# TREATMENT TECHNOLOGY FOR LOCAL RADIATION INJURIES AND THERMAL BURNS WITH USE OF MESENCHYMAL STEM CELLS

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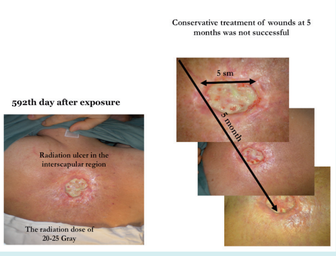
In clinical practice, burn lesions of various etiologies are quite common. In most cases burn injuries have a high social importance. The outcome of these injuries are often scars even in case of the small area of damage and average severity level of the process. Scars localized on the exposed parts of the body or in the joints cause contractures, various cosmetic skin damages or even non-healing, resistant to standard therapy, trophic ulcers - in the case of radiation burns. All this leads to a prolonged rehabilitation process and significantly reduces quality of life for these patients. Every year in Russia recorded more than 600 thousand cases of burns, with an overall mortality rate reaches 3.6%. The true skin regeneration is impossible without additional intervention in case of loss of dermis (third-degree B and fourth-degree burns), and healing is accompanied by scar formation. Borderline third A - degree burns can heal yourself, but then preserved epidermis is under threat of death. The most commonly reasons of skin lesions are - flame burns, contact burns and electric burns. The main reasons for the development of local radiation injuries (LRI) are incidents with ionizing radiation and aftereffects of radiotherapy. Up to 30% of all complications of radiotherapy has on LRI. Our attention was attracted by mesenchymal stem cells (MSCs), which have a trophic effect and participate in the process of damaged tissues repair. The aim of this work was development of the complex treatment method for burns of different etiologies with using autologous MSCs, which allows to improve engraftment of autografts, nonhealing ulcers close and accelerate epithelization of burn surfaces. We have developed an experimental model of local radiation injury with β - radiation from the source 90Sr/90Y to explore the use of mesenchymal stem cells in the treatment of LRI. The experiments were performed on male rats Wistar weighing 170-180g. In the experiments we studied the effect of transplantation of mesenchymal stem cells from bone marrow for run of the local radiation injuries in a local irradiation of the rat by beta source with 90Sr/90Y 140 Gy radiation dose under different conditions and methods of cell transplantation. We have recorded a short latent period of 6.7 days after the local b - irradiation of rats at a dose of 140 Gy, and we did not observe any visible changes on the irradiated surface of the skin.

The phenomenon of dry or moist dermatitis begin to develop with the 7-8-days. The entire surface layer of the skin in the affected area turned out to be necrotic by the 12th to 14th days. Radiation ulcers covered with a dense crust were observed for the all rats on the 21th day after irradiation (Slide 1).

We administered MSCs subcutaneously with at 5 points around the lesion on the 8th day after local irradiation of rats. We clearly observed reduction in lesion area during all periods of study under the influence of MSCs. Starting with 37-days in animals, with the administering of mesenchymal cells, there was recovery of the skin, whereas the ulcers were observed up to 100 - day in the control irradiated animals (Slide 2). Macroscopic data were confirmed by histological examination. Preparations of ulcer surface of the control group differed lymphocytic infiltration of the dermis, marked sclerosis of the dermis and focal destruction of the cutaneous muscle (Slide 3.4), while in the group of animals with cell therapy there was a complete restoration of the epithelial surface and a less pronounced sclerosis of the dermis (Slide 5). Our experimental data were the basis for the transition to a phase of limited clinical trials. The BURNASYAN FMBC staff was developed protocol of treatment of radiation and thermal burns with the use of autologous multipotent mesenchymal stromal cells with through research with the approval of the Ethics Committee and with the scope of that study. After informed consent signing, the study included patients with thermal injury II to IV severity, with the affected area up to 50% of body surface, and 5 patients with MLP II - IV severity. The cell material was obtained by puncture of the iliac bone under local anesthesia. The volume of aspirated bone marrow ranged from 50 to 100 ml for each patient.

## Clinical case number 1

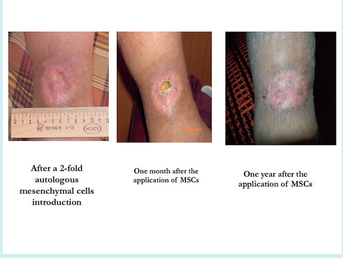
61-year-old male patient . Diagnosis: acute local effects of back LRI of severe degree: radiation fibrosis, late radiation ulcers, due to aftereffects of coronary stenting procedure.





## Clinical case number 2

74-years-old female patient. Diagnosis: acute effects of radiation damage to local tissue the lower third of the right leg, severe: radiation fibrosis, late radiation ulcers.



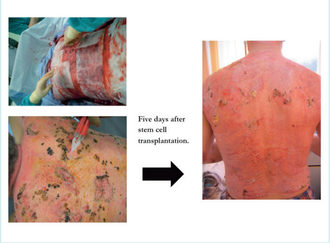

## Clinical case number 3

64-year-old male patient.
Diagnosis: keratinizing squamous skin cancer T3N0M0. Condition after excision and radiation therapy. Late radiation ulcer middle third of the outer surface of the right tibia.


## Clinical case number 5

38-year-old male patient.

Diagnosis: thermal burns II, IIIA, IIIB Art., Back, upper and lower extremities, head, a total area of 45%, 20% of them deep burns.




## Clinical case number 4

28-years-old female patient.
Diagnosis: thermal burns II, IIIA, IIIB degree of upper and lower limbs the total area of 35%, 8% of them - deep burns.


## Clinical case number 6

27-years-old female patient.
Diagnosis: burn wounds of the right and left upper limb III A - B degrees of total area of 15% on the rear surface of the trunk in both areas of burn wounds of blade III A - B degrees with a total area of 7-10%; burns on his face I-III A of degrees total area of up to 3%.


**The results:** The method of treatment of local radiation injuries with the use of autologous MSCs and standard surgical techniques made it possible to close nonhealing ulcers beam, avoiding of infection, amputation and additional operations for skin grafts. The use of MSCs in the treatment of burn wounds accelerates the healing of the wound surfaces, complete and rapid engraftment autografts. The therapeutic potential of MSCs is associated with their secretory activity: they produce a huge range of cytokines and growth factors, which, in turn, activate and attract regional circulating of stem cells in the lesion. In addition, MSCs have immunosuppressive and anti-inflammatory effects and reduce the number of cells entered into apoptosis.

**Conclusion:** The use of MSCs transplantation in the treatment of burns of different etiologies leading to a reduction in terms of healing of burn surfaces, complete epithelialization nonhealing ulcers in the case of local radiation injuries, to avoid additional transplants of skin, promotes the formation of normotrophic scars, prevents the development of contractures and keloids.