DOI: 10.15825/1995-1191-2026-1-8-16

THE LAUNCH OF THE UPPER EXTREMITY TRANSPLANTATION PROGRAM: CLINICAL CASES AND KEY ASPECTS OF ORGANIZING WORK IN A NEW AREA OF CLINICAL TRANSPLANTOLOGY

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The loss of an arm (or both arms), not only causes severe physical trauma but also leads to long-term psychological consequences and difficulties in occupational, domestic, and social maladjustment, substantially impairing quality of life. This complex problem is not always addressed effectively with modern high-tech bionic prostheses, which, while enabling the performance of many functional tasks, have inherent limitations. In selected cases, allograft transplantation of an upper limb from a deceased donor may be considered. Until recently, this treatment option was unavailable within the Russian healthcare system. This paper presents the key stages in establishing an upper limb transplant program, including its organizational structure, the roles of its individual components, and the outcomes of practical implementation. The efficacy and safety of the treatment method are illustrated through the first two clinical cases. The experience gained and the outcomes of the first clinical cases are intended to demonstrate the practical feasibility of developing a structured, effective upper limb transplant program that can address the growing demand for this type of high-tech medical care.

Keywords: hand transplantation, distal upper limb allograft, vascularized composite allograft, deceased donation, osteosynthesis, microsurgery, rehabilitation, functional outcomes, immunosuppression.

INTRODUCTION

"War is an epidemic of trauma" – a statement by pioneering 19th-century Russian surgeon Nikolay Pirogov, that vividly captures the devastating consequences of large-scale armed conflicts, which result in a sharp and sustained increase in the number of casualties.

Traumatic amputation of upper limb segments of varying extent, or their irreversible destruction, occurs both as isolated injuries and as part of combined injuries. Although significant advances in exoprosthetics – particularly modern bionic prosthetic technologies – have substantially improved functional rehabilitation, they can only partially restore lost limb function. In carefully selected patients, upper limb transplantation from a deceased donor may therefore be considered as a potential reconstructive option [1].

Upper limb transplantation remains a relatively underexplored area of clinical transplantology within the broader field of vascularized composite allograft (VCA), which also includes face, anterior abdominal wall, and genital transplantation [2]. Globally, the number of VCA procedures performed to date is substantially lower than that of solid organ transplants. This disparity is attributed not only to the technical complexity of the surgical procedures and ethical considerations surrounding the donation of visible body parts such as hands and face, but also to the inherently high immunogenicity of composite allografts. This immunogenicity arises from the presence of multiple heterogeneous tissue types within the graft, including skin, muscle, adipose tissue, and bone marrow components [3, 4].

Despite the use of intensive multicomponent immunosuppressive regimens, rejection rates remain high.

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Moreover, prevention and management of rejection significantly increases the risk of adverse effects associated with immunosuppressive therapy, including life-threatening complications. This highlights a central clinical dilemma in VCA: balancing functional and aesthetic restoration of the upper limb against the substantial risks associated with long-term immunosuppression [5].

Global experience accumulated in leading transplant centers in the field of cross-match–negative transplantation and transplantation in presensitized recipients – i.e., solid organ transplantation associated with a high risk of severe immunological complications – has contributed to the development of more effective and safer immunosuppressive protocols applicable to VCA [3, 4].

In addition, established principles of donor organ procurement, pharmacological cold storage, and transportation – well developed in solid organ transplantation – have been successfully adapted to upper limb VCA procedures. The concentration of such expertise within specialized transplant centers creates the necessary infrastructure and conditions for implementation and expansion of VCA programs.

Furthermore, replantation of amputated native limbs and their segments after traumatic injury, depending on the extent of reconstruction, closely replicates many key stages of transplant surgery. This provides an important clinical platform through which relevant specialists can acquire and refine their experience within routine surgical practice.

These factors, together with a high level of organization and effective functioning of the deceased organ donation system, have created the necessary conditions for the development and subsequent implementation of an upper limb transplant program through collaboration among specialists from leading transplant and trauma centers in Russia.

