IPGDx®

PrognostiCheck™ is a proprietary noninvasive measurement that depicts prognosis by illustrating the plasma cell membrane and the exchange between the intra and extracellular matrices. We use impedance plethysmography, a well-established vascular diagnostic technique to measure the values of resistance (R) and Reactance (Xc) and calculate phase angle (Pa). Phase angle is the arc tangent of Xc/R converted to degrees. Without regression analysis and across disease states and populations phase angle clearly illustrates;

- The presence and progression of disease
- Fluid Balance and Nutrition Status (without regression predictions)
- The effectiveness of a pharmacologic or non-pharmacologic treatment intervention
  - Giving an opportunity to modify it to try and optimize a response
- Predicts the timing of non-acute death
  - Facilitating the transition from curative-restorative to palliative-hospice care (Transitive Care™)

We characterize Phase Angle as a 'Vitality Index™' which can be positive, neutral or negative and use it as a qualitative indicator to be added to the existing clinical decision matrix. Since the Phase Angle illustrates changes that occur prior to those evidenced by cell counts, physical signs, biochemical assays and imaging techniques its value clearly complements the disease management process, providing the physician with valuable information sooner. The study is objective, precise, sensitive and technically feasible. Specific Phase Angle values are associated with improvement, disease progression and treatment efficacy and the timing of non-acute death. Phase angle is clearly associated with prognosis and survival as a powerful independent variable.

While the impedance measuring devices are FDA cleared (510(k)) Class II medical devices the specific application, PrognostiCheck™ is investigational and only recently submitted to FDA under a 513(g) request for classification.

Our interest is in exploring the specific potential of PrognostiCheck™ as an OTC item targeting patients with chronic disease states for monitoring disease progression, effectiveness of treatment and transition from curative-restorative to palliative-hospice care; 'Transitive Care™'. This technology and the resulting objective metric obtained from serial measurements would be the basis for a Health 2.0 application within a social networking medium. A brief description of the technology and a series of published data are included for your review.

What it is:

Impedance Plethysmography (IPG): the gathering of a variety of physiologic data based upon the measured electrical conductive properties of the body.

The study of electricity is well established, the properties clearly understood and its parameters accurately measured. When a safe electrical circuit is applied to a biological system or entity the measured electrical values correspond directly to physiological equivalents and plainly illustrate them. As the nature of the electrical component is completely defined and does not change the method is particularly effective to demonstrate the natural changes intrinsic in the biological entity.

IPG has been effectively used for over fifty-years in a variety of clinical medical practice and research applications. Ranging from the detection of blood clots that may lead to serious illness (venous thrombosis/pulmonary embolism), estimating the blood pumped by the heart (Left Ventricular Ejection Fraction) or body composition analysis (estimating body fat); IPG has a well established history of use.

In addition to its ability to accurately illustrate physiologic (pathophysiologic) parameters in a noninvasive manner it is the precision (test re-test reliability: 0.98-0.99) of IPG that makes it a valuable tool; as the changes it documents are the changes inherent in the biological system as the electrical properties don't change.

Challenges to the use and validity of IPG are based upon the manipulations of the measured electrical values by statistical regression analysis. Even when such manipulations are eloquently composed with the benefit of comparison to sophisticated standards they are limited by the size and character of the group studied, cannot be accurately applied outside of it and do not accurately predict findings in all group members equally. This 'best-fit' tool is impractical for general use. No where has this been more evident than in the area of estimating body composition where these methods are used and based upon the porous foundation of 'assumed biological constants'. These 'assumed constants' are used to satisfy and explain variation of the biological system being studied and are used as a 'bridge' to reach another objective or value. These 'assumed constants' and their product results are not sufficiently reliable to base a clinical medical decision upon as they often are neither reliable nor accurate.

In our applications of IPG we have chosen to provide only the specific measured electrical values, the understanding of what their physiologic equivalents are and to compare those results in a visible illustration. This qualitative standard provides the basis for a reliable decision matrix suitable for clinical practice that is understandable to patient and provider forming the basis of a practical health-tool.

