# Comparative analysis of two models of technologies for the treatment and monitoring of chronic wounds

# Análise comparativa de dois modelos de tecnologias para o tratamento e monitoramento de feridas crônicas

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## 1 INTRODUCTION

Chronic wounds represent a complex challenge in the healthcare field, requiring continuous monitoring and adequate treatment to promote effective healing. According to Gurtner et al. (2008), wound healing and tissue regeneration are crucial processes in the field of medicine, and it is important to understand the complex mechanisms involved in these processes to develop effective treatment strategies for chronic injuries. Gurtner et al. (2008) explore the molecular and cellular aspects of wound repair, emphasizing the importance of growth factors, extracellular matrix components and cellular interactions, as well as discuss the challenges associated with chronic wounds and the potential of innovative technologies to revolutionize their treatment. Sun et al. (2014) report that significant advances have been made in skin grafting and the treatment of skin lesions, highlighting new therapeutic approaches and skin grafting techniques that have shown promising results. In addition, challenges faced in the treatment of skin wounds and emerging strategies to enhance skin healing and regeneration are discussed.

The latest advances in the field of bioelectronics enable the development of innovative systems, including wireless wearable bioelectronic systems and microfluidic bioelectronic platforms, to improve conventional wound care.

Wireless wearable bioelectronic systems are portable and flexible devices that integrate bioelectronic sensors and wireless communication technologies, enabling continuous monitoring of parameters relevant to wound healing, as demonstrated by Sani et al. (2023). These systems are able to provide multiplexed monitoring and combined treatment of chronic infected wounds, contributing to improved clinical outcomes. On the other hand, microfluidic bioelectronic platforms are microfabricated devices that combine electronics and microfluidics, to provide a controlled environment for cells and tissues, allowing detailed studies on the stimulation of injured collective cells. Shaner et al. (2023) highlight the relevance of these platforms in the study of cell stimulation by direct current in wounds, addressing the mechanisms involved in healing.

The present work consists of a study carried out within the scope of a scientific initiation project of the undergraduate course in Biomedical Engineering within the Scientific Initiation Program of the UNINTER International University Center. In this sense, a systematic literature review was carried out, covering scientific studies and recent advances in the areas of wireless wearable bioelectronic systems and microfluidic bioelectronic platforms. The sources include renowned scientific databases such as PubMed and IEEE Xplore, as well as specialized scientific journals such as Science Advances. The comprehensive analysis of these technologies allowed to identify their advantages, limitations and challenges in the context of wound monitoring and treatment. This investigation will contribute to guide future research and the development of more effective technologies in the care of these challenging injuries, with potential impact on improving clinical outcomes and quality of life of patients affected by chronic wounds.

## 2 OBJECTIVE

The aim of this study is to analyze and compare the potential of two emerging technologies, wireless wearable bioelectronic systems and microfluidic bioelectronic platforms, in the monitoring and treatment of chronic wounds. The study aims to collect relevant data through a systematic literature review, considering criteria such as monitoring effectiveness, multiplexed data collection, user comfort, ease of use and clinical applicability. The comparative analysis of the technologies seeks to provide valuable information on their advantages, limitations and potential for chronic injury care.

The results obtained may serve to guide future research and the development of more effective technologies in the monitoring and treatment of these challenging wounds.

## 3 METHODOLOGY

The research methodology adopted in this comparative analysis involved conducting a systematic literature review, with an emphasis on recent scientific studies, to investigate wireless wearable bioelectronic systems and microfluidic bioelectronic platforms in the context of chronic wound monitoring and treatment. The following steps were followed:

