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REVIEW

Exploring Thermal Dynamics in Wound Healing: The Impact of Temperature and Microenvironment

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Abstract: Exploring the critical role of thermal dynamics in wound healing, this manuscript navigates through the complex biological responses initiated upon wound infliction and how temperature variations influence the healing trajectory. Integrating biothermal physics, clinical medicine, and biomedical engineering, it highlights the significance of thermal management in wound care, emphasizing the wound microenvironment's division into internal and external domains and their collaborative impact on tissue repair. Innovations in real-time wound temperature monitoring, especially through intelligent wireless sensor dressings, are spotlighted as transformative, enabling precise wound condition management. The text underscores the necessity for further research to elucidate thermal regulation's molecular and cellular mechanisms on healing processes. It advocates for standardized protocols for localized heating treatments, integrating them into personalized wound care strategies to enhance therapeutic outcomes, improve patient well-being, and achieve cost-effective healthcare practices. This work presents a forward-looking perspective on refining wound management through sophisticated, evidence-based interventions, emphasizing the interplay between thermal dynamics and wound healing.
Keywords: wound healing, thermal dynamics, wound microenvironment, intelligent dressings, localized heating treatment

Introduction

The disruption of epidermal integrity instigates a multifaceted biological response within the dermal stratum. This response encompasses immune activation,[1] vasodilation mediated by pro-inflammatory cytokines,[2] and an intensification of metabolic processes within the afflicted tissues.[3] Collectively, these phenomena modify the thermal profiles at both the lesion and its adjacent epidermal areas.

A seminal study conducted in 2015 elucidated the complex architecture of the wound microenvironment by dichotomizing it into external and internal components.[4] The external wound microenvironment is defined as the area immediately adjacent to the lesion's surface, interfacing directly with the ambient environment. In contrast, the internal wound microenvironment comprises the subepidermal layers, rich in cellular constituents and the extracellular matrix (ECM).[5] This bifurcation is crucial for understanding the dynamic interactions that dictate the course of wound healing.[6] Clinical interventions are strategically designed to modulate these microenvironments to optimize conditions conducive to reparative processes. Pertinent external variables affecting both acute and chronic wound contexts include thermal fluctuations,[7] mechanical pressure,[8] moisture levels,[9] and microbial colonization.[10] An intricate comprehension of both the synergistic and antagonistic interactions among these factors, as well as their aggregate impact on the healing trajectory, is paramount for the advancement of therapeutic approaches.

Within the discourse of wound management, the imperative of localized surveillance and modulation of the external wound environment is unequivocal. Current clinical guidelines advocate for the manipulation of pressure, humidity, and microbial load as fundamental elements of localized intervention protocols. Nonetheless, the regulation of wound

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temperature has not been adequately integrated into standard therapeutic regimens.[11,12] The nuanced interplay between thermal conditions and reparative processes in wounds represents a relatively unexplored field, necessitating enhanced empirical examination. This study endeavors to provide a comprehensive exploration and critical evaluation of the correlation between thermal parameters within the external wound microenvironment and the holistic process of wound healing, thereby contributing to the expansion of both theoretical and practical paradigms in clinical wound management.

Comprehensive Modeling of Human Biothermal Transfer Dynamics

The constitution of human tissues, encompassing a tripartite composition of solids, liquids, and gases, demonstrates a labyrinthine array of thermal transfer phenomena that diverge markedly from conventional mechanisms.[13] Embedded within the biological milieu, these tissues engage in metabolic activities that are distinct in nature from rudimentary chemical reactions, anchored by an intrinsically sophisticated apparatus for thermoregulation.[14] The spectrum of biothermal transfer within the human organism is delineated through a confluence of conductive, convective, and radiative modalities, rendering the narrative of thermal energy conveyance notably complex.[15] Scholarly endeavors have been directed towards the elucidation of these complexities, yielding theoretical constructs and algebraic expressions that encapsulate the quintessential principles of biothermal transfer in biological matrices. This intellectual journey has led to the creation of analytical models that allow for a detailed examination of thermal phenomena.

