EXPERIMENTAL INDUCTION OF DEEP DERMAL BURNS IN RATS: STRUCTURAL–FUNCTIONAL CHARACTERISTICS AND METHODOLOGICAL BASIS

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Abstract. Thermal trauma represents one of the most widely utilized and methodologically significant experimental models in pathological physiology for investigating mechanisms of wound repair, tissue regeneration, and hemostatic imbalance. The present study was designed to establish a rigorously standardized and highly reproducible model of deep third-degree dermal burns in laboratory rats, enabling comprehensive assessment of structural and functional transformations during the reparative process, as well as the evaluation of the effectiveness of local hemostatic preparations. A controlled contact burn was induced by applying a preheated metal probe to the depilated dorsal surface of anesthetized animals. Sequential morphological and histological examinations were performed on days 3, 7, 14, 21, 30, and 60 following injury. The obtained data confirmed the rapid onset of coagulative necrosis within the first 24 hours, accompanied by pronounced inflammatory cell infiltration and subsequent development of granulation tissue. The most intense fibroblast activity and collagen matrix deposition were observed between days 14 and 21, indicating the peak reparative phase. By day 60, the damaged area was predominantly substituted with mature fibrotic scar tissue, demonstrating partial re-epithelialization. The proposed experimental model ensures high reproducibility and is suitable for detailed investigation of morphofunctional responses in severe thermal injuries, as well as for testing therapeutic agents aimed at optimizing tissue regeneration.

Keywords: experimental burns, thermal injury, morphofunctional changes, rats, granulation tissue, fibrosis, wound healing.

Аннотация. Термическая травма является одной из наиболее широко применяемых и методологически значимых экспериментальных моделей в патологической физиологии для изучения механизмов репарации ран, регенерации тканей и нарушений гемостаза. Настоящее исследование было направлено на создание строго стандартизированной и высоковоспроизводимой модели глубоких дермальных ожогов III степени у лабораторных крыс, позволяющей комплексно оценивать структурно-функциональные изменения в процессе репарации, а также эффективность местных гемостатических препаратов. Контактный ожог вызывали путём приложения предварительно нагретого металлического зонда к

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депилированной дорсальной поверхности анестезированных животных. Последовательные морфологические и гистологические исследования проводились на 3, 7, 14, 21, 30 - 60 сутки после травмы. Полученные данные подтвердили быстрое развитие коагуляционного некроза в течение первых 24 часов, сопровождающееся выраженной инфильтрацией воспалительных клеток и последующим формированием грануляционной ткани. Наиболее интенсивная активность фибробластов и отложение коллагенового матрикса наблюдались в период с 14-го по 21-й день, что свидетельствует о пике репаративной фазы. К 60-му дню повреждённая область преимущественно замещалась зрелой фиброзной рубцовой тканью с признаками частичной реэпителизации. Предложенная экспериментальная модель обеспечивает высокую воспроизводимость и пригодна для детального изучения морфофункциональных реакций при тяжёлых термических повреждениях, а также для тестирования терапевтических средств, направленных на оптимизацию регенерации тканей.

Ключевые слова: экспериментальные ожоги, термическая травма, морфофункциональные изменения, крысы, грануляционная ткань, фиброз, заживление ран.

Annotatsiya. Termik shikastlanish patologik fiziologiyada yara bitishi mexanizmlarini, to‘qimalarning regeneratsiyasini va gemostaz buzilishlarini o‘rganishda keng qo‘llaniladigan hamda metodologik jihatdan muhim eksperimental modellaridan biridir. Mazkur tadqiqot laboratoriya kalamushlarida uchinchi darajali chuqur dermal kuyishlarning qat’iy standartlashtirilgan va yuqori darajada takrorlanuvchi modelini yaratishga qaratilgan bo‘lib, reparativ jarayon davomida yuz beradigan tuzilmaviy-funktsional o‘zgarishlarni kompleks baholash, shuningdek mahalliy gemostatik preparatlarning samaradorligini aniqlash imkonini beradi. Nazorat qilinadigan kontakt kuyishi oldindan qizdirilgan metall zondni narkoz ostidagi hayvonlarning junlari olinib tozalangan orqa (dorsal) yuzasiga qo‘llash orqali chaqirildi. Ketma-ket morfologik va gistologik tekshiruvlar jarohatdan keyingi 3, 7, 14, 21, 30 va 60-kunlarda amalga oshirildi. Olingan natijalar dastlabki 24 soat ichida koagulyatsion nekrozning tez rivojlanishini, kuchli yallig‘lanish hujayralari infiltratsiyasi va undan keyin granulyatsion to‘qima hosil bo‘lishi bilan kechishini tasdiqladi. Eng yuqori darajadagi fibroblast faolligi va kollagen matritsasining to‘planishi 14–21-kunlar oralig‘ida kuzatilib, bu reparativ fazaning eng yuqori cho‘qqisini ko‘rsatadi. 60-kunga kelib shikastlangan soha asosan yetilgan fibroz chandiq to‘qimasi bilan almashib, qisman qayta epitelizatsiya belgilari aniqlanadi. Taklif etilgan eksperimental model yuqori darajada takrorlanuvchanlikni ta’minlaydi va og‘ir termik shikastlanishlarda morfofunktsional javoblarni chuqur o‘rganish,