STAGES OF ORGANIZATION OF THE UPPER LIMB TRANSPLANT PROGRAM

In the first stage, candidate selection criteria were formulated based on international experience [3]. Transplant candidates were considered to be physically healthy male patients aged 18 to 50 years, with average anthropometric characteristics (height ~170 cm, weight ~70 kg), harmonious physique, and isolated amputation of one or both upper limbs not extending above the proximal third of the forearm, and without harmful habits.

Psychological health, strong motivation for upper limb transplantation, strict adherence to medical recommendations, and commitment to long-term treatment were considered essential prerequisites.

Patients who met the selection criteria underwent evaluation at the transplant center to confirm the isolated nature of the traumatic injury and to identify and manage any concomitant conditions. In all cases, the evaluation as part of the upper limb transplant preparation program concluded with the patient being placed on the waiting list for donor tissue from a deceased donor.

Potential upper limb donors proposed by regional organ donation coordination centers were evaluated according to the following criteria:

- absence of laboratory signs of systemic infection;
- maximum vasopressor therapy with norepinephrine at a dose not exceeding 500 ng/kg/min;
- physical integrity of the donor limb (absence of visible injury, joint deformities, sequelae of previous trauma or surgical interventions, arterial catheterization sites, or signs of thrombophlebitis;
- preserved integrity and functional adequacy of the peripheral vascular bed as confirmed by Doppler ultrasonography;
- absence of osteoarticular pathology based on X-ray findings in two projections;
- absence of tattoos.

Donor–recipient pairs were selected based on anthropometric compatibility (height and weight characteristics, as well as symmetry of the donor's hand in relation to recipient's contralateral hand with respect to shape and size. Compatibility according to blood group and human leukocyte antigen (HLA) profile was also taken into consideration.

Between September 2025 and February 2026, the upper limb transplant working group evaluated two donors who met the established selection criteria. Suitable recipients were identified from the waiting list based on blood group compatibility and anthropometric matching. Distal upper limb transplantations were subsequently performed on September 28, 2025, and February 2, 2026.

Recipient No. 1

Patient A., 48 years old, somatically compensated (healthy), sustained severe combined multiple trauma in 2019 that resulted in the loss of the right upper limb. The stump was located at the level of the proximal third of the forearm (Fig. 1). The patient reported a negative prior experience with prosthetic use. Comprehensive evaluation performed in August 2025 as part of the upper limb transplant preparation program confirmed the technical feasibility of transplantation and revealed no contraindications to the procedure.

Recipient No. 2

Patient B., 40 years old, underwent traumatic amputation of the left upper limb following a mine-blast injury sustained in 2023. The stump of the left upper limb was located at the level of the middle third of the forearm (Figs. 2, 3).

The functional performance of the exoprosthesis used by the patient was assessed as unsatisfactory and inadequate for the demands of an active lifestyle. Evaluation at the transplant center in 2025 revealed no significant

concomitant disease or contraindications to transplantation of the distal segment of the left upper limb.

DONOR STAGE OF DISTAL UPPER LIMB TRANSPLANTATION

In both cases, procurement of the composite upper limb allograft was performed as part of multi-organ retrieval involving the liver, kidneys, and heart. The upper limb procurement team operated simultaneously with the thoracic and abdominal organ retrieval teams.

The donor limb was positioned in abduction on a separate support table. The surgeon performing the explantation was positioned in the axilla. A fishmouth-shaped skin incision was made along the volar surface, extending from the medial to the lateral epicondyle of the humerus. The skin and subcutaneous tissue were dissected to the level of the brachial fascia, after which the proximal skin flap was mobilized proximally to expose the antecubital fossa. Superficial veins were clipped and divided.

For improved visualization of the neurovascular bundle, the biceps tendon was transected, allowing mobilization of the brachial artery for subsequent cannulation. Following proximal exposure of the brachial artery, dissection continued distally to the bifurcation into the radial and ulnar arteries. The ulnar, median, and radial nerves were subsequently identified and mobilized.

