Impedance Sensing Device for Monitoring Ulcer Healing in Human Patients

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***Abstract*— Chronic skin wounds affect millions of people each year and take billions of dollars to treat. Ulcers are a type of chronic skin wound that can be especially painful for patients and are tricky to treat because current monitoring solutions are subjective. We have developed an impedance sensing tool to objectively monitor the progression of healing in ulcers, and have begun a clinical trial to evaluate the safety and feasibility of our device to map damaged regions of skin. Impedance data has been collected on five patients with ulcers, and impedance was found to correlate with tissue health. A damage threshold was applied to effectively identify certain regions of skin as "damaged tissue".**

I. Introduction

Chronic skin wounds significantly threaten public health and the economy, costing an estimated $25 billion per year to treat. Pressure ulcers are a particularly morbid type of chronic wound – they affect over 2.5 million patients and cost approximately $11 billion per year in the United States alone [1]. Pressure ulcers are formed by constant pressure or rubbing applied to an area of skin, often over a bony prominence, that results in breakdown of the skin. Bedridden patients who are diabetic, obese, or elderly are at particularly high risk of developing pressure ulcers, and can incur these injuries simply from lying in the same position for the duration of a long surgery [1-3]. Other ulcers can also be formed from a variety of additional factors, including excessive rubbing or irritation, edema, and having a compromised immune system. These kinds of chronic wounds require that patients attend frequent doctor visits, often weekly or more often, to monitor the ulcer and undergo treatment. Monitoring of an ulcer can be very subjective and dependent on clinical experience, revealing the need for an objective tool that can help direct and standardize patient care.

A number of groups have studied electrical changes in cells and tissues *in vivo* and *in vitro*, and have correlated electrical properties with cell types [4-7]. A cell can be represented electrically as a combination of resistances and capacitances. Cytoplasm within the cell and extracellular fluid are ion-rich mediums that can be modelled as resistors, while the cell membrane can be modelled as a capacitor. Previous studies have examined the dielectric response of cell suspensions and tissues. Distinct *dispersions*, step changes in the complex permittivity of the material, are associated with particular molecular-level processes [8]. When utilized *in vivo*, impedance spectroscopy can detect subtle changes in tissue type and tissue health, enabling objective assessment and providing unique insight into the condition of a wound [6,9].

Our group has developed a device that non-invasively detects pressure-induced tissue damage, with functionality validated in an animal model [10]. We have since begun a clinical trial to evaluate the safety and feasibility of our device to map ulcers and to understand the relevant impedance profiles for human ulcers. Here, we detail our optimized device hardware and software for use on humans, and present new data collected on five patients with stage I, stage II, and stage III ulcers.

II. Impedance Sensor Device Design

An overview of the system is shown in Fig. 1a. The design consists of a flexible electrode array board that contacts the skin, which is connected to control hardware that enables signal to be sent and received via an LCR meter, with data being recorded on a laptop.

A. Flexible Electrode Array

The flexible electrode arrays used in this study were fabricated using copper on polyimide, plated with electroless nickel immersion gold (Tramonto Circuits, Stillwater, MN), as shown in Fig. 1b. We utilized two versions of the array in our clinical study – one that covered a circular area 0.7 inches in diameter, and another that covered a circular area 2 inches in diameter. The 0.7-inch board had 300 um diameter pads spaced 2.54 mm apart, while the 2-inch board had 635 um diameter pads spaced 7.333 mm apart. Selection of which array to use was based upon size and anatomical location of the ulcer on each patient.

In order to minimize contact impedance, we selectively applied SignaGel (Parker Laboratories Inc., Fairfield, NJ), a highly conductive electrode gel, to each electrode. To do this reproducibly, we patterned HT-6240 thin silicone rubber sheets (Stockwell Elastomerics, Philadelphia, PA) with small holes to use as a stencil over which to blade-coat the gel.

B. Impedance Sensor Hardware Design

Impedance magnitude and phase were measured using a Keysight Technologies E4980AL 20 Hz to 1 MHz Precision LCR meter. 2-point impedance measurements were taken by

