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Research Article

Preclinical Trials of Distant Non-invasive Electromagnetic Therapy Accelerating Burn Wounds Recovery in Model Animals

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Abstract

Introduction: The development of new approaches for local therapy and treatment of burns of varying depths remains a critical challenge in modern burn medicine.

Purpose of the Preclinical Study: To evaluate the efficacy of weak, pulsed, non-ionizing, non-thermal electromagnetic fields (EMFs) applied through non-invasive electromagnetic therapy in accelerating the healing of burn wounds in a rabbit model.

Materials and Methods: A non-randomized preclinical study was conducted at the educational vivarium of the Far Eastern State Agrarian University (Russia) using 24 rabbits (average age: 1.5 years; weight: 3.2 kg), divided equally into two groups. The control group received only 0.9% NaCl wound irrigation. The experimental group was exposed to non-invasive EMF therapy at a distance of 12 meters from the device, in addition to standard NaCl treatment. The total study duration was 30 days.

Results: The experimental group demonstrated significantly faster wound healing compared to the control. By day 21, the average wound area in the EMF-treated animals was reduced to approximately 1 cm^2, accompanied by extensive granulation tissue formation. Burn wounds were initially inoculated with a monoculture of Staphylococcus epidermidis (10^6 CFU/mL), and while similar bacterial growth was observed in both groups initially, pathogenic flora such as E. coli, Pseudomonas aeruginosa, and Proteus spp. were absent from the wounds of the EMF-treated group by the end of the study. Rabbits in the control group exhibited signs of sepsis and multiple organ failure, and all died between days 8-10. In contrast, all animals in the experimental group survived the full study period. Necropsy confirmed acute sepsis in the control group, whereas signs of endotoxemia were observed in a few experimental animals.

Conclusion: The application of non-invasive EMF therapy significantly accelerated burn wound healing in the rabbit model and demonstrated a systemic immunostimulatory effect, resulting in complete survival of animals in the treatment group.

Keywords: Non-Invasive Electromagnetic Therapy; Pulsed EMF; Non-Ionizing Radiation; Burn Wounds; Burn Disease; Ambustion; Preclinical Trials; HZ

Introduction

Modern combustiology encompasses not only innovations in extracorporeal detoxification, protein deficit correction, and restoration of coagulation homeostasis, but also in the advancement of local burn treatment techniques [1-8,13,15]. Among these, the development of novel methods for managing superficial (I-II degree) and borderline burns (IIIA-IIIB) is of high clinical relevance

[2]. These types of burns comprise 60-80% of all burn injuries per 100,000 patients annually [2,11].

While effective local treatment in superficial burns (I-II) primarily accelerates healing regardless of total burn area, appropriate management of borderline burns can drastically influence prognosis and outcome [2,7,8,11,13,16]. In third-degree burns, damage extends into the reticular dermis, making epithelial regeneration reliant on adjacent skin structures such as hair follicles and sebaceous glands [3-5]. Inadequate local therapy or secondary bacterial infection often results in burn wound progression and worsened disease severity [1-16].

Histologically, three burn zones are recognized:

- Coagulation zone: irreversible tissue necrosis [2,8-15].
- Stasis zone: characterized by compromised microcirculation and biochemical damage (e.g., lipid peroxidation and oxygen free radicals), making it prone to secondary necrosis if not managed [12,15,17,18].
- Hyperemia zone: marked by inflammation, redness, and swelling [2,8-15].

Innovations targeting the stasis zone with anti-inflammatory strategies could significantly improve outcomes for this patient cohort.

In addition to advancements in composite wound dressings, recent studies highlight the potential of external EMFs of varied intensities and durations in modulating burn wound healing [21-26]. The mechanism behind EMF action may involve nanobubble cluster formation in intercellular fluid, which alters ion exchange across cell membranes [27-28].

The COVID-19 pandemic prompted renewed interest in EMF therapy, with promising results using low-noise, non-invasive EMF technologies in patients with mild-to-moderate SARS-CoV-2 infection. These therapies were evaluated in randomized clinical trials at Samara State Medical University (Russia), demonstrating safety and efficacy in 222 patients [29].