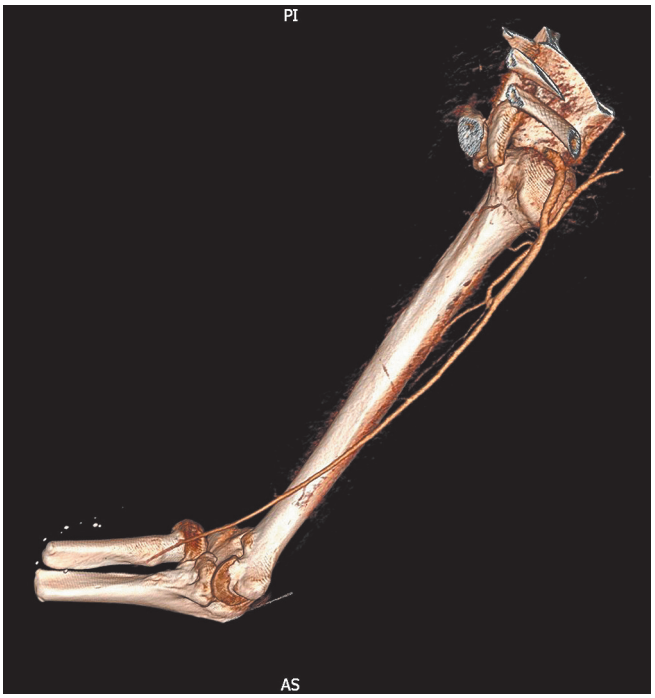

Fig. 1. 3D reconstruction of CT angiography of the stump of Patient A's right upper limb

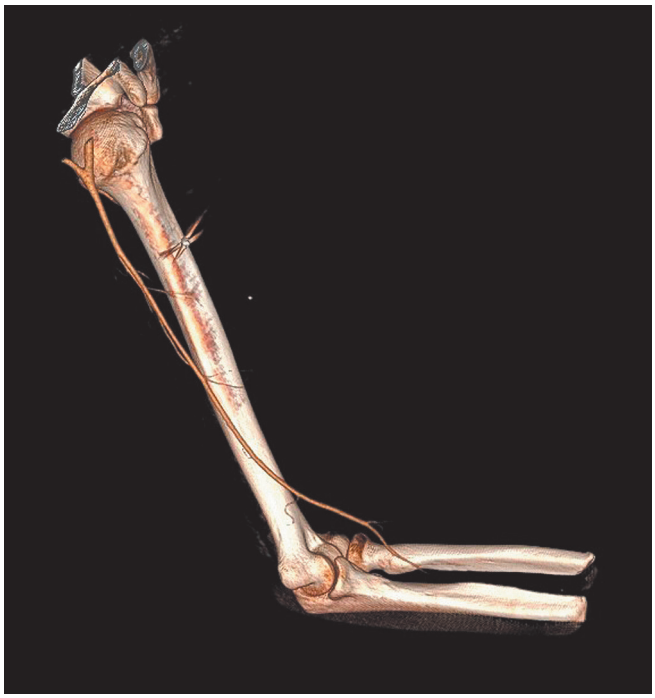

Fig. 2. 3D reconstruction of CT angiography of the stump of Patient B's left upper limb