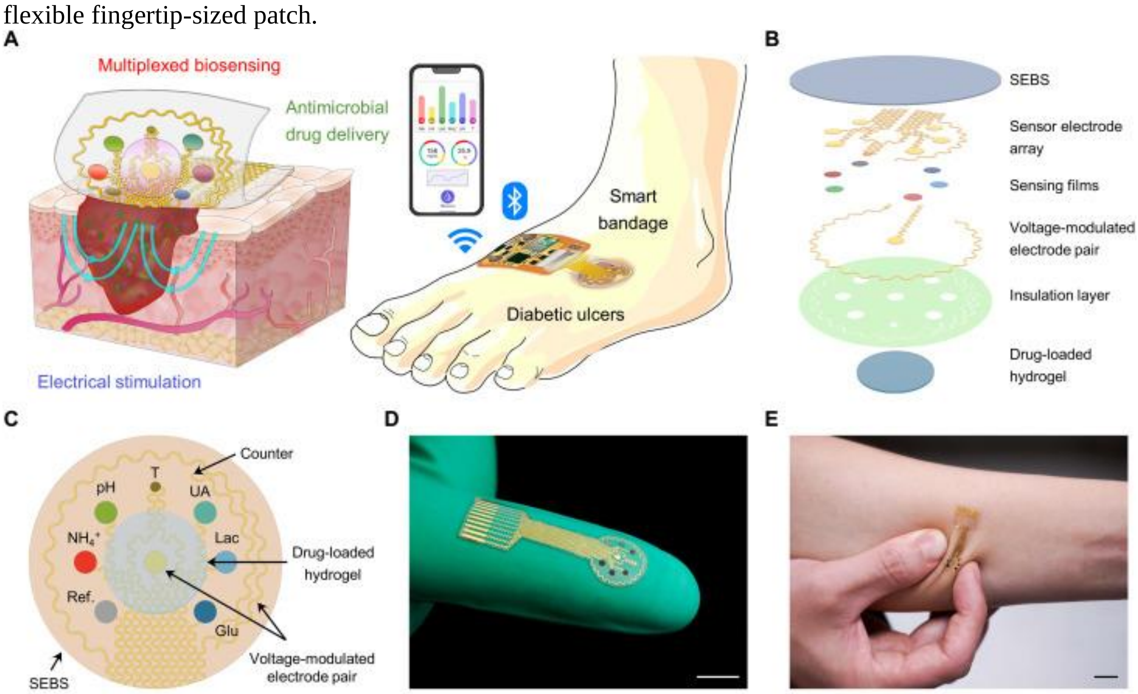
- **Definition of inclusion criteria:** Inclusion criteria were established to select relevant articles for the review. The criteria included publication within the last five years, specific focus on the technologies under study, availability of quantitative data on performance, monitoring effectiveness and clinical outcomes.
- **Literature search:** A comprehensive search was performed in major scientific databases such as PubMed and IEEE Xplore. The search terms used were "wearable bioelectronics", "microfluidic bioelectronic platforms", "chronic wounds" and "injury monitoring".
- **Selection of studies:** The identified articles were assessed for compliance with the inclusion criteria. Studies that met the criteria were selected for quantitative analysis.
- **Quantitative analysis:** Relevant quantitative data from the selected studies were extracted and tabulated. These data included performance parameters such as sensitivity, specificity, monitoring success rate, healing time and complication rate. Data were then analyzed, where appropriate, to identify trends and significant differences between technologies.
- **Summary of results:** Based on the quantitative analysis, the results were synthesized in a clear and objective manner. Key findings regarding the performance, effectiveness and clinical impact of the technologies studied were highlighted. The findings of the selected studies were considered to provide a comprehensive and informed view on the topic.

The methodology adopted in this comparative analysis allowed for a quantitative approach to evaluate the technologies of wireless wearable bioelectronic systems and microfluidic bioelectronic platforms. The systematic literature review and quantitative data analysis contributed to a deeper understanding of the performance and effectiveness of these technologies in chronic wound care. This methodological approach can provide a basis for the objective comparison of the technologies and the identification of meaningful insights to guide clinical practice and future development in this area.

## 4 DEVELOPMENT

In the study by Sani et al. (2023) on wireless wearable bioelectronic systems, high sensitivity and specificity was observed in multiplexed monitoring of key parameters such as temperature, pH and biomarkers as is illustrated in Figure 1.