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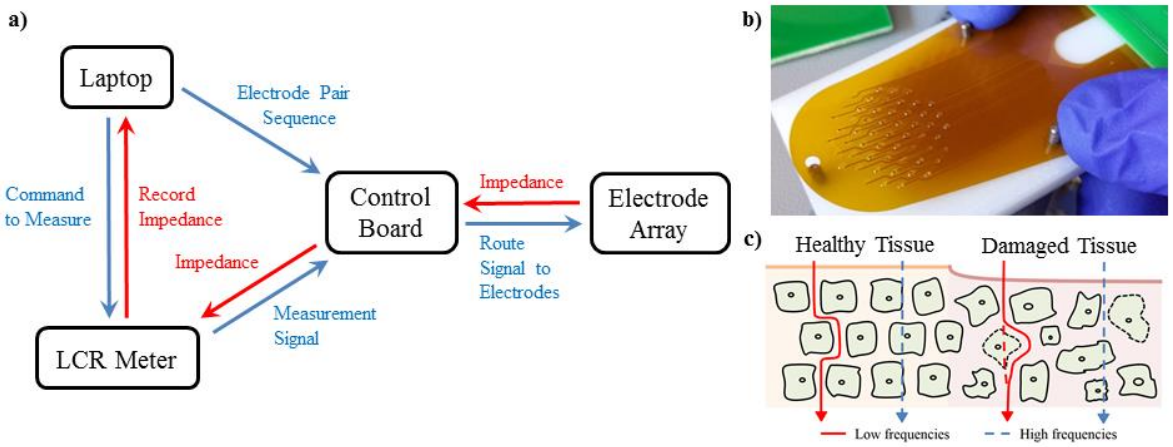

Figure 1. a) Overview of the impedance measurement system. **b)** 0.7-inch flexible electrode array board with hydrogel applied selectively to each electrode. **c)** Schematic of how low and high frequency signal travels through healthy and damaged tissue.

applying a 100-mV constant voltage sine wave output signal with a frequency of 100 Hz to 1 MHz. The control hardware allowed each electrode on the array to be independently selected, enabling the measurement of impedance between any two electrodes. A microcontroller on the board was programmed to make pairwise measurements between all nearest neighbor electrodes over a range of frequencies, routing test signal from the LCR meter to each pair of selected electrodes. This system is powered by four AA batteries.

C. *User Interface Software and Data Analysis*

We developed specific user interface software for use by clinical personnel in our study. For each patient, at least two sets of impedance measurements are taken, one set on healthy skin to serve as a baseline, and one set on the ulcer. Each set contains a measurement across each of 72 nearest-neighbor electrode pairs on the array at four frequencies (1, 15, 50, and 100 kHz), as well as a measurement across each of 11 select pairs on the array at 12 frequencies ranging from 100 Hz to 1 MHz. After a set of measurements is taken, the software can automatically plot the 72-pair data to produce visually intuitive maps of the measurement area. A nurse or physician can quickly examine these maps to understand the severity of an ulcer.

We used a number of custom MATLAB scripts to analyze the impedance data. To create the visually intuitive maps, the data is first filtered and averaged, then a simple interpolation is applied to smooth out the graphs. Additional post-processing is done to extract more frequency-dependent information from the data. Transfer functions are fit to the Bode plots, and we can compare the fits between the different types of tissue present in and around an ulcer. A contrast optimization process identified 15 kHz as the frequency at which the largest spread in impedance existed between healthy tissue and ulcerous tissue.

III. Electrode Spacing and Tissue Impedance

The human skin is a complex organ made up of three distinct layers: the epidermis, dermis, and the subcutis. Each layer of the skin will have a characteristic impedance spectrum determined by its structure.

Penetration depth of current through tissue depends on a combination of the frequency of current, electrode spacing, and the intra- and extracellular properties of the tissue being measured [5]. High frequency current can more easily penetrate through the capacitive cell membrane and traverse deeper into tissue than low frequency current. Fig. 1c depicts how signal travels differently through healthy tissue and damaged tissue. Electrode spacing also plays a crucial part in determining current path through tissue. When electrodes are spaced further apart, current is able to penetrate more deeply into the tissue, thus capturing more information about the deeper layers of skin [5]. A schematic is shown in Fig. 2a.

Impedance was measured between electrodes spaced at 0.1, 0.2, 0.3, 0.4, and 0.5 inches apart on healthy skin on the forearm of 3 subjects. If tissue is considered as a homogenous material, we would expect the impedance magnitude to increase linearly with spacing. In practice, however, impedance measurements, shown in Fig. 2b, do not increase significantly as electrode spacing increases due to the multi-layered nature of skin. The results suggest that the layers of skin (epidermis, dermis, and fatty subcutaneous tissue) have higher impedances than the underlying muscle [11], and therefore have the highest contribution to the overall impedance measurements regardless of the electrode spacing. High contact impedance could also contribute to the negligible effect of electrode spacing. In the event that tissue is damaged, the relative impedances of the three skin layers to muscle may shift and cause electrode spacing to have a larger impact on the impedance measurements.

IV. Measuring Pressure Ulcers in Patients

A. *Patient Selection*

Our study population includes males and females that are 18-80 years of age and require weekly wound assessments by a physician or registered nurse. Each patient must have an ulcer between stages I and III as defined by the National Pressure Ulcer Advisory Panel (NPUAP) classification [12]. These ulcers are located on common pressure points including the sacrum, ischium, trochanters, heels, and elbows. To ensure controlled measurements, the injury must be in a location with minimal hair.

