Advances in Wound Repair Technologies: From Surgical Interventions to Regenerative Therapies

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Abstract. Wound repair is a critical component of trauma management, profoundly influencing patient recovery, functional restoration, and aesthetic outcomes. Recent advancements in biomedical engineering, material science, and regenerative medicine have significantly advanced wound care, offering novel therapeutic strategies to address both acute and chronic wounds. This review systematically examines the structural and functional aspects of skin, the molecular and cellular mechanisms underpinning wound healing, and the latest innovations in surgical and non-surgical interventions. We highlight cutting-edge approaches, including precision debridement techniques, engineered skin substitutes, bioactive dressings, stem cell-based therapies, and bioelectric modulation. By integrating evidence from preclinical and clinical studies, this article provides a comprehensive framework to guide clinical decision-making and inspire future research in optimizing wound repair outcomes.

Keywords: wound repair, surgery, dressings, stem cells, electrical stimulation, growth factors

1 Introduction

In recent years, the growing prevalence of chronic diseases like diabetes, coupled with the aging of the population, has brought about a substantial increase in the incidence of chronic wounds. These wounds present significant clinical challenges owing to their prolonged healing period, high recurrence rate, and the potential to trigger severe complications. Furthermore, the emergence of cutting-edge technologies such as bioengineering and precision medicine has unlocked novel approaches for wound treatment. In this context, gaining an understanding of the latest advancements in wound repair technology is of vital importance for enhancing patient outcomes. The skin, being the largest organ in the human body, assumes multiple crucial roles. It serves as a robust barrier against the invasion of external microorganisms and facilitates the excretion of metabolic wastes. It also plays a key part in preventing excessive water evaporation from the body and regulating body temperature. Additionally, the skin is an integral component of the immune system, housing various immune cells that contribute to the body's defense mechanism [1]. A wound refers to a defect in the skin and soft tissues caused by either external injurious factors, such as mechanical trauma, burns, and

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chemical corrosion, or internal disease factors, including vascular disorders and autoimmune diseases. Once a wound is formed, the natural protective barrier constituted by the skin is disrupted. This disruption leaves human tissues vulnerable to invasion by bacteria, fungi, and other microorganisms, which can result in more severe infections and further damage to the surrounding tissues [2]. Besides, wounds can lead to the exposure and necrosis of deep tissues, as well as the loss of body fluids and essential nutrients [3]. Large and chronic wounds, in particular, can cause a severe depletion of the body's reserves, affecting the overall physiological functions and even posing a threat to life in severe cases. Wound repair is an intricate and dynamic process that involves the synergistic interplay of multiple biological mechanisms, including inflammation, cell proliferation, tissue remodeling, and the coordinated action of various clinical techniques [4]. In recent years, remarkable progress has been achieved in wound repair technology, offering a wider range of treatment options and better prognosis for patients with wounds. This article will focus on the advancements in wound repair technology, encompassing surgical treatment methods that have been refined with minimally invasive techniques, new types of dressings with enhanced moisture retention and antibacterial properties, electrical stimulation therapy that promotes cell activity and blood circulation, stem cell therapy that leverages the regenerative potential of stem cells, as well as other emerging therapeutic approaches.

2 Skin Structure

As shown in Figure 1, the skin is composed of epidermis, dermis, and subcutaneous tissue. The epidermis belongs to the stratified squamous epithelium histologically, mainly composed of keratinocytes, melanocytes, Langerhans cells, and Merkel cells. The epidermis and dermis are connected by a basement membrane band. The dermis is derived from the mesoderm and can be divided into the papillary layer and the reticular layer from shallow to deep, but there is no clear boundary between the two layers. The dermis belongs to irregular dense connective tissue histologically, composed of fibers, matrix, and cellular components, with fibers being the main component and a small amount of matrix and cellular components between fibers. Subcutaneous tissue is located beneath the dermis and is connected to tissues such as the muscle membrane. It is made up of fat lobules, also referred to as the subcutaneous fat layer, and loose connective tissue. Blood vessels, lymphatic vessels, nerves, sweat glands, and apocrine sweat glands are all found in subcutaneous tissue.

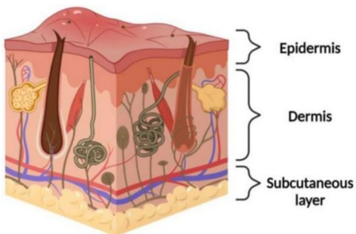

Fig. 1. Structure of the skin [5].

