Assessment of degree of hydration in dialysis patients using whole body and calf bioimpedance analysis

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Abstract. Prescription of an appropriate post hemodialysis (HD) dialysis target weight requires accurate evaluation of the degree of hydration. The aim of this study was to investigate whether a state of normal hydration as defined by calf bioimpedance spectroscopy (cBIS) could be characterized in HD and normal subjects (NS). cBIS was performed in 62 NS (33 m/29 f) and 30 HD patients (16 m/14 f) pre- and post-dialysis to measure extracellular resistance. Normalized calf resistivity at 5 kHz \(\rho_{N,5}\) was defined as resistivity divided by body mass index. Measurements were made at baseline (BL) and at a state of normal hydration (NH) established following the progressive reduction of post-HD weight over successive dialysis treatments until the \(\rho_{N,5}\) was in the range of NS. Blood pressures were measured pre- and post-HD between BL and NH range due to progressive decrease in body weight, and systolic blood pressure (SBP) significantly decreased pre- and post-HD between BL and NH respectively. This establishes the use of \(\rho_{N,5}\) as a new comparator allowing the clinician to incrementally monitor the effect of removal of extracellular fluid from patients over a course of dialysis treatments.

1. Introduction
In conventional hemodialysis (HD), excess body fluid is removed during 3-4 hours of ultrafiltration per treatment. An accurate measure of hydration status is essential in determining the prescriptions of target weight necessary over a period of time to achieve normal body hydration (NH) [1]. Current available methods to assess hydration status are not clinically useful because of limited accuracy and practicality [2].

Bioimpedance techniques measuring body fluid content have the advantages of being noninvasive, low cost and convenient. Bioimpedance using the 5 kHz current frequency vector methods have been proposed to indicate both hydration and nutrition [3]. Multi-frequency bioimpedance spectroscopy (BIS) measures extracellular and intracellular fluid volumes [4]. Both of these measurements may be useful in population studies but are less useful when applied to the individual HD patient because of problems inherent in whole body measurements [5]. During dialysis in ambulatory patients, the percentage decrease in ECV in the lower limbs is larger than in other body segments, presumably due to the prior effect of gravity on distribution of extracellular fluid [6, 7, 8]. We propose as a practical approach for evaluating degrees of hydration the measurement of change in electrical resistivity in the calf, as calculated from specific resistance per unit area.

The main aim of this study was to evaluate whether this method can be used to indicate degrees of body hydration in dialysis patients whose ECV is gradually reduced over a course of dialysis treatments by comparing calf resistivity, pre and post dialysis to that of normal subjects (NS) and also accompanying blood pressure changes.

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2. Materials and Methods

2.1 Study protocol
This study was approved by the Institutional Review Board of Beth Israel Medical Center. Informed consent was obtained from all subjects. Calf BIS (cBIS) was measured in 62 apparently normal subjects (NS) (33 male; 29 female). In 30 stable HD patients (16 male; 14 female) three baseline (BL) pre-HD and post-HD cBIS measurements were performed in sequential dialyses. If normalized calf resistivity at BL was lower than the minimal level (Mean minus SD) of NS, indicating a state of overhydration, post-HD dialysis target weights were reduced by 0.2 - 0.3 kg per treatment, until normalized calf resistivity was above the minimal level of NS range, the definition of a state of normal hydration (NH).

2.2 Measurements
cBIS using the Xitron 4200 device was measured continuously during HD to obtain resistance and resistivity with patients in a sitting position with legs horizontal. Four electrodes were placed on the lateral side of calf to inject current (0.8 mA) and to measure voltage [26]. One sensing electrode (ES1) was placed on the area of maximal calf circumference (CMax); while the other sensing electrode (ES2) was placed 10 cm below the ES1 in the circumference denoted as CMin (Fig.1). The two current-injecting electrodes (EI1 and EI2) were placed on the same side of the calf 5 cm above and below ES1 and ES2, respectively. CMax and CMin were measured using a soft measurement tape with 0.1 cm accuracy. Body mass (BM) was measured using a calibrated electric scale. Blood pressures were measured in NS and in patients pre- and post-HD using a calibrated electronic blood pressure device (A&D Engineering, Inc, Milpitas CA).

![Figure 1: Calf bioimpedance measurement with four electrodes](image)

2.3 Calculations
Extracellular resistance (R_E) and intracellular resistance (R_I) were calculated based on the Cole-Cole model using raw data of resistance and reactance with frequencies from 5 kHz to 1000 kHz. Calf extracellular (cECV) and intracellular fluid volumes (cICV) were calculated using Xitron software. Total calf fluid volume (TCV) was defined as cECV + cICV. The ratios of cECV/TCV were calculated as markers of degree of hydration. Resistivity (ρ5) was calculated from resistance (R5) at 5 kHz by Eq.1 as follows.

\[ \rho_5 = \frac{R_5 A}{L} \]  

(1)

where A and L are the cross sectional areas of the calf and the distance between the sensing electrodes, respectively. The cross sectional area was calculated by Eq 2, where CAve was the mean of the two measured calf circumferences (Cave = (CMax + CMin)/2).

\[ A = \frac{C_{ave}^2}{4\pi} \]  

(2)
To standardize for the effects of differences in body composition, resistivity $\rho_5$ was normalized by the body mass index (BMI) calculated as $BM \ [kg]$ divided by height$^2 \ [m^2]$, and reported as normalized resistivity ($\rho_{N,5}$) in units of $10^{-2} \Omega m^3/kg$ (Eq 3).

$$\rho_{N,5} = \frac{\rho_5}{BMI} \quad (3)$$

### 2.4 Data analysis

$\rho_{N,5}$ and blood pressure levels were compared between patients and NS. Data are presented as mean ± SD. The values between groups were compared by $t$-test using GraphPad Prism 4 (Graphpad Inc., San Diego, CA). A difference of $p<0.05$ was considered significant. The paired $t$-test was used to compare differences over time in the same patients.