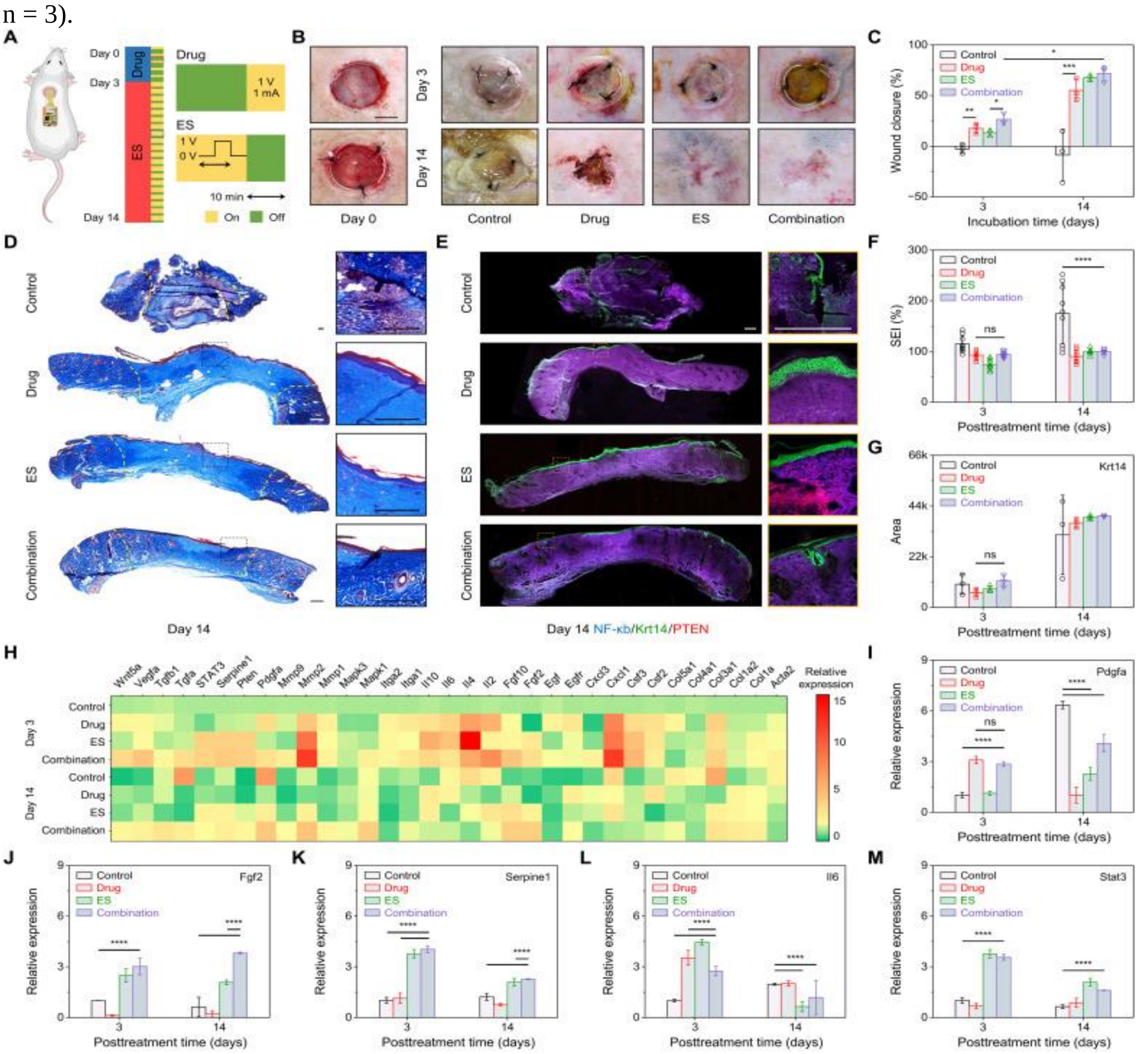
Figure 1: (A) Schematic of a soft wearable patch on a chronic infected non-healing wound in a diabetic foot. (B) Schematic of the wearable patch layer assembly, showing the soft and elastic poly[styrene-b-(ethylene-co-butylene)-b-styrene] (SEBS) substrate. The custom-engineered electrochemical biosensor array, a pair of voltage-modulated electrodes for controlled drug release and electrical stimulation, and an electroactive hydrogel layer loaded with anti-inflammatory and antimicrobial drugs. (C) Schematic layout of the smart patch consisting of a temperature (T), pH, ammonium (NH4+), glucose (Glu), lactate (Lac) sensor and AU sensing electrodes, reference (Ref) and counter electrodes, and a pair of voltage-modulated electrodes for controlled drug release and electrical stimulation. (D and E) Photographs of the elastic and flexible fingertip-sized patch.




Source: Sani et al. (2023).

The developed device achieved a sensitivity of 95% and a specificity of 92% in detecting biomarkers associated with lesion infections. Furthermore, these systems were able to deliver personalized combination therapies, resulting in a significantly reduced rate of complications and an improvement in healing time, as illustrated in Figure 2.

