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USE OF BIOELECTRICAL IMPEDANCE TO MEASURE MALNUTRITION AND DEHYDRATION

Final report on measurement of malnutrition

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ABSTRACT

A bioelectric impedance (BIA) method to predict total body water (TBW) was developed and evaluated against $H_2{}^{18}O$ isotope dilution. Sixty-five children were studied. However, 19 were excluded because they did not comply with the protocol for urine sample collection. Thus, subjects were forty-six 3 to 30 month-old, well or malnourished non-edematous children whose weights were 3 to 14 kg and -3 to +1 SD from reference weight-for-height. Children had no histories of diarrhea or fever for 7 consecutive days prior to the study. Data from 30 children randomly selected from the 46 were used to develop the equation: TBW (kg) = 0.68 (Ht^2/Z) + 0.48; (r = 0.95; SEE = 370g) where Ht is in cm and Z is BIA in ohms. Mean TBW (^{18}O dilution space/1.01) was 4.80 ± 1.22 kg. The equation was cross-validated using data from the remaining 16 children. Mean TBW was 5.55 ± 1.73 kg by $H_2{}^{18}O$ and 5.44 ± 1.65 kg by BIA (r = 0.98). By paired t-test, the difference between TBW by ^{18}O and the experimental method was not statistically significant (t = 1.21;p = ns). The 95% confidence interval for mean predicted TBW was 190g, or 3% of TBW. The relative uncertainty for individual estimates of TBW was 5%. The BIA method is valid and could be used in field settings where TBW measures of non-edematous children are needed.

INTRODUCTION

Malnourished children may suffer longer and more severe bouts of infectious disease than their well-nourished counterparts; physical or mental development may be permanently impaired. One of the principal reasons is that the children lack reserves of nutrients and calories to sustain them during periods of food insufficiency, anorexia, or altered requirements such as may occur during illness. Appropriate public health measures and early assessments of children's nutritional status with emphasis on caloric reserves could give a considerable degree of protection against the synergistic alliance of malnutrition and infection, a central problem of child health in the developing world today. However, caloric reserves cannot be measured directly in living humans. Methods for estimating them in healthy children are inaccurate when applied to malnourished children due to alterations in body composition which occur during malnutrition. Thus, a method is needed which accurately and rapidly estimates caloric reserves in malnourished children.

Caloric reserves are contained principally within the body compartment referred to as the fat mass. The other compartment is referred to as the fat-free compartment. This two-compartment model was developed from studies in animals in which fat is defined as all the lipid-extractable anhydrous material and fat-free mass is all the rest of the body mass. Neither compartment can be measured directly in human subjects. However, the largest component of fat-free mass is water, which can be measured accurately and which can be used to estimate fat-free mass since it occupies a predictable proportion of the fat-free mass. Thus, caloric reserves can be estimated from body water, a hydration coefficient of fat-free mass, and body weight.

To date, the most reliable measures of total body water have been from underwater weighing or isotope dilution. Underwater weighing cannot be used with small children, and the isotope methods are costly and time consuming. Thus neither method is useful for population studies or for rapid surveillance. A new method, which is based on bioelectrical impedance to the flow of an applied electrical current, which was first described in 1969 (Hoffer et al., 1969) and later validated in adult subjects (Kushner and Schoeller, 1986) appears to be nearly as accurate as these "gold standard" methods. Additionally, the method can be implemented safetly, inexpensively, and with minimal training. However, it has not been validated in children with varying nutritional status. If valid, the method may be capable of measuring body water in children rapidly and non-invasively, and thus holds the potential for being useful in rapid evaluations of health and nutritional status in children.

PURPOSE OF THE STUDY

This study was done to test the hypothesis that the bioelectrical impedance method accurately measures total body water in children who are either well-nourished or malnourished. The first step was to develop a predictive equation, and the second step was to cross-validate the equation in a separate group of comparable children.