3 Wound Healing Mechanisms

The wound healing process is shown in Figure 2. Different levels of tissue necrosis and bleeding from vascular rupture are present in the wound region in the early stages. An inflammatory reaction takes place within a few hours, causing localized redness and swelling through congestion, serous exudation, and white blood cell migration. Neutrophils make up the majority of the early white blood cell invasion, which changes to macrophages after three days. Blood and wound exudate include fibrinogen, which rapidly coagulates to create clots. Some clots dry out on the surface to form scabs, which shield the wound. The wound rapidly shrinks after two to three days as the entire layer of skin and subcutaneous tissue at the perimeter shifts toward the center. Granulation tissue begins to form from the wound's edges and bottom during the third day. Collagen fibers are produced by fibroblasts during the fifth and sixth day, and they become extremely active the next week before progressively slowing down. Since healthy granulation tissue supplies the nutrients and growth factors required for epithelial regeneration, it is essential for epidermal regeneration. Epithelial regeneration will be delayed if granulation tissue is unable to fill the wound and form scars for an extended period of time. In other cases, excessive granulation tissue growth caused by stimuli like infections and foreign bodies that are higher than the skin surface can also prevent epidermal regeneration, necessitating its removal clinically. Large wounds are difficult for the regenerated epidermis to cover entirely, and skin grafting is frequently necessary.

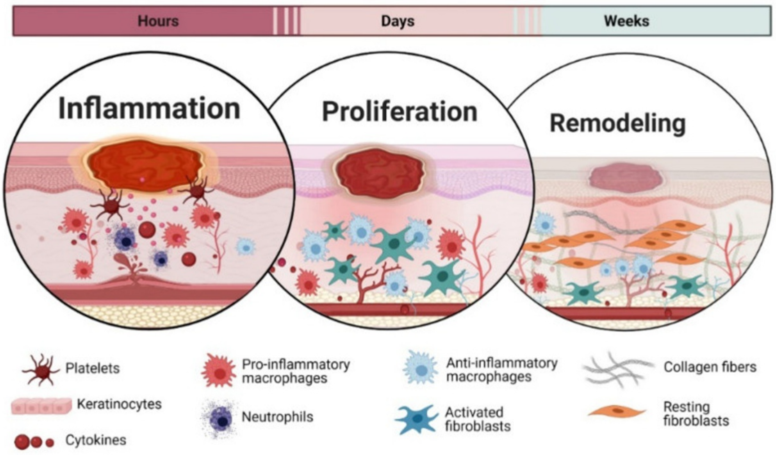

Fig. 2. The wound healing process [6].

4 Surgical Strategies

4.1 Debridement

The key steps of wound treatment in debridement surgery mainly include wound evaluation, wound cleaning, disinfection, removal of necrotic tissue and foreign objects, washing, and examination. Ultrasonic debridement utilizes the cavitation effect of ultrasound in washing jets: the micro-jets and high pressure generated by foam collapse remove bacteria from both the surface and deep layers of wounds. As one of the most clinically impactful debridement techniques for complex ulcers, it can replace traditional sharp debridement to treat more complex ulcer wounds [7].

4.2 Skin Graft Transplantation

Skin graft transplantation effectively closes wounds, reduces exudation, alleviates infection, and promotes wound healing. The specific application requires selecting the appropriate skin graft method based on the patient's condition and surgical needs. In cases of limited skin sources, Meek skin grafting meets the demand for large-area skin grafting, with a high skin graft survival rate, simple operation, and shortened surgical time. Due to these advantages, it is widely used in clinical practice and has high clinical impact [8].

4.3 Skin Flap Transplantation

Common surgical methods for skin flap transplantation include rotation, advancement, transposition, propeller, and vascular anastomosis free transplantation. The appropriate tissue flap and surgical technique should be selected based on factors such as the wound’s size, depth, and location to achieve the best repair effect. The perforator flap technique is flexibly designed, ensuring good appearance and function of the recipient area while minimizing damage to the donor area [9]. It is thus widely used for whole-body wound repair, though its application depends on the surgeon’s technical proficiency, limiting its widespread adoption in primary care settings.

4.4 Skin Soft Tissue Expansion Surgery

Skin soft tissue expansion surgery involves inserting a skin soft tissue expander under normal skin soft tissue. By regularly injecting sterile liquids (e.g., physiological saline) into the expander, its capacity is gradually increased, generating sustained tension stimulation on the surrounding skin soft tissue [10]. Based on the skin’s biomechanical properties, the stressed skin produces new tissue through fiber proliferation and rearrangement. As the expander’s capacity expands, the skin area in the traction zone increases, and this newly formed skin soft tissue can be used to repair tissue defects. This technique is particularly effective for repairing large defects in cosmetically sensitive areas (e.g., the face), but it requires multiple surgical sessions and a long treatment cycle, which may reduce patient compliance.