How it works:

Our body is made of materials that have varying degrees of conductivity based upon water and cells. In electrical science there is always a balance of forces, a positive and a negative. Impedance is the opposition to conduction; the voltage-drop or loss measured in the circuit.

To make the measurement the subject becomes the only unknown part of a safe electrical circuit. The circuit is safe because the electrical signal that is used is at a frequency and strength (current and voltage) so as not to stimulate or disturb any tissues. The measurement can be repeated as often as necessary to illustrate and report the information sought. The electrical circuit's field is set-up with two stick-on electrodes placed on the subject's skin with the signal passed between them. These ‘introduction’ electrodes are used to establish and maintain the electrical circuit through the IPG instrument at a highly-controlled, constant and stable level. Two more electrodes are placed within that field in relation to anatomical landmarks at the beginning and end of the area of interest, which may be the whole-body or a region/segment of the body, depending upon the event to be reported. These ‘detection’ electrodes are used by the IPG instrument to measure and record the change in the electrical signal. These changes relate with precision, sensitivity and specificity to cellular level physiology.

The measured impedance is vectored into two parts; Resistance (R) and Reactance (Xc) and the relationship between them is calculated as the Phase Angle (Pa).

R is inversely proportionate (opposite) to water content so when more water is added to the body such as in edema the R value decreases and when water is lost from the body such as in dehydration R increases. When more water is present conduction is improved and resistance is lessened and conversely when less water is present conduction is reduced and resistance is greater. The R is a fluid indicator, when higher the subject is dehydrated, when lower the subject has edema (heart failure, trauma, surgery and critical care) and when the same the subject’s water volume is stable.

Xc is proportionate to cell mass so when you are healthier and better nourished Xc is higher and when you are less healthy or malnourished Xc is less. The membrane of each cell holds the electrical signal resulting in the reactance value. When there are more cells and when the cells are healthier the Xc value is greater as they have a greater capacity to ‘hold’ the electrical energy. When the cells are not healthy or when there are fewer cells such as in wasting disorders the Xc value is lower as their capacity to hold the electrical signal is not as good. The Xc is a nutrition/metabolism indicator, when higher the subject is well-nourished, when lower the subject is malnourished and when the same over time the subject’s nutrition/metabolism is stable.

The Pa is the relationship between R and Xc defined mathematically (arc tangent Xc/R expressed in degrees). The higher the value of phase angle generally the healthier the subject indicating the ratio of cells and water is balanced and that the ability of the plasma cell membrane to hold the electrical signal is good. The Pa is the delay caused by the healthy cell membrane to hold the electricity as it passes through the circuit. When the Pa is less than average or in a low range the health of the subject is poor. The Pa may drop during an episodic illness such as the flu or a cold but then recover quickly thereafter, within a week. If the Pa does not recover the illness may be more severe. If the Pa continues to drop the illness is worsening and treatment needs to be adjusted or made more aggressive. When the Pa goes too low the patient cannot recover. The Pa is a sort of ‘Vitality Index’ which may be considered as ‘Positive’ (healthy), ‘Neutral’, or ‘Negative’ (unhealthy).

Why use it:

Changes in R, Xc and Pa do not explain the reason for the change and they must be taken in the context of the overall health of the subject and used in addition to the existing clinical dataset. However their value is that they clearly and reliably illustrate change before changes are seen through typical methods such as blood chemistries/cell counts, physical signs or imaging techniques. The basis for this is simply because they ‘see’ and report what is happening at the cellular level, an earlier level or compartment of physiology before the other values develop and can be reported. This makes the IPG values very sensitive to changes and trends of increase or decease can be reported at a time when treatment can be more effective and before a condition has more rigorously established itself. This ‘early-warning’ can provide valuable time to act, to detect disease and improve treatment and outcomes or at the end-of-life to preserve control, comfort and communication. In addition the characterization of the cell membrane and the exchange it mediates between the intracellular and extracellular environments illustrates the condition of the subject unlike any other methodology providing valuable information and insight.

