

## Imaging methods

*Computed tomography*—Because of the small difference in tissue density (fat at 0.901 and lean at 1.06) (11), the X-ray absorption coefficients of fat and lean tissue differ. Computed tomography (CT) uses this difference and is capable of imaging these two tissue components by producing a two-dimensional image with a resolution of 5 mm or less. This procedure has been used to determine regional adipose tissue deposition at a single site. However, the measurement of whole body adipose tissue mass requires repeated cross sections at many positions across the legs, trunk, arms, and head, which is followed by planimetry on each of the sections produced by the scan. The planimetry determines the ratio of adipose to lean areas at each section. Computerization of the integrated areas can be done. With assumptions made concerning the geometry of the various body parts, these data relating adipose to lean areas can be used to compute whole body component values (29-31).

This method can be used where a CT facility is available. The instrumentation required is well developed and ubiquitous but also complex and expensive. No subject discomfort or trauma is involved, although subjects are exposed to about 0.7 rads of ionizing radiation. This radiation dosage, the inherent cost of instrument operation, and the time required by highly trained personnel in making the many cross sections of the body and carrying out the data treatment may make this method undesirable to many clinicians for the determination of the total body fat fraction.

*Magnetic resonance imaging*—Magnetic resonance imaging (MRI) for body composition is a method which, in principle, is similar to CT. MRI involves repeated cross sections over the entire body and planimetry (which, like CT, may be automated) of the two tissue areas (lean and adipose) of each section. Like the X-ray technique, MRI produces images in the cross section showing the geometry of the adipose, lean, and skeletal fractions (32). The advantage of MRI is that the subject is not exposed to ionizing radiation. Instrumentation is complex, costly, and requires highly trained personnel, and the multiple sections required for a whole body study involve substantial periods of time using the device. Until this body composition method is refined to reduce cost and establishes standardization against a second method, the technique will be limited to basic research on body component measurement.

## Confinement chamber methods

*Acoustic plethysmography*—This method, recently introduced for the determination of body density, uses the sound wave resonance characteristics of an enclosed chamber. The Helmholtz law states that the resonant frequency of a chamber is inversely proportional to the square of the chamber's volume. Thus, an increase in a chamber's acoustic resonant frequency would be expected if its volume is reduced by placing an object in it. The technique is to reduce the volume by introducing the living subject into the chamber. If the new (higher) resonant frequency can be measured, the reduction in volume can be obtained. Knowing both the subject's volume and weight, the body density can be determined. Fat mass and fat-free mass are calculated from density [Eq (3)]. An acoustic device, designed for the determination of density in infants, uses a frequency at about 100 Hz (20).

Acoustic plethysmography is in an early development stage. It has been tested with small animals and in a limited study with infants. It has not been tested extensively on adults. The method is a safe, one-minute, noninvasive assay. It has good agreement with underwater weighing and has shown a coefficient of variation of less than 2%. Movement, temperature changes, and air in the lungs and gastrointestinal tract as well as ordinary respiration can introduce substantial errors in the analysis. The respiration problem is a serious one. Although acoustic plethysmography is a promising system, such a device is not available commercially and is not applicable to routine clinical use at this time. The adipose mass determination is indirect.

*Air displacement*—Air displacement is a relatively new technique requiring chamber confinement and utilizing the pressure-volume relationship spelled out in Boyle's law. This system utilizes chambers more complex than those of the acoustical method (33). Small animals have been tested with this technique, and limited data from studies on infants are available. Body volumes are obtained by means of pressure variations in the chamber; from the body volume and body weight, body density can be derived. From density, the values for the fat-

free mass and total body fat mass may be obtained indirectly [Eq (3)].

Procedure complexity, instrumentation cost, subject discomfort, and safety fall into the moderate to high category and are sufficiently great as to limit this technique's use. Air displacement is not available for routine application and is subject to the errors from breathing and movement usually found in chamber methods.

*Helium method*—A third method involving an isolation chamber is helium gas dilution. A sealed chamber, enclosing the subject, has a small amount of noble gas (helium) introduced (34). The dilution factor of the gas in the air of the chamber gives the subject's volume, as compared with the empty chamber. From total body weight and the derived body volume, body density is obtained, and the total body fat mass may then be determined indirectly in the same way as in the acoustical and Boyle's law methods. This approach has similar disadvantages described for the other enclosure methods.

