A Quantitative Method for Monitoring Wound Healing

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***Abstract*—Assessment and monitoring of chronic wounds is primarily based on visual inspection by medical professionals. The method is subjective and its reliability depends on the assessment criteria of the evaluator. This may cause problems in particular at home care where caretakers are not usually wound care specialists. Wound dressings have to be removed for each assessment which disturbs the wound healing process. Additionally this increases both workload and cost, as the wound dressings are often changed without medical necessity. Our research group has developed a quantitative method for evaluation and monitoring of the wound healing process. The method is based on differences in electrical conductivity of tissue types and is addressed using the bioimpedance measurement. The results indicate that the method is a potential tool for evaluating the status of a wound.**

Keywords—Bioimpedance; chronic; monitoring; skin; two-electrode; wound

I. INTRODUCTION

A. Chronic wounds

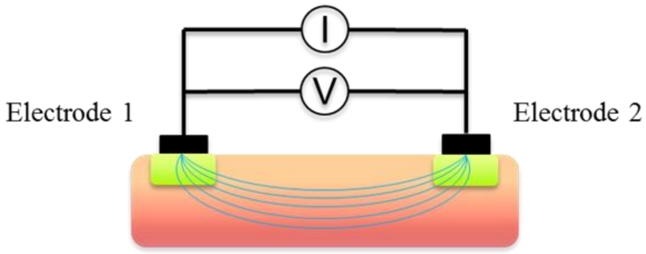
Chronic wound is not an unambiguously defined concept, however usually a wound that fails to heal within a few months is considered chronic [1]. Chronic wound is usually induced by a combination of an internal condition of the body and external trauma. Systemic factors such as diabetes, impaired vascular flow, obesity and aging expose to chronic wounds [2]. Diabetes, chronic venous or arterial insufficiency and pressure necrosis are responsible for approximately 70% of all chronic wounds [3]. The prevalence of chronic wounds is 1.3-3.6% in the western population. The burden is growing rapidly due to population aging and sharp rise in the incidence of diabetes and obesity [4]. A significant proportion of the costs are comprised of inpatient hospital days and wound care products [4], [5]. In addition to the costs, an individual chronic wound patient is exposed to a variety of psychosocial problems and physical disabilities [6].

B. Assessment and monitoring of chronic wounds

In clinical practice the assessment of a chronic wound is generally based on measuring the size and the depth of the wound and visual evaluation of the color of the wound [6]. Visual assessment is always influenced by a certain degree of subjectivity. Sometimes ultrasound or other imaging methods are used for determining the structure of the wound, and also laboratory tests of exudate samples or biopsied tissue are done [7], [8], [9]. These methods are fairly laborious and cannot be applied for daily assessment of healing of a wound. Additionally all these above mentioned methods require removal of the wound dressing.

There is a need for a quantitative at-line method to monitor the healing of chronic wounds while not disturbing the healing process and without necessity to remove the covering dressings. Bioimpedance based wound measurement may provide a solution to this monitoring problem.

We have developed a method for determining the status of a wound, based on an applied two-electrode bioimpedance measurement. In two-electrode bioimpedance measurement a single electrode pair is used for both feeding the excitation current and measuring the voltage (fig. 1). The output of two-electrode bioimpedance measurement basically consists of the electrode impedance of both electrodes, the electrode-skin interface (e.g. electrode paste), the skin impedance under both electrodes and the tissue impedance between the two measurement electrodes [10]. The outer layers of skin provide extremely high impedance compared to underlying tissues.



$$Z(f)_{tot} = Z(f)_{tissue} + Z(f)_{EI1} + Z(f)_{EI2}$$

Fig. 1. Illustration of two-electrode measurement configuration and the formation of measurement output. Z_{tot} refers to measured total impedance, Z_{tissue} to the tissue impedance, Z_{EI1} to electrode impedance of electrode 1 and Z_{EI2} to electrode impedance of electrode 2. Green layer under the electrodes refers to the skin impedance, which provides the largest contribution to Z_{tissue}, in particular at the low measurement frequencies.