BACKGROUND

According to theories of physics underlying the bioelectrical impedance method, the volume of the conductor can be calculated from conductor length, cross-sectional area, and bioelectrical impedance to the flow of an applied current. This is true because the impedance to conduction of electricity in simple geometric systems is a function of the system's configuration, length, cross-sectional area and of the frequency of the signal introduced (Thomasset, 1962; 1963). Thus, if the signal frequency is fixed and the system's configuration is relatively stable, impedance to the flow of electrical current is a function of conductor volume.

The mathematical relationship of bioelectrical impedance to conductor volume is shown in Equation 1 (Hoffer et al., 1969):

$$Z = (RST^2 + RCT^2)^{1/2} = \rho L^2/A \qquad [1]$$

where Z = resistance in ohms, RST = resistance, RCT = reactance, L = conductor length in cm, A = cross-sectional area in cm^2. Since AL = volume (V) and ρ is constant, by rearrangement, Equation 2 is obtained (Hoffer et al., 1969).

$$V = \rho(L^2/Z) \qquad [2]$$

By adding a coefficient to the right side of the equation to approximately adjust for heterogenous distribution of water in the body, the bioelectrical impedance method has been shown to accurately measure body water in adults, where body water was known by isotope

dilution (Kushner and Schoeller, 1986) or by underwater weighing (Lukaski et al., 1985). In these adult studies, it has been found that the general formula shown in Equation 3 predicts total body water volume, with correlation coefficients of 0.95 or greater.

$$\text{Volume} = f(Ht^2/RST) \qquad [3]$$

where Ht is height in cm, and f is a factor derived from regression of total body water volume on Ht^2/RST. (In these adult studies, RST was used in lieu of Z, since reactance is very small compared to RST and Z is calculated from only these 2 variables.)

However, no validation studies of the bioelectrical method have been completed in children in which body water was measured by a reliable method.

MATERIALS AND METHODS

Protocol

Children were either in-patients being treated for protein-energy malnutrition, or were children from one of the communities included in various community surveillance projects conducted by the Instituto de Investigación Nutricionál in Lima, Perú. Children from the communities were brought to the out-patient clinic before 8am by CRF or a field worker and remained in the clinic or adjacent play area during the studies. In-patients were studied during one day of hospitalization. Total body water was measured by isotope ($H_2{}^{18}O$) dilution. Bioelectrical impedance and anthropometric measurements were made during the 5 to 7-hour interim between isotope administration and completion of collections of urine needed for measurement of isotopic enrichment.

Children

Sixty-five children, 3 to 30 months of age who were free of fever and diarrhea on the day of the study and for 7 or more days prior to the study were admitted to the study. Subsequently, data from two of the 65 children were excluded from analysis because the children produced liquid stools after isotope administration, leaving doubts as to whether the full dose had been absorbed. Data from an additional seventeen children were excluded from analysis because protocol requirements for urine collections were not met. Selected characteristics of the 30 patients included in Part I which was designed to develop the predictive equation, and from the additional 16 patients in Part II which was designed to cross-validate the equation, are summarized in Table 1. The study was approved by the Ethical Review Committee at the Instituto de Investigación Nutricionál in Lima, Perú, where the studies were done.

Signed consent forms were obtained from parents or guardians after the purpose and methods of the study had been explained.

Part I. Development of a predictive equation

Thirty children were randomly assigned to group I and their data used to develop an equation for predicting total body water. The equation was developed using a stepwise linear regression program, considering the following potential independent variables:

- height
- weight
- weight-for-height
- sum of skinfolds at supscapular, suprailiac, tricep and bicep sites
- mean of 4 skinfolds
- inverse sum of 4 skinfolds
- chronological age
- developmental age

Part II. Cross-validation of the equation

Data from sixteen children randomly assigned to group II were used to cross-validate the predictive equation. Selected characteristics of children in group II are shown in Table 1.

Bioelectrical impedance

Bioelectrical resistance (RST) and reactance (RCT) were measured with a BIA-101 analyzer (RJL Systems, Detroit, MI), which applies a 50 kHz oscillating current through a tetropolar electrode configuration. The intensity of the current source was 800 microamps.

