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Development of a Multi – Electrode Electrical Stimulation Device to Improve Chronic Wound Healing

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***Abstract*—A new device has been developed for the application of Electrical Stimulation to improve healing of chronic wounds. The device enables the creation of a composite electrode hence matching the electrode(s) to the size and shape of the wound. Up to 49 electrodes in an array can be combined, delivering High Voltage Pulsed Current (HVPC) in the range 60 – 120 Hz with a pulse duration range from 90 – 110 µs and the possibility of treating the patient with direct current instead of HVPC. In addition, the software can import the measurements from the ImpediMap device, analysing the electrical impedance of the tissues involved. A test on healthy volunteers did not prove a statistically significant rise in skin temperature, $TcPO_2$ or impedance due to the stimulation, even though a slight reddening of the stimulated site was observed.**

I. INTRODUCTION

CHRONIC wounds are a major problem in the health care of the elderly patients or with patients with disabilities or diabetes. These wounds do not heal normally for weeks, months or even years, with a high impact on the quality of life of the patients and on the budget of health care systems. 4% of the annual NHS budget was spent on the prevention and treatment of pressure ulcers alone in 2004 [1]. Unfortunately, many ulcers do not respond to conventional treatments and hence research is required to develop cost-effective treatments which enhance wound healing, reduce associated pain and improve the quality-of-life of patients. Alternative techniques such as hyperbaric oxygen [2] and the application of vacuum [3] or electrical stimulation are under investigation. Electrical Stimulation in particular is a technique that should be considered as it covered by major health insurance companies such as Cigna HealthCare in the USA [4].

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II. LITERATURE REVIEW

At first glance, wound electrical stimulation appears a relatively recent technique that only attained popularity when voltage generators and batteries became small enough to manufacture portable devices in the late 60s. However, already in 1688 Digby used charged gold leaves to prevent excessive scaring of smallpox lesions [5]. The first "modern" trial of electrical stimulation was conducted by Carey and Lepley in 1962, where skin ulcers in rabbits were treated with an electrical current [5]. The first trial on humans was completed by Assimacopoulos in 1967, who had previously established in rabbits that the beneficial effects start at 50µA and that the best results can be obtained using direct current of amplitudes between 50-100µA [6], with the healing time decreased by 25% compared to control rabbits and denser and stronger scar tissue formed. He reported three human cases that he treated with the negative electrode over the ulcer, applying 50-100µA and the positive electrode positioned away from the principal vessels. The patients healed within 30-40 days whereas their ulcers had not responded to any conventional care for over a year prior to the investigation [7].

In 1969 Wolcott et al applied Low Intensity Direct Current (LIDC) of 0.2-1 mA to 67 ischemic ulcers. 8 Patients, who had two ulcers each, hence serving as their own controls, were treated with electrical stimulation on one and with conventional care on the other [8]. The first double-blind, randomised trial was conducted in 1985 by Carley and Wainapel [9] and achieved 150-240% faster healing rates compared to controls. The application of direct current has been limited due to the effects of electrolysis which may cause skin irritations and burns. This limitation caused scientists to investigate other techniques such as pulsed currents in the middle of the 1980s. Pulsed stimulation appeared as an attractive alternative to DC treatment, mainly in three forms: As low voltage pulsed current (LVPC), as high voltage pulsed current (HVPC) (both of which are monophasic pulses) and as biphasic current.

Low voltage pulsed current, also called Low Intensity Pulsed Direct Current (LIPDC), usually has an amplitude of around 10 – 50 mA at 100 Hz. Several double-blind multi-centre randomised controlled clinical trial (RCT) have been conducted successfully and led to reductions in wound size up to 4 times greater than for control groups [10]. The relatively high current amplitudes and therefore current densities, however, are quite likely to cause irritation in the skin. In high voltage pulsed currents with voltages between

100-250V, a very low total amount of energy is administered, which is not sufficient to cause the negative irritating effects while high enough to promote healing. The "active" electrode is usually positioned on the wound, with the much larger "passive" electrode at approximately 15cm distance from the wound surface [11]. The low RMS current applied by HVPC primarily induces electro-physiological effects, yet limits the electrochemical reactions seen with direct or LVPC currents.

