2013

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L C. Ward

K Sharpe

Dale Edgar
University of Notre Dame Australia, dale.edgar@nd.edu.au

V Finlay

F Wood

This article was originally published as:
Ward, L. C., Sharpe, K., Edgar, D., Finlay, V., & Wood, F. (2013). Measurement of localized tissue water - clinical application of bioimpedance spectroscopy in wound management. *Journal of Physics: Conference Series, 434*.

Original article available here:
http://iopscience.iop.org/article/10.1088/1742-6596/434/1/012043/pdf

Ward, L.C.; Sharpe, K.; Edgar, D.; Finlay, V.; and Wood, F. (2013) Measurement of localized tissue water – clinical application of bioimpedance spectroscopy in wound management. *Journal of Physics: Conference Series,* 434. doi: 10.1088/1742-6596/434/1/012043

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2013 J. Phys.: Conf. Ser. 434 012043

(http://iopscience.iop.org/1742-6596/434/1/012043)

Journal of Physics: Conference Series **434** (2013) 012043 doi:10.1088/1742-6596/434/1/012043

Measurement of localized tissue water – clinical application of bioimpedance spectroscopy in wound management.

LC Ward[1], K Sharpe[2], D Edgar[2,3], V Finlay[3] and F Wood[2,3]

[1] School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, QLD 4072, Australia
[2] Burn Injury Research Unit, University of Western Australia, Australia
[3] Fiona Wood (Burn Research) Foundation of WA, Perth, Australia

l.ward@uq.edu.au

Abstract. Wound healing is a complex process which can be impeded by the presence of accumulated cell fluid or oedema. A simple and convenient method for the assessment of wound oedema would aid improvement in patient care. In this proof of concept study we investigated whether bioelectrical impedance spectroscopy has the potential to provide such a tool. A number of important observations were made. Firstly, the method was highly reproducible and data can be obtained from electrodes located at different positions around the region of interest; important given the highly variable topography of surface wounds, e.g. burns. Secondly, the method was highly sensitive with the potential to detect changes of as little as 20 µl in extracellular fluid. Thirdly the relative changes in R0, R∞ and Ri following sub-cutaneous injections of saline were consistent with redistribution of water from the extracellular to intracellular space and /or removal from the local area as may occur during wound healing.

1. Introduction

The burden of chronic and acute wound care on the hospital system is immense and conditions involving these lesions are increasing in prevalence [1]. Wound healing is a complex but well described physiological process, which is common to all lesions and injuries in spite of their origin. Factors known to impede wound healing have been identified, amongst which is oedema. Oedema, which represents an expansion of the tissue's extracellular fluid compartment, impairs the healing process by increasing the diffusion distance between the nutrient source and the cell, compromising cell function and cellular waste removal, leading to cell death and a toxic wound environment. Bioimpedance spectroscopy (BIS) is a safe, rapid and non-invasive technique that has been used for the objective assessment of whole body and tissue fluid compartments. The technique lends itself to the assessment of conditions involving fluctuations of fluid within and between the intra-and extracellular fluid compartments, and could be useful in the assessment of periwound oedema. A preliminary report has suggested that it may also be useful for the assessment of epithelialization that occurs during wound healing [2].

We report here the results of studies, designed as a proof of concept, to demonstrate the potential and feasibility of the technique as a wound area-specific, non-invasive means of wound oedema monitoring.

2. Experimental

2.1 Assessment of the feasibility of localized impedance measurements. Bioimpedance measurements were made across a 60-mm diameter region of the dorsal surface of the forearm mid-way between the head of the ulna and the olecranon using an SFB7 (ImpediMed, Brisbane) bioimpedance spectrometer. Current drive electrodes (Ag-AgCl, Kendall Care 610) were located at the base of fingers and on the foot; voltage sense electrodes were located at 45° intervals around the circumference of the measurement area. Impedance was measured, in triplicate, between all combinations of electrode pairs at 256 discrete current frequencies (4-1000 kHz) across a body region and data analysed according to the Cole model using Bioimp version 4.8.0.0. to determine resistance at zero frequency (R0), infinite frequency (R∞) and Ri, the intracellular resistance. Data were obtained for six healthy control subjects.

2.2 Assessment of the ability of impedance measurements to detect localized changes in extracellular fluid. A 21-gauge needle was inserted subcutaneously into the forearm of a participant at the midpoint between sense electrodes located 40 mm apart along the midline and was left in situ for the duration of the study. Current drive electrodes were located on the hand and foot. Impedance measurements were repeated prior to and following injection of a 1 ml bolus of normal saline. Further injections (1 ml) to a total volume of 5 ml were made 3, 5, 7, 10 minutes from baseline. Impedance was recorded, in triplicate as described above, following each injection. The study concluded with continued monitoring of impedance during resorption of injected fluid over the subsequent 50 minutes.