*Fat-soluble gases*—Certain noble gases (eg, xenon, krypton) exhibit preferential solubility in adipose tissue. This characteristic can be used for direct measurement of the body's total fat mass. The process requires a holding chamber for the subject, with a measured amount of the soluble gas injected into the chamber (35-37). The gas' disappearance rate, as it is dissolved in the body's store of lipid, is the measure of the adipose mass. The method has been used on adults, infants, and animals. The release of the stored gas can also be assayed as a measure of the body fat mass.

Although this is one of few direct methods for adipose mass determination, the special, somewhat expensive equipment, complex mathematical corrections and data analysis, long study times in the chamber (up to four hours), and the difficulty of obtaining subject compliance make it unlikely that this system will achieve widespread routine clinical use.

**Isotope techniques**

The isotope dilution method, used extensively in body component assay, can be divided into stable isotope use and the radioactive nuclide tag (either naturally occurring or synthetic). This technique for adipose fraction measurement is well established and has been used substantially.

*Tritium dilution*—When tagged to the water molecule, tritium, a radioactive, man-made, byproduct material, is utilized through the simple fluid volume dilution process. It directly measures the total body water pool. The dilution factor is obtained by counting the isotope's radioactive beta emissions, usually by scintillation counting.

Using total body water obtained from the dilution factor, the lean body mass may be calculated from the expression:

$$L = 1.30\,TBW \qquad (11)$$

where L is lean body mass, TBW is total body water directly from the dilution factor, and 1.30 is a combined correction factor, covering losses due to exchangeable hydrogen, plus the water factor for lean tissue.

The body fat mass is obtained indirectly in a second step by the difference relation:

$$F = W - L \qquad (12)$$

where F is total body fat mass, W is body weight, and L is the lean body mass.

*Deuterium dilution*—The determination of body water and lean mass by dilution and the adipose mass by difference, using water tagged with heavy hydrogen, is in principle identical to the tritium procedure. Deuterium detection is more complex in that either IR spectroscopy, mass spectrometry, or the falling drop method are required. IR analysis of deuterium dilution may be the method of choice.

Dilution methods are available to all research facilities and have proven potential for clinical application. The procedures incur only minor subject inconvenience. Compliance is good. Cost, although not negligible for deuterium assay, is not high. The method has been described in detail in the literature (7,20,38,39).

*Potassium-40*—A naturally occurring radioactive isotope of potassium, Potassium-40 has an easily detected, penetrating gamma ray of 1.46 meV and a half-life of 1.3 billion years (obviating the problem of decay corrections). This isotope is of benefit to the clinician-researcher concerned with the body composition assay. Potassium-40 is an isotope of an element essential for human life and valuable in body composition study, but it may also be considered a bane, since man is subjected to about 30,000 energetic gamma rays and 250,000 highly penetrating beta particles each minute from this endogenous isotope. (This natural radiation dosage comprises about one sixth of the total background radiation to which man is exposed each year.)

Body composition measurements with Potassium-40 are made using a whole body counter. This device requires extensive shielding, which may involve the room itself, plus sophisticated electronics. The whole body measurements are compared with Potassium-40 calibration standards and from this the body's potassium content is computed. The methods and instrumentation along with complete descriptions concerning the devices and techniques are well described in the literature (7,40-42).

Using the whole body counting method, the total body content of potassium can be determined. The following expression relates body cell mass to the body's potassium content:

$$BCM = 0.0833\,K \qquad (13)$$

where BCM is the body cell mass, and K is the body potassium value (in mEq) obtained from $^{40}K$ whole body assay.

Body cell mass presumably makes up 57% of the lean body mass. With the lean body mass thus known, the body fat mass is the difference between the derived fat-free body mass and total body weight.

Whole body counting for Potassium-40 assay requires expensive, complex instrumentation and an area isolated by heavy

shielding. An error associated with exercise and radon intake has been identified (39). Despite these negative factors, the whole body Potassium-40 facility is somewhat commonplace. The system involves no subject discomfort and is rather simple. Counting time can be long, and the assay is difficult in infants because of their small $^{40}K$ content. Based on the rate of current installations, this method may become a relatively common, clinic-based body composition measurement device in the future.