II. MATERIALS AND METHODS

The healing of a wound starts from the base as the granulation tissue starts to reform and at the same time the edges of the wound start to close in [1]. It is important to not only monitor the spatial changes of the wound area but also the changes in the lateral direction. There are two ways to affect the measurement depth, one is inter-electrode spacing and the other is measurement frequency [10].

Martinsen et al. [11] investigated the effect of frequency to measurement depth in two-electrode configuration using a finite element model of the skin and electrodes. The study suggested that at a low frequency the Stratum Corneum, the dead cell layer of epidermis provides the largest contribution to the measured total impedance. The contribution seems to decline as the measurement frequency increases. This effect could be explained as follows using a simplistic electrical model of the skin and subcutaneous tissue. In the model the epidermis is modelled using a parallel combination resistance and capacitance, the dermis and subcutaneous tissues are modelled using a simple resistor [12]. The Stratum Corneum of the epidermis has very high frequency dependency in comparison to viable skin layers and subcutaneous tissue. At a low measurement frequency the impedance of tissue is mainly comprised of the impedance of epidermis. As the measurement frequency is increased, more current flows through the capacitive element of epidermis. Parallel combination of capacitive and resistive element results in a major decrease in the impedance of the epidermis. Frequency dependency of the dermis and subcutaneous tissue is much lower; therefore their relative contribution to the measured total impedance increases as the measurement frequency increases. Appropriate frequency selection may enable the monitoring of changes in electrical properties in different depth tissue layers.

We conducted a one month bioimpedance spectroscopy follow-up of a superficial acute wound. The measurements were done utilizing a Solartron 1260A Frequency Response Analyzer and Solartron 1294A Impedance Interface and Ambu Blue Sensor BRS –hydrogel electrodes.

TABLE 1 STUDY AND SUBJECT INFORMATION

Study and subject information	
Gender	Male
Age	31
Wound details	Superficial acute wound.
Duration of follow-up	Circa 1 month
Method	2-electrode bioimpedance measurement. Reference measured from intact skin adjacent to the wound.
Study equipment	Solartron 1260A and Solartron 1294A. Ambu Blue BRS –hydrogel electrodes.
Frequency range	10 Hz – 100 kHz.

The bioimpedance was measured using two-electrode configuration. The wound impedance was measured with an electrode placed on the wound (W) and an electrode placed on the reference site located on the intact skin (H1) (figs. 2 and 3). The wound impedance was referenced to the impedance measured from the intact skin site adjacent to the wound (H1 and H2 electrodes in figs. 2 and 3). The healing ratio was calculated according to equation 1.

$$Healing\,ratio\,(\%) = \left\{ \frac{\frac{Z(f_1)_{W,H1}}{Z(f_1)_{H1,H2}} + \frac{Z(f_2)_{W,H1}}{Z(f_2)_{H1,H2}} + \cdots + \frac{Z(f_n)_{W,H1}}{Z(f_n)_{H1,H2}}}{n} \right\} * 100\% \qquad (1)$$

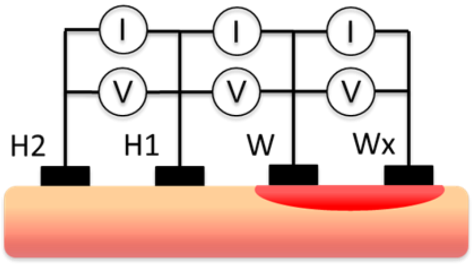


Fig. 2. A descriptive figure representing the measurement configuration. Impedance is measured with variety of excitation frequencies using electrodes W and H1 and the result is proportioned with the reference measurement taken from electrodes H1 and H2. Electrode Wx is additional electrode for measuring wound impedance using electrode W and Wx.

Fig. 3. Electrode placement on the wound according to figure 2. The wound is a superficial acute wound. The picture on the left was taken 1-2 days after the trauma. Electrode Wx is an auxiliary electrode and placed on the wound.