Objective: To conduct preclinical trials evaluating the safety and efficacy of the TOR electromagnetic therapy device in treating infected burn wounds in a rabbit model.

Materials and Methods

A prospective, non-randomized preclinical study was conducted at the vivarium of the Faculty of Veterinary Medicine, Animal Science, and Biotechnology, Far Eastern State Agrarian University (Blagoveshchensk, Russia), from June to December 2024. Twenty-four clinically healthy rabbits (mean age: 1.5 years; average weight: 3.2 kg) were used.

Burn Model: Standardized thermal burns were induced using a heated metal stamp (diameter: 5.5 cm), applied for 10 seconds to the interscapular region without pressure, creating a wound area of approximately 19 cm^2 (confirmed by the V. Schubert formula [30]: A = L × W, where L is length and W is width).

Study Groups

- **Group 1 (Control):** 12 rabbits received only 0.9% NaCl wound irrigation.
- **Group 2 (EMF-treated):** 12 rabbits received NaCl treatment and EMF exposure (from a device placed 12 m from the animal cages) on days 0, 3, 5, 8, 12, 17, 21, and 26.

The study duration was 30 days. No necrectomy was performed. Daily clinical monitoring included local wound assessment, thermometry, and overall health status.

Laboratory assessments

- **Blood tests:** Total protein, albumin, glucose, creatinine, urea, ALT, AST, bilirubin (total and direct), alkaline phosphatase, electrolytes (Na^+, K^+, Cl^-), cholesterol, triglycerides, GGT, alpha-amylase, LDH, total calcium, uric acid.
- **Microbiological evaluation:** Wound exudate cultures.
- **Red bone marrow:** Collected on days 0, 8, and 21.

Testing was conducted at the accredited "VET UNION" veterinary laboratory under contract No. 4089 (dated 10.06.2024), using certified equipment.

All procedures followed the "National General Ethical Principles of Animal Experimentation," in accordance with the European Convention for the Protection of Vertebrate Animals (March 18, 1986). Protocol approval was granted by the Bioethics Committee of the Far Eastern State Agrarian University (Protocol No. 2, dated 03.06.2024).

Results

In the control group, by day 5 post-burn, the average wound area increased by 11.3 cm^2. Between days 5 and 8 (with only two animals surviving), a further increase of 3.9 cm^2 was recorded. Conversely, in the EMF-treated group, significant wound contraction was observed beginning on day 5. By day 8 (after three EMF exposures), all animals showed an average reduction of 17.3 ± 5.1 cm^2 in wound area, with visible granulation tissue emerging in several cases. This healing trend continued throughout the study. By day 21 (after six treatments), the average wound area in the EMF group had reduced to approximately 1 cm^2. Six animals had achieved complete epithelialization, with early hair regrowth noted at the wound site.

Infections in both groups initially showed presence of Staphylococcus epidermidis (10^6 CFU/mL). However, by the end of the experiment, no E. coli, Pseudomonas aeruginosa, or Proteus spp. were detected in the EMF group wounds. Control group animals, in contrast, developed polymicrobial infections. Biochemical analysis showed stable values within physiological norms in the EMF group. All control animals died by day 10, exhibiting systemic signs of sepsis and multi-organ failure. Necropsy confirmed acute septicemia in the control group, and only minor signs of endotoxemia in a few EMF-treated animals. A detailed summary of wound healing progression is provided in table 1, with photographic documentation shown in figure 1.

	## Animal	Ambustion area, cm^2					
		Initial	5th day	8th day	12th day	17th day	21th day
Control							
1	1	19,1	25,1	33,7	-	-	-
2	2	19,1	32,7	-	-	-	-
3	3	19,1	33,7	-	-	-	-
4	4	19,1	29,6	-	-	-	-
5	5	19,1	25,7	-	-	-	-
6	6	19,1	36,7	-	-	-	-
7	7	19,1	38,1	-	-	-	-
8	8	19,1	23,3	-	-	-	-
9	9	19,1	37,4	-	-	-	-
10	10	19,1	22,9	-	-	-	-
11	11	19,1	31,6	-	-	-	-
12	12	19,1	27,4	34,8	-	-	-
M ± m		19,1 ± 1,3	30,3 ± 4,4	34,4 ± 11,7	-	-	-
Experimental							
1	1	19,1	10,5	7,8	8,9	4,9	Complete regeneration
2	2	19,1	23,9	18,7	17,2	-	-
3	3	19,1	22,4	17,2	15,4	15,1	0,59
4	4	19,1	24,7	18,6	17,2	16,1	Complete regeneration
5	5	19,1	24,3	16,4	19,8	15,4	Complete regeneration
6	6	19,1	18,7	18,3	13,7	-	-
7	7	19,1	30,6	22,2	15,3	15,3	0,11

