



## REVIEW ARTICLE - ENGINEERING

### Wound Healing Using Electrical Stimulation: A Review

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| <p><i>Article history:</i></p> <p>Received<br/>31 January 2023</p> <p>Accepted<br/>12 May 2023</p> <p>Publishing<br/>31 December 2023</p>                                 | <p>The wound healing process is considered one of the most important elements of progress in the health and medical reality alike, because it has a direct impact on the patient's life, especially those who suffer from chronic diseases such as diabetes mellitus and others. All over the world, especially in developing countries, many people are exposed to afflictions due to the lack of ability to heal wounds or the delay in their recovery. The healing of wounds is always attributed to the ability of the affected skin to produce an electric current that helps the migration of stem cells and platelets to the place of extraction for the sake of healing, this is why electrical stimulation ES devices played an important role in the process of stimulation and wound treatment through using the high voltage pulsed current HVPC, low voltage pulsed current LVPC, direct current DC or pulse current PC. In this study, we review some of the important works that touched on this field in terms of the aim of their studies and the outcome that was reached, and the results were extracted. We also discuss the problems that faced researchers, especially those problems that Their studies miss it.</p> |
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## 1. Introduction

At the cellular and organismal levels, internal and external electrical currents affect how cells behave and interact with each other and operate the internal biological electrical system by interchanging inside and outside cells, which is critical to maintaining the basic physiological processes of the body in general and the skin in particular [1]. The skin's primary purpose is to protect the body from the outside world while the first objective of healing is wound closure including numerous biological processes for repair and tissue regeneration because its loss of integrity as a result of injury or illness may result in severe impairment, where the healing process goes through four phases, one of which is the migration of the healthy epithelium surrounding the wound in the direction of the injury to cover it, also The most important function of human skin is to generate currents that maintain cellular tone and heal wounds in case of tissue damage [1, 2]. The properties of the current generated by the skin would accelerate the healing process, as in all the studies that were conducted to accelerate the wound healing process using electrical stimulation, it was found that this current relied on two types of current, which are continuous current and pulsating current, although there are two types of Constant and alternating current, pulse current is still not subject to this classification, it is a continuous current, but it falls at specific frequencies and is very effective in wound healing as the characteristics of the therapeutic current are no more than mA or micro amp max and with specific pulse frequencies, they are known By studying the pathological condition, while the amount of voltage ranges from 1 to 140 volts per millimeter of the wound area [3]. Wounds of all kinds, especially chronic ones, represent a great burden on the body. The matter may develop into a loss of growth factors as a result of the development of wounds, the continuous decrease in cellular activity, and the failure to generate appropriate currents that are necessary to activate the cells that work and help heal wounds as a result of their movement towards the site of the wound or injury [4]. Chronic wounds present a serious problem for patients and healthcare professionals Therefore, it has become a major problem on the financial level in terms of the therapeutic cost and healing complications, which prompted most researchers to study the effect of many therapeutic methods designed to accelerate wound healing, including the use of antiseptics and antibiotic growth factors, Pressurized oxygen, bioengineered skin substitutes, and physiotherapy methods such as electrical stimulation(ES) and nanogenerators [5, 6] also the polymeric hydrogel membranes which act as a wound dressing that increase the process of the treatment [7]. Electrical stimulation devices have played many important roles in medical treatments, and they have become the focus of attention and attraction for most researchers because of their important role in activating cells through signals that are shed with specific features and values that activate cells and increase the migration of fibrous and stem cells towards and places of wounds, and this is what helps On stimulating the skin to heal and heal wounds, research has become the subject of renewed medical treatment because of the advantages that these devices provide [8]. The process of treating and healing wounds has always been a complex process which contains many stages involved within the skin to complete this process, including the process of coagulation, cellular proliferation, and infections associated with this process,