III. RESULTS

Fig. 4 depicts the significant difference in the impedance of the open wound (day 4) and the completely healed wound (day 28). The green graph refers to the impedance measured using the electrodes H2 and H1, according to the electrode configuration in the fig. 2. This measurement is used as a reference. The orange graph is the impedance of the wound measured using electrodes H1 and W. The red graph shows the impedance measured using the electrodes W and Wx, both electrodes were placed on the wound. The red graph is shown primarily to illustrate the significant difference in impedance of wound and intact skin. The skin impedance can be tens or even hundreds of times higher than the wound impedance. The blue graph represents the electrode impedance.

On day 4 after the injury the wound impedance (H1 and W) was around half of the reference impedance (H2 and H1) at 10 Hz (fig. 4). On day 9 the wound had clearly started to heal and the impedance of the wound reached the reference at the higher measurement frequencies, 1 kHz to 100 kHz. On day 23, the wound had completely healed and the wound impedance had reached and exceeded the reference impedance throughout the measurement range.

The table in fig. 5 represent the healing ratios calculated according to equation 1. Colour coding in the table ranges from red to green, low ratio value to high. The wound was photographed on each day of measurement.

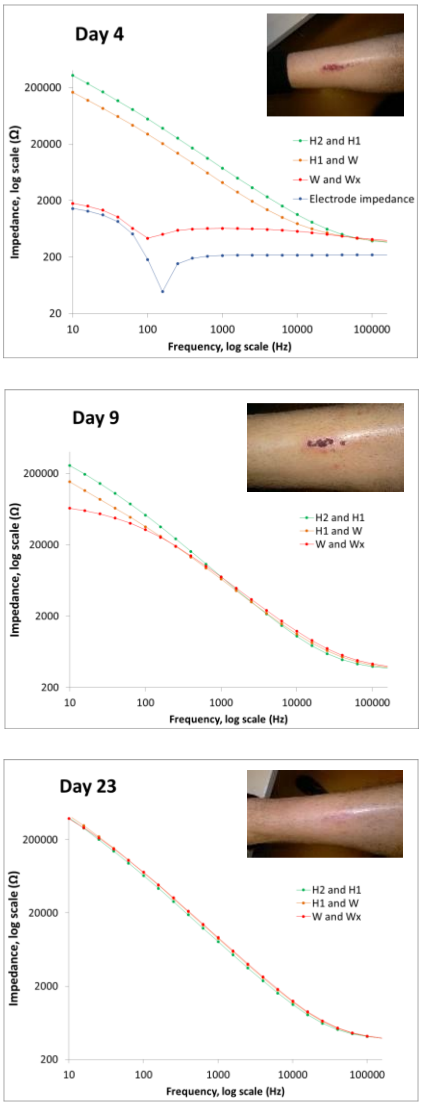
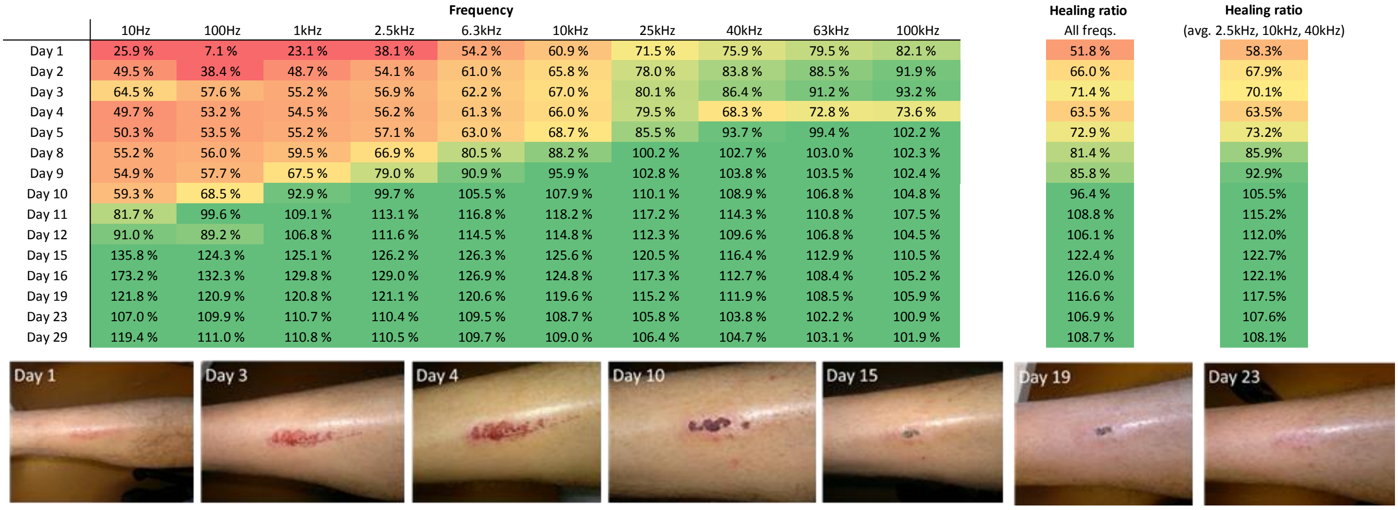