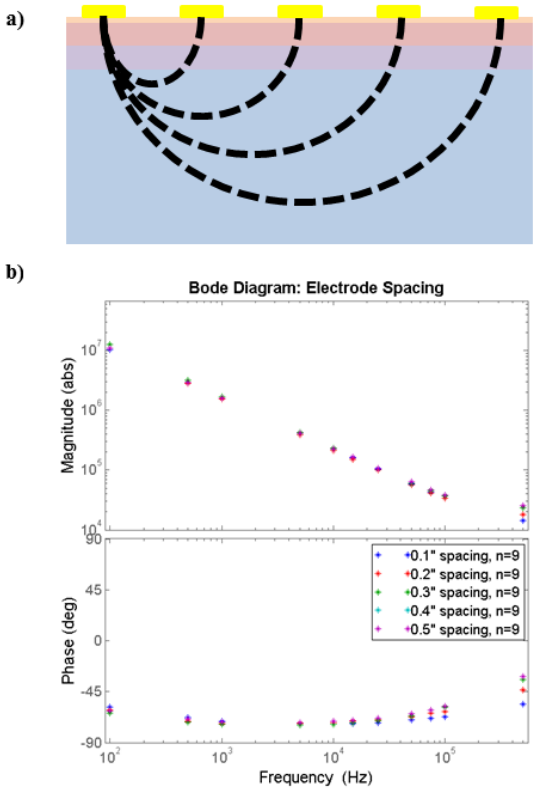

Figure 2. a) Schematic of penetration depth as a function of electrode spacing. **b)** Impedance magnitude and phase do not change significantly with respect to electrode spacing.

Patients with stage IV pressure ulcers were excluded due to the extreme topography of the ulcers, which impedes proper placement of the device. While the back of the head is an anatomical area that often develops ulcers in high-risk patients, wounds in this location are not practical for measurement as they require shaving the head, so they are also excluded from this study. Any area that has excessive body hair that the patient will not allow to be shaved will not be considered for measurement.

The five patients presented here had ulcers ranging from stage I to stage III on their leg, foot, or sacrum, and shaving was not necessary on any patient. Patients included two males and three females of ages 57-70. The flexible array board was adhered to the patient using Versatel™ contact layer wound dressings, which caused no irritation to the patient.

B. Correlating Impedance with Tissue Health

Tissue impedance was measured between 10^2 and 10^6 Hz across every nearest neighbor pair in the electrode array using a 100-mV_{RMS} constant voltage test signal generated by the Keysight Technologies LCR meter. For each patient, two measurements were taken: 1.) on "healthy" skin in an area adjacent to the ulcer and 2.) at the border of the ulcer. Wounded tissue in the ulcer was categorized as granulation tissue, slough, or necrotic tissue. Damaged tissue that did not fit into one of those 3 types were lumped into a general "ulcer" category. *Granulation tissue*, which forms on the surface of wounds, is a highly vascularized tissue that appears moist and bumpy. Across all 5 patients studied, the impedance of the granulation tissue in the ulcer is consistently lower in magnitude and less capacitive than the corresponding impedance of healthy tissue on the same patient, which is consistent with compromised cell membrane of the damaged tissue and the increase in ionic fluids introduced by the new vasculature. *Slough* is a thick, fibrous tissue, consisting of fibrin, pus, and other proteinaceous materials that need to be removed in order for the wound to heal properly. The impedance magnitude of slough is also lower than that of normal non-ulcerous tissue. *Necrotic tissue*, which typically appears as a red to dark brown scab-like tissue, consists of dead cells and debris and has low moisture levels, resulting in a high impedance magnitude similar to or slightly higher than that of normal healthy tissue. Bode plots depicting these differences between tissue types are shown in Fig. 3.

C. Determining a Damage Threshold

The spread in impedance magnitude and phase between the different tissue types was most apparent at the 15 kHz frequency. A magnitude and phase threshold is used to effectively identify "damaged tissue":

$$\text{Threshold: } |Z| < 100\ \text{k}\Omega,\ -30^{o} < \theta < 10^{o}$$

The same thresholds were applied to all impedance measurements. Pairs falling within the threshold range are labeled as "damaged tissue". The damage parameter indicates where the algorithm predicts tissue damage, including granulation tissue and slough (there were not enough data points to identify a separate threshold for necrotic tissue). The damage parameter is chosen to minimize the number of false positives, while still identifying the majority of damaged tissue regions. The damage threshold uses both the impedance magnitude and phase to identify "damaged tissue" to reduce the impact of the natural variation between patient skins and to make the threshold more reliable. The spatial map of the damage

