Body Composition Measurements from Whole Body Resistance and Reactance

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1.Abstract

Prior research has demonstrated relationships between whole body electrical resistance (R) and lean body mass (LBM). The present study investigates the use of reactance (X_c) in the measurement of body composition, and compares the accuracy of R and X_c measurements in normal versus malnourished states.

In 64 subjects, R and X_c were determined using a four-electrode impedance plethysmograph. Body composition was simultaneously determined by multiple isotope dilution.

23 subjects had a normal body composition and 41 were malnourished, as measured by isotope dilution. Data analysis revealed an inverse relationship between the isotope-measured LBM and R (r=.78), similar to previous findings.

Reactance was found to correlate inversely with ECM/BCM (r=.70), where ECM is the isotope-measured extracellular mass and BCM is the body cell mass. This is a new finding.

The LBM, ECM, BCM and fat mass, calculated from the impedance data, height and weight, correlate significantly with the respective isotope-method measurements, in both normally nourished and malnourished states.

The impedance method is more accurate in measuring normal body compositions than in measuring malnourished ones.

2. Résumé

Des recherches antérieures ont démontré qu'il existe une relation entre la résistance électrique totale de l'organisme (R) et sa masse maigre (MM). La présente étude a pour but d'examiner l'utilisation de la réactance (Xc) dans la mesure de la composition corporelle, et de comparer la précision des mesures de R et de Xc à l'état normal par opposition à un état de malnutrition.

Nous avons déterminé R et Xc chez 64 sujets, au moyen d'un pléthysmographe à impédance à quatre électrodes. La composition corporelle fut déterminée simultanément par multiples dilutions isotopiques.

Selon les mesures par dilution isotopique, 23 sujets avaient une composition corporelle normale et 41 souffraient de malnutrition. L'analyse des données a révélé l'existence d'une relation inverse entre la MM mesurée par méthode isotopique et la R (r=0,78), conformément aux résultats antérieurs.

Nous avons également observé une corrélation inverse entre la réactance (Xc) et MEC/MC (r=0,70), si MEC représente la masse extracellulaire mesurée par méthode isotopique et MC la masse cellulaire. Il s'agit d'une nouvelle constatation.

La MM, la MEC, la MC et la masse grasse, calculés à partir des données d'impédence, de la taille et du poids, ont une corrélation significative avec les mesures respectives par méthode isotopique, à la fois chez les sujets normaux et chez les sujets souffrant de malnutrition.

Pour la mesure de la composition corporelle, la méthode par impédance s'est révélée plus précise dans les cas normaux que dans les cas de malnutrition.

Table of Contents

	page
Abstract	1
LIST OF ABBREVIATIONS	5
PREFACE	6
INTRODUCTION	6
HISTORICAL REVIEW	9
THE PRESENT STUDY: ORIGINAL FINDINGS	11
ACKNOWLEDGEMENTS	12
LITERATURE REVIEW	13
IMPEDANCE MEASUREMENTS IN THE NORMALLY NOURISHED: RESISTANCE CORRELATES STRONGLY WITH LBM, TBW AND BCM, BUT REACTANCE HAS NO PREDICTIVE VALUE.	13
FAT-FREE MASS DETERMINATION BY IMPEDANCE COMPARED TO DENSITOMETRY AND ANTHROPOMETRY METHODS	15
COMPARISON OF IMPEDANCE MEASUREMENTS WITH D_2O MEASURED TOTAL BODY WATER IN NORMAL AND OBESE SUBJECTS	17
COMPARISON OF DEUTERIUM MEASURED TOTAL BODY WATER WITH IMPEDANCE MEASUREMENTS CORRECTED FOR ELECTROLYTE CONCENTRATION	18
EXPERIENCE WITH IMPEDANCE MEASURED USING OTHER ELECTRODE PLACEMENTS AND A 100kHz FREQUENCY	20
BODY COMPOSITION MEASUREMENTS BY MULTIPLE ISOTOPE DILUTION; THE INDIRECT MEASUREMENT OF TOTAL EXCHANGEABLE POTASSIUM	21
BODY COMPOSITION IN THE MALNOURISHED STATE	26
METHODS	28
OVERVIEW	28
IMPEDANCE METHOD	29
ISOTOPE-DILUTION METHOD	30
RESULTS	35
BASIC DATA AND DESCRIPTIVE STATISTICS	35
RELATIONSHIPS BETWEEN RESISTANCE, TBW AND LBM	39
RELATIONSHIPS BETWEEN REACTANCE, Na_e/K_e AND ECM/BCM	43
SOLVING FOR THE OTHER COMPONENTS OF BODY COMPOSITION	46
LBM: Impedance Measured Vs. Isotope Measured	46
TBW: Impedance Measured Vs. Isotope Measured	53
ECM/BCM: Impedance Measured Vs. Isotope Measured	58
Na_e/K_e: Impedance Measured Vs. Isotope Measured	65
BCM: Impedance Measured Vs. Isotope Measured	70
ECM: Impedance Measured Vs. Isotope Measured	75

FAT: Impedance Measured Vs. Isotope Measured 80

CONCLUSIONS: 85

DISCUSSION 90

REFERENCES 98

APPENDIX 100

2.LIST OF ABBREVIATIONS

	Meaning
%BF	percentage of body fat
^{22}Na	sodium-22 isotope
^{3}H	tritium isotope
BCM	body cell mass
D_2O-TBW ..	total body water measured by deuterium dilution
Db	body density
ECFV	extracellular fluid volume
ECM	extracellular mass
ECM/BCM ..	the ratio of extracellular mass to body cell mass
Eq	equation
FFM	fat free mass, equivalent to the lean body mass
Ht	height
Ht^2/R	the sqare of height divided by the resistance
K_e	total exchangeable potassium
LBM	lean body mass
Na_e	total exchangeable sodium
Na_e/K_e ...	the ratio of total exchangeable sodium to exchangeable potassium, defined on page 26 as an index of the nutritional state.
P	probability in the sense of statistical significance
R	electrical resistance
r	Pearson's coefficient of correlation
R_{Na+K}	ratio of the sodium plus potassium content divided by the water content of a tissue specimen, in the context of section 5.6.
SEE/mean .	standard error of the estimate divided by the mean of the dependant variable
TBK	total body potassium
TBW	total body water
TEI	transthoracic electrical impedance
X_c	electrical reactance
Z	impedance
Z/elec.dist.	impedance value divided by the distance between the inner pair of electrodes (in context of page 19)

3.PREFACE

3.1.INTRODUCTION.

In the past decade the medical community has become increasingly aware of the importance of the nutritional state in determining postoperative outcome, host resistance to infection, and capacity for tolerating a catabolic stress[1]. Accordingly, it is important to have a simple, safe and accurate technique for assessing the nutritional state.

The measurement of body composition provides a useful index of the nutritional state[2]. Body composition in the nutritional sense refers to a partitioning of the body weight into three main compartments; the body cell mass (BCM), extracellular mass (ECM) and fat. The BCM is the intracellular protoplasm and the metabolically active, energy producing component of body composition. The ECM comprises plasma , lymph and interstitial fluid. The sum of the ECM and BCM is the lean body mass (LBM). Since fat is relatively anhydrous, the LBM contains virtually all of the total body water (TBW).

The body composition techniques currently used in nutritional research, such as isotope dilution, whole-body counting of potassium-40, neutron activation analysis for total body calcium and

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[1] Muller JM, Keller HW, Brenner U, Walter M, Holzmuller W. Indications and Effects of Preoperative Parenteral Nutrition. World J. Surg. 1986;10:53-63.

[2] Shizgal HM. The effect of malnutrition on body composition. Surgery 1981;152:22-26.

nitrogen, computerized tomography and densitometry, are impractical for general clinical use. Simpler methods such as anthropometry and fat estimation by infrared or ultrasound are not sufficiently accurate.

Impedance plethysmography, since its commercial introduction in 1981, is rapidly becoming popular as a safe, simple and non-invasive measure of body composition and might gain widespread clinical use if further refinements in accuracy are achieved.

Impedance plethysmography connotes the measurement of the resistance and reactance to an electrical current applied to a living organism. The intra- and extracellular fluids of the body comprise an ionic conductive volume that offers resistance (R) to the flow of current, according to Ohm's law:

$$\text{(Resistance)} \quad R = \frac{V}{I} \quad \begin{matrix}\text{(voltage)} \\ \text{(current)}\end{matrix}$$

Because fat contains little water, conductance occurs primarily through the LBM.

Nyboer, who pioneered research relating impedance measurements to biological function in the 1940's, conceptualized that the reactance (X_c) measurement might be related to the body cell membranes acting as the dielectric of a capacitor. Basic electronics tells us that reactance is the apparent resistance of a capacitor in an AC circuit, and that its value decreases as the applied frequency increases, according to the proportion:

$$X_c \approx \frac{T}{6.28\ F\ k\ A}$$

where T is the thickness of the dielectric, F is the frequency and A is the area of one of the dielectric plates. At low frequencies (~ 1 kHz) of current applied to the body, the current passes mainly through the extracellular fluid while at higher frequencies (>500 kHz) it passes through both the extracellular and intracellular compartments. The impedance plethysmograph currently used by most investigators delivers a 50 kHz current of 800 microamps. This signal is clinically safe for measuring virtually any subject and is painless.

Nyboer was the first investigator to demonstrate that electrically measured biological volumes were inversely related to impedance (Z), resistance and reactance[3]. He proposed the equation:

$$Z = \sqrt{R^2 + X_c^2}$$

Because X_c is relatively much smaller than R, the R value is approximately equal to Z.

Bioelectrical resistance is mathematically related to the volume of the conductor, as shown in the following steps:

(a) Given $R \approx pL/A$

where L is the conductor length, A is the cross-sectional area of the conductor and p is volume resistivity,

(b) Multiplying equation A by L/L gives $R \approx pL^2/AL$

where AL is the volume (V). Substituting V for AL gives

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[3] Nyboer J. Electrical Impedance Plethysmography. Springfield, IL: CC Thomas, 1970, 2nd edition.

$R \approx pL^2/V$, and rearranging gives

(c) $V \approx pL^2/R$

Because of the complex geometry and bio-electrical composition of the human body, equation (c) is likely a simplistic approximation, but it is pertinent in that investigators[4] have found that the regression relationship between R and the isotope-measured total body water is strengthened best by correcting for the subject's geometry as Ht^2/R.

3.2.HISTORICAL REVIEW

Early research work on bioimpedance was focussed on vascular and respiratory applications. In 1907 Cremer[5] noted that capacitor measurements varied with the beat of a frog's heart. In 1932 Atzler[6] placed capacitor plates on either side of the thorax of a human and recorded dielectric changes related to cardiac activity. Mann[7] reported in 1937 that continuous impedance measurements of limbs varied rhythmically with the pulse. In 1940, Nyboer[8] designed

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[4] Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1985;41:810-817.

[5] Cremer H. Uber die Registrierung Mechanischer Vorgange auf electrischem Wege, speziell mit Hilfe des Saitengalvonometers und Saitenelektrometers. Munchen Med Wschr 1907; 54:1629.

[6] Atzler E, Lehmann G. Uber ein neues Verfahren zur Darstellung der Herztatigkeit (Dielektrographie). Arbeitsphysiol 1932; 5:536.

[7] Mann H. Study of Peripheral Circulation by Means of an Alternating Current Bridge. Proc Soc Biol Med. 1937; 36:670.

[8] Nyboer J. Electrical Impedance Plethysmography. Springfield, IL: CC Thomas, 1970, 2nd edition.

an impedance recorder to measure cardiac output. Thomasset[9], reporting in the early 1960's, was the first to use impedance in measuring total body water, and Hoffer[10] further defined the relationship between impedance and TBW in 1969.

There was little progress in this area during the 1970's. In 1985, Lukaski and co-workers[11] reported on comparisons between impedance measurements, LBM measured by deuterium, and total body potassium (TBK) measured by whole body counting in 37 healthy men. They found strong correlations between 1/R and LBM, TBW and TBK, optimised by correcting for the subject's height (as Ht^2/R).

To differentiate the normally nourished from the malnourished state, it is necessary to know the size of the body cell mass (BCM) relative to the extracellular mass (ECM). In the normal state, the ratio ECM/BCM is approximately 1:1, so it is understandable why resistance correlated well with TBK in Lukaski's study of healthy men, since it correlated strongly with LBM. However, in the malnourished state, the BCM becomes much smaller relative to the ECM.

One purpose of our study was to determine whether impedance could measure the relative changes in BCM and ECM that occur

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[9] Thomasset A. Bio-electrical properties of tissues. Lyon Med 1963;209:1325-52.

[10] Hoffer EC, Meador CK, Simpson DC. Correlation of whole-body impedance with total body water. J Appl Physiol 1969;27:531-4.

[11] see footnote #4

with malnutrition. Since resistance was related to LBM and TBW as shown by prior research, our curiosity was focussed on the other component of impedance, reactance.

Our second objective was to determine whether the relationship between R and LBM is accurate in malnourished states

3.3. THE PRESENT STUDY: ORIGINAL FINDINGS

Impedance and body composition measurements by multiple isotope dilution were performed on 64 hospitalized patients, the majority of whom were malnourished according to isotope-dilution results.

Reactance was found to correlate fairly strongly with the ratio ECM/BCM ($r = .70$), as $1/X_c$, from data analysis based on the entire group of 64 patients. This relationship for reactance is a new observation and it is useful because it enables a calculation of BCM and ECM based on impedance measurements. The mathematics are as follows:

Given that $LBM = ECM + BCM$,

then, dividing by BCM yields

$$\frac{LBM}{BCM} = \frac{ECM}{BCM} + 1$$

then solving for BCM gives

$$BCM = \frac{LBM}{(ECM/BCM + 1)}$$

where LBM is determined by $1/R$ and ECM/BCM by $1/X_c$.

ECM is then solved as LBM - BCM.

Similar to the findings of other investigators, the regression relating $1/R$ to LBM was optimised by correcting for the geometry of the subject, as Ht^2/R. The regression relating $1/X_c$ to ECM/BCM

was improved best by including Ht^2 as a second independent variable.

The measurement of LBM by Ht^2/R in the malnourished subjects was not as precise ($r = .83$, SEE/mean = 9.8% [12]) as in the normally nourished subjects ($r = .97$, SEE/mean = 7.1%). The measure of ECM/BCM by $1/X_c + Ht^2$ was comparable in the malnourished group ($r = .64$, SEE/mean = 11.7%) and the normal group ($r = .60$, SEE/mean = 9%).

The measure of ECM/BCM by $1/X_c$ was slightly better for the total group of 64 subjects ($r = .7$, SEE/mean = 23.8%) than for the malnourished subjects ($n=41$, $r=.58$, SEE/mean = 19.7%) but was poor for the normally nourished ($n=23$, $r = .25$, SEE/mean = 17.1%).

While reactance is certainly a measure of ECM/BCM, it is not sufficiently precise, using current techniques, to measure small changes in body composition.

3.4.ACKNOWLEDGEMENTS

Much of the lab work relating to processing of isotope-dilution specimens was done by Mr. Joseph Vincelli B.Ed. and Miss Linda Grey, two McGill University technicians associated with the Body Composition Laboratory of the Royal Victoria Hospital.

This study was funded by a grant from the Medical Research Council of Canada.

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[12] For regression analyses, the standard error of the estimate divided by the mean of the dependant (Y axis) value, is abbreviated as **SEE/mean** Y and is a measure of the accuracy of the regression relationship.

4.LITERATURE REVIEW

4.1.IMPEDANCE MEASUREMENTS IN THE NORMALLY NOURISHED: RESISTANCE CORRELATES STRONGLY WITH LBM, TBW AND BCM, BUT REACTANCE HAS NO PREDICTIVE VALUE.

Lukaski and coworkers[13] compared whole body resistance and reactance measurements with fat-free mass assessed by hydrodensitometry, total body water (TBW) determined by D_2O dilution, and total body potassium (TBK) from whole body counting, in 37 healthy male volunteers.

The resistance and reactance measurements were made with the RJL Systems plethysmograph, using two pairs of electrodes attached to the subject's hand and foot and an excitation current of 800microamperes at 50kHz. Comparison measurements were made using electrodes placed on the ipsilateral and contralateral sides of the body.

Their results are:

1. Electrode placement influenced the observed R but not the X_c values. Electrode configurations using the right arm had significantly lower ($P < 0.05$) R values than did the arrangements using the left arm, perhaps because in 32 out of the 37 subjects the right arm was dominant. The investigators used the lowest observed R value as representative of an individual on further analysis. The test-retest correlation coefficient was 0.99 for a

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[13] Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1985;41:810-817

single measurement and the reliability coefficient for a single measurement over 5 days was 0.99. As shown in Table 1 , strong relationships were found between R values and FFM ($r = -0.86$), TBW ($r = -0.86$), and TBK ($r = -0.79$). Significant ($P < 0.01$) increases in the correlation coefficients were observed when the predictor Ht^2/R was regressed against FFM ($r = 0.98$), TBW ($r = 0.95$), and TBK ($r = 0.96$).

Table 1 Correlation matrix of selected variables; measurements of 37 normally nourished subjects.

	Mass	FFM	Fat Mass	Density	TBK	TBW	Wt/Ht²	R	Xc	Z
Height	.63									
FFM	.91									
FatMass	.85	.55								
% Fat	.65	.29	.93							
Density	-.65	-.29	-.92							
TBK	.87	.97	.48	-.22						
TBW	.90	.96	.56	-.31	.96					
Wt/Ht²	.94	.79	.89	-.75	.71	.80				
R	-.76	-.86	-.45	.23	-.79	-.86	-.77			
Xc	-.50	-.54	-.31	.16	-.54	-.55	-.47	.71		
Z	-.77	-.86	-.45	.22	-.83	-.86	-.78	.99	.70	
Ht²/R	.86	.98	.49	-.22	.96	.95	.73	-.89	-.64	-.89

FFM : fat-free mass, equivalent to the lean body mass
TBK : total body potassium
TBW : total body water
R : whole body resistance
Xc : whole body reactance

3. Compared to resistance, reactance correlated poorly with TBK, FFM, Fat mass, TBW and density. The correlation coefficient relating R and impedance (Z) values ($r = 0.99$) was significantly greater ($P < 0.001$) than that between X_c and Z ($r = 0.70$). Thus, the contribution of X_c in measuring body composition was considered

negligeable.

4.2.FAT-FREE MASS DETERMINATION BY IMPEDANCE COMPARED TO DENSITOMETRY AND ANTHROPOMETRY METHODS

To further validate the relationship between bioelectrical conductance (ht^2/R) and fat-free mass determined by densitometry, Lukaski and coworkers[14] studied 114 male and female volunteers, aged 18-50 years, with a wide range of lean body mass (34-96kg) and percent body fat (4-41%). Anthropometry data, comprising skinfold thicknesses at the triceps, biceps, suprailiac crest, and scapula, were also collected in order to compare the prediction errors of body fatness derived from the tetrapolar impedance method and skinfold thickness, relative to hydrodensitometry.

Body density was determined from hydrostatic weighing with simultaneous measurement of residual volume by nitrogen washout of the lungs. Percent body fat (%BF) was calculated from body density (Db) according to the Brozek[15] formula:

$$\%BF = 100[(4.57/Db)-4.142].$$

Fat-free mass was calculated as the difference between body mass and fat mass, where fat mass equaled body mass times percent body fat.

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[14] Lukaski HC, Bolonchuk WW, Hall CB, Siders WA. Validation of tetrapolar bioelectrical impedance method to assess human body composition. J Appl Physiol 1986;60(4):1327-1332.

[15] Brozek J, Grande F, Anderson JT, Keys A. Densitometric analysis of body composition: revision of some quantitative assumptions. Ann NY Acad Sci 1963;110:113-40.

Bioelectrical impedance was measured by the same 800 microampere, 50kHz technique as the previous study, employing two pairs of wrist and ankle electrodes and taking the lowest observed resistance value as representative of an individual.

The results are:

1. Fat-free mass determined by densitometry correlated highly with fat-free mass predicted from impedance using the equation developed in the previous study of 37 male volunteers, with an r of .98 for males. For females, the correlation between densitometry-measured fat-free mass and values predicted from the combined (previous and present data) male impedance formula was also strong, r = .95. No statistical difference was found between either the slopes or the intercepts of the regression lines relating ht^2/R to fat-free mass of the male and female volunteers.

2. Relative to hydrodensitometry, the impedance estimate of body fatness had a lower predictive error or standard error of estimates than the anthropometric technique (2.7 vs. 3.9%). The r value was .93 for the correlation between densitometry and impedance measured percent body fat, and .88 for the correlation between densitometry and anthropometrically measured percent body fat.

4.3.COMPARISON OF IMPEDANCE MEASUREMENTS WITH D_2O MEASURED TOTAL BODY WATER IN NORMAL AND OBESE SUBJECTS

Kushner and Schoeller[16] compared total body water (TBW) measured by bioelectrical impedance and deuterium-isotope dilution in 58 subjects. They first developed sex-specific and group equations by multiple regression analysis in 10 obese and 10 non-obese men and women, and then prospectively tested the equations in a heterogeneous group of 18 patients.

Bioelectrical impedance measurements were collected using the technique standardized for the model B1A 101, RJL Systems, with a pair of electrodes each on the right hand and foot passing an 800 microampere current at 50kHz. The deuterium-dilution space was determined by saliva sampling before and after oral D_2O administration.

The following observations were made:

1. The mean coefficient of variation for within-day intra-individual bioimpedance measurements was small, at 1.3%.
2. Ht^2/R was the most significant independent predictor of D_2O-TBW, accounting for 94% of the total variability associated with D_2O-TBW (r=.97). The prediction of D_2O-TBW was further improved by adding weight to the multiple regression equation, giving a multiple correlation coefficient r of 0.99 and an

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[16] Kushner RF, Schoeller DA. Estimation of total body water by bioelectrical impedance analysis. Am J Clin Nutr 1986;44:417-424.

improvement in the standard error of the estimate (SEE) from 2.5 to 1.75. Adding age to the equation did not improve the prediction of D_2O-TBW.

3. Compared to the group equation, the male-specific and female-specific equation slightly reduced the SEE and total error, without improving the r values.

4. The equations predicted D_2O-TBW with high correlation for both non-obese and obese males and females; the regression slopes were not statistically different between the obese and non-obese subjects.

5. In cross validating the equations on a prospective population of 18 heterogeneous patients, the correlation coefficients remained excellent (r of .93 to.97) for both the group equation and the sex-specific equations. The difference between the impedance-calculated D_2O-TBW for all equations was not statistically different from the measured D_2O dilution space. The group equation was at least as good or better than sex-specific equations in the prospective portion of the study, suggesting that the use of one group equation for both males and females may be suitable.

4.4.COMPARISON OF DEUTERIUM MEASURED TOTAL BODY WATER WITH IMPEDANCE MEASUREMENTS CORRECTED FOR ELECTROLYTE CONCENTRATION

Schloerb and coworkers[17] also correlated total body water with bio-impedance but they included corrections for electrolyte concentrations in their regression equations.

Total body water was measured in 18 normally nourished adults by urine analysis following oral administration of deuterium. Impedance was measured using the RJL Systems analyzer with electrodes attached to the subject's right wrist and ankle.

TBW correlated strongly with Ht^2/Z ($r = 0.96$), where Z is impedance. Males and females conformed to the same regression equation:

$$TBW = 6.19 + 5683 \ Ht^2/Z$$

TBW correlated less well with impedance (Z)($r = 0.77$), height squared ($r = 0.80$), and body weight ($r = 0.84$).

The electrolyte correction factor for patients with altered serum sodium concentrations was incorporated in the regression as:

$$TBW = 6.19 + 5683 \ Ht^2/[Z + Na(.00719(Na - 1.0061))]$$

However, no mention is made concerning any improvement in accuracy by correcting for the serum sodium. The authors' conclusion that body cell mass can be estimated from total body water predicted by impedance would be untrue in malnourished states where the ratio of extracellular to intracellular water is

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[17] Schloerb PR, Gurian JH, Lord LM, Winiarski EA, Casey CM. Bioimpedance as a measure of total body water and body cell mass in surgical nutrition. European Surg Res 1986;18(S1):3.

not constant.

4.5.EXPERIENCE WITH IMPEDANCE MEASURED USING OTHER ELECTRODE PLACEMENTS AND A 100kHz FREQUENCY

Roos and coworkers[18] compared transthoracic electrical impedance (TEI) and total body extracellular fluid volume (ECFV) in 76 people. They used the IFM/Minnesota impedance cardiograph, model 304A, to measure transthoracic impedance; this device delivers a 100kHz alternating current from an outer pair of four electrodes placed circumferentially around the subject's neck and below the xiphisternal junction. Impedance is measured from a second pair of sensing electrodes, positioned nearer the midline, after 1.5 hours in the supine position and at end-expiratory apnoea. They found that the long recumbent period was necessary to achieve stable readings.

The impedance measurement was corrected for electrode placement by dividing impedance by the distance between the inner pair of electrodes (Z/elec. dist.).

ECFV was estimated as the bromide-82 distribution volume and was divided by the lean body mass as estimated from formulas established by Hume and Weyers using height and weight as the predictor variables.

They found that transthoracic impedance correlated with ECFV changes with an r = -0.76. The correlation between Z/elec.dist. and ECFV/LBM was -0.66 for men and -0.61 for women. They

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[18] Roos JC, Koomans HA, Boer P, Dorhout Mees EJ. Transthoracic electrical impedance as an index of extracellular fluid volume in man. Intensive Care Med 1985;11:39-42

concluded that, for repeated measurements in the same subject, a change in transthoracic impedance is possibly a sensitive index for a change in ECFV.

The Z/elec.dist. value was found to rise with inspiration, and so the measurements were performed at end-expiration. The authors attributed this increase to elongation of the thorax and electrode distance during respiration, since it was unlikely that major fluid shifts were occurring during respiration. They suggest that whole-body impedance(from the neck to the ankles) is less variable and might be more useful in determining ECFV.

4.6.BODY COMPOSITION MEASUREMENTS BY MULTIPLE ISOTOPE DILUTION; THE INDIRECT MEASUREMENT OF TOTAL EXCHANGEABLE POTASSIUM

The isotope-dilution techniques used in our lab for measuring body composition were perfected and validated by Shizgal and coworkers[19].

