Dokkyo Medical Journal
2(4): 275-280, 2023

Review Article

Current Status and Future of Reconstructive Surgery: Development of Novel and Artificial Flaps

Takuya Iida, Hirotaka Asato

Department of Plastic and Reconstructive Surgery, Dokkyo Medical University, Tochigi, Japan

Summary

Recent advances in reconstructive surgery, such as microvascular free flap transfer, have contributed to the development of other surgical specialties to achieve improved performance of surgery. Although microvascular free flap transfer is one of the most frequently used methods, it has several limitations and shortcomings, such as donor-site morbidity and insufficient flap function. We refined conventional methods of free flap transfer and developed various types of novel flaps to overcome these shortcomings. However, although many technical refinements are being developed, the restoration of complex organs to their original status remains difficult. We believe that there are two solutions for reconstruction of complex organs: 1) vascularized composite allotransplantation and 2) artificial flaps using regenerative medicine. In this article, we aimed to present the current status of reconstructive surgery and discuss its future.

Key Words: reconstructive surgery, adipose-derived stem cells, artificial flap

Current Status and Technical Refinement of Reconstructive Surgery

Reconstructive surgery is a surgical specialty that aims to restore normal function and appearance damaged by a disease or trauma. It collaborates with other surgical specialties, such as head and neck surgery, breast surgery, neurosurgery, dermatology, general surgery and so on, and maximizes their surgical activity by reconstructing the defect. One of the most frequently used methods in current reconstructive surgery is microvascular free flap transfer, which is the transfer of various tissues, such as skin, fat, muscle, bone, intestine, lymph nodes, and other tissues, from other parts of the body to reconstruct the defects (Fig. 1). This method has drastically changed the strategy of reconstructive surgery. However, it has several limitations and shortcomings, such as donor-site morbidity and insufficient flap function. To minimize donor-site morbidity and maximize flap function, we have refined conventional methods and developed various types of novel flaps, including the sensate superficial circumflex iliac perforator flap[1-6], free intercostal artery perforator flap[7], sensate superior gluteal artery perforator flap[8], and free thoracoacromial artery perforator flap[9]. We have also refined microvascular anastomosis techniques to ensure safer flap transfer[10,11].

Received March 29, 2023; accepted April 23, 2023; advance publication by J-STAGE January 31, 2024
https://doi.org/10.51040/dkmj.2023-013
Reprint requests to: Takuya Iida
t-iida@dokkyomed.ac.jp
Department of Plastic and Reconstructive Surgery, Dokkyo Medical University, 880 Kitakobayashi, Mibu, Tochigi 321-0293 Japan

