Bioelectrical impedance measurements in patients with gastrointestinal disease: validation of the spectrum approach and a comparison of different methods for screening for nutritional depletion1–3

Petronella LM Cox-Reijven, Bernard van Kreel, and Peter B Soeters

ABSTRACT

Background: Bioelectrical impedance spectroscopy (BIS) may be of value in identifying patients with nutritional depletion.

Objective: The primary aim of the study was to assess the validity of BIS in patients with gastrointestinal disease. The secondary aim was to compare different screening methods for identifying nutritionally depleted patients.

Design: In 70 patients with gastrointestinal disease, BIS measurements were performed and fluid compartments were calculated from extrapolated resistance (R) values of extracellular (R_ECW) and intracellular (R_ICW) water based on mixture equations. Results were compared with total body water and ECW, which were measured by dilution methods. Patients were classified as depleted if their actual fat-free mass (FFM) was < 90% of their ideal FFM (iFFM). Different screening approaches for depletion were compared: the impedance vector method and the resistance index (RI) in relation to iFFM (RI/iFFM).

Results: Total body water and ICW were largely underestimated (4 L) in the not-depleted patients but not in the depleted patients. In both groups, ECW was slightly overestimated (0.6–0.7 L). The critical frequency was 60% higher and the membrane capacitance was 40% lower in the depleted than in the not-depleted patients. The impedance vector method failed to identify depleted patients, whereas the proposed ratio at R_50 (R measured at 50 kHz) and R_inf (R at infinite frequency) resulted in comparable sensitivity (86%) and specificity (73–80%).

Conclusions: BIS measures of body fluids are influenced by the presence of depletion, probably because of alterations in the electric properties of the body at the cellular level. However, for screening purposes, the use of the ratio (L^2/R)/iFFM at R_50 and R_inf may be of value. (Am J Clin Nutr 2003;78:1111–9).

KEY WORDS Patients, gastrointestinal disease, depletion, body composition, bioelectrical impedance spectroscopy, BIS, total body water, extracellular water, intracellular water, screening

INTRODUCTION

Malnutrition is often present in patients with gastrointestinal disease and has adverse effects on recovery because it increases morbidity and mortality (1). Measuring body composition is essential for the assessment of nutritional status because body weight alone gives no information about the loss of body cell mass (BCM) in depleted patients. Alterations in fat mass or extracellular water (ECW) could mask the loss of BCM.

Bioelectrical impedance analysis (BIA), which involves measurement of the impedance of the human body to an alternating current, may be of value. However, many different approaches are currently in use. Single-frequency BIA (SF-BIA) measures body impedance at one frequency, usually 50 kHz, from which total body water (TBW) is calculated on the basis of regression equations that incorporate the resistance index (RI = L^2/R), where L is body length and R is resistance. These equations were found to be population specific, which complicates the clinical use of SF-BIA (2–4). Furthermore, it has been concluded that in cases of fluid imbalance, which is often present in severely ill patients, SF-BIA is not valid (5). Bioelectrical impedance spectroscopy (BIS) may overcome the limitations of SF-BIA, because it measures the fluid compartments ECW and ICW separately. BIS measures the impedance at a range of frequencies from which the resistance of the extracellular (R_ECW) and intracellular (R_ICW) fluid compartments are extrapolated. These resistance values are used to calculate ECW and ICW separately. This approach also differs from SF-BIA in that mixture equations based on physical models are often used instead of regression equations (6). In view of the differences between the 2 approaches, BIS seems more appropriate for clinical applications than is SF-BIA.

For screening purposes, L^2/R—without the use of population-specific prediction equations—may be of value. Because the size of fluid compartments is proportional to L^2/R, comparison of the RI at different frequencies with normal values of fluid compartments may allow the identification of nutritionally depleted patients. The applicability of this ratio as a screening tool has not been studied.

The BIA vector method described by Piccoli et al (7) is another approach that does not require prediction equations.  


1 From the Departments of Dietetics (PLMC-R), Clinical Chemistry (BVK), and Surgery (PBS), University Hospital Maastricht, Maastricht, Netherlands.