The technique involves measurement of total exchangeable sodium (Na_e) and total body water (TBW) by isotope dilution, using sodium-22 and tritium (^3H) respectively. Total exchangeable potassium (K_e) is calculated from the following formula:

$$K_e = R_{Na+K}\,(TBW) - Na_e$$

where R_{Na+K} is the ratio of the sodium plus potassium content divided by the water content in a sample of whole blood.

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[19] Shizgal HM, Spanier AH, Humes J, Wood D. Indirect measurement of total exchangeable potassium. Am J Physiol 1977;233(3):F253-259.

The theoretical considerations behind the indirect measurement of K_e are (a) the absence of an osmotic gradient between the intracellular and extracellular compartments, and (b) the observation that the major sources of body water osmolarity are the electrolytes, with sodium and potassium being the principal cations. It was postulated that the ratio (R_{Na+K}) of the sum of the freely exchangeable sodium and potassium divided by the water content would be identical for all tissues within an individual.

This was expressed mathematically as:

Equation A: $R_{Na+K} = \frac{Na_e + K_e}{TBW}$, which on rearranging gives:

Equation B: $K_e = R_{Na+K}(TBW) - Na_e$

Since in all tissues the total content of potassium is freely available for exchange, K_e is equivalent to the total potassium mass, Na_e underestimates the total sodium content of the body because much of the sodium content of bone is unavailable for exchange.

Equation B was used to calculate K_e; R_{Na+K} was calculated by measuring the sodium, potassium, and water content in a sample of whole blood. TBW was by measured by isotope dilution using tritiated water, and Na_e by using sodium-22.

Equation B was validated in a four part experiment. Part I tested the basic assumption that the ratio R_{Na+K} is the same in all tissues, by measuring the total mass of sodium, potassium, and water in muscle, kidney, liver, whole blood, spleen, heart and

lung in 14 normal rats. The tissues were dessicated to a constant dry weight, with the water content calculated as the difference between the wet and dry weights. The electrolyte content was obtained after dissolving the dried residue in nitric acid, with measurement of electrolyte concentration and solution volume. Although slight variations existed between the calculated R ratios for the seven different tissues, the differences were not statistically significant by an analysis of variance.

In part 2, the K_e was determined both indirectly using equation 2 and directly by carcass analysis in 19 normal rats and in four rats with uremia. The Na_e was determined by measuring the specific activity of sodium-22 24 hours after intravenous injection. TBW was measured by dessicating the entire animal to a constant dry weight. The K_e determined indirectly by equation B was compared, as the dependent variable Y, with the K_e measured by carcass analysis, as the independent variable X, in a least squares regression analysis. The actual regression, $Y = 0.99X$, was almost identical to the line of identity, $Y = 1.00X$, and the correlation between the two sets of measurements was excellent, ($r = 0.91$). The standard error of the estimate was 2.25 meq, which was 9% of the mean.

Similar results were obtained in part 3 of the experiment, in which K_e was simultaneously determined indirectly by equation 2 and directly by potassium-42 dilution in 15 normal dogs, five dogs with uremia, and 14 dogs in a hypo-osmolar state induced by pitressin and infusion of large volumes of water. Each animal was

injected intravenously with 15 microcuries of sodium-22, 500 microcuries of potassium-42, and 500 microcuries of tritiated water. The serum concentration of isotopes was determined by differential beta and gamma counting twenty-four hours later, and was corrected for the urinary loss. Comparing the direct and indirect measurements of K_e using the method described for part 2, the regression line was virtually identical to the line of identity. The correlation between K_e determined indirectly and that determined by potassium-42 was excellent (r=0.98). The standard error of the estimate was 47.6 meq, which was 6% of the mean.

In part 4 of the study, K_e was determined simultaneously by potassium-42 dilution and indirectly by the method of equation B in a heterogeneous group of 20 patients, many of whom were terminally ill. The experimental protocol was similar to that described in part 3. There was an excellent correlation (r=0.988) between the Ke measured indirectly and that measured directly by potassium-42. The line of identity and the regression line (Y = 1.02 X) almost coincided. The standard error of the estimate was 141.2 meq, which was 7% of the mean. The high correlation existed in spite of the fact that the K_e of a majority of patients in the group was abnormally low.

Additionally, in 25 normal volunteers K_e was determined indirectly by equation 2 and compared to the K_e measurements reported by Moore [20] obtained by potassium-42 dilution in 33

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[20] Moore FD, Olesen KH, McMurray JD, Parker HV, Ball MR, Boyden CM. The Body Cell Mass and Its Supporting Environment. Body Composition in Health and Disease. Philadelphia: Saunders,

normal volunteers. The indirect measurement of K_e involved the intravenous injection of 500 microcuries of tritiated water and 8 microcuries of sodium-22 to determine TBW and Na_e, respectively. The regression line and 95% confidence limits for the indirectly-determined K_e almost coincide with the regression line and confidence limits of the data published by Moore.

The authors conclude that the indirect measurement of K_e is experimentally validated, noting that the precision of the indirect K_e measurements is not as good as that obtained with potassium-42 dilution. The latter involves a single isotope dilution measurement, while the experimental error of the indirect measurement is the sum of the experimental errors of the measurement of R_{Na+K}, TBW and Na_e. An estimate of the precision of the indirect measurement is the standard error of the estimate of the regression line comparing the values of the direct and indirect techniques. In the group of 20 very ill patients (part 4), the standard error of the estimate was 134.9 meq, which represents 7% of the mean Ke.

The advantages of the indirect measurement of K_e over the direct method using potassium-42 are convenience and cost. The short half-life of potassium-42, 12.5 hours, necessitate frequent expensive shipments and make it inconvenient to use. The counting of potassium-42 is complicated by the need to correct for radioactive decay before and during the counting period. By contrast, the two isotopes used in the indirect measurement of

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1963;13-42 and 531-535.

K_e, sodium-22 and tritium, have half-lives of 950 and 4.5×10^3 days, respectively.

4.7.BODY COMPOSITION IN THE MALNOURISHED STATE

Using the technique described above for the indirect measurement of exchangeable potassium, Shizgal[21] has examined the effect of a chronic catabolic state or starvation on body composition.

Body composition studies were done in 75 patients who appeared clinically malnourished. The red cell mass was determined from the equilibrated concentration of chromium-51 tagged red cells. The plasma and extracellular water volumes were determined from the plot of the logarithm of the plasma concentration of radio-iodinated serum albumin and sodium-22 against time. Total body water was calculated from the equilibrated plasma concentration of tritium-labeled water, and intracellular water was calculated as the difference between total body water and extracellular water. The lean body mass was calculated from the total body water using the assumption that total body water comprises 75% of the lean body mass. Body fat was calculated as body weight minus lean body mass. Body cell mass was calculated from exchangeable potassium as follows:

$$BCM = K_e \times 0.00833$$

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[21] Shizgal HM. The effect of malnutrition on body composition. Surgery 1981;152:22-26.

The extracellular mass was derived as the lean body mass minus the body cell mass.

Another 20 patients were studied before and on the fifth day after an elective operation of moderate severity, usually resection of either the stomach or large intestine. During the initial five days post-operatively, these patients received a daily infusion of 3 liters of a 5% glucose solution containing sufficient electrolytes to maintain electrolyte balance, but no other caloric intake The range of normal body composition was established by isotope dilution studies on 25 normal volunteers.

The results can be summarized as follows.

1. The lean body mass of the 75 malnourished patients was not significantly different from that of the 25 normal volunteers. However, the composition of the lean body mass in the malnourished patients was abnormal, with a marked decrease in the body cell mass and a corresponding expansion of the extracellular mass. The mean body cell mass in the malnourished group was 14 7 $\pm$ 0.1 kg, compared with 24.7 $\pm$ 1.1 kg in the normal volunteers. In the malnourished group, the mean extracellular mass was 31.9 $\pm$ 0.9 kg compared with 25.8 $\pm$ kg in the normal group. In the group of 20 patients where body compositions preoperatively were compared with those at 5 days postop, the body cell mass was reduced by 13.9% while the extracellular mass was increased by 9.6%.

2. In that malnutrition is characterized by a decrease in the body cell mass accompanied by an increase in the extracellular

mass, the ratio of exchangeable sodium to exchangeable potassium (Na_e/K_e) is a sensitive index of nutritional status. In 25 normal volunteers, the mean Na_e/K_e was 0.98 $\pm$ 0.02, with the upper 95% confidence limit of 1.22. This led to a definition of malnutrition as the presence of a Na_e/K_e in excess of 1.22. In the 75 malnourished patients, the mean Na_e/K_e was 1.95 $\pm$ 0.08. In the 20 patients studied before and 5 days following a major operation, the Na_e/K_e increased from 1.04 $\pm$ 0.08 preop to 1.29 $\pm$ 0.11 postop.

Dr. Shizgal reports that a Na_e/K_e greater than 1.22 was virtually always associated with an abnormally decreased body cell mass, and that total parenteral nutrition increases the body cell mass only in those patients with a ratio greater than 1.22.

3. In the group of 20 patients studied pre- and postoperatively, the mean body cell mass decreased by 13.9% while the mean body weight decreased by only 3.9% because of a 9.6% increase in the extracellular mass, demonstrating that body weight changes are not a sensitive measure of the nutritional state. Body weight loss correlates more closely with loss of body fat than with changes in lean body mass or body cell mass.

5.METHODS

5.1.OVERVIEW

Impedance measurements and isotope-dilution body composition

studies were performed on 64 patients of the Royal Victoria Hospital between October 1985 and May 1986. Most of the subjects were clinically malnourished and were referred to the hyperalimentation service for a course of total parenteral nutrition. Approximately 65% of the patients were general surgical, and of these about 15% were critically ill and requiring intensive care. The other 35% of patients were referred from the department of medicine, including the intensive care unit and bone-marrow transplant unit, or from the gynecology and oncology services.

The impedance measurements were performed just prior to the injection of isotopes in each patient.

Written informed consent was obtained for the isotope study and verbal informed consent for the impedance measurements from each subject. The hospital Ethics Committee had previously approved the act of body composition analysis using isotopes.

5.2.IMPEDANCE METHOD

Resistance and reactance were determined using a four-terminal impedance plethysmograph (RJL Systems, model 101, Detroit, MI). The subject was measured in a relaxed, supine position on a bed, with the shoe and sock removed from the right foot. The dorsum of the right hand and foot was gently rubbed with an alcohol swab to defat the skin surface, and four aluminum spot electrodes were applied, one pair on the right hand and the other on the right foot. The proximal detector electrode on the

hand was positioned on the mid-dorsum of the wrist at the level of the ulnar tubercle. The current-introducing electrode was placed overlying the dorsum of the third and fourth metacarpals just proximal to the knuckles. The proximal detector electrode for the foot was positioned on the mid-dorsum of the ankle between the malleoli, while the distal current-introducing electrode was placed 1 cm proximal to the toes overlying the dorsum of the second and third metatarsals. The electrodes were pre-packaged with a layer of electrolyte jelly on the conductive side.

A painless, insensible alternating current of 800 microamperes at 50kHz was passed into the patient by switching on the built-in power supply of the plethysmograph. With another switch set to measure resistance, the plethysmograph displays a digital readout of the sum of the in-phase vectors. With the switch set to reactance, the display is the sum of the out-of-phase vectors. Less than two seconds were required for the digital display to settle at consistent readings for either resistance or reactance, and these were recorded. All recordings were made with the electrodes attached to the right limbs except where this was not feasible due to amputations, wounds or catheter dressings. For such exceptions, both electrode pairs were placed on the left side.

5.3.ISOTOPE-DILUTION METHOD

Body composition was determined using the tritium and

sodium-22 isotope-dilution technique described by Shizgal, as described in section 5.6, which provides an indirect measurement of total exchangeable potassium (K_e). The isotope injections were performed immediately following the impedance measurements for each patient.

The steps in this technique are as follows:

A. Preparation of Isotope Injections

Using sterile technique, 10cc's of tritium (^3H) solution were drawn into a labelled 10 cc plastic syringe tipped with a 22 gauge needle, and 2 cc's of sodium-22 (^{22}Na) solution were drawn into a 3cc plastic syringe tipped with a 25 gauge needle. Each syringe, with capped needle attached, was then weighed on an analytical balance.

B. Drawing of Baseline Samples and Injection of Isotopes

20cc's of blood were drawn from the patient for isotope processing as described below, to provide a measure of background radiation activity prior to the injection of the isotopes.

The 10cc's of ^3H solution and 2cc's of ^{22}Na solution were then injected intravenously into the patient using sterile precautions.

The 10cc's of the ^3H solution comprise a dose of approximately 500 microcuries. The radiation to the patient is 29 millirads assuming a biological half life of 10 days. The 2cc's of ^{22}Na are about 10 microcuries, exposing the patient to 96 millirads assuming a half-life of 10 days. The total radiation dose of 125 millirads is approximately equivalent to that of two liver-spleen scans.

The isotope syringes were reweighed following injection, with the difference between the full and empty weights used to calculate the precise amount of isotope administered.

C. Processing of Samples

20cc's of blood were drawn at 4 hours and 24 hours following the isotope injections. All urine and drainage fluids, such as from nasogastric tubes and wound or abscess sumps, were also collected during the 24 hour period following isotope injections.

The blood samples were centrifuged to separate the plasma fraction from the cell fraction. 3cc's of plasma were pipetted into each of two plastic gamma-counter vials. Another 3cc's of plasma were added to a test-tube containing 3cc's of 10% trichloroacetic acid. This mixture was then stirred and centrifuged, and 1cc of the supernatant was pipetted into each of three glass beta-counter vials containing 10cc's of aquasol.

The gamma urine or drain-fluid samples were prepared by adding 3cc's of the fluid to each of two gamma vials. To prepare the beta samples, the urine or drain-fluid was first decolorized by filtering with activated charcoal. The filtrate was then mixed with an equal volume of trichloroacetic acid, and 1cc of the supernatant was pipetted into each of three beta vials containing 10cc's of aquasol.

The various beta and gamma samples were then loaded into a beta liquid scintillation counter and gamma deep well crystal

detector, respectively, for differential counting of the radioisotope concentrations. Including sodium-22 and tritium standards corresponding to the vial used in preparing the injections made it possible to correct for differences in isotope activity.

The water content of the blood was measured, from the 24 hour specimen, by first determining the protein concentration using a total solids meter and then using a conversion chart relating water concentration to protein concentration.

The serum sodium and potassium concentrations were also determined from the 24 hour sample using either a flame photometer or the biochemistry services of the hospital.

D. Calculating Body Composition from the Isotope Data

The TBW was determined from the relationship:

$$TBW = \left(\frac{^{3}H \text{ counts/min injected} - ^{3}H \text{ counts/min excreted}}{\text{24-hour plasma tritium concentration}} \right)$$

...where the counts/min injected is determined from the amount injected and the activity of the standard, and the counts/min excreted is determined from the volume of urine and drainage fluids and their radioactivities.

The Na_e was determined in a similar manner:

$$Na_e = \left(\frac{^{22}Na \text{ counts/min injected} - ^{22}Na \text{ counts/min excreted}}{\text{24-hour plasma } ^{22}Na \text{ concentration}} \right)$$

Total exchangeable potassium (K_e) was determined from:

$$K_e = R_{Na+K} \times TBW - Na_e$$

...where R_{Na+K} is the ratio of the sum of the sodium plus

potassium content divided by the water content in a sample of whole blood.

The lean body mass (LBM) was determined by assuming that the total body water comprises 75% of the LBM, i.e.

$$LBM = 1.333 \times TBW$$

Body cell mass (BCM) was calculated as $K_e \times 0.00833$, while extracellular mass (ECM) was solved as the difference between the LBM and BCM.

Body fat was calculated as body weight minus LBM.

6.RESULTS

6.1.BASIC DATA AND DESCRIPTIVE STATISTICS

The basic data from isotope-dilution and impedance measurements on 64 patients, sorted according to the Na_e/K_e ratio, are listed in Table 2. The Na_e/K_e has been previously shown to be a useful index of the nutritional state (footnote 17, section 5.7), the upper limit of the normal nutritional state being a ratio not greater than 1.22. By this criterium, 41 of the 64 patients were malnourished ($Na_e/K_e > 1.22$) and 23 were normally nourished.

The relative sizes of the BCM, ECM and fat partitions of body composition for the whole study group and the normal and malnourished subgroups are shown as a bar graph of means in Figure 1.

Table 2. Body composition measurements, by isotope dilution and impedance, of 64 subjects, 41 of whom were malnourished as defined by a Na_e/K_e ratio > 1.22.

Nutr.State	Study No.	Sex	Age	FBW(Kg)	LBM(Kg)	Na_e/K_e	BCM(Kg)	ECM(Kg)	FAT(Kg)	Ht(cm)	Weight(Kg)	R(ohm)	X_c(ohm)
normal	3309	M	34	40.36	55.28	.72	29.22	26.06	2.72	180.34	58	537	57
normal	3276	M	26	41.05	56.23	.72	31.49	24.74	7.27	177.80	63.64	479	71
normal	3337	M	57	42.60	58.35	.77	31.45	26.90	30.25	185.42	88.60	605	73
normal	3307	M	25	38.34	52.52	.83	27.60	24.91	13.25	177.80	65.77	533	56
normal	3240	M	52	39.65	54.32	.83	27.98	26.34	41.84	187.96	96.36	580	69
normal	3242	F	48	48.92	67.01	.85	34.34	32.67	28.70	182.88	95.91	450	50
normal	3336	F	27	27.51	37.68	.85	19.07	18.62	9.32	157.48	47	767	81
normal	3308	M	23	35.14	48.14	.89	24.26	23.88	9.01	182.88	57.15	610	55
normal	3338	M	63	56.47	77.36	.91	37.19	40.16	26.14	173.99	105.50	313	37
normal	3249	F	61	34.19	46.84	.92	23.14	23.70	6.66	160.02	53.50	656	48
normal	3257	F	29	32.86	45.02	.92	21.83	23.18	23.02	167.64	68	633	57
normal	3269	M	57	38.14	52.25	.94	25.10	27.15	9.75	180.34	62	587	56
normal	3237	F	19	31.26	42.82	.94	20.13	22.69	12.52	167.64	55.45	646	77
normal	3321	M	37	48.41	66.31	.95	32.67	33.64	15.34	177.80	81.65	420	46
normal	3239	M	60	46.08	63.12	.97	29.47	33.66	32.14	180.34	95.45	496	55
normal	3270	M	46	33.64	46.08	.99	21.25	24.84	19.69	177.80	65.91	565	58
normal	3334	M	60	39.18	53.67	1.07	23.28	30.39	9.03	165.10	62.70	488	40
normal	3329	F	27	26.15	35.82	1.10	16.01	19.81	9.54	157.48	45.36	796	79
normal	3290	M	57	39.08	53.53	1.11	22.78	30.75	11.47	180.34	65	551	50
normal	3324	F	30	42.41	58.10	1.17	24.81	33.29	3.14	176.53	61.24	522	38
normal	3248	M	66	31.90	43.69	1.17	17.82	25.87	18.00	154.94	61.82	708	45
normal	3330	F	63	26.93	36.89	1.17	16.02	20.87	20.11	160.02	57	716	58
normal	3267	F	57	25.84	35.39	1.20	14.23	21.16	20.11	162.56	55.55	793	84
malnour.	3306	M	86	33.17	45.44	1.23	19.50	25.95	10.56	175.26	56	608	37
malnour.	3332	M	74	28.12	38.52	1.25	17.00	21.52	16.48	170.18	55	508	36
malnour.	3282	M	60	34.50	47.26	1.28	18.74	28.52	12.74	165.10	60	543	63
malnour.	3262	M	44	47.48	65.04	1.29	25.80	39.24	21.36	180.34	86.36	390	35
malnour.	3250	F	58	35.38	48.47	1.30	19.35	29.12	49.96	157.48	98.64	425	46
malnour.	3251	M	60	31.92	43.72	1.32	16.90	26.82	12.78	157.48	52	577	69
malnour.	3247	M	70	30.12	41.26	1.33	16.13	25.13	9.74	167.64	51	626	42
malnour.	3292	F	43	36.97	50.65	1.34	19.51	31.14	.85	170.18	51.50	564	32
malnour.	3273	M	44	40.79	55.88	1.35	21.60	34.28	29.12	180.34	85	471	52
malnour.	3243	F	75	24.53	33.61	1.36	12.82	20.79	14.02	162.56	47.73	883	49
malnour.	3289	F	64	30.83	42.23	1.36	16.80	25.43	19.01	170.18	61.36	624	54
malnour.	3284	F	31	29.27	40.09	1.37	14.81	25.28	12.98	154.94	53.18	672	46
malnour.	3335	F	73	21.03	28.80	1.38	10.67	18.13	10.50	152.40	39.30	1046	72
malnour.	3319	F	30	32.19	44.09	1.38	16.99	27.11	13.06	176.53	57.15	629	66
malnour.	3258	F	66	32.80	44.93	1.39	17.50	27.43	50.78	162.56	95.91	473	46
malnour.	3287	M	50	29.57	40.50	1.40	15.79	24.71	20.00	165.10	60.50	613	41
malnour.	3265	F	31	25.28	34.63	1.43	13.36	21.27	14.97	154.94	49.55	671	49
malnour.	3256	F	43	25.07	34.34	1.44	17.59	16.75	17.66	165.10	52	539	32
malnour.	3259	F	78	24.43	33.46	1.44	12.19	21.27	32.94	152.40	66.36	636	33
malnour.	3310	F	63	30.06	41.18	1.49	14.94	26.24	10.32	154.94	51.50	696	41
malnour.	3303	F	31	34.18	46.83	1.52	15.72	31.10	4.42	154.94	51.25	805	53
malnour.	3320	M	74	29.78	40.79	1.53	15.22	25.57	16.11	170.18	56.90	612	31

Table 2, continued from previous page

Nutr.	State	Study No.	Sex	Age	TBW(Kg)	LBM(Kg)	H_e/H_s	BCM(Kg)	ECM(Kg)	FAT(Kg)	Ht(cm)	Weight(Kg)	R(ohm)	X_c(ohm)
malnour.		3244	F	37	39.07	53.51	1.53	18.64	34.88	36.99	162.56	90.50	509	31
malnour.		3261	F	37	36.22	49.62	1.55	17.43	32.19	40.88	162.56	90.50	482	26
malnour.		3304	M	74	32.00	43.84	1.55	16.53	27.31	12.16	170.18	56	575	25
malnour.		3254	F	85	31.73	43.47	1.59	15.09	28.38	23.83	157.48	67.27	587	36
malnour.		3325	M	74	31.05	42.53	1.66	15.05	27.48	13.47	170.18	56	513	40
malnour.		3326	F	73	22.40	30.68	1.74	10.32	20.36	9.82	152.40	40.50	792	42
malnour.		3236	F	85	32.47	44.48	1.82	14.32	30.16	22.88	157.48	67.50	547	31
malnour.		3278	M	65	39.83	54.56	1.82	18.27	36.29	8.49	162.56	63.18	389	31
malnour.		3315	M	78	33.67	46.12	1.88	13.83	32.29	11.18	172.72	57.30	541	31
malnour.		3316	M	70	37.62	51.53	1.88	16.92	34.61	23.47	172.72	75	532	32
malnour.		3272	F	76	26.24	35.95	1.96	11.28	24.67	29.82	165.10	65.91	596	56
malnour.		3305	M	69	48.58	66.55	1.96	21.24	45.31	9.45	172.72	76	401	18
malnour.		3238	F	76	29.32	40.17	2.05	11.44	28.73	22.83	165.10	63.64	483	27
malnour.		3255	F	76	29.90	40.95	2.08	11.98	28.98	31.44	165.10	72.41	559	33
malnour.		3279	F	63	37.02	50.72	2.19	14.64	36.07	9.28	154.94	60	582	35
malnour.		3268	M	69	51.00	69.87	2.33	19.22	50.65	8.13	170.18	78.18	350	18
malnour.		3271	M	79	34.34	47.04	2.64	12.08	34.96	.96	157.48	48	622	27
malnour.		3241	F	70	33.56	45.97	2.69	11.58	34.39	4.03	157.48	51	399	19
malnour.		3283	M	70	48.20	66.03	2.77	17.68	48.35	9.26	172.72	52.73	393	24

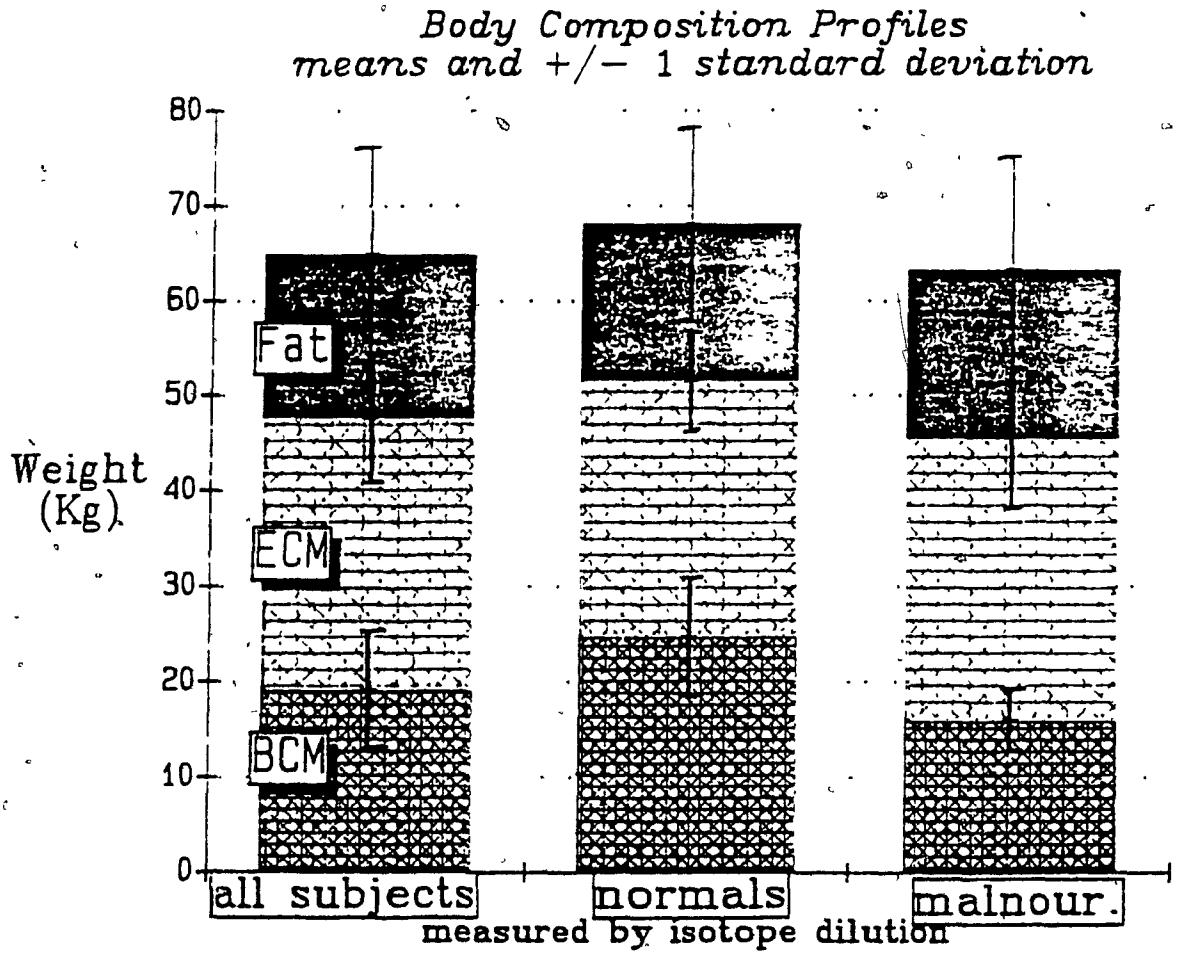

Figure 1.
Bar Graph of the Means of Body Composition Profiles with vertical lines indicating ± 1 standard deviation for BCM, ECM and FAT.
all subjects, n=64
normally nourished (Na_e/K_e not > 1.22), n=23
malnourished (Na_e/K_e > 1.22), n=41

The body composition profile of the normally nourished group was not significantly different from that of 25 previously studied healthy volunteers. The malnourished group had a significantly smaller BCM than the normally nourished group, ($P<.05$). The size of the LBM is represented as the combined height of the ECM and BCM bars, and the mean body weight is the total height of the bars (BCM + ECM + Fat). The mean body weight, LBM and fat sizes were not significantly different between the normal and malnourished groups, but there is a marked difference in the relative sizes of the BCM and ECM.