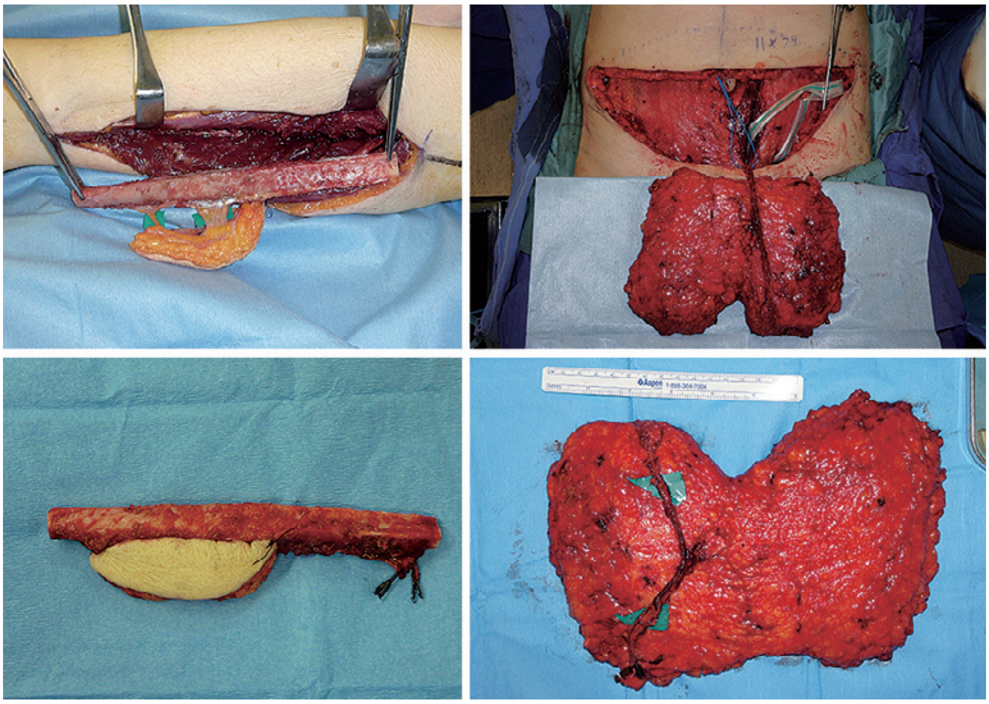

Figure 1

Microvascular free flap transfer. Various tissues, such as skin, fat, muscle, bone, intestine, lymph nodes, and other tissues, can be transferred from other parts of the body to the region containing the defects.

Future of Reconstructive Surgery

Restoration of complex organ to the original status remains a difficult procedure even with the current advances in microvascular free flap transfer. We believe that there are two solutions for realizing reconstruction of complex organs: 1) vascularized composite allotransplantation (VCA) and 2) artificial flaps using regenerative medicine/tissue engineering.

Vascularized Composite Allotransplantation (VCA)

VCA is a method of transplanting complex tissues, including skin, fat, muscles, bones, and nerves, harvested from deceased donors. Clinically performed VCA includes the face, hand, uterus, abdominal wall, penis and so on. The first VCA of the hand was performed by Dubernard et al. in 1998 in Lyon, France[12) while the first VCA of the face was performed by Devauchelle et al. (2005, Amiens, France)[13). Hand and face transplantation has been performed in considerable number of cases worldwide and is becoming an established surgical procedure. However, one of the most important problems in VCA is donor shortage, which hinders this procedure from becoming a commonly used technique.

In Japan, some plastic surgeons including us have been engaged in liver transplants from deceased donors for reconstruction of the hepatic artery (Fig. 2). However, a VCA has not yet been performed. Allotransplantation of non-vital organs is legally difficult compared to that of vital organs, such as the heart, lung, liver, and kidney. Legislation and social recognition are necessary to perform a VCA in Japan. However, VCA is a promising and evolving technique for future reconstructive surgeries.

Development of Artificial Flaps: Combination of Reconstructive Surgery with Regenerative Medicine/Tissue Engineering

Donor-site morbidity is one of the most important problems associated with reconstructive surgery. Donor shortage is also an important issue in VCA. Regenerative medicine/tissue engineering can offer a solution to these problems because it can be used to create large tissues and organs from a small number of cells. We developed a tissue-engineered skin equivalent based on an acellular dermal matrix[14). Currently, how-

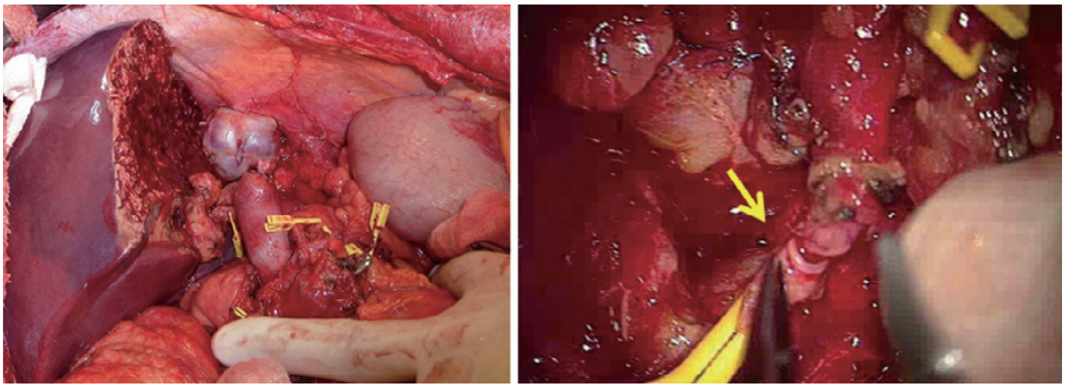

Figure 2

Living donor liver transplantation. Plastic surgeons are engaged in liver transplantation for microvascular hepatic artery reconstruction.