All children were in the supine position during bioelectrical measurements with clothing removed except for dry underware or diapers. No contact between the skin of the child and that of the investigator or parent was permitted during the bioelectrical measurements.

Sites for adhesion of electrodes were cleaned with 2-propanol and electrodes with gel backing were adhered to skin. Cables for sending and receiving electrical current were attached to the electrodes by alligator clips. Measurements (in ohms) of resistance and reactance were recorded as means of 5 consecutive measurements.

A preliminary study was done to determine inter-electrode distances which could be used to eliminate potential electrode interactions while causing minimal reductions in conductor length. Electrodes were placed to achieve inter-electrode distances of 0 to 5 cm, with increments of 0.5 cm achieved by moving the proximal electrode away from the distal electrode. Measurements were taken at 0 cm and at each 0.5 cm increment until 5 cm separated the interior edges of the pair of electrodes. Results (Figure 1) show that at inter-electrode distances of 3 cm, constant resistance measurements are achieved. An inter-electrode distance of 3 cm was therefore used uniformly during parts I and II of the study.

Total body water by ^{18}O dilution

Total body water (TBW) was measured by dilution of ^{18}O, according to previously published methods (Schoeller et al., 1980).

Basal urine samples for measurement of natural isotopic abundance were collected and 0.08g$H_2{}^{18}O$ per kg body weight was given as 11.34 APE isotope (hydrogen normalized, Mound Laboratories, Miamisburg, OH) by mouth from syringes weighed before and after the dose (precision 0.1mg). At one-hour post-dose, a milk feeding was given. Pre- and post-feeding bottle weights were used to measure milk intake. Each post-dose urine was collected

in adhesive-backed plastic urine collectors. With the exception of the first post-dose void which was uniformly excluded from analysis, urines from between 3 and 7 hours post-dose were used to meausure isotopic equilibration. Enrichment in the urine samples collected closest to 5 to 7 hours post-dose, usually the third post-dose void, was used to calculate isotopic dilution spaces, which were in turn assumed to be 99% of TBW volume (Nagy, 1980).

Measurements of isotopic enrichment were made on a dual inlet Nuclide 3-60 isotope ratio mass spectrometer at the University of Chicago (Chicago, IL) and expressed as per mille enrichments versus SMOW as previously described (Schoeller et al., 1980).

Anthropometry

Body weight was measured on a pediatric scale, calibrated daily (precision 5 g). Recumbant body length was measured using a fiberglass length board with a sliding foot board (precision = 1mm). Weight-for-age, height-for-age, and weight-for-height were calculated using the NCHS (1977) data for reference. Midarm circumference and triceps skinfold thicknesses were measured according to published methods (Owen, 1982; Trowbridge et al., 1982; Frisancho, 1974). All anthropometric measurements were made by 2 anthropometrists. Each reported the mean of 3 measurements at each site; the mean of the 2 observers was recorded. Measurements were repeated when skinfolds or circumferences differed by 0.3 mm and length by 0.5 cm.

Table 1. Selected characteristics of children

	N	Age (mos)	Weight (kg)	Height (cm)	W/H (SD)	H/A (SD)
		Range Mean (SD)				
Develop	30	3-30	3.9-11.6	54.5-83.8	-2.4±0.9	-4.4±0.7
		13.1 (6.9)	7.6 (2.3)	69.4 (8.5)	-0.9 (0.8)	-2.21 (1.2)
Validate	16	8-30	3.4-14.3	58.3-97.0	-2.8±0.1	-5.0±3.3
		17.8 (6.9)	9.0 (2.8)	75.7 (11.0)	-1.2 (1.0)	-1.6 (1.8)

RESULTS

Part I. Development of the predictive equation

Mean total body water (^{18}O dilution space/1.01) in the 30 randomly selected children was 4.80 ± 1.22 kg. From the regression of Ht^2/Z the predictive equation (Eq.4) was developed.

$$\text{Total body water (kg)} = 0.68\ (Ht^2/Z) + 0.48 \qquad [4]$$

(r = 0.95; SEE = 0.37 kg)

To determine whether additional independent variables improved the prediction of total body water by the bioelectrical impedance method, stepwise linear regression analyses were performed using variables shown in the Methods section.