6.2. RELATIONSHIPS BETWEEN RESISTANCE, TBW AND LBM

Relationships were sought between the various isotope-derived components of body composition, as the dependent variable, and the impedance measurements as the independent variable. Referring to Table 3, which lists a correlation matrix for all 64 subjects, resistance (R) correlated best (as 1/R) with LBM and TBW ($r = .78$).

Table 3. Correlation matrix of selected variables, data from all patients, n=64.

	TBW	LBM	Ht_e/I_e	ECM/BCM	BCM	ECM	FAT	Ht(cm)	Ht^2	Wt(kg)	1/Res	Ht^2/I	$1/I_c$
TBW	1												
LBM	1	1											
Ht_e/I_e	-.07	-.07	1										
ECM/BCM	-.08	-.06	.97	1									
BCM	.77	.77	-.65	-.68	1								
ECM	.81	.81	.49	.49	.24	1							
FAT	.05	.05	-.13	-.11	.10	-.02	1						
Ht(cm)	.62	.62	-.39	-.44	.73	.27	.07	1	Ht^2	Wt(kg)	1/Res	Ht^2/I	$1/I_c$
Ht^2	.62	.62	-.40	-.44	.74	.26	.07	1	1				
wt(kg)	.65	.65	-.20	-.18	.58	.45	.77	.45	.45	1			
1/R	.78	.78	.24	.19	.44	.78	.18	.36	.35	.61	1		
Ht^2/R	.88	.88	.03	-.03	.65	.73	.16	.67	.66	.65	.93	1	
$1/I_c$	.28	.28	.75	.70	-125	.66	-.11	-.11	-.12	.07	.56	.39	1

The relationship between 1/R and ECM is not as suitable, as will be shown later in this section.

Figures 2 and 3 demonstrate the scatterplots comparing 1/R with TBW and LBM. The normal subjects are distinguished from the malnourished as indicated by the legend.

The following regression formulas were developed and are represented graphically as the regression line in each of the plots. The ratio of the standard error of the estimate to the mean of the dependent (Y) value (SEE/mean Y) is presented as a measure of the recision of the regression prediction.

	Equation	r	P<	SEE/mean Y
Eq1.	TBW = 13912.05 x 1/R + 9.56	0.78	.001	13.5%
Eq2.	LBM = 19059.66 x 1/R +13.09	0.78	.001	13.5%

The relationships between 1/R and TBW, and between 1/R and LBM, are best improved by taking into account the subject's eometry as height^2, with the r improving to .88. The resultant formulas are:

	Equation	r	P<	SEE/mean Y
Eq3.	TBW = 0.44 x Ht^2/R + 11.99	0.88	.001	10.5%
Eq4.	LBM = 0.61 x Ht^2/R + 16.42	0.88	.001	10.5%

The correlation between Ht^2/R and ECM (r = .73) is weaker than the previously noted correlation between 1/R and ECM.

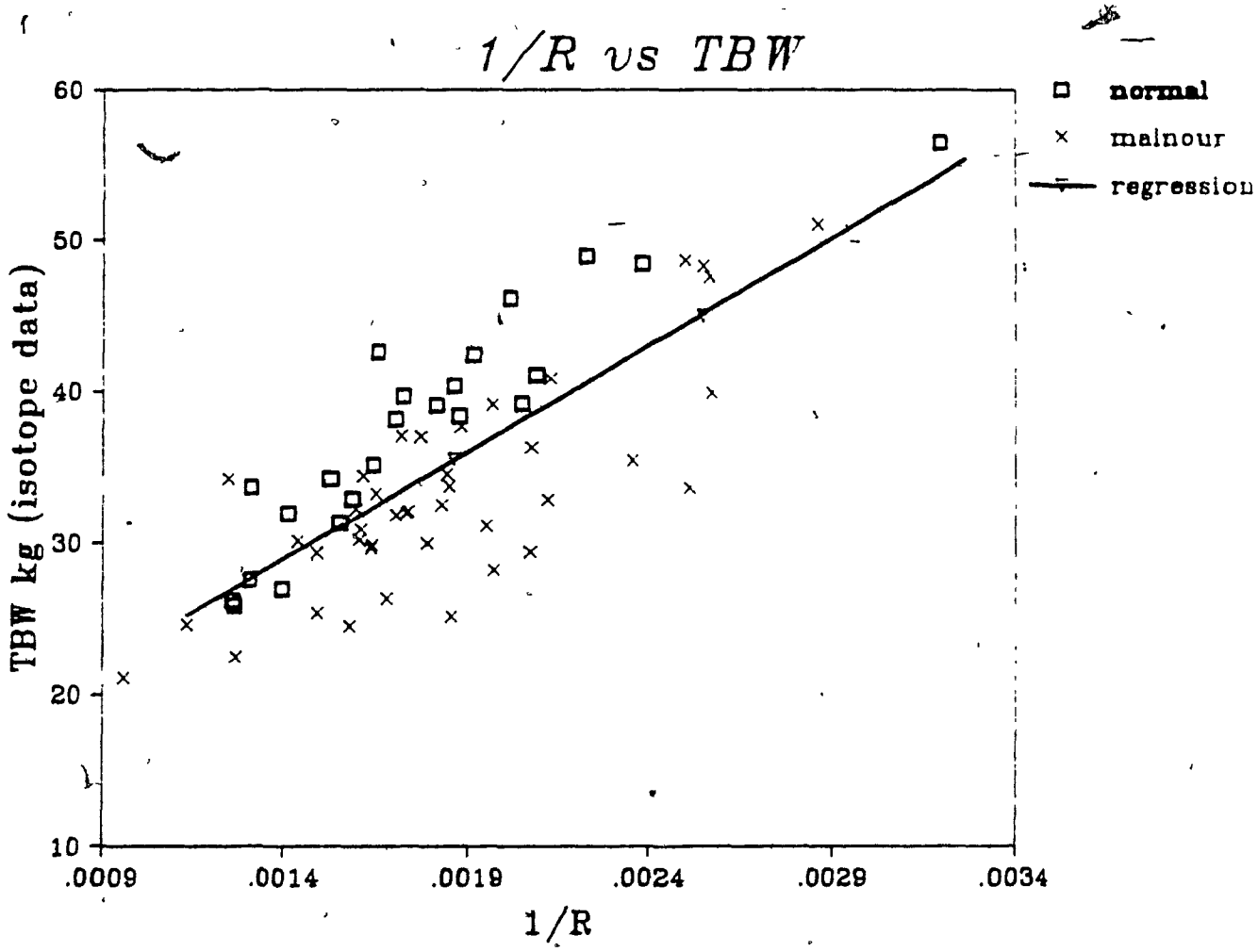

Figure 2.
Scatterplot comparing 1/resistance with TBW measured by isotope dilution, and showing the distribution of normal and malnourished points. The regression line is calculated from Equation 1

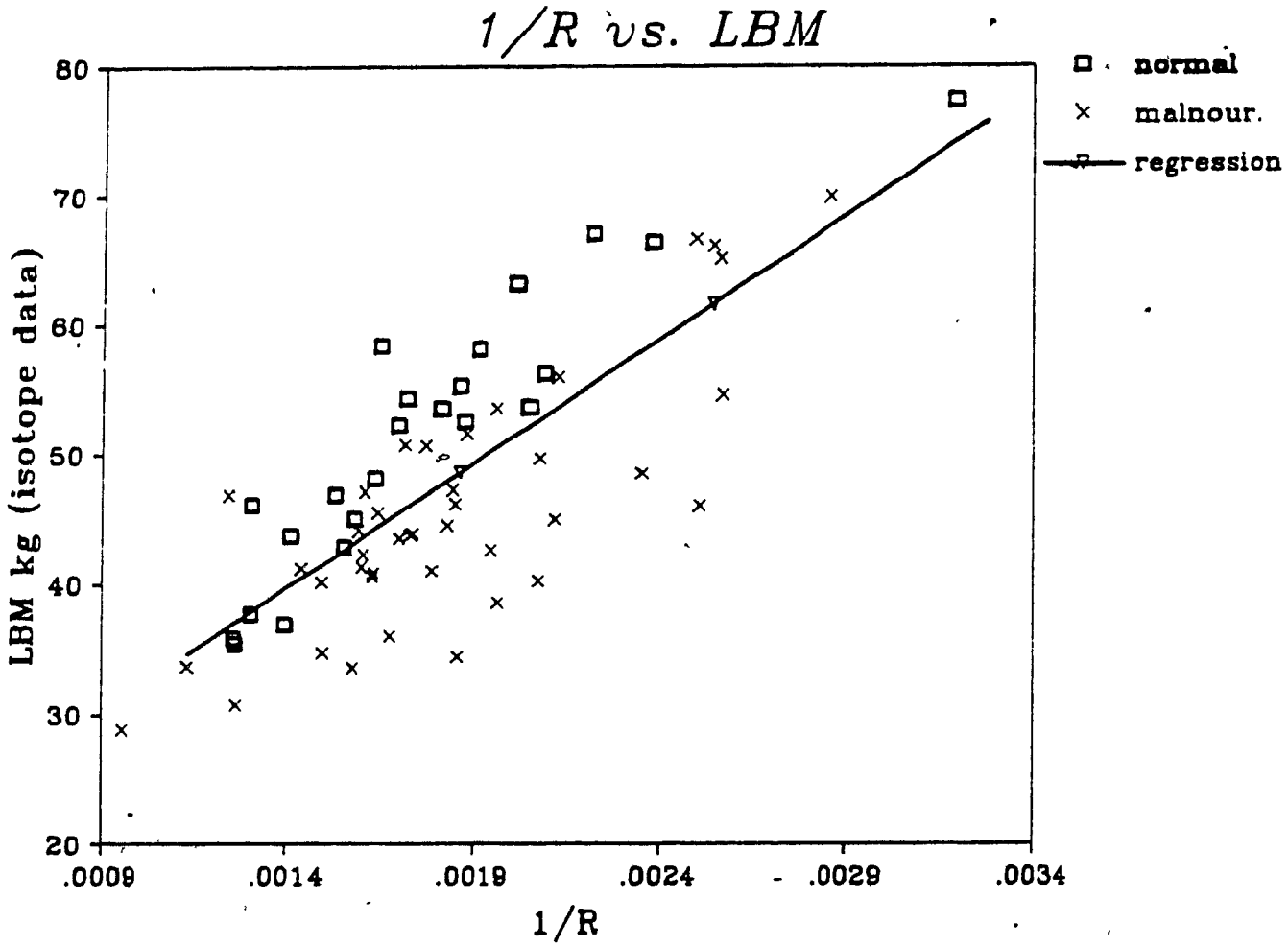

Figure 3
Scatterplot comparing 1/resistance with LBM measured by isotope dilution, and showing the distribution of normal and malnourished points. The regression line is calculated from Equation 2.

Referring again to Table 3, 1/R is found to correlate fairly strongly with weight (r=.61). However, including weight as a second independent variable neither improves the r nor the precision (SEE/mean Y) of the relationship between Ht^2/R and $\overline{LBM}$ or TBW.

6.3.RELATIONSHIPS BETWEEN REACTANCE, Na_e/K_e AND ECM/BCM

Referring again to Table 3, reactance (as $1/X_c$) was found to correlate best with the ratios of Na_e/K_e and ECM/BCM (r =.75 and .70 respectively) for the total group of 64 subjects. This is a new observation in that other investigators had considered the predictive value of X_c as negligeable, despite Nyboer's original hypothesis that reactance might measure the effect of cell membranes acting as a dielectric.

Comparing the correlation matrices of Tables 4 and 5 in which the normal subjects are analyzed separately from the malnourished, it is apparent that the relationships between $1/X_c$ and Na_e/K_e or ECM/BCM are weak in the normal group. Reactance is inaccurate in predicting small changes in Na_e/K_e or ECM/BCM.

Figure 4 shows the scatterplot comparing $1/X_c$ with Na_e/K_e.

The regression formulas relating Na_e/K_e and ECM/BCM with $1/X_c$, based on all 64 subjects, are:

Equation	r	P<	SEE/mean Y
Eq5. $Na_e/K_e = 35.84/X_c + 0.51$	0.75	.001	22.7%
Eq6. $ECM/BCM = 36.98/X_c + 0.68$	0.70	.001	23.8%

Table 4. Correlation matrix of selected variables, data from the 23 normally nourished subjects.

	TBW	LBM	Na_e/K_e	ECM/BCM	BCM	ECM	FAT	Ht	Ht^2	Wt	1/R	Ht^2/R	$1/X_c$
TBW	1												
LBM	1	1											
Na_e/K_e	-.39	-.39	1										
ECM/BCM	-.38	-.38	.97	1									
BCM	.94	.94	-.66	-.66	1								
ECM	.92	.92	-.02	-.00	.74	1							
FAT	.30	.30	-.10	-.09	.30	.27	1						
Ht	.66	.66	-.53	-.53	.72	.49	.31	1	Ht^2	Wt	1/R	Ht^2/R	$1/X_c$
Ht^2	.65	.65	-.54	-.53	.72	.48	.32	1	1				
Wt	.82	.82	-.31	-.30	.78	.75	.80	.61	.61	1			
1/R	.92	.92	-.31	-.29	.85	.87	.19	.44	.43	.70	1		
Ht^2/R	.97	.97	-.42	-.41	.93	.87	.27	.69	.68	.78	.95	1	
$1/X_c$	.59	.59	.26	.25	.37	.76	-.11	.07	.06	.31	.61	.52	1

Table 5. Correlation matrix of selected variables, data from the 41 malnourished subjects.

	TBW	LBM	Na_e/K_e	ECM/BCM	BCM	ECM	FAT	Ht	Ht^2	Wt	1/R	Ht^2/R	$1/X_c$
TBW	1												
LBM	1	1											
Na_e/K_e	.36	.36	1										
ECM/BCM	.34	.34	.94	1									
BCM	.72	.72	-.32	-.38	1								
ECM	.95	.95	.60	.61	.48	1							
FAT	-.06	-.06	-.27	-.24	.12	-.13	1						
Ht	.51	.51	-.07	-.15	.63	.37	-.02	1	Ht^2	Wt	1/R	Ht^2/R	$1/X_c$
Ht^2	.51	.51	-.07	-.15	.63	.37	-.03	1	1				
Wt	.51	.51	-.08	-.03	.54	.41	.80	.27	.27	1			
1/R	.78	.78	.40	.31	.56	.74	.19	.42	.42	.60	1		
Ht^2/R	.83	.83	.30	.21	.68	.75	.11	.69	.69	.56	.94	1	
$1/X_c$	.56	.56	.67	.56	.12	.66	-.18	.18	.18	.18	.65	.58	1

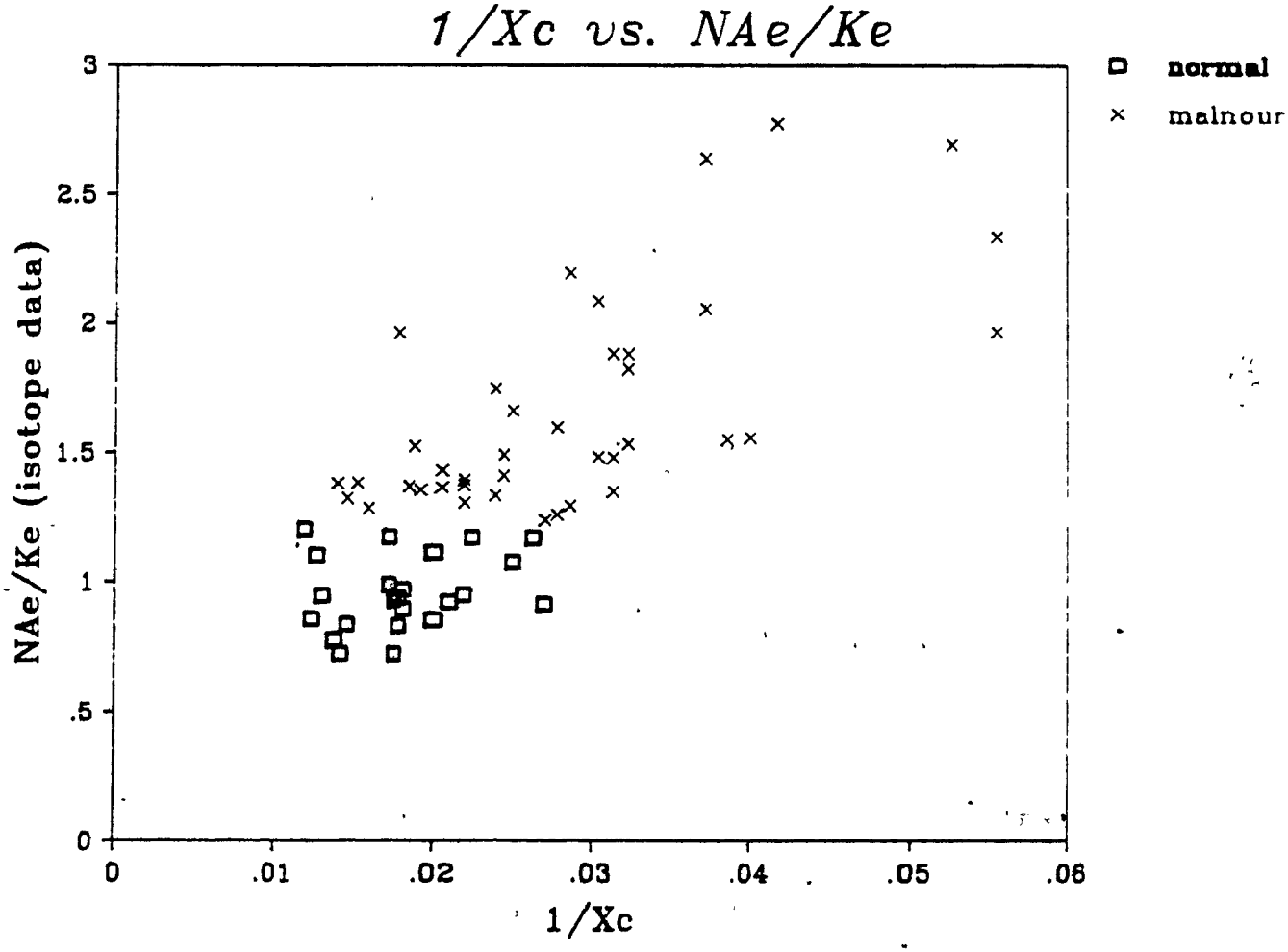

Figure 4
Scatterplot comparing 1/reactance with the Na_e/K_e ratio determined from isotope dilution measurements, and showing the distribution of normal and malnourished points.

The relationships between $1/X_c$ and Na_e/K_e, and between $1/X_c$ and ECM/BCM are improved by including Ht^2 as a second independent variable:

Equation	r	P<	SEE/mean
Eq 7. $Na_e/K_e = 34.09/X_c - .000047(Ht^2) + 1.87$	.81	.001	19.9%
Eq 8. $ECM/BCM = 34.73/X_c - .000060(Ht^2) + 2.42$	.79	.001	20.6%

6.4. SOLVING FOR THE OTHER COMPONENTS OF BODY COMPOSITION

The relationship between X_c and ECM/BCM is particularly relevant because the body cell mass (BCM) can be calculated from the ECM/BCM and LBM. The mathematics are as follows:

Because $LBM = ECM + BCM$

then $$\frac{LBM}{BCM} = \frac{ECM}{BCM} + 1$$

and BCM can be solved as $$\frac{LBM}{(ECM/BCM + 1)}$$

The extracellular mass (ECM) can then be calculated as the LBM minus the BCM, and fat can be solved as the difference between body weight and the LBM.

Using equations 4 and 8 to calculate LBM and ECM/BCM from the impedance and height measurements, the values for BCM, ECM, and fat can then be calculated for each subject.

6.5.LBM: Impedance Measured Vs. Isotope Measured

A measure of the accuracy of the LBM determination from impedance is obtained by plotting the LBM measured by isotope

dilution against the LBM values from impedance,(equation 4), as shown in Figure 5. The isotope-dilution LBM is the independent variable on the x-axis, and the impedance LBM is the dependant variable on the y-axis.

The regression line represents the regression of the impedance LBM on the isotope LBM. The equation is:

Equation	r	P<	SEE/mean Y
Eq 9. impLBM = 0.77 (isoLBM) + 11.11	0.88	.001	9.2%

where **impLBM** is the lean body mass measured from impedance data, and **isoLBM** is the lean body mass measured from the isotope data.

The line of identity is obtained by plotting the isotope LBM values on both axes. The degree to which the regression line approximates the line of identity is a measure of how closely the impedance LBM values correspond to the isotope values.

Comparing the scatter of the normal and malnourished points it can be seen that the normal points tend to fall below the lines of regression and identity, while the malnourished points tend to fall above. This bias is better appreciated by referring to Figure 6, which shows the difference between the impedance and isotope LBM values for each subject, sorted in order of increasing malnourishment according to the Na_e/K_e ratio. Values to the left of 1.2 on the x-axis are normal, while values to the right are increasingly malnourished.

It is clear that the impedance measurement of LBM (equation 4) underestimates the normal subjects and overestimates the malnourished subjects.

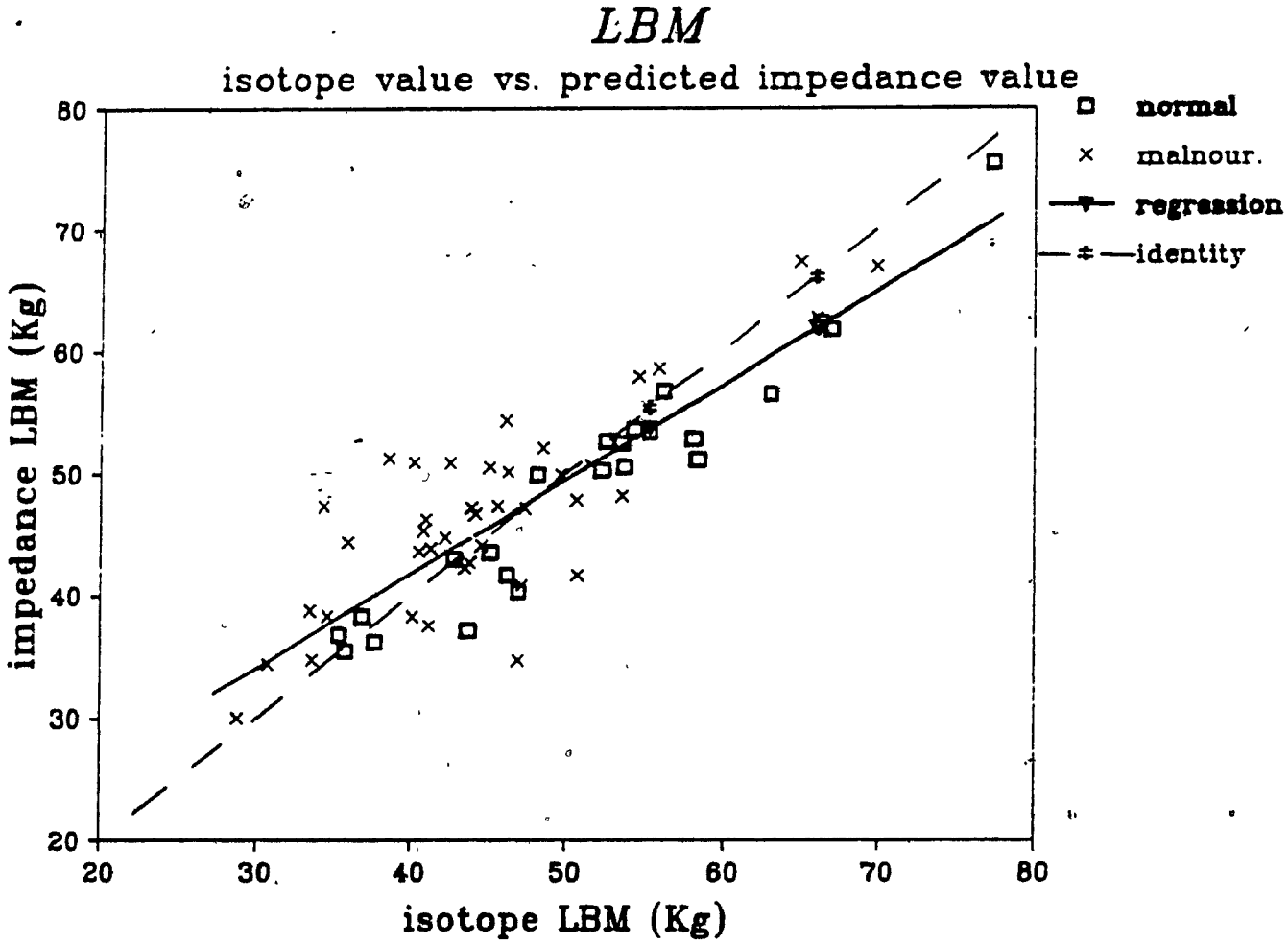

Figure 5
Scatterplot comparing the isotope-measured LBM with the LBM calculated from the impedance data using Equation 4. The regression line is calculated from Equation 9. The line of identity is obtained by plotting identical values on both the X and Y axes.