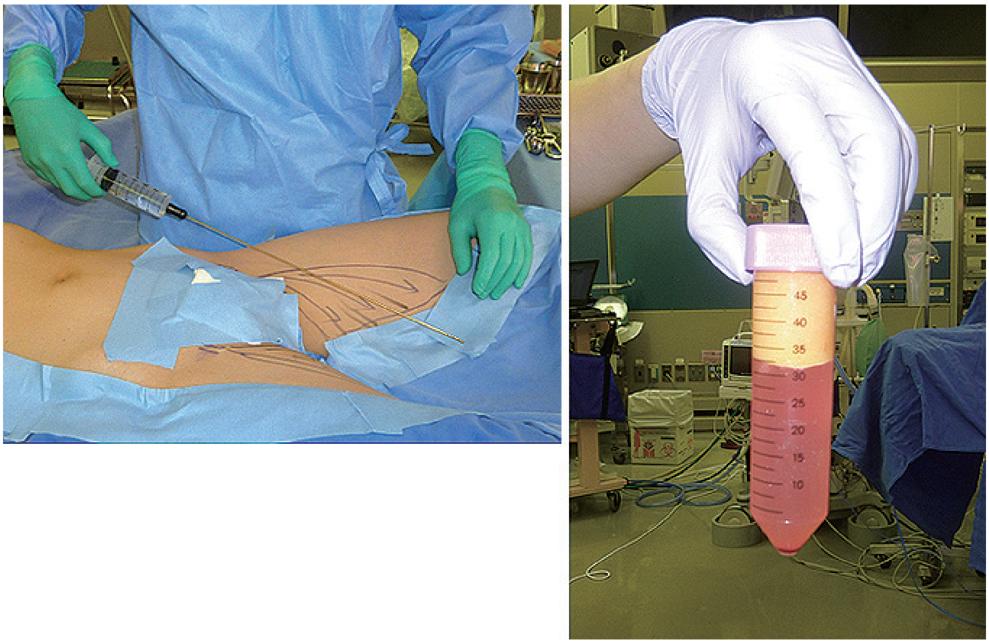

Figure 3

Liposuction is commonly performed in plastic surgery, which can provide adipose-derived stem cells (ASCS).

ever, the tissue can be clinically transplanted mainly at the cellular level; for example, cultured epithelial sheet for extensive burns (JACE®, J-TEC, JAPAN) and retinal sheet for retinitis pigmentosa. These thin sheets and spheroids can be nourished by diffusion and do not require the vascular system.

For manufacturing large organs, the vascular system is necessary for perfusion because diffusion from the culture medium or interstitial fluid alone does not reach the center of the tissue sufficiently, resulting in central necrosis. Therefore, the key is to incorporate the vascular network into the tissue to supply oxygen and nutrients. In the field of reconstructive surgery, there is the "prefabricated flap" concept; a new vascular network can be introduced into a tissue by burying it near a vascular pedicle. After a few weeks of neovascularization, vascularized tissue with a vascular pedicle can be transferred as a free flap based on the attached vascular pedicle.

By combining regenerative medicine with the "prefabricated flap" concept in reconstructive surgery, we are trying to develop a larger three-dimensional tissue model with a vascular pedicle that can be transplanted as a free flap than the currently available tissue-