8	8	19,1	20,7	11,9	9,2	19,8	Complete regeneration
9	9	19,1	23,4	19,0	8,9	10,4	2,28
10	10	19,1	17,9	17,4	18,9	5,5	Complete regeneration
11	11	19,1	27	24,8	17,2	13,6	Complete regeneration
12	12	19,1	22,1	15,2	17,2	-	-
M ± m		19,07 ± 1,3	22,18 ± 5,6	17,3 ± 5,1	14,9 ± 5,5	12,9 ± 6,1	-

Table 1: The infected burn wounds area of rabbits during the experiment.

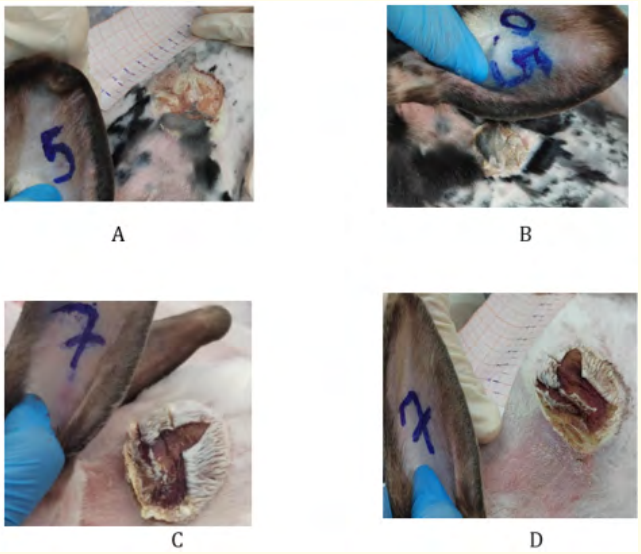

Figure 1: Dynamics of burn wound recovery from the 5th to the 21st day in both groups: A - 5th day, experimental group; B - 21st day, experimental group; C - 2nd day, control group; D - 8th day, control group.

When assessing the microbiocenosis of the animals' skin in both groups prior to burn wound modeling, most cases revealed the presence of a conditionally pathogenic monoculture of Staphylococcus epidermidis at a concentration of $\times 10^6$ CFU/mL. On the 5th day after wound induction, microbial analysis of the control group showed that nine rabbits had developed pathogenic monocultures or associations involving Enterobacter cloacae, Escherichia coli, Enterococcus faecalis, and Proteus mirabilis, with concentrations exceeding $\times 10^5$ CFU/mL. By the 7th day, Staphylococcus aureus and Pseudomonas aeruginosa were also identified in wound exudates, both as monocultures and in microbial associations.

On the 5th day in the experimental group, after EMF treatments, microbial contamination of the wounds revealed monocultures of Staphylococcus equorum, Pantoea agglomerans, Staphylococcus sciuri, Staphylococcus aureus, Staphylococcus xylosus, and Staphylococcus vitulinus, along with microbial associations involving Enterobacter cloacae and Staphylococcus aureus. By the 7th day, the microbial composition of wounds in the experimental group was limited to staphylococcal monocultures: Staphylococcus sciuri, Staphylococcus aureus, and Staphylococcus xylosus. Over the course of the study, particularly by the 21st and 30th days, the microbiocenosis of the skin in the experimental group underwent several changes. Notably, no highly pathogenic strains such as E. coli, Pseudomonas aeruginosa ("blue pus bacillus"), or Proteus species were detected on the wound surfaces at any point.

Analysis of the clinical blood test data showed persistent erythrocytopenia, a reduction in total hematocrit, and leukocytopenia throughout the duration of the experiment (Table 2).