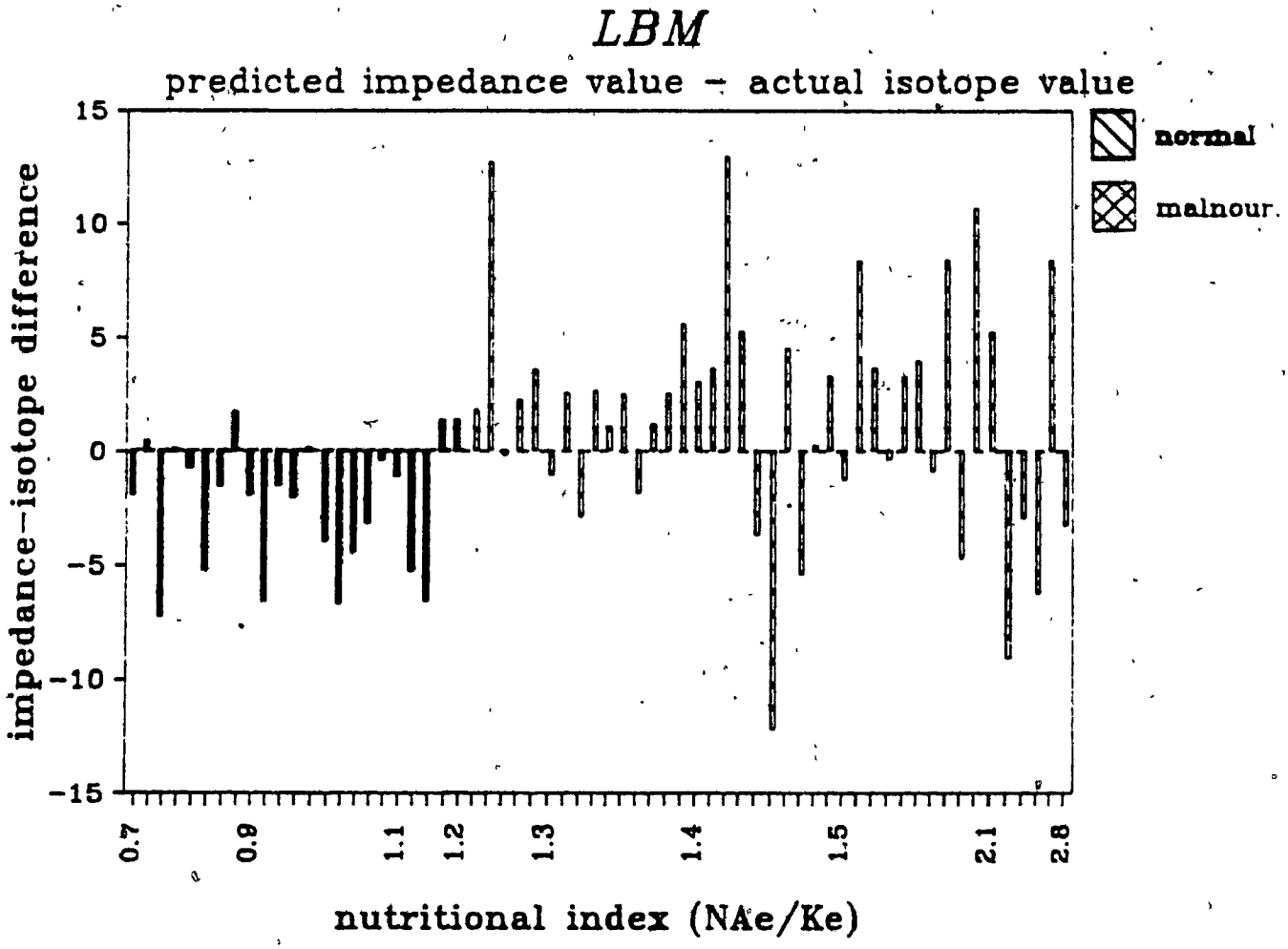

Figure 6
Bar graph of the differences between the impedance and isotope LBM values, sorted along the x-axis in order of increasing malnourishment according to the Na_e/K_e ratio. Values to the left of 1.2 on the x-axis are normal. The impedance calculations for lean body mass are based on Ht^2/R according to equation 4.

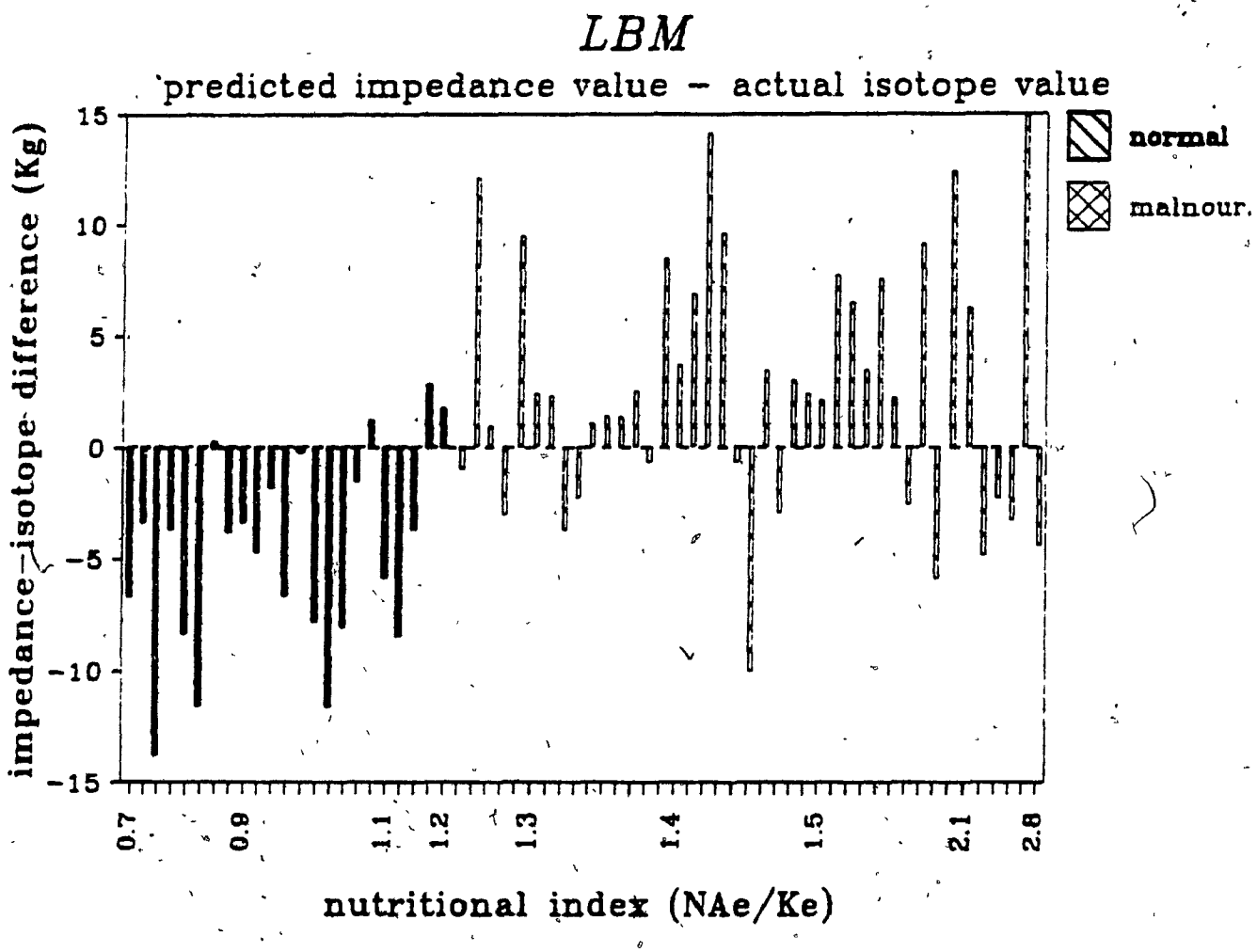

Figure 7
Bar graph of differences between the impedance and isotope LBM values. The impedance calculations for lean body mass are based on 1/R according to equation 2.

This disparity between normal and malnourished subjects is not due to including Ht^2 in the regression of equation 4. Figure 7 demonstrates similar differences when LBM is calculated by equation 2, the regression based on 1/R without Ht_2.

To understand how the relationship between 1/R and LBM differs between the normal and malnourished subjects, separate regression equations can be developed for each group. These are listed for comparison in Table 6.

Table 6

Equation	r	P<	SEE/mean Y
for normals, n=23			
Eq10. LBM = .64 $(Ht^2)/R$ + 17.43	.97	.001	5.6%
for malnour.,n=41			
Eq11. LBM = .56 $(Ht^2)/R$ + 17.36	.83	.001	11.8%
for all subjects, n=64			
Eq4. LBM = .61 $(Ht^2)/R$ + 16.42	.88	.001	10.5%

r is the Pearson coefficient
SEE/mean Y: Standard error of estimate / mean of dependant var.

Applying the normal equation to the normal subjects and the malnourished equation to the malnourished subjects, the impedance-derived measure of LBM can then be compared with the isotope LBM as shown in the scatterplot of Figure 8. Separate regression lines comparing normal impedance with normal isotope LBM, and malnourished impedance with malnourished isotope LBM, are plotted for comparison with the line of identity.

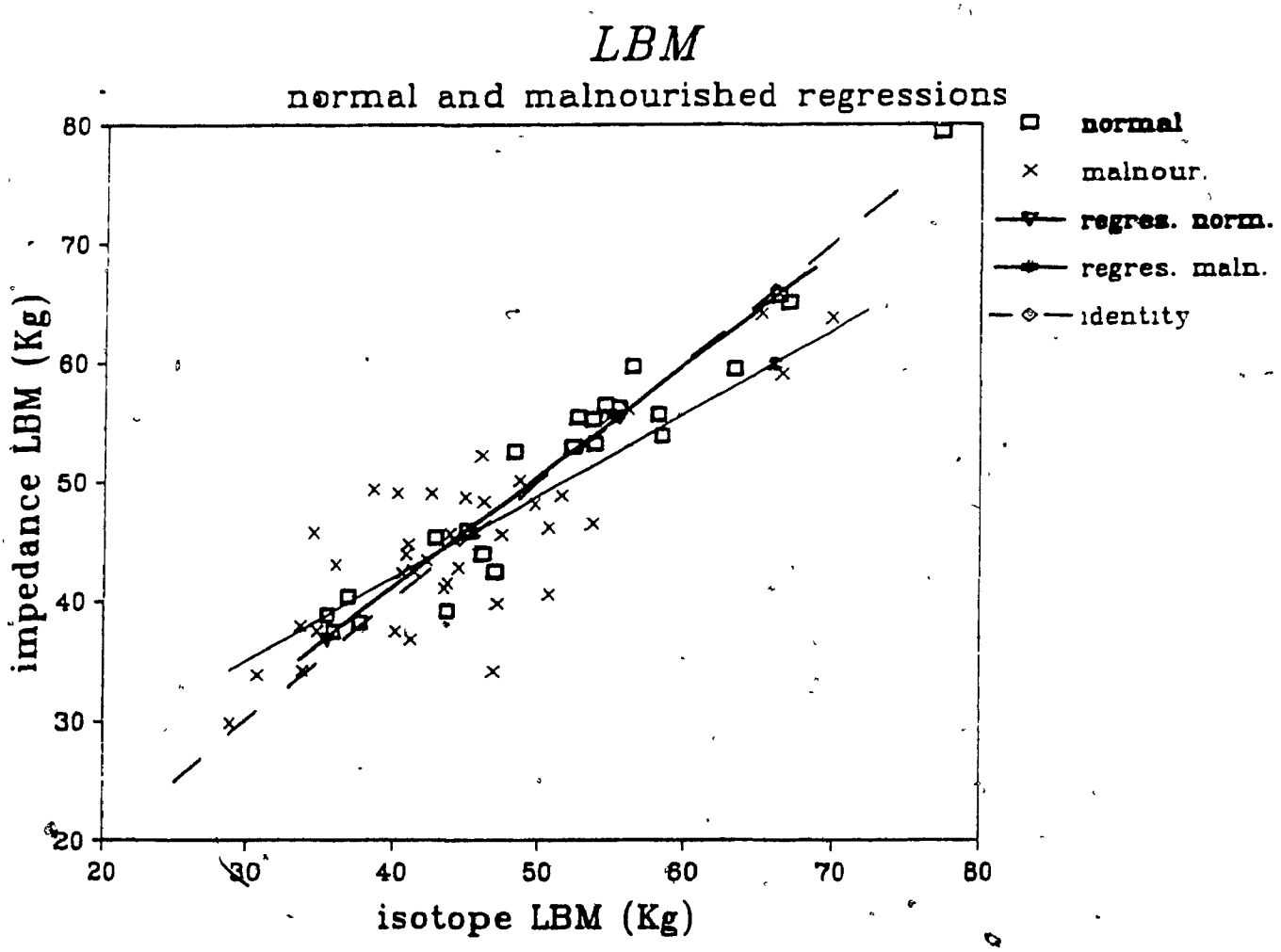

Figure 8
Scatterplot comparing the isotope-measured LBM with the LBM calculated from the impedance data using Equation 10 for the normal subjects and Equation 11 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 12, while the regression line for the malnourished subjects is calculated from Equation 13.

The equations for the regression lines of Figure 8 are:

	Equation	r	P<	SEE/mean Y
Eq.12 normal	impLBM = .94(isoLBM) + 3.41	.97	.001	5.4%
Eq.13 malnour.	impLBM = .69(isoLBM) + 14.29	.83	.001	9.8%

where **impLBM** is LBM measured by impedance, and **isoLBM** is LBM measured by isotope dilution.

It is evident that the normal regression line almost coincides with the line of identity and that the impedance equation for normals (equation 10) accurately predicts the isotope LBM. However, for the malnourished regression, both the slope (69) and the y-intercept (11.11) are quite different from the line of identity and the relationship between Ht^2/R and LBM in the malnourished group is not as precise

The relationship between LBM and Ht^2/R based on the normally nourished subjects (Equation 10) is comparable, in terms of r (.97) and standard error of the estimate (2.87), to that reported in Lukaski's study[22] of 37 healthy men (r = .98, SEE = 2.61).

6.6.TBW: Impedance Measured Vs. Isotope Measured

The same observations made above for LBM also apply for total body water (TBW). This is understandable because the isotope-dilution measurement of TBW is directly related to the measurement of LBM (TBW = .75 LBM).

The scatterplot of Figure 9 compares the isotope TBW with the

[22] Refer to section 4.1.

impedance TBW calculated by equation 3. The regression line represents the regression of the impedance TBW on the isotope TBW, according to the equation:

	Equation	r	P<	SEE/mean Y
Eq14.	impTBW = 0.76 x isoTBW + 8.16	.88	.001	9.2%

where **impTBW** is TBW measured by impedance, and **isoTBW** is TBW measured by isotope dilution.

Figure 10 demonstrates the difference between the impedance and isotope TBW value for each subject, and Table 7 lists the separate regression equations relating TBW and Ht^2/R for the normal, malnourished and total group.

Table 7

	Equation	r	P<	SEE/mean Y
for normals, n=23				
Eq.15	$TBW = .46(Ht^2)/R + 12.73$	.97	.001	5.6%
for malnour. n=41				
Eq.16	$TBW = .41(Ht^2)/R + 12.68$	.83	.001	11.8%
for all subjects, n=64				
Eq.3	$TBW = .44(Ht^2)/R + 11.99$	.88	.001	10.5%

SEE/mean Y : standard error of estimate / mean of dependant variable

Figure 11 plots impedance TBW for the normal and malnourished subjects, calculated from equations 15 and 16, against the isotope TBW.

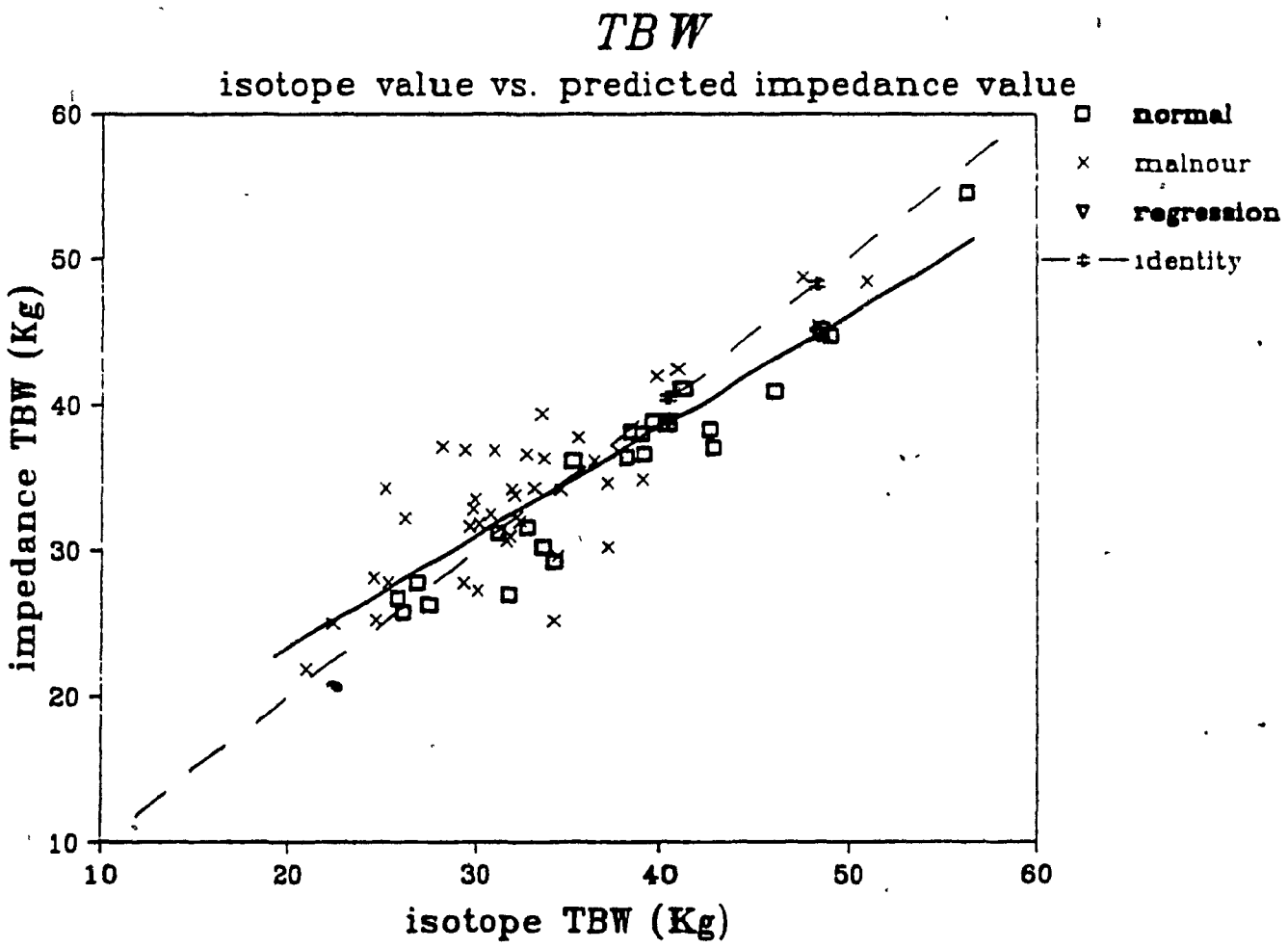

Figure 9
Scatterplot comparing the isotope-measured TBW with the TBW calculated from the impedance data using Equation 3. The regression line is calculated from Equation 14. The line of identity represents Y = X.

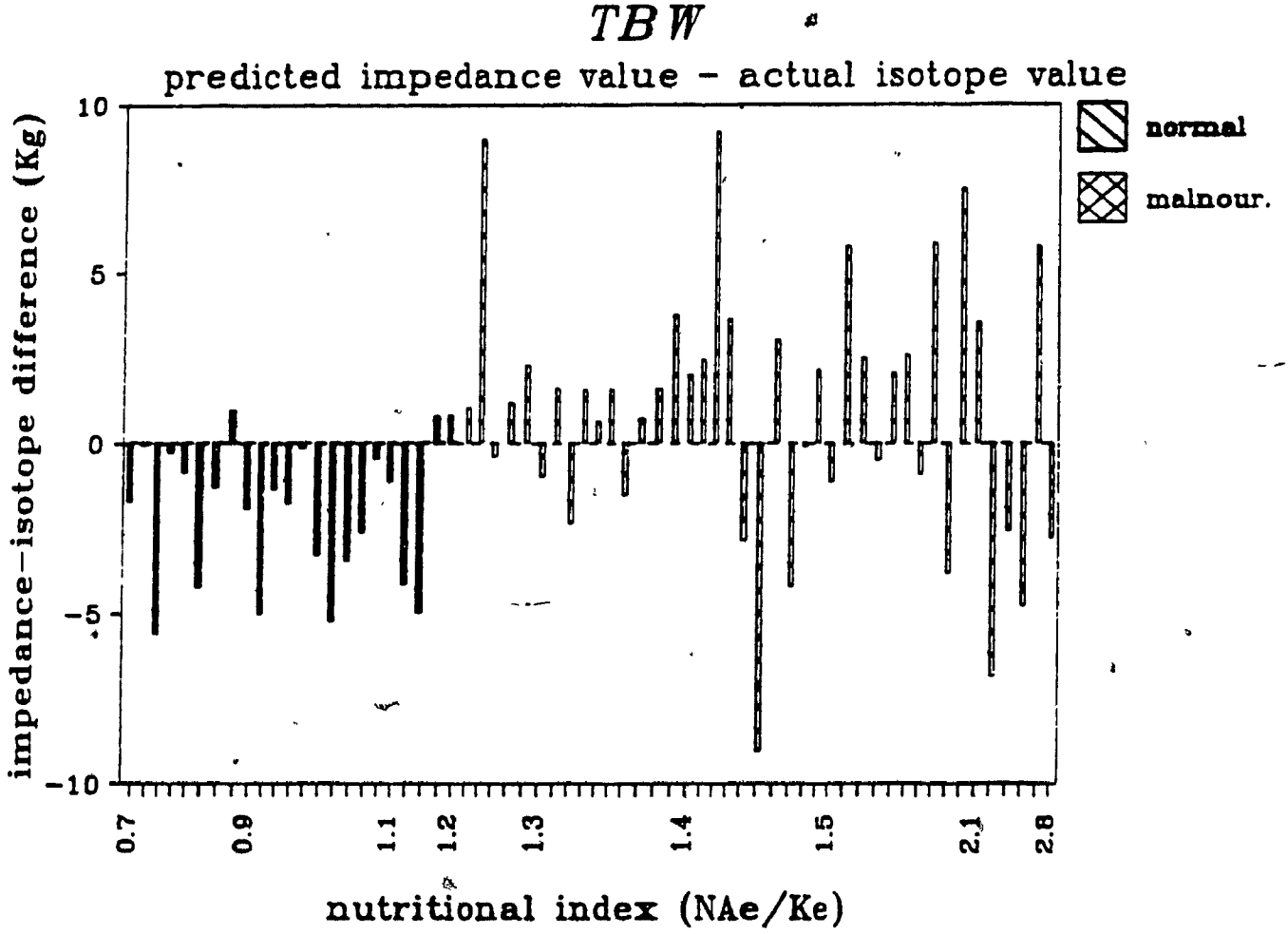

Figure 10
Bar graph of the differences between the impedance and isotope TBW values, sorted along the x-axis in order of increasing malnourishment according to the Na_e/K_e ratio.

