

DEVELOPMENT OF HOMOLOGOUS SKIN, BONE AND OTHER SOFT TISSUES TRANSPLANTATION IN SLOVENIA

RAZVOJ TRANSPLANTACIJE HOMOLOGNE KOŽE, KOSTI I DRUGOG MEKOG TKIVA U SLOVENIJI

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SUMMARY

In Slovenia, transplantation of tissues such as skin and bone was successfully following global trends throughout its history. First documented homologous skin graft was already mentioned back in 1901. Alongside with new discoveries in immunology and advancements in burn surgery, skin transplantation development surged in the second half of 20th century. Slovenia's first and currently the only skin bank was established in 1973, in Ljubljana. Throughout its existence it always managed to supply skin grafts for patients that were in vast majority burn victims. The bone bank was established twenty years earlier, in 1952. Homologous bone grafts helped patients with trauma injuries and tumour resections. Besides skin and bone grafts, cartilage and other soft tissues have also been used for transplantation – tympanic membrane and cartilage transplants being used in ear surgery. International inclusion of Slovenian physicians allowed comparable results and introduction of new methods at home and around the world.

Key words: transplantation; allograft; skin bank; bone bank, Slovenia.

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INTRODUCTION

The difference between transplantation of tissues such as skin, bone and cartilage, in comparison with transplantation of other organs such as heart, lung and liver, is that they can be transplanted between different persons (homotransplants, allografts) or different parts of the body of the same person (autotransplants, autografts). Differences also exist in terms of harvesting these tissues from either alive or deceased donors and their preserving and storage. The history of tissue transplantation is extensive and has over time intertwined with various fields in medicine.

WORLD'S HISTORY

Precise dating of the beginning of skin transplantation is questionable and is often referred to the techniques of Indians who presumably performed successful autologous skin transplantations around 400 years BC. The oldest documented descriptions of skin transplantation are found recorded in the early 19th century, when surgeon Sir Astley Cooper (1768-1841) successfully transplanted patient's skin on his amputated thumb in 1817 in London. That same year Christian Heinrich Büniger (1782-1842) from Marburg described a case of nose reconstruction with autologous skin transplant. At the time, skin autografts and allografts were being used in a non-discriminatory fashion. The first who successfully transplanted fresh homologous skin graft was Jacques-Louis Reverdin (1842-1929), in 1868 and the first, who extensively described the technique, was Girdner, in 1881. Towards the end of the 19th century, Karl Thiersch (1822-1895) together with Louis Léopold Ollier (1830-1900) laid the foundation of harvesting and use of patient's own thin skin grafts. The next big revolution, artificially grown skin, took place almost a hundred years later. Transplantation of autologous in vitro cultured keratinocyte cell cultures has become a reality thanks to James Rheinwald and Howard Green (1925-2015) ¹.

The first descriptions of attempts to transplant bones dates back to the 17th century, but the first successful breakthrough only came in 1867, when Ollier published the results of their work with autologous and homologous bone grafts in animals, and later, in 1879, when Sir William MacEwan (1848-1924) as the first transplanted a part of humerus in a human; the defect after extensive haematogenous osteomyelitis in the upper arm of the child was treated with multiple transplantation of fresh homologous bone grafts and conserved the functionality of the limb. Since then, history has shown a

diverse range of experiments with bone transplantation. The use of cortical bone grafts was introduced by Albee (1876-1945) in 1911, spongy bone grafts were put into use twenty years later – they were introduced by the Dallas B. Phemister (1882- 1951). Bone grafts were physically, chemically and biologically modified to produce clean, deproteinized and defatted grafts or completely demineralized grafts, where only the organic matrix of the bone was preserved. With the development of modern microsurgery, transplantation of whole bones or bone graft with blood vessels – vascularized bone graft also became a reality ².