A watershed moment in this scholarly trajectory was realized in 1948 with the conceptualization of the human arm as a cylindrical model, leading to the articulation of the seminal bioheat transfer equation, colloquially known as the "Pennes equation".[16] This theoretical innovation provided a substantive framework for the elucidation of thermal distribution patterns within biological tissues. Progressing beyond this foundational milestone, research further meticulously charted the intricacies of the human body's thermoregulatory functions, deploying mathematical equations to quantitatively delineate this mechanism.[17] The findings from this inquiry resonated with a high degree of fidelity to established physiological paradigms. Recent scholarly initiatives have introduced a cutting-edge model, meticulously tailored for the demographic contours of the Chinese populace.[18] This model is predicated on the objective of precisely prognosticating instantaneous average skin temperatures under the ambience of warm environmental conditions (26.0 ~ 33.8°C). This analytical tool extends its utility beyond mere temperature estimation to encompass the delineation of evaporative sweat regulation efficiency, the dynamics of skin blood flow, and the quantification of total heat dissipation ratios. Critically, it unveils the gender-specific thermal response disparities, augmenting the granularity of thermal physiological understanding.

In light of the criticality of temperature as an arbiter of physiological equilibrium, its quantification and interpretive analysis have ascended to a position of paramount importance within the diagnostic lexicon of medical science. The quest for precision in mapping and modeling the temperature landscapes across biological tissues has emerged as a vibrant focal point of inquiry within the interdisciplinary domains of biothermal transfer and biomedical engineering.[19,20] This pursuit is emblematic of a broader scientific commitment to harness computational innovations for the real-time simulation and intricate reconstruction of biotemperature fields, thereby advancing the frontiers of knowledge in biothermal phenomena and refining the precision of diagnostic methodologies.

Wound Temperature Measurement

Single-Point Thermometric Evaluation

The archetypical modalities for quantifying thermal variations predominantly rely on single-point detection mechanisms, incorporating instruments such as thermocouple thermometers,[21] infrared thermometers,[22] and infrared thermographic cameras (Figure 1).[23] In the landscape of empirical investigation, a preference is discernible towards non-contact measurement devices, attributed to their non-intrusive nature and the convenience they offer in operational deployment.[24] Nevertheless, a discernible fraction of investigative efforts integrates contact-based thermometric tools, including liquid crystal thermometry and thermocouple probes, delineating a methodological diversity.[25] The deployment of infrared thermometers, characterized by their portability, ease of manipulation, and economic viability, engenders a spectrum of viewpoints regarding their utility in elucidating the correlation between thermal dynamics at the wound site

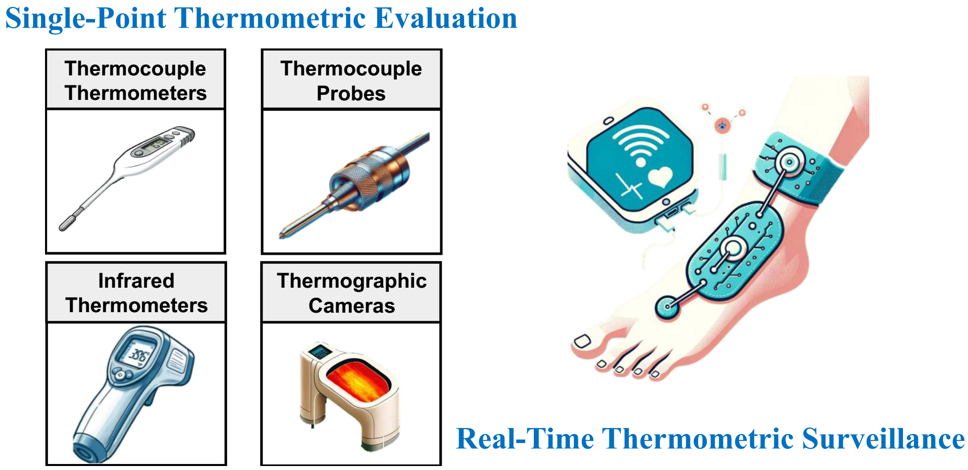

Figure 1 Overview of thermometric assessment tools. The left panel displays single-point measurement tools including thermocouple thermometers, probes, infrared thermometers, and thermographic cameras for diverse temperature assessments. The right panel introduces a real-time thermometric surveillance system with a smart wireless sensor dressing connected to digital platforms for continuous monitoring.