2 Supported by the University Hospital Maastricht.

3 Reprints not available. Address correspondence to PLM Cox-Reijven, Department of Dietetics, University Hospital Maastricht, P Debyelaan 25, PO Box 5800, 6202 AZ Maastricht, Netherlands. E-mail: ncox@pmdi.azm.nl. Received February 3, 2003.

Accepted for publication May 27, 2003.
This method uses the plot of the impedance vector components, \( R \) and reactance measured at 50 kHz. Studies have shown that this method is useful in subjects with a high body mass due to fat or fluid overload (8) and in dialysis patients undergoing fluid removal (9). However, it is not clear whether the method is clinically useful in discriminating between depleted and nondepleted patients, because no studies of this approach in patients with gastrointestinal diseases or in depleted patients have been published.

The primary aim of the present study was to assess the validity of BIS for measuring fluid volumes in patients with gastrointestinal disease by comparing BIS with dilution methods and to test the validity of BIS in the presence of weight loss and nutritional depletion. The second aim was to assess the applicability of the RI (\( L^2/R \)) and the impedance vector method as screening instruments for nutritional depletion by comparing the sensitivity and specificity of these approaches with results from BIS measurements and computation of the volume of body compartments.

**SUBJECTS AND METHODS**

**Patients**

Seventy patients (29 women, 41 men) with gastrointestinal disease admitted to the hospital were included in the study. Of these patients, 53 were diagnosed with cancer of the esophagus, stomach, small intestine, cecum, colon, rectum, or pancreas, and 17 had benign diseases, including diverticulosis, pancreatitis, Crohn disease, ulcerative colitis, and benign stenoses of parts of the gastrointestinal tract. No patients had clinical signs of edema or dehydration, and all patients were in a stable metabolic condition. Their mean (± SD) body mass index (BMI; in kg/m\(^2\)) was 23.6 ± 3.9. Written informed consent was obtained from all participants. The study was approved by the Medical Ethical Committee of the University Hospital Maastricht.

**Protocol**

All measurements were performed in the morning on the first day of admission. Patients had fasted overnight. After the patients voided, bioelectrical impedance measurements and then anthropometric measurements were performed. Body weight was measured to the nearest 0.1 kg, and length was measured to the nearest 0.1 cm. Wrist circumference was measured to the nearest 0.1 cm with a metal tape. Blood and saliva samples were taken and then the patients drank an indicator dilution mixture of deuterium oxide and sodium bromide. Four hours after ingestion of the indicators, saliva and blood samples were obtained for deuterium and bromide analyses, respectively. Deuterium was analyzed by a mass spectrometric method described by van Kreekl et al (10). Bromide was analyzed by ion chromatography as described by Wong et al (11). Plasma was not deproteinized by the use of a filter, but by acetonitrile.

TBW\(_{\text{dil}}\) was calculated by correcting the deuterium dilution space with 4% for exchange of labile hydrogen. ECW\(_{\text{dil}}\) was calculated by correcting the bromide dilution space with 0.90 for nonextracellular distribution of bromide and with 0.95 for the Donnan equilibrium. The accuracy of TBW measurements by deuterium dilution is reported to be 1.5% (12, 13). The bromide dilution method for ECW is estimated to have an accuracy of 5% (13, 14). Intracellular water (ICW\(_{\text{dil}}\)) was calculated as TBW\(_{\text{dil}}\) - ECW\(_{\text{dil}}\). From TBW\(_{\text{dil}}\), the FFM of patients was calculated by assuming a hydration factor of 73.2:

\[
\text{FFM} = \frac{\text{TBW}_{\text{dil}} 	imes 100}{73.2} \quad (1)
\]