The whole body Potassium-40 counter is a unique determinant of the body cell mass. This is an important body component in which the clinician has a strong interest, since this metabolizing body fraction is most likely to be influenced by diet, disease, and treatment.

*Potassium-42*—A synthetic, man-made radioactive isotope, Potassium-42 has been used occasionally as a body composition measurement tool to estimate total body potassium. The method used is the isotope dilution principle, and the quantities obtained are identical to those obtained by whole body counting for Potassium-40. Since the half-life of this isotope is very short, the method is not likely to be used for ordinary clinical application of adipose mass measurement but may have some use in basic research studies of body cell mass.

**Thermal neutron activation analysis**

In vivo neutron activation analysis (NAA) is a relatively new method for the measurement of whole body components. The physical principle is that of thermal (low energy) neutron capture by the nucleus of specific isotopes of targeted chemical elements. This nuclear capture interaction is accompanied by the immediate (prompt) emission of a photon from the isotope and the delayed photon radiation from the new unstable radioactive isotope of the element, which is created by the neutron capture. The creation of the unstable isotope of the endogenous element is the essential product of the process, since it can be measured by its radioactive decay and because it maintains the target element's chemical role in the body's metabolism.

An example of such a reaction is the bombardment of the body's Sodium-23, a stable isotope of sodium, by thermal neutrons. The immediate reaction to the neutron capture by the Sodium-23 atom's nucleus is the issuance of the prompt gamma ray, which has considerable photon energy. The neutron capture process produces the new sodium isotope, Sodium-24, which now contains the extra neutron and which in itself is radioactive with a half-life of about 15 hours. Sodium-24 emits 4.2 meV and 1.4 meV beta particles and a 1.4 meV gamma ray. This capture process may be written as:

$$^{23}Na\ (n,\gamma)\ ^{24}Na \qquad (14)$$

This NAA process allows the body compositionist to calculate the level of an element (in this case sodium) by using whole body counting. The prompt photon or the decay radiation of the product isotope may be counted. Gamma ray spectroscopy is used in this analysis.

The source of neutrons can be from either a reactor, an accelerator, or alpha bombardment on a low z element such as a radium-beryllium source.

This type of NAA does expose the subject to ionizing radiation, although a relatively small total body dose (about 30 mrem). This dosage is less than in some routine clinical X-ray procedures but does involve irradiation of the entire body rather than a small region, as in a chest X-ray.

A few of the important isotopes that may be produced by in vivo NAA are Nitrogen-13, Sodium-24, Magnesium-27, Aluminum-28, Chlorine-38, and Calcium-49. All are produced from the same parent element, using thermalized neutrons, and the common "neutron in, gamma out" [Eq (14)] reaction. The use of NAA for determination of total body nitrogen may be used as a measure of body cell mass. Total body potassium by NAA may be used to measure body cell mass and lean body mass. These are merely two examples of the applications which may be carried out by this method. Forbes (7), Ellis et al (20), and others (43,44) provide details on the several NAA activations available for the measurement of body composition. The determination of the body fat mass is an indirect step when using NAA.

In vivo NAA is a powerful system for the study of body composition but has some serious problems. The equipment, complex and costly, is physically large and cannot be installed in the ordinary clinic environment. Highly trained professional operators are required for its use as well as for evaluation of the data which is produced. Although NAA may provide body composition data unavailable by other techniques, its general medical use in following body composition changes in disease and the like in order to facilitate treatment is probably in the distant future. Currently, NAA will be limited to basic studies on body composition done at large, national research establishments, universities, and large research hospitals with neutron production facilities.

**Fast neutron activation analysis**

Most of the neutron activation analysis for determining in vivo body components is carried out with thermalized neutrons. Those applications have been summarized in the previous section.

Because few *direct* methods exist for the determination of in vivo measurement of body fat, this neutron activation method is important because it can analyze directly for body fat mass.

Because the body's adipose mass contains 64% of the carbon found in standard man, a total carbon measurement, combined with other elemental measurements, can provide an assay of the total body adipose mass. Such an analysis would be valid in both normal and in diseased states and thus could be valuable in the clinical setting.