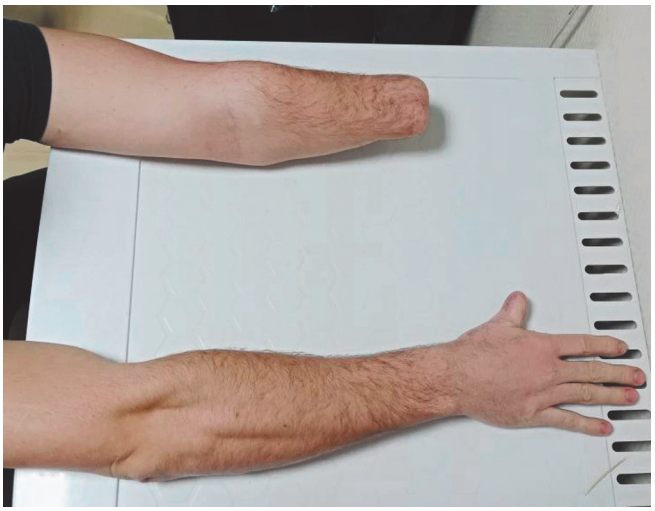

Fig. 3. External view of Patient B's upper limbs

After systemic heparinization, the brachial artery was cannulated using a straight 12-Fr arterial cannula. Custodiol was used as the preservation solution in a volume of 2 L, with a perfusion duration of 10 minutes. From the onset of cold perfusion, superficial and deep veins were transected to ensure passive outflow of the preservation solution.

Upon completion of cold perfusion, decannulation was performed, followed by transection of the brachial artery and accompanying veins. The radial, median, and ulnar nerves were then divided. The flexor muscle group was transected, after which the anterior capsule of the elbow joint was dissected. The limb was flexed at the elbow joint, and the previously formed skin flap was

retracted proximally. After palpating the olecranon, the triceps tendon was transected, exposing the posterior capsule of the elbow joint, which was subsequently divided. Elbow disarticulation completed the donor upper limb procurement procedure.

The graft was wrapped in sterile drapes soaked in preservation solution and packaged in three sterile transport bags. Total procurement time in both procedures did not exceed 60 minutes. The cooled allograft was transported in an isothermal container at +4 °C.

ANESTHESIOLOGICAL MANAGEMENT IN DISTAL UPPER LIMB TRANSPLANTATION

Preoperative preparation of the recipient was carried out at the transplant center simultaneously with graft procurement performed at a separate medical institution.

Intraoperatively, recipients were positioned supine on the operating table. Intravenous premedication included dexamethasone, chloropyramine, and atropine sulfate, followed by sequential induction of anesthesia using fentanyl (200 μg), 1% propofol (200 mg), and rocuronium bromide (100 mg). Direct laryngoscopy and orotracheal intubation with a 9.0-mm endotracheal tube were then performed.

Mechanical ventilation was maintained using lung-protective settings: peak inspiratory pressure of 10–12 cm H_2O, positive end-expiratory pressure of 4 cm H_2O, respiratory rate of 10 breaths/min, and tidal volume of 5–6 mL/kg. Oxygen concentration in the inspired gas mixture was maintained at 40–45%, while end-tidal carbon dioxide levels were maintained at 4–4.5%. Sedation depth was maintained using isoflurane at 1–2.5 vol%.

Anesthesia and neuromuscular blockade were maintained with continuous infusions of rocuronium bromide at 40–50 mg/h and fentanyl at 50–100 μg/h.

For infusion therapy and hemodynamic monitoring, central venous access was established through the internal jugular vein contralateral to the operative side. A femoral arterial catheter was inserted for invasive hemodynamic monitoring and intermittent arterial blood gas analysis. Additional monitoring included continuous noninvasive heart rate and oxygen saturation assessment. A Foley catheter was inserted for urine output monitoring and optimization of perioperative fluid therapy.

Given the need to avoid vasopressors and/or medications with vasopressor effects, continuous infusion therapy was administered throughout the procedure to maintain stable hemodynamic parameters. Infusion therapy included balanced crystalloid solutions, colloids (albumin and gelofusine), as well as nutritional support via a nasogastric tube using a 10% glucose solution. In addition, 40% glucose solution (800 mg) was administered intravenously, together with prokinetic agents to prevent gastrointestinal paresis. Target hematocrit values were maintained within the range of 25–30%.

At the initiation of vascular reconstruction, sodium heparin was administered intravenously at a dose of 30–35 U/kg to achieve target activated partial thromboplastin time (aPTT) values greater than 200 seconds. Thereafter, prolonged anticoagulant therapy was continued using titrated dosing regimens, maintaining target aPTT values within the range of 50–65 seconds.

Following restoration of blood flow through the principal vessels of the allograft, systemic vasodilators were administered to reduce the risk of reperfusion-associated vasospasm. Systemic glucocorticoids were also given at target doses as part of the combined immunosuppressive protocol.