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shuningdek to‘qima regeneratsiyasini optimallashtirishga qaratilgan davolovchi vositalarni sinovdan o‘tkazish uchun mos hisoblanadi.

Kalit so‘zlar: eksperimental kuyishlar, termik shikastlanish, morfofunktsional o‘zgarishlar, kalamushlar, granulyatsion to‘qima, fibroz, yara bitishi.

Introduction

Thermal burns continue to represent a major clinical and experimental challenge due to the multidimensional nature of their pathogenesis, which encompasses extensive tissue necrosis, pronounced inflammatory reactions, microcirculatory disturbances, oxidative stress, and impaired reparative capacity. Experimental modeling of such injuries in laboratory animals is essential for a deeper understanding of the sequential cellular and molecular events underlying wound healing, scar formation, and hemostatic dysregulation. These models also play a pivotal role in the preclinical evaluation of innovative pharmacological compounds and local therapeutic agents aimed at accelerating regeneration and reducing post-burn complications.

Rats are among the most commonly used small laboratory animals for burn modeling because they demonstrate well-studied physiological and immunological responses, possess a suitable skin structure for histopathological examination, and provide consistency in experimental outcomes. The creation of a reproducible, controlled, and ethically sound model of thermal injury is necessary for accurate assessment of morphological, biochemical, and functional alterations occurring throughout the wound healing continuum.

The present study sought to establish a standardized model of deep third-degree skin burns in rats that ensures high reproducibility, minimizes the influence of confounding variables, and adheres to modern bioethical principles. The methodology enables precise control of burn area and depth through regulated thermal exposure, thereby reducing inter-individual variability and the risk of secondary infection. Sequential analysis of morphofunctional parameters at predetermined time points was conducted to characterize the dynamics of tissue damage, inflammation, granulation, and scar formation. The generated data confirm the suitability of the proposed model for further use in biomedical research, including preclinical testing of hemostatic materials, wound dressings, anti-inflammatory agents, and stimulators of tissue regeneration.

Aim. The aim of this study was to develop a reproducible and ethically justified experimental model of deep third-degree thermal skin burns in laboratory rats under controlled conditions. The model was designed to allow systematic evaluation of morphofunctional changes in skin and subcutaneous tissues during the wound-healing process, and to provide a reliable platform for assessing the effectiveness of local hemostatic and reparative agents.

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Materials and Methods

The study was conducted on 30 clinically healthy white outbred male rats weighing 180–220 g. All experimental procedures complied with institutional animal care and ethical standards.

Before burn induction, the animals were anesthetized with intraperitoneal sodium thiopental (40 mg/kg). The dorsal region was shaved and cleaned with 70% ethanol to ensure uniform skin exposure.

A brass metal probe (diameter 2 cm, weight 80 g) was preheated in water to 96–98°C and applied to the dorsal skin for 10 seconds under controlled pressure to produce a full-thickness (third-degree) burn covering approximately 10% of the total body surface area. The burned region was left open to the air without any immediate treatment to observe natural wound progression.

Animals were housed individually in sterile cages and observed daily. Standard feed and water were provided ad libitum. To prevent secondary infection, wound areas were treated with 0.05% chlorhexidine solution once daily.

Tissue samples were collected on days 3, 7, 14, 21, 30, and 60 post-burn. Macroscopic observations included wound color, exudation, and epithelialization. Histological examination was performed on paraffin-embedded sections stained with hematoxylin and eosin and Masson's trichrome.

Results

Macroscopic Findings

Table 1 summarizes the macroscopic dynamics of the burn wound healing process. The first 24 hours were characterized by the formation of a dense necrotic crust with clear demarcation from surrounding tissue. By day 7, inflammatory edema and purulent exudate were observed. Granulation tissue formation became prominent by day 14 and reached maximum development between days 14 and 21.

Table 1.

