Journal of Diabetes Science and Technology
Volume 6, Issue 1, January 2012

COMMENTARY

Bioelectrical Impedance Assessment of Wound Healing

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Abstract

Objective assessment of wound healing is fundamental to evaluate therapeutic and nutritional interventions and to identify complications. Despite availability of many techniques to monitor wounds, there is a need for a safe, practical, accurate, and effective method. A new method is localized bioelectrical impedance analysis (BIA) that noninvasively provides information describing cellular changes that occur during healing and signal complications to wound healing. This article describes the theory and application of localized BIA and provides examples of its use among patients with lower leg wounds. This promising method may afford clinicians a novel technique for routine monitoring of interventions and surveillance of wounds.

J Diabetes Sci Technol 2012;6(1):209-212

Introduction

Wound healing is a dynamic, interactive cascade of molecular, cellular and biochemical processes.[1] Despite accumulating knowledge of the biology of wound healing, the estimated annual cost of treating wounds exceeds $20 billion in the United States, particularly for wounds of the lower body.[2] Although many therapeutic interventions are utilized to treat wounds, physician decisions are hampered by the lack of objective and convenient methods to monitor treatment effects and to assess wound healing.[3] Contemporary methods have limitations including cost, time commitment, reliability, and accuracy.[4,5] Thus, the need persists for an objective, suitable, and practical method to assess wound healing.

Assessment of the effectiveness of treatment to foster wound healing is a complex and broad field. Traditional methods estimate the dimensions of wounds including surface area and volume.[6,7] Physiological approaches utilize molecular and biochemical indicators that provide less subjective information.[3,8] Because successful wound healing is a dynamic process that integrates physiological and biochemical factors and mechanisms, reliance on a single aspect of the process may be inadequate. This article describes the use of localized bioelectrical impedance analysis (BIA) measurements to monitor cellular processes involved in wound healing.

Theory and Application of Bioelectrical Impedance Analysis in Wounds

Bioelectrical impedance analysis provides a safe, non-invasive and objective method to assess cellular level

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Abbreviations: (AC) alternating current, (BIA) bioelectrical impedance analysis, (ECF) extracellular fluid, (MRSA) methicillin-resistant Staphylococcus aureus, (PA) phase angle, (R) resistance, (Xc) reactance

Keywords: phase angle, reactance, resistance, wound healing

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architecture and function[9] that is applicable during the wound healing process. It utilizes a highly controlled electrical circuit that includes the wound. Four small adhesive electrodes (TYCO Healthcare; Mansfield, MA) are placed on the skin and adjacent to the margins of the wound. A high-frequency (50 kHz), low-voltage current [800 μA alternating current (AC)] that neither stimulates nor perturbs tissues is introduced, the voltage drop is measured, and impedance is determined by using Ohm's Law.[10] Because a phase-sensitive instrument is used (Quantum IV, RJL Systems; Clinton Township, MI), *in vivo* bioelectrical measurements include resistance (R) (reduction in voltage as the applied current passes through the wound) and reactance (Xc) (cell membrane capacitance due to the delay in transmission of the applied current as a result of bipolar lipid membranes) that indicate extracellular fluid (ECF) and electrolyte composition, and cell membrane mass and function, respectively. Another variable, phase angle (PA), calculated as the arc tangent of Xc/R and expressed in degrees, indicates cell membrane vitality and prognosis in malnutrition and chronic disease.[11,12] Thus, BIA characterizes the integrated healing process whereas other methods focus on individual components of the process.

Consistent patterns of change in BIA variables are seen in various models of wound healing. In a cell culture model,R increased significantly during growth of a functional monolayer but R decreased significantly after disruption of the monolayer.[13] Serial measurements of R after restoration of the monolayer increased significantly (e.g., positive slope). These findings indicate that R is a specific biomarker of cell growth with increases suggestive of healing and decreases characterizing a lack of healing.

Bioelectrical R measurements also successfully monitored the healing of surgically-induced wounds in rodents. Transcutaneous electrical resistance significantly decreased after incision of the skin. During a 20-day postsurgical recovery period, daily R values progressively increased with a positive slope that was related to histological measures of healing.[14]

Impedance measurements discriminated the risk for pressure ulcers in adults. Phase-sensitive measurements were made at the trochanter and coccyx of adults at different levels of risk for pressure ulcers.[15] Patients at high risk for pressure ulcers, compared to controls, had significantly reduced Xc, R, and PA values that are indicative of malnutrition, ECF accumulation, and reduced cellular vitality. Multiple linear regression analysis identified Xc together with serum albumin as significant predictors of risk for pressure ulcers with a coefficient of determination of 0.96. These findings suggest that Xc is an indicator of nutritional status and cell mass.

