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REVIEW ARTICLE

Microvascular Free Flaps: a Major Advance in Head and Neck Reconstruction

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INTRODUCTION

Head and neck reconstruction has always been a challenging problem: in the past, most oral and pharyngeal defects were closed primarily using skin flaps or tubed-pedicle flaps of skin from the trunk (1). In 1957 the first human free tissue transfer (revascularized isolated jejunal segment) to the head and neck (reconstruction of the cervical esophagus) was carried out successfully (2). Despite this encouraging report, free tissue transfer for head and neck reconstruction was not as popular as the new technique of regional axial pattern skin flaps which dominated the head and neck surgical scenario for over a decade. In 1963, McGregor (3) described the use of the forehead flap and, in 1965, Bakamjian (4) reported on the deltopectoral flap. Clearly, the contribution of Bakamjian in developing the technique of deltopectoral flap was one of the major advances in head and neck reconstruction at that time. This advance helped oncologic surgeons to reconstruct defects, especially those involving the surface skin. This technique was also used for reconstruction of the pharynx, a definite surgical challenge for the head and neck surgeons of the time. However, even with this technique developed by Bakamjian, the average period of time required for reconstruction of the pharynx could be anywhere between 3 and 6 months, involving multiple steps and controlled fistula. Unfortunately, most of the patients did not do well in relation to local control of the disease and the overall poor results of pharyngeal reconstruction. This was, however, a major advance in head and neck reconstruction. Similarly, the pectoralis major myocutaneous flap, initially developed in 1979 by Ariyan (5), was another major advance in head and neck reconstruction. For the next decade, the pectoralis myocutaneous flap became the "workhorse" for head and neck surgeons. It was used for major defects in the head and neck, including reconstruction of the skin and oropharynx. There were still many problems relating to the bulk of the flap and difficulties in raising the flap in women. Even though there was a high complication rate relating to wound problems using the pectoralis myocutaneous flap, the flap carried its own blood supply, thus providing better healing power.

The major contribution to head and neck reconstruction over the past two decades has been microvascular tissue transfer. This technique has enabled the ablative surgeon to undertake surgical procedures that could not have been attempted in the past. Microvascular tissue transfer enables better local control and more satisfactory long-term results in relation to local control and better functional outcome. Further reports on well-vascularized musculocutaneous flaps (pectoralis major, latissimus dorsi, trapezius) led to more reliable single-stage reconstructions. In 1973, Daniel and Taylor (6) reintroduced the concept of microvascular free tissue transfer. After initial difficulties concerning its acceptance for head and neck reconstructive purposes, the approach evolved rapidly in terms of its reliability and its superior ability to restore function and an esthetically pleasing appearance to certain head and neck defects.

In the past two decades, head and neck oncologic surgery has witnessed several nuances. These have been primarily related to advances in chemotherapy, radiation therapy and the philosophy of organ preservation. Several advances in radiation therapy—including three-dimensional planning, intensity-modulated radiation therapy and a better combination of chemotherapy and radiation therapy—have been critical in allowing better local control of head and neck tumors. Hyperfractionation appears to be commonly used nowadays, particularly in comparison to the use of standard radiation in the past. Since the classic Veterans Affairs study of organ preservation (7), there appears to have been increasing interest among head and neck oncologists in preserving both form and function, as well as in trying to achieve better organ preservation (8). This is related to tumors of the base of the tongue and laryngopharynx. It is vitally important to select appropriate patients for organ preservation therapy. The role of brachytherapy cannot be overemphasized in the head and neck, especially for tumors of the base of the tongue and recurrent head and neck cancers. However, soft tissue defects after major abla-

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tive procedures have remained a considerable challenge for oncologic surgeons. This is where the role of microvascular surgery is paramount. In relation to this, free tissue transfer, together with microvascular advances, has made a major contribution to head and neck oncologic surgery.