The information illustrated by measuring and reporting the R, Xc and Pa add to the subjects and healthcare providers dataset and decision matrix about prognosis, fluid status, metabolism and nutrition. Not only is this information helpful to assess and maintain general health but to detect the presence of disease, characterize its progression and the effectiveness of treatment. The patient's compliance with treatment can be improved when they understand the effects that effort has on their health. The type of treatment can be adjusted to optimally affect the patient. When treatment is not effective and a cure or restoration of health is not possible the transition to supportive care can be made based upon objective values so the patient and their family can understand, accommodate and make the best use of what time they have available.

When to use it:

The frequency of the measurement is based upon the phenomenon to be captured and illustrated. For general health concerns measurements are made on an annual or seasonal basis to assess the condition and effects at hand to adjust health practices. When an illness occurs the measurements are made more frequently to show what changes are occurring over time to demonstrate recovery or to support further more definitive investigation. During more serious illnesses the measurements may be made multiple times throughout the day to capture and track fluid changes which may occur rapidly. While changes in nutrition and metabolism are seen in days changes in fluids can occur in hours. Measurements for prognosis are based upon the dynamics of how aggressive the disease is progressing; the treatment changed and is followed two or three times weekly.

SELECTED PUBLICATION ABSTRACTS (complete publications available)

Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer

Gupta D, et al; American Journal Clinical Nutrition, 2004 Dec; 80(6):1634-8

Background: Phase angle, determined by bioelectrical impedance analysis (BIA), detects changes in tissue electrical properties and has been found to be a prognostic indicator in several chronic conditions-such as HIV, liver cirrhosis, chronic obstructive pulmonary disease, and lung cancer-and in patients receiving dialysis. Objective: This study was conducted to investigate the prognostic role of phase angle in advanced colorectal cancer. Design: We evaluated a case series of 52 patients with histologically confirmed stage IV colorectal cancer. BIA was conducted on all patients and phase angle was calculated. The Kaplan-Meier method was used to calculate survival. Cox proportional hazard models were constructed to evaluate the prognostic effect of phase angle independent of other clinical and nutritional variables. Results: Patients with a phase angle ≤5.57 had a median survival of 8.6 mo (95% CI: 4.8, 12.4; n=26), whereas those with a phase angle >5.57 had a median survival of 40.4 mo (95% CI: 21.9, 58.8; n=26; P=0.0001). Conclusion: Phase angle is a prognostic indicator in patients with advanced colorectal cancer. Similar studies of other cancer types with larger sample sizes are needed to further validate the prognostic significance of phase angle in cancer treatment settings.

Bioelectrical impedance analysis in clinical practice: a new perspective on its use beyond body composition equations

Barbosa-Silva MC, et al; Current Opinion, Clinical Nutrition Metabolic Care, 2005 May; 8(3):311-7

Purpose Of Review: The bioelectrical impedance analysis is not a direct method for estimating body composition. Its accuracy depends on regression equations, and recent papers have suggested that this approach should not be used in several clinical situations. Another option is to obtain information about the electrical properties of tissues by using raw bioelectrical impedance measurements, resistance and reactance. They can be expressed as a ratio (phase angle) or as a plot (bioelectrical impedance vector analysis). This review describes their use in clinical practice. Recent Findings: The phase angle changes with sex and age. It is described as a prognostic tool in many clinical situations. There are some controversies about considering it as a nutritional marker. Studies in burn victims and sickle-cell disease corroborate its ability to evaluate cell membrane function. Bioelectrical impedance vector analysis allows a semi-quantitative estimation of body composition from information from tissue hydration and soft-tissue mass in a plot. It can be used in healthy individuals or patients, for a population or individual evaluation of fluid imbalance or an assessment of soft-tissue mass. It has also been used as a prognostic tool in dialysis and cancer patients. Summary: The phase angle can be considered a global marker of health, and future studies are needed to prove its utility in intervention studies. Bioelectrical impedance vector analysis has increased its utility in clinical practice, even when the equations may be inaccurate for body composition analysis.