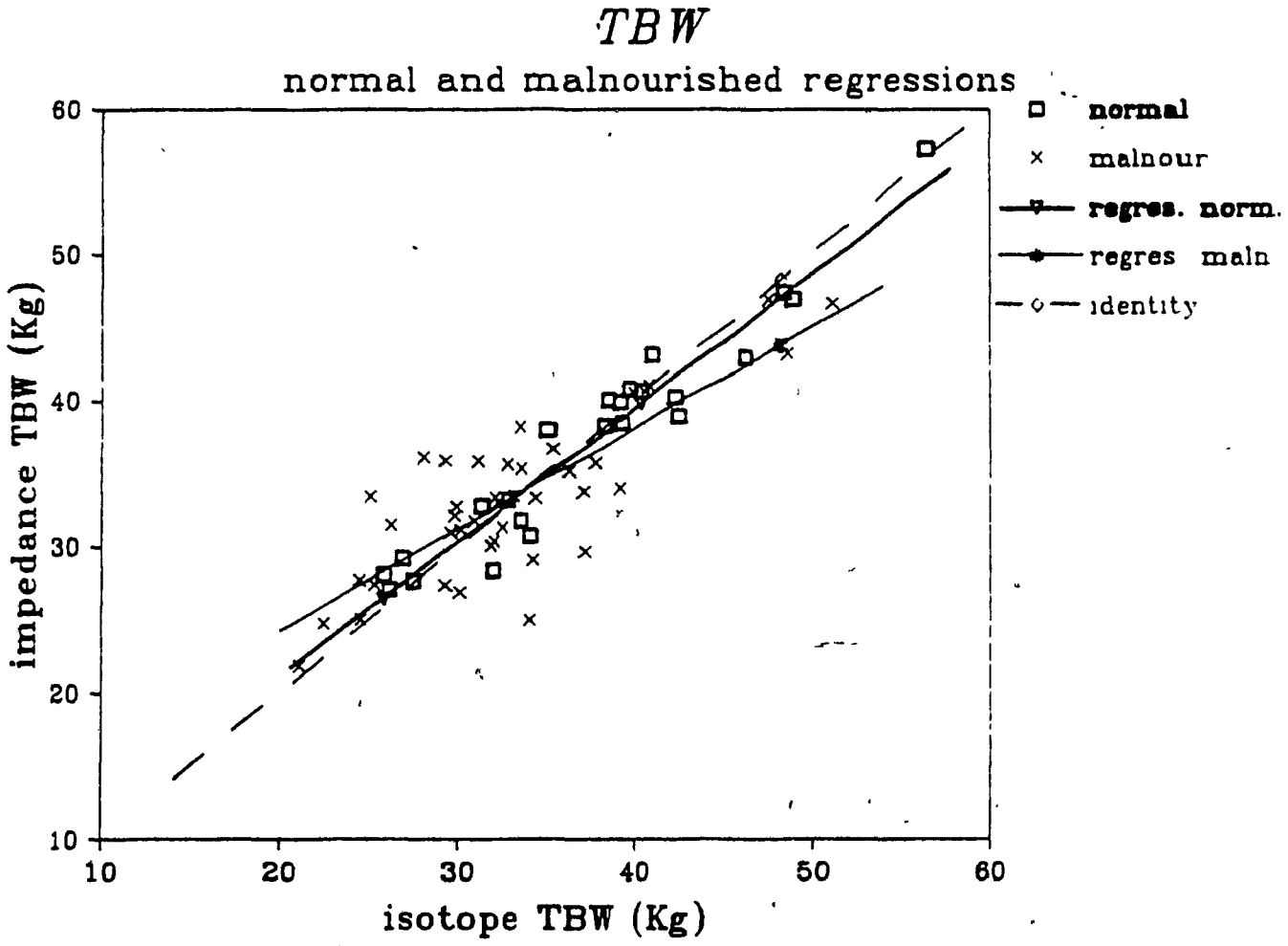

Figure 11
Scatterplot comparing the isotope-measured TBW with the TBW calculated from the impedance data using Equation 15 for the normal subjects and Equation 16 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 17, while the regression line for the malnourished subjects is calculated from Equation 18.

The normal and malnourished regressions lines compare the impedance TBW with the isotope TBW and are derived from the following equations:

Equation	r	P<	SEE/mean Y
for normals, n=23			
Eq.17 impTBW = .92 (isoTBW) + 2.65	.97	.001	7.1%
malnour.n=41			
Eq.18 impTBW = .69 (isoTBW) +10.42	.83	.001	9.8%

where **impTBW** is TBW measured by impedance, and **isoTBW** is TBW measured by isotope dilution.

The impedance measure of TBW is evidently more accurate in the normal subjects than the malnourished subjects.

6.7.ECM/BCM: Impedance Measured Vs. Isotope Measured

The accuracy of the measurement of the ratio of the extracellular to intracellular mass (ECM/BCM) by impedance can be assessed by plotting the impedance-measured ECM/BCM values, calculated according to equation 8, as the dependent variable on the Y axis, against the isotope values as the independent variable. This scatterplot is shown in Figure 12. The regression line represents the following equation:

Equation	r	P<	SEE/mean Y
Eq.19 impECM/BCM = .62 (isoECM/BCM) +.61	.79	.001	16.3%

where **impECM/BCM** is the ECM/BCM measured by impedance, and **isoECM/BCM** is the ECM/BCM measured by isotope dilution.

The normal and malnourished subjects are represented by different point markers as shown in the legend.

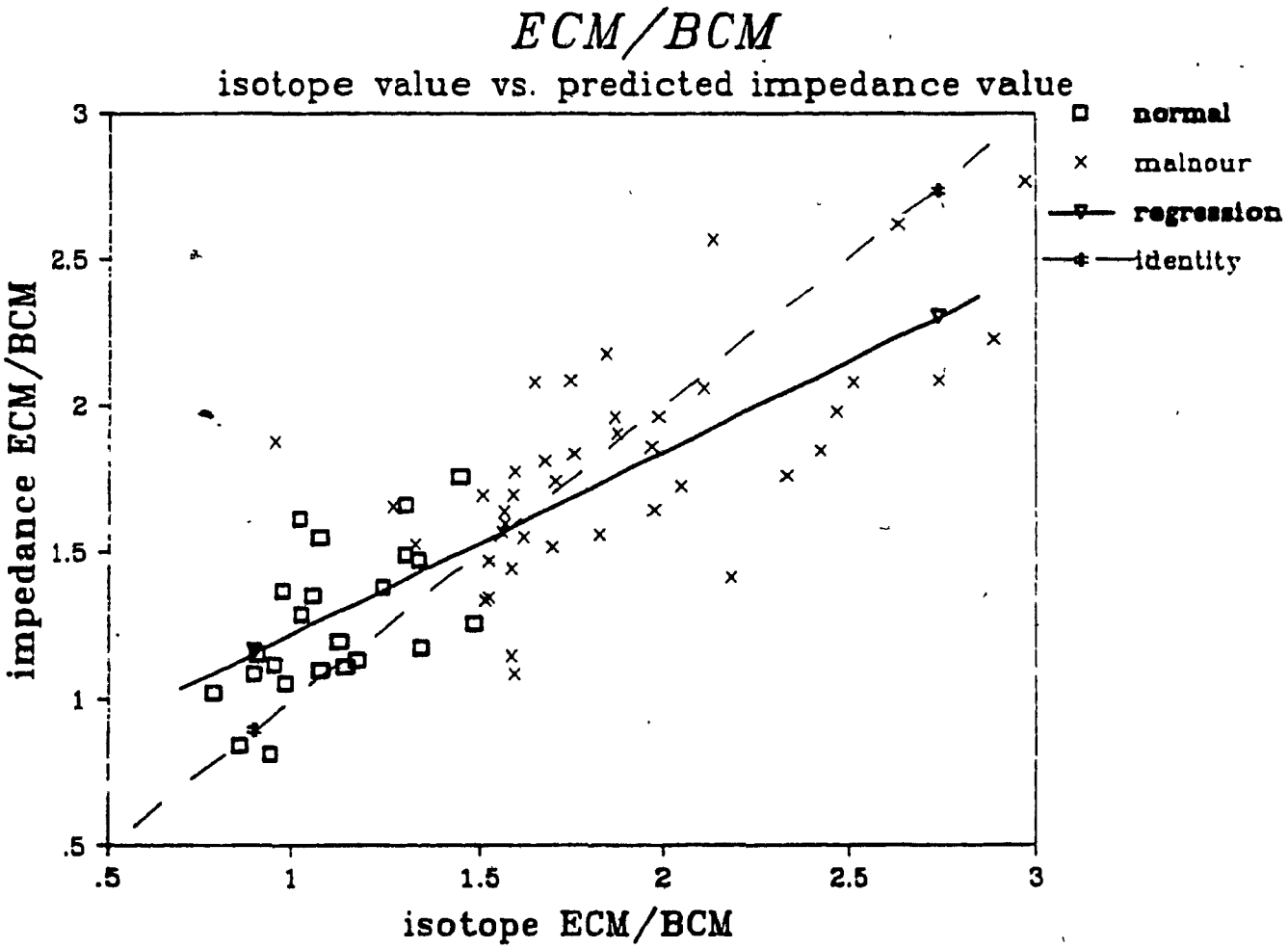

Figure 12
Scatterplot comparing the isotope-measured ECM/BCM with the ECM/BCM calculated from the impedance data using Equation 8. The regression line is calculated from Equation 19. The line of identity represents Y = X.

The distribution of the normal and malnourished points about the line of identity seems skewed, with fewer normals falling below and more malnourished falling below. Examining Figure 13 reveals that this is the case; equation 8 biases the impedance ECM/BCM measurements by overestimating in the normal subjects and slightly underestimating in the malnourished.

This discrepancy between the normal and malnourished impedance ECM/BCM is not caused by including Ht^2 as a second independent variable in equation 8. Figure 14 shows the difference between the impedance ECM/BCM calculated from equation 6, with $1/X_c$ as the single independent variable. The bias between normal and malnourished appears worse than that of equation 8.

Separate regressions for the normal and malnourished subjects are useful for understanding how the relationship between $1/X_c$ and ECM/BCM is different for these two groups. The separate regression equations are listed in table 8 along with equation 8 for comparison.

Table 8

Equation	r	P=	SEE/mean Y
for normals, n=23			
Eq.20 $ECM/BCM=12.53(1/X_c)-.000031(Ht^2)+1.81$	.60	.011	14.4%
for malnour. n=41			
Eq.21 $ECM/BCM=27.61(1/X_c)-.000046(Ht^2)+2.3$	.64	<.001	11.7%
for all subjects, n=64			
Eq.8 $ECM/BCM=34.73(1/X_c)-.00006(Ht^2)+2.42$	.79	<.001	20.6%

SEE/mean Y: standard error of estimate / mean of dependant variable.

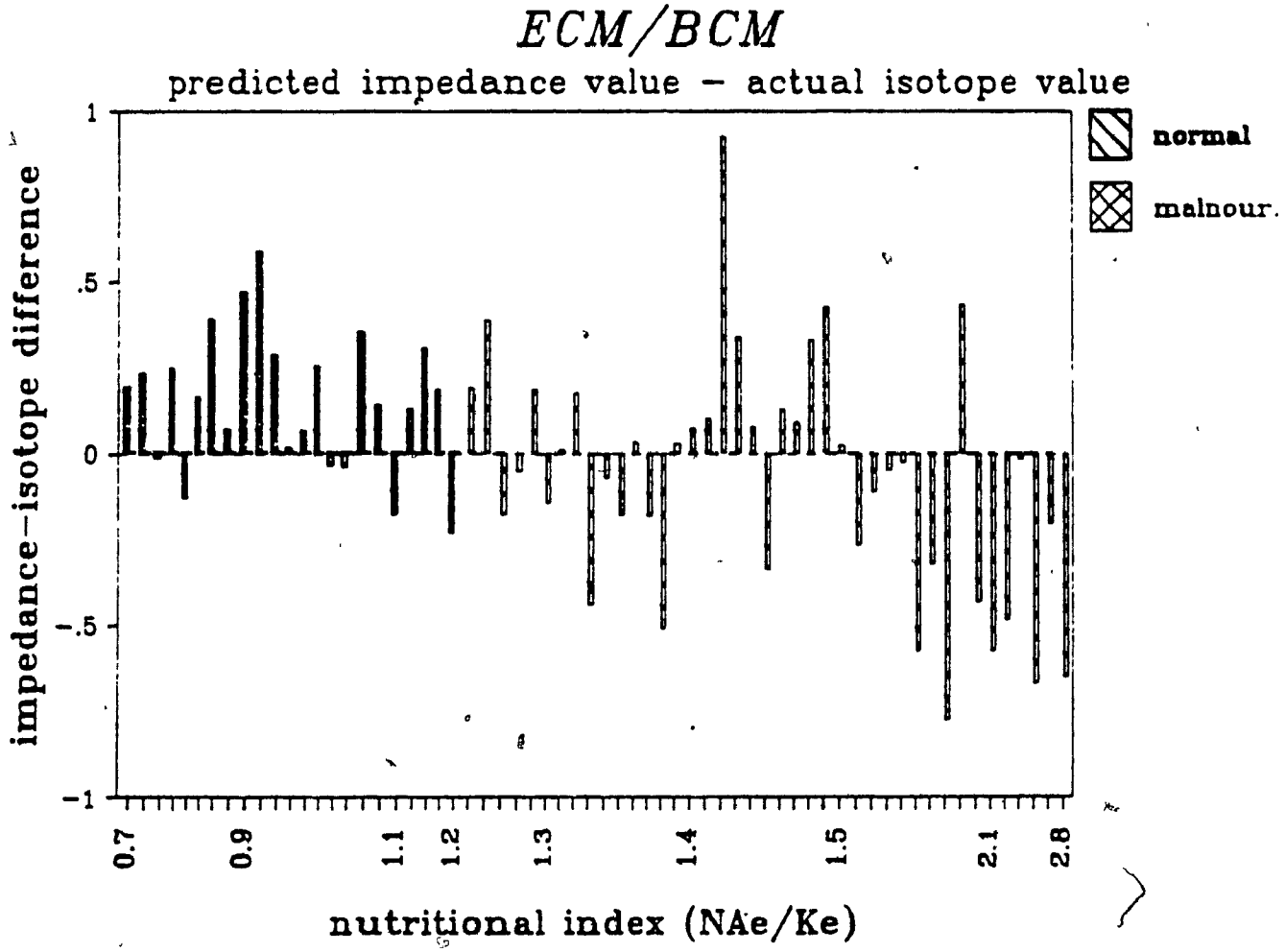

Figure 13
Bar graph of the differences between the impedance and isotope ECM/BCM values, sorted along the x-axis in order of increasing malnourishment. The impedance-measured ECM/BCM values are calculated using equation 8, with $1/X_c$ and Ht^2 as two independant variables.

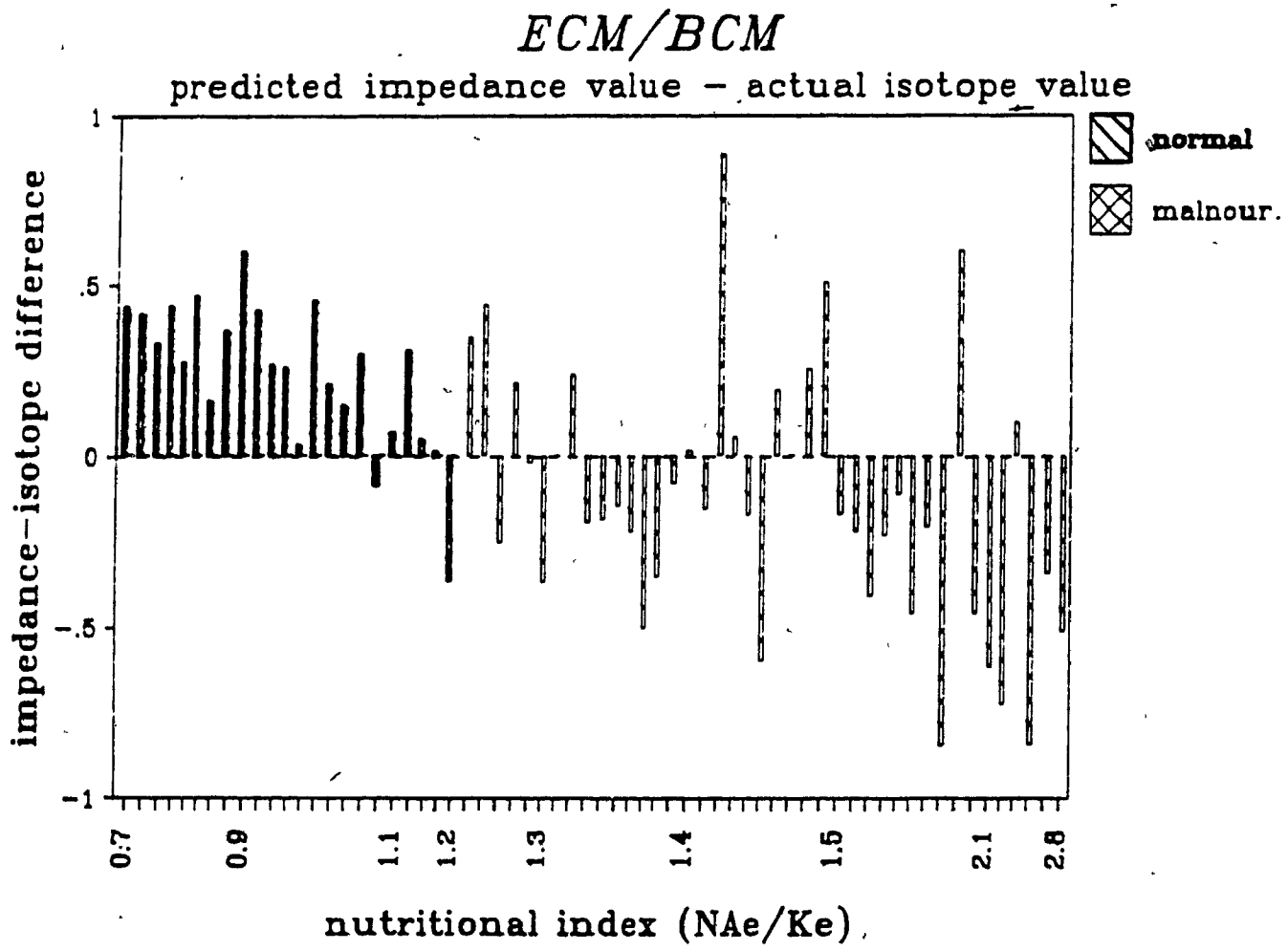

Figure 14
Bar graph of the differences between the impedance and isotope ECM/BCM values. The impedance-measured ECM/BCM values are calculated using
equation 6, with $1/X_c$ as the only independant variable.

Equations 20 and 21 can be used to generate impedance ECM/BCM values for the normal and malnourished subjects, and these are plotted against the isotope ECM/BCM as shown in figure 16.

The normal and malnourished regression lines were calculated from equations comparing the impedance ECM/BCM and isotope ECM/BCM for each group:

Equation	r	P=	SEE/mean
for normals, n=23			
Eq.22 impECM/BCM = .36*isoECM/BCM +.71	.60	.002	9%
for malnour. n=41			
Eq.23 impECM/BCM = .41*isoECM/BCM +1.11	.64	<.001	11.7%

where **impECM/BCM** is the ECM/BCM measured by impedance, and **isoECM/BCM** is the ECM/BCM measured by isotope dilution.

The slopes of both regressions lines are about .4 indicating a poor prediction of ECM/BCM using impedance data in both the normal and malnourished subjects.

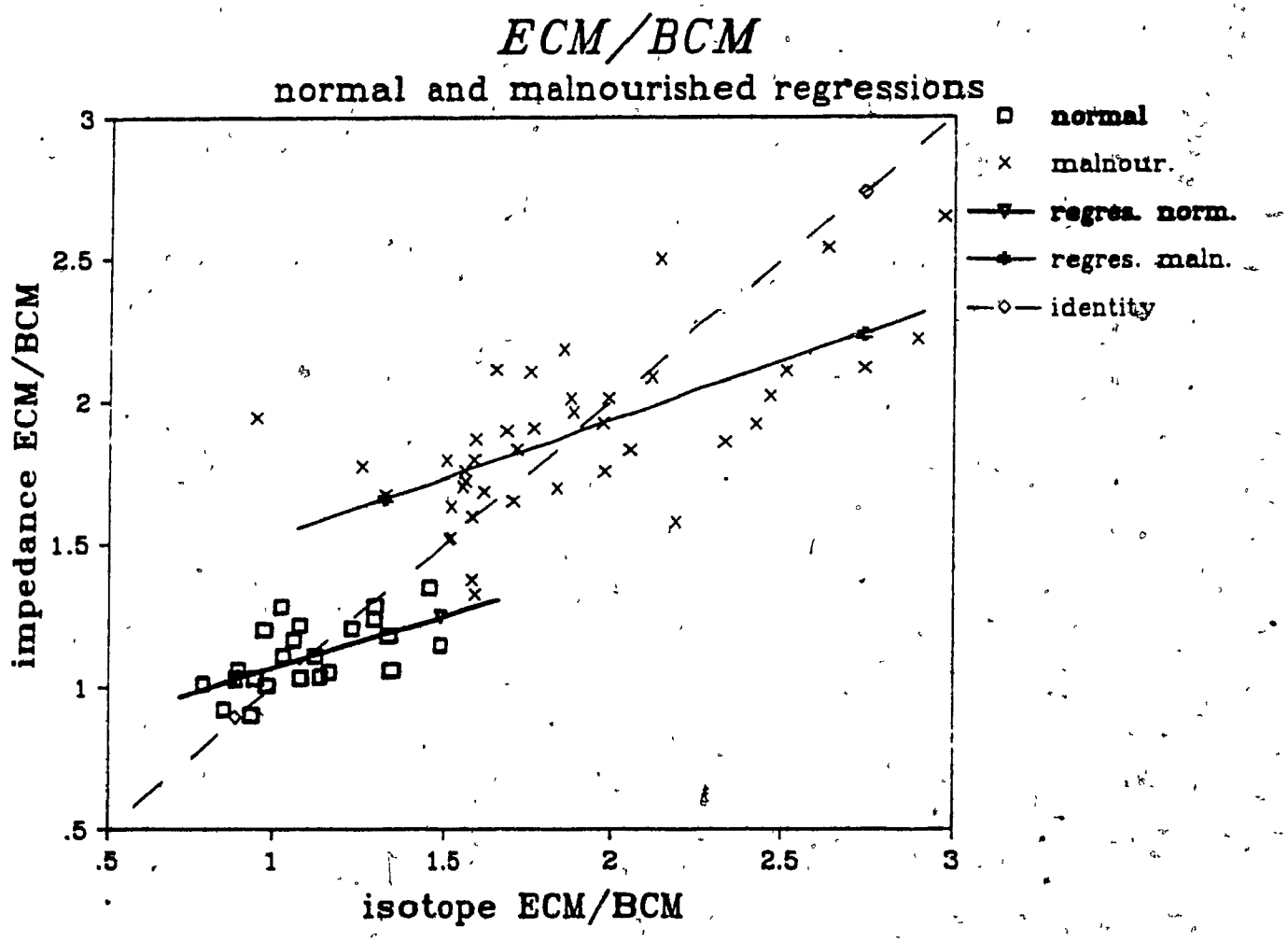

Figure 15
Scatterplot comparing the isotope-measured ECM/BCM with the ECM/BCM calculated from the impedance data using Equation 20 for the normal subjects and Equation 21 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 22, while the regression line for the malnourished subjects is calculated from Equation 23.

6.8.Na_e/K_e: Impedance Measured Vs. Isotope Measured

The observations regarding the use of impedance to predict the isotope Na_e/K_e ratio are qualitatively similar to those for ECM/BCM, although impedance is slightly more accurate at measuring Na_e/K_e than ECM/BCM. The relationship between the impedance Na_e/K_e predicted by equation 7 and the isotope Na_e/K_e is demonstrated in figure 16. The regression line is determined by the equation:

	Equation	r	P<	SEE/mean Y
Eq.24	$impNa_e/K_e = .66(isoNa_e/K_e) + .48$	.79	.001	16.4%

where **$impNa_e/K_e$** is the exchangeable sodium / exchangeable potassium ratio predicted from impedance data, and **$isoNa_e/K_e$** is the ratio measured by isotope dilution.

The slope of the regression (.66) is somewhat closer to the identity line than the regression slope for ECM/BCM (.62). Figure 17 demonstrates that equation 7 overestimates the Na_e/K_e for the normal subjects, and to a lesser degree underestimates for the malnourished group.

Separate regression equations relating impedance to the isotope Na_e/K_e are listed in table 9.

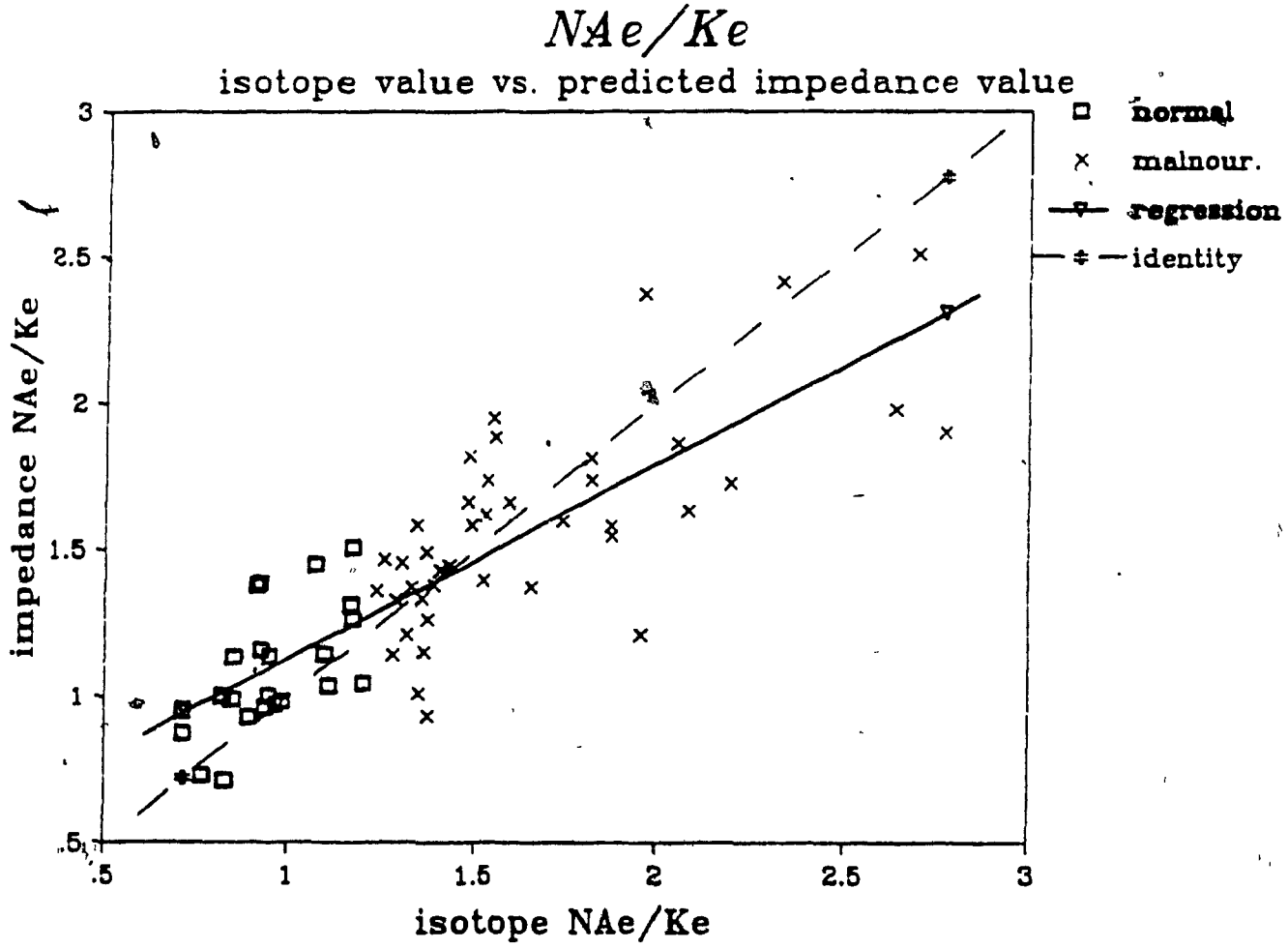

Figure 16
Scatterplot comparing the isotope-measured Na_e/K_e ratio with the Na_e/K_e ratio calculated from the impedance data using Equation 7. The regression line is calculated from Equation 24. The line of identity is obtained by plotting y-values equal to x-values.