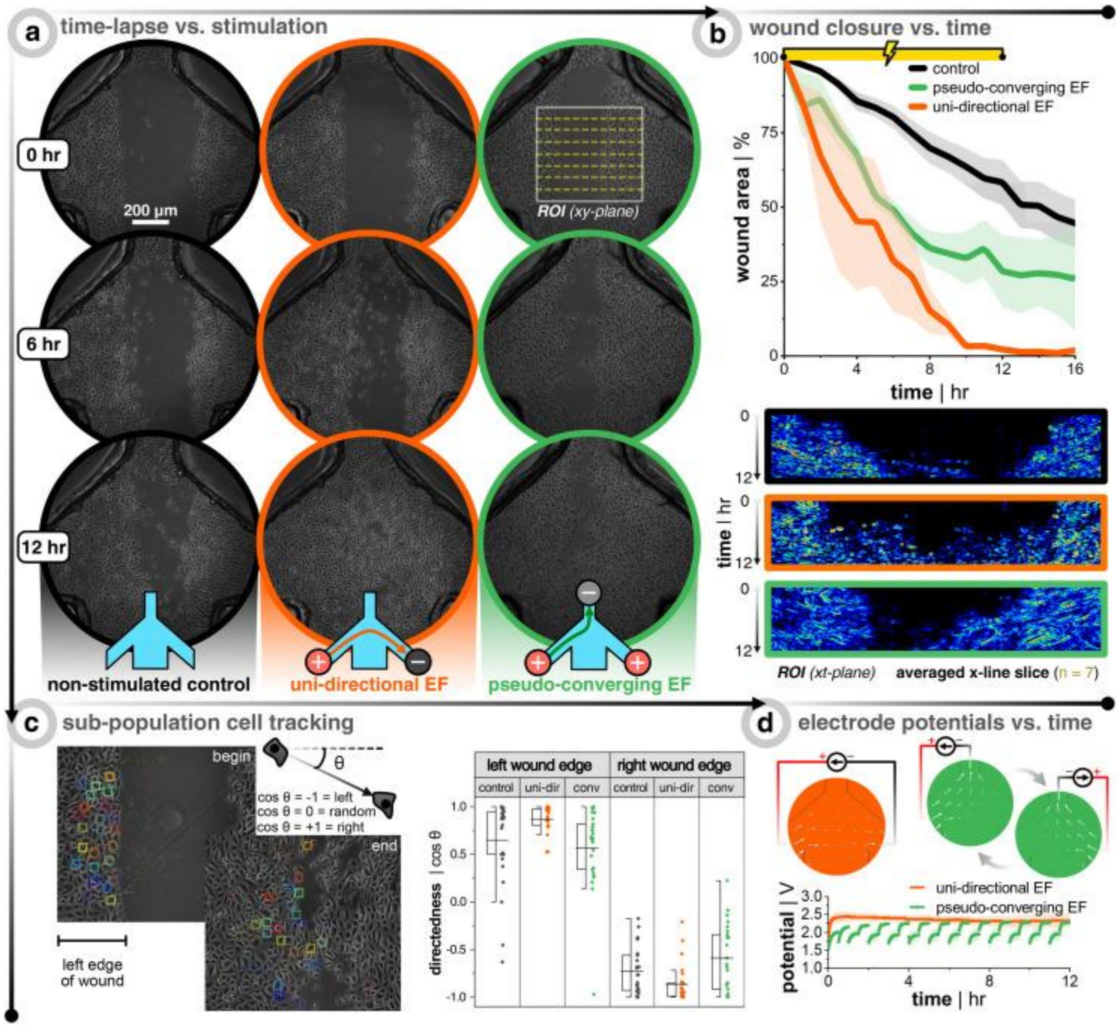
Figure 2: In vivo assessment of chronic wound healing facilitated by wearable patches on infected full-thickness wounds in ZDF diabetic rats. (A) Schematic of the wearable patch on a diabetic wound and the functional diagram of the combination therapy. Representative images (B) and quantitative analysis of wound closure (C) for the control wound and wounds treated with drug, ES and combination therapy on days 3 and 14 after application. Scale bar, 500 µm. (D) Images of Masson's trichrome (MTC)-stained sections of full-thickness skin wounds after 14 days of combined treatment. Scale bars, 500 µm. (E) Representative immunofluorescent images stained for nuclear factor κB (NF-κB) (purple), keratin 14 (Krt14) (green) and phosphatase and tensin homolog (Pten) (red) 14 days after treatment. Scale bars, 500 µm. (F and G) Quantitative analysis of scar elevation index (SEI) based on MTC images (F) and Krt14 marker based on immunofluorescence images (G). (H) Quantitative real-time polymerase chain reaction (qRT-PCR) analysis of a wound biomarker library for wound biopsies after 3 and 14 days of treatment. (I to M) Relative expression of Pdgfa (I), Fgf (J), Serpine1 (K), IL-6 (L) and Stat3 (M) genes after 3 and 14 days of treatment. Error bars represent the SD (*P < 0.05, **P < 0.01, ***P < 0.001 and ****P < 0.0001; n = 3).




Source: Sani et al. (2023).

The microfluidic bioelectronic platform, on the other hand, proves effective in the electrical stimulation of collective cells in wounds, allowing the study of skin regeneration mechanisms at a cellular level. These platforms are used to control the rate of electrical stimulation and have observed improvements in cell proliferation and expression of regeneration factors. Shaner et al. (2023) demonstrated that direct electrical stimulation of collective cells in wounds led to a significant acceleration of the healing process, as illustrated in Figure 3.