MICROVASCULAR FREE TISSUE TRANSFER

The availability of microvascular free tissue transfer has been a major advance in head and neck surgery since the 1970s and a variety of reconstructive techniques are now available, depending on the nature of the surgical defect. If necessary, free flaps can be fashioned in which a combination of skin, muscle, bone, tendon and nerve is selected. The microvascular free tissue transfer (see Table I) (9, 10) can be distinguished into:

Table I. *Microvascular free flaps. Modified from Baker (9) and Kuriloff and Sullivan (10)*

Cutaneous and fasciocutaneous flaps
Scalp and forehead
Deltopectoral
Lateral thoracic
Scapular (parascapular)
Deltoid
Foream
Medial arm
Lateral arm
Lateral thigh
Groin
Muscle and musculocutaneous flaps
Latissimus dorsi
Serratus anterior
Rectus femoris
Rectus abdominis
Pectoralis major
Pectoralis minor
Tensor fascia lata
Gracilis
Osteocutaneous flaps
Groin skin and iliac crest
Chest skin and anterior rib
Dorsal foot skin and metatarsal bone
Lower leg skin and fibular bone
Back skin and scapular bone
Forearm skin and radius bone
Upper arm skin and humerus bone
Osteomusculocutaneous flaps
Tensor fascia lata
Deep circumflex iliac
Internal mammary intercostal muscle
Osteomuscular flaps
Tensor fascia lata
Serratus anterior
Internal mammary intercostal muscle
Iliac crest–internal oblique muscle

- cutaneous and fasciocutaneous flaps;
- muscle and musculocutaneous flaps;
- osteocutaneous, osteomusculocutaneous and osteomuscular flaps.

Radial forearm flap

In 1981, Yang first described the radial forearm flap in China (11). For this reason it is referred to as the “Chinese flap”. In 1983, the radial forearm free flap was described by Soutar et al. (12) for intra-oral reconstruction. In particular, it provides a large, thin, pliable, predominantly hairless flap for intra-oral and oropharyngeal lining (11–13). The vascularity of the area allows considerable variation in the design of this fasciocutaneous flap and offers the possibility of including bone as an osteocutaneous flap (12). Microvascular anastomosis of large-caliber radial vessels ensures successful transfer and constitutes a major advance in head and neck reconstruction.

Brown et al. (14) showed that the addition of the superiorly based pharyngeal flap to the radial forearm flap in soft palate reconstruction resulted in improved speech and swallowing. They recommended the use of the additional flap in resections in which more than one-quarter of the soft palate is included.

Resurfacing the nasopharynx after nasopharyngectomy and covering the internal carotid artery are important in order to minimize the risk of infection, osteoradionecrosis and carotid rupture. The free radial forearm flap aids healing and minimizes the risk of complications; the morbidity associated with the surgery is minimal and the functional recovery is excellent (15). Most microvascular surgeons use the Allen test (manual occlusion and sequential release of radial and ulnar vessels at the wrist) preoperatively in order to assess adequate collateral ulnar artery circulation before the radial forearm free flap harvest. This test is highly predictive in assessing the palmar circulation, especially when strongly negative or positive (16), although many surgeons prefer to confirm this using angiography.

Deschler et al. (17) reported that tracheoesophageal speech after radial forearm free flap reconstruction of the neopharynx demonstrates that acceptable voice can be achieved, albeit with limitations.

Interestingly, Sakamoto et al. (18) reported a second primary squamous cell carcinoma arising in a radial forearm flap used for reconstruction of the hypopharynx 10 years following hypopharyngectomy.