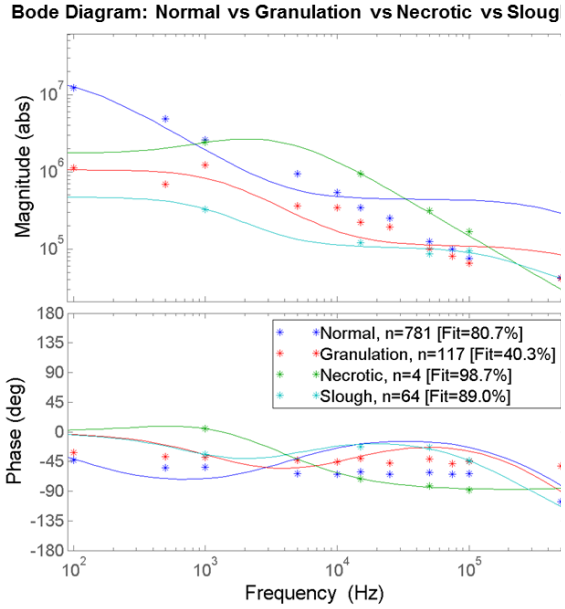

Figure 3. Impedance magnitude and phase as a function of frequency, averaged across all pairs from all 5 patients.

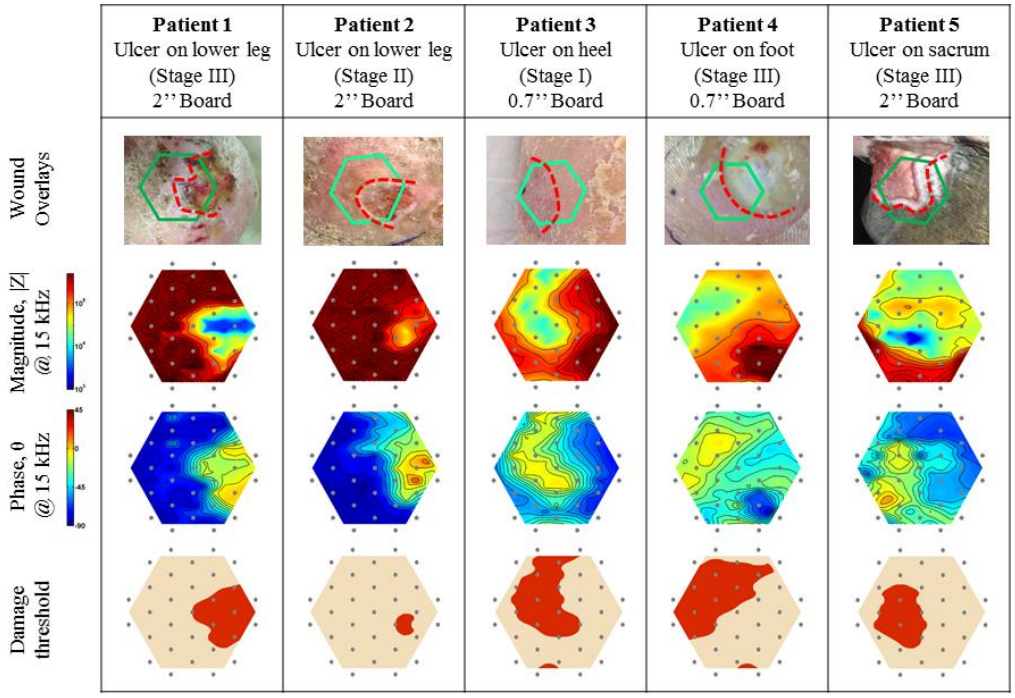

Figure 4. Impedance magnitude and phase are plotted on a color scale for each of the five patients. The damage threshold is used to identify the location of tissue damage on the skin. The green hexagon in the wound overlays represents the array measurement area, and the dashed red line represents the border of the ulcer.

parameter will enable physicians to quickly assess wound size, as shown in Fig. 4.

V. Conclusion

We have developed a non-invasive, bandage-like electronic sensor that is capable of examining differences between several tissue types (normal skin, granulation tissue, slough, and necrotic tissue) present in ulcers on human patients using impedance spectroscopy. Our device is notable in that it directly measures tissue health, rather than a secondary measure such as the amount of pressure applied. The device will enable physicians to more objectively monitor the efficacy of wound treatments and make adjustments as needed to improve patient outcomes.

Future work includes further optimizing the sensor and algorithm design and incorporating wireless functionality to improve portability and ease-of-use of the device. In addition, we plan to conduct full-scale clinical studies to track tissue changes over time as the patient heals and to assess tissue impedance in early stage ulcers and in high-risk patients who have not yet developed a pressure ulcer. The ultimate goal of this project is to develop a diagnostic device capable of detecting pressure ulcers early to prevent formation of these painful and costly sores.

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