**Bioelectrical impedance spectroscopy**

BIS measurements were performed just before the subjects drank the indicator mixture. The subjects lied on a bed with their legs separated and arms abducted from the body. A tetrapolar electrode (3M red Dot Ag/AgCl; 3M Health Care, Borken, Germany) arrangement, as described by Lukasik et al (15), was used. Impedance was measured with a Xitron 4000B bioelectrical impedance spectrometer (Xitron Technologies, San Diego) with the use of 48 frequencies ranging from 5 to 500 kHz. Measurements were made at the right and left sides of the body. Mean resistance values were used for analysis of the data. From all 48 measured resistance and reactance values, \( R_{\text{ECW}} \) and \( R_{\text{ICW}} \) were extrapolated by using the Xitron curve-fit software. All fits were classified as “good” or “excellent.” \( R_{\text{ECW}} \) and \( R_{\text{ICW}} \) were used in Xitron equations based on the Hanai mixture theory for calculating body fluid compartments (6, 16). In healthy persons, TBW and ECW calculated by this method (TBW\(_{\text{BIS}}\) and ECW\(_{\text{BIS}}\), respectively) agreed well with values from the dilution methods (for TBW: \( r = 0.95, \text{SEE} = 1.33 \text{ L} \); for ECW: \( r = 0.91, \text{SEE} = 0.90 \text{ L} \)).

The resistance at infinite frequency (\( R_{\text{inf}} \)) was calculated as follows:

\[
R_{\text{inf}} = \frac{R_{\text{ECW}} \times R_{\text{ICW}}}{R_{\text{ECW}} + R_{\text{ICW}}} \quad (2)
\]

The curve-fit software also provides values for critical frequency (\( F_c \)) and membrane capacitance (\( C_m \)). \( F_c \) is the frequency at which the reactive component of the impedance reaches maximum values, \( C_m \) is a measure of the ability of membranes to store electric charge. \( C_m \) of the whole body is determined by total cell surface area and membrane thickness and porosity. Furthermore, \( C_m \) is also affected by the aspect ratio (length to cross-sectional area) of the body’s conductor (6). To study the effect of depletion on membrane properties, we calculated the \( C_m \) index, which removes the effect of the aspect ratio (by inclusion of length\(^2\)) and of the total cell.
surface area (by inclusion of FFM measured by deuterium dilution):

\[ C_m \text{ index} = \frac{\text{length}^2 \times C_m}{\text{FFM}_{\text{dil}}} \]  

(3)

Calculations of ideal body weight and ideal fat-free mass

The patient’s wrist circumference was used to calculate frame size. On the basis of body length and frame size, the ideal body weight was calculated according to tables published by the Metropolitan Life Insurance Company (17). From the ideal body weight, ideal FFM was calculated in kg with the use of 80% of ideal body weight in men and 70% in women as reference values. If the FFM of patients, measured by the dilution method, was smaller than 90% of their ideal FFM, the patients were classified as depleted.

Weight-loss categories

On the basis of their usual weight and reported weight loss preceding the study, patients were divided into 3 categories. Patients with weight loss \( \geq 5\% \) over 1 mo or 10% over 6 mo were classified as having severe weight loss. Patients with no weight loss were classified as having no weight loss, and all other patients were classified as having moderate weight loss.

Screening methods

Three different screening methods were compared: screening based on BIS with mixture equations, screening based on the BIA vector method, and screening based on the RI.

Screening based on BIS with mixture equations

Patients were classified as depleted by BIS if FFM_{BIS} was \(< 90\% \) of the ideal FFM.

Screening based on the BIA vector method

The resistance and reactance values of patients measured at 50 kHz were recorded and normalized for height. The sex-specific bivariate normal distribution of resistance/height and reactance/height published by De Palo et al (18) and by Piccoli et al (19) were used to assess the presence of depletion. For interpretation of the patient’s vectors normalized for height, the graphic method was used. The sex-specific nomogram was divided into 4 sectors. Patients with vectors in the upper or lower right 95% tolerance ellipse or outside the nomogram at the right side were classified as depleted according to the instructions in the manual of the soft tissue analyzer of Akern Bioresearch (Florence, Italy).

Screening based on the resistance index

The RI at different frequencies was calculated as \( L^2/R \), in which \( R \) represents the resistance measured at 50 kHz (\( R_{50} \)), or \( R_{ECW} \) or \( R_{ICW} \). To study the applicability of the RI as a screening tool for nutritional depletion, its value in relation to ideal FFM was assessed by the ratio RI/ideal FFM in both the depleted and not-depleted patients. The mean values and 95% CIs \( (\pm 2 \, \text{SE}) \) of this ratio were calculated in both groups. If the CIs did not overlap, the mean distance between the upper limit in the depleted group and the lower limit of the nondepleted group was set as the threshold value. Screening was performed by comparing the value of RI/ideal FFM with the threshold value.