Indicators	Фон n = 10	Control, n = 12		Experiemntal, n = 12				
		5th n = 3	8th n = 2	5th n = 7	8th day n = 6	12th day n=9	17th day n = 9	21th day n = 9
WBC (leukocytes),10^9/l	3,0 ± 0,2	2,1 ± 1,0	2,8 ± 0,07	6,7 ± 6,3	2,8 ± 0,4	2,6 ± 0,3	2,7 ± 0,2	2,8 ± 0,4
Neu (neutrophils), 10^9/l	1,3 ± 0,4	1,0 ± 0,3	0,7 ± 0,04	-	0,7 ± 0,2	0,6 ± 0,1	0,7 ± 0,2	0,5 ± 0,2
Lym (lymphocytes), 10^9/l	1,2 ± 0,1	1,2 ± 0,1	1,7 ± 0,09	-	1,7 ± 0,2	1,8 ± 0,2	1,9 ± 0,2	1,9 ± 0,3
Mon (monocytes),10^9/l	0,1 ± 0,1	0,2 ± 0,1	0,16 ± 0,055	-	0,07 ± 0,01	0,06 ± 0,01	0,08 ± 0,02	0,09 ± 0,03
Eos (eosinophils), 10^9/l	0,2 ± 0,1	0,1 ± 0,01	0,03 ± 0,015	-	0,1 ± 0,04	0,05 ± 0,01	0,09 ± 0,03	0,09 ± 0,04
Bas basophils), 10^9/l	0,3 ± 0,1	0,2 ± 0,07	0,15 ± 0,005	-	0,2 ± 0,06	0,13 ± 0,01	0,2 ± 0,01	0,3 ± 0,03
Neu (neutrophils), %	46,7 ± 2,3	35,1 ± 7,2	26,9 ± 1,00	-	23,3 ± 4,1	20,8 ± 2,4	17,6 ± 2,6	15,4 ± 3,3
Lym (lymphocytes), %	43,6 ± 2,1	48,5 ± 10,7	60,0 ± 1,65	-	62,8 ± 6,3	68,8 ± 3,1	62,0 ± 4,8	67,7 ± 5,1
Mon (monocytes), %	3,8 ± 0,6	5,6 ± 1,3	5,9 ± 2,10	-	3,0 ± 0,5	2,8 ± 0,5	3,7 ± 0,6	3,1 ± 0,8
Eos (eosinophils), %	1,9 ± 0,8	3,2 ± 0,4	1,5 ± 0,60	-	3,1 ± 0,8	2,3 ± 0,3	3,2 ± 0,7	3,1 ± 0,9
Bas (basophils),%	4,2 ± 1,2	7,6 ± 1,9	5,6 ± 0,05	-	7,8 ± 1,4	5,3 ± 0,6	9,4 ± 0,6	10,6 ± 0,8
RBC (erythrosites), 10^{12}/l	3,3 ± 0,2	8,4 ± 6,1	2,3 ± 0,89	2,3 ± 0,2	1,9 ± 0,2	1,8 ± 0,1	2,9 ± 0,5	2,9 ± 0,6
HGB (hemoglobin), g/l	92,5 ± 7,0	124,7 ± 3,8	124 ± 1,00	49,4 ± 3,6	116 ± 2	119 ± 3	130 ± 8	138 ± 9
HTC (hematocrit), %	22,1 ± 1,8	13,3 ± 0,	913,5 ± 5,55	16,0 ± 1,3	12,8 ± 1,4	11,5 ± 0,9	17,7 ± 3,5	15,5 ± 3,7
PLT (platelets), 10^9/л	239 ± 17	199 ± 39	256 ± 48	88,4 ± 23,8	190 ± 29	120 ± 18	121 ± 15	123 ± 21
PCT (thrombocrit), %	0,127 ± 0,01	0,1 ± 0,02	0,16 ± 0,07	-	0,10 ± 0,01	0,07 ± 0,01	0,06 ± 0,01	0,08 ± 0,01

Table 2: Indicators of rabbit blood clinical analysis of over the entire experiment duration.

