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## NEW APPROACHES FOR FULL-THICKNESS GRAFTING OF THE FACE

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In addition to the physical injury, deep burns of the face also can cause psychological injury. The purpose of this study was to develop new technical methods for improving engraftment of full-thickness autografts. Since 2017, autologous fibroblasts have been used for skin facioplasty of one full thickness autograft in Scientific Research Institue, Reginal Clinical Hospital No 1. Isolation of fibroblasts was performed by using an enzymatic method and a skin sample with an area of 10 cm<sup>2</sup>. Cultivation of autologous fibroblasts was performed for 22 days according to a standard procedure. The prepared culture of autologous fibroblasts was used together with a full-layer autologous transplant to close the wound on the face. We found that autologous fibroblasts provided faster adaptation of the autograft. There were no signs of fibrous tissue over the long term. We concluded that fibroblasts promoted rapid engraftment and adaptation of the full-thickness autograft. Improvement of facial plastic surgery methods can help achieve maximum cosmetic treatment results.

Keywords: skin; full-thickness autograft; treatment; plastic; fibroblasts; cellular technology.

### НОВЫЕ ПОДХОДЫ К ВЫПОЛНЕНИЮ ПЛАСТИКИ КОЖИ ЛИЦА ПОЛНОСЛОЙНЫМИ АУТОТРАНСПЛАНТАТАМИ

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Глубокие ожоги лица являются не только тяжелой ожоговой, но и психологической травмой. Цель данной работы — разработка способов улучшения приживления кожных полнослойных аутотрансплантатов. С 2017 г. в ГБУЗ «НИИ-ККБ № 1» при выполнении пластики кожи лица одним полнослойным аутотрансплантатом были использованы аутофибробласты. Выделение фибробластов проводили ферментативным способом из образца кожи площадью 10 см<sup>2</sup>. Культивирование аутологичных фибробластов происходило по стандартной методике в течение 22 дней. Подготовленная культура аутологичных фибробластов была применена вместе с полнослойным аутологичным трансплантатом для закрытия раневой поверхности лица. Было отмечено, что с использованием аутологичных фибробластов происходит более быстрая адаптация аутотрансплантата, не формируется фиброзная ткань при длительном периоде наблюдения. На основании анализа данного клинического случая было показано, что фибробласты способствуют быстрому приживлению и адаптации полнослойного аутотрансплантата. Совершенствование способов пластики кожи лица позволяет достигнуть максимальных косметических результатов лечения.

Ключевые слова: кожа; полнослойный аутотрансплантат; лечение; пластика; фибробласты; клеточные технологии.

#### Introduction

Russian surgeons have made significant contributions to the development of replacement surgery; in particular, they have developed a method of full-thickness, free skin autografting [1]. The grafting methods described by Krasovitov and Parin are known worldwide [2, 3].

In the field of combustiology, surgical tactics are based on the excision of necrotic tissues followed by autografting with a split-free skin flap. While performing autografting in patients with burn injury, the achievement of a positive functional result is one of the primary tasks. In addition, achieving a cosmetic effect that primarily satisfies patients, particularly in terms of functionality, is equally important [4].

The achievement of a satisfactory cosmetic effect in the treatment of deep face burns is determined by its special significance in aesthetic and functional aspects. Currently, this issue remains one of the most challenging problems in the fields of combustiology and reconstructive surgery [5, 6]. It is noteworthy that deep facial burns are characterized by a high frequency and a significant severity in the course of functional disorders [7]. Subsequently, patients perceive facial scars not only as a physical defect but also as severe psychological trauma [8-10]. Uniform and rapid engraftment of a skin autograft on the face is crucial for the final aesthetic result. Conventional closure of the damaged facial skin with several split grafts leads to the formation of a "flat" face with an artificial look and a limited view. Moreover, transplanted skin can have a corrugated "wood-like texture" with an unnatural color; it also shows the formation of scar tissue, which is an indication for lengthy reconstructive surgeries [11]. Transplantation of a full-layer skin autograft is devoid of the abovementioned defects; however, the degree of its engraftment is worse because of the thickness and area of the flap used and the longer duration required for the restoration of blood circulation [12].

To improve cell epithelialization while performing autografting in the treatment of patients with severe burns and owing to the scarcity of donor resources, cellular technologies from the 20th century have been used, one of the priority treatment direction of which is obtaining fibroblasts [13, 14]. It should be noted that even in the absence of transfer risk of hemotransmissible infections, tissue reactions in immunocompromised patients receiving autologous fibroblasts remain crucial [15]. Regardless of the origin of fibroblasts (autologous or allogeneic), they can be used independently in the form of suspension and as a part of skin equivalents [16]. An example of the use of autologous fibroblasts is in the technology used for treating burns that is based on the use of these fibroblasts and a fibrin adhesive, which was developed by the workers of the Nizhny Novgorod Burn Center (Federal State Budgetary Institution, Privolzhsky, Federal Medical Research Center of the Russian Ministry of Health) [17, 18]. Nevertheless, cellular technologies include the closure of skin defects using perforated autografts. A literature review revealed isolated cases of the application of cellular technologies in facial skin grafting. For example, Li et al. reported on the results of the treatment of patients using bone marrow mononuclear stem cells for the closure of the wound surface in combination with combined split autografts [12]. To the best of our knowledge, there are no reports on the engraftment of a full-layer skin autograft in conjunction with cellular technologies, particularly on the face. The search for methods to improve the engraftment of a full-thickness skin autograft in case of face burns definitely warrants attention and optimization.