The fast neutron principle is based on detection of the 4.4 meV gamma rays, resulting from inelastic scattering of energetic neutrons on the Carbon-12 isotope. The threshold for this reaction is 4.8 meV or higher (20).

This energy requirement necessitates a specialized neutron source different from thermalized reactor neutrons or the low-energy plutonium and radium-beryllium or californium neutron sources.

The reaction is written:

$$^{12}C\ (n, n^{1}\gamma)\ ^{12}C \qquad (15)$$

where n is the fast neutron bombarding the $^{12}C$ nucleus, $n^{1}$ is the inelastic scattering of the neutron, and $\gamma$ is the emission of the energetic gamma ray. The end product is the unchanged carbon isotope, $^{12}C$.

This total body fat assay method has been developed both at Brookhaven National Laboratories (Brookhaven, NY) and in England. This direct method for total body fat mass analysis requires a sophisticated accelerator or neutron generator, complex electronic control and detector systems, and the usual expert staff. This costly, delicate, and somewhat bulky apparatus limits this method currently to university and large research hospital usage. No single commercially acceptable analysis system is available or suitable for routine use.

Although no subject discomfort is involved, the system does expose the subject to a measurable amount of ionizing radiation which can be a problem with subject cooperation and which is certainly a factor when choosing a method for routine use.

## Combined assay methods

The composition analysis results obtained from NAA have been most valuable in combination with other, more routine measurement methods. Cohn, who is a leader in this field, and colleagues (45,46) combined the dilution technique for body water determination with neutron activation of body calcium and nitrogen. Their determination of lean body mass is expressed as the sum of bone mineral, protein, and body water:

$$LBM = 6.25N + W + Ca/0.34 \qquad (16)$$

where LBM is lean body mass in kilograms, N is nitrogen in kilograms (by NAA), W is water in liters (by isotopic dilution), and Ca is calcium in kilograms (also by NAA).

The adipose mass can be obtained indirectly through the difference between the lean body mass and total body weight [Eq (12)].

Although other methods of analysis combined with NAA are possible, they are primarily of academic interest and are complicated and not applicable to the practical, routine determination of body fat mass. All the disadvantages of neutron irradiation also apply to these methods.

## Electrical methods

Mammalian tissue conducts electrical current. The lean tissue, which carries most of the body water and electrolytes, is the major conductor. The adipose tissue, which holds a minor fraction of the body's water and binds few electrolytes, is not a good conductor.

*Total body electrical conductivity*—Two electrical methods for estimation of total body composition have been utilized recently. The total body electrical conductivity (TOBEC) method is predicated on the principle that the lean tissue, because of its electrolyte and water content, is by and large the conductor in the body. Therefore, the measurement of the body's level of conductivity is a measure of the body water and lean body mass. The TOBEC method is carried out by placing the subject centrally in a large coil which produces an alternating electrical field, varying from 2.5 to 10 MHz. The power is about 7 mW/$cm^2$. The subject's body, when inserted into the coil, perturbs the electrical field. The degree of perturbation is directly related to its conductivity. The system's change in conductivity caused by this perturbation, with the subject in the field, as compared to the empty device, should therefore be proportional to the body's lean mass and indirectly to the total body fat mass.

The TOBEC system has been used extensively in animal measurements (47) and in a substantial number of human studies (48-50). Correlations as high as 0.98 have been reported in animal studies in which body water was determined by other established assay methods. The principle and the device have had extensive, routine use in the meat industry.

One commercial device for human measurements consists of a horizontal cylindrical coil which is 0.8 m in diameter and 2.2 m in length (20). The supine subject is moved gradually through the coil on a track, and the 64 conductivity measurements taken are averaged to obtain a value termed the "phase average." When standardized against another method (eg, isotope dilution for total body water), the method may be used to measure total body water. From total body water, the fat-free mass and indirectly, as a final step, the body's total fat mass may be obtained. High correlations have been reported in studies using the TOBEC device when comparing it to other standard methods of body composition measurement (eg, densitometry).