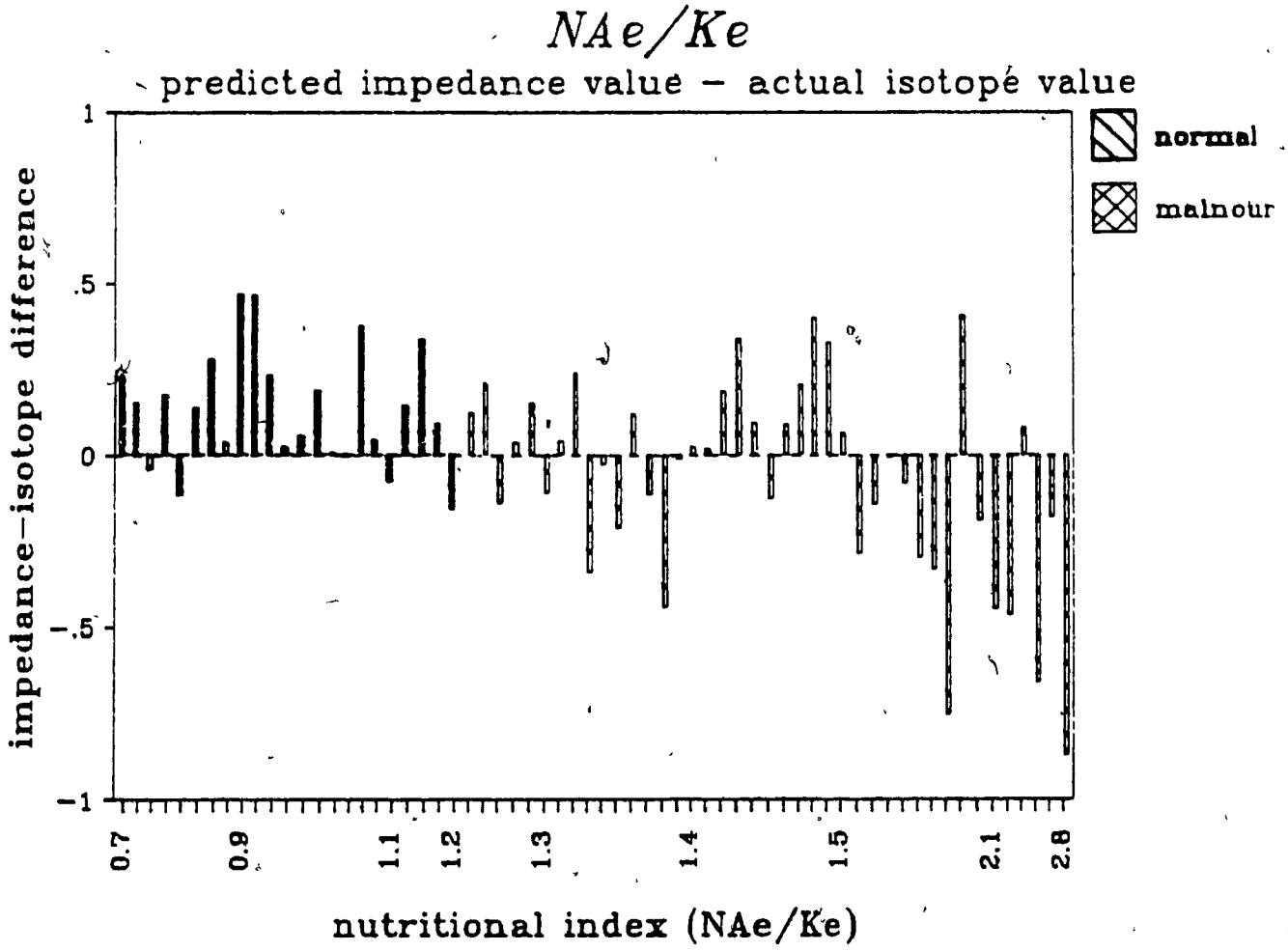

Figure 17
Bar graph of the differences between the impedance and isotope Na_e/K_e values, sorted along the x-axis in order of increasing malnourishment according to the isotope-measured Na_e/K_e ratio.

Table 9

Equation	r	P=	SEE/mean Y
for normals, n=23			
Eq.25 Na_e/K_e = 9.73(1/Xc)-.000023(Ht^2)+1.48	.61	.009	12.5%
~~for malnour. n=41~~			
Eq.26 Na_e/K_e =27.98(1/Xc)-.000031(Ht^2)+1.7	.70	<.001	18.1%
for all subjects, n=64			
Eq.7 Na_e/K_e =34.09(1/Xc)-.000047(Ht^2)+1.87	.81	<.001	19.9%

SEE/mean Y : standard error of the estimate / mean of the dependant variable.

From equations 25 and 26 the normal and malnourished group-specific Na_e/K_e can be calculated and then plotted against the isotope Na_e/K_e, as shown in figure 18.

The regression lines represent the following regressions of the impedance Na_e/K_e on the isotope Na_e/K_e for the normal group and malnourished group:

Equation	r	P=	SEE/mean
for normals, n=23			
Eq.27 **impNa$_e$/K$_e$** = .37(**isoNa$_e$/K$_e$**) +.61	.60	.002	7.3%
for malnour. n=41			
Eq.28 **impNa$_e$/K$_e$** = .49(**isoNa$_e$/K$_e$**) +.85	.70	<.001	12.7%

where **impNa$_e$/K$_e$** is the exchangeable sodium / exchangeable potassium ratio predicted from impedance data, and **isoNa$_e$/K$_e$** is the ratio measured by isotope dilution.

The slope for the normal regression (.37) is the same as that for ECM/BCM (.36), while the malnourished Na_e/K_e slope (.49) is better than the corresponding slope for ECM/BCM (.41), indicating that for the malnourished subjects, the relationship of impedance with Na_e/K_e is better than that with ECM/BCM.

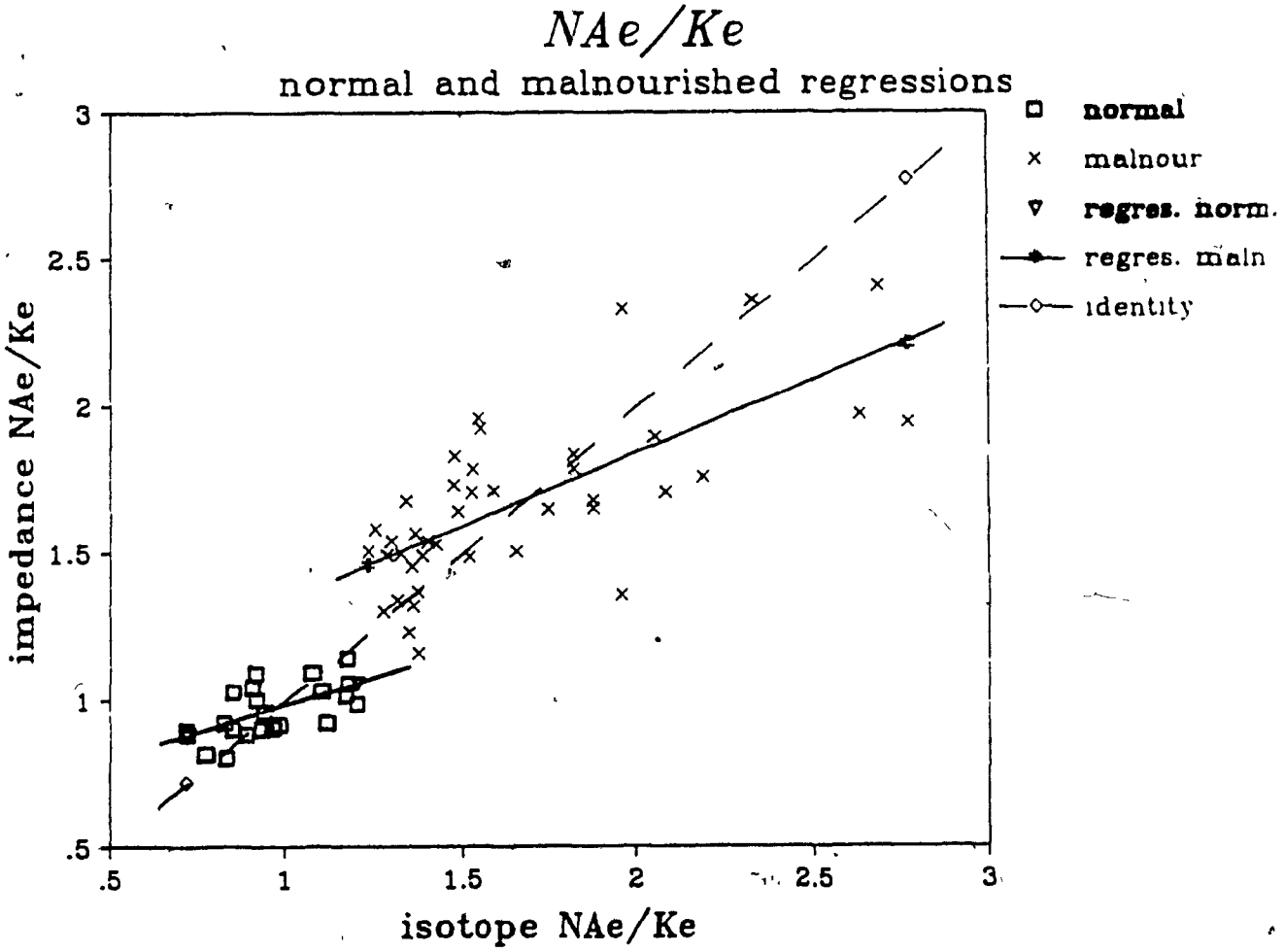

Figure 18
Scatterplot comparing the isotope-measured Na_e/K_e ratio with the Na_e/K_e ratio calculated from the impedance data using Equation 25 for the normal subjects and Equation 26 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 27, while the regression line for the malnourished subjects is calculated from Equation 28.

6.9.BCM: Impedance Measured Vs. Isotope Measured

On analyzing the body cell mass (BCM) predicted by impedance, the observations are found to be similar to those previously described for LBM and TBW; the regression describing all 64 subjects is biased, underestimating the BCM of the normally nourished subjects, and the regression is more precise for the normally nourished than for the malnourished subjects.

Figure 19 demonstrates a scatterplot comparing the isotope-measured BCM, as the independent variable on the x-axis, with BCM on the y-axis calculated from the equation.

Eq.29 $$BCM = \frac{LBM}{(ECM/BCM + 1)}$$

...where LBM is calculated by equation 4 and ECM/BCM by equation 8. The regression line represents the regression of the impedance BCM (y-axis values) on the isotope BCM (x-axis values):

	Equation	r	P<	SEE/mean Y
Eq.30	impBCM = .69(isoBCM) + 5.69	.87	.001	12.9%

where impBCM is the BCM calculated from Equation 29, and isoBCM is the BCM measured by isotope dilution.

The r (.87) is good but the regression slope (.69) is quite different from identity and cursory examination suggests that most of the scatterpoints representing the normal subjects fall below both the regression line and the line of identity. Indeed, plotting the difference between the impedance and isotope BCM sorted by nutritional index, as shown in figure 20, reveals that equation 29 biases the impedance-measured BCM, underestimating the normal subjects and overestimating the malnourished.

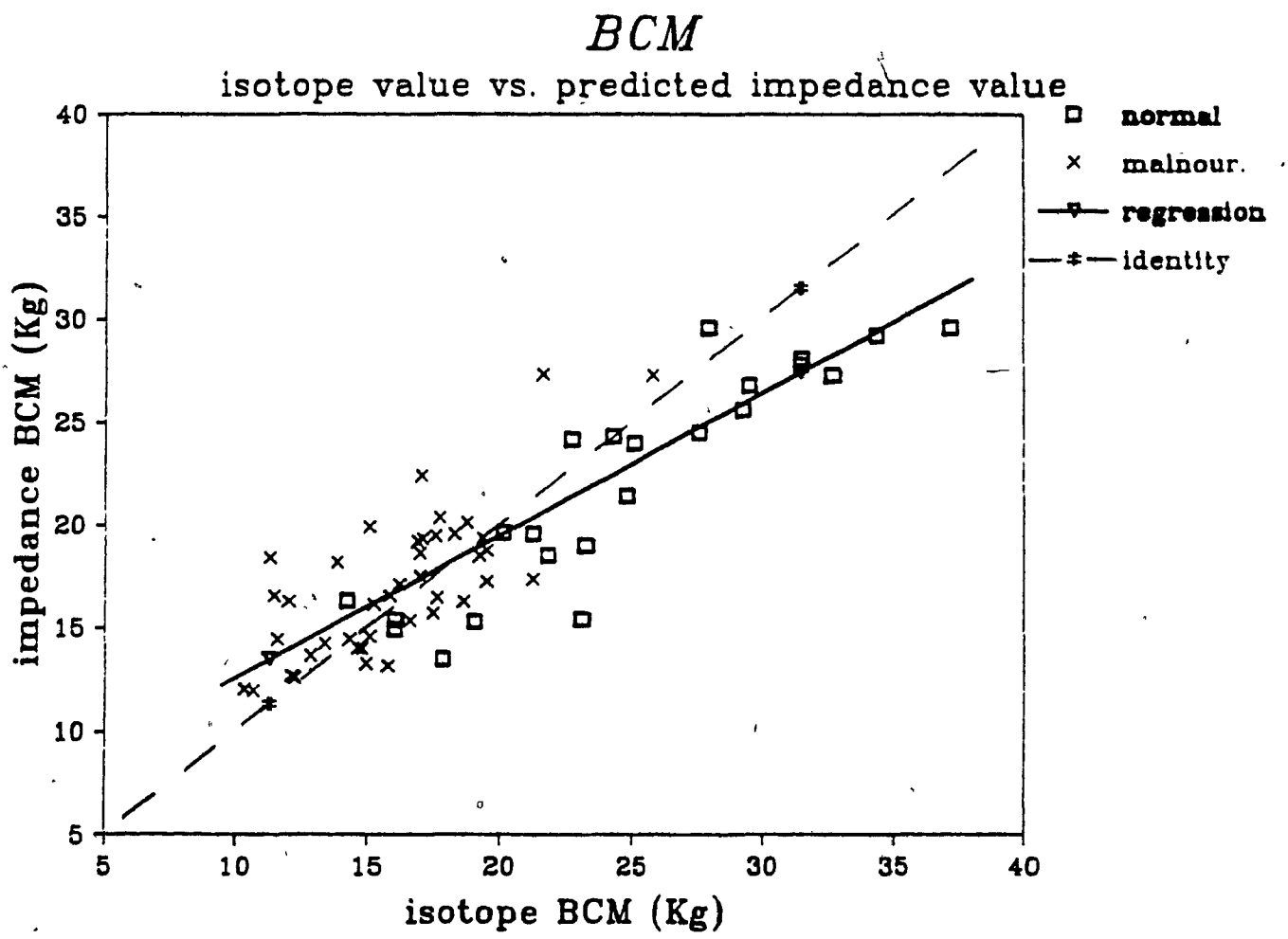

Figure 19
Scatterplot comparing the isotope-measured BCM with the BCM calculated from the impedance data using Equation 29. The regression line is calculated from Equation 30. The line of identity is obtained by plotting y-values equal to x-values.

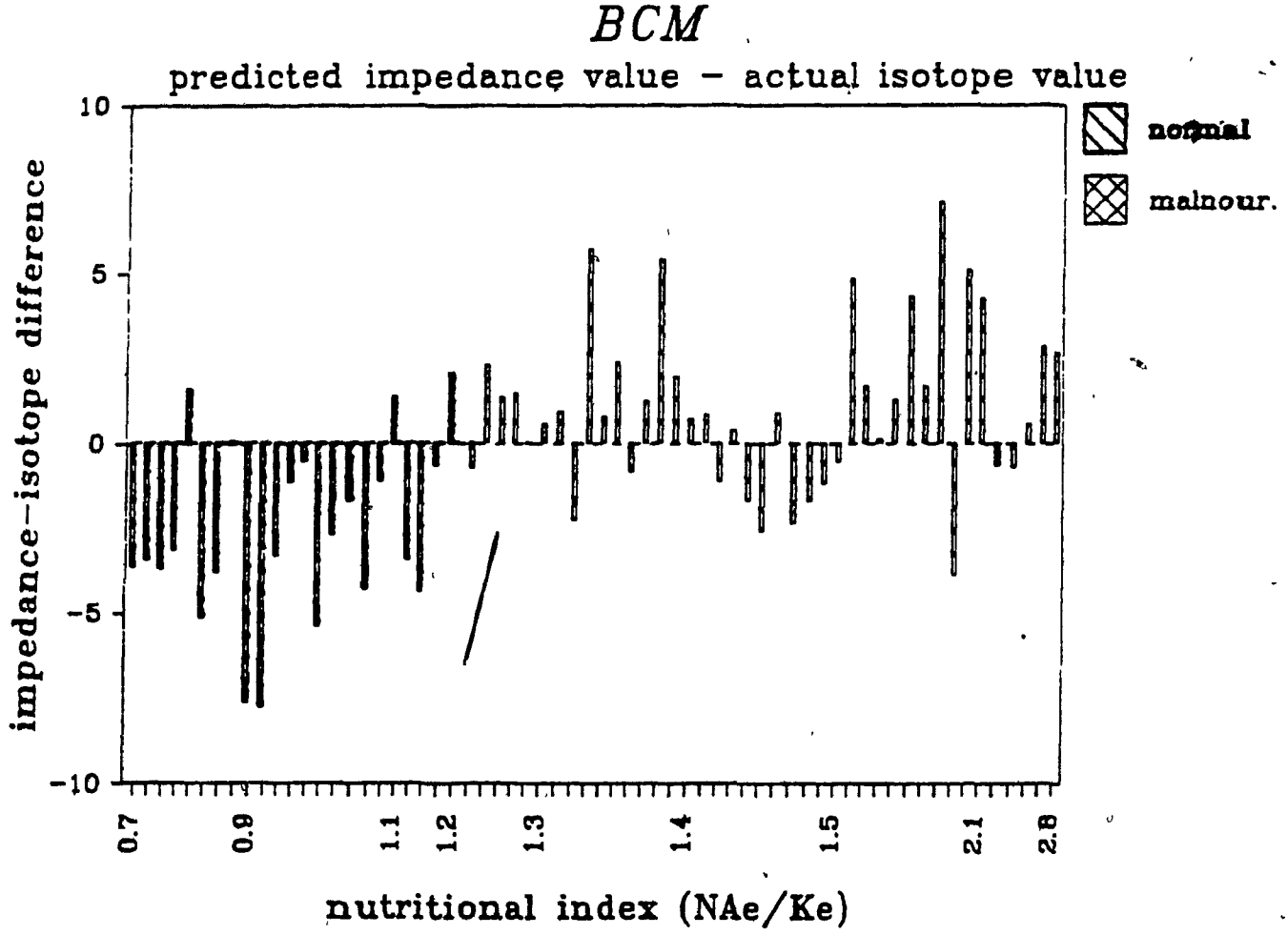

Figure 20
Bar graph of the differences between the impedance and isotope BCM values, sorted along the x-axis in order of increasing malnourishment.

To better appreciate this discrepancy, the impedance BCM for the normal subjects was calculated using the LBM and ECM/BCM values from equations 10 and 20, while the impedance BCM for the malnourished group was calculated from the malnourished-based equations 11 and 21. The normal and malnourished BCM values so-obtained are plotted on the y-axis against the isotope-BCM, as shown in figure 21.

Although there is considerable overlap of the normal and malnourished scatter points, the regression lines relating impedance BCM with isotope BCM are quite different, as listed in Table 10

Table 10

Equation	r	P<	SEE/mean Y
for normals, n=23			
Eq.31 impBCM = .83*isoBCM +4.08	.94	.001	7.6%
for malnour. n=41			
Eq32 impBCM = .66*isoBCM +5.36	.76	.001	11.9%

where impBCM is the BCM calculated from impedance data, and isoBCM is the BCM measured by isotope dilution.
SEE/mean : standard error of the estimate / mean of the dependant variable.

The normal regression line almost coincides with the identity line, and both the r (.94) and the SEE/mean (7.6%) are better than those for the malnourished and total group.

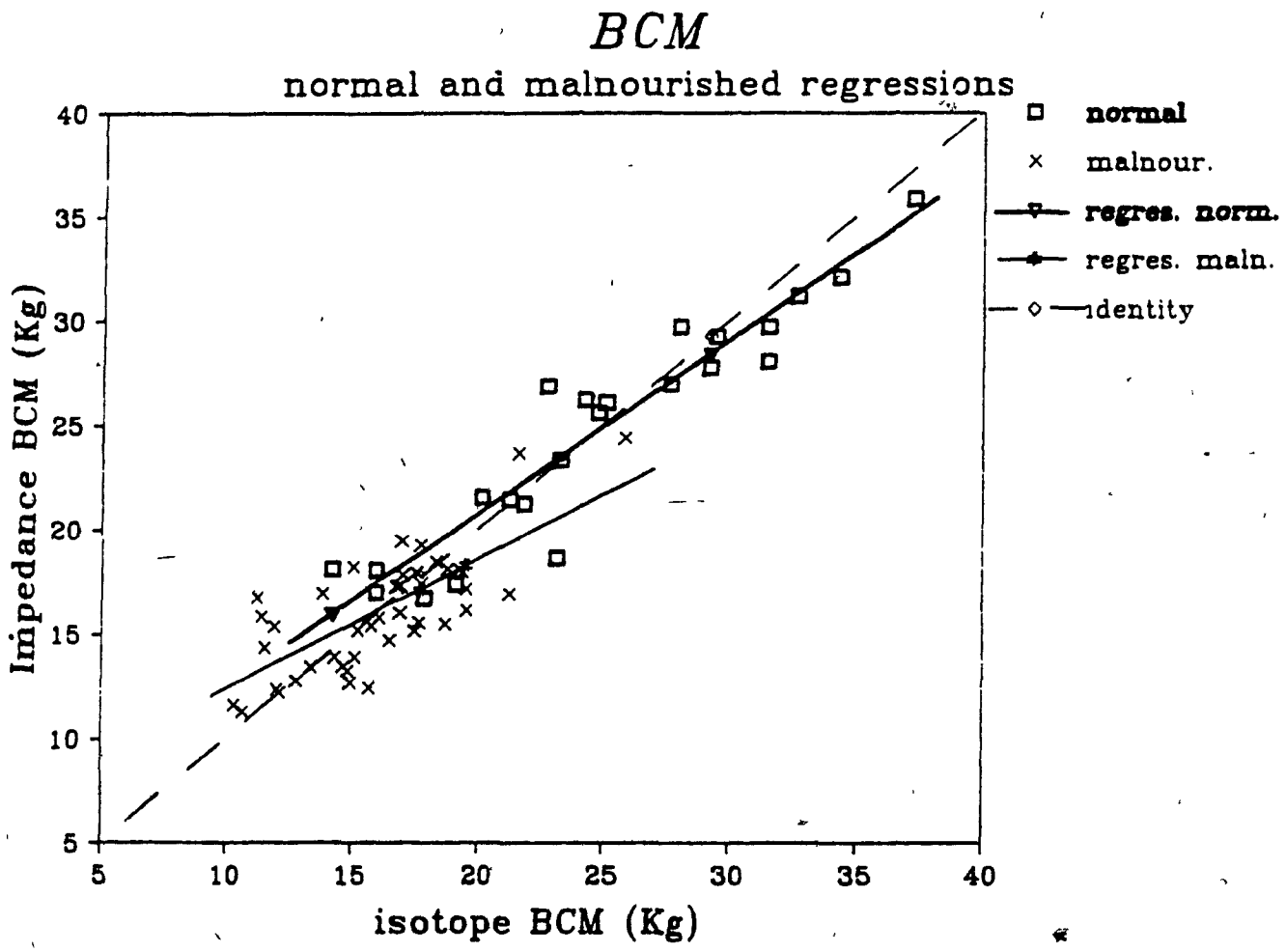

Figure 21
Scatterplot comparing the isotope-measured BCM with the BCM calculated from the impedance values derived from Equation 10 (LBM) and Equation 20 (ECM/BCM) for the normal subjects, and from Equation 11 (LBM) and Equation 21 (ECM/BCM) for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 31, while the regression line for the malnourished subjects is calculated from Equation 32.

6.10.ECM: Impedance Measured Vs. Isotope Measured

Similar to the findings for BCM, the measurement of extracellular mass (ECM) by impedance is also more accurate for normal subjects than for the malnourished, but the ECM partition is the only partition of body composition in which the regression equation developed for the total group seems unbiased, without overestimating or underestimating the normal or malnourished subgroups.

The ECM is calculated as:

Eq.33 ECM = LBM - BCM

where LBM is calculated from equation 4 and BCM from equation 29.

Figure 22 plots the impedance ECM, as the dependant variable, against the isotope-measured ECM, as the independent variable. The regression of the impedance ECM on the isotope ECM is plotted according to the equation:

	Equation	r	P<	SEE/mean Y
Eq.34	impECM = .77 (isoECM) + 7.03	.83	.001	12.1%

where **impECM** is the ECM calculated from impedance data, and **isoECM** is the ECM measured by isotope dilution.

The scatter of the data points for ECM is wider than that for BCM and the r is not as strong (.83 vs. .87) although the SEE/mean is the approximately the same (12.1%).