In 1988 Kloth et al conducted the first blinded placebo-controlled HVPC trial on humans [12]. In a retrospective study, 22 paired patients, who received a minimum of 4 weeks of electrical stimulation or of conventional treatment were compared. After the one year follow up period, 90% of the stimulation group had permanently healed whereas only 71% of the control group achieved complete healing [13]. The main parameters measured were microcirculation as detected by TcPO2, Videomicroscopy and Laser Doppler, and skin surface temperature. All of which indicated that microcirculation had improved considerably for electrical stimulation treated patients in a very short time.

Two very similar trials were conducted by Baker et al, one with patients with diabetes [14] and one with patients with spinal cord injuries and associated ulcers [15]. Asymmetric biphasic square waves (A) (initially positive), as used in Functional Electrical Stimulation, were compared with a symmetrical biphasic square wave stimulation (B) as used in TENS, a placebo group (C) and with a group stimulated by non-therapeutic micro-currents (D). This setup was intended to investigate the effect of biphasic stimulation polarity on wound healing. The healing rate of the SCI-patients was only 24%/wk if treated as group D. Group B and C healed at around 30%/week whereas group A healed at 36.5% a week. 11 Cross-over patients that were randomly assigned to A or B improved considerably from 10%/wk to 43%/wk.

In the second trial, asymmetric biphasic current as used for group A showed a healing rate twice as fast as the micro-stimulation or the sham treatment. The above trials proved that there is an influence of the polarity of the applied current on the healing process.

In 1999 Gardner et al performed a Meta Analysis in order to quantitatively "average" the outcomes of several independent studies. 28 studies were reviewed, 15 of which passed the criteria to be included. In total, 591 ulcers had been treated with electrical stimulation in these studies and 212 served as control or placebo.

No placebo effect could be proven; however, there was a considerable difference between the various stimulation techniques: 10.87%/wk for TENS, 12.59%/wk for DC and 15.5%/wk for pulsed currents. There was also a big difference between ulcer aetiologies. There is no overlap in confidence intervals between the total weekly healing rates, which increases the significance of the difference between stimulated and non-stimulated wounds. This meta-analysis therefore supports electrical stimulation "as an effective adjunctive therapy for chronic wound healing" [16].

Following in-depth analysis of literature on electrical treatments for wound stimulation, HVPC was determined to be the safest and most effective stimulation mode due to its typical twin-peaked unipolar waveform. The best effects of wound stimulation have been obtained with an average current of ~600 µA, increasing the protein synthesising activity [17]. Kloth and Luther suggested that an adjustable amplitude range of 100-200 V is most efficient when stimulating with HVPC [18].

III. Stimulation Device

When looking at stimulation devices aimed at wound healing it becomes apparent that they are usually only equipped with one or two pairs of electrodes. The electrodes used are of standard sizes and are not customized to the size and shape of the wound. In the human body, however, the electrical healing potential which found in acute wounds and is to be assisted by the applied electrical field is present at the direct wound perimeter, following its shape and contours.

A new device has been developed called ImpediStim that enables the clinician to 'create' an electrode out of an electrode array and to thus achieve the closest match to the wound shape and size. This composite electrode can take either polarity and stimulate with either HVPC or DC to furnish the clinician with a range of options for therapeutic stimulation.

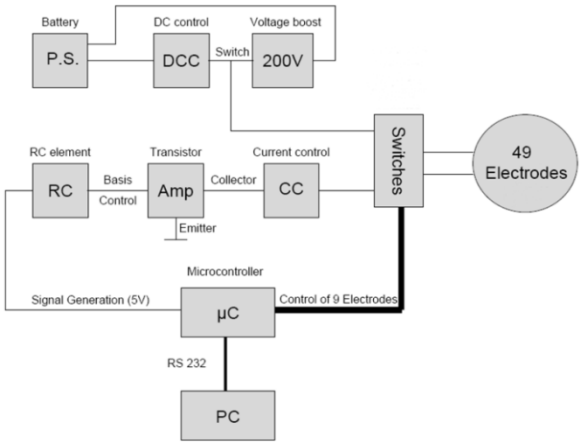

Fig. 1: Block Diagram of the ImpediStim Device

In addition, the new device can work together with the ImpediMap device [19] in order to measure and define the wound automatically. The impedance values are fed back into the software and enable the chosen individual electrodes to be incorporated into a signal composite electrode. The same electrode array is used for both measurement and stimulation, thus enabling the use of both devices in clinical trials. The impedance measurements can additionally be used to assess the success of the electrical treatment, all without removal of the dressing.