The TOBEC method involves complex and costly equipment, which is now commercially available but currently limited to a few large facilities where the method is undergoing evaluation. The method is safe, involves no subject discomfort, and has been tested for precision and accuracy at several research centers. A substantial amount of literature describes this method's principle and application to total body adipose component determinations.

*Bioelectrical impedance*—Methods using the bioelectrical impedance (BEI) technique for body composition assay have increased in the past decade. BEI is based on the simple premise that a measurement of the electrical impedance of the body is one way to estimate the mass of the total body water. The lower the measured resistance, the larger the conducting, electrolyte-containing, body fluid pool. Once this determination of resistance is made, the body composition, divided into total fat mass and the fat-free mass, may be obtained. As with the TOBEC method, this assay is based on the fact that the body's fluid is an ionic conductor.

A simple impedance analyzer, using the tetrapolar approach, consists of using four electrodes: two for producing a very low level of constant alternating current through the body, and the

other two serving as pickup electrodes. The pickup electrodes establish the body's resistance by measuring the voltage drop across these two points. The 50 kHz current is small, usually less than 1 mA. Alternating current is used, since this provides for measurement of the capacitative effect, which is developed in the cell wall by the insulating lipid of the cell wall. The BEI device also measures electrical reactance. These devices are not operated from line current but utilize low battery voltage. Therefore, they constitute no electrical hazard.

Kushner and Schoeller (51) carried out a BEI study with a substantial number of subjects and found a relatively high correlation value ($r = 0.986$) in a comparison between total body water, using a heavy water dilution, and the tetrapolar bioelectrical technique. Their expression for total body water is:

$$TBW = 0.5561\,H^2/R + 0.0955\,W + 1.726 \qquad (17)$$

where TBW is total body water in liters, R is body resistance in ohms, W is weight in kilograms, and H is height in centimeters. From total body water, fat-free mass is derived, and a following step gives the fat mass (indirectly).

Lukaski and coworkers (52) also found a high correlation ($r = 0.992$) with a much larger cohort. Their correlation was made between body resistance, determined by the tetrapolar BEI device, and densitometry, determined by underwater weighing. Their subjects covered a wider range in age and in adiposity than those in Kushner and Schoeller's study. Lukaski et al developed a somewhat different formula which yields fat-free mass:

$$FFM = 0.756\,H^2/R + 0.110\,W + 0.107\,(XC) - 5.463 \qquad (18)$$

where FFM is the fat-free mass in kilograms, H is height in centimeters, R is resistance in ohms, W is weight in kilograms, and XC is reactance in ohms.

The high correlations found by some workers have encouraged widespread application of this type of BEI body composition assay.

The BEI assay involves attaching input and pickup electrodes on the hand and foot, either on the same or opposite sides of the body. The instrumentation is commercially available, relatively simple, and may be obtained at a modest cost. The test is done with ease and may be completed with simple software from commercial suppliers, or the computations may be done locally with internally developed software. The system involves no subject discomfort and is completely safe. Some discussion exists regarding the applicability of this method in disease states, in the emaciated such as in anorexia nervosa, in morbid obesity, or in cases where edema is present. The analysis is useful to trace over time relative changes in: edema at specific body sites, adipose mass regionally, and whole body fluid volume.

The system's instrumentation is in a good state of development and is available from various commercial sources. The system's present level of use is relatively high and may be found in routine clinical applications in clinics concerned with dyscrasias such as obesity. Because research is still under way on the application of tetrapolar BEI to other than the normal body state, measurements of abnormal body composition should be accompanied by scrupulous study of the current literature on the subject.

### Dual photon differential absorptiometry

Dual photon absorptiometry (DPA), using radioactive isotopes as photon sources, has been used clinically for the study of bone density and soft tissue components at single sites and small regions of the body. Until recently, DPA has not been applied for determination of total body components. However, the technique has been used for measurement of the entire body for the determination of whole body lean and adipose fractions. Research involving human subjects by Mazess et al (53,54) and Gotfredsen et al (55) has resulted in body composition determinations for soft tissue.

DPA utilizes a rectilinear scan system capable of covering the adult body. A 1 Ci gadolinium-153 source provides two penetrating photons of 44 and 100 keV. The two distinct energies provide the differential absorptiometry. Approximately 2,000 pixels, which cover the entire soft tissue region of the body, are measured in a 90-minute scan. An "R" value is a quantity proportional to the ratio of adipose to lean fractions derived for each pixel. The R values of all soft tissue pixels are averaged, and from this value the total body water and lean and fat fractions are obtained (53).