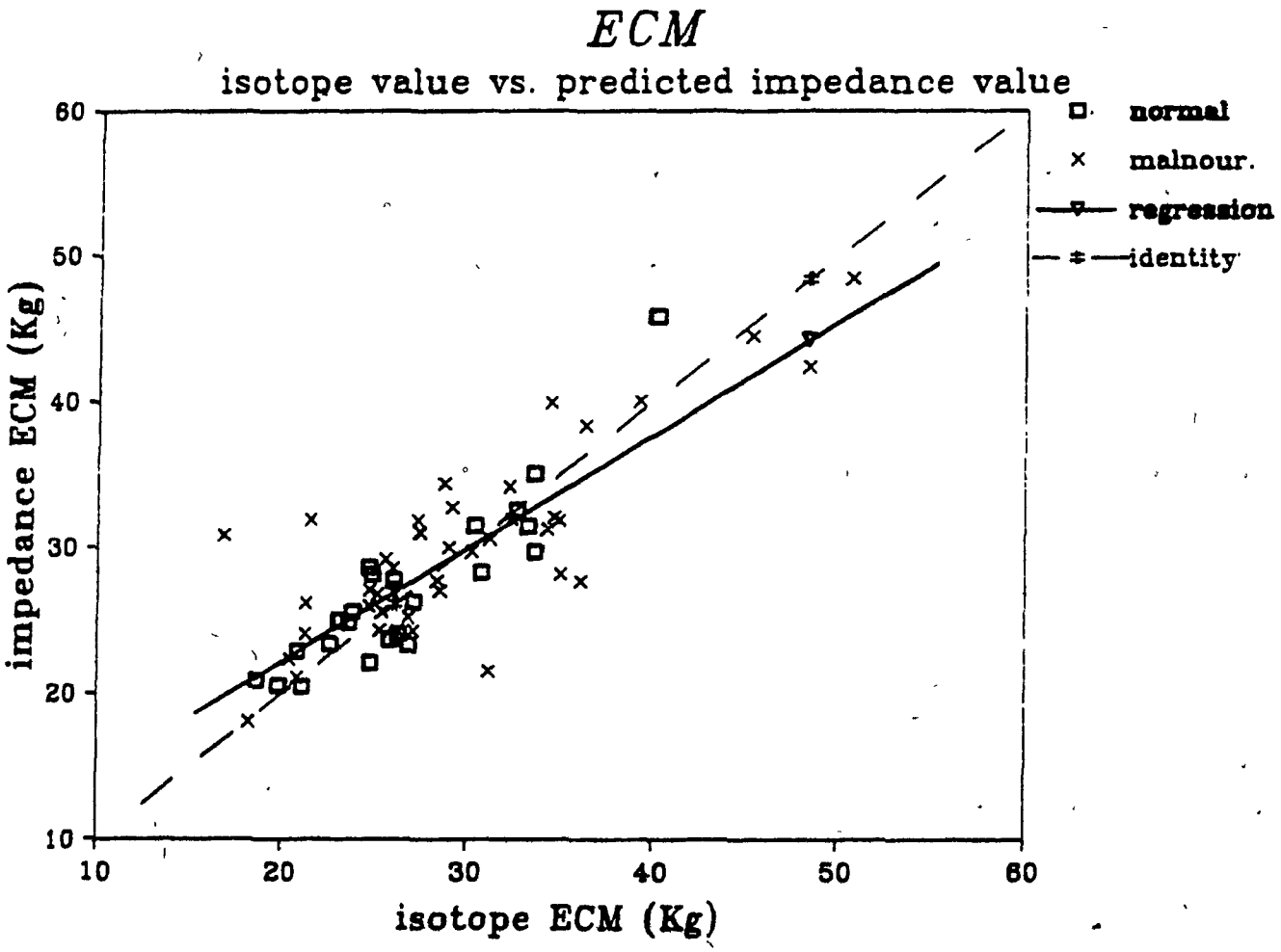

Figure 22
Scatterplot comparing the isotope-measured ECM with the ECM calculated from the impedance data using Equation 33. The regression line is calculated from Equation 34.

Referring to Figure 23, the impedance - isotope differences in the measured ECM are sorted according to the Na_e/K_e ratio. The distribution about 0 on the Y axis is fairly even, suggesting that equation 34 fairly represents both the normal and malnourished subjects despite it being derived from the LBM and BCM equations which give biased results, both underestimating the normal subjects and overestimating the malnourished subjects.

For Figure 24, equation 33 was recalculated using the "normal" equations 10 and 20 for the normally-nourished subjects and the "malnourished" equations 11 and 21 for the malnourished subjects. The two new sets of impedance ECM data, as the y-axis, are plotted against isotope ECM on the x-axis.

The normal and malnourished regression lines are derived from equations 35 and 36, listed in Table 11.

Table 11

Equation	r	P<	SEE/mean Y
for normals, n=23			
Eq.35 impECM = .90 (isoECM) + 2.94	.90	.001	8.6%
for malnour. n=41			
Eq.36 impECM = .62 (isoECM) + 11.22	.80	.001	11.7%

where **impECM** is the ECM calculated from impedance data, and **isoECM** is the ECM measured by isotope dilution.

Considering the slopes, r and SEE/mean, the ECM relationship developed for the normal subjects is more precise than that for the malnourished.

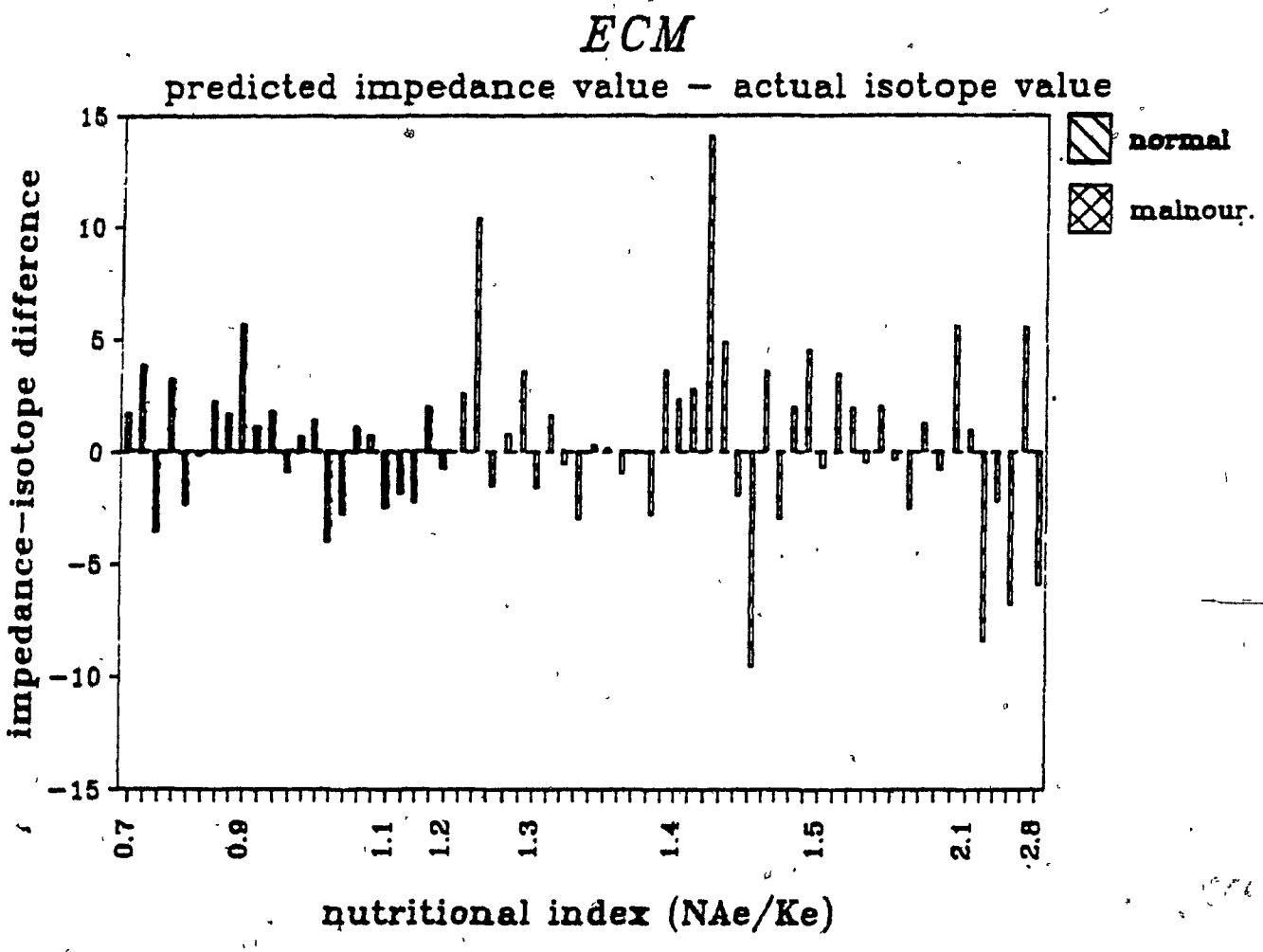

Figure 23
Bar graph of the differences between the impedance and isotope ECM values, sorted along the x-axis in order of increasing malnourishment.

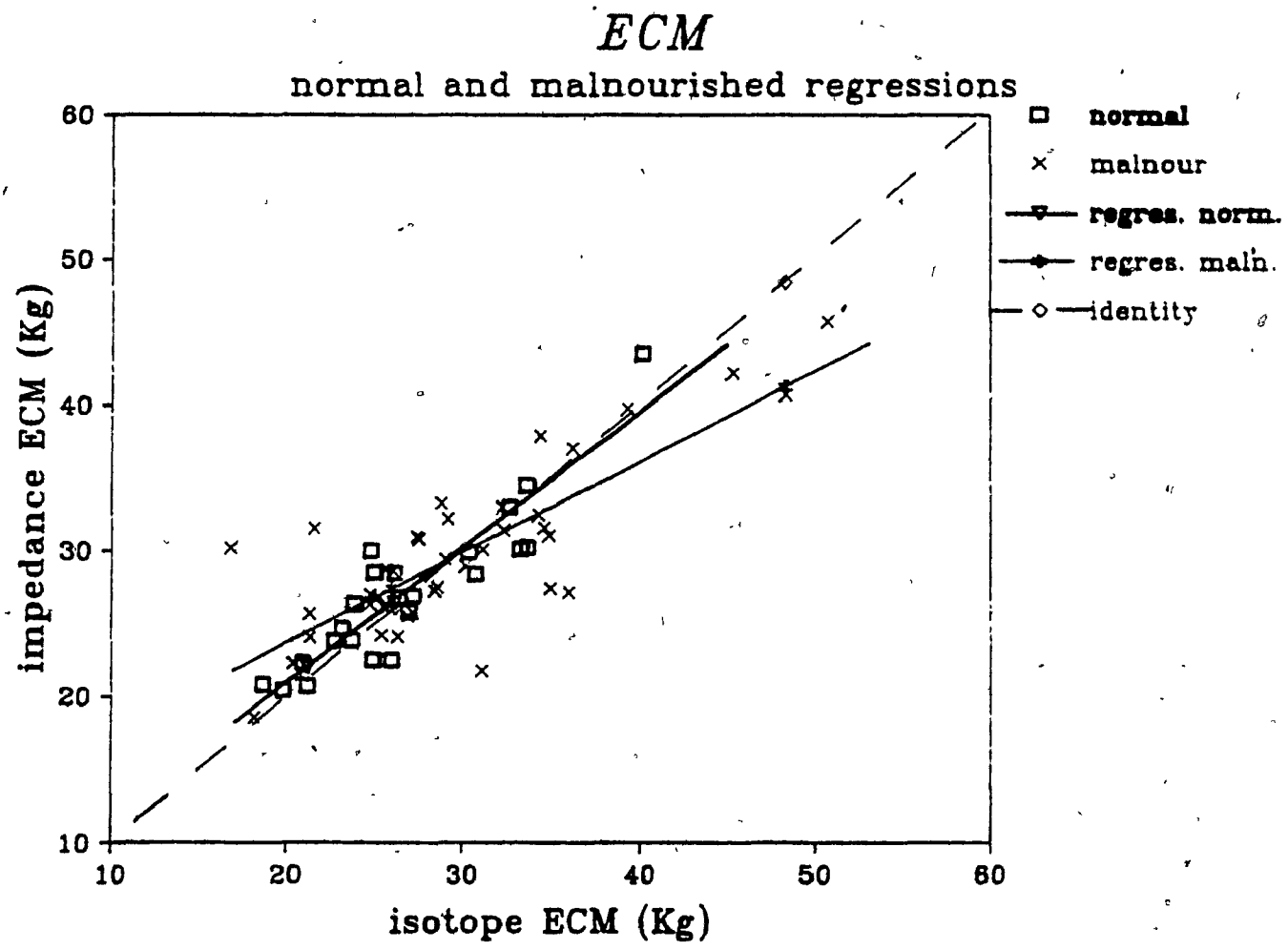

Figure 24
Scatterplot comparing the isotope-measured ECM with the ECM calculated from the impedance values derived from Equations 10 and 20 for the normal subjects, and from Equations 11 and 21 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 35, while the regression line for the malnourished subjects is calculated from Equation 36.

6.11.FAT: Impedance Measured Vs. Isotope Measured

Because the fat partition of body composition is conceptually the difference between the body weight and the lean body mass, impedance fat is calculated as:

Eq.37 Fat = Body Wt. - LBM

... where LBM is calculated by equation4 and the body weight was measured on hospital scales.

Figure 25 plots the impedance-calculated fat on the y-axis against the isotope-fat on the x-axis. The regression line is determined by the equation relating the impedance-fat as the dependant variable to isotope-fat as the independent variable:

	Equation	r	P<	SEE/mean Y
Eq.38	imp Fat = .94(iso Fat) + .46	.89	.001	32.6%

where **impFat** is the fat measured from impedance data, and **isoFat** is the fat measured from isotope-dilution data.
SEE/mean : standard error of the estimate / mean of the dependant variable.

The large SEE/mean value of 32% is understandable when one considers that the SEE approximates the SEE for LBM while the mean fat value (16.8 Kg) is much smaller than the mean LBM (47.9 Kg).

The negative fat values plotted in Figure 25 are mathematically correct according to Equation 38 but are, of course, physically impossible. As shown in Figure 26, where the difference between the impedance and isotope measured fat is sorted into normal and malnourished groups, equation 37 overpredicts the fat measurement in the normal subjects and tends to underestimate for the

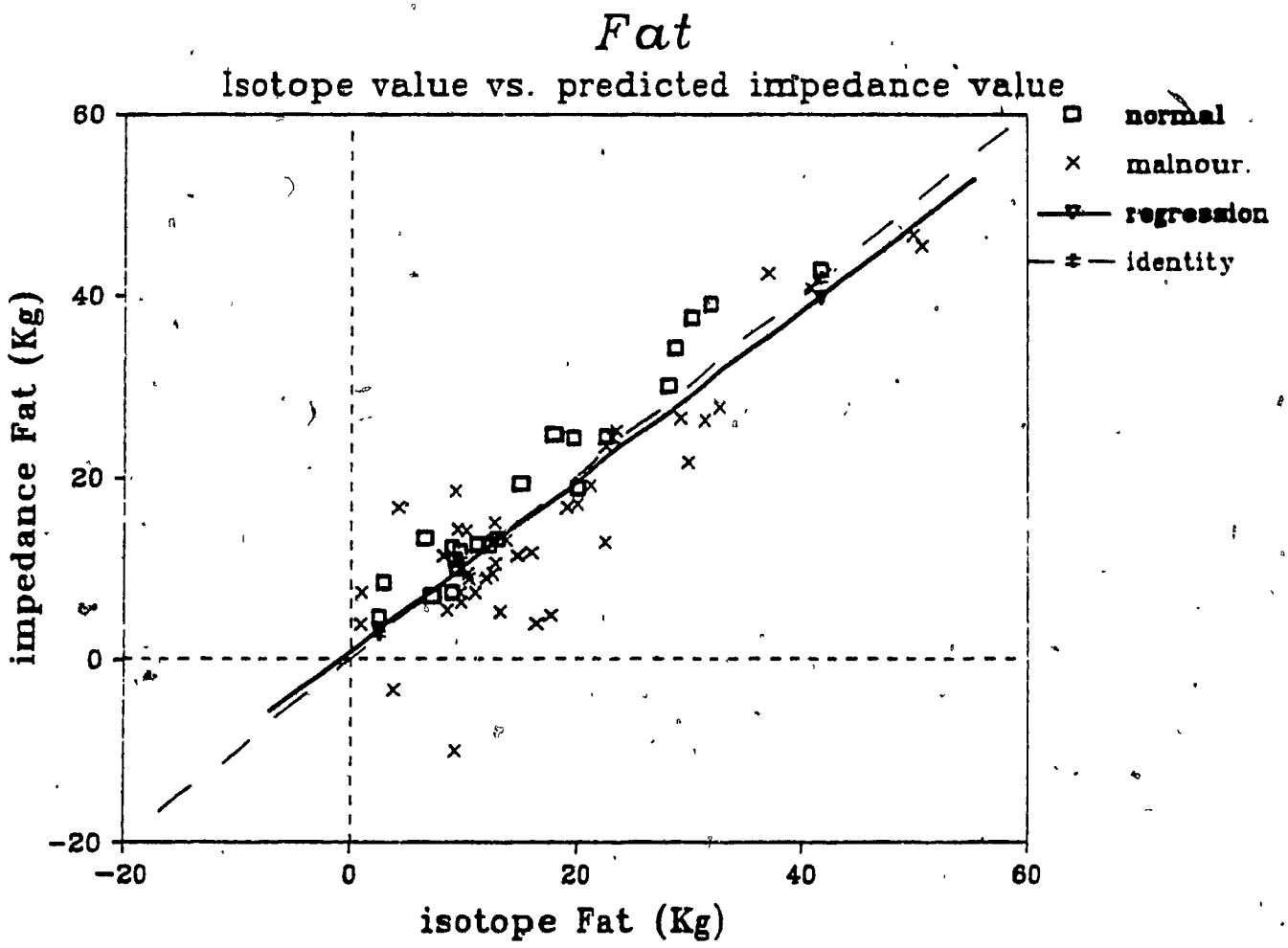

Figure 25
Scatterplot comparing the isotope-measured fat mass with the fat calculated from the impedance data using Equation 37. The regression line is calculated from Equation 38. The line of identity is obtained by plotting the y-values equal to the x-values.

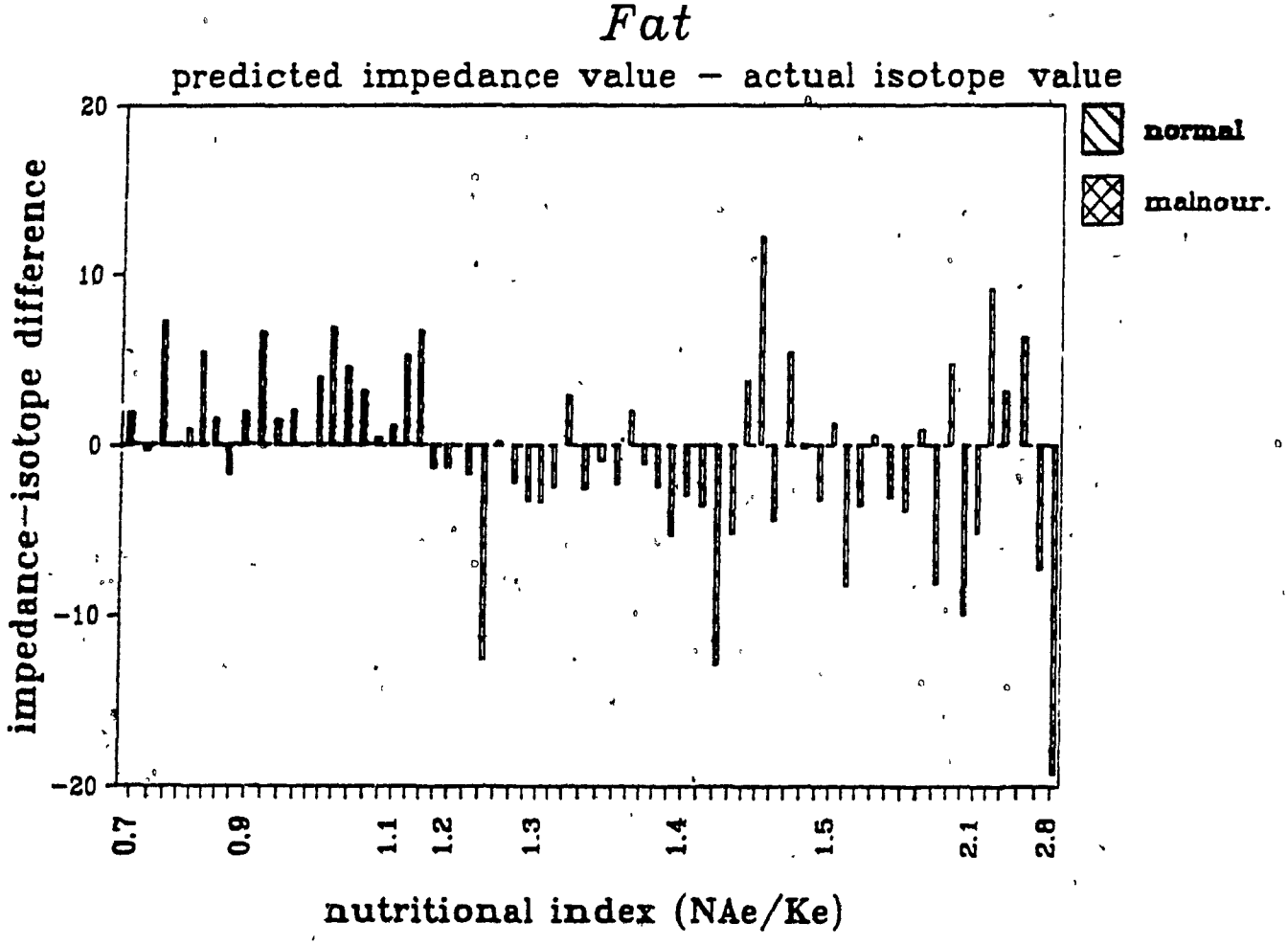

Figure 26
Bar graph of the differences between the impedance and isotope Fat values, sorted along the x-axis in order of increasing malnourishment.

malnourished. This bias is understandable since the equation 4 for LBM underestimates the normals and overestimates the malnourished.

By substituting the normal and malnourished regression equations for LBM (equations 10 and 11) in equation 38, separate normal and malnourished regression lines can be developed, as demonstrated in Figure 27, describing the relationship between impedance fat as the dependant variable and isotope fat as the independent variable. The equations that describe these regression lines are listed in Table 12

Table 12

Equation	r	P<	SEE/mean Y
for normals, n=23			
Eq.39 impFat = 1.05(isoFat) -.92	.97	.001	17.4%
for malnour. n=41			
Eq.40 impFat = .92(isoFat) +.84	.89	.001	33.4%

where **impFat** is the fat calculated from impedance data, and **isoFat** is the fat calculated from isotope-dilution data.
SEE/mean: standard error of the estimate / mean of the dependant variable.

Understandably, the observations are the same as those for LBM; the relationship between impedance and the fat mass is more precise for the normal subjects than for the malnourished.

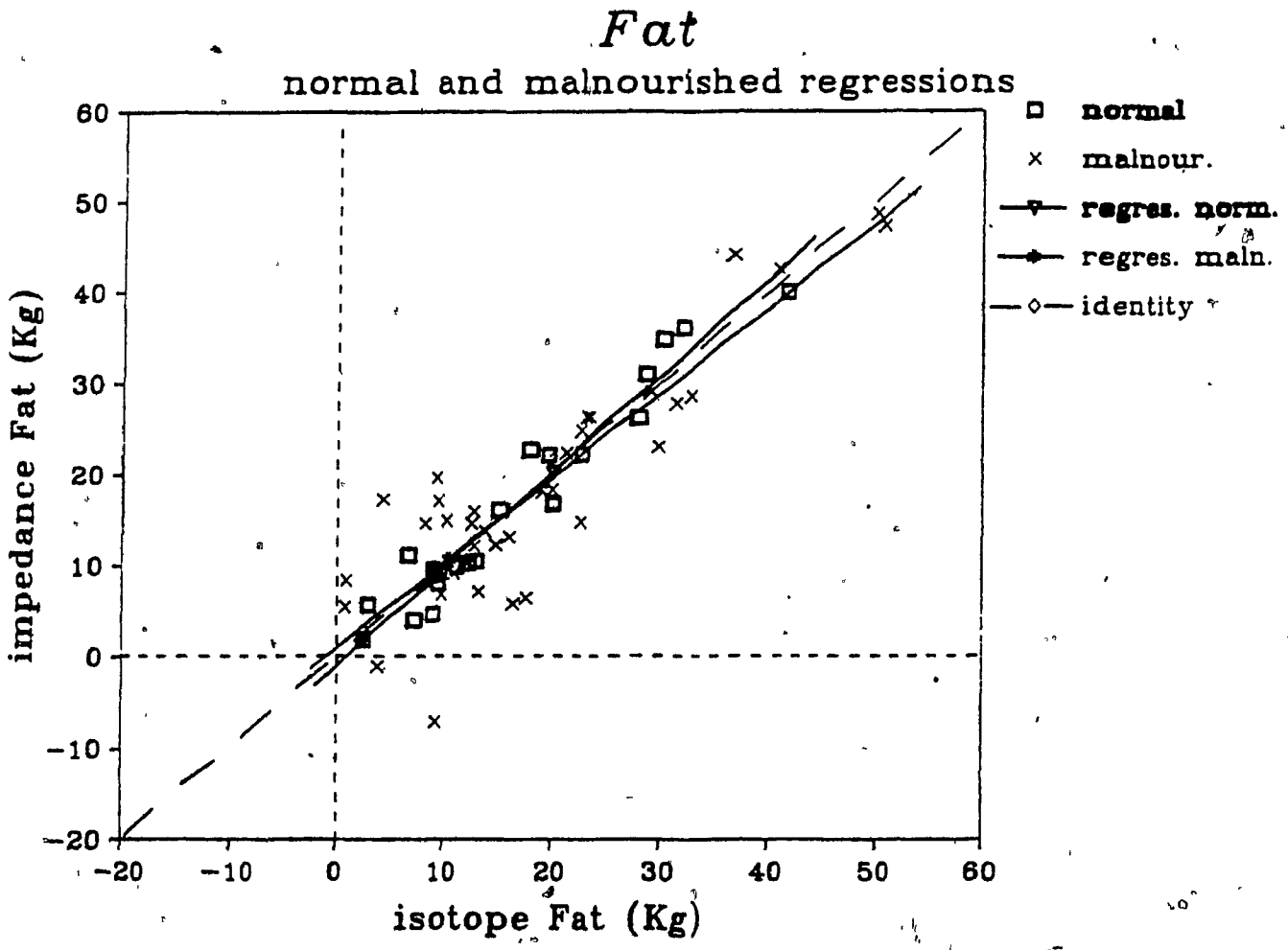

Figure 27
Scatterplot comparing the isotope-measured Fat with the Fat calculated from the impedance values derived from Equation 10 for the normal subjects and from Equation 11 for the malnourished subjects. The regression line for the normal subjects is calculated from Equation 39, while the regression line for the malnourished subjects is calculated from Equation 40.