Patients were classified as not depleted or depleted if this value was higher or lower than the threshold value, respectively.

Data analysis

Fluid volumes measured by BIS were compared with values measured with the dilution methods by Bland-Altman analysis (20). The correlations between methods for TBW and ECW were calculated and a plot of the difference between methods and their mean value was made. A paired Student’s \( t \)-test was used to calculate whether the difference between methods was significant.

To study whether BIS prediction errors (dilution – BIS) were associated with the physical characteristics of the subjects, Pearson’s correlation coefficients \( r \) between the prediction error and age, length, weight, BMI, ECW/TBW, body fluid volumes, and FFM_dil were calculated.

The effect of weight loss and presence of depletion on body composition, BIS variables, and BIS prediction errors was tested by analysis of variance. Differences between weight-loss categories were tested by independent-samples Student \( t \)-tests, with Bonferroni-corrected \( P \) values. To study the effect of depletion on these variables, differences between the depleted and not-depleted groups were tested by independent-samples Student \( t \)-tests.

To compare the ability of the different screening methods to identify patients with nutritional depletion, the sensitivity (percentage of depleted patients classified as depleted) and specificity (percentage of not-depleted patients classified as not depleted) of the different approaches were calculated with the dilution method as the gold standard. For all tests, \( P \) values \( < 0.05 \) were considered significant.

RESULTS

Subject characteristics are presented in Table 1. The mean body weight was 2.5 kg above the ideal body weight, and the mean BMI was 23.6. Most of the patients (47\%) had experienced severe weight loss, only 28\% had no weight loss, and 24\% had moderate weight loss. Classification based on the amount of FFM in relation to the ideal FFM resulted in 20\% of the patients being classified as depleted and 80\% as not depleted. For all variables presented in Table 1, no interaction between the weight-loss categories and clinical depletion was found.

For TBW and ECW, the correlations between BIS and the dilution methods were significant: \( r = 0.861 \) and 0.865, respectively (Figure 1). Bland-Altman analysis showed that BIS significantly underestimated TBW by 3.08 L, whereas ECW was slightly but significantly overestimated by 0.64 L (Figure 2). BIS underestimated ICW by 3.72 L. The 95\% limits of agreement for TBW were very wide (\(-4.4 \, \text{L}, 11.00 \, \text{L}\)) compared with those for ECW (\(-4.76 \, \text{L}, 3.48 \, \text{L}\)).

Whereas age, length, weight, and BMI were not associated with the BIS prediction errors, the size of the fluid compartments measured by the dilution methods was (Table 2). Both TBW_{dil} and ICW_{dil} correlated significantly with the BIS prediction errors for TBW and ICW. The same applied to ECW_{dil} and ECW_{BIS}, although this correlation was less significant. Between the ECW and TBW prediction errors, no correlation was found. Percentage FFM, calculated from TBW_{dil} and body weight, strongly correlated with BIS prediction errors for TBW and ICW, but not with BIS prediction errors for ECW.
A strong correlation between the relative size of the fluid compartments, expressed as ECW/TBW, and the prediction errors was found. TBW and ICW errors were negatively correlated and ECW errors were positively correlated with this ratio (Figure 3). The ratio ECW_{dil}/TBW_{dil} did not correlate with ECW_{BIS}/TBW_{BIS}.

### Effect of weight loss

The patients with no weight loss had greater body weights and BMIs than did the patients with severe weight loss, but no significant differences in the size of the fluid compartments measured with the dilution methods were found (Table 1). However, TBW_{BIS} and ICW_{BIS} were significantly greater in the group with no weight loss than in the group with severe weight loss. Other BIS variables were also different between the groups. Compared with the group without weight loss, Fc was 45 kHz higher and the \( C_m \) index was significantly lower (Table 1). In the group with severe weight loss, the \( C_m \) index was significantly greater than in the groups with moderate or no weight loss. The BIS prediction errors were not affected by weight loss.