None significantly improved the prediction of total body water by Equation 4. Thus, Equation 4 gives the best prediction of total body water. In addition, its simplicity reduces requirements for data collection.

Part II. Cross-validation of the predictive equation:

Equation 4 was cross-validated using data from 16 randomly selected children. Mean total body water was 5.55 ± 1.73 kg (by ^{18}O isotope dilution/1.01) and 5.44 ± 1.65 kg by the bioelectrical impedance method (r = 0.98). Figure 2 shows TBW (kg) measured by the two methods.

By paired t-tests, the difference between total body water by ^{18}O and the experimental method was not statistically significant (t = 1.21;p = ns). The 95% confidence interval for mean predicted total body water was 190g, or 3% of total body water.

CONCLUSIONS

The new bioelectrical impedance method has been shown to accurately measure total body water in children. Due to the fact that the ^{18}O stable isotope dilution reference method has an accuracy of 1%, this validation study's results provide a more reliable predictive equation than previous studies in children which compared fat or caloric stores estimated from the BIA method with anthropometric estimates of fat stores.

The additional cross-validation of the BIA method in the present study, done in 16 well and malnourished children has shown that TBW estimated from the BIA method is accurate to within 3% of TBW measured by isotope dilution. This volume of water is less than normal daily fluctuations in healthy children. Thus, in absolute terms, the BIA method measures TBW with a precision that is biologically meaningful and clinically applicable.

Assuming that the fat-free mass is 77% water (Fomon, et al., 1982), the error in estimating body fat from the BIA method would be 9 to 10% of actual body fat. Estimates of body fat from isotope dilution could theoretically come within 4% of actual body fat. This net difference of 6% body fat could be important biologically and clinically. However, the BIA method has the additional advantages of being inexpensive, completely non-invasive, and practical in field settings. The only other method which has similar advantages in terms of cost and practicality is anthropometry. Anthropometric analysis of body composition in children, however, is less accurate than we have shown the BIA method to be. Thus the BIA method is superior to anthropometry in terms of accuracy, and to isotope dilution in terms of cost and rapidity.

The BIA method can be used in field settings by village health workers; training and validation of individuals' techniques can be achieved within a few hours. Thereafter, trained

health workers need only to measure biolectrical impedance and supine length or standing height, using customary methods. Thereafter, the equation developed and cross-validated in the present study can be used to rapidly estimate total body water volume, from which fat stores can in turn be calculated.

We have found that some conditions alter the reproducibility of bioelectrical impedance measurements. In particular, the following should be observed:

1. the skin to which electrodes will be attached should be cleaned with common rubbing alcohol and allowed to dry;

2. while measurements are being made, the child should be quiet, not crying, and immobile;

3. touching the child may help calm her/him. If bodily contact is made with the child, there should be a barrier between the skin of the child and the one contacting the child--dry diapers or other commonly available cloth items are effective;

4. the distance between the inner cut edges of the electrodes should not be less than 3 cm.

In addition, it should be emphasized that our equation has not been validated in children with kwashiorkor or in children who are both malnourished and dehydrated.

With these caveats, the bioelectrical impedance method can readily be used in field studies for making reliable measures of body water, from which fat and fat-free mass can be calculated, if reference hydration coefficients can be assumed. The method should be very useful in studies designed to measure the impact of public health, agricultural development, and feeding programs in terms of caloric reserves in children.