Fig. 4. *Impedance spectroscopy results of wound and intact skin. On day 4, the wound is open. On day 23, the wound is completely healed. Notice that the frequency scale of the upmost graph starts from 20 Hz.*



	Frequency										Healing ratio	Healing ratio
	10Hz	100Hz	1kHz	2.5kHz	6.3kHz	10kHz	25kHz	40kHz	63kHz	100kHz	All freqs.	(avg. 2.5kHz, 10kHz, 40kHz)
Day 1	25.9 %	7.1 %	23.1 %	38.1 %	54.2 %	60.9 %	71.5 %	75.9 %	79.5 %	82.1 %	51.8 %	58.3%
Day 2	49.5 %	38.4 %	48.7 %	54.1 %	61.0 %	65.8 %	78.0 %	83.8 %	88.5 %	91.9 %	66.0 %	67.9%
Day 3	64.5 %	57.6 %	55.2 %	56.9 %	62.2 %	67.0 %	80.1 %	86.4 %	91.2 %	93.2 %	71.4 %	70.1%
Day 4	49.7 %	53.2 %	54.5 %	56.2 %	61.3 %	66.0 %	79.5 %	68.3 %	72.8 %	73.6 %	63.5 %	63.5%
Day 5	50.3 %	53.5 %	55.2 %	57.1 %	63.0 %	68.7 %	85.5 %	93.7 %	99.4 %	102.2 %	72.9 %	73.2%
Day 8	55.2 %	56.0 %	59.5 %	66.9 %	80.5 %	88.2 %	100.2 %	102.7 %	103.0 %	102.3 %	81.4 %	85.9%
Day 9	54.9 %	57.7 %	67.5 %	79.0 %	90.9 %	95.9 %	102.8 %	103.8 %	103.5 %	102.4 %	85.8 %	92.9%
Day 10	59.3 %	68.5 %	92.9 %	99.7 %	105.5 %	107.9 %	110.1 %	108.9 %	106.8 %	104.8 %	96.4 %	105.5%
Day 11	81.7 %	99.6 %	109.1 %	113.1 %	116.8 %	118.2 %	117.2 %	114.3 %	110.8 %	107.5 %	108.8 %	115.2%
Day 12	91.0 %	89.2 %	106.8 %	111.6 %	114.5 %	114.8 %	112.3 %	109.6 %	106.8 %	104.5 %	106.1 %	112.0%
Day 15	135.8 %	124.3 %	125.1 %	126.2 %	126.3 %	125.6 %	120.5 %	116.4 %	112.9 %	110.5 %	122.4 %	122.7%
Day 16	173.2 %	132.3 %	129.8 %	129.0 %	126.9 %	124.8 %	117.3 %	112.7 %	108.4 %	105.2 %	126.0 %	122.1%
Day 19	121.8 %	120.9 %	120.8 %	121.1 %	120.6 %	119.6 %	115.2 %	111.9 %	108.5 %	105.9 %	116.6 %	117.5%
Day 23	107.0 %	109.9 %	110.7 %	110.4 %	109.5 %	108.7 %	105.8 %	103.8 %	102.2 %	100.9 %	106.9 %	107.6%
Day 29	119.4 %	111.0 %	110.8 %	110.5 %	109.7 %	109.0 %	106.4 %	104.7 %	103.1 %	101.9 %	108.7 %	108.1%