| Nomenclature & Symbols |                             |      |                            |
|------------------------|-----------------------------|------|----------------------------|
| ES                     | Electrical Stimulation      | DC   | Direct Current             |
| PC                     | Pulsed Current              | LVPC | Low Voltage Pulsed Current |
| HVPC                   | High Voltage Pulsed Current | MPC  | Monophasic Current         |
| mA                     | milliamps                   | mV   | millivolts                 |

so the process of healing wounds was accompanied by many developments in this field and the inclusion of some engineering and medical applications such as nanomaterials and generators [4, 5, 9]. Nanoelectric stimulation and other networks of medical fibers have high adaptability to the body and the ability to overcome most of the problems related to medical bandages to keep pace with developments in the medical field and accelerate the complex healing process [9-11]. The necessity of using stimulation devices may be when the internal electric fields of the skin decrease due to a certain disease such as chronic diabetes mellitus, so that these currents are responsible for wound healing and their decrease leads to a twenty-five percent reduction in the healing process [12]. The areas of application of electrical stimulation differed in the treatment and healing of many types of wounds. It had a direct impact on the treatment of severe wounds, as well as the treatment and healing of complex wounds, especially in the treatment of ulcers of patients suffering from diabetic foot, and the direct threat these wounds cause to their lives, whether in the short or long term. These devices had a direct effect on the physical properties of the skin and helped in the healing of ulcers by stimulating the proliferation of therapeutic cells and reducing bacterial activity [13]. Finally, through the introduction above, we can understand that the skin has major mechanical functions, as it represents the largest organ in the human body, as it helps maintain balance by acting as a selective barrier between the inside and outside and providing protection. of pathogens and harmful physical and chemical agents, while regulating the movement of heat, water, and electrolytes through them [14].

## 2. Properties of Electrical Stimulation

For decades, people have used the energy of an electric field to speed up the healing of chronic wounds, so this energy has been shown to help direct cell migration toward wound areas[3]. Human skin works on the automatic generation of cellular current, which works on the internal balance of the human body, in addition to maintaining cell activity and the process of repairing damaged tissue [1]. The skin loses the property of generating current and maintaining the internal cellular balance in the case of patients with chronic diseases, which reduces the wound healing process by a large percentage that may reach twenty-five percent[12, 15] Here comes the role of electrical stimulation devices to accelerate the healing process and help patients with chronic wounds. In this section we will show the type of current and voltage used in electrical stimulation for wound healing as described in [3].

### 2.1. Voltage

When two electrodes are attached to the body, voltage (V) is the electromotive force (EMF) that can move charged particles (ions across cell membranes in damaged tissues). A volt is a unit of electrical pressure that is similar to water pressure and represents the electromotive force (EMF) required to push a current of 1 A through a resistance of 1 ohm. where the amount of voltage ranges from 1mv to hundreds per mm area of the wound during the healing procedures which could be high voltage HV or low voltage LV.

### 2.2. Current

There are two types of current used in the ES device, direct current DC or pulsed current PC, The two electrodes used in direct current (DC) and monophasic pulsed current (MPC) are polarized concerning one another, with the cathode being negatively charged and the anode being positively charged (anode). To ostensibly duplicate or stimulate the disrupted endogenous polarized current that is present after the damage of the integument, currents with polarity are employed for wound healing. where the amount of current used in the ES ranges from microamps to miliamps based on the wound type, Figs. 1 and 2 show the two types of the current waveform used in the ES device.