3. Results

3.1 Assessment of the feasibility of localized impedance measurements.

Impedance measurements were highly reproducible, with mean a coefficient of variation of 2.3%. Figure 1 represents a map of the measured resistances (R0) between pairs of electrodes for a representative subject.

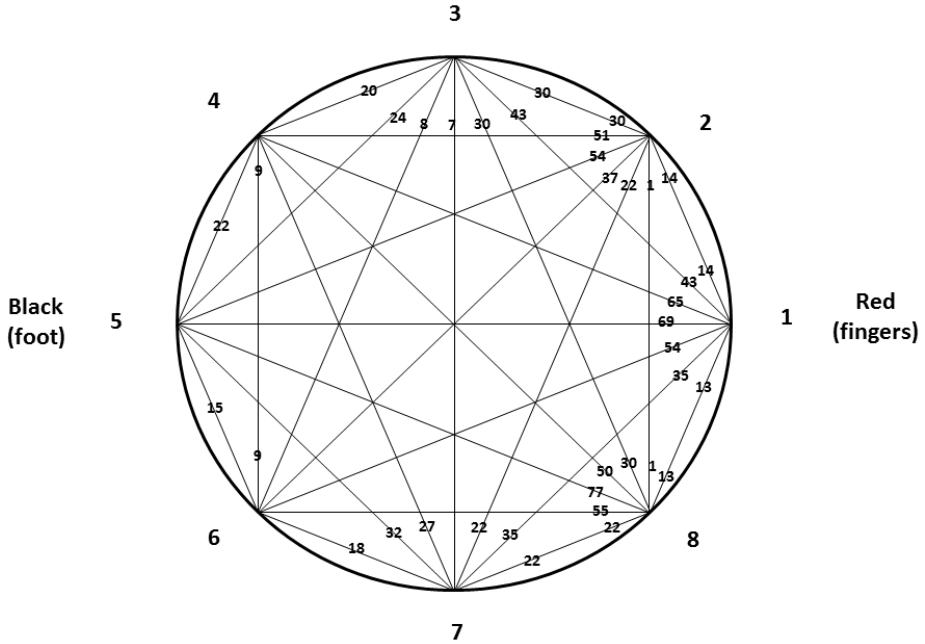

Figure 1. Map of resistances measured between surface electrodes located on the dorsal surface of the forearm. Voltage sense electrodes (numbered 1 to 8) were located at 45° intervals around the circumference of a circle 60 mm in diameter; current drive electrodes were located on the hand and foot. Lines and numbers within the circle indicate the measured resistance (ohm) between the pair of electrodes connected by the line.

Resistance measurements ranged from 1 to approximately 80 ohm between adjacent or diametrically opposite electrode pairs respectively and between different subjects. Impedance measurements were achievable for all electrode combinations with the exception of electrodes located orthogonal to the direction of current flow in some subjects. The sum of impedances for each pair of adjacent electrodes equalled (within ± 2%) that of equatorially placed electrodes along the line of current flow. For example in Figure 1, the sum of resistances between electrode positions 1-8-7-6-5 is 68 ohm compared to 69 ohm for 1-5 directly. In this participant, electrode positions for pairs 2-8, 4-6 and 3-7, although aimed to be orthogonal to the direction of current flow (red-black), this was not fully achieved as resistances of 1, 9 and 7 ohm respectively were recorded.

3.2 Assessment of the ability of impedance measurements to detect localized changes in extracellular fluid. The change in R0, R∞ and Ri are presented in Figures 2a,b,c respectively. The times of injection of each bolus (1 ml) of saline are indicated by the vertical lines.