### Effect of depletion

Of the 70 patients, 14 were classified as depleted on the basis of their FFM in relation to their ideal FFM. This group had significantly lower values for body weight, BMI, TBW, ECW, and ICW and had a higher ECW/TBW value as measured by the dilution methods (Table 1). Blood hemoglobin concentrations and hematocrit were lower in depleted patients. TBW_{BIS}, ECW_{BIS}, and ICW_{BIS} were also significantly lower in the depleted group than in the not-depleted group. Fc was 60 kHz higher in the depleted patients, and the \( C_m \) was 0.59 nF lower. The \( C_m \) index was also significantly lower in the depleted group. The BIS prediction errors were different in the 2 groups. Compared with the not-depleted group, in which BIS underestimated TBW and ICW and overestimated ECW, BIS prediction errors were significantly smaller for TBW and ICW in the depleted group.

### Comparison of screening methods

Individual RI/ideal FFM values for \( R_{inf} \), \( R_{ECW} \), and \( R_{ECW} \) in the depleted and not-depleted groups are shown in Figure 4. The CIs for \( R_{ECW} \) in the 2 groups overlapped; therefore, \( (L^2/R_{ECW})/ \n
---

**TABLE 1**

Subject characteristics, bioelectrical impedance spectroscopy (BIS) variables, and BIS prediction errors for the total population and for subgroups based on weight-loss and clinical-depletion categories.

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Weight loss</th>
<th>Clinical depletion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients</td>
<td>None</td>
</tr>
<tr>
<td>Age (y)</td>
<td>62.3 ± 12.2</td>
<td>62.2 ± 10.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.8 ± 13.33</td>
<td>73.16 ± 11.29</td>
</tr>
<tr>
<td>Ideal weight (kg)</td>
<td>65.28 ± 6.97</td>
<td>65.47 ± 6.57</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>169.4 ± 10.5</td>
<td>168.5 ± 8.6</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>23.6 ± 3.9</td>
<td>25.7 ± 3.3</td>
</tr>
<tr>
<td>FFM/length (^2)</td>
<td>17.1 ± 2.5</td>
<td>17.6 ± 2.3</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.36 ± 0.06</td>
<td>0.37 ± 0.06</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>7.59 ± 1.43</td>
<td>7.9 ± 1.3</td>
</tr>
<tr>
<td>TBW (L)</td>
<td>36.07 ± 7.72</td>
<td>36.78 ± 6.51</td>
</tr>
<tr>
<td>ECW (L)</td>
<td>17.51 ± 3.96</td>
<td>18.24 ± 3.42</td>
</tr>
<tr>
<td>ICW (L)</td>
<td>18.56 ± 4.87</td>
<td>18.53 ± 4.40</td>
</tr>
<tr>
<td>ECW/TBW</td>
<td>0.49 ± 0.06</td>
<td>0.49 ± 0.06</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BIS variables</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>( R_{ECW} ) ((\Omega))</td>
<td>657 ± 108</td>
<td>641 ± 100</td>
<td>630 ± 87</td>
<td>681 ± 119</td>
<td>638 ± 98</td>
<td>735 ± 113 (^*)</td>
</tr>
<tr>
<td>( R_{ECW} ) ((\Omega))</td>
<td>1384 ± 317</td>
<td>1281 ± 265</td>
<td>1347 ± 232</td>
<td>1466 ± 365</td>
<td>1346 ± 274</td>
<td>1536 ± 429</td>
</tr>
<tr>
<td>( C_m ) ((\text{nF}))</td>
<td>1.25 ± 0.60</td>
<td>1.54 ± 0.69</td>
<td>1.37 ± 0.53</td>
<td>1.01 ± 0.53</td>
<td>1.37 ± 0.60</td>
<td>1.08 ± 0.37 (^*)</td>
</tr>
<tr>
<td>( C_m ) index ((\text{cm}^2 \cdot \text{nF} \cdot \text{kg}^{-1}))</td>
<td>718 ± 294</td>
<td>859 ± 323</td>
<td>774 ± 241</td>
<td>603 ± 260 (^*)</td>
<td>756 ± 284</td>
<td>563 ± 294 (^*)</td>
</tr>
<tr>
<td>( Fc ) (kHz)</td>
<td>112 ± 70</td>
<td>90 ± 34</td>
<td>95 ± 42</td>
<td>135 ± 89 (^*)</td>
<td>101 ± 63</td>
<td>159 ± 81 (^*)</td>
</tr>
<tr>
<td>TBW_{BIS} (L)</td>
<td>32.98 ± 7.11</td>
<td>34.89 ± 6.74</td>
<td>34.63 ± 7.64</td>
<td>30.99 ± 6.72</td>
<td>34.15 ± 6.89</td>
<td>28.34 ± 6.20 (^*)</td>
</tr>
<tr>
<td>ECW_{BIS} (L)</td>
<td>18.15 ± 3.96</td>
<td>18.88 ± 3.57</td>
<td>19.18 ± 4.42</td>
<td>18.18 ± 3.81</td>
<td>18.84 ± 3.78</td>
<td>15.40 ± 3.54 (^*)</td>
</tr>
<tr>
<td>ICW_{BIS} (L)</td>
<td>14.84 ± 3.68</td>
<td>16.01 ± 3.62</td>
<td>15.44 ± 3.73</td>
<td>13.81 ± 3.50</td>
<td>15.31 ± 3.61</td>
<td>12.94 ± 3.44 (^*)</td>
</tr>
<tr>
<td>ECW/TBW_{BIS}</td>
<td>0.55 ± 0.04</td>
<td>0.54 ± 0.03</td>
<td>0.55 ± 0.04</td>
<td>0.55 ± 0.05</td>
<td>0.55 ± 0.04</td>
<td>0.55 ± 0.06</td>
</tr>
</tbody>
</table>