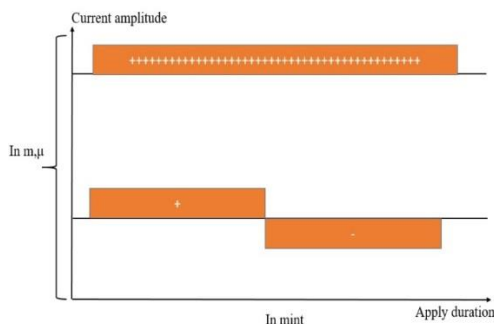


Fig. 1. The Direct current waveform

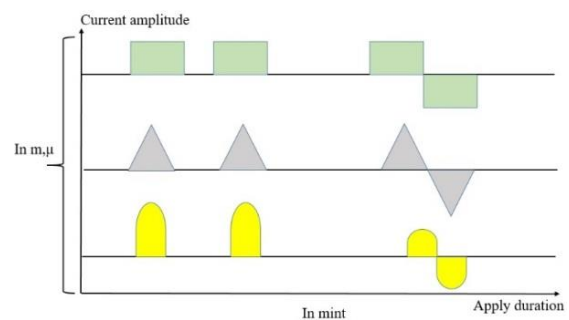


Fig. 2. The pulsed current waveform

Therefore, electrical stimulation can be applied in several ways, depending on the type of wound and the response of the skin to the healing state:

- LVDC Low Voltage Direct Current.
- HVDC High Voltage Direct Current.
- LVPC Low Voltage Pulsed Current.
- HVDC Low Voltage Pulsed Current.

Where the studies and works related to the use of electrical stimulation for the treatment of wounds, as in[3, 8, 12] showed that the basic structure for placing electrodes and using the electrical stimulation device is as shown in Fig. 3:

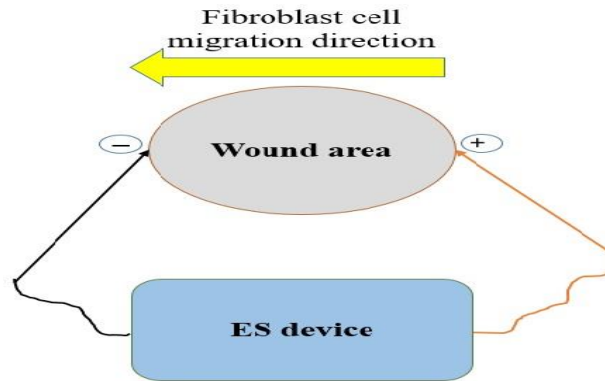


Fig. 3. The electrode placement of the ES device in the wound healing procedure

### 3. Literature Survey of Related Works

In this part, we review the most important studies related to the field of wound healing and treatment using various techniques, in addition to providing summaries explaining the aim of the study according to the principles, materials used, results obtained, and the most important problems in these studies, as follows:

A. Sebastian, et al., 2015[16]; In this study, the researchers intended to treat and heal wounds by modifying the reaction of SIVA1 p53 protein. The authors based on a Wounded tissue model outside the body in the form of a donut of living tissue with a thickness of 4 mm from the inside and a size of 8 mm. which was treated by an ES device applied by 100 mv for 16 days 1ma and comparing the result with and without ES. It was found that the speed of wound healing increased by seven days in the case of not using electrical stimulation. But The model used works on only one model using continuous electrical stimulation technology for long periods of therapeutic time to demonstrate the effect of electrical stimulation that targets genetic biopsies, so to prove the validity of the results, the patient or tissue examination must be provided before the comparison process takes place to calculate the therapeutic effect. from a genetic mutation affecting this gene.

Snyder, et al., 2017[17]; In this paper, the researchers sought to treat wounds by increasing the migration of stem cells to the wound site through electrical stimulation. Through this study, the effect of electrical stimulation on cell migration was examined by using mimic wound model treated with an ES device with 25 to 100 mv and current 2 mA to 3 mA and wound monitoring using Timelapse Microscopy for migration monitoring. The random migration occurs after 10 mint of the procedure with 100 mv and greater in 200. Based on the principle used This study needs to improve the wound healing mechanism by making the design contain the range of chronic and acute types of wounds, i.e. generating different types of electrical stimulation currents.