When examining bone marrow punctures in both groups, no significant deviations were observed in erythroid, granulocytic, or megakaryocytic lineages.

Analysis of biochemical changes in the control group on the 5th and 8th days revealed that the primary abnormalities were associated with increased activity of liver transaminases, indicating the development of cytolytic syndrome. Triglyceride levels were found to be 15% below the reference norm. By the 8th day, a twofold increase in cholesterol levels (hypercholesterolemia) was detected in the control animals. During the same period, elevated amylase levels (amylasemia) were also recorded, exceeding the reference value by 23% (Table 3).

Indicators	Control			Experimental					
	Initial	5th day	8th day	Initial	5th day	8th day	12th day	17th day	21st day
	N = 12	N = 3	N = 2	N = 12	N = 8	N = 10	N = 9	N = 9	N = 9
ALT, u/l	57,5 ± 6,4	72 ± 23	66,5 ± 11,5	56,6 ± 3,5	58 ± 3	44 ± 3	59 ± 4	60 ± 3	49 ± 4
AST, u/l	55 ± 8	44 ± 14	28,5 ± 11,5	29,6 ± 3,3	24,5 ± 3,4	36,5 ± 10,5	59 ± 12	50 ± 11	66 ± 8
Albumen, g/l	38 ± 0,7	34 ± 3	36 ± 3	34,6 ± 0,5	33,1 ± 0,4	33,8 ± 1,2	36 ± 1	33 ± 2	36 ± 1
Alpha-amylase, u/l	334 ± 29	253 ± 80	411 ± 177	179 ± 5	187 ± 9	188 ± 7	199 ± 3	263 ± 11	250 ± 15
Total bilirubin, µmol/l	1,9 ± 0,2	1,7	1,7	1,7	1,7	1,8 ± 0,1	1,8 ± 0,1	1,8 ± 0,1	1,8 ± 0,05
Gamma-GT, u/l	8 ± 1	6,6 ± 1,6	10 ± 1	6,4 ± 0,4	7 ± 1	6,6 ± 0,7	5 ± 0,3	5 ± 0,8	5 ± 0,3
Creatinine, 10^9 µmol/l	103 ± 7	122 ± 6	113 ± 26	99,1 ± 3,6	100 ± 3	112 ± 6	97 ± 6	151 ± 14	141 ± 14
Ureal, mmol/	7,8 ± 0,3	7,3 ± 0,8	9 ± 4	7,3 ± 0,2	4,4 ± 0,2	5,1 ± 0,3	4,8 ± 0,3	5,7 ± 0,3	4,6 ± 0,2
Crude protein, g/l 112	74 ± 4	69,3 ± 5,3	67,5 ± 12,5	62,6 ± 1,2	61 ± 1	62,2 ± 1,6	68 ± 3	65 ± 2	66 ± 2
Triglycerides, mmol/l	1,06 ± 0,13	0,9 ± 0,2	0,9 ± 0,2	0,8 ± 0,1	1,4 ± 0,3	1 ± 0,1	1,5 ± 0,1	1,52 ± 0,02	1,54 ± 0,02
Cholesterol, mmol/l	1,3 ± 0,2	1,7 ± 0,4	3 ± 2	1,7 ± 0,1	1,6 ± 0,1	1,8 ± 0,1	1,8 ± 0,1	1,7 ± 0,1	1,8 ± 0,1
Alk Phos, U/l	64,1 ± 11,3	13,3 ± 5,6	66 ± 23	39,3 ± 3,9	38,1 ± 4,4	71 ± 12	66,2 ± 4,2	64 ± 3	58 ± 3
Phosphatase alkaline, u/l	3,5 ± 0,1	4,0 ± 0,1	3,5 ± 0,5	3,5 ± 0,03	3,1 ± 0,6	3,1 ± 0,1	3,1 ± 0,1	3,2 ± 01	3,1 ± 0,1

Table 3: Indicators of rabbit blood biochemical analysis of over the entire experiment duration.

In the experimental group, all major biochemical parameters remained within reference ranges throughout the duration of the study, and any deviations observed were not considered diagnostically significant.

The overall results of the preclinical trials were both remarkable and unexpected for the research team (Table 4).