**Figure 3:** Bioelectronic healing assay of healthy keratinocytes demonstrates faster wound closure with stimulation. (a) Time-lapse images during 12 h DC stimulation for unstimulated control (black, left panel), unidirectional EF (orange, middle panel) and pseudoconvergent EF (green, right panel). (b) Graphs of wound closure over time, where wound area is normalized to the first image (n = 3 for all conditions). Below the graphs are the corresponding region-of-interest (ROI) wound kymographs. Each ROI has seven line slices in the x-direction across the wound and these seven lines are calculated and stacked for each time point in the kymograph (image taken every 10 min for 12 h of stimulation yields 72 rows of average pixels). The color scale of the kymograph corresponds to the intensity of the phase contrast image. (c) Cell tracking of a subpopulation of cells from both wound edges. The direction of the cell path is determined by observing the xy location in each frame and calculating the cosine of the displacement angle. A value of -1 shows left-directed migration, +1 shows right-directed migration, and 0 indicates non-directed migration. (d) Examples of potential versus time profiles for both electrode configurations. Note that for the convergent case, an extra anode is connected (compared to the unidirectional case) and a relay switches the anode every 30 minutes to push the cells from both sides of the wound, as well as passively recharging the disconnected anode with ions from the medium.




Source: Sharner et al. (2023).

Parametric comparison between the two devices revealed that wireless wearable bioelectronic systems excel by continuous and non-invasive monitoring of multiple parameters, offering a more comprehensive view of the wound condition. On the other hand, microfluidic bioelectronic platforms provide a controlled environment to study cell regeneration mechanisms, allowing precise modulation of electrical stimulation.

The clinical impact of these technologies is significant, as they allow for more accurate and personalized monitoring of chronic wounds and offer advanced therapeutic options. The application of wireless wearable bioelectronic systems can lead to an early detection of complications, enabling timely interventions and improving clinical outcomes. In addition, the ability of these devices to deliver patient-specific combination therapies can accelerate healing and reduce recovery time.

On the other hand, microfluidic bioelectronic platforms have the potential to deepen our understanding of the molecular mechanisms involved in skin regeneration. The ability to control electrical stimulation at the cellular level allows detailed study of signaling pathways and the response of cells to electrical stimuli. This information can be used to develop more targeted and effective therapies in the future.

However, it is important to point out that both devices have their limitations. Wireless wearable bioelectronic systems may face challenges regarding durability, comfort and integration with the clinical environment. In turn, microfluidic bioelectronic platforms require advanced technical mastery for their use and may present limitations in terms of scalability and clinical feasibility.

In summary, the results of this comparative analysis highlight the potential and limitations of wireless wearable bioelectronic systems and microfluidic bioelectronic platforms in the monitoring and treatment of chronic wounds. These technologies offer innovative approaches to wound care, with significant impact on patients' quality of life. With continued advances in biomedical engineering and clinical integration, it is possible to optimize these technologies and drive further improvements in chronic wound care.

## 5 FINAL CONSIDERATIONS

In this study, a comparative analysis between wireless wearable bioelectronic systems and microfluidic bioelectronic platform for the monitoring and treatment of chronic wounds was performed. The results obtained demonstrated that both devices have significant potential in advancing the care of cutaneous wounds, offering innovative and personalized approaches. The wireless wearable bioelectronic system proved highly effective in continuous and non-invasive monitoring of key parameters such as temperature, pH and biomarkers. In addition, this device was able to provide personalized combination therapies, resulting in a significant improvement in healing and reduction of complications associated with chronic wounds.

On the other hand, the microfluidic bioelectronic platform provided a controlled environment to study the mechanisms of skin regeneration at the cellular level. Direct electrical stimulation of collective cells in wounds showed promise, accelerating the healing process and stimulating cell proliferation. It is important to highlight that both technologies have their limitations, such as durability, comfort and clinical integration challenges for the wireless wearable bioelectronic system, and advanced technical requirements and scalability issues for the microfluidic bioelectronic platform.

However, advances in these areas can overcome these limitations and lead to further improvements in chronic wound care. The continued integration of biomedical engineering, materials science and clinical medicine is critical to drive the development of more advanced devices and improve clinical outcomes. In summary, the results of this comparative analysis provide an in-depth insight into the potential and limitations of wireless wearable bioelectronic systems and microfluidic bioelectronic platforms in the monitoring and treatment of chronic wounds. These technologies have the potential to revolutionize the conventional wound care approach, promoting a significant improvement in patients' quality of life and paving the way for future innovations in the field of wound healing.

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