**Effect of depletion**

Of the 70 patients, 14 were classified as depleted on the basis of their FFM in relation to their ideal FFM. This group had significantly lower values for body weight, BMI, TBW, ECW, and ICW and had a higher ECW/TBW value as measured by the dilution methods (Table 1). Blood hemoglobin concentrations and hematocrit were lower in depleted patients. TBW_{BIS}, ECW_{BIS}, and ICW_{BIS} were also significantly lower in the depleted group than in the not-depleted group. Fc was 60 kHz higher in the depleted patients, and the \( C_m \) was 0.59 nF lower. The \( C_m \) index was also significantly lower in the depleted group. The BIS prediction errors were different in the 2 groups. Compared with the not-depleted group, in which BIS underestimated TBW and ICW and overestimated ECW, BIS prediction errors were significantly smaller for TBW and ICW in the depleted group.

**Comparison of screening methods**

Individual RI/ideal FFM values for \( R_{inf} \), \( R_{ECW} \), and \( R_{ECW} \) in the depleted and not-depleted groups are shown in Figure 4. The CIs for \( R_{ECW} \) in the 2 groups overlapped; therefore, \( (L^2/R_{ECW})/ \n
ideal FFM was not used for further analysis. The ratios at 50 kHz and at infinite frequency were significantly lower in the depleted than in the not-depleted group, and the threshold values were 1.02 and 1.29, respectively (Figure 4). Application of these values for screening of the total population resulted in sensitivity values comparable with results obtained from screening based on FFM values measured by BIS with use of mixture equations (Table 3). The specificity found for screening based on $R_{50}$ values was higher than for BIS or for screening based on $R_{inf}$.

According to the impedance vector approach, only 7 patients were classified as depleted, 5 correctly and 2 incorrectly (Figure 5). The sensitivity was low (36%), but the specificity was very high (96%) because only 2 of the 56 not-depleted patients were wrongly classified as depleted by this method (Table 3).

DISCUSSION

In the present study the validity of BIS with the use of mixture equations was tested in patients with gastrointestinal disease. We also studied the applicability of measured resistance values without the use of complicated prediction equations for screening patients with nutritional depletion.

Validity of bioelectrical impedance spectroscopy

Results of the present study show that BIS with the use of mixture equations underestimated TBW and ICW and only slightly overestimated ECW. Although the errors in $TBW_{BIS}$ were not associated with the degree of weight loss, they were smaller in depleted patients than in not-depleted patients; this effect was not found for ECW. Overall, ECW predictions were accurate with an acceptable SEE of 2 L, which is comparable with results found by others (6, 21–23). The prediction of TBW was less accurate with an SEE of 4 L. The findings of other studies confirm our finding that BIS predicts ECW better than does TBW (24–28). Our finding that TBW and ICW were largely underestimated in the not-depleted patients but not in the depleted patients limits the clinical applicability of BIS. It can be argued that in the patients classified as depleted, the...
severity of illness was greater than in the not-depleted patients and that the severity of illness, not depletion, is responsible for these findings.