Currently, the optimal treatment parameters for wound healing have yet to be firmly established. Clinical trials are

required that assess unequivocally the effects of stimulation frequency, polarity and amplitude on the different stages of the healing process.

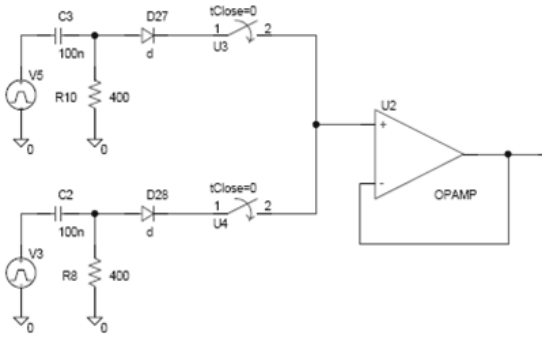

Figure 2: Signal Generation to achieve the typical twin peaked HVPC pulse

The ImpediStim device, whose block diagram is shown in Fig. 1, offers these options with up to 200 V over a frequency range of 60 – 120 Hz, with a pulse duration range from 90 – 110 µs and the possibility of treating the patient with direct current instead of HVPC. The polarity can be chosen individually for every of the up to 49 electrodes in the array.

At the heart of the device is an analogue circuit, utilizing two RC elements, connected as a differentiator to create the typical HVPC twin pulse as shown in Fig. 2. In order to use low cost electronic components, the signal generation takes place at a low voltage range and is thereafter amplified within the power transistor circuit which also increases the accuracy of the pulse duration, frequency and amplitude, see Fig. 3.

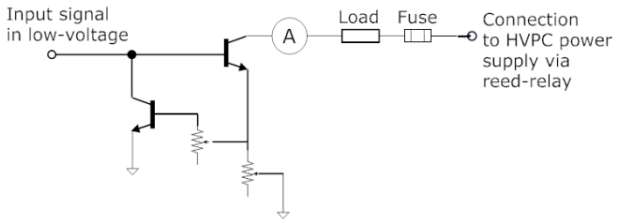

Figure 3: Signal amplification from 12V amplitude to 200V amplitude

The output is achieved by the use of a rail-to-rail, single supply amplifier in the form of a voltage follower to give the same output signal characteristic as at the input. Alternative voltage followers assessed destroyed or obscured the signal from the desired exponential function which is shown in Fig. 4. In order to ensure the correct reference potential in the collector path of the power transistor, reed-relays were used to address the up to 49 electrodes. The control of the DC/DC converter with a 12V input and 200V was established by the use of a serial open-collector transistor.

The wound stimulation interface (WSI) which controls and sets the parameters for the wound stimulation unit such as frequency, treatment time, pulse duration and signal polarity, was designed on VB.net and communicates via RS232. The WSI has the common Microsoft Windows style for ease of use. The software for the PIC16F877 microcontroller, the latter is from Microchip and controls the hardware, was implemented with a MPLAP ICD 2 in-circuit debugger and a C compiler from Custom Computer Service (CCS).

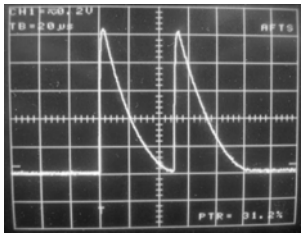
Figure 4: Signal output in low-voltage range (measurement taken with a /10 probe therefore the amplitude has to be multiplied by 2)

IV. In-Vivo Testing

The effectiveness of the newly designed electrical stimulation unit was evaluated on several volunteers at the University of Ulster. The aim was to monitor the changes in impedance, Saturation of Peripheral Oxygen (SPO2) and temperature over time following stimulation and thus to acquire an insight into the effects electrical stimulation has on skin and the underlying tissues, eventually aiming at improved understanding of stimulation-induced healing of chronic ulcers. The main research question to be addressed was, to what extent does Electrical Stimulation influence blood flow in healthy tissue and can this be the key mechanism for the improvement in wound healing achieved with such Electrical Stimulation?