5 Negative Pressure Wound Repair (NPWT)

NPWT is a well-established clinical technique with significant impact on burn and flap transplantation wounds: it can seal burn wounds without skin grafting, remove secretions and necrotic tissue from wounds and cavities, prevent wound infection, promote local blood circulation, and reduce edema. Moreover, the combined application of NPWT and skin flap transplantation enhances therapeutic effects and significantly increases the graft survival rate [11]. However, NPWT equipment is relatively expensive, and its long-term use may increase the economic burden on patients, especially in low- and middle-income regions where accessibility is limited.

6 Dressing

Wound dressings are diverse and cater to different wound types. Traditional dressings (e.g., gauze, cotton cloth, stretch cloth) absorb wound exudate, isolate bacteria, and keep wounds dry. Although they can cover wounds, they have limited exudate absorption capacity, easily adhere to wounds, and may cause secondary damage during dressing changes [12]. In recent years, new wound dressings with different ingredients and advantages have addressed these shortcomings.

6.1 Hydrogel Dressing

Hydrogel is a water-soluble, hydrophilic polymer material with chemical tunability, favorable physical and biological properties, and a three-dimensional cross-linked network that absorbs and retains large amounts of water. As a functional wound dressing, hydrogel is one of the most clinically adopted new dressings: compared with traditional dressings, it maintains wound moisture, continuously absorbs exudate, and can be degraded in a timely manner (when prepared from chitosan or polypeptides), avoiding secondary injury during dressing replacement [13]. More importantly, structural design and functional integration can enhance its performance, making it critical for wound healing. However, hydrogels have low mechanical strength and are not suitable for wounds with excessive exudate or high tension.

6.2 Sponge Dressing

Sponge dressings are fabricated from freeze-dried solutions or gels, with an interconnected porous structure (pore size: 50 μm–1 mm). They rapidly absorb blood, expand, and apply pressure to wounds for rapid hemostasis; they can also carry bioactive substances (e.g., anti-inflammatory, antibacterial, or angiogenic factors). Common materials include natural polymers such as alginate, chitosan, and gelatin. Diabetic foot ulcer (DFU) wounds produce excessive exudate, which may cause immersion and infection—traditional dressings have insufficient water absorption and require frequent replacement [14]. Owing to their high porosity, strong water absorption, and breathability, sponge dressings are widely used in DFU treatment, though they are still in the early stages of clinical popularization due to higher costs than traditional dressings.

6.3 Foam Dressing

Foam dressings are generally made of polymer materials (mostly polyurethane) via a foaming process, and most have a three-layer structure (adhesive layer, foam layer, waterproof layer) [15]. The foam layer's three-dimensional structure and pores provide excellent breathability, exudate absorption, and water retention. Additionally, these dressings are soft and have shape recovery, alleviating local pressure to a certain extent. As a commonly used clinical dressing for moderate-to-high exudate wounds, foam dressings still have drawbacks: they need frequent replacement, easily adhere to wound surfaces (causing secondary damage), and are not suitable for low-exudate wounds.

6.4 Microneedle Patch

A new type of dressing incorporating microneedle technology can overcome biological barriers, penetrate biofilms, and enhance the local concentration and bioavailability of active substances [16]. Microneedle systems can be categorized into solid, coated, hollow, soluble, and hydrogel types: solid microneedles improve drug utilization by creating microchannels in the wound bed, though they may cause uneven local drug distribution; coated microneedles feature active substances adhered to the needle tips, and while this design limits drug loading capacity, it enhances efficiency through increased surface roughness; hollow microneedles enable continuous delivery of liquid formulations and can promote angiogenesis, but their poor mechanical strength poses a risk of needle fracture; soluble microneedles, typically fabricated from polymers like hyaluronic acid, gradually dissolve to release drugs, reducing inflammation and promoting angiogenesis to accelerate wound healing. Although microneedle-based systems have demonstrated advantages in painless, minimally invasive transdermal drug delivery and diabetic foot ulcer (DFU) treatment—making them closer to clinical translation—their efficacy on chronic wounds with excessive exudate remains limited, and further research is needed to fully evaluate their safety and therapeutic potential in such contexts.