At the conclusion of the procedure, after the recipient's upper limb had been temporarily immobilized with a plaster splint, a VCA catheter was placed under ultrasound guidance to provide prolonged peripheral analgesia. A 0.5% solution of ropivacaine was administered into the brachial plexus region via a supraclavicular approach to ensure effective postoperative pain control.

Anesthesia was discontinued with the administration of opioid receptor antagonists and sugammadex. The patient was then awakened in the operating room under continued sedation with dexmedetomidine at a dose of 1–1.5 μg/kg/h.

The patients were transferred to the surgical ward for further monitoring and postoperative management.

KEY STAGES OF IMPLANTATION OF A COMPOSITE VASCULARIZED ALLOGRAFT IN THE DISTAL UPPER LIMB

In both cases, an incision was made at the distal end of the forearm stump. The flexor and extensor muscle groups were identified and isolated using a combination of blunt and sharp dissection techniques.

Simultaneously, in a neighboring operating room, the composite allograft was prepared. Bone segments were resected to the required length, and the muscle compartments, together with the associated neurovascular structures, were carefully isolated. After a comparative assessment of the recipient's second forearm length and the stump length, the graft bones were trimmed accordingly.

Osteosynthesis of the ulna was performed using a nine-hole plate with 3.5-mm screws, while fixation of the radius was achieved using a nine-hole plate secured with six screws. After removal of excess muscle from the general flexor group, the superficial muscle group and deep portions of the flexors were isolated.

In both cases, arterial reconstruction was performed by end-to-end anastomosis between the donor and recipient brachial arteries. Under optical magnification, venous outflow was restored through anastomoses of the accompanying veins, including one saphenous vein. In total, the first case involved four venous anastomoses and one

arterial anastomosis, while the second case required five venous anastomoses and one arterial anastomosis.

After blood flow was restored, flexor and extensor tendons were reconstructed. Following mobilization and preparation, epineural sutures were placed on the median, ulnar, and radial nerves. The deep extensor muscle groups on the posterior aspect of the forearm were then sutured.

After completion of reconstruction, the wound was sutured layer by layer. The final appearance of the surgical site is shown in Fig. 4. The limb was immobilized in a position of elbow flexion and approximately 20° of wrist extension. Limb positioning and immobilization were guided by Doppler ultrasound assessment of graft arterial and venous flow. Continuous monitoring using peripheral pulse oximetry was employed to assess microcirculatory perfusion and graft viability.

IMMUNOSUPPRESSIVE THERAPY IN DISTAL UPPER LIMB TRANSPLANTATION

In both cases, preoperative immunosuppressive preparation included initiation of tacrolimus therapy at a dose of 2 mg administered 3 hours before transplantation. In the early postoperative period, the drug was delivered via a nasogastric tube. Subsequent administration followed a standard 12-hour dosing regimen, with dose adjustments performed to achieve target trough concentrations of 12–15 ng/mL.

Induction immunosuppression consisted of two intravenous administrations of basiliximab at a dose of 20 mg, given intraoperatively and on postoperative day 4. Immediately prior to allograft reperfusion, intravenous methylprednisolone was administered at a dose of 10 mg/kg body weight.

Maintenance immunosuppressive therapy included continued tacrolimus administration with individualized dose adjustment, together with oral methylprednisolone at a dose of 16 mg daily. One week after transplantation, mycophenolate mofetil was initiated at a dose of 2000 mg/day.

EARLY POSTOPERATIVE PERIOD

In both cases, the postoperative course was uneventful. Postoperative management was conducted according to a standardized treatment protocol. The primary goal of treatment was to maintain target hematocrit levels, adequate graft perfusion, appropriate anticoagulation parameters, and prevention of vascular thrombosis, inflammatory complications, and pain syndrome.

During the first 7 postoperative days, infusion therapy was restricted to 1,500–2,000 mL/day. Blood electrolyte levels, acid–base balance, and anticoagulation parameters were monitored every 3 hours.