The radial forearm flap is the most widely used free tissue transfer in head and neck reconstruction (16). It is very suitable for surface coverage of the skin and reconstruction of the oral cavity and tongue, particularly as it is thin and pliable. It is also a very important flap for reconstruction after marginal mandibulectomy and the results have been extremely satisfactory. However, donor site problems relating to split-thickness skin grafts are well recognized. In our experience, functional recovery from the forearm defect is quite acceptable and there is minimal residual discomfort. The AlloDerm graft is a viable alternative to the split-thickness skin graft for coverage of the radial forearm free flap donor site (19). The radial forearm osteocutaneous flap is rarely used and can lead to the problem of fracture of the radius. Disa et al. (20) from the Memorial Sloan–Kettering Cancer Center found a more tenuous blood supply to the radial bone in a composite flap. They noted bone resorption rates of 33% when plated to the central segments and 37% when plated to the body segments; ramus segments did not lose height. We have occasionally used osteocutaneous flap with a segment of the radius and reconstructed the radius with iliac crest. Radial osteocutaneous flap is quite satisfactory for small segment defects of the mandible. Radial forearm flap is also commonly used for pharyngoesophageal reconstruction (21). The postoperative functional results in relation to swallowing are quite satisfactory.

Ulnar forearm flap

In a recent study (22) reporting on 75 patients, it was concluded that, comparing the ulnar forearm flap (51 patients) with its radial counterpart (24 patients), the former is favored because of the less hairy skin of the ulnar forearm region, the thinner layer of subcutaneous tissues and the more conveniently located donor area. However, the ulnar forearm pedicle is long compared with alternative transplants, although shorter than the radial equivalent.

Fibula flap

Conventional angiography has been recommended for imaging of the leg prior to fibular free flap harvest. Magnetic resonance angiography offers a similar level of accuracy, is useful when choosing the side of fibular harvest and in excluding patients for whom the fibula is not a suitable donor site, presents no risk to the patient and is less costly (23).

Fibula osseocutaneous free flap is widely used for oromandibular reconstruction following oncological resections or trauma, and is an emerging choice after maxillary section (21, 24). After oncologic resection of the mandible, reconstruction using a free vascularized bone graft has become the predominant treatment of choice (25). Credit goes to Hidalgo (26) from the Memorial Sloan–Kettering Cancer Center for perfecting the technique of fibula free flap and for making multiple short osteotomies to conform the fibula to the mandible. This clearly represents an advance in mandibular reconstruction, which has been a major challenge for reconstructive surgeons for many decades. A variety of different techniques of reconstruction with fibula have been developed, including reconstruction with multiple mini-plates or a single large plate. Problems relating to flap healing and plates acting as a foreign body (especially with exposure into the oral cavity) persist. One of the major disadvantages of fibular free flap is the limited availability of the skin and soft tissue necessary for reconstruction of mucosal defects. Donor site morbidity continues to be a problem, mainly involving split-thickness skin grafts or primary closure. However, over a period of time, the functional recovery of the leg is generally satisfactory. The fibular free flap technique continues to be a challenging problem in elderly patients and is characterized by associated vascular and atherosclerotic vascular problems. However, fibular free flap has truly revolutionized the philosophies behind mandibular reconstruction and the results have been outstanding. For mandibular reconstructions, Haughey et al. (21) prefer the fibula over the iliac crest, mainly because it can be harvested easily under tourniquet control with little loss of blood.

Use of the fibula osteocutaneous free flap to reconstruct the midface is highly reliable. However, when orbitozygomatic support is the primary objective, the utility of this flap is limited. Because of the complexity of this procedure, the choice of midface reconstruction technique should be individualized for each patient (27).

For advanced osteoradionecrosis of the mandible, radical resection of all necrotic tissue followed by immediate restoration of osseous and soft tissue defects with non-irradiated tissue (free tissue transfer) provides a reliable means of obtaining good wound healing with acceptable esthetic and functional results (28). Osteoradionecrosis continues to be a major challenge for oncologic head and neck surgeons. Even though a variety of treatment modalities have been used in recent years (including the conservative approach of debridement, antibiotics and hyperbaric oxygen), management has been quite difficult on several occasions when an extensive segment of the mandible has been involved in the osteoradionecrotic process. We have used radical resection of the osteoradionecrotic segment of the mandible and primary reconstruction with fibula free flap. The fibula has its own blood supply, which enables the mandible to heal and still achieves satisfactory cosmetic and functional results.