Examples of Use of Bioelectrical Impedance to Assess Wound Healing or Complications

Electrode Placements

Figure 1 shows the placement of the four surface electrodes used to introduce the electrical current (two distal electrodes with black clips) and the adjacent electrodes (two electrodes with red clips) to determine the voltage drop; this electrode arrangement is used to determine the R, Xc, and PA at the wound. Prior to placement of the electrodes, these sites were cleaned with alcohol to remove any emollients or other chemicals that may influence conduction of the applied current.

Uncomplicated Wound Healing

Figure 2 describes the patterns of serial changes in R, Xc, and PA angle during healing of a wound (19 mm in length, 17 mm in width, and 2 mm in depth) that was traumatic in etiology. After treatment, R increased for 18 days after which it decreased transiently at days 20 through 25 because of erythema and then increased further until epithelialization at day 39. Reactance increased at day 10 then stabilized until it increased until day 39. Phase angle followed a pattern similar to that observed with Xc. The general pattern is a longitudinal increase in R, Xc, and PA (11, 90, 50%, respectively) during

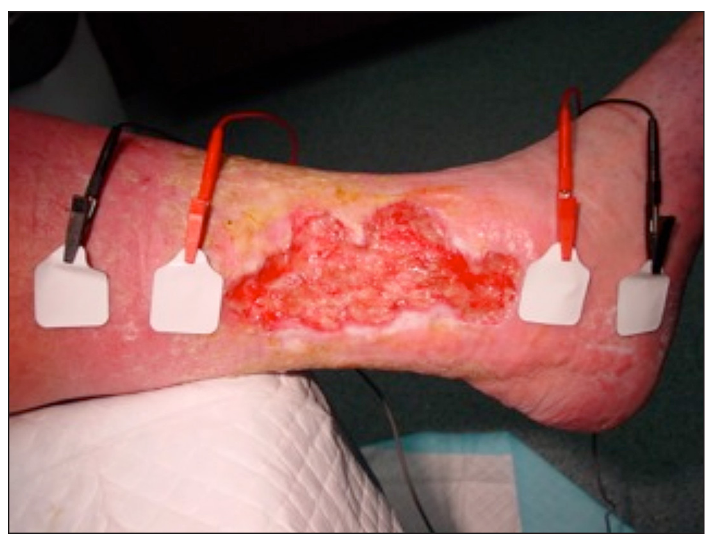

Figure 1. Description of the placement of electrodes for measurement of bioelectrical impedance of a wound. The two electrodes distal to the wound administer the 50 kHz AC and the two electrodes adjacent to the wound detect the voltage drop across the wound.

uncomplicated healing that is consistent with decreased ECF, increased cell mass, vitality and epithelialization.

Wound Healing After a Graft

Medical procedures administered to facilitate wound healing acutely affect impedance parameters (**Figure 3**). Debridement of a nonhealing, surgical incision (25 mm in length and width and 100 mm in depth) of the knee following surgical repair of a ligament elicited a transient decrease in R, Xc, and PA (2, 28, and 30%, respectively) that indicates a distinct disruption in cell membranes and function with a minimal change in ECF. Trauma to tissues associated with wound preparation and application of the skin graft resulted in decreased R, Xc, and PA values (23, 65, and 59%, respectively) indicating a greater disruption in cell architecture than ECF. Marked increases in R, Xc, and PA values (28, 210, and 178%, respectively) after recovery from the graft procedure suggest decreased ECF and substantially increased number of cells and wound repair.

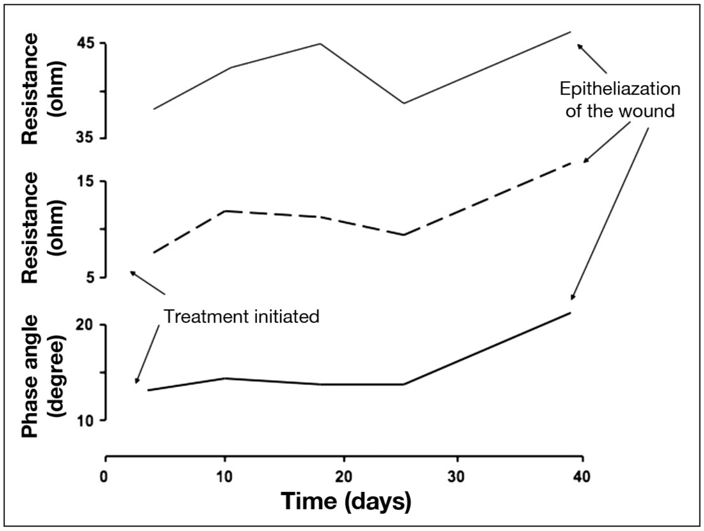

Figure 2. Longitudinal measurements of R, Xc, and PA in uncomplicated wound healing. After initiation of treatment, successful wound healing is characterized by increases in R, Xc, and PA that reflect a decreased ECF and increased cell growth.