and the consequent healing trajectory.[26] Detractors highlight the susceptibility of infrared thermometric readings to perturbations from a multitude of exogenous and endogenous factors, casting aspersions on their reliability within the domain of wound diagnostic research.[26] In contrast, proponents assert that, under a regime of controlled environmental parameters, infrared thermometry emerges as a credible modality for the assessment of wound temperature, thereby facilitating an analytical lens into the state of wound convalescence.[27]

The fidelity of single-point thermal monitoring methodologies is contingent upon a complex interplay of factors, encompassing ambient thermal conditions, the systemic temperature of the patient, circulatory dynamics, and the presence of exudative fluids, which collectively precipitate variances in the resultant measurements.[28,29] The paucity of a globally endorsed standard for executing these measurements amplifies the challenges associated with the universal adoption and implementation of single-point wound temperature monitoring within both clinical and investigative contexts. This scenario underscores an imperative for methodological refinement and the formulation of standardized procedural frameworks to bolster the reliability and generalizability of these techniques in the broader discourse of wound management and scholarly inquiry.

Pioneering Developments in Real-Time Thermometric Surveillance

Recent scholarly discourse and investigative endeavors have heralded the advent of advanced intelligent wireless sensor dressings.[30–32] These novel interventions represent a confluence of biocompatible materials and micro-engineered temperature sensors, epitomizing the fusion of biomedical engineering and sensor technology. Utilizing sophisticated mechanisms such as radio-frequency identification (RFID) systems or platinum-based sensors, these sensor-integrated dressings facilitate uninterrupted and meticulous monitoring of thermal variations at the wound site.[33,34] This innovation surmounts the limitations endemic to conventional single-point thermometric approaches, notably their diminished stability and pronounced vulnerability to a broad spectrum of environmental and physiological perturbations.

The utility of intelligent wireless sensor dressings extends beyond mere thermal measurement, enabling comprehensive real-time analysis of fluctuating parameters critical to the wound healing milieu.[35,36] This integrative monitoring capacity permits a detailed evaluation of the wound microenvironment's suitability for healing, embodying a proactive approach to wound management.[37] Moreover, these advanced dressings are endowed with the capability to wirelessly transmit the amassed data to contemporary digital devices, including smartphones and tablets, via Bluetooth technology (Figure 1).[38,39] This facilitates the prompt dissemination of vital health metrics to medical practitioners and integrates seamlessly with cloud-based infrastructures, ensuring the longitudinal conservation of wound-related data. Such integration heralds a significant leap forward in remote healthcare provision, aligning with the principles of personalized medicine. This digital convergence in wound care management underscores a paradigmatic shift towards customizing therapeutic interventions to meet the unique physiological and clinical profiles of individual patients, thereby enhancing the efficacy and precision of medical care.

The Relationship Between Wound Temperature Monitoring and Wound Healing Status

Temperature has been acknowledged as a critical factor influencing wound healing.[40] In the distinct stages following the formation of acute and chronic wounds, variations in wound temperature exhibit specific trends. These temperature changes are influenced by environmental conditions and local blood flow and can modulate vascular active molecules, facilitating vasoconstriction and dilation.

Acute Wounds

Surgical Wounds

Studies show that normal surgical wounds can exhibit localized temperature increases in the initial days post-operation, returning to baseline within two weeks.[41] Zheng et al analyzed the impact of preoperative warming on reducing the risk of surgical site infections (SSI), finding that using mixed warming methods before surgery significantly lowers the incidence of SSI, recommending their adoption in surgical protocols.[42] Another study also highlights that maintaining normothermia with active warming techniques to keep body temperature above 36°C during surgery is a crucial strategy among others to significantly reduce the risk of surgical site infections.[43]