Macroscopic stages of burn wound healing in rats

Observation day	Macroscopic appearance	Healing phase
3	Necrotic crust formation, edema, hyperemia	Necrosis and inflammation
7	Beginning of demarcation, purulent exudate	Inflammatory phase
14	Active granulation tissue growth	Proliferative phase
21	Wound contraction, decreased exudate	Early remodeling
30	Granulation replaced by fibrous tissue	Remodeling and scar formation

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60	Mature scar, no active inflammation	Final epithelialization

Histological and Morphological Findings

On day 3, histological analysis revealed massive coagulative necrosis with inflammatory cell infiltration consisting of neutrophils and macrophages. Capillary thrombosis and local hemorrhages were frequent.

By day 14, granulation tissue showed intensive fibroblast proliferation and newly formed capillaries. Collagen deposition increased sharply during this period. Between days 21 and 30, fibroblasts differentiated into myofibroblasts, initiating scar contraction. By day 60, dense collagen bundles replaced granulation tissue, forming mature fibrous scars with partial re-epithelialization.

Table 2.

Histological dynamics of tissue repair after deep thermal burn

Day	Predominant cell types	Structural characteristics	Functional interpretation
3	Neutrophils, macrophages	Necrosis, edema, vascular congestion	Inflammation, tissue degradation
7	Macrophages, fibroblasts	Granulation tissue onset	Transition to repair
14	Fibroblasts, endothelial cells	Active angiogenesis, collagen synthesis	Peak reparative phase
21	Myofibroblasts	Wound contraction, collagen cross-linking	Remodeling begins
30	Fibrocytes, keratinocytes	Scar tissue formation, epithelial migration	Late remodeling
60	Fibrocytes	Mature fibrotic scar	Functional closure

Discussion

The present study successfully developed a reproducible and standardized rat model of deep third-degree thermal burns, accurately reflecting the morphofunctional dynamics observed in severe human burn injuries. The model replicates key pathological features, including coagulative necrosis, intense inflammatory infiltration, granulation tissue formation, and subsequent fibrotic scarring, providing a reliable platform for experimental studies on wound healing and tissue regeneration.

Compared to previously described models, the current methodology offers precise control over thermal parameters, including temperature, contact duration, and burn area, which minimizes inter-animal variability and enhances experimental reproducibility. Histological analyses revealed that the peak reparative phase, occurring between 14 and 21 days post-injury, is characterized by pronounced

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fibroblast proliferation, angiogenesis, and organized collagen fiber deposition, all of which are critical for effective tissue repair. By 60 days, the wound area is predominantly replaced by mature fibrotic scar tissue, restoring the epidermal barrier, although the biomechanical and elastic properties of the skin remain only partially recovered. These findings are consistent with previous reports that deep thermal injuries induce prolonged remodeling involving cytokine-mediated fibroblast activation, extracellular matrix synthesis, and vascular reorganization.

The established model demonstrates significant potential for preclinical evaluation of therapeutic interventions, including fibrin- or collagen-based scaffolds, bioactive wound dressings, and local hemostatic agents. Furthermore, it allows for detailed biochemical and molecular assessments, including the measurement of oxidative stress parameters, pro- and anti-inflammatory cytokines, and angiogenic factors at different stages of healing. This comprehensive approach provides an essential foundation for translational research aimed at improving the management of severe thermal injuries and optimizing strategies for tissue regeneration.

Conclusion

The developed experimental methodology provides a reliable, reproducible, and ethically compliant model for inducing deep third-degree thermal burns in laboratory rats. This approach allows precise regulation of burn parameters, including temperature, contact duration, and affected surface area, thereby ensuring minimal inter-animal variability and consistent reproduction of morphofunctional changes that closely mirror those observed in severe clinical burns.

Analysis of the healing process demonstrated that the peak reparative phase occurs between 14 and 21 days post-injury, characterized by intensive fibroblast proliferation, angiogenesis, and organized collagen deposition. By 60 days, the wounds are predominantly replaced by mature fibrotic scar tissue, accompanied by partial restoration of the epidermal layer and re-establishment of the skin barrier, although full functional elasticity is not completely restored.

Given its reproducibility and ability to accurately mimic the dynamics of deep thermal injury, this model is highly suitable for preclinical evaluation of novel wound-healing agents, local hemostatic compounds, and tissue-regenerative therapies. Moreover, it enables detailed morphofunctional, histological, and biochemical assessments, including the analysis of oxidative stress markers, inflammatory mediators, and angiogenic factors throughout the different stages of healing. Consequently, this model represents a valuable tool for advancing translational research in experimental burn pathology and for optimizing therapeutic strategies aimed at improving skin repair and regeneration.

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