This system is based on the difference in the absorption coefficients for the two photon beams for a given tissue mix of the two components (lipid and lipid-free tissue) (56,57). The R value is defined by:

$$R = \ln(I_{01}/I_1)/\ln(I_{02}/I_2) = \mu_1 PX/\mu_2 PX = \mu_1/\mu_2 \qquad (19)$$

where subscripts 1 and 2 refer to the two component system, $\mu$ is mass absorption coefficient, P is density, X is thickness, $I_0$ is unattenuated beam, and I is transmitted beam. Density and thickness are the same for both beams and fall out of this expression. Thus, as the tissue fractions change, the R value changes over a given range. If the proper choice of radioactive isotope and photon energies is made, the relation of R to tissue component ratio is essentially linear (58,59). This makes for simple system standardization.

This scanning method for whole body soft tissue analysis is a promising technique. The method involves costly equipment and requires knowledgeable personnel for its use. Surprisingly, the radiation dosage is small (less than 5 mrad for the whole body). The measurement period is lengthy (1.5 hours) but does not involve subject discomfort or serious compliance problems. Equipment is now commercially available and is adaptable to routine use.

## Summary

Noninvasive methods for body fat fraction determination can be divided into two categories: 1) those that have well understood principles, available instrumentation, tested procedures, good calibration, and no substantial disadvantage, thereby mak-

**Table**
**Methods for In Vivo Fat Mass Measurement**

| Methods | Criteria* | | | | | |
|---|---|---|---|---|---|---|
| | Safety | Compliance | Instrumentation | Methodology | Cost | Clinical Usefulness |
| Anthropometry | 4 | 4 | 4 | 2 | 4 | 4 |
| Bioelectrical impedance | 3 | 4 | 3 | 3 | 3 | 2 |
| Deuterium dilution | 4 | 4 | 1 | 2 | 2 | 1 |
| Radiotracer dilution | 2 | 2 | 2 | 4 | 2 | 1 |
| Whole body counting $^{40}K$ | 4 | 4 | 1 | 2 | 0 | 0 |
| Underwater weighing | 2 | 1 | 1 | 3 | 2 | 1 |
| TOBEC | 3 | 4 | 0 | 1 | 0 | 0 |
| Displacement | 2 | 1 | 1 | 2 | 2 | 1 |
| Dual photon absorptiometry | 2 | 2 | 0 | 2 | 0 | 1 |

*Methods suitable for in vivo fat mass measurement are compared for safety, compliance, instrumentation, methodology, and cost. Zero is the poorest rating, four is best. "Safety" and "Compliance" require no definition. "Instrumentation" includes device size, availability, complexity. "Methodology" combines the level of current calibration, measurement procedures, data collection methods. "Cost" combines initial instrument purchase, plus operating and attending staff expense. "Clinical Usefulness" is defined through a combination of factors, such as: ease of operation; short measurement time, requiring only nonspecialist personnel; reasonable cost; tested and established devices and principles; and a history of extensive clinical routine use.

The ratings are not given as absolutes. If total body, plus body segment fat mass change were both to be assayed, dual photon absorptiometry or BEI would be the best candidates. Anthropometry, despite this table's rating, would not be a first choice.

ing them candidates for routine applications; and 2) those that have one or more disadvantages which makes routine application less attractive.

In a complete review of the several methods available for body adipose mass measurement, the clinician-researcher may find the selection a daunting prospect. Most will be inclined to use a familiar and available method which in fact may be a poor choice for the patient population or dyscrasia in question.

Nine methods suitable for adipose fraction assay are listed in the Table. Six criteria of safety, compliance, instrumentation, methodology, cost, and clinical usefulness are graded and compared. Since all criteria cannot be included in the Table, some methods can be best evaluated from detail provided in the literature. Clinicians considering a choice of techniques for adipose measurement must rate the systems according to the requirements of their specific usage, capabilities, and the disease to be treated. These special parameters should influence the choice of method.