7.CONCLUSIONS:

1. In a comparison of impedance measurements with isotope-dilution measurements in 64 subjects, whole body resistance was found to correlate well with lean body mass (1/R vs. LBM, r = .78, SEE/mean = 13.5%). On separating the 64 subjects into normally nourished (n = 23) and malnourished (n = 41) groups according to the Na_e/K_e ratio, the relationship between 1/R and LBM was found to have greater precision in the normally nourished group (r = .92, SEE/mean = 8.4%) compared to the malnourished group (r = .78, SEE/mean = 13.3%).

2. As reported by previous investigators[19], the relationship between 1/R and LBM was optimised by including a correction factor for the subject's height, expressed as Ht^2/R. This correction improved the r and SEE/mean as demonstrated in Table 13:

Table 13 Comparison of 1/R vs. LBM with Ht^2/R vs. LBM

Group	1/R vs. LBM r	1/R vs. LBM SEE/mean LBM	Ht^2/R vs. LBM r	Ht^2/R vs. LBM SEE/mean LBM
All subjects, n=64	.78	13.5%	.88	10.5%
Normals, n=23	.92	8.4%	.96	5.7%
Malnourished, n=41	.78	13.3%	.82	12.1%

r : Pearson coefficient
SEE/mean : standard error of the estimate / mean of the dependant variable

[19] Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1986;41:810-817.

Applying a correction factor for body weight to the relationship between Ht^2/R and LBM did not improve the statistics.

3. The r and SEE/mean values described above for LBM are identical for the respective relationships between the total body water (TBW) and $1/R$ or Ht^2/R. This is because our isotope method calculates LBM as the product of the isotope-measured TBW and a constant (TBW x 1.333).

4. Reactance was found to correlate inversely with the isotope-measured ratio of extracellular to intracellular mass ($1/X_c$ vs. ECM/BCM, r = .70, SEE/mean = 23.8% for all 64 subjects). The relationship between $1/X_c$ and ECM/BCM was found to be weak in the normally nourished group (r = .25, SEE/mean = 17.1%, n=23) compared to the malnourished group (r = .58, SEE/mean = 19.7%, n=41).

5. The statistics for $1/X_c$ are improved by including Ht^2 as a second independent variable, as shown in Table 14.

Table 14. Comparison of $1/X_c$ vs. ECM/BCM with $(1/X_c + Ht^2)$ vs. ECM/BCM

	$1/X_c$ vs. ECM/BCM		$(1/X_c+Ht^2)$ vs. ECM/BCM	
Group	r	SEE/mean ECM/BCM	r	SEE/mean ECM/BCM
All subjects, n=64	.70	23.8%	.79	20.6%
Normals, n=23	.25	17.1%	.60	14.4%
Malnourished, n=41	.58	19.7%	.64	18.6%

where $1/X_c$ is the inverse of reactance, and ECM/BCM is the ratio of the extracellular to intracellular mass measured by isotope dilution.

6. The body cell mass (BCM) can be calculated from the impedance-measured LBM and ECM/BCM as :

$$BCM = \frac{LBM}{ECM/BCM + 1}$$

The extracellular mass (ECM) can then be calculated as the LBM minus the BCM, and the fat mass is calculated as body weight minus LBM. In this way the impedance method was devised to measure all partitions of body composition from measurements of resistance, reactance, height and weight.

The regression formulas of the impedance method, based on the total group of 64 subjects, are summarized in Table 14.

Table 15. Formulas for calculating body composition from impedance data, height and weight.

(a) $LBM = 0.61(Ht^2/R) + 16.42$	
(b) $ECM/BCM = 34.73(1/X_c) - .00006(Ht^2) + 2.42$	
(c) $BCM = \frac{LBM}{(ECM/BCM) + 1}$	where LBM is calculated from (a) and ECM/BCM is calculated from (b).
(d) $ECM = LBM - BCM$	where LBM is calculated from (a) and BCM is calculated from (c).
(e) Fat = Body weight - LBM	,LBM is calculated from (a).

7. The precision of the BCM, ECM, LBM and fat measurements using the impedance method can be evaluated by regression equations comparing the impedance-measured partition, as the dependant variable, with the corresponding isotope-measured partition, as the independent variable. The statistics of these

regressions are listed in Table 16, with analysis of the total group of subjects and the normal and malnourished subgroups for comparison purposes.

The precision of the impedance method in measuring BCM, ECM, LBM and fat is better in the normal subjects compared to the malnourished.

Table 16.
Comparison of statistics of the regressions Y = mX + b, where Y is body composition measured by impedance, using the formulas listed in Table 15, and X is body composition measured by isotope dilution.

Partition of Body Composition

	BCM		ECM		LBM		Fat	
Group	r	SEE/mean	r	SEE/mean	r	SEE/mean	r	SEE/mean
All subjects n=64	.87	12.9%	.83	12.1%	.88	9.2%	.89	32.6%
Normals n=23	.91	10.5%	.90	9.4%	.97	5.4%	.97	15.0%
Malnour. n=41	.74	14.1%	.81	12.8%	.83	10.3%	.88	37.7%

SEE/mean : the standard error of the estimate, divided by the mean of the body composition partition as measured by impedance.

The large SEE/mean for fat (32.6%) is understandable when considering that the fat measure is calculated as body weight minus LBM. The SEE for fat (5.48) is comparable in size to the SEE for LBM (4.42), but the mean fat mass is much smaller than the mean LBM (16.8 Kg vs. 47.9 Kg).

8. The formulas listed in Table 15 represent analyses of the total

group of 64 subjects, the majority (64%) of whom were malnourished according to isotope-dilution results. The formulas for LBM and BCM are found to bias the calculated measurements by underestimating the measurements of the normally nourished subjects and overestimating in the malnourished group. Conversely, the formula for fat overestimates the normal subjects and slightly underestimates the malnourished. The formula for ECM appears unbiased.

9. In contrast to previous investigators, reactance is found to be important in the measurement of body composition, especially in malnourished states characterized by an expansion of the extracellular mass and contraction of the body cell mass.

However, the relationship between reactance and ECM/BCM is not as strong as the relationship between resistance and lean body mass. Referring to the SEE/mean values of Table 16, the 9% to 33% error of body composition measurements from impedance may be too high for some clinical applications. Further refinement is needed.

The impedance plethysmograph used for this study delivers a current of fixed frequency and amperage. Conceivably, measuring with other frequencies at different intensities might improve the accuracy of body composition measurements.

8. DISCUSSION

While there is statistical evidence and electrophysiologic reasoning in support of the relationship between LBM and Ht^2/R, the rationale for choosing $(1/X_c + Ht^2)$ as the optimal solution for ECM/BCM is open to question. A problem with this interpretation for X_c is its inaccuracy in the normally nourished subjects, where $1/X_c$ correlates poorly with ECM/BCM ($r = .25$). However, $1/X_c$ also correlates fairly well with ECM in both the normal ($r=.76$) and malnourished subjects ($r=.66$). Therefor, one could speculate that $1/X_c$ might correlate well with the product of ECM/BCM and ECM, i.e. ECM^2/BCM.

The following relationship is obtained:

for all 64 patients:

Equation	P<	r	SEE/mean
$ECM*ECM/BCM = 2026.41*1/X_c - 3.05$	.0001	.80	32%

This relationship is not improved (in terms of r or SEE/mean) by including Ht^2 or weight as second independent variables.

ECM can be solved from ECM^2/BCM and LBM as a quadratic equation:

$X^2 + aX - ab = 0$ where X is ECM, a is ECM^2/BCM, and b is ECM+BCM, i.e. LBM.

Applying the general solution to a quadratic equation, the solution for ECM is:

$$ECM = \frac{-(ECM^2/BCM) + \sqrt{(ECM^2/BCM)^2 - 4((-ECM^2/BCM) \times LBM)}}{2}$$

Using the above equation to calculate ECM and solving for BCM as LBM - ECM. the regression comparisons between the impedance measured ECM and BCM and the corresponding isotope-measured values are as follows:

for all patients, n=64:

Equation	P<	r	SEE/mean Y
impECM = .73 isoECM + 7.97	.001	.83	11.6%
impBCM = .70 isoBCM + 5.55	.001	.86	13.6%

for normals, n=23:

Equation	P<	r	SEE/mean Y
impECM = .94 isoECM + 1.83	.001	.94	6.8%
impBCM = .79 isoBCM + 2.63	.001	.92	9.3%

for malnourished, n=41:

Equation	P<	r	SEE/mean Y
impECM = .66 isoECM + 10.54	.001	.79	12.8%
impBCM = .86 isoBCM + 3.31	.001	.73	15.7%

where **impECM** and **impBCM** are the respective impedance measured values, and **isoECM** and **isoBCM** are the isotope measured values.

The results listed above can be compared with those presented previously for the relationship between $1/X_c + Ht^2$ and ECM/BCM:

for all patients, n=64:

Equation	P<	r	SEE/mean Y
impECM = .77 isoECM + 6.98	.001	.83	12.2%
impBCM = .69 isoBCM + 5.69	.001	.87	12.9%

for normals, n=23:

Equation	P<	r	SEE/mean Y
impECM = .97 isoECM +.98	.001	.90	9.4%
impBCM = .79 isoBCM +2.64	.001	.91	10.5%

for malnourished, n=41:

Equation	P<	r	SEE/mean Y
impECM = .70 isoECM + 9.57	.001	.81	12.8%
impBCM = .78 isoBCM + 4.51	.001	.74	14.1%

Thus, the relationship between ECM^2/BCM and $1/X_c$ seems to provide a slightly better measurement of ECM and BCM in the normal subjects compared to the relationship between ECM/BCM and $(1/X_c + Ht^2)$, while the latter relationship is slightly stronger for the malnourished subjects.

However, the relationship between $1/X_c$ and ECM^2/BCM does not remove the bias in the impedance measurement of BCM. Referring to Figure 28, on plotting the differences between the impedance-measured BCM and the isotope-measured BCM, the same trend of underestimation of the normal subjects and overestimation of the malnourished subjects is present as was found using Equation 29 (Figure 20), which is based on the relationship between $(1/X_c + Ht^2)$ and ECM/BCM.

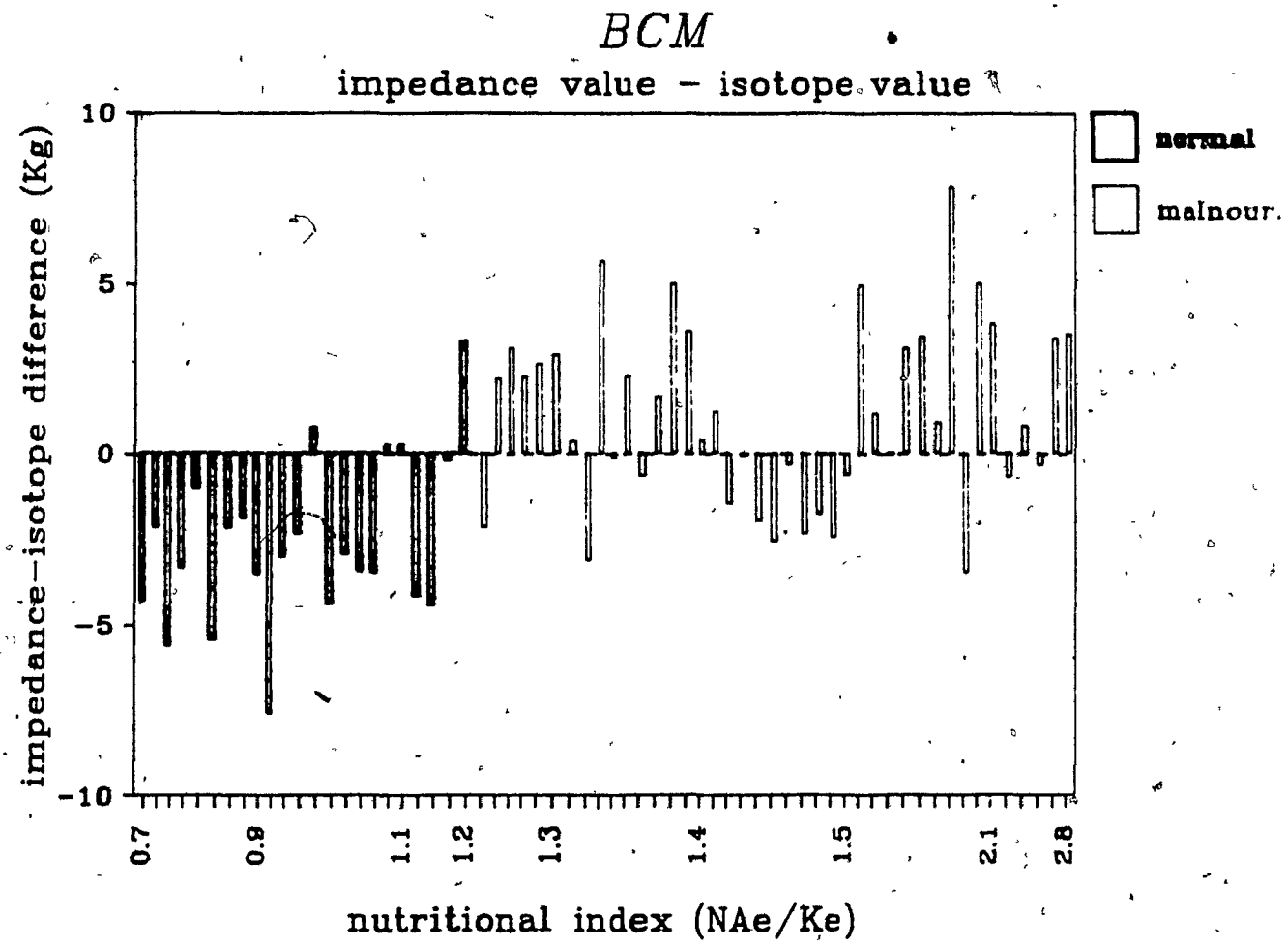

Figure 28
Bar graph of the differences between the impedance and isotope BCM values, sorted along the x-axis in order of increasing malnourishment. The impedance BCM is calculated as the difference between the LBM and the ECM, where the LBM is calculated using equation 4 and ECM is calculated as:

$$ECM = \frac{-(ECM^2/BCM) + \sqrt{(ECM^2/BCM)^2 - 4((-ECM^2/BCM) \times LBM)}}{2}$$

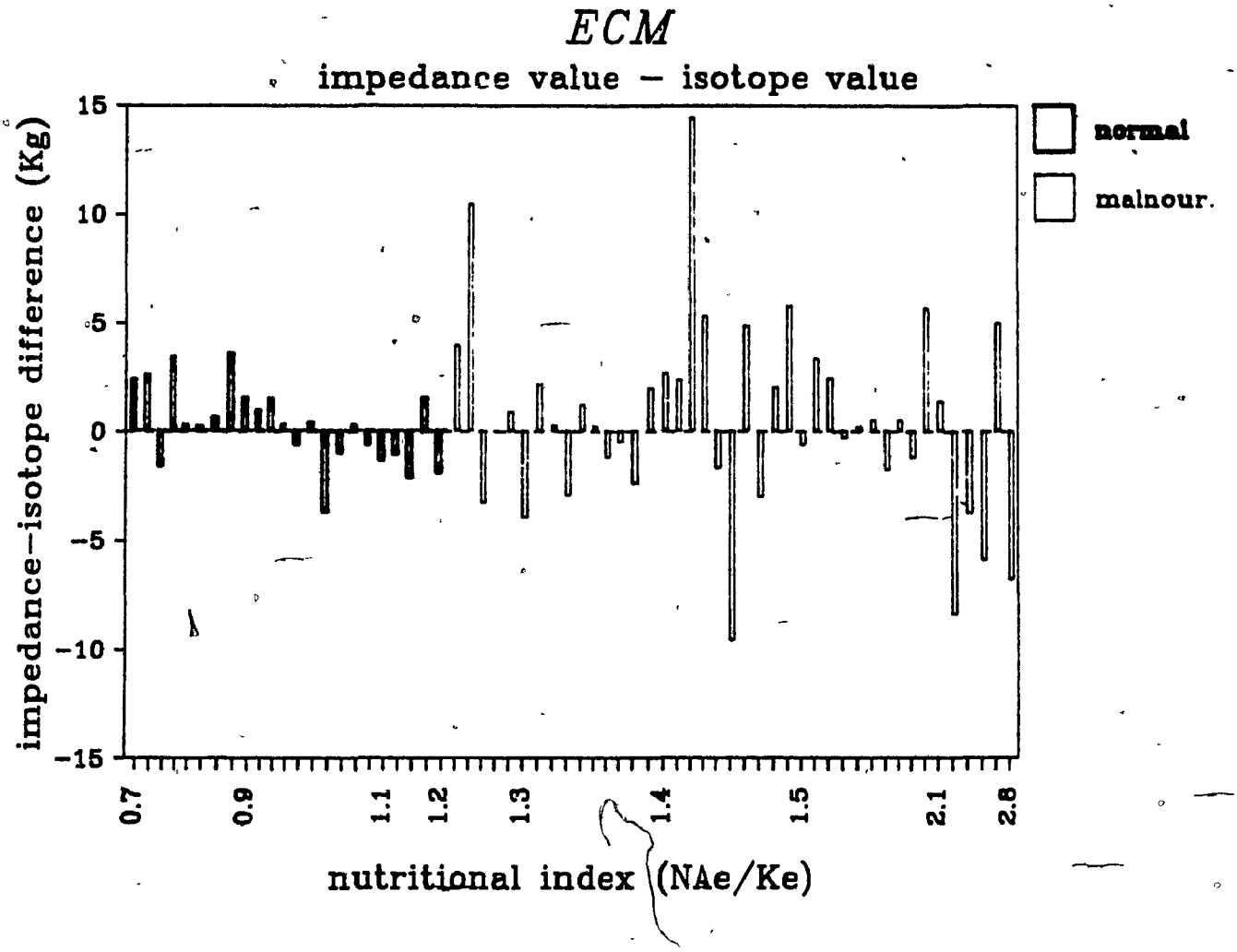

Figure 29
Bar graph of the differences between the impedance and isotope ECM values, sorted along the x-axis in order of increasing malnourishment. The impedance calculation for ECM is based on the following formula:

$$ECM = \frac{(ECM^2/BCM) + \sqrt{(ECM^2/BCM)^2 - 4((-ECM^2/BCM) \times LBM)}}{2}$$

The ECM calculated from the quadratic solution of the relationship between $1/X_c$ and ECM^2/BCM shows no obvious bias between the normally nourished and malnourished subjects, as shown in Figure 29. This is the same observation as that noted for ECM calculated using Equation 33 (Figure 23).

The explanation for the bias observed in the impedance measurements of BCM and LBM is somewhat of a mystery, although there is some evidence from this study and from prior research to suggest that using a signal frequency higher than 50 kHz might both remove the bias and improve the precision of the BCM and LBM measurements. It is improbable that the bias is due to our isotope-dilution measurements because the technique used was previously validated in comparison with other techniques, such as the direct measurement of exchangeable potassium and whole-carcass analysis, and no bias was observed.

The evidence in favor of using a higher frequency is as follows: (A) The impedance method of this study, using a 50 kHz frequency, underestimates the LBM and BCM measurements in the normally nourished subjects compared to the malnourished subjects. The LBM measurement is based on the measure of resistance and height and not on reactance. Removing height from the relationship does not resolve the bias. However, no bias was found in the measured extracellular water (ECM), which is based on both reactance and resistance measurements.

Compared to malnourished subjects, normally nourished subjects have a larger fraction of the total body water distributed in the

intracellular space. The bias of our impedance calculations could reflect an incomplete penetration of the intracellular space by the 50 kHz signal. Theoretically, the result of such an incomplete penetration would be an underestimation of the intracellular water, i.e. body cell mass, and also of the total body water. This underestimation would be more apparent in the normally nourished subjects since more of their total body water is intracellular. Since there was no obvious bias in the extracellular water measurement, perhaps the 50 kHz signal is appropriate for reactance measurements, while resistance measurements would benefit from a higher frequency.

(B) Lofgren has shown that intracellular conduction is excluded at low frequencies but is included at higher frequencies [20].

(C) In studying the electrical characteristics of tissues at various frequencies, Nyboer concluded that resistance and capacitance both have high values at frequencies below 10 kHz; capacitance drops to a minimum in the frequency range of 100 to 1000 kHz while resistance continues to diminish beyond 1000 kHz [21].

Based on this information, further body composition studies comparing isotope-dilution measurements with impedance measurements using multiple frequencies from 50 to, say, 500 kHz might identify a frequency at which there is no bias in the measured BCM and LBM between normal and malnourished states.

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10.APPENDIX: The following paper was published in the Surgical Forum, 1986;XXXV11:42-44, and was presented at the American College of Surgeons 72nd Annual Clinical Congress, in New Orleans, October 1986.

SURGICAL FORUM

BODY COMPOSITION MEASUREMENTS FROM WHOLE BODY RESISTANCE AND REACTANCE

David McDougall, MD,
and Harry M. Shizgal, MD, FRCS(C), FACS

A RELATIONSHIP has been demonstrated between whole body bioelectrical resistance (R) and total body water. The present study was undertaken to determine the relationship between whole body reactance (X_c) and body composition. X_c is related to impedance (Z) by the relationship $Z^2 = R^2 + X_c^2$.

MATERIALS AND METHODS

In 64 patients, R and X_c were determined using a four-electrode impedance plethysmograph (RJL Systems, Detroit). An 800-microamp, 50-kHz current was applied via a pair of electrodes attached to the dorsum of the hand and foot, with a second set of proximal sensing electrodes. Body composition was simultaneously determined by multiple isotope dilution (1).

RESULTS AND DISCUSSION

A normal body composition was present in 23 patients and a malnourished body composition in 41. Data analysis revealed an inverse relationship between lean body mass (LBM) and R, while the ratio of the two components of LBM, the extracellular mass (ECM) and the body cell mass (BCM), was inversely related to the X_c. The ratio of exchangeable sodium to exchangeable potassium (Na_e/K_e), a sensitive index of the nutritional state, was also inversely related to X_c. The statistics of the resultant regressions were improved by including the subject's height (H_t), as an independent variable, to correct for the subject's geometry. The following regressions were obtained:

$$LBM = 16.4 + 0.61(H_t)^2/R \qquad r = 0.88,\ P < 0.001$$
$$ECM/BCM = 2.4 + 34.8/X_c - 5.97 \times 10^{-5}(H_t)^2 \qquad r = 0.79,\ P < 0.001$$
$$Na_e/K_e = 1.87 + 34.1/X_c - 4.66 \times 10^{-5}(H_t)^2 \qquad r = 0.79,\ P < 0.001$$

Since LBM = BCM + ECM, and body fat = body weight − LBM, body composition can be determined from the measurement of R, X_c, and H_t. A statistically significant correlation exists between the components of body composition determined by isotope dilution, as the independent

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variable, and those determined by impedance plethysmography, as the dependent variable (Table 1). The correlation coefficients (r) for the normal subjects, malnourished subjects, and both groups combined have been included in Table 1. For all the variables, a better correlation existed for the subjects with a normal body composition. The precision of the impedance determinations was estimated by dividing the standard error of the estimate (SEE) by the mean of the dependent variable. Although there was a good correlation between the two measurements, the error was significant. The relationship between the isotope dilution measurement of BCM and the impedance determination is depicted in Figure 1.

Table 1—Relationship between body composition components as determined by isotope dilution and impedance plethysmography

	Normally nourished and malnourished				Normally nourished	Malnourished
Variable	Regression*	r	P	SEE/Mean (%)	(r)	(r)
BCM	$Y = 5.69 + 0.69X$	0.87	<0.001	12.9	0.91	0.74
ECM	$Y = 6.98 + 0.77X$	0.83	<0.001	12.2	0.90	0.80
LBM	$Y = 11.11 + 0.77X$	0.88	<0.001	9.2	0.96	0.83
Body fat	$Y = 0.46 + 0.94X$	0.97	<0.001	32.6	0.97	0.88

X = isotope dilution measurement, Y = impedance plethysmography determination.

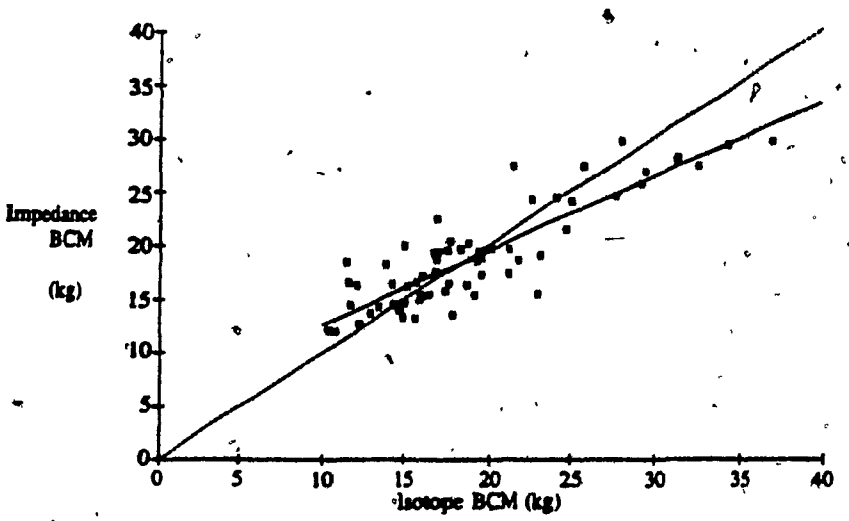

Fig 1—BCM as measured by impedance plethysmography, plotted against BCM as measured by isotope dilution. The solid line is the regression and the broken line is the line of identity.

CONCLUSIONS

The simultaneous measurement of R and X_c provides a simple and noninvasive means of measuring body composition. However, the accuracy of the determinations remains a problem.

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