Predictive value of APACHE II score is improved by combination with bioelectrical impedance analysis in multiple trauma patients

PHJ Mueller, et al; Critical Care 1998, 2(Suppl 1):P162

Background: Indication to extensive critical care could be ameliorated by combining APACHE II (AP II) scores with the Phase-Angle (PA, ~), a global parameter of nutritional status derived from Bioelectrical Impedance Analysis (BIA). Methods: 40 (30 male/10 female) multiple trauma patents (age: 16-81 years) with a stay of >5 days on the Intensive Care Unit (ICU) were studied retrospectively. Routinely obtained daily measurements of nutritional status (BIA 101 Impedance Analyzer, RJL-Systems) included calculations of PA. Results: 10/40 patients (25%) died during ICU stay (Table). In all patients with AP II scores ~20 (APACHE II-Class ~5) determination of outcome would have been correct by Phase-Angle: all deceased patients had a PA <3, while surviving patients had a PA >4 (P < 0.05). Discriminate analysis of this data reveals a probability of 100% for prediction of survival and 94% for lethal outcome respectively. Conclusion: Even in this small sample of multiple trauma patients there is a clear cutoff level of PA >4 for prediction of survival. We suggest the routine use of BIA for observation of ICU patents, but further studies are needed to establish the prognostic relevance of this method.

Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer

Gupta D, et al; British Journal Nutrition, 2004 Dec; 92(6):957-62

Bioelectrical impedance analysis (BIA) is an easy-to-use, non-invasive and reproducible technique to evaluate changes in body composition and nutritional status. Phase angle, determined by BIA, has been found to be a prognostic indicator in several chronic conditions, such as HIV, liver cirrhosis, chronic obstructive pulmonary disease and lung cancer, and in patients undergoing dialysis.

The present study investigated the prognostic role of phase angle in advanced pancreatic cancer. We evaluated a case series of fifty-eight stage IV pancreatic cancer patients treated at Cancer Treatment Centers of America at Midwestern Regional Medical Center (Zion, IL, USA) between January 2000 and July 2003. BIA was conducted on all patients using a bioelectrical impedance analyzer that operated at 50 kHz. The phase angle was calculated as capacitance (Xc)/resistance (R) and expressed in degrees. The Kaplan-Meier method was used to calculate survival. Cox proportional hazard models were constructed to evaluate the prognostic effect of phase angle independent of other clinical and nutritional variables. The correlations between phase angle and traditional nutritional measures were evaluated using Pearson and Spearman coefficients. Patients with phase angle <5.0 degrees had a median survival time of 6.3 (95% CI 3.5, 9.2) months (n 29), while those with phase angle >5.0 degrees had a median survival time of 10.2 (95% CI 9.6, 10.8) months (n 29); this difference was statistically significant (P=0.02). The present study demonstrates that phase angle is a strong prognostic indicator in advanced pancreatic cancer. Similar studies in other cancer settings with larger sample sizes are needed to further validate the prognostic significance of the phase angle.

Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis

Selberg O, European Journal of Applied Physiology, 2002 Apr; 86(6):509-16

This study investigates whether bioimpedance indexes rather than derived body compartments would be adequate for nutritional assessment. Evidence is provided that the phase angle as determined by conventional tetrapolar whole body bioelectrical impedance analysis at 50 kHz (1) was largely determined by the arms and legs and not the trunk, (2) was higher in control subjects than in hospitalized patients [mean (SD) 6.6 degrees (0.6) degrees vs 4.9 degrees (1.2) degrees, P<0.001], (3) discriminated poorly between cirrhotic patients of different Child-Pugh class, and (4) was positively correlated with muscle mass (r=0.53) and muscle strength (r=0.53) in these patients (each P<0.01). In a prospective study of patients with liver cirrhosis Kaplan-Meier and log rank analyses of survival curves demonstrated that patients with phase angles equal to or less than 5.4 degrees had shorter survival times than patients with higher phase angles [6.6 degrees (1.4) degrees] and that phase angles less than 4.4 degrees were associated with even shorter survival times (P<0.01). The prognostic roles of the phase angle and standard nutritional parameters such as total body potassium, anthropometric measurements, and impedance derived fat free mass, body cell mass and fat mass were evaluated separately by Cox regression which eliminated all variables except the phase angle as predictors of patient survival time (P<0.01). We concluded that for the clinical assessment of patients the phase angle may be superior to commonly used body composition information.