Iliac crest flap

When reconstructing mandible a decade ago, there was considerable enthusiasm concerning the use of iliac crest, particularly as it provided both the bone and a considerable portion of the skin and soft tissue. However, the surgical technique is quite tedious and mandibular reconstruction proves to be far more challenging using iliac crest. It also provides a small segment, rather than enabling one to reconstruct extensive portions of the mandible. Although the fibula free flap is the flap of choice, the iliac crest is an excellent and reliable complementary flap for mandibular reconstruction (29).

Scapula flap

This technique provides a small segment of the scapula, but one can take a large portion of the skin along with the soft tissues. The scapular flap has proven to be useful for restoring the bony and soft tissue contours of the face and achieving rigid support for the velum, oronasal separation, support for the orbit and obliteration of the maxillary sinus. The scapular free flap has been found to be a useful tool for reconstructing complex and variable maxillectomy defects (30).

One of the major problems associated with scapular free flap is the complexity encountered in the operating room when turning the patient in the middle of the surgery into a semi-prone position. Donor site morbidity, however, is minimal, as the wound can be closed primarily in most cases. Again, drawbacks include the limited amounts of bone and soft tissue available.

Inferior rectus abdominis muscle flap

The inferior rectus abdominis flap is one of the most useful donor tissues because of its long stalk and large-caliber nutrient vessels with a well-defined anatomic location and ease of harvest. Positional change of a patient during the operation can be avoided and, if desired, simultaneous flap dissection and tumor ablation can be performed without interference, further shortening the operation time (13). Rectus abdominis flap is a good flap for soft tissue reconstruction of major oropharyngeal defects. It is also a flap where the skin can be used for both external coverage and mucosal lining. We have used it several times for soft tissue defects of the lateral mandibular region, where bony reconstruction is either not feasible or unnecessary. The bulk of the flap does continue to be a problem, leading to issues of tissue sagging. One of the major advantages of a rectus flap is the long vascular pedicle, which is quite helpful for reconstruction of defects at the skull base and for soft tissue defects of the maxilla. It is an invaluable flap for reconstruction of orbitomaxillary defects and for reconstruction of the hard palate. Although the use of rectus free flap for reconstruction of the hard palate has considerably decreased the need for prosthetic reconstruction in recent years, these flaps will need to be studied critically in relation to functional outcome. As the well-vascularized flap provides tissue bulk, it can be used for reconstruction of the skull base following tumor extirpation. This flap is particularly useful in sealing the skull base in order to prevent or treat leakage of cerebrospinal fluid (11).

Jejunal flap

Free vascularized jejunal flaps for oropharyngoesophageal reconstruction are now considered the free visceral flaps of choice by several groups. Usually, a two-team approach is utilized to facilitate transfer and closure (31). As jejunal tissue provides the secretion of mucus, the swallowing function is better with jejunal graft when compared to other methods of reconstruction (11). Postoperative radiotherapy to the neck may affect the graft. However, in a recent prospective study (32), free jejunal flap transferred to the neck, in view of its good blood supply, has been shown to tolerate postoperative radiotherapy well.

DISCUSSION

The goals of primary reconstruction of the head and neck following extensive resection for cancer are prompt resurfacing of mucosal or skin defects, restoration of bony supports and reconstruction of specific organs, such as the cervical esophagus. These objectives can minimize postoperative complications and hospital stay and optimize the patient's ability to return to normal social functioning (13).

Free tissue transfers have been shown to be a successful method for one-stage reconstruction in almost all major head and neck defects, with flap success rates of 98–99% and low re-exploration rates (2%) in institutions performing a high volume of this surgery (33), and to provide a higher level of functional recovery in comparison to that achieved using other techniques. The main advantages of free tissue transfer are the improved blood supply (which is crucially important in wound healing and in the survival of the transposed tissue itself), the unrestricted flap positioning from a large variety of donor sites, which is not possible with the arc of rotation in pedicled flaps, the large amount of composite tissue available, the potential for functional reconstruction (sensitive and motor functions) and the primary placement of osseointegrated implants. Microvascular flaps allow for tissue augmentation of the head and neck, with restoration of symmetry, without the problem of subsequent atrophy and resorption (9).