Fig. 5. Impedance spectroscopy results of wound and intact skin. On day 4, the wound is open. On day 28, the wound is fully healed. On the left the individual wound vs. reference ratios are calculated and then converted to a percentage number. Healing ratios on the right are calculated according to the equation 1.

IV. DISCUSSION

Our proposal to evaluate the status of a wound is based on an applied two-electrode bioimpedance measurement. The two-electrode configuration represents so called “true impedance”, in which areas of negative sensitivity do not exist unlike in the other basic bioimpedance measurement configurations. This makes it easier to place electrodes and to interpret the results. In two-electrode measurement the sensitivity is dictated by current density which peaks right under the electrodes and decreases with distance from the electrodes [10], [13]. The sensitivity peaks at the area of interest in the case of a cutaneous wound.

In the wound measurement one electrode is placed on the wound and the other on the intact skin. The electrode placed on the intact skin is shared by the skin impedance measurement, which is used as a reference. High impedance of the stratum corneum layer of epidermis is volatile and fairly high daily variations can be observed in the impedance of intact skin. The mutual (H1) electrode binds the wound measurement and reference together. The mutual electrode creates a sort of baseline in a way that unwanted volatility of skin impedance is reduced when the wound-skin ratio is calculated. Yet another advantage of this setup is that it decreases possibility of electrical short-circuit through highly conductive ionic wound exudate, which is typical for venous ulcer. To increase the reliability of the reference measurement it may be advisable to measure impedance at slightly higher frequencies so that the contribution of volatile stratum corneum layer is reduced and measurement depth is increased.

The results represented in fig. 5 depict that indications of healing of the wound can be seen first at the higher frequencies. At first days of the follow-up the largest changes occur at the higher frequencies, while low frequency results do not seem to indicate any significant change. The jump in the healing ratio between day 5 and day 9 is primarily due increase of wound impedance at frequencies above 1 kHz. After day 9 also frequencies below 1 kHz start to show significant increase.

The well-known downside of the two-electrode configuration is that the measurement results also include the impedance originating from the electrodes and leads. Because of this high and even quality electrodes should be used and the effect of the electrode impedance minimized or controlled. In most cases it is also impossible to make a distinction between electrode impedance and tissue impedance [14]. Despite of this the total electrode-impedance can be easily measured by connecting electrodes face-to-face. We did measure the electrode-impedance of the Ambu Blue Sensor BRS electrodes and the electrode-impedance was at the same level as the impedance measured using the wound electrode W and Wx at the first day of follow up. The level of electrode-impedance (fig. 4) was such low in comparison to the results of the skin measurement or wound measurement using H1 and W electrodes, especially at lower frequencies, that we did not perceive it as seriously detrimental to the results. The higher the measurement frequency is, the larger the relative effect of electrode-impedance seems to be. If the electrode impedance is proven to have an adverse effect on the results, a simple subtraction might be enough to overcome this problem. Calculating the ratio of wound and skin impedance may also somewhat reduce the adverse effect of the electrode impedance itself.

V. CONCLUSIONS

The developed bioimpedance based method is an auspicious tool for quantitative evaluation of the status of a wound. The follow-up of the superficial wound did show that the applied two-electrode method is suitable for wound monitoring. The results also indicated that frequency selection may have a role in detecting of early changes in the wound base. In the future more and different types of wounds should be monitored using the method.

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