7 Electrical Stimulation

As shown in Figure 3, wound formation disrupts the epithelial barrier, reducing the electric potential at the injury site compared to intact regions farther away; this potential difference generates a current flow toward the wound, creating a transverse electric field that points inward to the wound center. The endogenous electric field persists for hours to days, and within a 500 μm to 1 mm radius of the wound edge, electrical signals orchestrate cellular responses until re-epithelialization is complete, after which the signals cease—these bioelectric cues are among the earliest signals guiding epithelial cell migration toward the wound [17]. The mechanisms by which electrical stimulation promotes repair involve three key processes: first, it accelerates cell migration and proliferation, particularly enhancing epidermal stem cell potency, directional migration, and multilineage differentiation, while also boosting fibroblast and keratinocyte activity to hasten wound closure; second, it upregulates collagen synthesis while suppressing inflammation, providing a structural scaffold for tissue regeneration and reducing healing time; third, it facilitates nerve regeneration by promoting axonal growth, neurotransmitter regulation, and functional reinnervation, enabling full sensory and motor recovery. As a mature clinical adjuvant therapy for chronic wounds (e.g., DFUs), electrical stimulation plays a critical role in efficient wound healing, though its application is restricted by the need for specialized equipment and patient compliance with regular treatment sessions.

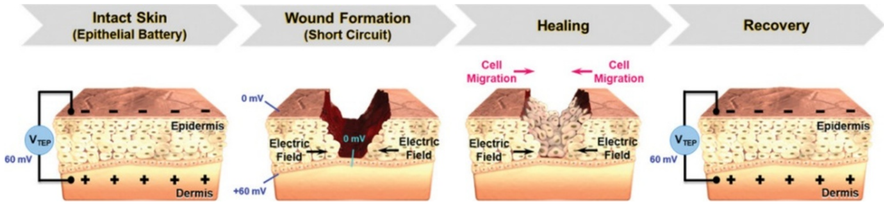

Fig. 3. The electric field at wound site [18].

8 Stem Cells

Stem cells are a group of cells capable of self-renewal and multipotent differentiation, allowing them to develop into various functional cell types under specific conditions. Mesenchymal stem cells (MSCs), a key subset of pluripotent stem cells, can be categorized based on their tissue origin, including bone marrow-derived MSCs, umbilical cord blood-derived MSCs, adipose-derived MSCs, and dermal MSCs. These cells play a vital role in wound repair by directly proliferating and differentiating into diverse cell types, thereby addressing the varying demands of different wound stages [19]. Additionally, MSCs offer a potential solution to the lack of skin appendages in tissue-engineered skin. Through direct cell-to-cell contact and the secretion of cytokines such as transforming growth factor-β (TGF-β), hepatocyte growth factor (HGF), and interleukins, MSCs modulate immune responses by suppressing the activation, proliferation, and differentiation of immune cells. This mechanism helps mitigate excessive inflammation, promotes angiogenesis and fibroblast proliferation, and enhances host fibroblast migration to the wound site—ultimately accelerating tissue regeneration. Notably, MSCs lack specific surface markers, resulting in low immunogenicity and reduced risk of rejection in allogeneic transplantation. As stem cell research advances, further clinical studies are expected to validate the safety and efficacy of MSC-based therapies in wound healing.

9 Growth Factor

Growth factors are closely related to repair cells and play a key role in wound repair. The growth factors mainly involved in the wound healing process include platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor-1 (IGF-I), etc. These growth factors play a major role in promoting the division and proliferation of various tissue cell types, synthesis and deposition of the extracellular matrix, formation of fibrous tissue and granulation tissue, as well as enhancing collagen synthesis capacity and regulating processes such as epithelial regeneration, interstitial proliferation, and neovascularization following trauma [20].

10 Conclusion

Wound repair is a continuous and complex process; the key is to address the treatment needs of different stages by considering individual wound characteristics and patient conditions, while developing comprehensive and personalized repair plans. The emergence of new technologies and materials—such as advanced dressings, stem cell therapies, electrical stimulation, and growth factor applications—has introduced innovative approaches to wound treatment. However, these advancements still face practical challenges: high costs limit the accessibility of technologies like NPWT and stem cell therapy in low-resource settings; regulatory barriers (e.g., standardized protocols for MSCs) delay the translation of preclinical discoveries to clinical practice; and technical requirements (e.g., surgeon proficiency for perforator flaps) restrict the adoption of certain techniques. It is anticipated that as the understanding of wound healing mechanisms deepens, and with ongoing efforts to address cost, accessibility, and regulatory issues, an increasing number of therapeutic modalities will emerge—offering more effective, equitable solutions for wound management.

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