Tissue transplantation was also present in, for example, ear surgery. Ludwig Wullstein (1906-1987) and F. Zöllner are considered the founders of tympanoplasty as they were the first to perform plasty of the stapes with modulated malleus in 1953. Zollinger was the first to use autologous incus harvested from a living donor for a surgical procedure of auditory nerve neurinoma. The first transplanted eardrum from a deceased donor was performed by Ned Chalot 1960. In 1964 Jean Marquet transplanted the eardrum together with the malleus. Marquet was also the first to start with conserving these types of allografts and is considered the founder of allotransplantation in this field ³.

The continuing article of the development of tissue transplantation in Slovenia is almost entirely limited to the use of homologous transplants - allografts.

SKIN GRAFTING

The first record of the use of homologous skin transplant was described by Franc Derganc (1877- 1939) in the case of a patient, who was treated in 1896 at the new hospital on Zaloška street in Ljubljana for the big lump at the back of his neck. The patient was operated by Edvard Šlajmer (1864-1935), who excised the lump and sutured the wound. As the lump reoccurred in 1901, there was not enough skin available to cover the new wound on the neck, so they harvested it from patient's thighs. Too much skin was cut off, so one part of it was used on another patient, to cover a wound on his nose ⁴.

A revolution in the field of skin homotransplantation represents the year 1951, when plastic surgeon Mirko Derganc (1914 – 1981) returned from his training in the United Kingdom and brought the indications and surgical techniques for the use of homotransplants. In November of the same year, six months after the establishment of the first Department of Plastic Surgery

at the Ljubljana Surgical Clinic, he performed the first skin homotransplantation in a case of burn treatment; a child who burned in a burning crib and had deep burns, covering almost 40% of the body surface, was covered with homotransplants harvested from the mother. Gradually homotransplants were replaced with child's skin autografts⁴. Plastic surgeon Franjo Zdravič (1919-1999) extensively studied the field of skin homotransplants and in 1971 obtained a thesis on this topic. His thesis consists of twenty years of clinical work and the problem of immune reactions in skin homotransplants as its experimental part on which he worked in Rochester, the USA, in 1960 and 1961.

In a 20-year period from 1951 to 1971 the Ljubljana Department of Plastic Surgery treated 864 burn victims, alongside with around 2,100 patients at the Department of Dermatology, and approximately 3,500 burn victims at the Paediatric Clinic. Out of these, 688 were operated. Autografts were used in 79 % of patients and in 7.6 % of cases homologous tissues were taken from either living or deceased donors. Zdravič indicates 61 cases of burn treatment with homotransplants for this period^{11,12}.

Burns have always been by far the most common indication for the use of homologous skin grafts. First experiences with homotransplants in the treatment of burns in Slovenia are time-divided into two periods. In the period between the years 1951 and 1964, skin homotransplants were only used for extensive and deep burns when autotransplants were not available or their use would impose too much risk for the patient. From 1964 onwards, the indications were extended to the extensive dermal burns and were consistently applied to the concept of early tangential excision, which was introduced in 1961 by Zora Janžekovič (1918-2015).

A new era of transplantation of skin in Ljubljana began in 1971, when the surgical treatment of burns finally united under one department in the new building of the University Medical Centre Ljubljana. In 1993, the department introduced autologous grafts with in vitro cultured keratinocytes, which is described by Franc Planinšek and Zoran Marij Arnež⁵.

SKIN BANK

The first skin bank in Slovenia was founded two years after the organization of the clinical Department of Plastic Surgery, in 1973, and was located in Ljubljana University Medical Centre (UMC). Donors at the time were patients' relatives or patients who died at the UMC. Harvesting from the

deceased donors was first performed in the morgue and later on transferred to the operating theatre or at the Department of Pathology of Ljubljana Faculty of Medicine.