Relationship of bioelectrical impedance parameters to nutrition and survival in peritoneal dialysis patients

Mushnick R, et al; Kidney International Supplement, 2003 Nov ;(87):S53-6

Background: Malnutrition is highly prevalent in peritoneal dialysis (PD) patients and is associated with higher mortality in these patients. In this study, we have prospectively examined the relationship of bioimpedance indexes to the nutritional status and survival in PD patients. Methods: We enrolled 48 PD patients beginning in November 2000. On enrollment, bioelectrical impedance analysis (BIA) (BIA-101; RJL/Akern, Clinton Township, MI, USA) was performed and monthly blood was analyzed for biochemical markers, including pre-albumin.

Patients were followed until April 2003. Results: The mean age of PD patients was 51 +/- 15 (SD) years. Fifty-eight percent of the patients were female and 23% of the patients were diabetic. Mean body mass index (BMI) was 25.7 +/- 5.0 kg/m^2. Mean resistance, reactance, and phase angle were 521 +/- 104 ohms, 57 +/- 19 ohms, and 6.16 +/- 1.6 degrees, respectively. During the study period, 8 patients (17%) expired. The Kaplan-Meier method was used to compute observed survival. The cumulative observed survival of PD patients with enrollment phase angle greater than or equal to 6 degrees was significantly higher (P = 0.008) than that of patients with phase angle less than 6. Using Cox's multivariate regression analysis, phase angle was an independent predictor (relative risk = 0.39, P = 0.027) of more than two years' survival in PD patients. Serum pre-albumin was directly correlated with phase angle (r = 0.54, P < 0.0001), reactance (r = 0.55, P < 0.0001), and resistance (r = 0.29, P = 0.06). Conclusion: BIA indexes reflect nutritional status and may be useful in monitoring nutritional status in PD patients. Phase angle is a strong prognostic index in PD patients. It is useful to incorporate pre-albumin and BIA parameters in the regular assessment of PD patients, whose survival may be improved by better management of malnutrition and overall health status.

The validity of bioelectrical impedance phase angle for nutritional assessment in children

Nagano M, et al; J Pediatric Surgery, 2000 Jul; 35(7):1035-9

Background/Purpose: Bioelectrical impedance analysis (BIA) is a quick and noninvasive method for estimating body composition. Many prediction equations have been reported recently using bioelectrical impedance to calculate fat free mass (FFM) and fat mass (FM). These equations are based on the assumption that the composition and density of FFM are stable. In children, the composition and density of FFM vary according to age and clinical state, so the use of these equations is limited. However, phase angle is directly determined from resistance (Rz) and reactance (Xc) without equations and reflects body cell mass. The authors, therefore, investigated the validity of phase angle for nutritional assessment in children. Methods: Bioelectrical impedance analysis and anthropometric measurements were performed in 81 patients, including 71 well-nourished and 10 malnourished children. Results: Phase angle correlated with body weight (R = 0.818) and arm muscle circumference (r = 0.901) in well-nourished children. Malnourished patients showed lower phase angle than that of well-nourished children. Conclusion: Bioelectrical impedance phase angle is a useful parameter for nutritional assessment in children.