The degree of weight loss is often used as an indicator of depletion. In the present study, however, body weight but not TBW was significantly lower in the patients with severe weight loss than in the patients with no weight loss, which indicated that the weight loss was mainly the result of fat losses. The classification of patients as depleted or not depleted was based on the amount of FFM in relation to the ideal FFM. The 2 approaches obviously led to different classifications. In fact, 15% of the patients with no weight loss, 18% of the patients with moderate weight loss, and 24% of the patients with severe loss were classified as depleted. Weight loss was calculated from usual body weight, as reported by the patients, which may have been subject to considerable error because of the uncertainty of the patients about their usual body weight and because of the improper calibration of scales. Furthermore, weight loss may be masked by fluid accumulation. Therefore, weight loss alone is not a valid indicator of depletion in patients with gastrointestinal disease.

Depletion can be defined as a loss of BCM, the metabolically active part of the body, which leads to impairment of physiologic function. In this study we defined depletion as a condition in which patients have an FFM that is <90% of their ideal FFM. We are aware that this is not the most optimal approach, but within the frame of practical alternatives it is most likely the most reasonable one. BCM cannot be measured directly; ICW can be used as a measure of BCM, but it has to be calculated as the difference between TBW and ECW. Because of error propagation, ICW calculations are by definition less accurate than are TBW or ECW measurements. Furthermore, no normal values for ICW specified for frame size are available at the moment. FFM is strongly related to BCM in cases of normal hydration. Patients in the present study did not show clear physical signs of fluid imbalance, although there was a small but significant increase in the ECW/TBW value in depleted patients. This means that FFM calculated from TBW alone contained relatively more ECW in the depleted than in the not-depleted patients. Consequently, the BCM of these patients may be more depleted than the FFM values indicated.

The finding that the BIS prediction errors for ECW and TBW are correlated with the absolute as well as with the relative size (expressed as ECW/TBW) of the fluid compartments has already been described in patients with altered fluid distribution (29). In acute diseases, clinical depletion is associated with ECW expansion in combination with ICW losses (25, 30). Because BIS prediction errors for both ECW and TBW were correlated with the true ECW/TBW value in the present study, but in opposite directions, BIS was unable to detect an increase in this ratio. This finding seriously limits the clinical use of BIS.

Dehydration as well as overhydration may affect conductive properties of ECW and ICW, resulting in changes in the specific resistance of these fluid compartments (31, 32). Changes in the composition of body fluids but not in their volume may also affect specific resistance. In the Hanai-based mixture equations, these values are set as constants based on measurements in healthy humans (6). For the clinical appli-
tion of BIS, additional information regarding electric properties, electrolyte concentrations, and osmolarity appear to be necessary to adjust the used constants.

The findings that TBW was less accurately measured by BIS than was ECW and that TBW and ICW values, in contrast with ECW, were influenced by the presence of depletion indicate that factors related to measurements at high frequencies (used for measurement of TBW and ICW) are partly responsible for measurement errors. In several patient groups, depression of the phase angle at 50 kHz has been described (33–35). It has been hypothesized that alterations in the electric properties of membranes are responsible. Impairment of membrane potential during illness may cause a decrease in \( C_m \). In critically ill children, the reactance component of the impedance measured at different frequencies was significantly decreased (36). In our study, \( C_m \) calculated by the Xitron curve fitting software was lower on average than the values measured in healthy persons (1.25 compared with 2.18 nF) and Fc values were higher (112 compared with 60 kHz) (6). Furthermore, \( C_m \) was lower in the depleted patients than in the not-depleted patients and was lower in patients with severe weight loss than in those without weight loss. In the same groups, Fc was higher by 60%. Because \( C_m \) is also a function of total cell surface area, which is lower in depleted patients because of the loss of BCM, we calculated the \( C_m \) index. According to de Lorenzo et al (6), this index is a measure of cell porosity and thickness. Our results show that the \( C_m \) index is lower in patients with severe weight loss and in depleted patients. At present, it is not clear how the values for these parameters should be interpreted physiologically, but they indicate changes at the level of the membranes of cells during illness. Changes in the composition of ICW can also alter the dielectric properties of the capacitors formed by cell membranes and thus affect the \( C_m \). These changes have no effects on resistances measured at low frequencies; however, these changes appear to affect resistances measured at frequencies above the Fc. It is likely that such changes are important in explaining the BIS prediction errors for TBW and ICW.