Continuous monitoring of peripheral pulse oximetry in the transplanted limb was maintained throughout the early postoperative period. Under gastroprotective therapy, cyclooxygenase-1 and cyclooxygenase-2 inhibitors were administered, together with prolonged peripheral regional analgesia. In addition, continuous infusion of prostaglandin E1 at a dose of 60 μg/day and prolonged continuous heparin administration were used to prevent vascular complications.

After 7 days, anticoagulation therapy was transitioned from continuous heparin infusion to intermittent admi-

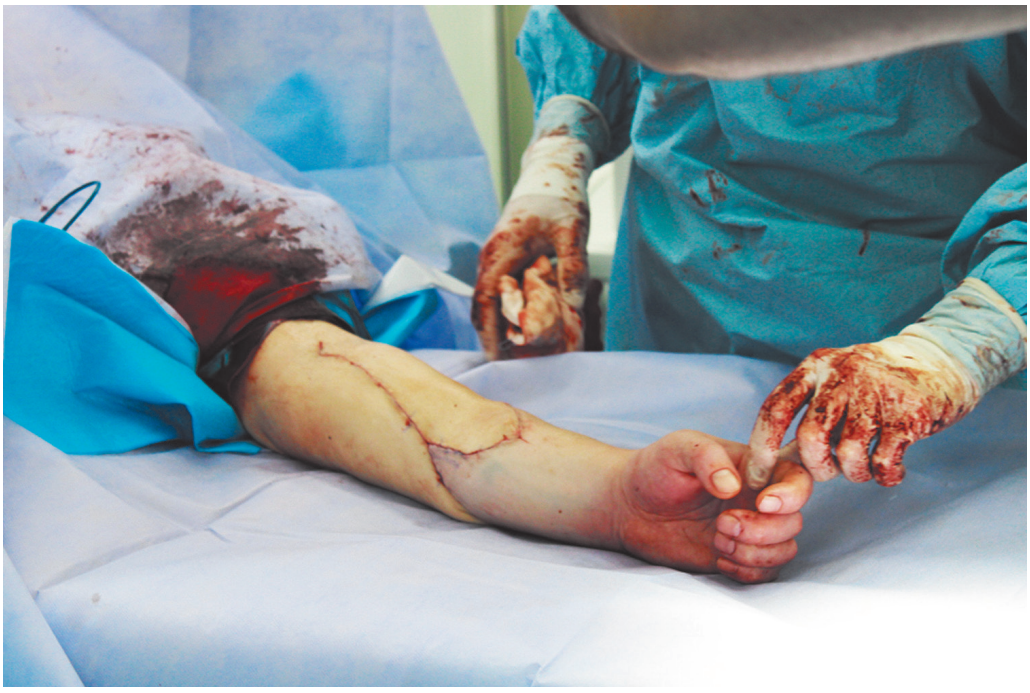

Fig. 4. Final appearance of the surgical site following completion of the transplant

nistration of low-molecular-weight heparins combined with oral antiplatelet therapy. Antimicrobial prophylaxis included intravenous broad-spectrum antibiotics and antifungal agents, followed by a switch to oral formulations.

Postoperative wounds healed by primary intention in both cases. Delayed bone repair in the osteosynthesis region was observed in both recipients; therefore, osteogenic hydroxyapatite-based compounds were prescribed.

Fig. 5. Demonstration of motor function in Patient A's transplanted hand on postoperative day 120

RESULTS

This article outlines the key stages in the organization and initial implementation of a domestic program for allograft transplantation of the distal upper limb, as undertaken during the preparation and performance of the first two clinical cases.

Recipient A is currently under outpatient follow-up and reports gradual restoration of cutaneous sensation extending from the postoperative scar toward the distal part of the transplanted hand. Thanks to comprehensive rehabilitation measures, the patient demonstrates mobility in all fingers and is regaining motor skills required for daily activities (Fig. 5).

An X-ray of the surgical site shows a well-formed bone callus (Fig. 6). Regular clinical and laboratory follow-up shows no evidence of graft rejection. With tacrolimus concentrations maintained within the target therapeutic range, no adverse effects related to immunosuppressive therapy have been observed. The patient continues rehabilitation and alongside regular outpatient follow-up.