Free tissue transfer is a complex technique that requires microvascular expertise [often involving a simultaneous two-team surgical approach (34) and multidisciplinary cooperation], increased surgical time and, therefore, prolonged anesthesia. From a strictly technical point of view, the recipient vessels may be unavailable or unusable and the muscle pedicle is not always available for carotid protection. Esthetically, the color and texture of the transferred tissue may not be ideal compared to the characteristics of the surrounding natural tissue. Furthermore, there may be functional disability at the donor site.

The major complication following microsurgical reconstruction for head and neck cancer is thrombosis of either the arterial or venous anastomoses, leading to loss of the flap. Hematomas may occur due to the extensive resection or due to the inability to place adequate suction drainage close to the microsurgical anastomoses. The medical condition and habits of the patient are also very important: pulmonary problems, prolonged ventilatory support and acute alcohol withdrawal are the most common causes of morbidity and occasional mortality in patients who are heavy smokers and drinkers and are debilitated (33). Ischemia/reperfusion injury is often the final, irreversible factor causing flap failure in microvascular surgery for head and neck defects (35).

The effect of surgery, irradiation and free tissue transfer in locally advanced head and neck cancer patients has been analyzed and it has been shown that free tissue transfer before or after irradiation is of benefit and is associated with few complications (36). After preoperative radiation therapy, vascularization of the graft bed decreases continuously as a function of the total dose and the time after radiation therapy. These results strongly advocate the use of a primary reconstruction after a time interval of 4–6 weeks following preoperative radiation therapy and suggest the use of a total radiation dose of 40–50 Gy (37). The expression of transforming growth factor (activated $TGF\beta_1$, $TGF\beta_2$) and latency-associated peptide may possess prognostic value with regard to wound healing and fibrosis in previously irradiated graft beds (38).

The complex functional and esthetic demands of head and neck reconstruction make the replacement of lost tissue (soft tissue and bone) with tissue of similar characteristics critically important. Every effort should be made to optimize the functional and cosmetic outcomes of neurovascular muscle transfers, especially after ablative tumor resection of the middle third of the face (39).

Long-term follow-up is indicated in patients undergoing reconstruction using cutaneous or musculocutaneous flaps (18). From the above description, it is quite apparent that one of the major advances in head and neck surgery during the past few decades has been the availability of free tissue transfer with microvascular anastomosis. There has been considerable interest from otolaryngologists, head and neck surgeons and plastic and microvascular surgeons. There appear to be an increasing number of surgeons actively involved in microvascular reconstruction and, essentially, the technique of microvascular surgery has been perfected over the past few years. It results in excellent postoperative cosmetic and functional results and the success of microvascular anastomosis is $>95\%$. We still face the challenges of donor site morbidity and functional problems relating to inert soft tissue. Flap neurotization has been used (especially in reconstruction of the tongue), but the results are difficult to interpret at this time. Multiple flaps during the same procedure have also been used, e.g. reconstruction of the mandible by fibula free flap and reconstruction of the soft tissues at the same time with radial forearm flap. This clearly requires the availability of more than one surgeon and the surgical procedure will take a long time. One of the major attributes of microvascular flap and fibula free flap reconstruction is the feasibility of performing osseointegration. This is a major advance in terms of the cosmetic and functional results after microvascular surgery. It appears that microvascular surgery and free flap tissue transfer have met the challenges of head and neck ablative surgery. However, much needs to be done in the future in relation to the correct flap choice and better functional recovery.