Early-Stage Burn Wounds

Determining the temperature of burn wounds assists in diagnosing the depth of burns. Studies employing contact-type rapid-response thermocouple probes to measure wound temperature within 10 hours post-burn reveal that, compared to adjacent normal skin, elevated wound temperatures indicate shallower burn depth or shorter healing times.[44] Such thermometric methods achieve a 78% accuracy rate in assessing burn depth, surpassing the 60% accuracy of evaluations based on clinical experience. However, the correlation between wound temperature and injury depth is not evident in hands, faces, feet, or beyond 10 hours post-burn.[44] Other research indicates that the optimal timeframe for using infrared thermal imaging to diagnose burn wound depth is within 3 days post-injury, as the correlation between wound temperature and burn depth diminishes after this period.[45] Furthermore, Ganon et al validated the use of the Flir One Thermal Imager® for early burn wound assessment in pediatrics, demonstrating its ability to distinguish between superficial and deep burns by measuring skin temperature differences, thereby aiding in the early decision-making process for treatments such as skin grafting.[46] Carrière et al highlighted the validity of using infrared thermography with a new, more sensitive thermal imager for assessing burn wound healing potential, showing its effectiveness in discriminating between different healing time frames when compared to Laser Doppler Imaging, marking it as a promising tool for burn wound triage and evaluation.[47]

Chronic Wounds

In chronic wounds, a sudden increase in local temperature is a typical sign of infection and inflammation. Most chronic wounds, often occurring in the lower limbs, exhibit temperatures approximately 5°C lower than core body temperature due to compromised blood supply and oxygenation.[48]

Chronic Venous Leg Ulcers

Studies utilizing handheld thermometers to monitor the temperature of chronic venous leg ulcers show that infected wound sites exhibit skin temperatures more than 2°C higher than corresponding healthy skin on the opposite limb, indicating a strong correlation between elevated periwound skin temperature and infection.[48] The infrared thermography can identify distinct temperature patterns in the lower legs of patients with chronic venous diseases (CVD), showing potential for early detection and classification based on the severity of CVD, including the presence of florid ulcers.[49]

Diabetic Foot Ulcers

In clinical trials employing infrared thermometers to measure the temperature of diabetic foot ulcers and surrounding skin, results indicate that smaller temperature differences between the wound and intact skin on the opposite foot predict a positive wound status and a tendency towards healing, suggesting that wound temperature effectively reflects inflammatory changes and healing trends in diabetic foot ulcers.[50] These studies collectively reveal that wound temperatures can significantly rise during the initial stages of injury and in cases of abnormal healing, but tend to decrease back to normal as the healing process normalizes.[51] Research combining temperature measurement with image evaluation has shown diagnostic sensitivities >60% and specificities >79% for detecting wound infections, whereas temperature measurement alone has shown a diagnostic sensitivity of up to 90% but a specificity of <25%.[52] However, a systematic analysis of existing literature suggests a lack of sufficient evidence to recommend wound temperature as a predictive indicator for wound healing.[53] Another meta-analysis also revealed that daily foot temperature monitoring at six points can significantly reduce the incidence of foot ulcers in patients with diabetes by prompting increased preventive measures in response to temperature differences greater than 2.2°C between the left and right corresponding sites.[54] Future research, if it further clarifies and confirms the role of wound temperature variations in early diagnosis and predicting infections and healing outcomes, could establish wound temperature measurement as an effective non-invasive method for early assessment of wound status and prognosis.

Pressure Injury

Clinical research demonstrates that measuring wound temperature can accurately predict the anatomical locations of ulcers before the formation of pressure injuries, proving more accurate than the commonly used Braden scale for pressure injury risk assessment.[55,56] This technique can monitor healing progress and improve management and prevention of ulcers.[27] Another study indicates that, three weeks post-pressure injury formation, wound temperatures significantly exceed those of surrounding skin, suggesting the presence of infection or other healing-compromising factors.[57]