By the 8th day of the experiment, 10 animals from the control group had died. The remaining two were withdrawn from the study. In contrast, all animals in the experimental group survived until the end of the observation period.

Anatomical examination of the deceased control animals revealed clear signs of acute sepsis, including venous stasis in all parenchymal organs, marked vascular injection, and multiple hemorrhages on the serous membranes. Additional findings included toxic hepatitis, cholangitis with biliary dyskinesia, nephritis with hemorrhagic foci, and septic splenitis with splenic infarctions. The two control animals removed from the experiment also showed signs of advanced burn disease and toxicemia, with predominant damage to the liver and pancreas. In the experimental group, the pathomorphological features of endotoxemia were notably less severe.

Animal number	Days of experiment							
	1st	3rd	4th	5th	6th	7th	8th	21nd
Control								
C1	Wound modeling						euthanized	
C2			dead					
C3				dead				
C4					dead			
C5						dead		
C6						dead		
C7					dead			
C8						dead		
C9				dead				
C10					dead			
C11				dead				
C12							euthanized	
Experiment								
E1	Wound modeling							
E2							Planned euthanasia	
E3								
E4								
E5								Planned euthanasia
E6							Planned euthanasia	
E7								Planned euthanasia
E8								
E9								Planned euthanasia
E10								
E11								
E12							Planned euthanasia	

Table 4: Mortality dynamics and days of scheduled culling throughout the experiment.

Discussion

As a result of the preclinical trials involving EMF therapy in rabbits with modeled burn wounds (ambustions), the effects of weak, non-ionizing, non-thermal pulsed electromagnetic fields (PEMF) on the healing of superficial and borderline-depth burns were studied.

When analyzing the mechanisms behind the accelerated wound healing observed with EMF exposure, two primary pathways of influence can be identified. On one hand, EMFs act on ion-exchange channels in cell membranes, increasing the regenerative potential of epithelial cells preserved in the appendages of the skin within the zones of burn-related paranecrosis. This promotes cell proliferation and improves microcirculation in the surrounding dermal layers [31-40]. These effects contribute to uniform granulation tissue formation and facilitate consistent epithelialization [31,33,35-38,42-45], ultimately preventing secondary deepening of the burn wounds and enhancing wound contraction.

On the other hand, EMFs appear to suppress acute-phase inflammatory responses: lipid peroxidation is inhibited, the generation of reactive oxygen species is reduced, and cellular antioxidant systems are activated [17-20,44-49]. As a result, the cellular and tissue-level inflammatory processes become more balanced, creating a more favorable environment for regeneration.

It is also important to consider that all regenerative cellular processes occur in the context of a specific microbial environment, which can significantly influence healing outcomes [38-41]. The present experiment demonstrated that the presence of highly pathogenic "noisy" microflora on wound surfaces interferes with the establishment of stable microbial communities-even among conditionally pathogenic organisms. The reduction of such pathogenic interference in the experimental group likely contributed to faster wound healing.

In addition to these local cellular effects, EMFs also appear to exert an organoprotective function. The therapy likely plays a role in stabilizing cell membranes under the systemic stress of burn-induced endotoxemia. This was reflected in the preservation of normal biochemical blood parameters in the experimental group, despite the presence of burn pathology [42-49]. This observation was further supported by necropsy findings in the experimental animals, which showed only minimal organ changes. The indirect organoprotective effect of EMF therapy may be associated with reduced toxic burden due to prevention of wound deepening, limited microbial contamination, and enhanced wound cleansing and regeneration processes. Together, these factors likely contributed to the 100% survival rate observed in the experimental group despite the presence of burn disease.

Conclusions

- In rabbit models with burns of I-III degree, treatment with a non-invasive electromagnetic therapy device significantly accelerated wound healing.
- Weak, non-ionizing, non-thermal pulsed electromagnetic fields (PEMF) may serve as an effective adjunct in the treatment of burns classified as I-IIIA, and can be used in combination with standard wound care protocols.
- Preclinical trials demonstrated that, in addition to local cellular effects, EMF therapy has a systemic immunostimulatory impact that supported full survival of rabbits in the experimental group under conditions of burn disease. However, the precise mechanisms behind this systemic effect require further investigation.

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