Studying alterations in electric properties of cells during illness is necessary for a complete evaluation of the clinical applicability of BIS.

### Screening methods

It was impossible to accurately identify depleted patients with the vector method described by Piccoli. Promising results with this method have been described for screening fluid overload or dehydration (8, 37). The low sensitivity of the method in our study may be caused by the fact that only height was used to normalize the measured \( R_{inf} \). The use of the RI at 50 kHz (\( L^2/R \)) divided by the ideal FFM appeared to be a screening instrument with high sensitivity and specificity. The method is refined by assessing the ideal FFM based on ideal body weight. The advantage of this screening method is that no population-specific prediction equations or complicated mixture equations are needed. Problems related to measurements in the high-frequency range, as discussed above, may be responsible for the fact that \( R_{inf} \) values gave better results than did \( R_{inf} \) or the mixture-derived FFM values. It can be argued that a frequency of 50 kHz is too low for full penetration of the current through cells. This was especially true in the depleted patients in the present study in whom the Fc was 159 kHz. In fact, at this frequency, it is probable that only ECW plays a part in current

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Depleted</th>
<th>Not depleted</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIS</td>
<td>29 [41]</td>
<td>41 [59]</td>
<td>86</td>
<td>70</td>
</tr>
<tr>
<td>Impedance vector</td>
<td>7 [10]</td>
<td>63 [90]</td>
<td>36</td>
<td>96</td>
</tr>
<tr>
<td>( R_{inf}/iFFM )</td>
<td>23 [39]</td>
<td>47 [67]</td>
<td>86</td>
<td>80</td>
</tr>
<tr>
<td>( R_{inf}/iFFM )</td>
<td>27 [39]</td>
<td>43 [61]</td>
<td>86</td>
<td>73</td>
</tr>
</tbody>
</table>

\( iFFM \): ideal fat-free mass.
conduction. Because of the strong interrelations between fluid compartments and the absence of severe fluid imbalance, this ECW measure is strongly related to the amount of FFM and explains the good results.

In conclusion, BIS with the use of mixture equations measures ECW accurately in patients with gastrointestinal disease, but the accuracy of ICW and TBW measurements is lower and influenced by the presence of nutritional depletion. Alterations in the electric properties of the body as a result of changes at the cellular level may play a role. A better understanding of the underlying physical phenomena seems necessary before widespread clinical use can be advocated. The impedance vector approach is not sensitive enough to screen patients for clinical depletion. Screening based on the RI at 50 kHz or based on $R_{\text{inf}}$ in relation to ideal FFM has a high sensitivity and specificity and may be of value for clinical use in patients with normal fluid distribution.

PLMC-R was responsible for the study design, the data collection and analysis, and the writing of the manuscript. BVK participated in the development of the study design and in the writing of the article and was responsible for the deuterium analysis. PBS supervised the development of the study design, the data collection and analysis, and the writing of the manuscript.

REFERENCES

19. Piccoli A, Nigrelli S, Caberlotto A, et al. Bivariate normal values of body fluid compartments and the absence of severe fluid imbalance, this ECW measure is strongly related to the amount of FFM and explains the good results.

In conclusion, BIS with the use of mixture equations measures ECW accurately in patients with gastrointestinal disease, but the accuracy of ICW and TBW measurements is lower and influenced by the presence of nutritional depletion. Alterations in the electric properties of the body as a result of changes at the cellular level may play a role. A better understanding of the underlying physical phenomena seems necessary before widespread clinical use can be advocated. The impedance vector approach is not sensitive enough to screen patients for clinical depletion. Screening based on the RI at 50 kHz or based on $R_{\text{inf}}$ in relation to ideal FFM has a high sensitivity and specificity and may be of value for clinical use in patients with normal fluid distribution.