Long, Y., et al., 2018[18]; In this study, the researchers used the technology of nanogenerators to treat wounds by using intermittent current for electrical stimulation. Depending on the principle of nanogenerators, the researchers found The greater the movement of the body, the greater the voltage produced by the skin that results from the generator that converts the mechanical movement into electrical, and it may reach a maximum of 2.2 v When the body is in full activity and movement, the design showed a difference in wound healing, starting on the third day. Some points should be taken into consideration in this study The poisoning that may affect the bandage must be treated, otherwise, it will adversely affect the wounds. The greater the movement of the body, the higher the voltage generated from the generator and vice versa, and this may not be appropriate for the types of wounds. This application is used in this study for treatment for long periods compared to the amount of voltage generated by the same amount Little. also, the treatment completely depends on the movement activity and this may not be suitable for the patients with low vital activity and movement.

Hu, W. et al., 2019[19] found that electrical stimulation has a significant impact on the process of improving the proliferation of stem cells, which in turn helps in the process of wound healing. so their study used RD-TENG nanogenerator as the ES generator applied on SWCNT thin film containing mouse fibroblast cell line L929 in a dish through carbon electrodes. the result was monitoring using a Digital microscope for monitoring the migration of fibroblast cells and they found by comparing the conditions with and without using the nanogenerator shows the optimal current value was 50  $\mu$ A to increase the proliferation and migration of the fibroblast cells within 2 days. But Before conducting the application of this study, we need genetic tests to know the status of the RNA chain and the status of the genetic mutation to ensure the validity of the results practically. Also, the mechanism of generating the electric field requires more movement to generate the electrical stimulation.

Liang, Y., et al., 2020 [20]; In this paper, the researchers used a constant continuous stimulus source for Studying the effect of electrical stimulation on the living body of pigs on a specific wound of the body and studying the migration of creatinine cells in terms of direction, distribution, and condition. The optimal shape and uniform cell distribution was by applying +100mv while -100mv showed the reverse and the distribution of keratinocytes looks random and not in site of the wound of pig in vivo wound case. the stable duty cycle of the power generator takes a long period for wound healing also may not be suitable for other types of wounds so these problems must be in the focus area.

Wang, X. F., et al., 2021[21]; In this study, the researchers intended to develop an electrical stimulation device to treat the wounds of patients with diabetic foot disease, where a flexible wearable device was designed with medical gauze that helps prevent moisture and germs. The results were tested on a group of rats and the results were satisfactory and the effect of the intermittent current was good in terms of affecting the migration of fibroblast stem cells. This research is considered very important for the development of the mechanism of wound treatment and an important step for the development of the work of the devices, but the failure to test the work of the device on some of the genetic properties of humans such as a blood sample or platelets leads to the non-confirmation of the results for human use and needs to be proven in the future.

Atieh Abedin-Do, et al., 2022 [22], In this study, the effect of electrical stimulation on diabetic human skin is shown, in addition to the effect of stimulation on the growth of fibroblasts and its effect on wound healing, the authors based on that the Electrical stimulation stimulates the

skin to grow and thus stimulates the growth of fibrous stem cells to close the wound site. They conclude The use of low-intensity electrical stimulation can accelerate the cell growth process and stimulate diabetic skin to grow and thus heal wounds in a shorter period of five days without the use of electrical stimulation where the effect of the ES appears on 6h to 24 h. this study lack of dealing with different types of wounds so The ideal device for treating wounds should be variable in terms of frequency, voltage, and current to treat different types of wounds, while the researchers relied on changing the voltage only.

Through previous studies, the importance of electrical stimulation in the treatment of normal and chronic wounds were noted, and the ability of electrical stimulation to accelerate the complex healing process in several ways and areas for applying therapeutic mechanisms. Where the mechanism of applying electrical stimulation has been developed using conventional or ready-made devices, as well as through Nano-applications. Few studies have aimed at designing devices and focused on studying the effect of electrical stimulation on wounds and accelerating the healing process by increasing the migration of stem cells and fibroblasts.