Recipient B, who received a shorter vascularized allograft, demonstrated the ability to partially flex the fingers in the immediate postoperative period, attributed to the preservation of his own forearm muscles in the stump (Fig. 7).

Within 1.5 months after the transplant, an episode of acute rejection was diagnosed based on characteristic clinical findings, including hyperemia, erythematous changes in the graft skin, and graft edema. Laboratory tests indicated increased activity of the T-cell–mediated

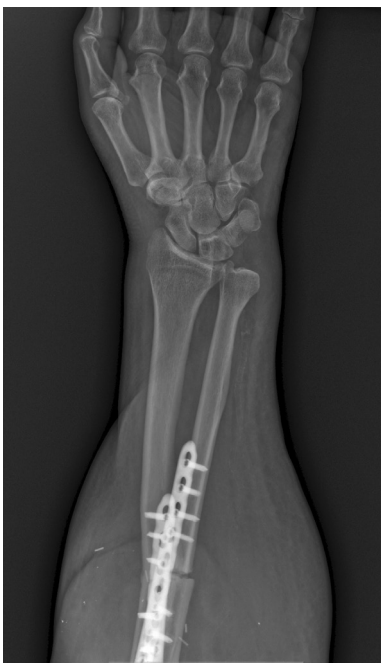

Fig. 6. X-ray of Patient A's surgical site on postoperative day 120

Fig. 7. Demonstration of motor function in Patient B's transplanted hand on postoperative day 145

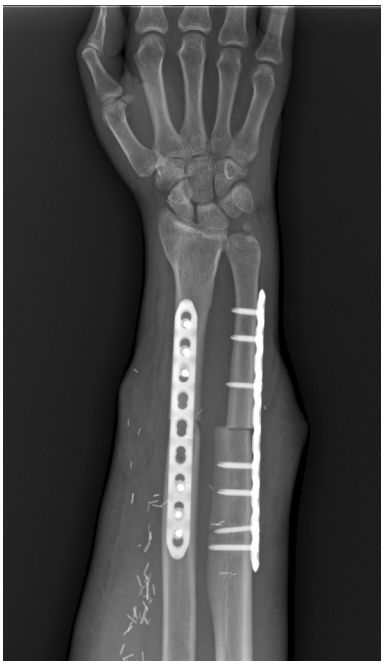

Fig. 8. X-ray of Patient B's surgical site on postoperative day 45

immune response, and treatment with anti-thymocyte globulin was initiated at a dose of 1.5 mg/kg.

Within 24 hours of the first administration, the clinical manifestations described above resolved completely and did not recur. The patient continues comprehensive rehabilitation therapy. A radiograph of the surgical site is shown in Fig. 8.

DISCUSSION AND CONCLUSIONS

Internationally, the number of VCA procedures – particularly upper limb transplantation – remains significantly lower than that of solid organ transplants [1–3]. This is mainly due to limited indications, strict recipient selection criteria, and inherent surgical and immunological challenges. The growing number of patients requiring this type of medical care in recent years underscores the need to develop dedicated upper limb transplant programs.

The combined clinical experience and scientific expertise of leading transplant and trauma centers within the Russian Ministry of Health, including Shumakov National Medical Research Center of Transplantology and Artificial Organs and Priorov National Medical Research Center of Traumatology and Orthopedics, have made it possible to rapidly implement the ambitious task of establishing a new field of clinical transplantology for our country at Shumakov National Medical Research Center of Transplantology and Artificial Organs.

The data presented in this study should be regarded not as a demonstration of a final outcome, but rather as an intermediate stage in addressing key fundamental challenges that previously represented major barriers to the implementation of such procedures in the Russian Federation.

This article did not aim to comprehensively address issues related to referral pathways for transplant candidates or the establishment of a formal waiting list system. Further development of the upper limb transplant program, and of the field more broadly, will require detailed consideration of these aspects, which remain topics for future investigation and publication.

The authors declare no conflict of interest.

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The article was submitted to the journal on 17.03.2026