Uremic malnutrition is a predictor of death independent of inflammatory status

Pupim LB, et al, Kidney Int. 2004 Nov; 66(5):2054-60

Background: Several studies have pointed out the influence of nutritional parameters and/or indices of inflammation on morbidity and mortality. Often, these conditions coexist, and the relative importance of poor nutritional status and chronic inflammation in terms of predicting clinical outcomes in chronic hemodialysis (CHD) patients has not been clarified. Methods: We undertook a prospective cohort study analyzing time-dependent changes in several established nutritional and inflammatory markers, and their influence on mortality in 194 CHD patients (53% male, 36% white, 30% with diabetes mellitus, mean age 55.7 +/- 15.4 years) throughout a 57-month period. Serial measurements of serum concentrations of albumin, pre-albumin, creatinine, transferrin, cholesterol, and C-reactive protein (CRP), as well as normalized protein catabolic rate, post-dialysis weight, and phase angle and reactance by bioelectrical impedance analysis were performed every 3 months. Clinical outcomes were simultaneously assessed using indicators of mortality. Results: Serum albumin, serum pre-albumin, serum creatinine, and phase angle were significant predictors of all cause mortality, even after adjustment for serum CRP concentrations. Serum CRP concentrations were not significantly associated with mortality. Serum albumin concentrations and phase angle were also independent predictors of cardiovascular deaths in the multivariate model. Conclusion: The nutritional status of CHD patients predicts mortality independent of concomitant presence or absence of inflammatory response. Prevention of, and timely intervention to treat uremic malnutrition by suitable means are necessary independent of the presence and/or therapy of inflammation in terms of improving clinical outcomes in CHD patients.

Altered tissue electric properties in lung cancer patients as detected by bioelectric impedance vector analysis

Toso S, et al; Nutrition, 2000 Feb; 16(2):120-4

Modifications of body composition are frequent in cancer patients. Bioelectric impedance analysis can specifically detect changes in tissue electric properties, which may be associated with outcome. We evaluated the distribution of the impedance vectors from 63 adult male patients with lung cancer, stages IIIB (33 patients) and IV (30 patients), in supportive therapy. Body weight change over the previous 6 mo. was the same in both groups (stable/increased 36% and decreased in 62%). Patients were compared with 56 healthy subjects matched for gender, age, and body mass index (25 kg/m2).

Impedance measurements (standard tetrapolar electrode placement on the hand and foot) were made with 50-kHz alternating currents. The resistance and reactance of the vector components were standardized by the height of the subjects and were plotted as resistance/reactance graphs. The impedance vector distribution was the same in patients with either stage IIIB or IV cancer. The mean vector position differed significantly between cancer patients and control subjects (Hotelling ^{T2} test, $P < 0.01$) because of a reduced reactance component (i.e., a smaller phase angle) with preserved resistance component in both cancer groups. Patients with a phase angle smaller than 4.5 degrees had a significantly shorter, i.e., 18 mo., survival. Body weight loss was not significantly associated with survival. In conclusion, impedance vectors from lung cancer patients were characterized by a reduced reactance component. The altered tissue electric properties were more predictive than weight loss of prognosis.

Bioelectrical Impedance Analysis as a Predictor of Survival in Patients with Human Immunodeficiency Virus Infection

Michael Ott, Harold Fischer; et al; Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 9:20-25 1995

Summary: In patients with AIDS, short-term survival has been related to body weight, body composition, and serum nutritional parameters, but their prognostic impact at earlier stages of the HIV infection is not known. With an individual follow-up period of 1,000 days, we investigated the prognostic relevance of electrical tissue conductivity (resistance R, reactance Xc, phase angle Ø, extracellular mass (ECM), body cell mass (BCM) measured by bioelectrical impedance analysis), of the $CD4^+$ cell count, and of serum parameters indicating malnutrition in 75 HIV-infected male patients at Walter Reed stages 3-5. After initial recording, 29 patients (38.7%) died from AIDS during this period. Among 12 parameters estimated with a semi parametric Cox regression model adjusted for therapy (pentamidine, azidothymidine), the phase angle Ø (parameter estimate: 1.043, 95% confidence interval of 0.61 to 1.47) $P < 0.0001$ the ECM/BCM ratio, Xc, BCM, serum cholesterol, number of $CD4^+$ cells, and serum albumin had