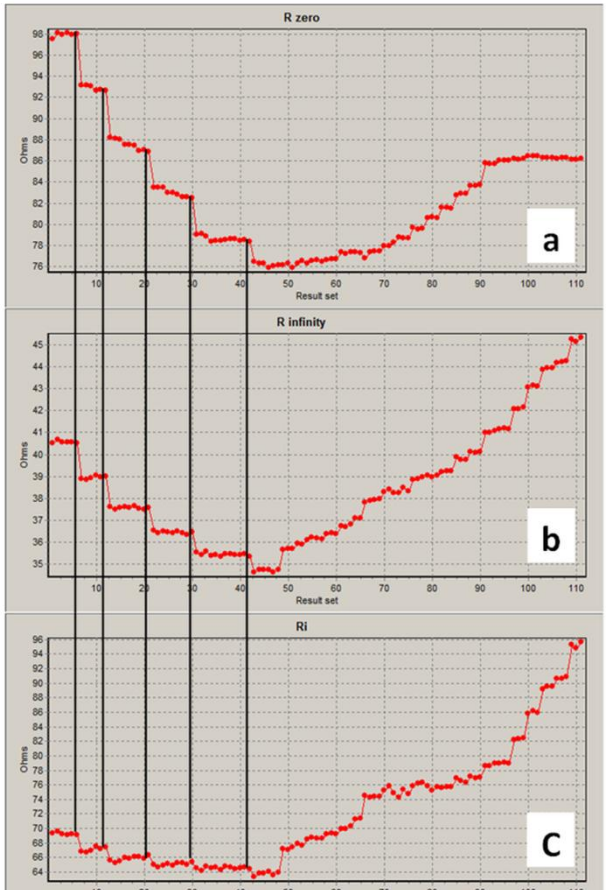

Figure 2. Change in tissue resistance during subcutaneous injection and resorption of saline.
Panel a: Change in R0 (inversely proportional to change in extracellular water volume).
Panel b: Change in R∞ (inversely proportional to change in total tissue water volume).
Panel c: Change in Ri (inversely proportional to change in intracellular water volume).
Vertical lines indicate time of injection of 1 ml of saline.

The relationship between resistance and fluid volume is described by the following

$$R \propto \frac{l}{V} \qquad (1)$$

where l is the distance between the measurement electrodes, R is resistance and V is the volume of fluid. R0 decreased by 4.9 ohm with the first subcutaneous injection of 1 ml of saline. The drop in resistance decreased progressively with each injection to 2.1 ohm by the fifth injection. The corresponding decreases in R∞ were 1.6 and 0.7 ohm respectively and the decreases in Ri were 2.2 and 0.9 ohm respectively.

Following the last injection of saline (at result data set 45) resistance progressively of all three fluid compartments increased as fluid was resorbed and redistributed between the intra and extracellular compartments. Notably resistance of no compartment returned to baseline values by 50 minutes post-injection.

4. Discussion

It is clear from these preliminary data that impedance measurements can track in a quantitative manner accumulation of fluid and its subsequent resorption in a localized tissue region. A number of important observations can be made from this pilot study. Firstly, the method appears to be robust with respect to electrode positioning. Wounds are frequently not regular in shape and it will not always be possible to locate electrodes such that current drive and sense electrodes are in-line.

Nevertheless, it is clear from the positioning study that an impedance will be measurable unless sense electrodes are perfectly orthogonal to the direction of current flow, suggesting that electrodes may be located at clinically acceptable locations even of not electrically ideal. Secondly, the method is potentially very sensitive. The impedance device used in this pilot study measured resistance with a resolution of 0.1 ohm. We were able to detect a change of approximately 5 ohm in R0 per ml of saline injected. This implies an ability potentially to detect changes in fluid volume of as little as 20 µl. Thirdly, during the period of injection the resistance of the intracellular compartment decreased to a much smaller and diminishing extent suggesting that the injected fluid was being predominantly sequestered in the extracellular space. Fourthly, the rate of increase in R0 following the last injection was much slower than that observed for the decrease in resistance during injections and approached a plateau after approximately 35 minutes. Conversely, the increase in $R\infty$, an index of both extra-and intracellular fluid showed a continued increase for as long as monitoring was continued (50 min). These observations are consistent with redistribution of water from the extracellular to intracellular space and/or removal from the local area.

Acute and chronic wounds are the feature of many illnesses including diabetes, venous stasis and burns. Pathological fluid accumulation around the site of wound is known to impair reparation, even in volumes imperceptible to the human eye. Whilst there are numerous medical interventions designed to reduce oedema, assessing their efficacy has been difficult on account of the relative paucity of simple and reliable tools to measure swelling. This pilot study shows that focal bioimpedance spectroscopy has great promise as a painless, non-invasive and potentially quantitative tool for the measurement of localized oedema; particularly, if as suggested by this study, it is capable of perceiving changes in tissue fluid volume of as little as a ml or potentially much less.

The instrument used in this trial was designed primarily for body composition assessment although it has been applied in variety of clinical settings, notably assessment of lymphedema. Its use here is a novel application of this technology and, hence, care must be taken in the interpretation of the results. The electrode arrangement described in this study should not be construed as representing the optimal arrangement. The region spanned by the measurement electrodes was 40 mm but clearly wounds are highly variable in shape and size and further studies are required to replicate the above findings for different electrode spacings and orientations. Wounds are also of variable depth and hence volume. The volume of tissue defined by the impedance measurement in these studies is unknown.

The present study measured acute changes in fluid only; the measurement of fluid distribution in the tissues long-term brings its own challenges. In order to detect any true changes in fluid accumulation and distribution in a particular location, both the configuration and placement of the electrodes must be replicated exactly at each measurement occasion; raising issues of both inconsistency and inconvenience. Preliminary studies in burns patients have underscored these difficulties. These studies continue, seeking not only to test the validity of this method for the purpose of wound monitoring, but also looking at ways of overcoming any practical issues in its implementation. Although much further investigation is required, this single study demonstrates the potential of bioimpedance spectroscopy for wound monitoring represents an exciting step toward objective evaluation of wound changes and their management.

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