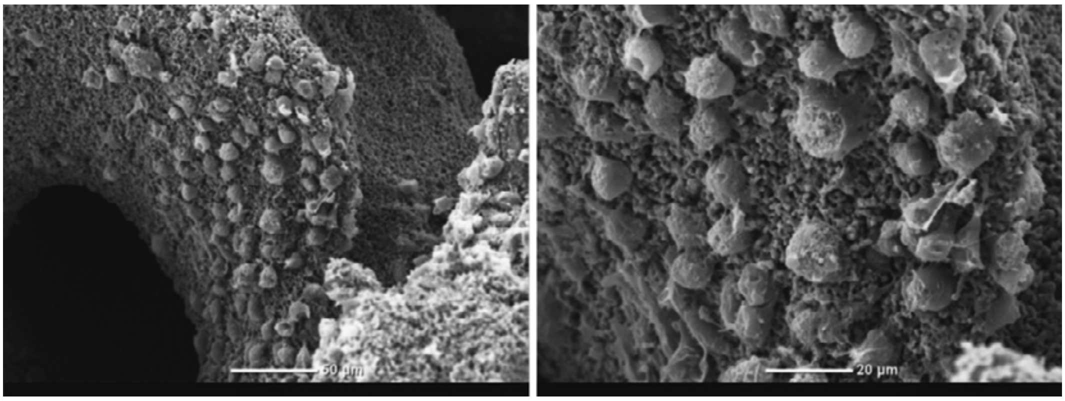

Figure 4 Electron microscopic image of adipose-derived stem cells (ASC)-seeded artificial bone. ASC adhesion to the surface and the internal structure of the artificial bone were observed.

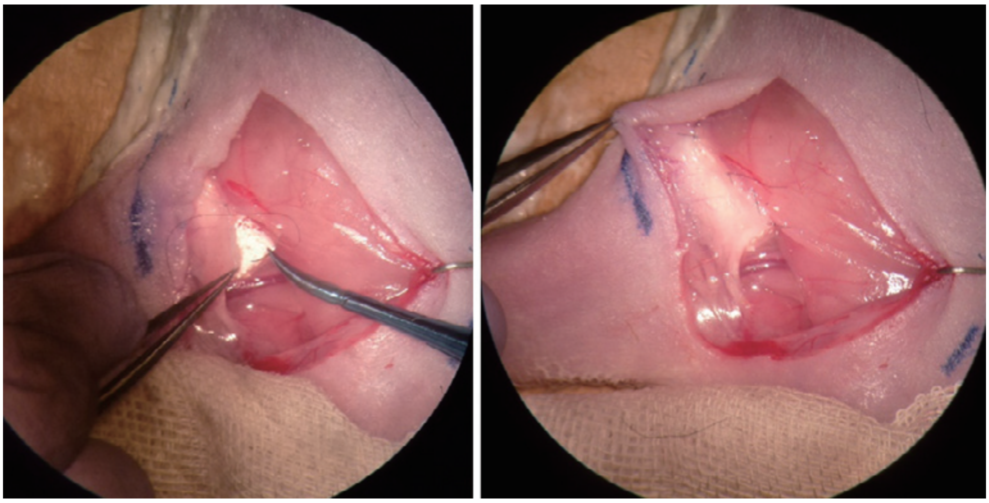

Figure 5 Transplantation of adipose-derived stem cells (ASC)-seeded artificial bone into nude rats. The ASC-seeded artificial bone was transplanted into the inguinal region of nude rats under an operating microscope. It was covered with fascia near the superficial inferior epigastric artery to create a vascularized bone flap.

engineered bone equivalent.

Our Studies on the Development of Artificial Flaps

We have been developing transplantable tissues by seeding mesenchymal stem cells onto scaffolds, such as β-tricalcium phosphate (β-TCP) artificial bone, and then, transplanted them into rats to manufacture artificial flaps. The details are as follows:

Isolation and Culture of Human Adipose-derived Stem Cells (ASCs)

Adipose tissue was harvested by liposuction under the approval of the ethical committee (Fig. 3). It was washed with phosphate-buffered saline (PBS), mixed with 0.075% collagenase solution, and processed in a constant-temperature shaker at 200 rpm for 30 min at 37° C. The solution was centrifuged (760 × *g*, 5 min) to separate adipocytes, and the pellet was collected and washed with PBS. The pellets were passed through 100, 70, and 40 μm cell strainers, and the cells were incubated in Dulbecco's modified Eagle's medium containing 15% fetal bovine serum at 37° C under 5% CO_2. The cells that adhered and proliferated during the culture process were designated as ASCs, and the cells obtained from the second passage were used for experiments.