significant prognostic influence on survival, whereas age, body weight, body mass index, resistance, serum protein, and serum triglycerides did not. In a model with four covariates $CD4^+$ cells, phase angle, pentamidine, azidothymidine, the prognostic impact of the $CD4^+$ cell count (parameter estimate: - 0.549) was lower compared with the phase angle Ø parameter estimate: - 0.799); ($P < 0.0001$) and did not gain statistical significance ($P = 0.0626$). The phase angle Ø was the best single predictive factor for survival among all 12 parameters (comparison of the respective Cox models with the likelihood ratio test). Body composition as reflected by the phase angle Ø is a major determinant of long term survival in HIV infection, thereby representing an important parameter for monitoring disease progression.

Bioelectrical Impedance Analysis Predicts Survival in Hemodialysis Patients

G.M Chertow, et al; Renal Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, **Published as "BLUE RIBBON AWARD" Abstract # T164, A0969, page 1442, journal of the American Society of Nephrology, September 1996, Volume 7, #9

Abstract: We performed a cross-sectional study of BIA (Bioelectrical impedance analysis, BIA 101-Q, RJL Systems, Clinton Township, MI) in 3009 HD (hemodialysis) patients with follow-up to 12 (median 8) months to evaluate the relation between impedance and survival. 296 deaths were documented over the study period; patients were censored at transplantation or if lost to follow-up. Mean (± SD) age was 60.5 ± 15.5 years, 47% were females, 47% African-American, and 36% diabetic. Dialysis vintage was 3.8 ± 3.7 years. Mean reactance (Xc) was 40.9 ± 13.8 ohms; mean resistance (R) was 497.7 ± 99.0 ohms. The mean Xc/R ratio 0.084 ± 0.030; Xc/R was directly correlated with albumin (r=0.24), pre-albumin (r=0.27), and creatinine (r=0.40), and inversely correlated with age (r= -0.33) and Quartile's index (r= -0.15). Xc/R was significantly higher in men Africa Americans, and non-diabetics (P< 0.0001 compared with women, Caucasians, and diabetics, respectively). To obviate linearity assumptions, Xc/R was ranked into quintiles, and the relative risks of death (RR) and 95% confidence intervals (95% CI) within each quintile were estimated from proportional hazards regression, with and without covariate adjustment. Survival in patients within the upper three quintiles of Xc/R; The RR in the two lowest quintiles was 2.7 (95% CI 1.1 to 2.2, P=0.009), respectively. After adjustment for age, sex, race, diabetes, albumin, creatinine, and urea reduction ratio, the RR in the lowest quintile was 1.5 (95% CI 1.2 to 2.1, P=0.003). Results were similar when Xc and R were adjusted for body stature. Conclusion: Xc/R is correlated with biochemical surrogates of nutritional status in hemodialysis patients, and provides prognostic power even after adjustment for case mix and laboratory variables. Longer-term follow-up and longitudinal assessment of Xc/R will be required to determine the optimal role for BIA in HD patient assessment.

Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment

Schwenk A, et al; American Journal of Clinical Nutrition, 2000 Aug; 72(2):496-501

Abstract: Background: Highly active antiretroviral treatment (HAART) reduces the risk of wasting in HIV infection and may alter the prognostic weight of wasting. The phase angle from bioelectrical impedance analysis (BIA) can be interpreted as a surrogate marker for the catabolic reaction to chronic HIV infection and opportunistic disease. Objective: Our objective was to assess the prognostic ability of the phase angle in HIV-infected patients in the era of HAART. Design: Two cross-sectional observation studies were conducted in 1996 and 1997 at a German