A. Method

Eight volunteers were recruited; five were stimulated with HVPC whereas the other three received sham treatment. Once the volunteers had given informed consent, four main measurements were taken before stimulation commenced: The initial electrical impedance was measured using the bespoke ImpediMap device. The temperature at the skin site to be stimulated, the temperature 5 cm away from the stimulated skin and the temperature at the participants' temples were measured using an infrared forehead thermometer device from Petit Hanson. The measurement of the SPO2 in the limb as well as the pulse rate was performed via a finger pulse oximeter device from Finger Pulse Oximeter on the index finger. Stimulation was then commenced for 30 min and the measurement was repeated directly following stimulation, then 1 and 6 hours later. The composite electrode was compiled out of a screen-printed 25- electrode array as used for the impedance measurements, see Fig.5. HVPC was applied at 100 Hz, with a pulse duration of 100 µs and a maximal amplitude of 200 V. The volunteers were advised to increase the amplitude until it was perceived as painful and to settle for an intensity slightly below that. Ethical approval was granted by the appropriate filter committee at the University of Ulster.

B. Results

Two of the volunteers increased the amplitude to a point where muscle twitching was observed. For these two volunteers a slight increase in temperature of around $\Delta T \approx$

1.5°C was measured, none was noticed for the other subjects. None of the other parameters changed significantly for any of the subjects. A reaction on the skin was observed on all five volunteers with HVPC stimulation, see Fig. 5. The skin was red under the treatment electrodes as well as under the dispersive electrodes indicating an increase in perfusion even though it could not be detected with the measurement techniques used.

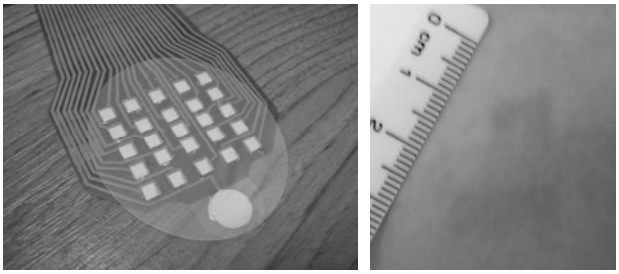

Figure 5: Electrode Array used for Impedance Measurement as well as for application of Electrical Stimulation (left). Reddening of the skin under the stimulating electrodes (right).

C. Discussion

Stimulation for 30 minutes did not show any significant changes in skin temperature, skin impedance or $TcPO_2$ measurements. Whereas a change could be visually observed, it could not be proven with any of the measurements used. A similar phenomenon was observed by Savrin and Rajmond who detected a rise in skin temperature in patients with spinal cord injuries but could not replicate this phenomenon in healthy volunteers [20].

In order to be able to detect significant differences between stimulated skin and non-stimulated skin, either the applied current amplitude or the timeframe over which stimulation is applied should be increased. Alternatively, different measurement techniques could be utilised, such as Laser Doppler, a technique which is based on the scattering of laser light, which would pick up an increase in microcirculation with very high sensitivity.

V. Conclusion

The ImpediStim is a device that is capable of delivering Electrical Stimulation in the form of HVPC or DC to a composite electrode which can be formed by the user out of an existing array of electrodes used to monitor the site. It is designed to process the impedance measurements of the underlying tissue in order to define the wound perimeter and thus aide in choosing the composite electrode layout.

Initial trials on healthy volunteers showed a visual reddening of the skin, however, no increase in circulation could be proven with the measurement apparatus used. This should, however, in itself not be seen as a fault in the device design but rather as a prompt to change stimulation parameters, if a measureable perfusion increase is the aim of the experiment. As can be seen in other trials [20], however, electrical stimulation at this level of intensity probably has a different influence on volunteers with a healthy circulatory system compared to patients with chronic ulcers, which are usually caused by ischemia-reperfusion, and hence by defective perfusion. What this trial has shown, however, is that the device is user-friendly, easy to use and capable of being managed by the patient him/her-self. This opens up the possibility of increased self-management by the patient whereby they can measure the impedance, and thus the wound healing progress, and apply stimulation to the wound to improve wound healing.

Clinical trials have been arranged for the device to investigate the effect of HVPC on chronic ulcers and the effect of changing stimulation parameters.

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