Seeding and Culture of ASCs on Artificial Bone

Artificial bone made of β-TCP (75% porosity, 5 × 10

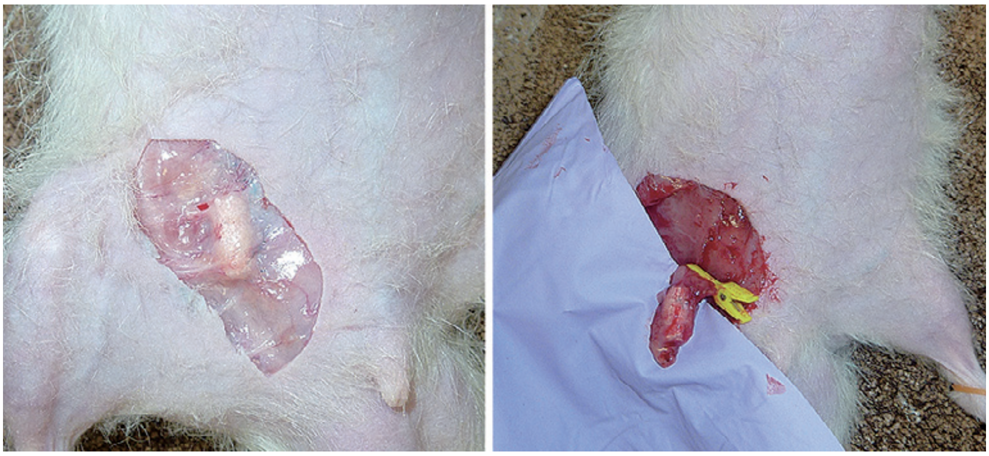

Figure 6 Flap elevation 8 weeks post transplantation.
The ASC-seeded artificial bone was elevated as a vascularized bone flap 8 weeks post transplantation, when the blood vessels had developed sufficiently.

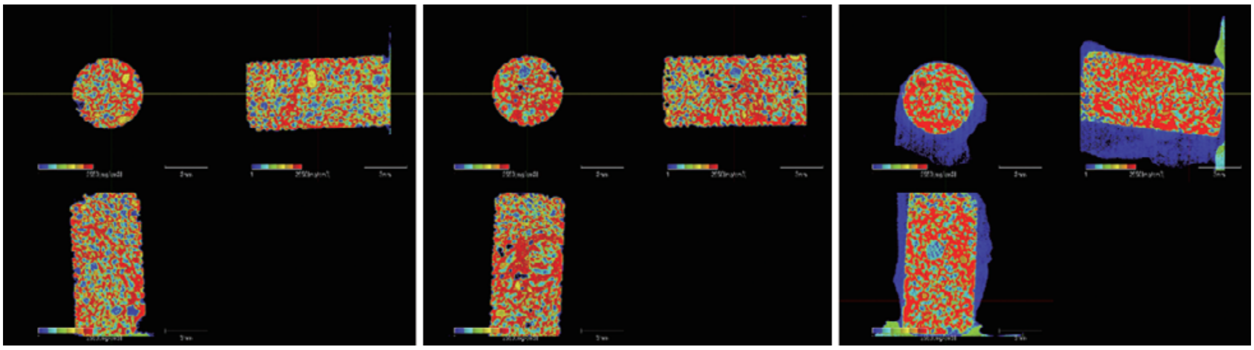

Figure 7 Evaluation of bone mineral density (BMD) using micro-CT.
BMD measured using micro-CT shows increased calcification in the transplanted ASC-seeded artificial bone (right). Left: Type A (ASC − , implantation −); Center: Type B (ASC + , implantation −); and Right: Type B (ASC + , implantation +).

mm in size, and cylinder in shape) was placed in a 96 well plate and incubated with ASC suspension (2 million cells/300 μl). The cells were incubated for 38 h, fixed, and examined under an electron microscope (Fig. 4).

Transplantation of ASC-seeded Artificial Bone into Nude Rats

The ASC-seeded artificial bone was transplanted into the inguinal region of nude rats (SPF F344/Njcl-nu/nu). The superficial inferior epigastric artery was dissected under a microscope, and artificial bone was inserted and covered with the surrounding fascia using 9-0 nylon (Fig. 5). Eight weeks after transplantation, when the capillary vascular network around the bone was sufficiently developed, it was elevated as a vascularized artificial bone flap. The pedicle was clamped for 30 min to create a condition similar to that of the free flap transfer (Fig. 6).