university outpatient HIV clinic. In the 1996 and 1997 cohorts, HAART was prescribed to 17 of 212 and 168 of 257 patients at baseline and to 179 of 212 and 234 of 257 patients during observation, respectively. Whole-body BIA was assessed at 50 KHz. Time to clinical progression and survival were calculated by using Cox proportional hazard models with time-dependent covariates. Median observation times were 1000 and 515 d for the 1996 and 1997 cohorts, respectively. Results: Higher phase angle was associated with a lower relative mortality risk, adjusted for viral load and $CD4^+$ cell count, of 0.49 (95% CI: 0.30, 0.81) per degree in 1996 and of 0.33 (95% CI: 0.18, 0.61) in 1997. The influence of phase angle on time to clinical progression, adjusted for viral load and $CD4^+$ cell count, was not significant in 1996 but the relative risk was 0.58 (0.36, 0.83) in 1997. Conclusion: Despite the favorable effects of HAART on the nutritional status of HIV-infected persons, low phase angle remains an independent adverse prognostic marker of clinical progression and survival.

Bioelectrical impedance analysis for assessment of severity of illness in pediatric patients after heart surgery

Shime N, et al; Critical Care Medicine 2002 Mar; 30(3):518-20

Objective: To investigate whether perioperative changes in bioelectrical impedance reflect the severity of illness in pediatric patients after heart surgery. Design: Prospective, controlled study. Setting: University-affiliated children's hospital. Patients: A total of 107 patients admitted to a pediatric intensive care unit after congenital heart surgery. Interventions: None. Measurements And Main Results: Single frequency (50 kHz) bioelectrical impedance was measured in the lower extremities before surgery and immediately, 16 hrs, and 40 hrs after admission (D0, D1, D2) to the pediatric intensive care unit. Postoperative changes in bioelectrical impedance were assessed by calculating values relative to the preoperative data (bioelectrical impedance ratio). These bioelectrical impedance ratios at D0 in both the non-surviving and surviving patients were 0.84 +/0.06 and 0.85 +/- 0.01 (mean +/- SE), respectively, indicating that the initial decrease caused by surgical stress itself was not directly related to the prognosis. The bioelectrical impedance ratio showed an increase toward preoperative values in surviving patients (0.94 +/- 0.02) at D1, and they showed a sustained decrease (0.70 +/- 0.06) in non-surviving patients. Patients with a bioelectrical impedance ratio at D1 of < 0.8 showed a higher mortality (25%) compared with those patients with a day-1 bioelectrical impedance ratio of > or = 1.0 (0%). The duration of the stay in the pediatric intensive care unit, mechanical ventilation, and inotropic support were all significantly longer in the patients with the lower bioelectrical impedance ratio. Conclusions: Measurement of the relative changes in postoperative bioelectrical impedance, which reflects perioperative alterations in body composition, provides a quantitative estimation of the critical illness in pediatric patients after heart surgery.

Localized bioimpedance analysis in the evaluation of neuromuscular disease

Rutkove SB, Muscle Nerve 2002 Mar; 25(3):390-7

Localized bioimpedance analysis is a novel, noninvasive technique with potential application to neuromuscular disease. In this procedure, high-frequency alternating current is passed through muscle, and parameters related to the consequent voltage pattern are evaluated. Currents flowing perpendicular to muscle fibers encounter many more cell membranes than do currents flowing parallel to them, producing surface voltage patterns that are altered by disease. Using this technique, 45 normal subjects and 25 patients with various neuromuscular diseases were studied, including 4 with amyotrophic lateral sclerosis, 4 with inflammatory myopathy, and 11 with inclusionbody myositis. Two parameters, the spatially averaged phase and the effective longitudinal resistivity, were altered in patients with neuromuscular disease. Reductions in phase correlated to disease progression, whereas normalization of phase correlated with disease remission. In patients with inclusion-body myositis, a unique pattern of reduced phase and elevated resistivity was identified. These findings suggest that localized bioimpedance analysis has the potential of playing a substantial role in the diagnostic and therapeutic evaluation of neuromuscular disease.