The Table 1 shows a summary of previous work on electrical stimulation that has been used in the treatment of specific conditions using different techniques, materials, and principles:

Table 1. The summary of the wound healing studies based on the principle of Design

| Refer | Aim of the study  | Principle of design   | Material   |
|-------|---|---|--|
| [16]  | This study targets a necrotic cell-regulatory protein named SIVA which is located in the SIVA1 gen, this study shows the effect of the ES on the SIVA.  | Electrical stimulation helps to increase the effect of protein in the areas exposed to the wound to increase the speed of healing.  | 1. Wounded tissue model outside the body in the form of a donut of living tissue with a thickness of 4 mm from the inside and a size of 8 mm.<br>2. ES device applied by 100 mv for 16-day period 1mA.<br>3. comparing the result with and without ES. |
| [17]  | Examining the effect of electrical stimulation on chronic wounds and observing its effect on HDFs migration.  | The study is based on the principle that the wounded tissue produces an electric current and field during the wound-healing process.  | 1. mimic wound model.<br>2. ES device with 25 to 100 mv and current 2 mA to 3 mA.<br>3. Timelapse Microscopy for migration monitoring.   |
| [18]  | The use of Discrete current of the electrical stimulation to treat rat wounds and to monitor the therapeutic effect.  | Converting the mechanical displacement resulting from the movement of the skin into an electric field that is applied using a bandage to the place of inventory. Producing electrical stimulation by converting mechanical displacements into electrical energy with variable ranges ranging from 10–50 $\mu$ A for different conditions of the test. | 1. Nanogenerator.<br>2. Rat with the wound.<br>3. Digital microscope for wound monitoring.   |
| [19]  | Knowledge of the effect of electrical stimulation by nanogenerators on the proliferation of stem cells (fibroblast cells) and their behavior.   | The direction and amount of electrical stimulation directly affect the direction, shape, and state of distribution of keratinocytes at the wound site.  | 1. RD-TENG nanogenerator.<br>2. SWCNT thin film contains mouse fibroblast cell line L929 in the dish.<br>3. electrodes.<br>4. Digital microscope for monitoring the migration of fibroblast cells.   |
| [20]  | Studying the effect of electrical stimulation on the living body of pigs on a specific wound of the body and studying the migration of creatinine cells in terms of direction, distribution, and condition. | The gauze used is classified as preventing the growth of germs and maintaining the level of moisture, so it speeds up the healing process using electrical stimulation.   | 1. Pig for vivo wound case.<br>2. power DC generator.<br>3. Electrodes.  |
| [21]  | This study aims to test the effect of electrical stimulation in the presence of medical gauze Chitosan-Vaseline and its efficiency in healing wounds for patients with diabetes.                            | Electrical stimulation stimulates the skin to grow and thus stimulates the growth of fibrous stem cells to close the wound site.  | 1. Flexible printed ES device LVMPC (4 to 40 v) and HVMPC (40 to 100 v).<br>2. chitosan –Vaseline gauze dressing.<br>3. group of rate.<br>4. Digital Microscope.   |
| [22]  | In this study, the effect of electrical stimulation on diabetic human skin is shown, in addition to the effect of stimulation on the growth of fibroblasts and its effect on wound healing                  |   | 1. ES device with (100,80,40 and 20 mv\mm).<br>2. Diabetic human skin fibroblasts sample.<br>3. optical microscopy for fibroblasts cell count  |

#### 4. Result

Based on the review of previous studies, we found that electrical stimulation helps in treating wounds by activating fibroblast cells and moving them toward the wound area by applying an amount of current similar to the value of the current that is generated by healthy skin or that has not lost its cellular properties as a result of chronic diseases. Electrical stimulation is applied in four different ways depending on the wound phase with two types of current and voltage (LV, HV, DC, and PC). The value of the therapeutic voltage ranges from 1 millivolt to one hundred or two hundred volts, while the current ranges from 1 micro amp to one hundred milliamps, according to the medical condition of the injured person, whether he suffers from chronic diseases or such as the chronic diabetic foot. The treatment period for chronic wounds may last up to several days with continuous sessions. The period for one session ranges from 5 minutes with a high current intensity to 40 minutes with a low current intensity, and so on, so that the relationship is inverse between the amount of current and the period for one session.