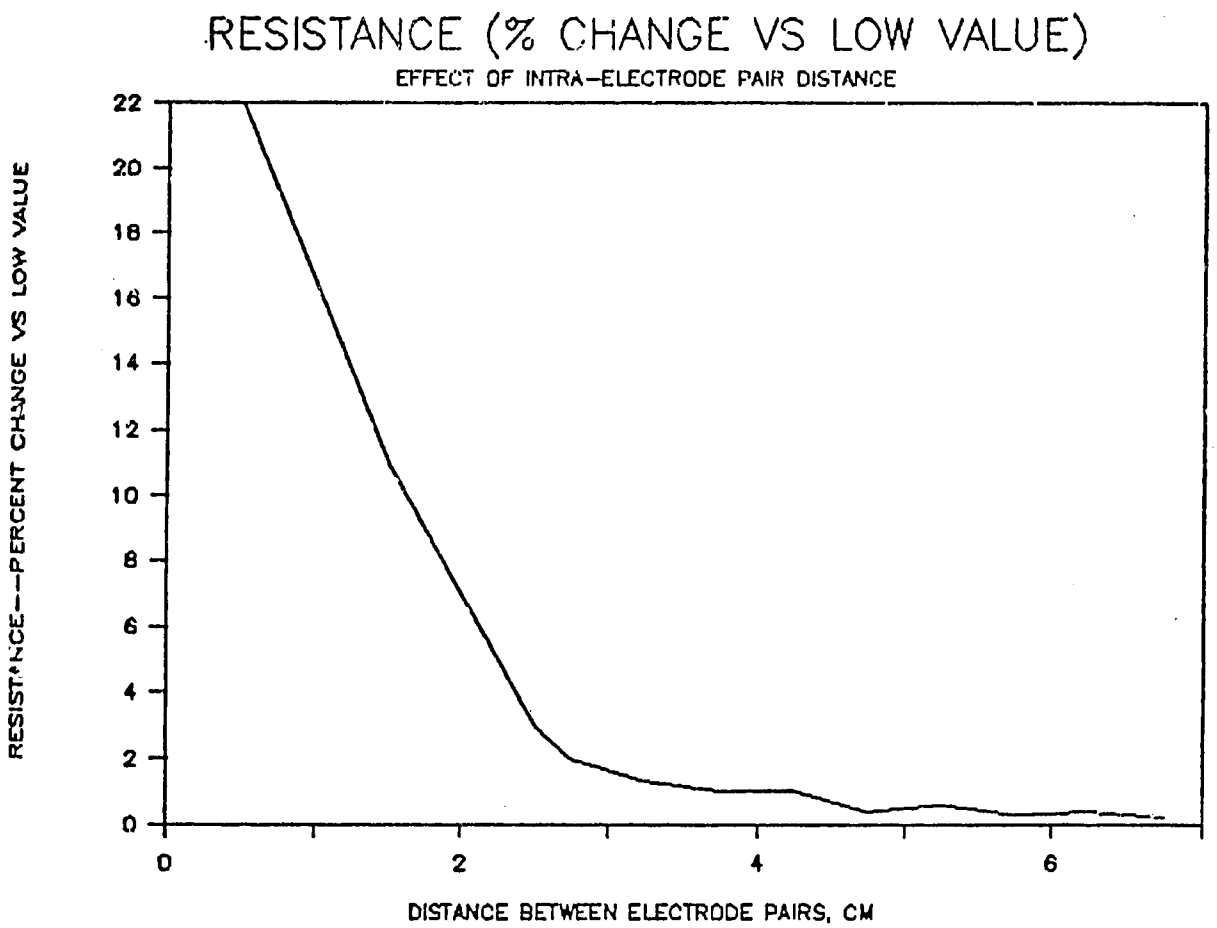
RESISTANCE (% CHANGE VS LOW VALUE)
EFFECT OF INTRA-ELECTRODE PAIR DISTANCE
RESISTANCE--PERCENT CHANGE VS LOW VALUE
22
20
18
16
14
12
10
8
6
4
2
0
0
2
4
6
DISTANCE BETWEEN ELECTRODE PAIRS, CM

FIGURE 1.