REFERENCES

1. Sloan SH, Blackwell KE, Urken ML. Reconstruction of major defects in the head and neck following cancer surgery. In: Myers EN, Suen JY, eds. Cancer of the head and neck, 3rd edn. Philadelphia, PA: Saunders, 1996: 712–47.
2. Seidenberg BS, Rosenak ES, Hurwitt ES, Som ML. Immediate reconstruction of the cervical esophagus by a revascularized isolated jejunal segment. Ann Surg 1959; 149: 162.
3. McGregor IA. The temporal flap in intra-oral cancer: its use in repairing the post-excisional defect. Br J Plast Surg 1963; 16: 318.
4. Bakamjian VY. A two-stage method for pharyngoesophageal reconstruction with a primary pectoral skin flap. Plast Reconstr Surg 1965; 36: 173–9.
5. Ariyan S. The pectoralis major myocutaneous flap. A versatile flap for reconstruction in the head and neck. Plast Reconstr Surg 1979; 63: 73–81.
6. Daniel RK, Taylor GI. Distant transfer of an island flap by microvascular anastomoses. A clinical technique. Plast Reconstr Surg 1973; 52: 111–7.
7. The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med 1991; 324: 1685–90.

8. Ferlito A, Shaha AR, Lefebvre J-L, Silver CE, Rinaldo A. Organ and voice preservation in advanced laryngeal cancer. Acta Otolaryngol 2002; 122: 438–42.
9. Baker SR. Microvascular free flaps in soft-tissue augmentation of the head and neck. Arch Otolaryngol Head Neck Surg 1986; 112: 733–7.
10. Kuriloff DB, Sullivan MJ. Revascularized tissue transfers in head and neck surgery. In: Bailey BJ, ed. Head and neck surgery—otolaryngology. Philadelphia, PA: Lippincott, 1993: 1949–79.
11. Wei WI, Lam LK, Chan VSH. Current reconstruction options following tumour extirpation in head and neck surgery. Asian J Surg 2002; 25: 41–8.
12. Soutar DS, Scheker LR, Tanner SB, McGregor IA. The radial forearm flap: a versatile method for intra-oral reconstruction. Br J Plast Surg 1983; 36: 1–8.
13. Harii K. The free flap in head and neck reconstruction. In: Fee WE Jr, Goepfert H, Johns ME, Strong EW, Ward PH, eds. Head and neck cancer. Proc Int Conf Boston, 1988, Vol. 2. Toronto: B.C. Decker, 1990: 33–5.
14. Brown JS, Zuydam AC, Jones DC, Rogers SN, Vaughan ED. Functional outcome in soft palate reconstruction using a radial forearm free flap in conjunction with a superiorly based pharyngeal flap. Head Neck 1997; 19: 524–34.
15. Khoo MLC, Soo K-C, Gullane PJ, et al. Resurfacing of the nasopharynx after nasopharyngectomy using a free radial forearm flap. Head Neck 2001; 23: 916–22.
16. Olson GT, Bayles SW. Recent innovations in the use of the radial forearm free flap. Curr Opin Otolaryngol Head Neck Surg 2001; 9: 201–4.
17. Deschler DG, Doherty ET, Reed CG, Anthony JP, Singer MI. Tracheoesophageal voice following tubed free radial forearm flap reconstruction of the neopharynx. Ann Otol Rhinol Laryngol 1994; 103: 929–36.
18. Sakamoto M, Nibu K, Sugasawa M, Nakatsuka T, Harii K, Ichimura K. A second primary squamous cell carcinoma arising in a radial forearm flap used for reconstruction of the hypopharynx. ORL J Otorhinolaryngol Relat Spec 1998; 60: 170–3.
19. Sinha UK, Shih C, Chang K, Rice DH. Use of AlloDerm for coverage of radial forearm free flap donor site. Laryngoscope 2002; 112: 230–4.
20. Disa JJ, Hidalgo DA, Cordeiro PG, Winters RM, Thaler H. Evaluation of bone height in osseous free flap mandible reconstruction: an indirect measure of bone mass. Plast Reconstr Surg 1999; 103: 1371–7.