Based on the previous studies, which are summarized in Table 1, most of the problems were identified in the designs related to the electrical stimulation process in the field of wound healing, where the identification of problems was based on the design structure, the therapeutic scope, the applicability of the study in practice, in addition to the extent of compatibility With most types of wounds and the mechanism of providing devices capable of dealing with most ulcers and chronic or acute wounds, the Table 2 shows a summary of most of the problems of previous studies.

Table 2. The problem statement based on the previous studies

| Refer | Problems  |
|-------|---|
| [16]  | The model used works on only one model using continuous electrical stimulation technology for long periods of therapeutic time to demonstrate the effect of electrical stimulation that targets genetic biopsies, so to prove the validity of the results, the patient or tissue examination must be provided before the comparison process takes place to calculate the therapeutic effect. from a genetic mutation affecting this gene.   |
| [17]  | This study needs to improve the wound healing mechanism by making the design contain the range of chronic and acute types of wounds, i.e. generating different types of electrical stimulation currents.  |
| [18]  | The poisoning that may affect the bandage must be treated, otherwise, it will adversely affect the wounds. The greater the movement of the body, the higher the voltage generated from the generator and vice versa, and this may not be appropriate for the types of wounds. This application is used in this study for treatment for long periods compared to the amount of voltage generated by the same amount of Little. also, the treatment completely depends on the movement activity and this may not be suitable for the patients with low vital activity and movement. |
| [19]  | Before conducting the application of this study, we need genetic tests to know the status of the RNA chain and the status of the genetic mutation to ensure the validity of the results practically. Also, the mechanism of generating the electric field requires more movement to generate the electrical stimulation.  |
| [20]  | the stable duty cycle of the power generator takes a long period for wound healing also may not be suitable for other types of wounds.  |
| [21]  | This research is considered very important for the development of the mechanism of wound treatment and an important step for the development of the work of the devices, but the failure to test the work of the device on some of the genetic properties of humans such as a blood sample or platelets leads to the non-confirmation of the results for human use and needs to be proven in the future.  |
| [22]  | The ideal device for treating wounds should be variable in terms of frequency, voltage, and current to treat different types of wounds, while the researchers relied on changing the voltage only, so the DC or PC of the ES must be taken into account during the test the effect of the ES on the wound healing.  |

## 5. Conclusion

The process of treating acute and chronic wounds represents a major problem in the field of health care and is also a measure of the extent of the development of health reality, especially in developing countries. Chronic wounds and ulcers represent a direct and very dangerous threat to patients suffering from diabetes, which may threaten their lives if they are not dealt with. With the problem directly and correctly. Many techniques have been applied in various fields to develop a mechanism for treating wounds and accelerating the healing process. The most important of them was the electrical stimulation process, which represents a simulation of the basic function of the skin tissue in the healing process. The skin tissue plays an essential role in the process of Hospitalization where an electric current is generated that stimulates stem cells and fibroblasts to multiply and move towards the wound site, but in the case of patients who suffer from diabetes or genetic problems, the skin may lose its function in stimulating cells, and here begins the important role in the wound healing process.

Many studies were conducted to achieve the property of healing by using electrical stimulation using several techniques and examinations outside the body or in the laboratory. Most of the objectives and the principles on which these studies are based were diagnosed with the identification of most of the problems facing each study. We concluded through most of the studies and the problems that were identified that The design of any electrical stimulation device must work according to a range of types of wounds, whether chronic or acute. Therefore, the devices must provide variable characteristics and values of voltages and currents with variable frequencies targeting a specific range or type of wound, so that some cases need pulsed current PC and others need a direct current DC of variable or constant intensity, so we intend in most designs to contain all the scope of wounds by designing devices that can provide constant or variable electrical stimulation according to the patient's condition.

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