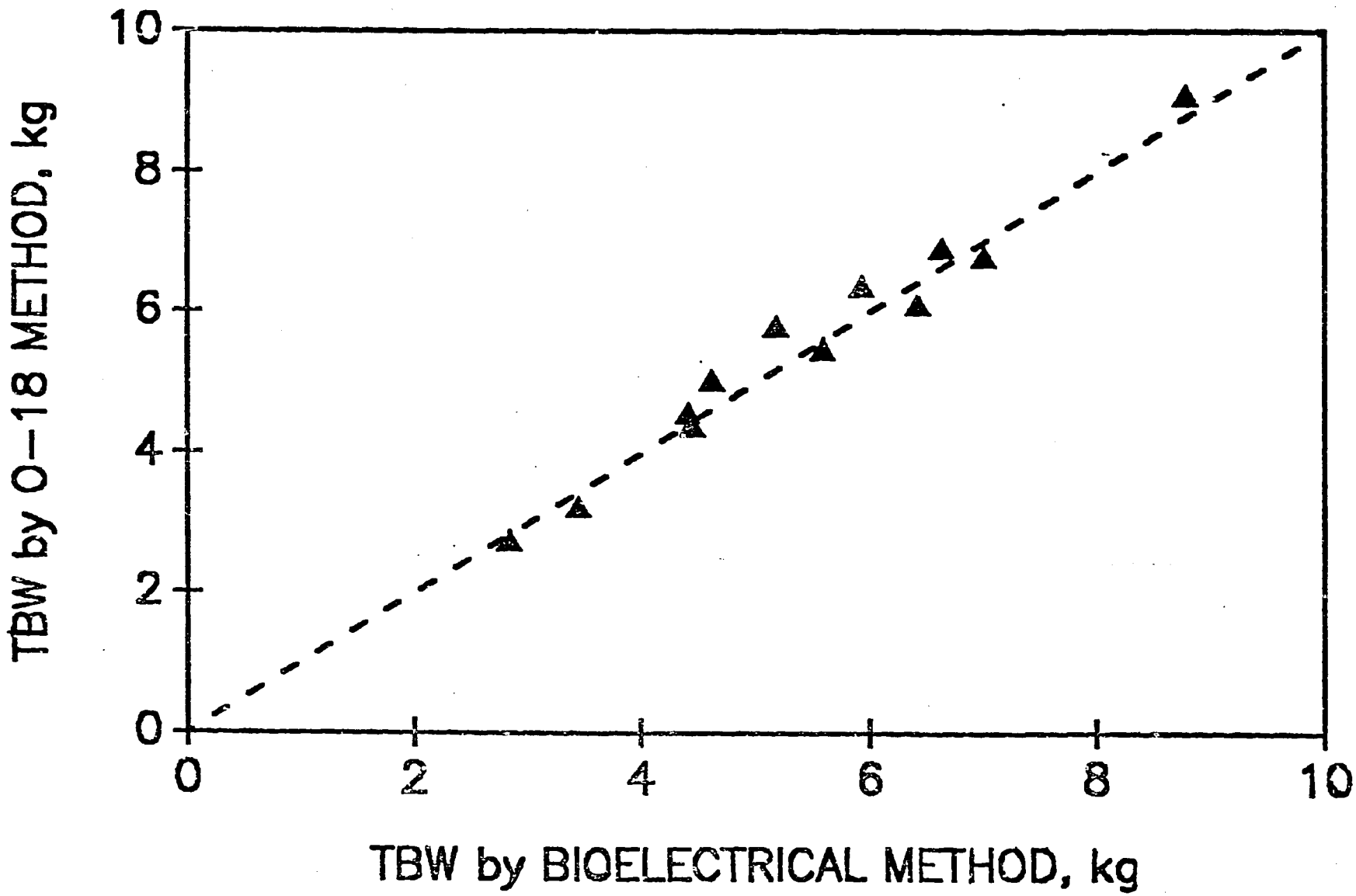

FIGURE 2.

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