Anthropometry is in widespread use and rated high under the limited criteria of the Table. Nevertheless, serious questions persist regarding its accuracy, precision, and use on the aged, diseased, and the young. Systematic caliper error is also a matter of concern. However, anthropometry is undoubtedly the method of choice for certain clinical applications.

Tetrapolar bioelectrical impedance is in some routine clinical use at the present time. Its standardization is expanding the current range of subjects, from the initial core of healthy young adults to the older and very young populations as well as to those who are obese or underweight. Current literature should be followed where BEI is routinely applied since small modifications of the calculations still occur.

Stable and radioactive isotope tracers for dilution determinations meet some routine use requirements. With radionuclides, radiation dosage is a compliance and safety factor to be considered. Deuterium dilution tests do not carry the ionizing radiation stigma, but assay detection devices and the exacting measurement techniques required are not as straightforward as with the radiotracer.

Potassium-40 whole body counting is attractive for a clinical body composition facility and is currently used in some large research hospitals. However, the facility's size and cost of the method provide serious disincentives. Potassium-40 is inapplicable to the very young (small) subject. The method also requires a high level of sophisticated technical supervision.

Total body electrical conductivity is in only limited use but holds promise for routine application. The high cost of instrumentation and need of trained professionals are handicaps, except for the larger institutions. As with tetrapolar BEI, the current literature should be followed for ongoing TOBEC standardization covering broader subject populations.

Density determination by underwater weighing and displacement both are attractive since they are widely used, have an extensive scientific literature, and have frequently been applied as a standard for evaluation of other biophysical body composition assay schemes. Some devices avoid submergence of the head, thus aiding in subject compliance. However, most units are large and somewhat costly, and built-in units require substantial space and maintenance.

Controversy exists between the Archimedeans and the electrical conductivity proponents. Each group questions the other's dogma and steadfastness to its time-honored position as the correct method for body component assay. However, each method has its place in fat fraction assay.

The electrical conductivity methods do not have the long history or extensive body of literature that can be found for the underwater weighing methods. As a consequence, the electrical conductance and impedance methods are to be used with more caution. With the electrical methods it is prudent to establish

that the formulas used were developed with the same specific subject group (eg, aged, infants, etc) as the population considered for the clinical study.

Dual photon absorptiometry has been used clinically for bone densitometry and is an attractive method for soft tissue (adipose) assay. Its ionizing radiation raises a safety question and a certain negative subject compliance response. Currently, the major disadvantage of this technique is the relatively high cost of large and complex instrumentation plus the specialized professional supervision required. As with TOBEC, instrument cost should lessen with the method's increased use.

In evaluating the measurement systems described herein, the clinician-researcher is well advised to review the scientific literature for ongoing developments in this rapidly expanding field. Consultation with biophysical professionals in the specialty is also recommended.

A primary question which must be resolved is: Has this adipose measurement method been standardized for the dyscrasia of concern, or is it only calibrated for normal adults or some other subpopulation? This can be a critical query, where accuracy of an isolated single measurement is important for the determination of body adipose mass on a patient. However, it is not as critical, where sequential assays over time are made, to follow *relative* change in the adipose fraction. In such a case, the calibration and standardization for the population group may not be necessary, since the data required have to do with percentage change of the component and not its absolute value in kilograms. Relative change in a critical body fraction may be more important to the physician than a single, highly accurate value of a given body fraction. Percentage change will reflect the efficacy of the treatment.

The methods that do not hold immediate promise for routine application for adipose mass assay are those whose principle is not well evaluated, the system not fully calibrated, the process overly complex, instrumentation unavailable, testing costly, and compliance difficult. Biophysical procedures in this category include fast neutron activation analysis, noble gas solution in body lipid, computed tomography, magnetic resonance imaging, all confinement chamber methods, and the infrared interactance principle. However, these procedures can be successfully applied to basic clinical research on body composition, provided that they are under supervision of professionals with experience in the study of body composition biophysics.

The newest candidates that hold future promise for routine adipose mass determinations include whole body dual beam absorptiometry, total body electrical conductivity, and bioelectrical impedance. Recent publications dealing with body composition measurement provide in-depth information on these and other measurement systems (7,20,43,60,61).

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