### 3. Results

Table 1 summarizes results obtained in NS and patients post-HD. Body height, body mass, systolic blood pressure (SBP), BMI, $C_{ave}$ and calf cross-sectional area (A) were higher in males. Calf resistance ($R_5$), resistivity ($\rho_5$) and normalized resistivity ($\rho_{N,5}$) were significantly lower in males.

Table 1 Summary of results from normal subjects (NS) and patients (P) in men (M) and females (F)

|                  | M-NS          | F-NS          | M-P-BL  | M-P-NH  | F-P-BL  | F-P-NH  |
|------------------|---------------|---------------|---------|---------|---------|---------|
| BM kg            | 80.3±17$^a$   | 59.1±8.8      | 74.4±14$^b$ | 73.2±14 | 72.6±18.9 | 70.8±18 |
| BMI kg/m$^2$     | 25.4±4.9$^a$ | 22.3±3        | 24.8±5$^b$ | 24.4±4.9 | 27.6±7.3 | 26.9±7.1 |
| $C_{ave}$ cm     | 35.4±3.6$^a$ | 32.0±2.1      | 31.8±3.9 | 31.6±4.1 | 31.3±3.7 | 31.1±4.1 |
| $R_5$ Ω         | 51.9±6.8$^a$ | 59.1±8.6      | 54.8±10$^b$ | 62.8±11 | 62.9±11$^b$ | 72.6±12.4 |
| $\rho_5$ Ω cm   | 518.6±100     | 482.7±83      | 437±82$^b$ | 494.1±95 | 494.6±131 | 557±129 |
| $\rho_{N,5}$ 10$^{-2}$ Ω m$^3$/kg | 20.5±1.99$^a$ | 21.7±2.6 | 17.4±2.8$^b$ | 20±1.5 | 18.4±1.8 | 20.9±1.8 |
| cECV/(TCV)       | 0.26±0.03$^a$ | 0.3±0.03      | 0.29±0.08$^b$ | 0.27±0.08 | 0.33±0.1 | 0.32±0.11 |

$^a$ Difference between males and females in NS  
$^b$ Difference between BL and NH state in patients post-HD

The standard deviations and coefficient of variation (CV) for normalized resistivity ($\rho_{N,5}$) in NS were less than the non-normalized values ($\rho_5$) (Fig.2). Mean of $\rho_{N,5}$ increased significantly in HD patients from BL to NH state pre- and post-HD and no difference in $\rho_{N,5}$ between patients at post-HD NH and NS (Fig.3).

![Figure 2 Normalized resistivity and resistivity in NS](image1)

![Figure 3 Comparison of patients to NS](image2)

Values of the mean minus the standard deviation are defined as minimal levels to establish the range of hydration in normal males (18.5 $10^{-2}$ Ωm$^3$/kg) and in females (19.1 $10^{-2}$ Ωm$^3$/kg) respectively
Normalized resistivity ($\rho_{N,5}$) in NS differed significantly between males and females but there were no significant differences between age groups.

With decrease in BM pre- and post-HD, calf resistance at 5 kHz ($R_5$), resistivity ($\rho_5$) and normalized resistivity ($\rho_{N,5}$) of patients increased significantly post-HD in males and females between BL and NBH (Table 1). Mean of ($\rho_{N,5}$) was no difference between NS and patients post-HD (Fig.3). cECV decreased significantly in both genders but cECV/TCV decreased significantly only in male patients between BL and NH. Pre-HD systolic blood pressure decreased (131.1±13 vs 123.8±14 mmHg, p<0.05) and post-HD (124.4±20 vs 114.0±17 mmHg, p<0.05) between BL and NH.

3. Discussion
This study illustrates that a gender-specific range for normalized calf resistivity ($\rho_{N,5}$) can be established in healthy control subjects (Fig. 2), and used as a reference to estimate the hydration status of dialysis patients. Fluid removal from BL to NH by ultrafiltration during dialysis was accompanied by increases in calf normalized resistivity (Fig.3) and significant decreases in mean SBP in all patients which suggest that this measurement can be used to provide guidance for prescription for fluid removal during the course of dialysis treatments.

Because the lower limbs are more hydrated than other body segments, calf bioimpedance provides more accurate information about body hydration than other body segments as excess fluid is finally removed. In addition, segmental measurement of the calf is preferable to that of the whole body because the geometric structure of the calf is uniform, resembling the segment of a cylinder. Resistivity at 5 kHz ($\rho_5$) varies widely in normal subjects (Fig. 2, right). Variability may be explained in part by the resistance measured at the skin surface of the calf reflecting the different electrical properties of components of body composition, such as fat, muscle and fluid. To minimize this variability, resistivity was normalized to body mass index (BMI), giving a new variable designated as normalized resistivity ($\rho_{N,5}$) (Fig.2, left). The unit of $\rho_{N,5}$ $\Omega m^3/kg$, can be interpreted also for its physical meaning. Since $m^3/kg$ is equal to $1/kg/m^3$, which is the reciprocal of density, the parameter $\rho_{N,5}$ can be interpreted as ohm per density of tissue, reflecting the relationship of hydration to body density.

Calf $\rho_{N,5}$ significantly increases in HD patients following progressive decrease in body water by ultrafiltration, with measurement variance being reduced by normalizing to BMI. Comparison of $\rho_{N,5}$ with healthy subjects was useful to evaluate degrees of hydration in HD patients. The parameter $\rho_{N,5}$ could also be applied to chronic kidney disease (CKD) patients to detect degrees of overhydration.

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