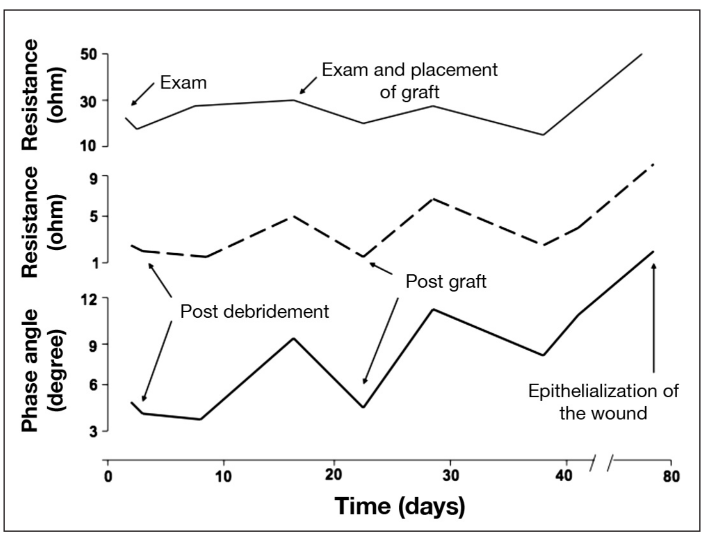

Figure 3. Serial changes in BIA variables in response to debridement of a wound and application of a skin graft that result in healing. Short-term decreases in R, Xc, and PA values follow debridement and skin graft that suggest modest increases in ECF and loss of cells, followed by overall increases during recovery from the procedures leading to wound healing.

Complications During Wound Healing

Infection of wounds results in discernible changes in the magnitude and direction of BIA data (**Figure 4**). In contrast to debridement (**Figure 3**), methicillin-resistant Staphylococcus aureus (MRSA) infection of a wound (25 mm in length and width and 4 mm in depth) due to diabetic neuropathy elicited substantial decreases in R, Xc, and PA (16, 63, and 56%, respectively) that alters the temporal increase in the parameters during healing. Importantly, the rate of change in R, Xc, and PA signaled the presence of infection before detection with laboratory methods. This pattern suggests that infection increases ECF and decreases cell numbers and vitality.

Summary and Conclusion

Emerging evidence from studies in various experimental models of wound healing supports the value of BIA in routine clinical assessment of the effects of treatment of wounds. The general pattern of modest decreases in R, Xc, and PA acutely after debridement with considerably greater decreases in advance of infection, and substantial

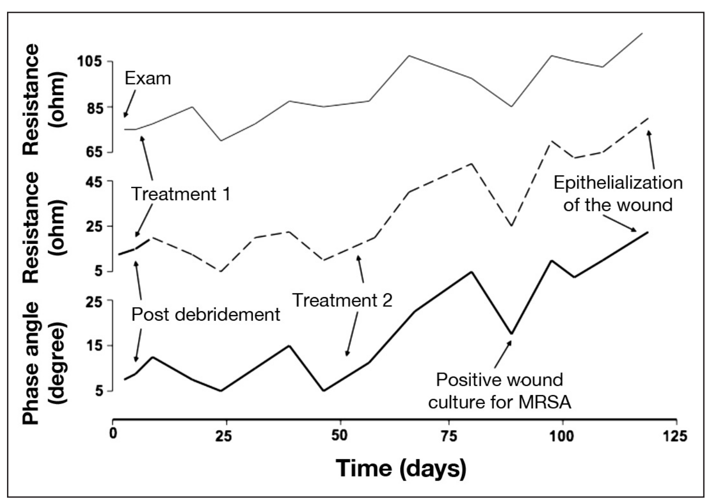

Figure 4. Effects of wound infection on BIA variables. MRSA infection marked decrease R, Xc, and PA values that exceed changes seen with usual treatments.

increases in R, Xc, and PA after treatment and healing is consistent with the hypothesis that BIA noninvasively illustrates cellular level structure and processes. The R value is inversely proportional to ECF and directly proportional to the fibrin clot and epithelialization and thus indicates successful wound healing. Similarly, Xc is proportional to cell mass. Because cell membranes consist of bilayers of lipid, they act as capacitors. Increases in Xc indicate epidermal proliferation and granulation whereas Xc decreases with infection and cell loss. Healthy membranes cause a delay in the transit of voltage and current; thus, the greater the PA, the healthier the cell membranes, and decreases in PA reflect impaired membrane function.

Use of BIA to monitor wound healing affords a safe, practical, and objective method to ascertain the effectiveness of therapy and to screen for presence of infection. Bioelectrical impedance analysis measurements are highly reliable with low within-subject variability (<2 ohm for R and Xc; <1° for PA), and high test-retest reliability (r = 0.99). Care is advised to ensure proper contact of electrodes adjacent to the wound and appropriate connection of source and detector electrodes to the BIA device. Use of BIA to monitor wound healing poses no hazard to the patient when precautions are taken to avoid contamination of the wound. It provides insights into cellular processes of healing and thus may advance development of cost-effective patient care.

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