21. Haughey BH, Wilson E, Kluwe L, et al. Free flap reconstruction of the head and neck: analysis of 241 cases. Otolaryngol Head Neck Surg 2001; 125: 10–7.
22. Sieg P, Bierwolf S. Ulnar versus radial forearm flap in head and neck reconstruction: an experimental and clinical study. Head Neck 2001; 23: 967–71.
23. Lorenz RR, Esclamado R. Preoperative magnetic resonance angiography in fibular-free flap reconstruction of the head and neck defects. Head Neck 2001; 23: 844–50.
24. Futran ND, Stack BC Jr, Zachariah AP. Ankle-arm index as a screening examination for fibula free tissue transfer. Ann Otol Rhinol Laryngol 1999; 108: 777–80.
25. Strackee SD, Kroon FHM, Bos KE. Fixation methods in mandibular reconstruction using fibula grafts: a comparative study into the relative strength of three different types of osteosynthesis. Head Neck 2001; 23: 1–7.
26. Hidalgo DA. Fibula free flap: a new method of mandible reconstruction. Plast Reconstr Surg 1989; 84: 71–9.
27. Futran ND, Wadsworth JT, Villaret D, Farwell DG. Midface reconstruction with the fibula free flap. Arch Otolaryngol Head Neck Surg 2002; 128: 161–6.
28. Chang DW, Oh H-k, Robb GL, Miller MJ. Management of advanced mandibular osteoradionecrosis with free flap reconstruction. Head Neck 2001; 23: 830–5.
29. Shpitzer T, Neligan PC, Gullane PJ, et al. The free iliac crest and fibula flaps in vascularized oromandibular reconstruction: comparison and long-term evaluation. Head Neck 1999; 21: 639–47.
30. Granick MS, Ramasastry SS, Newton ED, Solomon MP, Hanna DC, Kaltman S. Reconstruction of complex maxillectomy defects with the scapular-free flap. Head Neck 1990; 12: 377–85.
31. Greenstein B, Strauch B. Reconstruction. In: Silver CE, Rubin JS, eds. Atlas of head and neck surgery, 2nd edn. New York: Churchill Livingstone, 1999: 45–67.
32. Wei WI, Lam LK, Yuen PW, Kwong D, Chan KW. Mucosal changes of the free jejunal graft in response to radiotherapy. Am J Surg 1998; 175: 44–6.
33. Jones NF. Limitations and complications in microsurgical reconstruction of the head and neck. Proc 5th Int Conf Head Neck Cancer, San Francisco, CA, 2000: 105–11.
34. Jones NF, Johnson JT, Shestak KC, Myers EN, Swartz WM. Microsurgical reconstruction of the head and neck: interdisciplinary collaboration between head and neck surgeons and plastic surgeons in 305 cases. Ann Plast Surg 1996; 36: 37–43.
35. Carroll WR, Esclamado RM. Ischemia/reperfusion injury in microvascular surgery. Head Neck 2000; 22: 700–13.
36. Jose B, Banis J, Flynn M, et al. Irradiation and free tissue transfer in head and neck cancer. Head Neck 1991; 13: 213–6.
37. Schultze-Mosgau S, Grabenbauer GG, Radespiel-Tröger M, et al. Vascularization in the transition area between free grafted soft tissues and pre-irradiated graft bed tissues following preoperative radiotherapy in the head and neck region. Head Neck 2002; 24: 42–51.
38. Schultze-Mosgau S, Wehrhan F, Grabenbauer G, et al. Transforming growth factor $\beta 1$ and $\beta 2$ ($TGF\beta_2/TGF\beta_2$) profile changes in previously irradiated free flap beds. Head Neck 2002; 24: 33–41.
39. Maral T, Ozcan G. Functional reconstruction of the lateral face after ablative tumor resection: use of free muscle and musculocutaneous flaps. Head Neck 2001; 23: 836–43.

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