**Aim.** The study aimed to develop methods to improve the engraftment of full-layer skin autografts.

#### **Clinical case**

Since 2010, in the burn center of the Budgetary Public Health Facility, S.V. Ochapovsky Research Institute–Regional Clinical Hospital No.1, seven autograft surgeries were performed with a single full-layer graft in patients with total deep face burns or scar deformities (six in the acute period after trauma and one with total scar deformities); three of these patients were <18 years old.

The following main technical methods for surgical treatment that assist engrafting a full-layer autograft on a granulating wound were identified: 1) excision of granulation tissues to a fibrous layer, 2) excision of marginal scarring, and 3) uniform pressure on the full-layer graft.

In March 2017, a Patent of the Russian Federation was applied for the proposed method of skin autografting [application no. 2017115873/20 (027469)].

In the presented clinical case, surgical intervention and necessary studies were performed after obtaining approval from the Local Ethical Committee and receiving informed consent from the patient.

Patient D was admitted to the Burn Department of the Budgetary Public Health Facility on October 01, 2017 with the diagnosis of 31% IIIB-IV degree thermal burns (flame burns) of the face, neck, trunk, and upper limbs of and burns of the upper respiratory tract. On admission from the district on Day 2 after the trauma, there was a deep burn on the face, trunk, and limbs with scab formation. On the same day, under surgical conditions, a free skin split autograft with a thickness of 0.25 mm and an area of 10 cm<sup>2</sup> was collected from the anterior surface of the right thigh with electrodermatome DE-60 and sent to the laboratory for obtaining a dermal fibroblast culture. For the isolation of fibroblasts, an enzymatic method using a 0.15% collagenase solution and 0.25% trypsin solution was utilized. After treatment with enzymes, the dermis was placed in a 25-cm<sup>2</sup> culture flask and a nutrient medium comprising a DMEM solution and 10% autoserum was added and cultured to form a monolayer of fibroblasts. Fibroblasts were grown to the required amount by passaging. On the day of surgery, cells were removed from the flasks, resuspended in a normal saline solution at a rate of  $\geq$ 25,000 cells per cm<sup>2</sup> of the wound surface and the autograft. The total duration for obtaining the fibroblast culture was 22 days. Surgery was performed 24 days after the trauma under general anesthesia (artificial lung ventilation). The face wound dimension at the time of autografting was  $2 \times 22$  cm (Fig. 1).

Surgical intervention started with the excision of the upper layers of granulations using a scalpel and a dermatome. A wound with lower granulation layers was formed without exposing the subcutaneous



Fig. 1. Three weeks after the flame burn, granulation tissue was formed



Fig. 4. Facial skin grafting using a full-layer skin graft



Fig. 2. Excision of the granulation and wound edges; view before autografting

Fig. 5. Treatment result on postopera-

tive day 6



Fig. 3. Application of autofibroblasts to a full-layer autograft



Fig. 6. Treatment results 1.5 months after surgery

fat. Deviating 0.5–1 cm from the granulations and around the oral cavity, nasal passages, and eyes, a bordering incision was made with a scalpel; the edges of the wound and marginal epithelialization were then cut from the inside of the wound to the healthy skin (Fig. 2).

After achieving hemostasis, an entire full-layer free skin autograft  $(25 \times 22 \text{ cm})$  was taken from the left thigh. A suspension of autofibroblasts was applied by irrigating the inner surface of the full-layer autograft and the face wound after excising the granulations and was left for 25 min prior to the transplantation (Fig. 3).

Thereafter, autografting was performed using a full-layer autograft on the face (Fig. 4).

The surgery duration was 5.5 h. Tiling and compression bandages were applied to the wound post transplantation.

Six days after surgery, complete adaptation of the full-thickness skin autograft was observed (Fig. 5).

During 2.5 months of observation after transplantation, no scar tissue developed in the area of grafting with a full-layer autograft in conjunction with the autofibroblasts.

#### Discussion

In our clinic, we developed methods for facial skin grafting using full-layer autografts on a granulating wound with various options for harvesting a full-layer autograft. Patents of the Russian Federation (No 2618166, 2618907, and 2622979) were granted for the developed methods [19-21]. We proposed a method of grafting with a full-layer skin autograft (certificate of acceptance for invention No 2016128423) [22]. Since 2010, six surgeries for the transplantation of a single full-layer autograft with total face burns and scar deformities have been performed with positive cosmetic results and no indications for reconstructive surgeries noted in the long term [23, 24]. However, the engraftment of the full-layer autograft was slow, taking up to 14-17 days, owing to slow vascular invasion in the graft and its adaptation [25]. In order to improve adaptation, in this study, we used autologous fibroblasts, resulting in a shorter engraftment period (6 days). The choice of autologous fibroblasts was based on the use of one's own cells, thus eliminating the risk of hemotransmissible infection transfer and creating a favorable microenvironment for

engraftment. The results of our study showed the prospects of the use of autologous fibroblasts for a faster engraftment of a full-fledged flap.

#### Conclusion

This method enables the creation of conditions for rapid engraftment and adaptation of a single full-layer free skin autograft on a granulating wound after its excision owing to the use of autofibroblasts. Performing autografting with a single full-layer skin autograft using autofibroblasts reduces the risk of coarse scar tissue development over a long postoperative period and contributes to optimal cosmetic results. Based on these data, it can be preliminarily concluded that the use of autologous fibroblasts in conjunction with autografting with a full-thickness flap is promising; however, further research and accumulation of clinical data are warranted.

## Funding and conflict of interest

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