The Impact of Wound Temperature Treatment on Wound Healing

For both acute and chronic wounds, it is imperative to ameliorate systemic factors and provide an optimal wound microenvironment to facilitate timely and orderly healing and functional recovery. Beyond maintaining a moist micro-environment, alleviating hypothermic states and sustaining normothermic conditions within the wound vicinity can also expedite wound healing. During the healing process, the temperature of the wound exerts a significant influence on various repair-related effector cells. Studies have demonstrated that early-stage wound temperatures falling below core body temperature can hinder collagen deposition and reduce the presence of late-stage inflammatory cells and fibroblasts, thereby delaying the healing process.[58] Especially, 33°C represents a critical threshold temperature for the occurrence of various biological changes within the wound; temperatures below this threshold lead to decreased activity of neutrophils, fibroblasts, and keratinocytes.[59,60] Moreover, investigations revealed that during the replacement of dressings on acute traumatic wounds, the immediate post-removal average wound temperature is measured at 32.6°C, slightly below the minimum requisite of 33°C for cellular activity.[61] Prior to applying a new dressing, the average temperature drops to 29.9°C, indicating a persistently hypothermic state throughout the dressing change process.[62]

Observations suggest that elevating the temperature of pressure injury wounds to between 36–38°C significantly reduces wound area.[63] Thermal radiation dressings, as a therapeutic device, have been proven to increase capillary blood flow perfusion and blood oxygen partial pressure, thereby promoting the healing of pressure injuries.[64] Various modalities exist for heating treatment. A study utilizing thermal radiation dressings to heat both normal skin on human thighs and surgical wounds (set at 38°C for 2 hours of heating followed by 2 hours of rest, over a period of 7 days) maintained wound temperatures between 36.0–37.5°C.[65] This demonstrated that local heating can enhance microvascular blood flow and subcutaneous oxygen content in both normal and injured skin, potentially offering resistance to infection without increasing collagen deposition at the wound site. In addition, thermal radiation dressings (set at 38°C, three times a day for 1 hour) were used for the treatment of Stage I–II uninfected pressure injuries over 6 weeks or until healing showed that, compared to standard treatment with alginate dressings, this method significantly improved wound healing rates.[66] Subsequent research using heated dressing systems for intermittent heating of wounds for 5 hours (set at 38°C, heating for 3 hours followed by a 2-hour rest without the system) found that, compared to a control group using standard dressings, the proportion of CD3+ T lymphocytes in the wound increased after 24 and 48 hours of dressing use, while neutrophil and macrophage counts showed no significant difference.[67] This suggests lymphocyte infiltration into the local wound microenvironment, thereby enhancing the innate immune response within the wound healing milieu.

Conclusion

The healing of various acute and chronic wounds in clinical settings is influenced by numerous factors pertaining to the external microenvironment of the wound. Wound temperature, as a pivotal indicator of the wound's external micro-environment, has been identified in research as having potential for predicting infection and assessing healing outcomes, though further validation is necessary. Clarification of the interrelationship between wound temperature and wound healing could offer novel insights and foundational support for clinical treatment methodologies and the development of smart dressings.

By employing intelligent wireless sensor dressings, it is possible to observe comprehensively the variations in wound temperature within the external microenvironment, enabling real-time assessment of wound status. Furthermore, these smart dressings facilitate modulation and adjustment of the wound microenvironment, reduce the frequency of dressing changes, and promote wound healing. Significantly, this approach has the potential to alleviate patient discomfort and decrease hospitalization costs.

In addressing hypothermic wound states, localized heating treatments have been shown to enhance capillary blood flow perfusion and blood oxygen partial pressure, increase the activity and collagen deposition of neutrophils, fibroblasts, and keratinocytes, and elevate the proportion of lymphocytes at the wound site. This, in turn, strengthens the innate immune response within the wound healing microenvironment, thereby improving the wound condition and fostering repair. However, further research is necessary to elucidate the precise mechanisms by which localized heating modulates the proliferation and function of wound repair-related effector cells and to validate its efficacy in clinical intervention for wound infection. The optimal constant temperature required for the wound microenvironment and the duration of heating treatments remain to be established. Nonetheless, localized heating treatment represents an innovative approach for regulating the local wound microenvironment and the associated healing processes.

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Disclosure

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