Before the establishment of the skin bank grafts were stored in refrigerators at $+4^{\circ}\text{C}$. This method of conservation was adequate, but its main drawback was short utility period of preserved tissues. Skin grafts typically maintained their vitality up to 7 days and have been usually completely useless after three weeks. Although the skin bank never had problems with providing sufficient amount of the needed tissues, the need to improve the conservation of tissues was growing. Skin allografts were later stored in specially adapted freezers at -28°C . Since 1994, the allografts were additionally processed and stored in 85% glycerol ⁶. The number of burn victims, donors and recipients of grafts from the skin bank during its first years of operation (1973-1976) and in the period 1995-1998 were as follows: in the first period, the department treated 1821 patients with burns. At that time there were 57 donors and 136 recipients. In the second period, the number of patients dropped to 762, the number of donors to 19 and the number of recipients to 31. In the latter period, harvesting was performed only on deceased donors and no longer on the living ⁶. Another skin bank in Slovenia was established in Maribor but was abandoned due to administrative requirements.

BONE BANK AND BONE TRANSPLANTATION

In 1952, only five years after the first bone bank with deep freezing in the world, Slovenia established its first bone bank at the Orthopaedic Clinic in Ljubljana. The initiator of the establishment was Bogdan Breclj (1906-1986). At first, the bone grafts were preserved with merthiolate, supplied by Lek pharmaceutical company in Ljubljana and later stored at -30°C ⁸. In the first 45 years after the establishment of the bone bank there was no infection or graft rejection reported ¹³. Homologous and autologous bone transplants were throughout history limited to the spongy bone. Homotransplants of large cortical parts of bone have proved successful only in the surgical resection of bone tumours. One of the first such procedures performed in Ljubljana was described in the case of a patient with a bone tumour on his left tibia. The tumour was removed and replaced by a 20 cm long bone graft from the bank ⁷.

EAR SURGERY

Boris Povhe was the first in Slovenia to use an allograft in tympanoplasty at the Otorhinolaryngology Clinic in Ljubljana in 1979. By the end of the twentieth century they performed 24 such procedures¹⁰. Data shows that the functional success of tympanic homologous grafts was comparable to those in the international literature¹⁰.

CONCLUSION

While comparing different periods of the tissue transplantation in Slovenia, we can obtain a general impression of the development in Slovenia, which has evolved in the context of global guidelines. Periods of development coincided or followed new discoveries primarily in the field of immunology. Due to the modern methods of preservation, survival of homologous grafts extended and the immunogenicity effects of tissues were reduced. However, partly due to the high costs of tissue banks, the use of allografts is nowadays not widespread and a lot of physicians prefer artificial materials.

Professional integration and training of Slovenian individuals abroad has contributed enormously to the development of tissue transplantation at home. The constant introduction of advanced methods in daily practice allowed high-quality work and indirectly contributed to the accepted global standard of care.

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SAŽETAK

Transplantacija tkiva kao što su koža i kosti uspješno je pratila globalne trendove kroz povijest u Sloveniji. Prvi dokumentirani homologni kožni presadak spominje se već 1901. Uz nova otkrića u imunologiji i napredak u kirurgiji opekline, razvoj transplantacije kože povećao se u drugoj polovici XX. stoljeća. Prva slovenska i trenutačno jedina banka kože osnovana je 1973. u Ljubljani. Tijekom svog postojanja uvijek je uspijevala opskrbiti pacijente koji su u velikoj većini bili žrtve opekline. Koštana banka osnovana je dvadeset godina prije, 1952. Homologni koštani presadci pomogli su pacijentima s ozljedama traume i resekcijama tumora. Osim kožnih i koštanih presadaka, hrskavica i druga mekana tkiva također su korišteni za transplantaciju - timpanična membrana i transplantati hrskavice koriste se u operaciji uha. Međunarodno uključivanje slovenskih liječnika omogućilo je usporedive rezultate i uvođenje novih metoda u zemlji i širom svijeta.

Ključne riječi: *transplantacija; alograft; banka kože; koštana banka; Slovenija.*