Evaluation of Ossification of Post-implantation Tissues

The harvested tissue was fixed in paraformaldehyde and bone mineral density (BMD) was measured using micro-CT to evaluate the degree of ossification. The BMD of Type C (ASC+, implantation+) was higher than that of Type A (control; ASC-, implantation-, artificial bone only) and Type B (ASC+, implantation-) (Fig. 7). Therefore, it was considered that the tissue that was created using the aforementioned procedure has increased mechanical strength and could potentially be a substitute for an artificial bone flap.

Presently, small artificial bones have become preliminarily available, whereas large bones are necessary for clinical use. In addition, with recent advances in 3D printing technologies, the creation of large 3D organs is expected in the near future. We will continue to develop an artificial flap for clinical use by combining reconstructive surgery, regenerative medicine, and other medical technologies.

Conclusions

We have presented the current status and discussed future of reconstructive surgery. To realize artificial flaps, collaboration with other fields, including regenerative medicine and transplantation surgery, is necessary.

Conflict of interest

None

References

1) Iida T, Narushima M, Yoshimatsu H, et al.: A free vascularised iliac bone flap based on superficial circumflex iliac perforators for head and neck reconstruction. J Plast Reconstr Aesthet Surg **66**: 1596-1599, 2013.
2) Iida T, Mihara M, Yoshimatsu H, et al.: Reconstruction of the external auditory canal using a super-thin superficial circumflex iliac perforator flap after tumour resection. J Plast Reconstr Aesthet Surg **66**: 430-433, 2012.
3) Iida T, Mihara M, Narushima M, et al.: A sensate superficial circumflex iliac perforator flap based on lateral cutaneous branches of the intercostal nerves. J Plast Reconstr Aesthet Surg **65**: 538-540, 2012.
4) Iida T, Yoshimatsu H, Hara H, et al.: Reconstruction of Large Facial Defects Using a Sensate Superficial Circumflex Iliac Perforator Flap Based on the Lateral Cutaneous Branches of the Intercostal Nerves. Ann Plast Surg **72**: 328-331, 2013.
5) Iida T, Yamamoto T, Yoshimatsu H, et al.: Supermicrosurgical free sensate superficial circumflex iliac artery perforator flap for reconstruction of a soft tissue defect of the ankle in a 1-year-old child. Microsurgery **36**: 254-258, 2015.
6) Iida T: Superficial Circumflex Iliac Perforator (SCIP) Flap: Variations of the SCIP Flap and Their Clinical Applications. J Reconstr Microsurg **30**: 505-508, 2014.
7) Iida T, Narushima M, Hara H, et al.: Supermicrosurgical free sensate intercostal artery perforator flap based on the lateral cutaneous branch for plantar reconstruction. J Plast Reconstr Aesthet Surg **67**: 995-997, 2014.
8) Iida T, Isozaki Y, Numahata T, et al.: Sacral defect reconstruction using a sensate superior gluteal artery perforator flap based on the superior cluneal nerves: A report of two cases. Microsurgery **41**: 468-472, 2021.
9) Iida T, Yoshimatsu H: Anatomical Study and Clinical Application of Free Thoracoacromial Artery True-Perforator Flap for Reconstruction of the Face. J Craniofac Surg **30**: 205-207, 2019.
10) Iida T, Yoshimatsu H, Yamamoto T, et al.: A pilot study demonstrating the feasibility of supermicrosurgical end-to-side anastomosis onto large recipient vessels in head and neck reconstruction. J Plast Reconstr Aesthet Surg **69**: 1662-1668, 2016.
11) Iida T, Mihara M, Yoshimatsu H, et al.: Versatility of a near-infrared vein visualization device in plastic and reconstructive surgery. Plast Reconstr Surg **130**: 636e-638e, 2012.
12) Dubernard JM, Owen E, Lefrançois N, et al.: First human hand transplantation. Case report. Transpl Int **13** (Suppl 1): S521-S524, 2000.
13) Devauchelle B, Badet L, Lengelé B, et al.: First human face allograft: early report. Lancet **368**: 203-209, 2006.
14) Iida T, Takami Y, Yamaguchi R, et al.: Development of a tissue-engineered human oral mucosa equivalent based on an acellular allogeneic dermal matrix: a preliminary report of clinical application to burn wounds. Scand J Plast Reconstr Surg Hand Surg **39**: 138-146, 2005.